

Bauhinia unguolata L.: Medicinal Utilization, Botanical Aspects, Biological Properties and Chemical Constitution Reported in the Literature

Myrth Soares do Nascimento Remígio^{1,2}, Andressa Santa Brígida da Silva², Alessandra Rossi¹, Wagner Luiz Ramos Barbosa^{2,*}

¹Department of Food and Drug, University of Parma, Parco Area delle Scienze, Parma, ITALY.

²Laboratory of Chromatography and Mass Spectrometry, Faculty of Pharmacy, Federal University of Pará, Belém, PA, BRAZIL.

ABSTRACT

Bauhinia unguolata L. (Leguminosae) is a plant species popularly known as “mororó” or “pata-de-vaca”, whose leaves are used in Brazil as infusion, mainly to treat diabetes. Due to its wide utilization and its therapeutic potential, this species has been investigated, producing data that were organized and arranged in this review, in order to provide an overview of different aspects of the species. A search for articles published until December 2021 on medicinal utilization, botanical characterization, bioactivities, and chemical constitution of the species was carried out, consulting the databases PubMed, Scopus, Lilacs, SciELO, Google Scholar, and Capes Journal Portal. The selected articles describe 31 different terpenes, characterized in essential oils from *B. unguolata* leaves; in addition, other 20 substances, including flavonoids, alkaloids, steroids, and triterpenoids, in other derivatives obtained from leaves, roots, or stems of the species were described. In these articles, different activities were reported, such as antioxidant, anti-inflammatory, antidepressant/anxiolytic, antimicrobial, antiproliferative, larvicidal, cytotoxic and wound healing. The published data on the species allow to infer a potential of use as a therapeutic ingredient with antioxidant activity, which is the most investigated activity and has been related to phenolic compounds, especially flavonoids. Despite the popular use of leaves of the species, as an infusion to treat diabetes, to be well described in the literature, no records were found in the evaluation of their antidiabetic potential or about the characterization of substances present in aqueous extracts from *B. unguolata*.

Keywords: Bioactivities, Flavonoids, Medicinal Uses, “pata-de-vaca”, Phytochemical Constituents, Terpenes.

Correspondence:

Prof. Wagner Luiz Ramos Barbosa,

Laboratory of Chromatography and Mass Spectrometry, Faculty of Pharmacy, Federal University of Pará, Augusto Corrêa St, 01, CEP 66.075-900- Belém, PA, BRAZIL.

E-mail: barbosa@ufpa.br

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INTRODUCTION

Genus *Bauhinia* (Leguminosae) comprises 300 to 350 plant species that, due to the shape of their leaves, are popularly known in Brazil as “pata-de-vaca”, “casco de vaca”, “unha de boi”, “pata de boi”, or also “mororó”, “miroró da caatinga”, among others.^[1-3] Many of these plants are used as remedies in folk medicine in various regions of the world, including Africa, Asia and Central and South America.^[4,5] The hypoglycemic activity attributed to *Bauhinia* species is the most reported in the literature, which also describes activities such as antimicrobial, anti-inflammatory, analgesic, antidiuretic, anticoagulant, antifibrinogenic and antioxidant to species of the genus.^[6,7]

Among the *Bauhinia* species popularly used to treat health problems, there is *Bauhinia unguolata* L., a plant species whose leaves, like by other species of the genus, are used in Brazil, as infusion, mainly to treat diabetes.^[8,9] The species occurs in the neotropical zone, from Mexico to southeastern Brazil close to São Paulo, being also found in the Amazon rainforest.^[10] In Mexico, it is distributed on the Gulf slope, widely on the Pacific slope and the Yucatan peninsula, in addition to Belize, Guatemala,

El Salvador, Nicaragua, Costa Rica, Panama, Colombia, Venezuela, Peru, Brazil, Bolivia and Paraguay.^[11]

B. unguolata species has as synonymia *B. benthamiana* Taub., *B. cavanillesii* Millsp., *B. galpiniivar. unguolata* L., *B. inermis* (Cav.) Pers., *B. inermis* Forssk., *B. macrostachya* Benth., *B. unguiculata* Sesse and Moc., *Cansenia unguolata* (L.) Raf., *Pauletia inermis* Cav. and *P. unguolata* (L.) A. Schmitz.^[12] In addition, Tropicos (2022)^[13] refers to the following varieties *B. unguolata* var. *ungulata*, *B. unguolata* var. *cuyabensis* Vaz, which occurs in a dry corridor from Midwest to Southeast Brazil;^[10] *B. unguolata* var. *parvifolia* (Ducke) Vaz and *B. unguolata* var. *obtusifolia* (Ducke) Vaz that occur in the states Maranhão, Pará, Rondônia, Goiás, Piauí and Tocantins.^[10]

The species *B. unguolata* L. has been investigated, due to its popular medicinal use and its therapeutic potential, to characterize its biological properties and chemical constitution. The bibliographic search carried out for this work shows that 31 terpenes were detected in essential oils obtained from leaves of *B. unguolata*. In addition, another 20 substances, including flavonoids, alkaloids, steroids and triterpenoids, have been described in derivatives obtained from leaves, roots or stems of this *Bauhinia* species. Activities such as antimicrobial, antioxidant, anti-inflammatory and cytotoxic were confirmed, some of which attributed to the substances characterized in the tested samples. This work presents a review of articles published until December 2021 about the species, until this time it was not possible to find, in the literature, publications reviewing the available information about *B. unguolata*.



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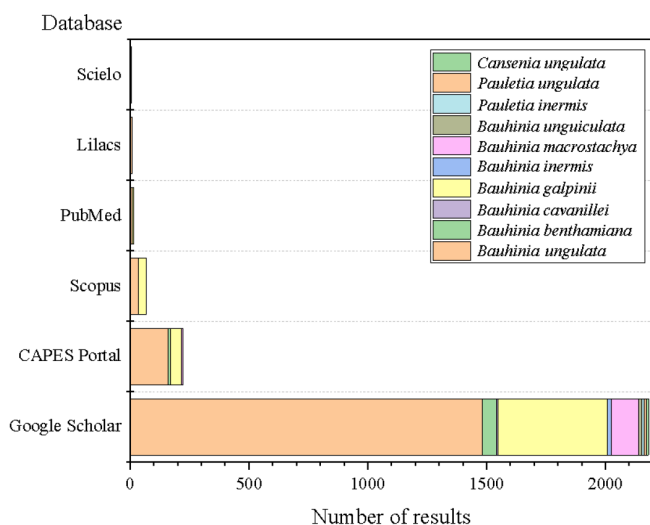
MATERIALS AND METHODS

The literature search was carried out accessing databases including PubMed, Scopus, Lilacs, SciELO, Google Scholar and Capes Journal Portal to fetch articles published and available until December 2021. The binomial of the species, its synonyms and the combination of them with the terms, “chemical”, “compounds”, “toxicological” and “pharmacological” were used as keywords. The inclusion criteria used in the file selection were scientific articles about *B. unguolata* focusing on botanical description, medicinal uses, chemical constitution, toxicological evaluation and bioactivities *in vivo* or *in vitro* from extracts, fractions or isolated substances from the species. Only scientific articles published in journals were selected. Theses, dissertations, monographs and conference abstracts were not considered.

RESULTS

The bibliographic search carried out using the botanical name of the species provided a higher number of references from the Google Scholar and Capes Journal Portal databases, where approximately 2,200 and 220 titles were found, respectively, excluding citations (Graph 1), while the lowest number of references was obtained from the SciELO platform. In all databases consulted, most articles corresponded to *B. unguolata*, followed by the synonyms *B. galpinii* and *B. macrostachya*.

