

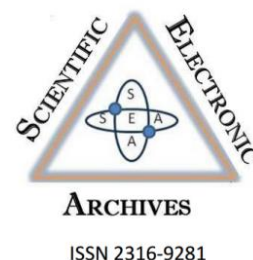
Scientific Electronic Archives

Issue ID: Sci. Elec. Arch. Vol. 17 (2)

March/April 2024

DOI: <http://dx.doi.org/10.36560/17220241876>

Article link: <https://sea.ufr.edu.br/SEA/article/view/1876>



Clarisia racemosa: phytochemical characterization and biological activities a brief literature review

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Abstract. *Clarisia racemosa* is a valuable resource in the wood industry, commonly used as raw material for furniture, boat construction, civil engineering, and various other applications. However, this species is used in other sectors as well. Research has shown that this plant has therapeutic potential for medicinal purposes. This review aims to present the various biological activities of the *Clarisia racemosa* plant. This study was conducted by postgraduate students in the Morphotechnology program at the Federal University of Pernambuco, from September 1st to October 6th, 2023, as part of a course on scientific article and patent preparation. The research findings confirmed that the species has the ability to promote various beneficial activities, including antioxidant, antitumor, toxicological, insecticidal, antimicrobial, antiparasitic, and photoprotective effects. This review aims to increase the value of species found in the Brazilian flora by obtaining products with high added value.

Keywords: Amazon Forest, natural products, herbal medicines, biological activities

Introduction

Humanity has relied on natural products for medicinal purposes for a long time (Elshafie et al., 2023). The use of these products is associated with their structural diversity and pharmacological characteristics, even in empirical studies (Tanveer et al., 2023). Plants are often regarded as living chemical factories that produce a wide range of secondary metabolites (Elshafie et al., 2023; Tanveer et al., 2023). These metabolites play a crucial role in the development of numerous pharmaceutical drugs. They can serve as precursors for the development of new medicines and can also be used in their natural form as herbal remedies (Nguyen et al., 2023).

The Amazon rainforest region is renowned for its exceptional plant diversity, with approximately 30,000 species (Silva Santos et al., 2022). Although many studies have documented the presence of secondary metabolites in Amazonian plants, our current understanding of the chemical diversity in this ecosystem remains limited due to the vast number of species. Among the various plant species, *Clarisia racemosa* (Albuquerque Nerys et al., 2022).

Clarisia racemosa is a medium to large tree native to Tropical America. It can grow up to 40 meters tall and has large, oval-shaped leaves that alternate. The flowers are small, with white or yellow petals, and are typically arranged in raceme-type inflorescences, which is why they are called "racemosa". The plant produces woody capsules containing seeds, and the trunk is typically straight (Costa, 1992; Ferraz & Varela, 2003; Santos, 2008). This tree is commonly used as raw material for

constructing furniture, boats, and various wooden products Loureiro; Silva; Alencar, 1979; Sudam, 1979; Jankowsky, 1990).

Despite extensive knowledge about the commercial applications of this plant, its biological properties remain largely unknown. This literature review aims to report the various biological activities of the plant *Clarisia racemosa*, including *in vitro* and *in vivo* toxicity (Souza de Melo, 2014; Albuquerque Nerys et al., 2022), antitumor (Melo, 2015), antiparasitic properties (Cruz Filho et al., 2023), insecticidal activity (Júnior et al., 2018), antioxidant and photoprotective effects (Albuquerque Nerys et al., 2022).

Clarisia racemosa

Clarisia racemosa Ruiz & Pavón is a tree species that is native to various countries in South America and Mexico (Santos, 2008). The genus *Clarisia*, consisting of three species (*Clarisia biflora*, *Clarisia ilicifolia*, and *Clarisia racemosa*), was named after the Spanish biologist Miguel Barnades Clares. These species are found in tropical America and various regions of Brazil, including the southeast, north, and center-west.

The taxonomic classification of *Clarisia racemosa* is based on various frameworks. Cronquist (1981) utilizes a morphological approach, while Joly (1998) adapts Engler's framework, which incorporates morphological, phylogenetic, and chemical composition aspects of the plant (Cronquist, 1981; Joly 1998). Table 1 presents the taxonomic framework of the *Clarisia racemosa* species.

Table 1. The taxonomic framework of *Clarisia racemosa*. Adapted from Cronquist (1981) and Joly (1998), respectively. The species has different popular names because it is found in many different geographic locations.

