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Arrabidaea chica (Humb. and Bonpl.): A plant with multipurpose medicinal applications

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Abstract
Arrabidaea chica is a bush-like plant from the Bignoniaceae family, widely spread in the tropics, mainly in South America's Amazon region. It is commonly known as crajiru, and it is popularly used in alternative medicine for its anti-inflammatory actions, anemia, and against infection and cytotoxic and leishmanicidal potential. Our objective is to review the related medical effects of *Arrabidaea chica.* Databases such as MEDLINE/PUBMED, EMBASE, and Scielo were consulted, and PRISMA guidelines were followed to build the review. In animals with peritonitis, it decreases the leukocyte migration, decreases the concentration of the proinflammatory cytokine, and increases Interleukin 10. It also shows hepatoprotective, anti-ulcerogenic, antifungal effects (Candida), leishmanicidal activity, anti-*Helicobacter pylori* anti-*Enterococcus faecalis*. Another action is the photoprotector activity, mainly against ultraviolet radiation, UVA, and UVB. It also presents the penetration rate similar to the traded sunscreens and the absence of renal or liver toxicity. It also shows a decrease in the reactive species of oxygen, preventing lipid peroxidation. As a result of the findings in these studies, it is possible to conclude that *A. chica* can be used in different pharmacological segments. However, more studies must be performed to identify the type and concentration of the extract and the way of delivery.

Keywords: *Arrabidaea chica,* antioxidant, anti-inflammatory, photoprotection

1. Introduction
The main etiological aspect of chronic-degenerative diseases is multifactorial. Besides, they represent a high prevalence and occurance group in the present time, and they are characterized for a set of elements that, over time, cause changes that lead to severe damage to the human body. Several plant compounds can prevent the occurrence or the complications of these diseases due to the antioxidant and anti-inflammatory actions [1, 2]. Among countless plants that are sources of antioxidants, we find the *Arrabidaea chica*, also named *Fridericia chica*, a bush-like plant from the Bignoniaceae family spread out on the tropics region, mainly in the South America Amazonic region. It is commonly known as "crajiru,""pariri," or, yet, "carajuru," and it is used popularly in alternative medicine for its possible anti-inflammatory actions, anemia and infections fighting, and its cytotoxic and leishmanicidal potential [3-5]. Some studies show that *A. chica* leaves have compounds like flavonoids, anthocyanins, and phenolic compounds in general, whose properties include antioxidant action and UV protection [6, 7].
Besides these characteristics, this plant has been little studied. For this reason, this study aims to revise the effects of *A. chica* on health.

2. Methods
2.1 Focused question
This review was performed to answer the focused question*: Can Arrabidaea chica exert beneficial effects on health?*

2.2 Language
Only studies in English were selected.

2.3 Databases
This review has included studies available in MEDLINE–PubMed (National Library of Medicine, National Institutes of Health), EMBASE, and SciELO (Scientific Electronic Library Online) databases.

The descriptor used was "*Arrabidaea chica* and health." The use of the above descriptor helped identify studies related to Arrabidaea chica's use and its biological effects. The authors of this review have followed PRISMA (Preferred Reporting Items for a Systematic Review and Meta-Analysis) guidelines [8].

2.4 Study selection
Abstracts, conferences, letters to editors, and other sources were consulted but not included. Furthermore, other relevant studies about *Arrabidaea chica* were included to introduce the subject. This study included studies that reported the biological effects of the plant. The inclusion criteria applied in this review were experimental studies, and interventional studies. We also included studies with animal models and studies performed *in vitro*. The exclusion criteria for this search were reviews, studies not in English, editorials, case reports, and poster presentations.
Other studies were used to build the discussion but were not included in Table 1 and Table 2.

2.5 Data extraction
The search period ran from 2008 to 2020, and after reading the 49 identified articles, only 19 of them were devoted to this review's study objectives. These studies are discussed in the item "discussion," and the retrieved articles (Figure 1) were described in Table 1 (studies performed with animal models and some with both animal and *in vitro* models) and Table 2 (studies performed exclusively *in vitro*).

3. Results
3.1 Search and selection of the relevant articles
The flow diagram shows the selection of the articles and the inclusion and exclusion process of this study. Twenty-nine studies were selected to build this review. Among these studies, none was performed in humans, fourteen used animal models, and fifteen were performed exclusively *in-vitro*.