All articles found were analyzed and from them 34 were selected to compose this review, according to the previously defined inclusion criteria. Additionally, ten important references to the topic were added that are not included in the searched data bases, then the review includes 44 references. Based on the information covered in the selected works, they were distributed in the sections “Botanical aspects”, “Medicinal utilization”, “Phytochemistry” and “Bioactivities”. Although a considerable number of references about *B. galpinii* have been found, these articles were not considered, since they are about *B. galpinii* N. E. Br and not about its variety *B. galpinii* var. *ungulata* L., considered synonymous to *B. unguolata* L., according to the consulted botanical database.^[12]



Graph 1: Number of results found using the botanical name and its synonyms, according to the databases consulted.

Botanical Aspects

Taxonomy

The main taxonomic data on *B. unguolata* were reported by Vaz and Tozzi,^[10] who, based on the description made by Wunderlin *et al.*^[14] affirm that the species, in Brazil, is representative of the *Cansenia* series, section *Pauletia*, subgenus *Bauhinia* and genus *Bauhinia*. The Wunderlin classification, which proposed a reorganization of the *Cercideae* tribe based on morphological aspects of the species, considered *Bauhinia* as a large genus in which the subgenera *Bauhinia*, *Piliostigma*, *Barklya* and *Phanera* were included.

The taxonomy of the genus *Bauhinia*, however, is quite complex and, based on later findings on species of the *Cercideae* tribe, other taxonomic descriptions have been proposed, also resulting in changes in the classification of the genus *Bauhinia*. Considering aspects of the chemical constitution of the *Cercideae* tribe species and data from previous classifications, Lewis and Forest,^[15] for example, presented as discrete genera those that Wunderlin *et al.*^[14] considered subgenera of a broad genus *Bauhinia*. They propose an amount of 12 genera in *Cercideae* (*Bauhinia*, *Piliostigma*, *Barklya*, *Phanera*, *Breniera*, *Lysiphyllum*, *Lasiobema*, *Tylosema*, *Gygaspiphon*, *Cercis*, *Adenolobus* and *Griffonia*).

In 2010, Wunderlin^[16] proposed a new reorganization of *Cercideae* tribe, based on the works of Lewis and Forest^[15] and Sinou *et al.*^[17] and on his more than thirty years own experience investigating *Cercideae*, and distributed the tribe's genera in two sub-tribes and *Bauhinia*, besides eight other genera, was classified in the sub-tribe *Bauhiniinae*. As from Vaz and Tozzi^[10] and considering more recent works found in this research, a flowchart about the taxonomy of the species is proposed in Figure 1, where *Cansenia* is shown as a serie of *Pauletia* section.

Morphoanatomical data

Vaz and Tozzi^[10] provide key information on identification, synonymy, description, geographic distribution and habitat, as well as comments on taxonomy referring to 35 species and 4 varieties of *Bauhinia*, section *Pauletia*, *Cansenia* series, and report the form of shrubs, sub-shrubs or small trees for *B. unguolata*. Its leaves are bilobed, with ovate-oblong to oblong-triangular lobes, straight and apex parallel, slightly converging or even slightly divergent, even elliptical or suborbiculate, apex long accentuated or acute to obtuse or rounded. The upper face is glabrous, and the lower one is pubescent, with hair on the entire surface. Glandular trichomes and somewhat prominent primary veins are observed, the secondary are less prominent to immersed and the tertiary fully immersed.

In later research, which aimed to describe the genus *Bauhinia* in the biotic province of the Yucatan peninsula, *B. unguolata* was recognized as a native species of the region, and key information for its identification, morphological descriptions, distribution maps, species photographs, information on common names and uses in the region were presented.

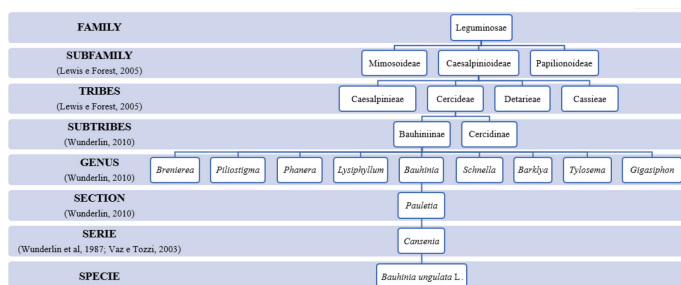


Figure 1: Flowchart of the taxonomy of the species *Bauhinia unguolata* L.

The species was described as shrubs, rarely trees, from 2 to 7 m in height, andromonoic, with leaves containing 7 to 9 ribs, bilobed, oval-lanceolate, cartaceous to subcoriaceous. The lobes of the leaves have an acute apex and a subchord to rounded base, with lanceolate stipules. Its inflorescences are presented in short racemes, with 10 to 30 flowers. It blooms bisexual and has tubular, ferruginous hypanthium. The calyx is spathaceous, 2-4-split, presenting spiraled, strigulous, ferruginous and reflexed lobes in anthesis. The petals are sessile, linear, patent, white, with 10 fertile stamens, didynamous, without staminodes, connates at the base, and the ovary is tomentous and ferruginous. The male flowers are similar, and the legume of the species is elastically dehiscent, linear and strigulous, with oblong-elliptical seeds.^[11]

The morphology of leaves, inflorescence, flowers and fruits may vary among individuals of this species, however, the type of rudimentary stem column, with a bearded internal appendage, and the upper petal, measuring about 2 mm in width, are common characters to all individuals. Despite some morphological variability, *B. unguolata* presents local patterns, artificially recognized in the form of the species' varieties, which can be found by observing the morphology and size of some structures present in leaves and inflorescences, for example. Based on these standards, the *B. unguolata* var. *ungulata*, *B. unguolata* var. *cuyabensis* Vaz, *B. unguolata* var. *parvifolia* (Ducke) Vaz and *B. unguolata* var. *obtusifolia* (Ducke) Vaz, could be described.^[10,13]

More recently, a study, aiming to produce data for the quality control of *B. unguolata* L. derivatives and provide information for its taxonomy description, reports morphoanatomical analyses of leaves collected in the state of Ceará (Brazil).^[18] The authors observed that the consistency of the leaves is chartaceous, presenting an oval-oblong shape, the blade base is truncated, and the apex is acute. The abaxial face is sericeous-pubescent, with glands and a palminervous type venation. The petiole and pulvines are canalicular, with insertion of the proximal pulvine between the extrafloral nectaries, and their mobile region is glabrous. Among the anatomical characters, the authors describe the presence of anomocytic, anisocytic and paracytic stomata distributed on both the abaxial and adaxial surfaces of the leaves, which are therefore considered amphistomatic.

