

Review - Environmental Sciences

Anti-Inflammatory Plants from Caatinga Biome

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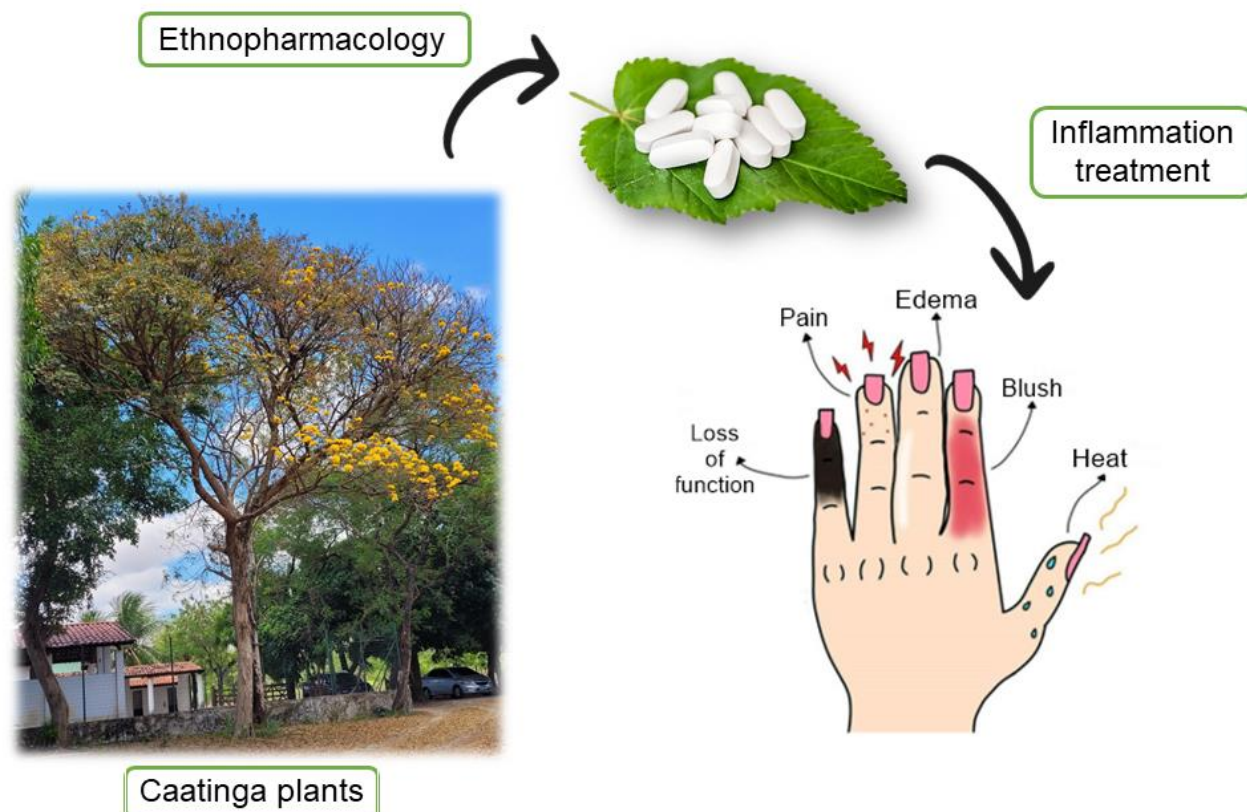
HIGHLIGHTS

- The Caatinga biome is exclusive to Brazil.
- Caatinga plants have anti-inflammatory properties.
- Plant bark is the part most used to treat inflammation.
- The Fabaceae family is the one with the largest number of species with anti-inflammatory reports.

Abstract: The Caatinga biome, known for its unique ecosystem and plant diversity, offers a rich source of botanical resources with anti-inflammatory properties. This review aims to analyze the plant species present in the Caatinga, focusing on their traditional applications, phytochemical composition, and mechanisms of action against inflammation. Additionally, it seeks to promote the conservation and sustainable use of this biodiversity, aiming for the development of herbal medicines, supplements, and pharmaceutical agents that can treat inflammation, aligning with global trends towards natural and holistic health approaches. The research consulted databases such as CAPES, PubMed, Scielo, Science Direct, and others, analyzing Brazilian publications from 2013 to 2023, using search terms like "anti-inflammatories," "Caatinga," and "natural products". The Fabaceae family stood out for having the most species with anti-inflammatory activity, with bark being the most commonly studied plant part. The findings could contribute to the development of new natural treatments for inflammation and emphasize the importance of preserving terrestrial ecosystems, which provide valuable resources for human health.

Keywords: Anti-inflammatory potential; Caatinga biome; Phytochemical composition.