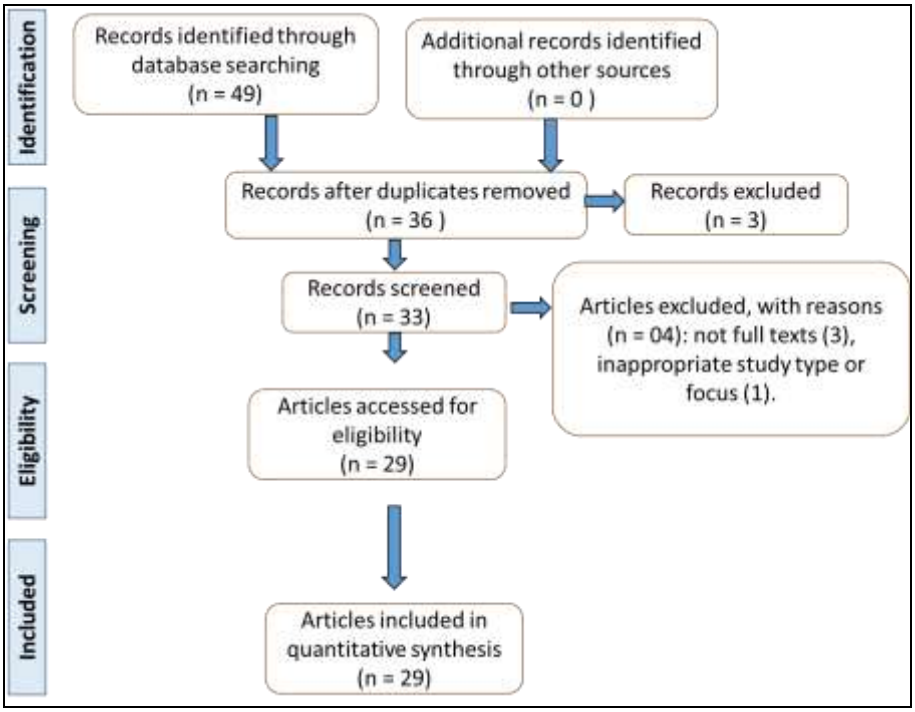

Fig 1: Flow diagram showing the results for the study selection (according to PRISMA, Moher *et al*, 2009).

4. Discussion
4.1 *Arrabidaea chica*
Arrabidaea chica is a bush-like plant from the *Bignoniaceae* family, widely spread out in the tropical regions. This plant can be found mainly in Amazonic regions in Brazil, especially in its northern region. Among this plant's popular uses, we can highlight the anemia and carcinogenesis fighting actions, anti-inflammatory and antiulcerogenic capacities, andanti-infection, including showing leishmanicidal potential. It is worth to mention, yet, the large presence of antioxidants in *A. chica*, what gives this plant diverse applications in medicine, such as prevention and reduction of risks of metabolic and cardiovascular diseases. Moreover, it shows a significant photoprotective activity, making it possible to use this plant for this purpose [4, 9, 10]. Some studies show the presence of several phytochemical compounds with antioxidant potential in the composition of *A. chica*. Martins *et al*. [6] showed that in the leaves of the plant, there are substances such as flavonoids, anthocyanins, and phenolic compounds in general, whose properties include antioxidant effects and ultraviolet photoprotection. Furthermore, Barbosa *et al*. [11] showed the existence of three flavonoids in the plant composition. The first phytocompound was identified as "I," and it has biochemical characteristics of flavonoids; Vicenin 2 and Kaempferol were isolated. Devia *et al*. (2002) [12] identified two new deoxyanthocyanins, besides the pigment "carajurina," which had already been previously isolated in a study made by Zorn *et al*. (2001), whose findings also include the presence of flavone acacetin and others 3 deoxyanthocyanins.
Furthermore, Martins *et al*. [13] detected the presence of ions of great metabolic importance, such as calcium, magnesium, and iron in the leaves and tea of *A. chica*. In another study, Magalhães *et al*. [14] found copper, iron, manganese, and zinc in the plant dried leaves and tea, and iron is the most abundant ion in the leaves, while manganese showed its greatest concentration in the infusion. Figure 2 shows some effects of *A. chica*.

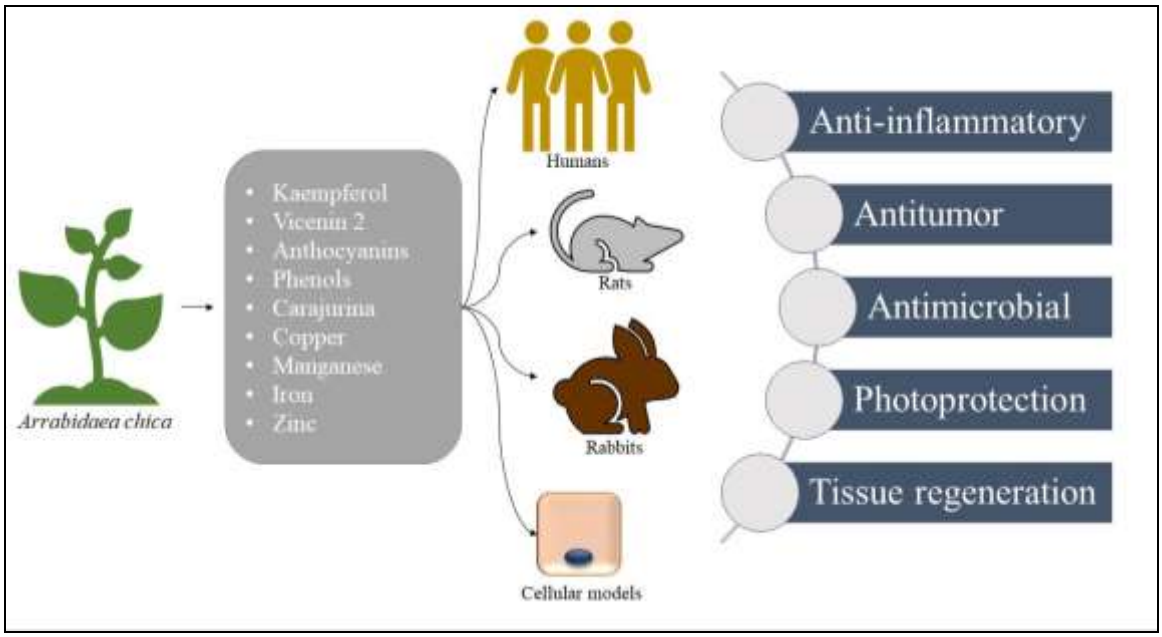

Fig 2: Components present in *A. chica* and their main biological effects in several models.

