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Pharmacological Potential of Fridericia Chica: Traditional Knowledge and Chemical Composition

Potencial Farmacológico da Fridericia Chica: Conhecimento Tradicional e Composição Química

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ABSTRACT

The *Fridericia chica* is a shrub widely distributed throughout the Brazilian territory. In traditional knowledge, it is used for various pathologies. It is a plant of interest in phytotherapy as it is part of the National List of Medicinal Plants of Interest to the Brazilian Unified Health System – RENISUS. Among the scientific studies conducted, the potential antioxidant, analgesic, anti-inflammatory, immunomodulatory, healing, gastroprotective, antibacterial, antifungal, antiprotozoal, antiviral, antitumor, antiangiogenic, photoprotective, diuretic, and hepatoprotective properties have been demonstrated. Furthermore, the assays report the low toxicity of the extracts. Therefore, *Fridericia chica* is a plant with pharmacological potential for the development of new medications. This article contributes to the dissemination of the species' pharmacological potential and the imminent observation of traditional knowledge.

Keywords: Medicinal Plants; Anti-Inflammatory; Crajiru; Pharmacological Potential

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RESUMO

A *Fridericia chica* é um arbusto amplamente distribuído pelo território brasileiro. No conhecimento tradicional é utilizada para diversas patologias. É uma planta de interesse na fitoterapia por compor a Relação Nacional de Plantas Medicinais de Interesse ao Sistema Único de Saúde Brasileiro – RENISUS. Dentre os estudos científicos realizados foram demonstrados o potencial antioxidante, analgásico, anti-inflamátorio, imunomodulador, cicatrizante, gastroprotetor, antibacteriano, antifúngico, antiprotozoário, antiviral, antitumoral, anti-angiogênico, fotoprotetor, diurético e hepatoprotetor. Ademais, os ensaios relatam a baixa toxicidade dos extratos. Dessarte, *Fridecia chica* é uma planta com potencial farmacológico para desenvolvimento de novos medicamentos. Este artigo contribui para disseminação do potencial farmacológico da espécie e a iminente observação do conhecimento tradicional.

Palavras-chave: Plantas Medicinais; Antiinflamatório; Crajiru; Potencial Farmacológico

INTRODUCTION

Fridericia chica (Bonpl.) L.G.Lohmann, also known as *Arrabidaea chica* (Humb. & Bonpl.) B. Verlot, is a shrub belonging to the *Bignoniaceae* family, genus *Arrabidaea* (BEHRENS, 2012; “Ficha de Espécies - SiBBr”, [s.d.]). The species is widely distributed in the African and American continents, from Mexico to Argentina. It can be found throughout all states of Brazilian territory, and is native to the Amazon region (ALVES et al., 2010; BIESKI et al., 2015; “Ficha de Espécies - SiBBr”, [s.d.] (SCHIOZER et al., 2008).

Brazil potentially hosts the highest number of species, with three distinct varieties cultivated in the Amazon region, with Variant I being predominant in traditional use in Amazonas. Various varieties are described in the literature, such as acutifólia, angustifólia, cúprea, chica, thyrsoidea, and viscid (ALVES et al., 2010; MISSOURI, [s.d.]; SCHIOZER et al., 2008). Depending on the region, it is commonly known as chica, carajuru, carajiru, carajunu cipó-cruz, coá-piranga, cuica, crajiru, creje, krawiru, oajuru pariri, and puca panga (BEHRENS, 2012; EMBRAPA, 2005; SCHIOZER et al., 2008).

Traditionally, it finds application in the treatment of wounds, skin diseases, cancer, sun protection, local pain, fever, gastric ulcers, menstrual cramps, uterine inflammation, infections, rheumatism, kidney colic, malaria, parasitic diseases, cardiovascular, renal, and metabolic diseases, anemia, diarrhea, edema in pregnant women, and oral pathological changes (BIESKI et al., 2015; BEHRENS, 2012; EVANGELISTA et al., 2013; FERREIRA et al., 2019).

The leaves are the plant part used in the preparation of teas obtained through infusions, maceration, and decoction. Additionally, baths can be prepared (FERREIRA et al., 2019; MARTINS et al., 2009). The dark red pigment extracted from the leaves is utilized as a body and clothing dye and for dyeing dry fibers and utensils (BEHRENS et al., 2012; QUEIROZ et al., 2007). It is explored in the cosmetic industry due to its astringent and antimicrobial properties (SCHIOZER et al., 2008).

Figure 1: *Fridericia chica (Bonpl.) L.G.Lohmann - (sin. hom. Arrabidaea chica (Bonpl.) Verl.) – BIGNONIACEAE. S*pecimen and presentations forms.

(A) Arboreal Plant **(B)** Bunch Leaves **(C)** Dried leaves

Local: Pharmaceutical Sciences Faculty. Federal University of Amazonas, Manaus, Amazonas, Brazil. Photos: Author.

Phytochemistry

The composition and quantity of minerals can vary depending on the tea extraction method and species variation. In dried leaves, the presence of calcium, copper, iron, magnesium, manganese, and zinc has been detected. In tea prepared by infusion, concentrations of calcium, copper, iron, magnesium, manganese, and zinc have been

described. Through decoction, the presence of copper, iron, manganese, and zinc has been verified (DOS SANTOS et al., 2009; MARTINS et al., 2009).

Regarding secondary metabolites, the presence of flavonoid groups is noteworthy, especially anthocyanidins, 6,7,3'-trihydroxy-4,41-dimethoxyflavilone, 6,7,3',4-tetrahydroxy-5-5 methoxy-flavilone, acacetin, carajurin, and carajurone, with the latter two being responsible for the reddish pigmentation. The presence of 3-deoxyanthocyanidins is rare in plants and is more stable than anthocyanins (BATALHA et al., 2022; DEVIA et al., 2002; PAULA et al., 2014; SCHIOZER et al., 2012; ZORN et al., 2001). Other phenolic compounds found in the plant include apigenin, scutellarein, hispidulin, luteolin (SIRAICHI et al., 2013b), vicenin, kaempferol (BARBOSA et al., 2008), tannins, phytosterols (TAFFARELLO et al., 2013), and alkaloids (COE et al., 2010).