Traditional/folk medicine uses in Central and South America

The main medicinal use of the species is to treat diabetes. Silva *et al.*^[19] report that in rural communities of Piauí, a state in northeastern Brazil, barks of the species are used as an anti-diabetic under the synonymy *B. unguiculata*. The species is also used by urban communities in the state for the same therapeutic purpose,^[20] however, leaves are more commonly used and the use of them, as an infusion for the treatment of diabetes, was observed in a city in Pará, a state in the Brazilian Amazon, under the synonym *B. benthamiana* Taub.^[9] Brazilian indigenous people from the Northeast^[21] also use the species to treat diabetes, however, the first reference found on its use reports the preparation of a tea with leaves of the species, which is used as an antidiabetic and for kidney problems in the Amazonian state of Roraima, the authors used the synonym *B. macrostachya* Benth.^[8] This last article cited is a record of the use of this species for more than 30 years by the population, in a safe and effective way and this is important, since it justifies its use as traditional in Brazil, according to the current regulation.^[22]

Despite its wide use mainly as an anti-diabetic, other properties are attributed to *B. unguolata* in Brazil. In the northeast, for example, barks are used to treat diarrhea,^[23] and in the Midwest, leaves and flowers they are used by riverine people as an infusion, decoction or maceration for the treatment of intestinal constipation, cancer, obesity, hypercholesterolemia and diarrhea.^[24] In Central America,

under the synonymy of *B. inermis*, leaves of the species are also used as sudorifics.^[25] Besides to the medicinal uses described so far, in Northeastern Brazil, barks of the species are used as insecticides and domestic repellents against mosquitoes and *Aedes aegypti* L., and in plantations, to combat ants and worms.^[26]

Phytochemistry

Essential oils

The bibliographic survey performed for this review shows the characterization of several terpenes has been reported in essential oils obtained from leaves of the species, including monoterpenes α and β -pinene and cyclic and acyclic sesquiterpenes (Table 1), substances whose skeletons are shown in Figure 2. In qualitative terms, these sesquiterpenes are predominantly bicyclic, denoting those with cadalane skeleton with 7 substances characterized in *B. unguolata*: α and γ -muurulene, γ and δ -cadinene, α -cadinol, α -calacorene and cubenol. Furthermore, a tricyclic sesquiterpene, α -copaene, three bicyclic, spathulenol, β -caryophyllene and caryophyllene oxide, and a monocyclic, α -humulene (Figure 3) were found in this species in higher amount than the previously cited, in the investigated essential oils, which varies according to the sample considered.^[27-29]

Table 1: Sesquiterpenes detected and characterized in essential oils obtained from *B. unguolata* L. leaves.

Classification	Skeleton	Substance	Reference
Acyclic	Farnesane (1)	Farnesol	[28]
		Nerolidol	
Monocyclic	Bisabolane (2)	α -bisabolol	[28]
		α -bisabolol oxide B	
	Elemene (3)	β -elemene	[27-29]
		8- α -11-elemendiol	[27]
	Germacrane (4)	Germacrene D	[27]
Humulene (5)	α -humulene	[27,29]	
	Humulene epoxide II		
Bicyclic	Cadalane (6)	α -muurulene	[29]
		γ -muurulene	[27,28]
		γ -cadinene	[27-29]
		δ -cadinene	[28]
		α -cadinol	[27,29]
		α -calacorene	[29]
	Caryophyllene (7)	β -caryophyllene	[27-29]
		Caryophyllene oxide	
	Eudesmane (8)	Epi- γ -eudesmol	[28]
		β -selinene	[29]
Guaiene (9)	α -guaiene	[29]	
	6,9-guaiadiene		
Tricyclic	Aromadendrane (10)	Aromadendrene	[28]
		Allo-aromadendrene	[27,29]
	Bourbonene (11)	Spathulenol	[27-29]
		β -bourbonene	[29]
Copaene (12)	α -copaene	[27,29]	
	β -copaene	[29]	
	Copaene	[28]	
Cubebane (13)	α -cubebene	[29]	
Tetracyclic	Cyclosativane (14)	Cyclosativene	[29]

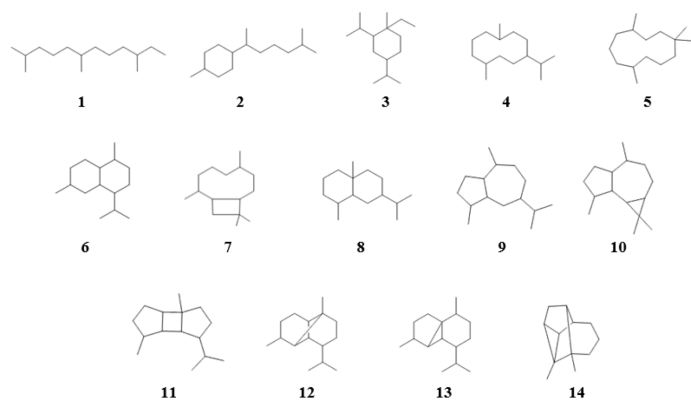


Figure 2: Skeletons of sesquiterpenes detected and characterized in essential oils obtained from *B. unguolata* L. leaves.

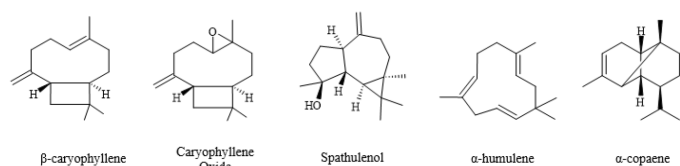


Figure 3: Main sesquiterpenes characterized in essential oils obtained from *B. unguolata* L. leaves.

The first characterization of volatile constituents of *B. unguolata* was carried out by Gramosa *et al.*^[27] who analyzed an essential oil obtained from leaves of the species, by GC/MS and GC/FID, detecting thirteen sesquiterpenes, among which it was quantified, mostly spathulenol (47.7%) and caryophyllene oxide (18.3%). Using the same techniques, Medeiros *et al.*^[28] also detected in a leaf essential oil eighteen terpenes, among them the following major substances: β -caryophyllene (15.9%), caryophyllene oxide (9.2%), α -humulene (8.1%), and a lower spathulenol content (only 2.1%), in comparison to that observed by Gramosa *et al.*^[27] More recently, the work developed by Sousa *et al.*^[29] reports the characterization and the content of 22 substances present in the essential oil of the species, among them: caryophyllene oxide, sesquiterpene in higher content (23%); followed by (E)-caryophyllene (or β -caryophyllene) (14.5%), and α -copaene (7.2%). The authors infer that the variation in the content of the substances, in comparison to previous works, is related to geographic differences between the sites where the leaves used to obtain the oils were collected, among other factors.

Other Substances found in *B. unguolata*

Analysis of samples obtained by different techniques, from roots, stems and leaves of *B. unguolata*, provided twenty substances, among which flavonoids, alkaloids, steroids and triterpenoids (Table 2), whose structures are shown in Figure 4. The substances first characterized in this species were detected in fractions obtained from an ethanol extract from leaves. The ethyl acetate fraction provided the flavonol quercetin, quercetin arabinofuranoside and quercitrin, in addition, 3-O-methyl-D-pinitol; and from the alkaloid fraction were isolated the β -carbonyl alkaloids harmana and eleagnine.^[30]

Sousa *et al.*^[31] isolated the flavanon liquiritigenin and the flavanols guibourtinidol and fisetinidol from ethyl acetate fractions obtained from ethanol extracts of roots and stem wood of the species, also

Table 2: Substances characterized in derivatives of *B. unguolata* L.

Classification	Substance	Plant section	Sample	Reference
	Eriodictyol (1)	Stem bark	Ethanol extract	[31]
	Fisetinidol (2)	Roots Stem wood Stem wood	Ethyl acetate fraction Ethyl acetate fraction Ethyl acetate fraction	[31] [31] [32]
Flavonoids	Guibourtinidol (3)	Roots Stem wood Stem wood	Ethyl acetate fraction Ethyl acetate fraction Ethyl acetate fraction	[31] [31] [32]
	Liquiritigenin (4)	Roots Stem wood Stem wood	Ethyl acetate fraction Ethyl acetate fraction Ethyl acetate fraction	[31] [31] [32]
	Naringenin (5)	Stem bark	Ethanol extract	[31]
	Quercetin (6)	Leaves	Ethyl acetate fraction	[30]
	Quercetin arabinofuranoside (7)	Leaves	Ethyl acetate fraction	[30]
	Quercitrin (8)	Leaves	Ethyl acetate fraction	[30]
Alkaloids	Harmaine (9)	Leaves	Alkaloid fraction	[30]
	Eleagnine (10)	Leaves	Alkaloid fraction	[30]
	Betulinic acid (11)	Stem bark	Hexane extract	[31]
Triterpenoids	Glutinol (12)	Stem bark	Hexane extract	[31]
	Taraxerol (13)	Stem bark	Hexane extract	[31]
	Taraxerone (14)	Stem bark	Hexane extract	[31]
Steroids	Sitosterol (15)	Stem bark	Hexane extract	[31]
	Stigmasterol (16)	Stem bark	Hexane extract	[31]
	3-O-methyl-D-pinitol (17)	Leaves	Ethyl acetate fraction	[30]
Other substances	Pacharin (18)	Stem bark	Ethanol extract	[31]
	2'-hydroxy-3,5-dimethoxy-4-methylbisbenzyl (19)	Roots	Ethyl acetate fraction	[31]
	2'-hydroxy-3,5-dimethoxybisbenzyl (20)	Roots	Ethyl acetate fraction	[31]