GRAPHICAL ABSTRACT



INTRODUCTION

The plants found in the Caatinga biome have a wide variety of secondary metabolites produced as defense mechanisms against biotic and abiotic stresses. These compounds constitute a class of natural molecules that play important roles in protecting plants against pathogens, herbivores, ultraviolet radiation, oxidative stress, and other environmental challenges [1]. These compounds contribute for the human being health since they display antioxidant, anti-inflammatory, anticancer, antimicrobial, antiparasitic, among others, mainly discovered by research of medicinal plants used in ethnomedicine [2].

Several types of compounds isolated from plants with anti-inflammatory activity have been reported as phenolic compounds and their antioxidant power contributes for combating various inflammatory mechanisms, and among these compounds stand out flavones, flavonols, flavanones, isoflavones, chalcones, phenolic acids, lignans and tannins [3].

Compounds of the terpenoid class, such as triterpenoids, diterpenoids and monoterpenoids, from the class of alkaloids and aryl-propanoids has also demonstrated this action. As an example, Acheflan®, the first phytotherapics produced in Brazil, contains the essential oil from a native plant *Varronia curassavica* Jacq. (synonym *Cordia verbenacea* DC.), which contains α -humulene (a monoterpene), claimed to be the anti-inflammatory principle. This product is indicated for the treatment of topical inflammatory processes, such as tendinitis and muscle pain, and in painful inflammatory conditions associated with limb trauma, sprains, and bruises.

Inflammation is a complex response of the immune system that occurs due to injury, infection, or stress [4]. It is an essential process for protecting the body, promoting healing, and restoring internal balance. Inflammation can occur anywhere in the body and involves a series of coordinated cellular and molecular events.

MATERIAL AND METHODS

In this work, we outline a comprehensive literature search on plants from the Caatinga biome that exhibit anti-inflammatory activity. To carry out this investigation, we carried out a systematic bibliographic review, following the criteria established by the PRISMA methodology (Main Items for Reporting Systematic Reviews

and Meta-Analyses) [5] to conduct our research, we employed a strategy that involves consulting online journal databases, such as CAPES, Google Scholar, PubMed, Scielo, Science Direct, SciFinder, Scopus and Web of Science. The search terms "anti-inflammatories," "Caatinga," and "natural products" were used to guide our investigations. These terms were combined without the use of Boolean operators.

The inclusion criteria established the selection of original open access articles, developed in Brazil, with a period of 10 years for publications published between 2013 and 2023, in Portuguese and English. Book chapters were also consulted to obtain additional data. The exclusion criteria involved review articles (systematic, integrative and narrative), opinion articles, publications on species not originating in Brazil, monographs, dissertations and theses, as well as works that were not aligned with the objective of the study after reading the summaries (Figure 1).

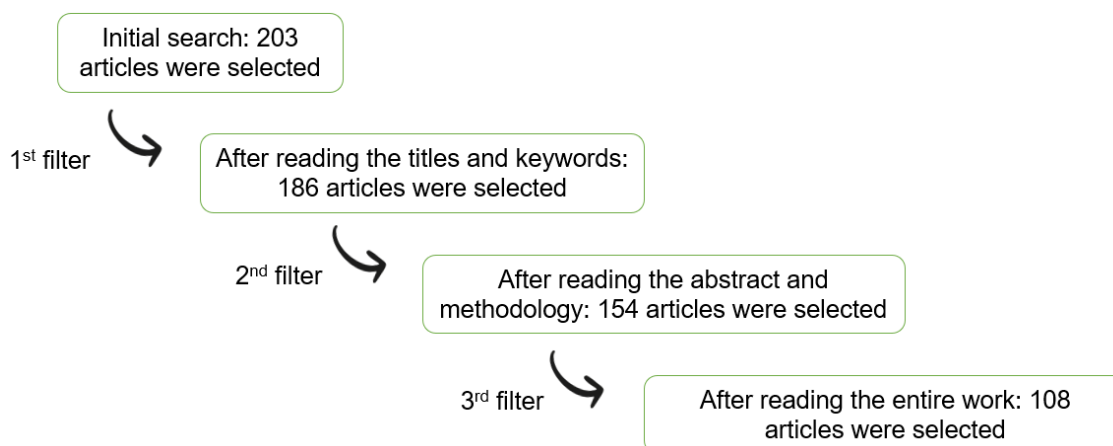


Figure 1. Criteria for displaying the study.

RESULTS

Brazil is made up of six biomes with distinct characteristics: Amazon, Caatinga, Cerrado, Atlantic Forest, Pampa and Pantanal. Each of these environments is home to different types of vegetation and fauna. The Caatinga is a biome exclusive to the Brazilian Northeast and is characterized by vegetation adapted to semi-arid conditions and high temperatures. Occupying an area of about 862,818 km², equivalent to 10.1% of the national territory [6] and encompasses the states of Alagoas, Bahia, Ceará, Maranhão, Pernambuco, Paraíba, Rio Grande do Norte, Piauí, Sergipe and north of Minas Gerais (Figure 2). The name Caatinga derives from the Tupi language and means "white forest", in relation to the whitish trunks due to the dry climate and absence of foliage [7].