The Antioxidant Potential

To evaluate the antioxidant capacity of the plant's dry extract, tests were conducted using the 1,1-diphenyl-2-picrylhydrazyl (DPPH), beta-carotene, and total antioxidant potential determination (TRAP) methods. These tests demonstrated the high antioxidant activity of the extract and revealed a dose-dependent relationship with its antioxidant potential. It is suggested that the antioxidant effect is attributed to the presence of phenolic compounds acting synergistically, with a particular emphasis on the roles of esculetin and apigenin (MARTINS et al., 2016; SIRAICHI et al., 2013b). Other studies have also confirmed the antioxidant potential of the species, associating it with the presence of anthocyanidins (JORGE et al., 2008; TAFFARELLO et al., 2013). Siqueira et al., (2022) highlighted antioxidant activity against reactive oxygen and nitrogen species in different extracts of the plant.

The Analgesic, Anti-Inflammatory, and Immunomodulatory Potential

In an experimental model of neuropathic pain in rats, a study was conducted to assess the efficacy of fractions from the plant's ethanolic extract. The test group animals were treated for 15 days with a dose of 1 mg/kg/day, exhibiting behavioural responses

indicative of the attenuation of neuropathic pain compared to the negative control group (LIMA et al., 2022a).

The anti-inflammatory properties of *Fridericia chica* are recognized in traditional medicine. Assays have evaluated the anti-inflammatory potential of the extract and confirmed the species' anti-inflammatory capacity. Zorn et al, (2001) demonstrated the potential of the lipophilic extract to completely inhibit the NF-κB transcription factor. Moreover, it suggests that one of the compounds present in the plant behaves similarly to quercetin, potentially preventing the transcription factor from binding to DNA.

In an *in vivo* study, peritonitis was induced in mice, and those pre-treated with hydroalcoholic extract showed a reduction in pro-inflammatory cytokines TNF-α, IL-1β, a 44% decrease in inflammatory infiltrate, along with a reduction in mononuclear cells and neutrophils. The effect on neutrophils of the isolated compound 5-O-methylesculetin was greater compared to dexamethasone, highlighting the immunomodulatory potential of the species in this acute inflammation model (LIMA et al., 2020).

Another *in vivo* study evaluated the aqueous extract in edema induced by venom from Amazonian snakes, reporting its ability to inhibit venom action and promote anti-edematogenic effects when administered subcutaneously and intraperitoneally. Histopathological findings also revealed inhibitory effects on granulocyte infiltrate and myocytolysis. The author suggests a possible influence of nitric oxide in the anti-inflammatory mechanism and relates the action of flavonoids present in the plant to their ability to inhibit phospholipase A, a component of snake venoms (OLIVEIRA et al., 2009).

The *in vitro* inhibition of cyclooxygenases 1 and 2 by the hydroalcoholic extract revealed the potential to non-selectively inhibit both enzymes, also reporting the ability to produce in vivo analgesia with results similar to meloxicam. This suggests its potential effectiveness in the treatment of osteoarthritis, with amentoflavone potentially interacting favorably with cyclooxygenase 2 to promote the effect (VASCONCELOS et al., 2019). Additionally, the anti-inflammatory activity of the extract may be related to the inhibition of lipoxygenases, as demonstrated in the assay conducted by Torres et al., (2018).

The Healing Potential

The *in vitro* and *in vivo* study conducted by Jorge et al., (2008) demonstrated the wound-healing capacity of the plant extract on skin lesions. The *in vitro* assay assessed

the extract's potential to stimulate fibroblast growth, revealing its high capacity to promote the growth of these cells and increase collagen synthesis through mechanisms similar to those of allantoin and vitamin C. *In vivo* results showed that rats treated topically with the extract experienced a significant reduction in the lesion area and, within 10 days, progressed to complete healing (96%). Histopathological analysis of the lesion treated with the extract for 10 days showed a higher presence of collagen compared to the saline-treated group. Examining the composition of *A. chica* extracts, it was found that crude extracts could stimulate fibroblast growth, with the compound with an m/z 463 ion inducing the greatest cell growth (TAFFARELLO et al., 2013).

In a study evaluating the extract's effect on tendon healing, rats treated topically with *A. chica* showed superior results in organizing collagen fibers compared to the negative control group. They also exhibited a significant amount of dermatan sulfate after treatment and 14 days post-injury (ARO et al., 2013). The hydroalcoholic extract of the plant demonstrated cytoprotective activity for fibroblasts and osteoblasts exposed to bisphosphonates, drugs with the potential to induce osteonecrosis (ZAGO et al., 2020).

The plant's healing potential may involve the stimulation of fibroblasts and collagen synthesis. Its antioxidant and anti-inflammatory capabilities are linked to the presence of anthocyanidins, while anthocyanins contribute to its wound-healing activity. These findings support traditional knowledge regarding the plant's use in wound treatment. The plant extract can be employed in various pharmaceutical technologies for the development of bioactive dressings that facilitate the healing process and exhibit antimicrobial activity (LIMA et al., 2019; SALLES et al., 2020; SOUSA IMO et al., 2013).