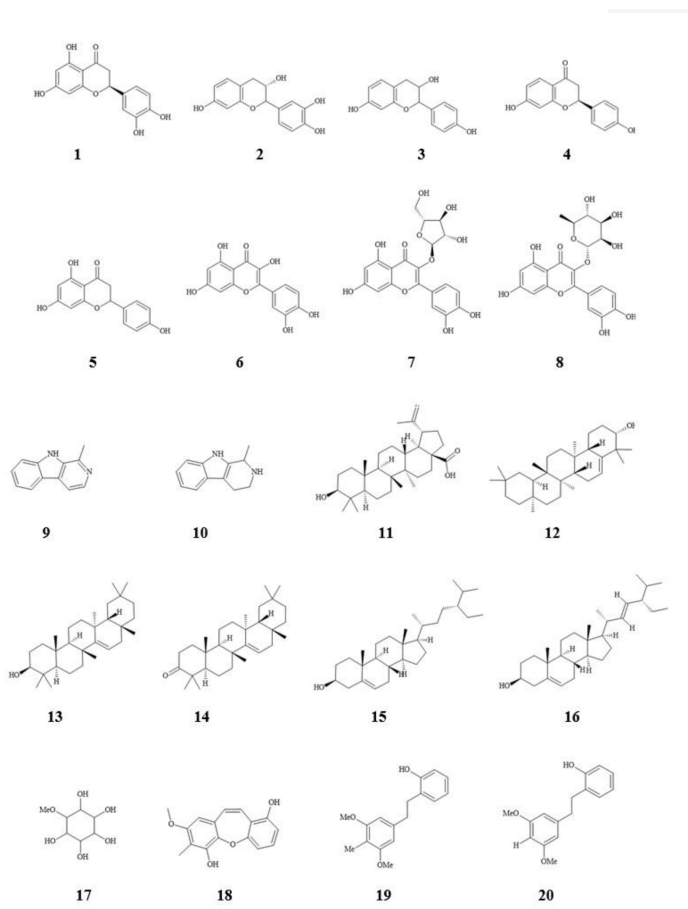


Figure 4: Structures of substances characterized in derivatives of *B. unguolata* L.

identifying two bisbenzyl substances (2'-hydroxy-3,5-dimethoxybisbenzyl and 2'-hydroxy-3,5-dimethoxy-4-methylbisbenzyl) found in the roots, the last one not yet described at the time. In the stem bark, the authors identified the triterpenoids betulinic acid, taraxerol, taraxerone and glutinol, the flavanones naringenin and eriodictyol, pacharin and a mixture of the steroids sitosterol and stigmasterol. More recently, the flavonoids liquiritigenin, guibourtinidol and fisetinidol were again characterized in a fraction of ethyl acetate obtained from stem wood of the species, reinforcing the marked presence of these substances in different parts of *B. unguolata*.^[32]

From seeds of the species, a lectin of specific binding to the galactose called BUL was isolated, with molecular mass of circa 30 kDa and 4.6% of carbohydrates in its composition. This glycoprotein was able to inhibit the growth of phytopathogenic fungi and showed *in vitro* antiproliferative activity against human colon adenocarcinoma cell lines.^[33]

Bioactivities

The surveyed literature describes some bioactivities investigated in *B. unguolata* derivatives, which are summarized in this topic. Until the elaboration of this review, the anti-inflammatory, antioxidant, antimicrobial, antiproliferative, healing, larvicidal, cytotoxic, antidepressant, anxiolytic and wound healing properties were demonstrated, in addition to the gelatinolytic activity of MMP-2 and MMP-9 and the inhibitory effects of acetylcholinesterase and of factors Xa, XII and Plasma Kallikrein (Table 3). Despite the widespread use of

the species to treat diabetes, no papers describing the assessment of its anti-diabetic potential were found in the research.

Antioxidant Activity

Port's *et al.*^[34] determined the total phenolic and flavonoids in infusions obtained from *B. unguolata* var. *obtusifolia* and eight other plant species, popularly used in the Amazon region, and evaluated their antioxidant capacity using the DPPH free radical method and the β -carotene/linoleic acid system assay. The infusion prepared with leaves of *B. unguolata* was able to capture DPPH radicals, with IC_{50} 210.66 μ g/mL, an intermediate value compared to the other tested infusions, whose values ranged between 46.7 and 502.53 μ g/mL. Concerning the analysis performed on the β -carotene/linoleic acid system, it was observed that the infusion inhibited the production of free radicals by the peroxidation of linoleic acid, presenting, however, an antioxidant capacity of 20.12 μ g BHT/mL, a lower value when compared to the most active infusion, 93.29 μ g BHT/mL. The antioxidant activity was positively correlated with the total phenolic content and suggests that this property is related to the phenolic compounds in the sample, quantified at 23.67 mg GAE/g.

The evaluation of the antioxidant potential of a crude ethanol extract obtained from *B. unguolata* leaves, and its fractions, revealed that all samples, especially the Ethyl Acetate fraction (FAE), were active. Concerning the total antioxidant capacity, evaluated by phosphomolybdenum complex reduction, the samples were active at 200 μ g/mL, a FAE concentration that reduced 100% molybdenum VI to molybdenum V conversion, similarly to Rutin standard. In evaluating the samples for DPPH radical capture, IC_{50} values between 7.68 and 124.74 μ g/mL were found, the lowest of them recorded for FAE, which was similar to that observed for Rutin, 6.35 μ g/mL. By the TBARS test (thiobarbituric acid reactive substances), which evaluates the reduction of the lipid peroxidation, FAE recorded up to 42.18% activity, a value with no statistically significant difference to the test using BHT standard (butyl-hydroxy-toluene).^[35] The authors suggested that the antioxidant activity observed was related to the flavonoid quercetin, quercetin arabinofuranoside and quercitrin, previously characterized in leaves of the species by Maia Neto *et al.*^[30]

The phosphomolybdenum complex reduction method was also used to determine the antioxidant activity of a flavonoid-rich ethyl acetate fraction (FABU) obtained from stem wood of *B. unguolata*. The sample showed greater activity than BHT, used as a control, and the antioxidant effect promoted by 1 mg of the fraction corresponded to that presented by 1.70 mg of BHT. The antioxidant potential of the sample was also evaluated by treating RAW 264.7 macrophages stimulated by lipopolysaccharide (LPS) with different concentrations of the fraction (15.63 - 62.5 μ g/mL) and then measuring the production of reactive oxygen species (ROS), nitric oxide (NO), hydrogen peroxide (H_2O_2) and TBARS. A decrease in ROS, NO and H_2O_2 was observed in cells stimulated with LPS in the presence of the fraction, indicating its capacity to interfere in the cascade of ROS and RNS production. The FABU also reduced the TBARS production and inhibited lipid peroxidation, proving to be a promising natural antioxidant complex. The authors related the flavonoids liquiritigenin, guibourtinidol and fisetinidol isolated from the fraction to the observed activities.^[32]

FABU was able to inhibit lipid peroxidation of cell membranes, when tested *in vivo*, due to the action of free radicals, in excised mice treated for five days with gels containing the fraction. Analysis of a tissue section removed from the wound after the treatment period revealed that gels containing 0.25% and 0.50% FABU produce an effective reduction in tissue malondialdehyde (MDA) levels, product of lipid peroxidation in animals, in comparison to non-treated group.^[36]

Table 3: Biological activities characterized in derivatives of *B. unguolata* L.