4.2 *Arrabidaea chica* and its medical effects

This revision shows that *A. chica* can bring countless health benefits such as anti-inflammatory properties, tissue regeneration, antitumoral effect, photoprotection against ultraviolet radiation (UV), and protection against several infectious agents, such as viruses, fungi, and protozoa. The study by Costa Salles *et al*. 2020 [15] showed an important role of the use of *A. chica* associated with *P. pubescens* in tissue regeneration, facilitating the healing process. This function is attributed to its capacity for controlled release of fibroblasts and absence of cytotoxic effects, in addition to its well-known anti-inflammatory function, thus showing its potential use in dental and medical areas. Lima *et al*. [16] performed a study whose objective was to manufacture bioactive wound dressings with a poly-α-hydroxyester core and incorporate *A. chica* extract components. The result showed antimicrobial activity with reduced bacterial concentration with *S. aureus*. Mendes *et al*.[17] performed a study to evaluate the physical properties and the long-term bond strength of a 2.5% polyphenol-enriched extract of *A. chica* incorporated into both the phosphoric acid and the primer of a three-step total-etch adhesive or into an aqueous solution as a dentin pretreatment. It was concluded that the application of *A. chica* as a dentin pretreatment did not affect bond strength or the micromorphological characteristics of the hybrid layer. The experimental studyof Moragas-Tellis *et al*.[5]evaluated the anthocyanidin profile of *A. chica* morphotypes collected in two seasons (summer and winter), comparing their activity against Leishmaniainfection. There is little information about the antileishmanial activity of *A. chica* reported. The analysis of *A. chica* extracts shows that anthocyanidin profiles change dramatically according to the morphotype and season. The activities observed against promastigote forms of *L. amazonensis* suggest that carajurin content may be influencing the antileishmanial activity of *A. chica* and, in this case, could be related as a biological marker of the species. Pires *et al*.[18] conducted a study with the objective to produce and evaluate the properties of chitosan-alginate membranes with a standardized extract of *A. chica*. The results showed that the addition of *A. chica* did not influence the physicochemical characteristics of the dressings produced. However, the dressings presented high released of the *A. chica* extract incorporated into the membranes, and it canshow therapeutic advantages by releasing the plant's bioactive Rocha *et al*. [19] investigated whether *A. chica* extract (ACE) can attenuate breast carcinoma development. Thirty Wistar rats were used, divided into five groups: normal control, 7,12-dimethyl-1,2-benzanthracene (DMBA), DMBA with *A. chica* extract, DMBA with Vincristine, DMBA with *A. chica* extract, and Vincristine. After 16 weeks was realized 2-[18F] fluoro-2-deoxy-D-glucose (18F-FDG) PET scan imaging, fluorescence imaging in vivo, biochemical analysis, and histopathological exam. According to the results, it was established that the combined use of *A. chica* enhances the effect of chemotherapy and decreases adverse effects. Vasconcelos *et al*. [20] investigated the use of *A. chica* as an alternative to osteoarthritis treatment and evaluated motor activity, incapacitation, mechanical hyperalgesia, mechanical allodynia, histopathological and radiographic analysis. The results showed that *A. chica* extract significantly reduced hyperalgesia, allodynia, and the weight distribution deficit between the left and right paws. In other words, *A. chica* extract has the potential to be used in the treatment of osteoarthritis. Violante *et al*. [21] performed *in vitro* studies aiming to evaluate *A. chica* antimicrobial action and its toxicity. The hydroethanolic extract obtained from the plant was subjected to analysis and fractionation, obtaining two main fractions: one rich in carajurone and the other containing mainly the scutellarein compound. The extracts demonstrated no cytotoxicity in an *in vitro* model. The extract showed good and moderate action against several gram-positive and negative bacteria, as well as the fraction containing carajurone. On the other hand, the fraction containing scutellarein demonstrated no antibacterial activity against the tested bacteria. The study attributes these actions to a possible mechanism of permeability of the bacterial cell wall and plasma membrane. Wiziack Zago *et al*.[22] showed that the use of *A. chica* at low concentration could offer acid cytoprotection in primary human gingival fibroblasts and murine pre-osteoblasts. The extract was capable of partially avoiding fibroblast activating caspase, decreasing cell damage. Some *in vivo* and *in vitro*studies showed the plant's anti-inflammatory actions and the plant extracts. Torres *et al*. [23] conducted a study to evaluate the in vitro antioxidant, antimicrobial, and anti-inflammatory activity of the Bignoniaceae family species, including *A. chica*. This plant