The research group Laftex (Laboratório de Fitoquímica, Farmacologia e Toxicologia Experimental - Unicamp) developed a healing gel with standardized extract from *Fridericia chica*. They examined the wound-healing activity of the extracts, the toxicity of the crude extract, as well as the pharmacological, physical, chemical, and pharmacological stability of formulations containing the extract (PEDROZA et al., 2013; SOUSA, 2013). The studies progressed and culminated in a clinical trial that assessed the safety, proving to be safe for patients (JORGE et al., 2020). The evaluation included the effect on oral mucositis in patients with head and neck cancer (QUEIROZ et al., 2018), showing positive results (data not yet published). The clinical trial is advancing to phase

three, currently being conducted in patients with onco-hematological diseases who developed oral mucositis due to chemotherapy (data not yet published).

The Gastroprotective Potential

Traditional Brazilian communities have reported the use of the plant's tea to treat gastric ulcers (BIESKI et al., 2015). An assay utilizing nanotechnology suggested that encapsulation of the standardized extract could be employed for the treatment of acute gastric ulcers. In *in vivo* tests using the ethanol-induced ulcer model, there was a 58% reduction in the lesion compared to the control group treated with saline. This method also allowed for a reduction in the required dose to achieve the same pharmacological effect compared to the free extract. In the non-steroidal anti-inflammatory drug (Indomethacin) induced ulcer model, there was a 58% reduction in the lesion compared to the control group (SERVAT-MEDINA et al., 2015).

Figueiredo et al., (2023) evaluated the potential to treat acute and chronic gastric ulcers in a live model, highlighting the gastroprotective effect of the hydroalcoholic extract. The study indicated that the extract increases mucus production and reduces gastric acidity. The antiulcerogenic properties of the extract can be attributed to the presence of flavonoids, apigenin, esculetin, and carajurone.

The Antimicrobial Potential

Antibacterial

The hydroalcoholic extract demonstrated activity against *Enterococcus faecalis* and *Helicobacter pylori* (MAFIOLETI et al., 2013). Furthermore, it demonstred effectiveness against *Streptococcus pyogenes, Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa*, and *Salmonella typhimurium.* These findings suggest a potential mechanism of action involving alterations in bacterial membrane permeability and nucleotide leakage (VIOLANTE IMP, 2021). Gurgel et al., (2023) pointed out the antimicrobial capacity of the endophytic fungal community colonizing the plant, with isolated fungi exhibiting potential against both gram-positive and gram-negative bacteria, as along with antioxidant properties.

The antibacterial activity of the extract may be attributed to the presence of specific phenolic compounds, with campferol, esculetin, and carajurone notably standing

out (MAFIOLETI et al., 2013; VIOLANTE IMP, 2021). These reports highlight the plant's antimicrobial potential, aligning with traditional knowledge.

Antifungal

The study conducted by Höfling et al., (2010) underscores the potent inhibitory of the dichloromethane extract in vitro against the *Candida genus*, indicating a robust capacity to inhibit fungi within this genus. However, it revealed little to no action against the tested strains for the methanolic extract. Although the methanolic extract demonstrated activity at 24 hours, strains developed resistance to it after 48 hours.

In addition to its action against the *Candida genus*, potential against T. mentagrophytes was reported at a minimum inhibitory concentration of 3.125 mg/ml, aligning with traditional knowledge for skin-related conditions. Lima et al., (2022b) presented the antifungal activity of the hydroalcoholic extract in a model of vulvovaginal candidiasis, demonstrating the potential of the extract to treat even severe forms of candidiasis caused by *Candida albicans*.

The antifungal property of the plant may be related to the presence of tannins, anthocyanins, quinones, and flavonoids, as these compounds are renowned for their antimicrobial activity (BARBOSA et al., 2008; HÖFLING et al., 2010).

Antiprotozoal

The leishmanicidal activity was observed with the ethanolic extract, which reduced the viability of the promastigote form of *L. amazonensis* by 50% *in vitro*. Notably, the antileishmanicidal action became evident within the first 24 hours of treatment, and by 72 hours, there was complete absence of parasite viability. The concentration of 500 µg/mL proved to be the most effective for leishmanicidal action within the evaluated time intervals. The inhibitory concentration (IC50) of the ethanolic extract for the promastigote form of *L. amazonensis* was determined to be 155.9 µg/mL (CORTEZ DE SÁ et al., 2016).

Furthermore, the extract was also tested for its action against *Trypanosoma cruzi*, demonstrating activity against the trypomastigote form of the parasite, leading to cell lysis. The presence of triterpenoid acids is suggested to contribute to this effect, along with the presence of flavonoids (BARBOSA et al., 2008).

Antiviral

Cruz et al. (2022) elucidate the antiviral effects of the ethanolic extract from this plant species. In this assay, in vitro inhibition was observed in the multiplication cycle of the DENV2, MAYV, and ZIKV viruses, which respectively cause dengue, Mayaro fever, and Zika virus. The author highlights the contribution of flavonoids from the plant species as potential antiviral compounds.

In another assay, the hydroalcoholic extract demonstrated antiviral activity against the MAYV virus. The active agent acts on both the early and late stages of viral replication. Additionally, it exhibits virucidal activity at low concentrations and reduces virions during the post-infection period studied (LOPES et al., 2022).

Antitumor and Anti-angiogenic Potential

In *in vivo* studies, the antitumor activity of the plant extract was evaluated. In the induced breast cancer model, a reduction in tumor size and presence was observed in the treatment with the extract, especially when combined with half the dose of vincristine. Additionally, there was a reduction in biochemical and hematological parameters, indicating lower toxicity for the group treated with the extract combined with half the dose of chemotherapy. An increase in tissue antioxidant enzymes was observed, suggesting protection against oxidative stress and tissue damage (ROCHA et al., 2019).

Brandão et al. (2022) demonstrated the antiproliferative effect of the chloroformic extract of *A. chica* on breast cancer cells, confirming antioxidant and anticarcinogenic activity. The study further presented the extract's action in hormonal modulation. In another in vivo study, the aqueous and ethanolic extracts showed antitumor effects against Ehrlich's tumor. The ethanolic extract promoted an increase in the number of neutrophils and levels of α1 and β-globulin compared to the control, while the aqueous extract reduced tumor growth associated with a decrease in TCD8 cells and natural killer cells. The percentage of TCD4 cells in the blood was reduced in the treatment with the extracts, suggesting a possible antitumor and immunomodulatory role (RIBEIRO et al., 2012).