	Cronquist (1981)	Engler (Joly, 1998)
Division	Magnoliophyta	Angiospermae
Class	Magnoliopsida	Dicotyledoneae
Subclass	Hamamelidae	Archichlamydeae
Order	Urticales	Urticales
Family	Moraceae	Moraceae
Gender	<i>Clarisia</i>	<i>Clarisia</i>
Species	<i>Racemosa</i>	<i>Racemosa</i>

Table 2 shows the commonly used names of the plant in different countries. The wood from this tree is highly valuable and widely used in carpentry, joinery, civil engineering, and naval construction. Indigenous populations commonly use it to easily make canoes from whole trunks. According to Loureiro, Silva, Alencar (1979), Sudam (1979), and Jankowsky (1990), dismissal is a common practice in organizations.

The tree species can reach heights of up to 40 meters. The trunk contains numerous laticiferous tubes. The cortex is usually a dark grayish-brown color (Santos, 2008; Santos et al., 2008). The leaves are simple and alternate, varying in length (4-15 cm), width (2-6 cm), and shape (elliptical, oval, or oblong). The branches of the stem release a white, sticky latex (Santos, 2008). The fruit is ellipsoidal and changes to an orange-yellow color when it is ripe. The maximum

length of it ranges from 2 to 3.5 cm. The seeds are almost spherical, weighing an average of 1g and measuring up to 1.5 cm in length (Santos et al., 2008; Gardner, 2023). The plant's roots are easily identifiable when they emerge from the soil surface

because of their red color (Santos, 2008; Santos et al., 2008; Gardner, 2023). Figure 1 illustrates the different parts of a tree, such as fruits, leaves, branches, roots, and trunk.

Table 2. The popular names of the plant *Clarisia racemosa* vary in different countries. Adapted from Costa (1992), Ferraz & Varela (2003), and Santos (2008).

Countries	Popular names
Bolivia	Mascajo; Mururé; Oiti; Vacati e Vitaca,
Brazil	Guariúba; Guariúba Amarela; Oiticia Da Mata; Oitícica; Oitícica Amarela; Oitícica; Quariuba; Tatajuba Amarela e Turupay.
Colombia	Ají; Mora; Moral; Oitícica Amarilla; Oity e Quebracho. Moral Bobo; Murere e Pituca.
Ecuador	Árbol Del Pan
Mexico	Amarillo; Capinuri; Mashonaste ; Mata Palo e Tulpay Ache; Aji; Amanllo; Arbol del pan; Arracacho; Bainha de espada; Bainha; Cajimán; Carac; Caraco; Catruz; Cuaruiba; D espada; Diconroque; Dinde; Guariuba amarela; Guariuba; Huariuba; Imauba; Janita; Killo-muena; Machunaste; Matapalo; Maxunasti; Moral comido de mono; Moralbabo; Murure; Oiti amarelo; Pellejo De Indio Chichillica; Piamich; Sota; Yasmich e Zota.



Figure 1. The components of a *Clarisia racemosa* tree include fruits, leaves, branches (A), trunk, and roots (B), which together form the tree (C). Adapted from Powo (2023) and Plantidtools (2023)

Wood composition analysis

Wood has a complex chemical structure due to the intertwining of its main constituents, cellulose (hexoses), hemicellulose (pentoses), and lignin. Additionally, they contain extractives and mineral salts (Sluiter et al., 2010). The wood composition values ranged from 40.58% to 50.51% for cellulose, 16.54% to 24.1% for hemicellulose, 25% to 34.72% for lignin, 3.82% to 16.01% for extractives, and 0.3% to 1.67% for ash (Corrêa, 1990; Frazão 1990; Printes et al. 2004; Santana & Okino 2007; Santos, 2015; Inga & Castillo 2016; Albuquerque Nerys et al. 2022). This variation can be attributed to factors such as seasonality, climatic conditions, and quantification methods (Sluiter et al., 2010). This review will focus solely on the extractives found in *Clarisia racemosa*, despite the presence of various constituents in the plant.