demonstrated good antioxidant action in the three methods used, as well as good inhibition of lipoxygenase, demonstrating a possible anti-inflammatory effect and a broad antimicrobial action against strains of *Staphylococcus aureus* and *Candida*, which demonstrates its great range of activities and supports the traditional use of the plant as an anti-infectious agent. Lima *et al*. [3] induced a peritoneal inflammatory process in rats, treating them previously with hydroethanolic extract of *A. chica*. The study showed a reduction of peritonitis by decreasing leukocyte migration andreducing the concentration of the proinflammatory cytokine, while it increased Interleukin 10, which is characterized by its anti-inflammatory action. Michel *et al*. [24] also submittedrats to a disk-shaped spongy material implant under the subcutaneous fibrovascular tissue to create local inflammation, treating the animals with ethanolic extract and aqueous extract from *A. chica*. The study revealed a reduction in the accumulation of neutrophils, but without significant alterations in cytokines' level, showing, yet, a proliferative effect *in vitro*, besides the attenuation of the inflammatory process. Other work, carried out by Lima de Medeiros *et al*. [25] showed that the presence of quinilones and flavonoids in the extract of *A. chica* is probably associated to the reduction of liver inflammation, through the decreasing of the levels of the enzyme in the liver injury, in Wistar rats with liver damage induced through carbon tetrachloride, treated with different concentrations of hydroethanolic extract of the plant. Oliveira *et al*. [26] induced edema in mice paws through *Crotalus* and *Bothrops* snakes venom. The treatment was carried out with aqueous extract only but using three available administration routes: oral, intraperitoneal, and subcutaneous. The administrated extracts led to the reduction of the inflammatory effects induced through the used venoms, mainly due to the granulocytes infiltrate inhibiting and the decreasing of the muscle fibers degeneration. Ribeiro *et al*. [27] evaluated the antitumoral activity of *A. chica* in rats using the aqueous and ethanolic extracts. The study led to a reduction of the TCD4+cells. Furthermore, it promoted an increase in the number of neutrophils and some globulins. These findings suggest that the ethanolic extract directly affects tumoral cells, showing a significant tumor reduction after tendays of treatment with both extracts. Besides the anti-inflammatory effects, several studies showed the pro-regenerative action of *Arrabidaea chica* on different tissues. Servat-Medina *et al*. [28] used mice to demonstrate nanoparticles' antiulcerogenic action from the *A. chica* extract in different concentrations. The study revealed that the lowest concentrations provided the cell variability maintenance, while higher concentrations promoted cell proliferation stimulus. Aro *et al*. [29] also used Wistar rats, subjecting them to tendontransection, and treating them with topic saline *A. chica* extract. In the beginning, treated animals and the control group showed collagen fibrils segments. However, afterward, it was possible to note higher levels of birefringence and the glycosaminoglycan responsible for stimulating the fibroblast proliferation, dermatan sulfate, in the group's tendons treated in relation to the control group. Nevertheless, on the 21º day, it was possible to note lower dermatan sulfate levels and chondroitin in the treated animals. In conclusion, the use of *A. chica* in this study appears to have contributed for a better organization of the collagen protein in the injuried tendons. In other study, Aro *et al*. [30] had carried out the same procedure in the same animal model aforementioned, observing the reduction of type I and III collagens in the groups treated with the plant. It was also possible to see a rising in the levels of hydroxyproline in the treated groups. Still, in the same line of study, Jorge *et al*. [31] induced a lesion in Wistar rats, treating them with *A. chica* by topic administration. They observed that the plant promoted lesion reduction by 96%, while the control group showed a reduction of only 36%. Besides, the study showed that, *in vitro*, there was a raising of the collagen synthesis and a moderated antioxidant action. The findings suggest that the regenerative capacity of A. chica applied on the lesion is associated to the stimulus of fibroblasts and a major production of collagen. Furthermore, some studies demonstrated the action of *A. chica*against infections caused by different agents, mainly *Leishmania* and *Trypanosoma cruzi* protozoa. Cortez de Sá *et al*. [32] realized a study *in vitro* using peritoneal macrophages infected with *Leishmania amazonensis* in its promastigote form, treating them with ethanolic extract of *A. chica* and its fractions. The study showed important leishmanicidal activity, as well as an evident cytotoxic potential. Therefore, the treated group showed a better process of cure, even in the more severe lesions. However, these findings occurred only at the beginning of the treatment. Rodrigues *et al*. [33] used the extract of *A. chica* against promastigotes of *Leishmania amazonensis* and *Leishmania infantum*, showing that the acids and sterols present in the extract are possibly related to an action against the protozoa. Miranda *et al*. [34] observed the significant action of *A. chica* against the epimastigote, amastigote, and trypomastigote forms of *Trypanosoma cruzi*. Barbosa *et al*. [11] also demonstrated considerable trypanocidal activity through the ethanolic extract of the plant. Furthermore, it validated the popular use of the plant for fungal skin diseases by demonstrating fungi growth inhibition, mainly *Trichophyton mentagrophytes*. Höfling *et al*. [35] also studied the action of *A. chica* against species of the genus *Candida*. However, methanolic and dichloro-methanolic extracts were used. It was observed that the dichloro-methanolic extract showed good actions against the *Candida* strains. However, the methanolic extract did not show a significant effect. Mafioleti *et al*. [36] showed that in mice and rats treated with hydroethanolic extract of *A. chica* it was provided a significant action against *Helicobacter pylori*, as well as against *Enterococcus faecalis*, showing good antimicrobial action, associated mainly with the presence of flavones and flavonoids in the extract used. Kohn *et al*. [37] evaluated the potential of *A. chica* against the avian metapneumovirus in embryonic cells of chicken, having a rate of 99% on inhibiting the viral replication of the initial stages.However, more studies are necessary to determine how this action occurs. Santos *et al*. [38] showed through mice that the extracts did not show genotoxicity and mutagenicity. Nonetheless, the same study showed no signs of mutagenicity in Salmonella strains after the administrations of the plant extract and its fractions. Siraichi *et al*. [39] subjected rabbits to a process of photoacoustic spectroscopy and treated them with topic formulations of *A. chica* extract. The study showed high absorption under a relevant UV radiation spectrum, including UVA and UVB. It was noted that the penetration rate was similar to the sunscreens traded worldwide and the absence of renal and hepatic toxicity. Ribeiro *et al*. [4] also studied the photoprotective capacity of *A. chica*, but *in vitro*, through a cellular culture of fibroblasts subjected to UV radiation and treated with plant extract. This study also revealed a significant photoprotective potential, besides demonstrating reactive oxygen species reduction, preventing lipid peroxidation.