In *in vitro* studies, a cytostatic effect was observed for the myeloma lineage (UACC-62). The ethanolic extract showed antiproliferative activity against immortalized human T lymphocyte cells (Jurkat) and human promyelocytic leukemia (HL60), with a pro-apoptotic effect on the latter. Levels of VEGF remained unchanged after treatment with the aqueous and ethanolic extracts, and the evaluation of angiogenesis indicated a

decrease in this process (TAFFARELLO et al., 2013). The presence of flavonoids, especially campferol and luteonin, may justify the observed antitumor and antiangiogenic effects (MICHEL et al., 2015).

Photoprotective Potential

Siraich et al. (2013a) highlighted the photoprotective potential of a formulation containing extracts and fractions of A. chica leaves. The assay indicates that the formulation offers protection against both UVB and UVA radiation. Notably, the *A. chica* formulation is free from inorganic compounds, making it a natural alternative for sun protection. Furthermore, the *A. chica* formulation showed no toxic effects in albino rats, as assessed by biochemical, hematological, and histological parameters. The author attributes the protective activity of the extract to the presence of flavonoids in the species.

Potential in Renal Function and Hepatic Function

Renal Function

In the renal system, the diuretic action of different fractions of the extract has been documented. In an in vivo analysis, the urinary volume of mice was monitored every 2 hours over a 6-hour period. It is suggested that this effect could justify the plant's popular use in treating urinary tract diseases, with luteonin being the compound responsible for promoting this function (AMARAL et. Al., 2012).

Hepatic Function

The hydroalcoholic extract, tested both *in vivo* and *in vitro* on Wistar rats and isolated mitochondria to assess hepatic energy metabolism, suggested an inhibitory effect on hepatic glucose production, potentially related to mitochondrial energy metabolism. In the mitochondrial isolate, the extract reduced the respiratory coefficient, inhibited oxidase enzyme activity, inhibited microsomal glucose 6-phosphate enzyme, and stimulated ATPase enzyme. Additionally, there was an increase in cellular content of glucose 6-phosphate. The hepatic perfusion assay indicated a stimulation in oxygen consumption and inhibition of gluconeogenesis (DE SOUZA et al., 2009).

In another *in vivo* assay, evaluated in a hepatic intoxication model, biochemical markers of hepatic function — specifically, aspartate transaminase (AST), alanine transaminase (ALT), and bilirubin- were evaluated. A reduction in levels of ALT, AST, and serum bilirubin was observed, indicating a hepatoprotective effect. This potential may be related to the presence of quinones and flavonoids in the extract (LIMA DE MEDEIROS et al., 2011).

Toxicity

In terms of toxicological aspects, different extracts were examined, revealing low toxicity levels for *A. chica*. The hydroalcoholic extract did not indicate cytotoxicity *in vitro. In vivo*, the lethal concentration for 50% of *Artemia salina larvae* (LC50) was 11732 µg/ml (COE et al., 2010). Notably, no mortality was observed at the tested concentrations of the ethanolic extract and its fractions in *Artemia salina* (AMARAL et al., 2012). For the aqueous and ethanolic extracts tested orally *in vivo*, no toxic effects were observed in animals. Mice did not show signs of toxicity, such as weight loss, tearing, salivation, or sedation. Renal and hepatic function was verified by measuring urea, creatinine, alanine transferase, and aspartate transferase, with no difference between the treated groups and the control group (MICHEL et al., 2015).

The absence of changes in hematological and hemometric indices suggests that the tested extracts (aqueous and ethanolic) are not toxic to the animals. A subchronic toxicity assessment was conducted for the hydroalcoholic extract in rats, and non-dose-dependent weight and food intake alterations were observed (RIBEIRO et al., 2012). There were no significant changes in analyzed biochemical and hematological parameters over 30 days, except for leukocytosis at a dose of 200 mg/kg. No cardiac, pulmonary, renal, hepatic, splenic, gastric, or cerebral lesions were observed. Additionally, there was no significant difference in organ weight between the treated groups and the control group. Doses above 3000 mg/kg did not exhibit signs or symptoms of acute toxicity, and the lethal dose (LD50) of the extract could not be determined as none of the tested animals died (MAFIOLETI et al., 2013).

The fraction tested *in vitro* showed no mutagenic effects in *Salmonella* bacteria and no mutagenic or genotoxic effects *in vivo* (DOS SANTOS et al., 2013; GEMELLI et al., 2015). However, the plant extract has cytoprotective activity in human cells (ALVAREZ-ORTEGA et al., 2021, 2023) and nematodes exposed to toxic agents

Chart 1: Relationship between the pharmacological potential, traditional knowledge, and the chemical composition of the plant.