Activities	Tested samples (Plant section)*	Observed effects	Substances	Reference
Antioxidant	Infusion (L)	Intermediate capacity to capture DPPH radicals, compared to other infusions tested; Inhibition of free radicals in the β -carotene/linoleic acid system.	Phenolic compounds	[34]
	Ethanol extract and fractions (L)	Reduction of the phosphomolybdenum complex by all samples, highlighting the FAE, with 100% reduction, similar to rutin; Capture of DPPH radicals by all samples and FAE was the most active; Inhibition of lipid peroxidation by the samples, recording up to 42.18% reduction by FAE.	Quercetin** Quercetin arabinofuranoside** Quercitrin**	[35]
	Ethyl acetate fraction (Sw)	Reduction of the phosphomolybdenum complex greater than that presented by BHT (control). The antioxidant activity of 1 mg of fraction corresponded to that presented by 1.70 mg of BHT; Reduction of ROS, NO and H ₂ O ₂ levels in RAW 264.7 cells stimulated with LPS, reduction in TBARS production and inhibition of lipid peroxidation.	Liquiritigenin Guibourtinidol Fisetinidol	[32]
	Ethyl acetate fraction (Stw)	Inhibition of lipid peroxidation in excised mice, treated with gels containing the fraction. Analysis of a tissue section taken from the lesion site after the treatment showed that the use of gels with 0.25% and 0.50% FABU resulted in an effective reduction in tissue malondialdehyde (MDA) levels in the animals compared to the untreated group with fraction.	Liquiritigenin Guibourtinidol Fisetinidol	[36]
Antimicrobial	Essential oil (L)	Growth inhibitory activity of <i>Staphylococcus aureus</i> , <i>Salmonella typhimurium</i> and <i>Candida albicans</i> by oil, which ranged from 80-85% with the three largest concentrations tested (250, 125 and 62.5 $\mu\text{g} / \text{mL}$).	18 terpenes (β -caryophyllene, caryophyllene oxide and α -humulene were the majority)	[28]
	BUL lectin (S)	Growth reduction of <i>Fusarium lateritium</i> , <i>F. moniliforme</i> , <i>F. oxysporum</i> fungi, <i>F. solani</i> , <i>Aspergillus niger</i> and <i>Colletotrichum lindemuthianum</i> ; Greater activity against <i>F. solani</i> and <i>F. moniliforme</i> (40 and 30% inhibition, respectively).	N/A	[33]
Anti-inflammatory	Ethyl acetate fraction (Sw)	Reduction in the relative levels of genes expressing the pro-inflammatory mediators IL-1 β and TNF- α in mice submitted to surgical excision and treated with gels containing the fraction.	Liquiritigenin Guibourtinidol Fisetinidol	[36]
Acetylcholinesterase inhibition	Hexane extracts (F, B, L)	Inhibition of the enzyme by the extracts. The sample prepared with flowers was the most potent.	N/D	[39]
	Essential oil (L)	Inhibition of more than 95% of the enzyme by the oil, which showed to be more active than the standards eserine and galantamine tested in the work.	18 terpenes (β -caryophyllene, α -bisabolol, α -pinene, β -pinene and caryophyllene oxide may be related to activity)	[28]
Cytotoxic	Essential oil (L)	High toxicity of the sample against <i>Artemia salina</i> , with LC ₅₀ 144.75 $\mu\text{g} / \text{mL}$.	N/D	[28]
	2'-hydroxy-3,5-dimethoxy-4-methylbenzyl (R)	Cytotoxicity against HL-60, MCF-7, NCI-H292 and HEP-2 cell lines, being more active against HL-60 and HEP-2, with IC ₅₀ 4.3 and 6.5 $\mu\text{g} / \text{mL}$, respectively.	N/A	[31]
Antiproliferative	BUL lectin (S)	Inhibition of HT-29 cell proliferation in a dose-dependent manner, starting at 60 $\mu\text{g} / \text{mL}$ and reaching 80% inhibition with 160 $\mu\text{g} / \text{mL}$ of the lectin.	N/A	[33]
Larvicidal	Essential oil (L)	Death of part of the instar III larvae of <i>Aedes aegypti</i> by the oil after 24 h, with a LC ₅₀ value calculated at 75.1 \pm 2.8 $\mu\text{g} / \text{mL}$.	19 sesquiterpenes, among which caryophyllene oxide	[29]

continued...

Table 3: Cont'd

Activities	Tested samples (Plant section)*	Observed effects	Substances	Reference
Inhibition of the gelatinolytic activity of MMP-2 and MMP-9	Hydroalcoholic, hexane, chloroform and ethyl acetate partitions (St)	Inhibitory activity of MMPs by the tested samples, highlighting the hydroalcoholic and ethyl acetate partitions, whose inhibition percentage was greater than 90%; The ethyl acetate partition was considered the most potent among the tested samples.	Flavonoids and alkaloids	[40]
Healing	Ethyl acetate fraction (Sw)	Progressive reduction of an injured area by surgical excision, especially in mice treated with gel containing 0.5% FABU fraction, which showed the best healing effect compared to the others tested, including the standard.	Liquiritigenin Guibourtinidol Fisetinidol	[36]
Inhibition of fractions Xa and XII and plasma kallikrein	BuXI (S)	The BuXI protein inhibited factor XII and kallikrein, which showed, after incubation, K_i 8.0×10^{-8} and 0.7×10^{-8} M, respectively; Factor Xa was strongly inhibited by BuXI, presenting a K_i of 1.4×10^{-8} M at the end of the process.	N/A	[41]
Antidepressant and anxiolytic	Alkaloid extract (L)	Significant increase in the number of stalks in the last three days of treatment when compared to the negative control group (elevated plus maze test); Increase in the time spent by the animals in the bright field when compared to the negative control (light/dark test); No changes in water consumption, feed and excreta production during the 14 days after the administration of a single dose (2000 mg/kg) of the extract and occasional changes in the animals' breathing. The treatment with the alkaloid extract did not promote significant cellular changes in the liver of animals.	Alkaloids	[44]

* B: branches, F: flowers, L: leaves, S: seeds, St: Stem, Sw: stem wood, R: roots.

** Substances not detected in the sample, but their presence and relation to characterized activity were suggested by the authors, based on previously published results.

N/A: Not applicable.

N/D: Not determined by authors.