5. Conclusions

Our review shows that *A. chica* and its products can be used

in the pharmaceutical industry as a source of bioactive compounds that can work as a complementary therapy for the treatment of several diseases due to its high antioxidant, anti-inflammatory, bactericidal, antifungal, antiviral, leishmanicidal, anti-cancer properties, regenerative, and photoprotective activities.

6. Conflict of interests

The authors declare no conflict of interests or funding support.

Table 1: Effects of *A. chica* on studies performed both *in vitro* and animal models

Reference	Model of the study	Main results	Relevant comments
Lima *et al*., 2020 [3]	LPS-induced peritonitis in mice.	Oral pretreatment with *Arrabidaea chica* led to a decreasing in leukocyte migration to the peritoneal cavity, such as reducing the concentrations of proinflammatory cytokines and an increase in the levels of anti-inflammatory cytokine (IL-10).	These results support the traditional anti-inflammatory use of *Arrabidaea chica*, possibly due to better control of cytokines and due to the inhibition of leukocyte migration.
Rocha *et al*., 2019 [19]	Wistar rats submitted to breast cancer induction by 7,12-dimethyl1,2-benzanthracene injection	The study demonstrated that extract of *A. chica* alone or associated with vincristine can reduce MDA, ALT, AST, GGT, and ROS. Furthermore, the combination of *A. chica* and chemotherapy can positively influence the treatment, reducing some of its adverse effects and the required chemotherapy dose.	It was used in vivo microPET equipment, fluorescence imaging, and biochemical analysis for the evaluation of mammary carcinoma response and adverse effects to *A. chica* extract, compared to conventional chemotherapy with vincristine.
Vasconcelos *et al*., 2019 [20]	Wistar rats with osteoarthritis induced by sodium monoiodoacetate and in vitro tests of inhibition of COX by the hydroethanolic extract of *A. chica*	It has been shown that *A. chica* to inhibit the enzyme COX-2 and showed antinociceptive activity, producing improvements in incapacitation, hyperalgesia, and motor activity.	The study shows the anti-inflammatory and analgesic properties of *A. chica* extract through in vitro by inhibition of cyclooxygenase and in vivo due to the improvement in animals' clinical and radiological parameters osteoarthritis.
Servat-Medina *et al*., 2015 [28]	Human embryonic skin fibroblasts and adult male Wistar rats treated with *A. chica* NPs in three different doses	AcE-NP demonstrated the viability of the cells at the lowest concentrations investigated, and in high concentrations, a stimulant way to the proliferation of cells. An anti-ulcerogenic action of AcE-NP was observed in gastric ulcers. NPs with the presence of *Arrabidaea chica* extract led to ulcer reduction.	The application of *A. chica* extract as a candidate for the pharmaceutical activity of ulcerative wound healing can be considered. Good biocompatibility was presented by NPs of *A. chica*, culminating in an antiulcerogenic effect on the experimental animal model.
Michel *et al*., 2015 [24]	Male Swiss mice implanted with a disk-shaped sponge and treated with aqueous-AE and ethanol- EE extracts of *Arrabidaea chica*	The decrease in neutrophil accumulation and hemoglobin content in spongy implants, with no change in cytokine levels (IL-2, IL-4, IL-5, IFN-γ, TNF-α, and VEGF) and albumin/globulin in the animals analyzed due to the action of ethanol and aqueous extracts of *Arrabidaea chica*. Signs of clinical, laboratory and histopathological toxicity were not observed.	Aqueous and ethanolic extracts of *Arrabidaea chica* attenuated inflammatory and angiogenesis components of the subcutaneous fibrovascular tissue. The ethanolic extract of *A. chica*, mainly the F1 fraction, has shown a proliferative effect *invitro* and can be used to develop chemo-preventive substances.
Mafioleti *et al*., 2013 [36]	Rats (Wistar) and mice (*Mus musculus*), administered with HEAc, using a panel of bacteria and yeast of medical interest.	When administered *in vivo* at doses up to 3000 mg/kg, HEAc did not generate signs and acute toxicity symptoms in rats. Administration for 30 days resulted in leukocytosis and reversible decrease in non-dose-dependent body weight, but no clinical modifications that may have shown signs of subchronic toxicity were observed. The HEAc showed a marked action against *Helicobacter pylori* and moderate action against *Enterococcus faecalis*.	HEAc may be considered safe, as well as that the results suggest utility in infections by *Helicobacter pylori* and *Enterococcus faecalis*. The antimicrobial effect is probably associated with the presence of flavones and flavonols in HEAc.
Siraichi *et al*., 2013 [39]	Male albino rabbits submitted by photoacoustic spectroscopy, treated with topic formulations with the extract and fractions from leaves of *Arrabidaea chica.*	The formulation showed a significant intensity of optical absorption over a significant spectral of UV radiation, including UVA and UVB. The penetration rate was similar to that of commercial sunscreens. No signs of renal or hepatic toxicity were observed.	The high optical absorption and the absence of toxicity suggest a remarkable photoprotective property of *A. chica*, representing a potential to be used in pharmacological preparations. The formulation with *A. chica* leaves is a promising natural and inorganic free compound for protection against UVA and UVB radiation.
dos Santos *et al*., 2013 [38]	*Salmonella* strains and male mice administrated with Ac-CF.	The mutagenic effects were analyzed using the Salmonella strains, and the results demonstrated that Ac-CF did not show mutagenicity in the strains of *Salmonella typhimurium* and presented negative results for mutagenicity genotoxicity in	The fraction does not appear to generate genetic risks, such as mutagenicity and genotoxicity.