Pharmacological Potential	Traditional Knowledge	Chemical Compound
Analgesic, Anti-inflammatory, and Immunomodulator (Zorn, 2001; Lima, 2020; Lima, 2022; Oliveira,2009; Vasconcelos, 2019; Tarres, 2018).	Used in pain, uterine inflammation, rheumatism, and kidney colic. (Behrens, 2012, Bieski, 2015).	Flavonoids, Amentoflavone, Scutellarein (Lima,2020; Oliveira, 2009; Vasconcelos, 2019).
Healing (Taffarello, 2013; Jorge ,2008; Aro, 2013; Zago, 2020; Lima, 2019; Salles, 2020; Sousa, 2013; Pedroza, 2013; Jorge, 2020; Queiroz 2018).	Used for wounds and skin diseases. (Behrens, 2012; Bieski, 2015).	Anthocyanins (Taffarello, 2013)
Gastroprotective (Servat-Medina, 2015; Figueiredo, 2023).	Used in gastric ulcers. (Bieski, 2015).	Flavonoids, Apigenin, Scutellarein, Carajurone (Figueiredo, 23).
Antimicrobial (Barbosa, 2008; Mafioleti, 2013; Violante, 2021; Gurgel, 2023; Lima, 2022; Hofling,2010; Cortez, 2016; da Cruz, 2022; Lopes, 2022).	Used for infections, malaria, parasitosis (Bieski, 2015).	Triterpenoid acids, anthocyanins, camphorol, carajurona, esculetarein, flavonoids, quinones, and tannins. (Barbosa, 2008; Mafioleti, 2013; Violante, 2021; Lima, 2022; da Cruz, 2022;).
Antitumoral and Anti-Angiogenic (Taffarello, 2013; Rocha, 2019; Brandão,2021; Ribeiro, 2012; Michel, 2015).	Used in cancer. (Bieski, 2015).	Campeferol, Luteonin (Michel,2015).
Photoprotection (Siraichi JTG, 2023).	Used as a sunscreen (Chagas, 2012).	Flavonoids (Siraichi JTG, 2023).
Diuretic (Amaral, 2012).	Used for edema in pregnant women (Ferreira, 2019).	Luteonin (Amaral, 2012).
Hepatoprotective (de Souza, 2009; Lima de Medeiros, 2011).	Used in metabolic diseases (Bieski, 2015).	Quinones, Flavonoids (Lima de Medeiros, 2011).

Chart 2: Translation: Relationship between the pharmacological potential and the assay model.

Pharmacological Potential	**Test Model**		
	In vitro	*In vivo*	
		Animal	Humans
Antioxidant	Siraichi, 2013; Taffarello, 2013; Martins, 2016; Jorge, 2008; Siqueira, 2022.	---	---
Analgesic, Anti-inflammatory, and Immunomodulator	Zorn, 2001; Vasconcelos, 2019; Torres, 2018.	Lima, 2022; Lima, 2020; Oliveira, 2009.	---
Healing	Taffarello, 2013; Jorge, 2008; Zago, 2020; Lima, 2019; Salles, 2020; Sousa, 2013.	Jorge, 2008; Aro, 2013; Sousa, 2013; Pedroza, 2013.	Jorge, 2020; Queiroz,2018.
Gastroprotective	---	Servat-Medina,2015; Figueiredo, 2023.	---
Antimicrobial	Barbosa, 2008; Mafiolete, 2013; Violante, 2021, Gurgel, 2023; Lima, 2022; Hofling,2012; Cortez, 2016; da Cruz,2022; Lopes, 2022.	---	---
Antitumoral and Anti-Angiogenic	Taffarello, 2013; Brandão, 2022, Ribeiro, 2012.	Rocha, 2019; Brandão, 2022; Ribeiro, 2012.	
Photoprotection	---	Siraichi JTG, 2013.	---
Diuretic	---	Amaral, 2012.	---
Toxicity	Coe, 2010; Gemelli, 2015; Alvarez-Ortega, 2020; Alvarez-Ortega, 2021.	Coe, 2010; Mafioleti, 2013; Ribeiro, 2012; Michel, 2015; Amaral,2012; dos Santos, 2013; Olivero-Verbel,2021.	---

Final Considerations

In the meantime, one can perceive the relevant role of *F. chica* in the development of new therapeutic standards. This plant species holds considerable pharmacological potential to treat challenging clinical conditions due to the presence of chemical compounds with establish including flavonoids, triterpenic acids, and tannins. Furthermore, it presents itself as a secure alternative. Moreover, the significant indication of traditional knowledge in the selection of new species for drug development is observed.

Clique aqui para inserir texto.

Thus, *F. chica* is a plant species with pharmacological potential for the development of new drugs with different clinical indications, as indicated by traditional knowledge. This article contributes to the dissemination of the pharmacological potential of plant species and the imminent observation of traditional knowledge.

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REFERENCES

ALVAREZ-ORTEGA, N; CABALLERO-GALLARDO, K; TABOADA-ALQUERQUE, M et al. Protective effects of the hydroethanolic extract of fridericia chica on undifferentiated human neuroblastoma cells exposed to α-zearalenol (α-ZEL) and β-zearalenol (β-ZEL). **Toxins**, v. 13, n. 11, 1 nov. 2021.

ALVAREZ-ORTEGA, N; CABALLERO-GALLARDO, K; JUAN, C et al. Cytoprotective, Antiproliferative, and Anti-Oxidant Potential of the Hydroethanolic Extract of Fridericia chica Leaves on Human Cancer Cell Lines Exposed to α- and β-Zearalenol. **Toxins**, v. 15, n. 1, 1 jan. 2023.

ALVES, M. S. M.; MENDES, P. C.; VIEIRA, J. G. P. et al. Análise farmacognóstica das folhas de Arrabidaea chica (Humb. & Bonpl.) B. Verlt. Bignoniaceae. **Brazilian Journal of Pharmacognosy**, v. 20, n. 2, p. 215–221, 2010.

ARO, A. A.; FREITAS, K. M.; FOGLIO, M. A. et al. Effect of the Arrabidaea chica extract on collagen fiber organization during healing of partially transected tendon. **Life Sciences**, v. 92, n. 13, p. 799–807, 19 abr. 2013.

BARBOSA, W. L. R.; PINTO, L. N.; QUIGNARD, E. et al. Arrabidaea chica (HBK) Verlot: Phytochemical approach, antifungal and trypanocidal activities. **Brazilian Journal of Pharmacognosy**, v. 18, n. 4, p. 544–548, out. 2008.