Antimicrobial Activity

An essential oil, obtained from leaves of *B. unguolata*, was tested *in vitro* against strains of five pathogenic micro-organism and showed growth inhibitory activity on *Staphylococcus aureus*, *Salmonella typhimurium* and *Candida albicans*, which ranged from 80 to 85% with the three highest concentrations (250, 125 and 62.5 µg/ml) of the tested sample. The chromatographic analysis of the oil allowed the characterization of eighteen terpenic substances and revealed the majority presence of β-caryophyllene, caryophyllene oxide and α-humulene.^[28]

The BUL lectin, a protein isolated from *B. unguolata* seeds, was evaluated *in vitro* for its ability to inhibit the growth of phytopathogenic fungi *Fusarium lateritium*, *Fusarium moniliforme*, *Fusarium oxysporum*, *Fusarium solani*, *Aspergillus niger* and *Colletotrichum lindemuthianum*, distributing 160 µg of the glycoprotein in plates containing the microorganisms. It was observed that BUL reduced the growth of all tested fungi, being more effective against *F. solani* and *F. moniliforme* (40 and 30% inhibition, respectively) and showing less inhibition against *F. lateritium* (about 5% growth reduction). This activity was considered fungistatic.^[33]

The analysis of other derivatives of the species, regarding their antimicrobial potential, revealed different results from those observed for the essential oil or for the BUL lectin. The evaluation of a hydroalcoholic extract and fractions (hexane, chloroform, ethyl acetate and residual hydroalcoholic) obtained from leaves of the species, for example, showed a low inhibitory potential for the growth of *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis* and *Pseudomonas aeruginosa* strains, and the samples were considered inactive.^[37] Similarly, an ethyl acetate fraction obtained from stem wood of *B. unguolata* was tested

against *Candida albicans*, methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* strains, and were presented MIC values greater than 500 µg/mL, not demonstrating significant antimicrobial activity.^[32]

On the other hand, an aqueous extract obtained from leaves of *B. unguolata* and tested for the modulating activity of antibiotics (amikacin, gentamicin, ciprofloxacin and imipenem) against strains of *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* was showed relevant synergistic activity on the drugs used, especially imipenem and ciprofloxacin, for which synergism was observed with the three bacteria tested.^[38]

Anti-inflammatory Activity

A flavonoid-rich ethyl acetate fraction obtained from stem wood of *B. unguolata* (FABU) was tested at 15.63-62.5 µg/mL for its anti-inflammatory activity on RAW 264.7 macrophages stimulated by lipopolysaccharide (LPS) and did not change the levels of cytokines TNF-α, TGF-β and IL-10 produced, indicating its low immunomodulatory potential.^[32] On the other hand, the treating mice submitted to surgical excision with gels containing FABU promoted a significant reduction in the relative levels of genes expressing the pro-inflammatory mediators IL-1β and TNF-α in injured region of these animals, compared to those that did not receive the treatment, suggesting that the fraction acts by regulating the inflammatory environment during the first stages of the healing process.^[36]

Healing Activity

The FABU was evaluated for its healing potential in a model that used mice in the experimentation. An injury made on the animals' back was

treated daily, for five days, with two different doses of the ethyl acetate fraction, incorporated in a 940 carbomer gel and then the lesion size was evaluated. The authors observed that during treatment, in addition to no bacterial growth, there was a progressive reduction in the injured area, especially in animals treated with the gel containing 0.5% FABU, which showed a better healing effect compared to the other samples tested, including the standard used in the test.^[36]

Acetylcholinesterase Inhibition

Hexane extracts, obtained from flowers, branches and leaves of *B. unguolata*, were investigated for their ability to inhibit acetylcholinesterase using a thin layer chromatography method. Of the samples tested, only the extract from the leaves did not show activity and the one obtained from the flowers was the most potent, suggesting that this is the plant organ with highest concentration of enzyme-inhibiting substances.^[39] An essential oil from leaves of the species was analyzed *in vitro* and inhibited the acetylcholinesterase in a percentage higher than 95%, and being more active than the eserine and galantamine, standards also analyzed in the test. This activity was related by the authors to constituents detected in the sample, including β -caryophyllene, which was the major substance in the oil (15.9%) and α -bisabolol, which represented 4.7% of the constituents present. The authors also highlight the presence of α -pinene, β -pinene and caryophyllene oxide, which could have a synergistic action in the inhibitory effect of acetylcholinesterase by the essential oil.^[28]

Cytotoxic Effect

The cytotoxic effect of an essential oil obtained from leaves of *B. unguolata* was evaluated against *Artemia salina* and showed a high toxicity, with LC_{50} 144.75 $\mu\text{g/mL}$, indicating its potential for biological activities.^[28] On the other hand, a hydroalcoholic extract and fractions (hexane, chloroform, ethyl acetate and residual hydroalcoholic) of *B. unguolata* proved to be non-cytotoxic when analyzed by the same model.^[37] The *in vitro* evaluation of 2'-hydroxy-3,5-dimethoxy-4-methylbisbenzyl isolated from *B. unguolata* roots against cell lines HL-60 (human promyelocytic leukemia), MCF-7 (human adenocarcinoma of the breast), NCI-H292 (human lung carcinoma) and HEP-2 (human cervical adenocarcinoma), revealed its cytotoxic potential, which was higher against HL-60 and HEP-2, with IC_{50} 4.3 and 6.5 $\mu\text{g/mL}$, respectively.^[31]

Antiproliferative Activity

The *in vitro* antiproliferative potential of the BUL lectin isolated from *B. unguolata* seeds was evaluated against human colon adenocarcinoma (HT-29 cell line), using glycoprotein concentrations ranging from 20 to 160 $\mu\text{g/mL}$. The tested lectin inhibited cell proliferation in a dose-dependent manner, starting its activity at 60 $\mu\text{g/mL}$ and reaching 80% inhibition with the highest concentration tested. The preliminary results observed by the authors suggest that BUL possesses the potential to be used as a tool in studies involving cancer cells.^[33]

Larvicidal Activity

Sousa *et al.*^[29] evaluated the larvicidal activity of an essential oil obtained from leaves of *B. unguolata* against instar III larvae of *Aedes aegypti*. Briefly, the parasites were kept in contact with the sample at concentrations ranging from 50 to 500 $\mu\text{g/mL}$ for 24 hr and the number of dead larvae was evaluated after this period. Based on these results it was possible to determine the LC_{50} value of the oil, calculated at 75.1 ± 2.8 $\mu\text{g/mL}$. The authors related the larvicidal activity to sesquiterpenes detected in the sample, including caryophyllene oxide, characterized as the major substance in the oil.

Inhibition of Gelatinolytic Activity of MMP-2 and MMP-9

The inhibition of the gelatinolytic activity of MMP-2 and MMP-9, proteases related to tumor invasion and metastasis in several types of cancer, represents an important property presented by *B. unguolata* L. In this investigation, the hydroalcoholic, hexane, chloroform and ethyl acetate partitions obtained from a crude extract of stems of the species were tested, and the inhibitory activity was observed for all samples tested, highlighting the hydroalcoholic and ethyl acetate partitions, with inhibition greater than 90%. The phytochemical investigation of the ethyl acetate partition revealed the presence of steroids, tannins, coumarins, alkaloids and flavonoids in the sample, however, the analysis of fractions obtained by chromatographic separation of this partition regarding the present metabolites and inhibitory potentials of MMPs, revealed that the activity of the sample is related to its flavonoids and/or alkaloids.^[40]

Inhibition of Factors Xa and XII and Plasma Kallikrein

From seeds of *B. unguolata* the protein BuXI was isolated and characterized as an inhibitor of serine proteases factor Xa, factor XII and plasma kallikrein, involved in the blood coagulation cascade. This determination was carried out by incubating the BuXI factor with the enzymes at different concentrations. At the end of the process, the residual activity of the enzyme was evaluated, based on its dissociation constant (K_i). As a result, it was observed that the protein inhibited factor XII and kallikrein, which presented, after incubation, a K_i of 8.0×10^{-8} and 0.7×10^{-8} M, respectively. In addition, factor Xa was strongly inhibited by BuXI, with a K_i 1.4×10^{-8} M at the end of the process, and this result characterized the protein as a plant protease inhibitor with greater affinity for factor Xa described so far.^[41] Further work was carried out to characterize the interactions between blood coagulation proteases and the BuXI inhibitor.^[42,43] The inhibitory effect of the protein isolated from *B. unguolata* on coagulation factors is important, as it suggests its potential as an anticoagulant agent.