		mice. Mutagenic and genotoxic/antigenotoxic effects *in vivo* were evaluated using the micronucleus test in bone marrow, blood, and liver after administration of Ac-CF in mice. Ac-CF demonstrated antigenotoxic activities, reducing oxidative DNA damage in more than 50% in liver and blood.	
Aro *et al*., 2013b [30]	Wistar rats submitted to transection of the tendon and treated with topical applications of saline of the *A. chica* extract.	The study demonstrated the presence of many segments of small collagen fibrils in the transectional region of the tendons at day 7, in the control and treated group. Higher values of birefringence could be noticed in the tendons of the animals treated with *A. chica* extract with a topical application on the 14th day. A greater amount of dermatan sulfate was also observed after treatment with the plant during the same period. However, fewer dermatan and chondroitin sulfate were observed in the treated animals on day 21.	The use of *A. chica* contributes to collagen's better organization and provides an increase in the amount of dermatan sulfate on the 14th day of the tendon healing process. However, further studies are needed on the use of this plant in healing.
Aro *et al*., 2013a [29]	Wistar rats submitted to transection of the tendon and treated with topical applications of saline of the *A. chica* extract.	*A. chica* extract in the injured tendon region increased the amount of hydroxyproline in the seventh (91.5 ± 18.9) and in the 21st (95.8 ± 11.9) days after the tendinous lesion. A reduction in type I and III collagens was observed in the groups treated with the plant extract seven days after tendon injury. The extract stimulated MMP-2 synthesis on the 21st day after the injury and reduced the amount of latent and active isoforms of MMP-9 on the 14th day.	*A. chica* led to an increase in the amount of collagen and better recovery of gait during tendinous scarring.
Ribeiro *et al*., 2012 [27]	Ehrlich ascites carcinoma cells in Swiss albino mice.	Aqueous and ethanolic extracts of *A. chica* decreased solid tumor growth after ten days of oral treatment. Group treated with ethanolic extract showed a higher number of neutrophils, α 1 and β globulin values, and a reduction of α two globulin values. The ethanolic extract also generated a reduction of $CD4^+$T cells but did not modify the number of inflammatory mononuclear cells, suggesting that the ethanolic extract has direct actions on the tumor cells.	Reduction of tumor growth with the aqueous extract is associated with lower $CD4^+$T lymphocyte count (antitumor activity is possibly related to the anti-inflammatory action). No toxic effects were observed in the animals.
Lima de Medeiros *et al*., 2011 [25]	Male Wistar rats with induced hepatic injury triggered by CCl4 (carbon tetrachloride).	The use of 300, 500 or 600 mg/kg of hydroethanolic extract of the leaves resulted in decreased GPT levels of 85.34%, 88.59%, and 93.72%, respectively. The suppression of GOT values was 56.86%, 65.27%, and 68.95%, respectively. The findings indicate the protective character of *A. chica* and its ability to maintain the functional integrity of liver cells.	The reduction of hepatic injury enzymes is probably related to quinones and flavonoids in the extract of *A. chica*.
Oliveira *et al*., 2009 [26]	Albino mice with paw edema induced by venoms from *Bothrops* moreover, *Crotalus* species and treated with the aqueous extract of *A. chica* (oral, intraperitoneal and subcutaneous)	The results demonstrated that the effect of inhibition provided by the aqueous extract for the genus *Bothrops* via the subcutaneous and intraperitoneal routes after 12 hours was 55.87% and 65.70%, respectively. For the genus *Crotalus*, the extract subcutaneously's inhibitory action after 3 hours was 33.55% and from 6 hours of 79.81%. After 3 hours, it was 48.02% in the intraperitoneal route, and after 6 hours, it was 92.52%. Histopathologically, the granulocyte infiltrates, and myocytolysis were the most significantly inhibited inflammatory actions.	The aqueous extract of *A. chica* may exert an inhibitory effect on the proinflammatory actions caused by the venom of *Bothrops* and *Crotalus* snakes.
Jorge *et al*., 2008 [31]	Cell culture and Wistar rats with induced wound and treated with topic *A. chica*.	There was an increase in collagen production *in vitro* and moderate antioxidant activity. *A. chica* caused 96% reduction in wound size *in vivo* (saline group showed only 36% healing).	The efficiency observed in *A. chica* is possibly associated with the stimulation of fibroblast growth and collagen synthesis.