BATALHA, A. D. DE S. J.; SOUZA, D. C. M.; UBIERA, R. D. et al. Therapeutic Potential of Leaves from Fridericia chica (Bonpl.) L. G. Lohmann: Botanical Aspects, Phytochemical and Biological, Anti-Inflammatory, Antioxidant and Healing Action. **BiomoleculesMDPI**, 1 set. 2022.

BIESKI, I. G. C.; LEONTI, M.; ARNASON, J. T. et al. Ethnobotanical study of medicinal plants by population of Valley of Juruena Region, Legal Amazon, Mato Grosso, Brazil. **Journal of Ethnopharmacology**, v. 173, p. 383–423, 15 set. 2015.

BRANDÃO, D. C.; LIMA, P. M A P; MARTINS, I. C. et al. Arrabidaea chica chloroform extract modulates estrogen and androgen receptors on luminal breast cancer cells. **BMC Complementary Medicine and Therapies**, 2022.

BEHRENS, M. D. B.; Tellis, C. J. M.; CHAGAS, M. S. Arrabidaea chica MONOGRAFIA / MONOGRAPHY. p. **Revista Fitos**, Vol. & no04, dez. 2012.

COE, F. G.; PARIKH, D. M.; JOHNSON, C. A. Alkaloid presence and brine shrimp (Artemia salina) bioassay of medicinal species of eastern Nicaragua. **Pharmaceutical Biology**, v. 48, n. 4, p. 439–445, 2010.

CORTEZ DE SÁ, J.; ALMEIDA-SOUZA, F.; MONDÊGO-OLIVEIRA, R. et al. Leishmanicidal, cytotoxicity and wound healing potential of Arrabidaea chica Verlot. **BMC Complementary and Alternative Medicine**, v. 16, n. 1, 4 jan. 2016.

DA CRUZ, A. F. G.; REIS, A. C. C.; SOUSA, J. A. C. et al. High-Resolution Mass Spectrometry Identification and Characterization of Flavonoids from Fridericia chica Leaves Extract with Anti-Arbovirus Activity. **Molecules**, v. 27, n. 18, 1 set. 2022.

DE SIQUEIRA, F. C.; BARBOSA-CARVALHO, A. P. P.; COSTA LEITÃO, D. S. T. et al. Scavenging Capacity of Extracts of Arrabidaea chica Leaves from the Amazonia against ROS and RNS of Physiological and Food Relevance. **Antioxidants**, v. 11, n. 10, p. 1909, 27 set. 2022.

DE SOUZA, A. S.; PAGADIGORRIA, C. L. S.; ISHII-IWAMOTO, E. L. et al. Effects of the Arrabidaea chica extract on energy metabolism in the rat liver. **Pharmaceutical Biology**, v. 47, n. 2, p. 154–161, 2009.

DEVIA, B.; LLABRES, G.; WOUTERS, J. et al. New 3-deoxyanthocyanidins from leaves of Arrabidaea chica. **Phytochemical Analysis**, v. 13, n. 2, p. 114–120, 2002.

DOS SANTOS, M. I. R.; DE OLIVEIRA SOARES, A.; ARAÚJO, L. M. et al. Determination of Cu, Fe, Mn, and Zn in the leaves and tea of arrabidaea chica (Humb. & Bompl.) Verl. Biological Trace Element Research, v. 132, n. 1–3, p. 239–246, 2009.

DOS SANTOS, V. C.; LONGO, T. B.; GARCIA, A. L H. et al. Evaluation of the mutagenicity and genotoxicity of Arrabidaea chica Verlot (Bignoneaceae), an Amazon plant with medicinal properties. **Journal of toxicology and environmental health**. Part A, v. 76, n. 6, p. 381–90, 1 mar. 2013.

EMBRAPA. Crajiru (Arrebidaea chica Verlot). Disponível em: <**http://ainfo.cnptia.embrapa.br/digital/bitstream/item/24786/1/folder-crajiru.pd**f>. Acesso em: 8 fev. 2021.

EVANGELISTA, S. S.; SAMPAIO, F. C.; PARENTE, R. C. et al. Fitoterápicos na odontologia: Estudo etnobotânico na cidade de Manaus. **Revista Brasileira de Plantas Medicinais**, v. 15, n. 4, p. 513–519, 2013.

FERREIRA, R. S. R. D. S.; RODRIGUES SARQUIS, Í.; RODRIGUES SARQUIS, I. et al. The Use of Medicinal Plants in the Riverside Community of the Mazagão River in the Brazilian Amazon, Amapá, Brazil: Ethnobotanical and Ethnopharmacological Studies. **Evidence-based Complementary and Alternative Medicine**, v. 2019, 2019.

Ficha de Espécies - SiBBr. Disponível em: **<https://ferramentas.sibbr.gov.br/ficha/bin/view/especie/fridericia_chica#HHabitat2FSubstrato**>. Acesso em: 8 fev. 2021.

FIGUEIREDO, F. DE F.; DAMAZO, A. S.; ARUNACHALAM, K. et al. Evaluation of the gastroprotective and ulcer healing properties by Fridericia chica (Bonpl.) L.G. Lohmann hydroethanolic extract of leaves. **Journal of Ethnopharmacology**, v. 309, p. 116338, 12 jun. 2023.

GEMELLI, T. F.; DA SILVA PRADO, L.; SANTOS, F. S. et al. Evaluation of Safety of Arrabidaea chica Verlot (Bignoniaceae), a Plant with Healing Properties. **Journal of Toxicology and Environmental Health**, Part A, v. 78, n. 18, p. 1170–1180, 17 set. 2015.

GURGEL, R. S.; DE MELO PEREIRA, D. Í.; GARCIA, A. V. F. et al. Antimicrobial and Antioxidant Activities of Endophytic Fungi Associated with Arrabidaea chica (Bignoniaceae). **Journal of Fungi**, v. 9, n. 8, 1 ago. 2023.