Antidepressant and Anxiolytic Activity

An alkaloid extract obtained from leaves of *B. unguolata* was evaluated for its ability to reduce the depressive behavior of mice, and its acute toxicity was also evaluated.^[44] Initially, depression was induced in the animals by forced swimming and after this step, the alkaloid extract was administered by gavage, for 12 days, 30 min before the behavioural tests (light/dark test and elevated plus maze test). As for the elevated plus maze test, it was observed that the animals treated with the extract showed a significant increase in the number of stalks in the last three days of treatment when compared to the negative control group, which indicates an improvement in the depressive state of the mice and suggests the activity anxiolytic of the extract. Similarly, in the light/dark test, an increase in the time spent by the animals in the bright field was observed compared to the negative control, which represents an indication of non-anxious and non-depressive behaviour in the mice. As for acute toxicity, it was noted that the administration of a single dose (2000 mg/kg) of the extract did not promote changes in water consumption, feed and excreta production during the 14 days after treatment. Only occasional changes in the animals' breathing were observed, which could be related to stress during the experiment. In addition, the histological analysis of the livers revealed that the treatment with the extract did not promote significant cellular changes, indicating a low level of toxicity of the extract.

CONCLUSION

Despite the limited number of articles published about *Bauhinia unguolata*, the selected works deal with different bioactivities and provide information on many metabolites present in different derivatives investigated, indicating that the phytochemical and biological data

published on this species allow to infer a potential of use as a therapeutic ingredient with antioxidant activity, which is the most investigated activity and has been related to phenolic compounds, especially flavonoids, detected in the species. It is also observed and reported that *Bauhinia* spp. is popularly used as an infusion to control diabetes, however, the search has found no published data reporting the evaluation of the antidiabetic or hypoglycemic activity of *B. unguolata*. As for the phytochemical analysis of the leaves, the selected works focused on the investigation of its essential oils, with no data being found on the substances present in aqueous extracts, which represent the main popular form of use reported for *Bauhinia* leaves, according to the consulted references.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

BHT: Butylated hydroxytoluene; **BUL:** Lectin from *Bauhinia unguolata*; **BuXI:** *Bauhinia unguolata* factor Xa inhibitor; **DPPH:** 2,2-diphenyl-1-picrylhydrazyl; **FABU:** Flavonoid-rich ethyl acetate fraction obtained from stem wood of *B. unguolata*; **FAE:** Ethyl acetate fraction; **GAE:** Gallic acid equivalents; **GC-FID:** Gas chromatography-flame-ionization detection; **GC-MS:** Gas chromatography-mass spectrometry; **IC₅₀:** Half maximal inhibitory concentration; **IL-10:** Interleukin 10; **LC₅₀:** Lethal concentration 50; **LPS:** Lipopolysaccharide; **MDA:** Malondialdehyde; **MIC:** Minimum inhibitory concentration; **MMP-2:** Matrix metalloproteinase 2; **MMP-9:** Matrix metalloproteinase 9; **RNS:** Reactive nitrogen species; **ROS:** Reactive oxygen species; **TBARS:** Thiobarbituric acid reactive substances; **TGF-β:** Transforming growth factor beta; **TNF-α:** Tumor necrosis factor alpha.

REFERENCES

- Corrêa MP. Dicionário das plantas úteis do Brasil e das exóticas cultivadas. Rio de Janeiro: Imprensa Nacional; 1926.
- Di Stasi LC, Hiruma-Lima CA. Plantas medicinais na Amazônia e na Mata Atlântica. 2nd ed. São Paulo: Editora Unesp; 2002.
- Vaz AMSF, Tozzi AMGA. Sinopsis de *Bauhinia* sect. Puletia (Cav.) DC. (Leguminosae: Caesalpinioideae: Cercideae) no Brasil. Rev Bras Bot. 2005;28(3):477-91. doi: 10.1590/S0100-84042005000300006.
- Achenbach H, Stöcker M, A. Constenla M. Flavonoid and other constituents of *Bauhinia manca*. Phytochemistry. 1988;27(6):1835-41. doi: 10.1016/0031-9422(88)80455-2.
- Silva KL, Cechinel Filho V. Plantas. Plantas do gênero *Bauhinia*: Composição química e potencial farmacológico. Quím Nova. 2002;25(3):449-54. doi: 10.1590/S0100-40422002000300018.
- Cechinel Filho VC. Chemical composition and biological potential of plants from the genus *Bauhinia*. Phytother Res. 2009;23(10):1347-54. doi: 10.1002/ptr.2756, PMID 19170142.
- Nogueira ACde O, Sabino CDVS. Revisão do gênero *Bauhinia* Abordando Aspectos Científicos das Espécies *Bauhinia forficata* Link e *Bauhinia variegata* L. de interesse para a indústria farmacêutica. Rev Fitos. 2012;7(2):77-84.
- Van den Berg ME, Silva MHLd. Contribuição ao conhecimento da flora medicinal de Roraima. Acta Amaz. 1988;18(suppl 1-2):23-35. doi: 10.1590/1809-43921988185035.
- Scoles R. Sabiduría popular y plantas medicinales: El ejemplo de la comunidad negra de Itacoá, Acará, Pará. Boll Mus Emilio Goeldi Sér Ciénc Natl. 2006;1(2):79-102. doi: 10.46357/bcnaturais.v1i2.744.
- Vaz AMSF, Tozzi AMGA. *Bauhinia* ser. Cansenia (Leguminosae: Caesalpinioideae) in Brazil. Rodriguesia. 2003;54(83):55-143.
- Torres-Colín R, De Stefano RD, Can LL. El género *Bauhinia* (Fabaceae, Caesalpinioideae, Cercideae) en la península de Yucatán (México, Belice y