LPS: lipopolysaccharide; IL-10: Interleukin 10; AcE: *A. chica* standardized extract; NP: nanoparticles; IL-2: Interleukin 2; IL-4: Interleukin 4; IL-5: Interleukin 5; IFN-γ: interferon γ; TNF-α: tumor necrosis factor α; VEGF: Vascular endothelial growth factor; HEAc: hydroethanolic extract of the leaves of *Arrabidaea chica;* UV: ultraviolet; Ac-CF: *A. chica* chloroformic fraction; MMP: metalloproteinases; GPT: glutamic pyruvic transaminase; GOT: glutamic oxaloacetic transaminase.

Table 2: Effects of *A.chica* in studies performedexclusively *in vitro* experiments.

Reference	Model of the study	Main results	Relevant comments
Costa Salles *et al*., 2020 [15]	8 polymer membranes were obtained by the electrospinning process with two plant extracts inassociation: *P. pubescens* and *A. chica.* Scanning Electron Microscopy images and Cytotoxicity and cell proliferation were evaluated.	Electrospun membranes associated with plant extracts *P. pubescens* and/or *A. chica* presented a controlled release profile of the active compounds induced fibroblastformation, suggesting that they are promising and suitable for applications in guided tissueregeneration.	The membranes showed no cytotoxic effects. *A. chica* showed fibroblast proliferation activity demonstrating these membranes could release plant extracts and potential application for wound healing and guided tissue regeneration
Lima, L. *et al*., 2020 [16]	*Pseudomonas aeruginosa* and *Staphylococcus aureus*, treated with coated electrospun bioactive wound dressings with Alginate coating and *A. chica.*	Dressings coated with *A. chica* extract proved to be able to stimulate wound healing and useful for guided tissue regeneration and changed the rate of transmission and permeation of water vapor in approximately 95%, compared to the control. Furthermore, it led to a reduction of gram-positive bacterial concentration on the surface.	The developed alginate-coated wound dressings functionalized with *A. chica* can actively interact with the wound microenvironment and facilitate wound healing.
Mendes *et al*., 2020 [17]	Fifty dentin surfaces received the treatments (n = 10): CON (control) – application of the three-step adhesive system (dentin pretreatment with AC; ACP - AC incorporated into the primer.Microtensile bond strength tests were performed after 24 h, 6, and 12 m of storage.	The use of *A. chica* incorporated into the primer led to lower bond strength values since *A. chica* modified the physical properties (particle size, polydispersity index, and zeta potential) of the primer but did not change thedegree of conversion. Application of *A. chica* as a dentin pretreatment did not affect bond strength or the hybrid layer's micro morphological characteristics.	Incorporatingthe polyphenol-enriched extract into the phosphoric acid seems to be a valid procedure that can be considered in future assays.
Moragas-tellis *et al*., 2020 [5]	Anthocyanidin profile was evaluated.	*A. chica* extracts show that anthocyanidin profiles change according to the morphotype and season. Only carajurone was evaluated in all analyzed extracts. Carajurin can be considered as a pharmacological marker for the antileishmanial potential of the species	The activities observed against promastigote forms of *L. amazonensis* suggest that carajurin content may be influencing the antileishmanial activity of *A. chica*.
Pires *et al*., 2020 [18]	Chitosan and alginate membranes containing the standardized extract of *A. chica.*	In conclusion, the addition of the standardized of *A. chica* extract to the membranes does not significantly influence the physicochemical characteristics of the dressings produced. Despite this, it is possible to obtain therapeutic advantages by releasing the plant's bioactive compound.	Chitosan with alginate films can show a dense or porous flexible structure, with characteristics tunable for different applications.
Violante *et al*., 2020 [21]	Hamster ovary cell – K1 (CHO-K1 cells), *Streptococcus pyogenes, Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Salmonella typhimurium, Enterobacter cloacae, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Shigella flexneri, Proteus mirabilis* and *Burkholderia cepacia*	HEFc and the fraction containing the scutellarein presented no toxicity in CHO-K1 cells. HEFc showed good antibacterial action against *Streptococcus pyogenes* and *Staphylococcus aureus* and moderate effect for *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Salmonella typhimurium*. The fraction containing carajurone presented good action against *Staphylococcus aureus* and *Staphylococcus epidermidis* and moderate Effect against *Streptococcus pyogenes.* However, the fraction of the extract conteining scutellarein showed no action against the bacteria tested.	HEFc antibacterial mechanism of action appears to be related to changes in the bacterial cell wall's permeability and cytoplasmic membrane. The results justify the common use of *F. chica* for the treatment of several infectious diseases.
Wiziack Zago *et al*., 2020 [22]	Primary human gingival fibroblasts and murine pre-osteoblasts were treated with zoledronic acid or *A. chica* extract for 24h and 48 h. At both times, cells were submitted to viability assay and caspase 3/7 activation evaluation.	A drastic damage effect of zoledronic acid appeared after 48h in both epithelial (55.8%) and pre-osteoblastic cells (39.7%) in cell viability assay. When treated with zoledronic acid combined with *A. chica* extract, cells showed higher viability values: 74.1%-82.3% for fibroblasts and 66% for pre-osteoblasts. Moreover, the combined treatment presented lower caspase 3/7 activation in fibroblasts and pre-osteoblasts.	*A. chica* extract showed promising cytoprotective effects against zoledronic acid-induced damage actions; however, further studies are necessary to establish action mechanisms.
Torres *et al*., 2018 [23]	12 pathogenicstrains of *Staphylococcus aureus* and 7 strains of *Candida.* Evaluation of antioxidant and lipoxygenase-inhibiting activities.	*A. chica*presented good antioxidant activity, notable inhibition of lipoxygenase and wide antimicrobial activity compared to other species belonging to the *Bignoniaceae* family.	*F. chica* presented antimicrobial and anti-inflammatoryeffects supporting its traditional use as antiseptic agents.
Ribeiro *et al*., 2018 [4]	L929 (ATCC CCL1) fibroblast cell line cells subjected to UV radiation and post-treated with crude extract of *A.*	Post-treatment with *A. chica* attenuated oxidative damage that was induced by both UVA and UVB irradiation. It also attenuated	*A. chica* crude extract may be a promising non-sunscreen photoprotector that can improve