The composition of phytochemicals in *Clarisia racemosa* extracts

Various secondary metabolites have been found in *Clarisia racemosa*. Cunha, Pinto & Braz-Filho (1994) isolated two flavonoids, artocarpine and isoartocarpine, from the hexane and chloroform extracts of *Clarisia racemosa* Ruiz. Hernes and Hedges (2004) confirmed the presence of tannins and triterpenes in the green leaves and bark of *Clarisia racemosa*. The tannin content in the leaves was 1.61%, with triterpenes at 0.20%. The peel contained 0.06% tannins and 0.88% triterpenes. No traces of these compounds were detected in the plant cone. Duran Ruiz (2014) qualitatively identified the presence of alkaloids, flavonoids, leucoanthocyanidins, saponins, tannins, triterpenes, and quinones.

Santos (2015) reported that the wood contained 0.95% total polyphenols and 0.71% tannins. Melo (2015) conducted a phytochemical study on the leaves and wood of the *Clarisia racemosa* species. The study focused on the hexane and dichloromethane fractions of the leaves, as well as the ethyl acetate fraction of the wood, and

identified nine constituents. In the hexane fraction of the leaves, 1 fatty alcohol (tetratriacontanol) and 1 fatty acid (palmitic acid) were identified. In the dichloromethane fraction of the leaves, 5 triterpenes (β -amyrin acetate, lupeol acetate, taraxerol acetate, lupeol, and α -amyrin) and 1 fatty ester (decanoyl 7-oxotetraeicosanoate) were identified. Finally, 1 flavanone known as 5,7,3',4'-tetrahydroxyflavanone was identified in the wood.

Albuquerque Nerys et al. (2022) utilized liquid chromatography coupled with mass spectrometry (UHPLC-MS) to identify phenolic compounds. The study found 17 compounds in the hydroalcoholic extract, including shikimic acid, caffeoylquinic acid, vanillic acid, (-) epicatechin, rutin, luteolin, and ferulic acid. The main signals were determined by vanillic acid, rutin, luteolin, and ferulic acid.

Biological activities of *Clarisia racemosa*

Toxicity

There is limited research on the cytotoxicity of *Clarisia Racemosa*. However, Albuquerque Nerys et al. (2022) assessed the cytotoxic effects of a hydroalcoholic extract from this plant. The authors found that the plant extract did not show any cytotoxic activity on erythrocytes in *in vitro* assays, even at concentrations as high as 500 $\mu\text{g/mL}$. The plant extract did not exhibit a 50% erythrocyte hemolysis (IC_{50}). No significant hemolysis of erythrocytes was observed, even at higher concentrations of the *Clarisia racemosa* extract.

This finding is significant because erythrocytes, which are anucleated cells without mitochondria, are among the first cells to be affected in adverse conditions. The cellular response of organisms depends on the permeability of substances through their cell membrane (Mameri et al., 2021). Additionally, these cells have a vital function in transporting different substances throughout the body. Any structural changes can result in a loss of cellular functionality, which can disrupt homeostasis (Mondal et al., 2023).

The cytotoxicity of the *Clarisia racemosa* extract on J774 macrophage cells was investigated by Albuquerque Nerys et al. (2022). The results showed that the extract had an IC_{50} value of $160.5 \pm 1.8 \mu\text{g/mL}$, indicating its effective concentration for promoting 50% cell viability. The authors found that the extract did not cause significant death of macrophage cells. However, they observed an increase in the production of nitric oxide when cells were cultivated with varying concentrations of the extract.

Macrophages and erythrocytes are frequently used cellular models in assays that assess the cytotoxic activity of organic extracts (Tsai et al., 2020). Macrophages are cells that play a crucial role in the body's response to harmful substances or foreign bodies. They are involved in processes such as phagocytosis and the release of mediators. The presence of damage to these cells indicates an immune system impairment (Park et al., 2022). In a recent *in vivo* study conducted by Albuquerque Nerys

et al. (2022), it was determined that the hydroalcoholic extract was non-toxic at a concentration of 2000 mg/kg.

The results of *in vitro* tests on macrophages and hamster blood cells demonstrated that the *Clarisia racemosa* extract exhibited low toxicity both *in vitro* and *in vivo* (Albuquerque Nerys et al., 2022).

Antitumor activity

Secondary metabolites in plants show promise as antitumor agents. Melo (2015) conducted a study to assess the anticancer properties of the methanolic extract from the leaves of *Clarisia racemosa*. The study found that the dichloromethane and hexane fractions of the extract had cytotoxic effects on a human lymphoma cell line. The dichloromethane fraction demonstrated effectiveness against colon adenocarcinoma, poorly metastatic melanoma, and human peripheral blood mononuclear cells. Albuquerque Nerys et al. (2022) discovered that the hydroalcoholic extract exhibited antiproliferative activity against MCF-7, T47D, DU-145, and Jurkat tumor cells, with IC_{50} values ranging from 0.31 to 1.06 $\mu\text{g/mL}$, respectively.