HÖFLING, J.F.; ANIBAL, P.C.; OBANDO-PEREDA, G.A. et al. Antimicrobial potential of some plant extracts against Candida species. **Brazilian Journal of Biology**, v. 70, n. 4, p. 1065–1068, 2010.

JORGE, M. P.; MADJAROF, C.; RUIZ, A. L. T. G. et al. Evaluation of wound healing properties of Arrabidaea chica Verlot extract. **Journal of Ethnopharmacology**, v. 118, n. 3, p. 361–366, 13 ago. 2008.

JORGE, M. P.; MARIA, P.; ZAGO, W. et al. Clinical Safety Evaluation of an Herbal Gel Containing 2.5% Arrabidaea chica Verlot Standardized Extract. **Clinical case Reports international**, v. 4, n. 1, p. 12–14, 2020.

LIMA DE MEDEIROS, B.; DOS SANTOS COSTA, K.; RIBEIRO, J. F. A. et al. Liver protective activity of a hydroethanolic extract of Arrabidaea chica (Humb. and Bonpl.) B. Verl. (pariri). **Pharmacognosy Research**, v. 3, n. 2, p. 79–84, abr. 2011.

LIMA, F. C. V. M.; OLIVEIRA, A.; LOPES, A. J. O. et al. Effect of Arrabidaea Chica Verlot on Posttraumatic Neuropathic Pain in Rats. Neurodegenerative Diseases: **Current Research,** v. 2, n. 1, 18 out. 2022a.

LIMA, J. C. S.; DE OLIVEIRA, R. G.; SILVA, V. C. et al. Anti-inflammatory activity of 4′,6,7-trihydroxy-5-methoxyflavone from Fridericia chica (Bonpl.) L.G.Lohmann. **Natural Product Research,** v. 34, n. 5, p. 726–730, 2020.

LIMA, L. L.; TAKETA, T. B.; BEPPU, M. M et al. Coated electrospun bioactive wound dressings: Mechanical properties and ability to control lesion microenvironment. **Materials Science and Engineering C**, v. 100, p. 493–504, 1 jul. 2019.

LIMA, W. G.; ARAÚJO, M. G. F.; BRITO, J. C. M. et al. Antifungal effect of hydroethanolic extract of Fridericia chica (Bonpl.) L. G. Lohmann leaves and its therapeutic use in a vulvovaginal candidosis model. **Journal of Medical Mycology**, v. 32, n. 3, p. 101255, 1 ago. 2022b.

LOPES, G. F. M.; LIMA, W. G.; SANTOS, F. R. S. et al. Anti-Mayaro virus activity of a hydroethanolic extract from Fridericia chica (Bonpl.) L. G. Lohmann leaves. **Journal of Ethnopharmacology**, v. 299, p. 115685, 2022.

MAFIOLETI, L.; DA SILVA JUNIOR, I. F.; COLODEL, E. M. et al. Evaluation of the toxicity and antimicrobial activity of hydroethanolic extract of Arrabidaea chica (Humb. & Bonpl.) B. Verl. **Journal of Ethnopharmacology**, v. 150, n. 2, p. 576–582, 25 nov. 2013.

MARTINS, A. S.; ALVES, C. N.; LAMEIRA, O. A. et al. Avaliação de minerais em plantas medicinais amazônicas. **Revista Brasileira de Farmacognosia**, v. 19, n. 2b, p. 621–625, 2009.

MARTINS, F. J.; CANESCHI, C. A.; VIEIRA, J. L.F. et al. Antioxidant activity and potential photoprotective from amazon native flora extracts. **Journal of Photochemistry and Photobiology B: Biology**, v. 161, p. 34–39, 1 ago. 2016.

MICHEL, A. F. R. M.; MELO, M. M.; CAMPOS, P. P. et al. Evaluation of anti-inflammatory, antiangiogenic and antiproliferative activities of Arrabidaea chica crude extracts. **Journal of Ethnopharmacology**, v. 165, p. 29–38, 13 maio 2015.

MISSOURI. Tropicos.org. Missouri Botanical Garden. Disponível em: <**https://tropicos.org/name/Search?name=Arrabidaea chica**>. Acesso em: 8 fev. 2021.

OLIVEIRA, D. P. C.; BORRÁS, M. R. L.; FERREIRA, L. C. L. et al. Atividade antiinflamatória do extrato aquoso de Arrabidaea chica (Humb. & Bonpl.) B. Verl. sobre o edema induzido por venenos de serpentes amazônicas. **Revista Brasileira de Farmacognosia**, v. 19, n. 2b, p. 643–649, 2009.

OLIVERO-VERBEL, J.; DE LA PARRA-GUERRA, A.; CABALLERO-GALLARDO, K. et al. The aqueous extract of Fridericia chica grown in northern Colombia ameliorates toxicity induced by Tergitol on Caenorhabditis elegans. Comparative Biochemistry and Physiology Part C: **Toxicology & Pharmacology**, v. 244, p. 109026, 2021.

PAULA, J. T.; PAVIANI, L. C.; FOGLIO, M. A. et al. Extraction of anthocyanins and luteolin from Arrabidaea chica by sequential extraction in fixed bed using supercritical CO2, ethanol and water as solvents. **Journal of Supercritical Fluids,** v. 86, p. 100–107, 1 fev. 2014.

PEDROZA, M. et al. ATIVIDADE CICATRIZANTE DE MICROENCAPSULADOS DE EXTRATO BRUTO ETANÓLICO OBTIDO DE Arrabidaea chica (HUMB. & BONPL.) VERLOT. [s.l: s.n.]. . Acesso em: 8 abr. 2020.

QUEIROZ, DE S. H.; DE FREITAS, H. A.; CÉLI, O M. C. F. Preparo do corante de crajirú (Arrabidaea chica (Bonpl.) B. Verl.) e sua aplicação em Histologia. [s.l: s.n.]. . Acesso em: 15 fev. 2021.