	chica.	the deleterious effects of UV radiation by quenching intracellular ROS and mitochondrial O2 and preventing lipid peroxidation.	the effectiveness of available commercial sunscreens against late UVR-induced damage.
Miranda *et al*., 2017 [34]	Monkey kidney epithelial cells (*Macaca mulatta*) and Y strain of *T. cruzi*.	*The* isolated component from *A. chica* extract (pheophorbide a) presented action against forms of *T. cruzi* Trypomastigotes. It was also possible to isolate a component called photosensitizer in *A. chica*'s extract, used in photodynamic therapy treatment.	*A. chica* presented a significant effect against epimastigote, amastigote, and trypomastigote *T. cruzi* forms, due to the isolated component "pheophorbide an" in its extract.
Cortez de Sá *et al*., 2016 [32]	Peritoneal macrophages obtained from 4-week-old female BALB/c mice with *Leishmania amazonensis* promastigotes, treated with *A. chica* ethanolic extract and its fractions.	*A. chica* presented satisfactory results in the leishmanicidal potential, in concentrations between 60 and 155.9 µg / mL. When analyzing the cytotoxicity, a decrease of 50% in viable cells, at a concentration of 189.9 µg/mL, was observed. Results regarding the healing process showed that the treated group showed signs of resolution in more severe lesions. However, this pattern was present only at the beginning of treatment.	*A. chica* has leishmanicidal and cytotoxic potential. However, its healing properties should be further studied.
Kohn *et al*., 2015 [37]	Chicken embryo related cell with Avian Metapneumovirus	*A. chica* presented an inhibition ratio of 99% in the early viral replication phases, indicating that these extracts may act during the adsorption stage.	*A. chica* extracts can inhibit 99% of aMPV *In vitro*.
Rodrigues *et al*., 2014 [33]	Promastigote forms of *Leishmania. amazonensis* and *L. infantum* treated with five fractions of the crude hexane extract of *A. chica. Chica.*	The extract of *A. chica* has an action against *L. amazonensis* and *L. infantum*. Acids and sterols are possibly the components most related to activity against *Leishmania*.	*A. chica* can be a promising phytotherapeutic agent.
Höfling *et al*., 2010 [35]	*Candida* species (*albicans*, *dubliniensis*, *parapsilosis*, *tropicalis*, *guilliermondii*, *utilis*, *krusei*, *lusitaniae*, *glabrata*, and *rugosa* treated with extracts from plants *A. chica*.	The dichloromethane extract of *A. chica* presented good action against Candida yeasts within 24 hours, showing resistance to this extract after 48 hours; however, its methanol extract presented none or less activity.	The dichloromethane extract of *Arrabidaea chica* presents action against *Candida* species.
Barbosa *et al*., 2008 [11]	*Candida albicans*, *Aspergillus niger*, *Trichophyton rubrum*, *T. mentagrophytes*, and *T. cruzi* trypomastigotes (strain Y) obtained from infected mice treated with *A. chica* extract.	Three flavonoids were isolated from *A. chica* extract and its fractions. Complete inhibition of *Trichophyton mentagrophytes* growth and significant trypanocidal action from the ethanolic extract and its fractions were observed. Acute toxicity was not observed, even at a dose of 1000 mg/kg.	The popular use of *A. chica* for fungal skin diseases is valid and the expected trypanocidal effect.

HEFc: Hydroethanolic extract obtained from the dry leaves of *Fridericia chica*; UV: ultraviolet; ROS: reactive oxygen species; aMPV: Avian Metapneumovirus.

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