Insecticidal activity

Secondary metabolites have the potential to act as insecticidal agents by inhibiting the growth of various insects. Júnior et al. (2018) conducted a study on the insecticidal properties of *Clarisia racemosa* wood against termites (*Cryptotermes brevis*). Wood has natural properties that can prevent termite infestation.

Antimicrobial Activity

Natural products have been essential in eliminating microorganisms. Albuquerque Nerys et al. (2022) evaluated the antimicrobial activity of the hydroalcoholic extract of *Clarisia racemosa* wood against different bacterial strains (*Staphylococcus aureus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*) and yeast strains (*Candida albicans*, *Candida glabrata*, *Candida guilliermondii*). The inhibitory concentration results against strains of *Staphylococcus aureus* and *Enterococcus faecalis* ranged from 512 to 1,024 $\mu\text{g/mL}$, respectively. The extract inhibited the yeasts *Candida albicans* and *Candida glabrata* at concentrations of 1024 $\mu\text{g/mL}$ each. Silva (2021) conducted a study showing that the hydroalcoholic extract of *Clarisia racemosa* has inhibitory effects on the growth of *Sporothrix* spp. Studies have demonstrated the antimicrobial activity of phenolic compounds in the extract in laboratory settings.

Antiparasitic activity

Recently, Cruz Filho et al. (2023) conducted a study on the antiparasitic properties of the hydroalcoholic extract of *Clarisia racemosa*. The researchers discovered that the extract caused structural changes in the promastigote forms of *L. amazonensis* and in the adult worms of *S. mansoni*. The extract demonstrated effectiveness in inhibiting

the growth of the trypanostigote form of *T. cruzi* and had some antiparasitic activity against strains of *P. falciparum*.

In vitro antioxidant activity

Antioxidants play an important role in inhibiting and eliminating free radicals. These tests have been widely used in plants due to the abundance of phenolic compounds found in the extracts (Lopes et al., 2010). Albuquerque Nerys et al. (2022) found that the extract of *Clarisia racemosa* was capable of promoting antioxidant activity in the DPPH, ABTS, and phosphomolybdenum assays.

In vitro photoprotective activity

The search for photoprotective molecules has increased, and phenolic compounds have proven to be a promising alternative capable of providing protection against UV radiation (Almeida Andrade et al. 2019). Only one study was found that used *Clarisia racemosa* extract as a photoprotector, conducted by Albuquerque Nerys et al. (2022). The authors confirmed that the components found in the extract had the ability to enhance photoprotective activity, with a sun protection factor of 8.0. This result shows that the extract of *Clarisia racemosa* is a promising and safe alternative to be used as an additive in sunscreens.

Formulations using *Clarisia racemosa* extract

In recent years, nanotechnology has gained significant attention and visibility, particularly in the pharmaceutical and cosmetic sectors (Mansur et al., 2020; Cao et al., 2022). Currently, there is no literature on the use of *Clarisia racemosa* extract in nanoformulations. A recent study by Albuquerque Nerys et al. (2022) discovered the biological potential of the hydroalcoholic extract derived from the wood of this plant. The extract has physicochemical characteristics and contains phenolic compounds, flavonols, flavonoids, and tannins. It has been demonstrated to function as an antioxidant, neutralizing free radicals, and as an antiglycant, minimizing harm to skin proteins. Additionally, it has antimicrobial properties that prevent the reproduction of *Staphylococcus aureus*.

Silva (2021) conducted an evaluation of the antifungal activity of *C. racemosa* for the treatment of sporotrichosis. The study included a pre-formulation analysis of the plant drug and the development of liquid and dry extracts using spray-drying and fluidized bed techniques. The dry extract by fluidized bed was selected for pre-formulation studies. Different standardized strains were used to test the antifungal activity of both types of extracts. The results showed activity against *Sporothrix* spp.

Conclusion

The review work demonstrated the potential biological activities of the *Clarisia racemosa* plant. These findings indicate that this species can serve as a valuable raw material for the production of high-value products that can be utilized in the biomedical and pharmaceutical industries.

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