QUEIROZ, N. D. C. A.; JORGE, M. P.; SOUSA, I. M. O et al. Arrabidaea chica for oral mucositis in patients with head and neck cancer: A protocol of a randomised clinical trial. **BMJ Open**, v. 8, n. 10, p. 6–10, 2018.

DO AMARAL, R. R.; SANTOS, A. A.D; SARAIVA, A. et al. Biological Activities of Arrabidaea chica (Bonpl.) B. Verl. Leaves. Disponível em: **<https://www.researchgate.net/publication/274836479_Biological_Activities_of_Arrabidaea_chica_Bonpl_B_Verl_Leaves**>. Acesso em: 22 jun. 2020.

RIBEIRO, A. F. C.; TELLES, T. C.; FERRAZ, V. P. et al. Effect of Arrabidaea chica extracts on the Ehrlich solid tumor development. **Brazilian Journal of Pharmacognosy,** v. 22, n. 2, p. 364–373, 2012.

ROCHA, K. B. F.; OLIVEIRA, C. N.; AZEVEDO, Í. M. et al. Effect of arrabidaea chica extract against chemically induced breast cancer in animal model. **Acta Cirurgica Brasileira**, v. 34, n. 10, 1 out. 2019.

SALLES, T. H. C.; VOLPE-ZANUTTO, F.; DE OLIVEIRA SOUSA, I. M. et al. Electrospun PCL-based nanofibers Arrabidaea chica Verlot – Pterodon pubescens Benth loaded: synergic effect in fibroblast formation. **Biomedical Materials**, v. 15, n. 6, p. 065001, 3 set. 2020.

SCHIOZER, A. L.; MARÇO, P. H.; BARATA, L. E.S. et al. Exploratory analysis of Arrabidaea chica deoxyanthocyanidins using chemometric methods. **Analytical Letters**, v. 41, n. 9, p. 1592–1602, 2008.

SCHIOZER, A. L.; CABRAL, E. C.; DE GODOY, L. A.F. et al. Electrospray ionization mass spectrometry fingerprinting of extracts of the leaves of Arrabidaea chica. **Journal of the Brazilian Chemical Society**, v. 23, n. 3, p. 409–414, 2012.

SERVAT-MEDINA, L.; GONZÁLEZ-GÓMEZ, A.; REYES-ORTEGA, F. et al. Chitosan–tripolyphosphate nanoparticles as Arrabidaea chica standardized extract carrier: Synthesis, characterization, biocompatibility, and antiulcerogenic activity. **International Journal of Nanomedicine**, v. 10, p. 3897–3909, 2015.

SIRAICHI, J. T. G.; PEDROCHI, F.; NATALI, M. R M et al. Ultraviolet (UVB and UVA) Photoprotector Activity and Percutaneous Penetration of Extracts Obtained from Arrabidaea chica. **Applied Spectroscopy**, v. 67, n. 10, p. 1179–1184, 2013a.

SIRAICHI, J. T. G.; FELIPE, D. F.; BRAMBILLA, L. Z. S. et al. Antioxidant Capacity of the Leaf Extract Obtained from Arrabidaea chica Cultivated in Southern Brazil. **PLoS ONE**, v. 8, n. 8, 29 ago. 2013b.

SOUSA. AVALIAÇÃO DA ESTABILIDADE DO EXTRATO SECO E FORMULAÇÕES DE BASES SEMI SÓLIDAS, CONTENDO ARRABIDAEA CHICA VERLOT, PARA USO. [s.l: s.n.]. . Acesso em: 8 abr. 2020.

SOUSA IMO; RIVERA, G.A.; PINT, D. et al. The role of spray-drying atmosphere on fridericia chica (bonpl.) L.G. Lohmann standardized extract production for wound healing activity. **Nat Prod Res**., 22DC.

TAFFARELLO, D.; JORGE, M. P.; DE OLIVEIRA SOUSA, I. M. et al. Atividade de extratos DE Arrabidaea chica (HUMB. & BONPL.) VERLOT OBTIDOS POR PROCESSOS BIOTECNOLÓGICOS SOBRE A PROLIFERAÇÃO DE FIBROBLASTOS E CÉLULAS TUMORAIS HUMANAS. **Quimica Nova**, v. 36, n. 3, p. 431–436, 2013.

TORRES, C. A.; PÉREZ ZAMORA, C. M.; NUÑEZ, M. B. et al. In vitro antioxidant, antilipoxygenase and antimicrobial activities of extracts from seven climbing plants belonging to the Bignoniaceae. **Journal of Integrative Medicine**, v. 16, n. 4, p. 255–262, 1 jul. 2018.

VASCONCELOS, C. C.; LOPES, A. J. O.; SOUSA, E. L. F. et al. Effects of extract of arrabidaea chica verlot on an experimental model of osteoarthritis. **International Journal of Molecular Sciences**, v. 20, n. 19, 1 out. 2019.

VIOLANTE I.M.P., CAROLLO, C.A.; SILVA, L.I. et al. Cytotoxicity and antibacterial activity of scutellarein and carajurone-enriched fraction obtained from the hydroethanolic extract of the leaves of Fridericia chica (Bonpl.) L.G. Lohmann. **Nat Prod Res.**, 2021.

ZAGO, P. M. W.; SOUSA, I. M. O.; SERVAT-MEDINA, L. et al. Standardized arrabidaea chica extract shows cytoprotective effects in zoledronic acid-treated fibroblasts and osteoblasts. **Clinical, Cosmetic and Investigational Dentistry**, v. 12, p. 327–333, 2020.

ZORN, B.; GARCÍA-PIÑERES, A. J.; CASTRO, V. et al. 3-Desoxyanthocyanidins from Arrabidaea chica. **Phytochemistry**, v. 56, n. 8, p. 831–835, 12 abr. 2001.