- Guatemala). Rev Mex Biodivers. 2009;80(2):293-301.
- The plant list. A working list of all plant species [Homepage on the Internet] [cited Jun 4 2022]. Available from: <http://www.theplantlist.org/tp1.1/record/ild-20070>.
- Tropicos, Missouri Botanical Garden. [Homepage on the Internet] [cited Jun 4 2022]. Available from: <https://www.tropicos.org/name/Search?name=Bauhinia%20ungulata>.
- Wunderlin R, Larsen K, Larsen SS. Reorganization of the Cercideae (Fabaceae: Caesalpinioideae). Biol Skr. 1987;28:1-40.
- Lewis G, Forest F. Tribe Cercideae. In: Lewis G, Schrire B, Mackinder B, Lock M, editors. Legumes of the world. Kew: Royal Botanical Garden; 2005. p. 57-68.
- Wunderlin R. Reorganization of the Cercideae (Fabaceae: Caesalpinioideae). Phytoneuron. 2010;48:1-5.
- Sinou C, Forest F, Lewis GP, Bruneau A. The genus *Bauhinia* s.l. (Leguminosae): A phylogeny based on the plastid trnL-trnF region. Botany. 2009;87(10):947-60. doi: 10.1139/B09-065.
- Pereira LBS, Costa-Silva R, Felix LP, Agra MdF. Leaf morphoanatomy of "mororó" (*Bauhinia* and *Schnella*, Fabaceae). Rev Bras Farmacogn. 2018;28(4):383-92. doi: 10.1016/j.bjp.2018.04.012.
- Da Silva MP, De Barros RFM, Moita Neto JM. Farmacopeia natural de comunidades rurais no estado do Piauí, Nordeste do Brasil. Desenvolv Meio Ambiente. 2015;33:193-207.
- Santos ABN, Araújo MP, Sousa RS, Lemos JR. Plantas medicinais conhecidas na zona urbana de Cajueiro da Praia, Piauí, Nordeste do Brasil. Rev Bras Plant Med. 2016;18(2):442-50. doi: 10.1590/1983-084X/15_149.
- Moraes SM, Joana D, Dantas P, Raquel A. Plantas medicinais usadas pelos índios Tabepas do Ceará. Rev Bras Farmacogn. 2005;15(2):169-77.
- Agência nacional de vigilância sanitária. Resolução RDC 26. de 13 de maio de 2014. Dispõe sobre o registro de medicamentos fitoterápicos e o registro e a notificação de produtos tradicionais fitoterápicos. Brazil: 2014.
- Coutinho JMCP, Lins Neto EMF, Monteiro JM. Plantas medicinais utilizadas na Comunidade Santo Antônio, Currais, Sul do Piauí: um enfoque etnobotânico. Baptistel AC. Rev Bras Plant Med. 2014;16:406-25.
- Ribeiro RV, Bieski IGC, Balogun SO, Martins DTO. Ethnobotanical study of medicinal plants used by Ribeirinhos in the North Araguaia microregion, Mato Grosso, Brazil. J Ethnopharmacol. 2017;205(May):69-102. doi: 10.1016/j.jep.2017.04.023, PMID 28476677.
- Hirschhorn HH. Botanical remedies of south and Central America, and the Caribbean: An archival analysis. Part I. J Ethnopharmacol. 1981;4(2):129-58. doi: 10.1016/0378-8741(81)90032-5, PMID 7311595.
- De Farias JC, Bomfim BLS. Plantas inseticidas e repelentes utilizadas em uma comunidade rural no Nordeste brasileiro. Espacios. 2016;37(2):1-11.
- V Gramosa N, De Freitas JVB, Neto MNDL, Silveira ER, V Gramosa N. Volatile components of the essential oil from *Bauhinia unguolata* L. J Essent Oil Res. 2009;21(6):495-6.
- Medeiros SRNA, Melo-Filho AA, Costa HNR, Silva Fdos S, Santos RC, Takahashi JA, et al. Chemical profile, antimicrobial activity, toxicity on artemia salina and anti-acetylcholinesterase enzyme essential oil from *Bauhinia unguolata* L. (Fabaceae) leaves. J Med Plants Res. 2016;10(29):442-9.
- Sousa LM, De Carvalho JL, Gois RWS, Da Silva HC, Santiago GMP, Lemos TLG, et al. Chemical composition, larvicidal and cytotoxic activities of the essential oils from two *Bauhinia* species. Rec Nat Prod. 2016;10(3):341-8.
- Neto MM, Neto MA, Filho RB, Lima MAS, Silveira ER. Flavonoids and alkaloids from leaves of *Bauhinia unguolata* L. Biochem Syst Ecol. 2008;36(3):227-9. doi: 10.1016/j.bse.2007.08.006.
- Sousa LM, De Carvalho JL, Da Silva HC, Lemos TLG, Arriaga AMC, Braz-Filho R, et al. New cytotoxic bibenzyl and Other Constituents from *Bauhinia unguolata* L. (Fabaceae). Chem Biodivers. 2016;13(12):1630-5.
- Rodrigues RdO, Yachite JNU, Braga MA, Sousa ARd, Sasahara GL, Fonseca SGdC, et al. Antioxidant and anti-inflammatory Activities of *Bauhinia unguolata* L. (Fabaceae) on LPS-stimulated RAW 264.7 cells. Pharmacogn J. 2019;11(1):37-42. doi: 10.5530/pj.2019.1.7.
- Silva HC, Pinto LdS, Teixeira EH, Nascimento KS, Cavada BS, Silva ALC. BUL: A novel lectin from *Bauhinia unguolata* L. seeds with fungistatic and antiproliferative activities. Process Biochem. 2014;49(2):203-9. doi: 10.1016/j.procbio.2013.10.020.
- Chisté RC, Godoy HT, Prado MA. The phenolic compounds and the antioxidant potential of infusion of herbs from the Brazilian Amazonian region. Port's PS. Food Res Int. 2013;53(2):875-81.
- Paula Cda S, Canteli VCD, Hirota BCK, Campos R, De Oliveira VB, Kalegari M, et al. Potencial antioxidante *in vitro* das folhas da *Bauhinia unguolata* L. Rev Ciénc Farm Básica Apl. 2014;35(2):217-22.
- De Oliveira Rodrigues RO, Yachite JNU, Sasahara GL, Albuquerque AA, Da Cruz Fonseca SG, De Vasconcelos Araújo TD, et al. Antioxidant, anti-inflammatory and healing potential of ethyl acetate fraction of *Bauhinia unguolata* L. (Fabaceae) on *in vitro* and *in vivo* wound model. Mol Biol Rep. 2020;47(4):2845-59. doi: 10.1007/s11033-020-05332-7, PMID 32239466.

37. Paula Cda S, Christina M, Konopatzki BC, De Souza AM, Bezerra C, Miguel OG. Caracterização fitoquímica, toxicidade e avaliação preliminar da atividade antibacteriana das folhas de *Bauhinia unguolata* L. *Rev Bras Farm.* 2015;96(2):1315-34.
38. Lacerda G, Brito Monteiro Á, Tintino SR, De Araújo Delmondes G, Fernandes CN, Santiago Lemos IC, *et al.* Modulatory activity about antibiotics by aqueous extract of the leaves of *Bauhinia unguolata* L. *Rev Cuba Plant Med.* 2017;21(3):309-17.
39. Santos KM, Gonçalves PS, Paiva MJ, Lacerda GA. Acetylcholinesterase inhibition starting from extracts of *Bauhinia variegata* L., *Bauhinia var. candida* (Aiton) Buch.-Ham., and *Bauhinia unguolata* L. *Rev Soc Bras Med Trop.* 2011;44(6):781-3. doi: 10.1590/s0037-86822011000600025, PMID 22231255.
40. Dos Santos KM, De Fátima Nunes DA, Gomes INF, Da Silva SL, De Azambuja Ribeiro RIM. Inhibition of gelatinase activity of MMP-2 and MMP-9 by extracts of *Bauhinia unguolata* L. *Biosci J.* 2015;31(2):584-90. doi: 10.14393/BJ-v31n2a2015-23477.
41. Oliva MLV, Sallai RC, Sampaio CAM, Fritz H, Auerswald EA, Tanaka AS, *et al.* *Bauhinia* serine proteinase inhibitors: Effect on factor X, factor XII and plasma kallikrein. *Immunopharmacology.* 1996;32(1-3):85-7. doi: 10.1016/0162-3109(95)00058-5, PMID 8796274.
42. Oliva MLV, Andrade SA, Batista IFC, Sampaio MU, Juliano M, Fritz H, *et al.* Human plasma kallikrein and tissue kallikrein binding to a substrate based on the reactive site of a factor Xa inhibitor isolated from *Bauhinia unguolata* seeds. *Immunopharmacology.* 1999;45(1-3):145-9. doi: 10.1016/s0162-3109(99)00146-0, PMID 10615004.
43. Oliva MLV, Andrade SA, Juliano MA, Sallai RC, Torquato RJ, Sampaio MU, *et al.* Kinetic Characterization of Factor Xa Binding Using a Quenched Fluorescent Substrate Based on the Reactive Site of Factor Xa Inhibitor from *Bauhinia unguolata* Seeds. *Curr Med Chem.* 2003;10(13):1085-93. doi: 10.2174/0929867033457548, PMID 12678803.
44. Santiago LR, Santos KM, Silva LT, Santos CF, Fonseca JVD, Caldas IG, *et al.* Extratos alcaloidicos de *Bauhinia* diminuem comportamento depressivo de camundongos com baixa toxicidade. *Conexão Cien.* 2021;16(3):42-62.

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