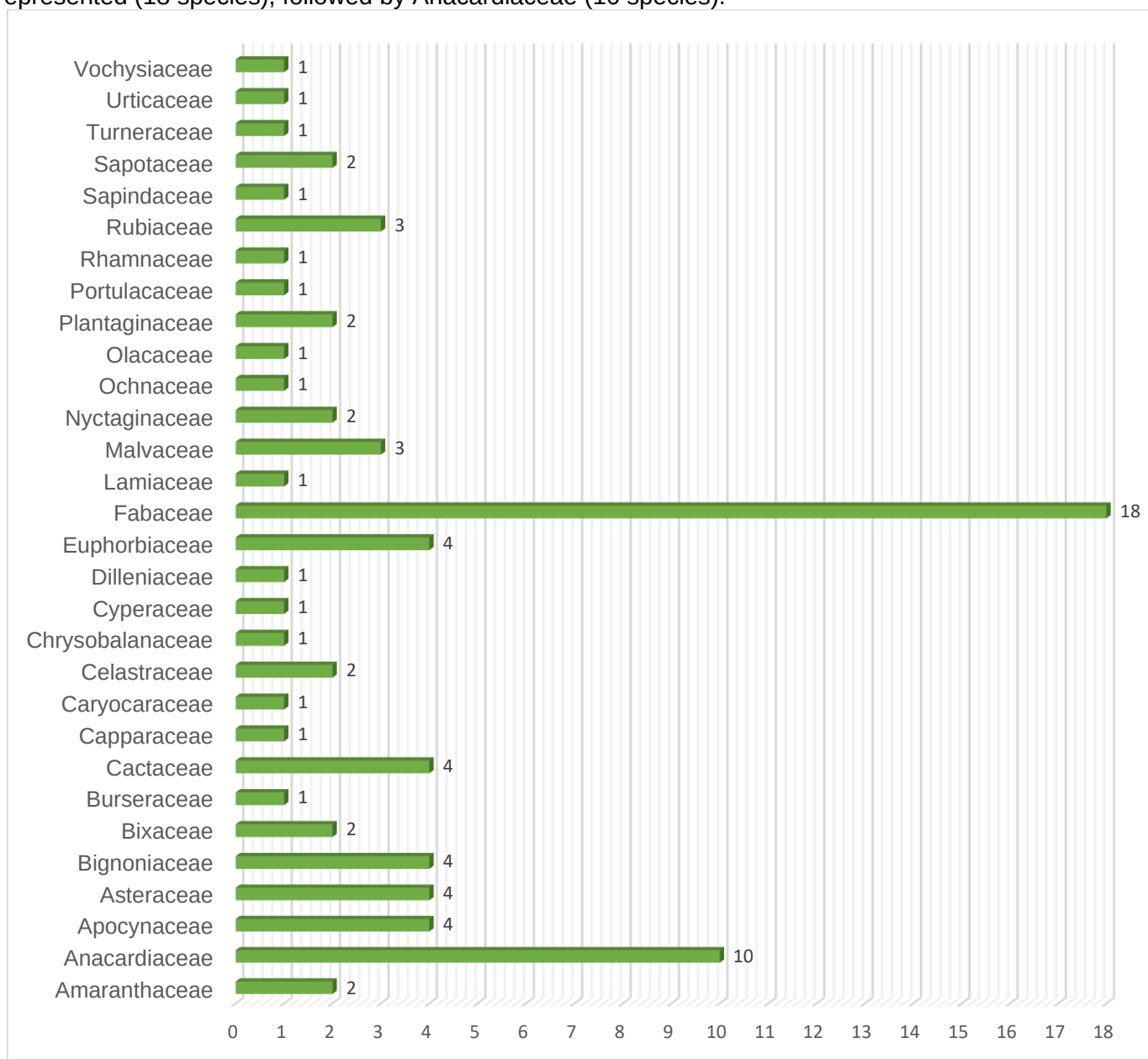


Figure 2. Brazilian Biomes [8].

With a floristic survey carried out throughout the Brazilian territory, the Caatinga biome presented a total of 4.322 species of seed plants, 744 of which are endemic to this biome, which corresponds to 17.2% of the total of registered taxa [9]. The main characteristics of the Caatinga vegetation are shallow and stony soil, low trees, crooked trunks that have thorns and leaves that generally fall during the dry season. Such mechanisms are responses of organisms to the physical environment, enabling the survival of species in edaphoclimatic conditions of the northeastern semi-arid region [10].

Studies indicate that approximately 1.512 species occur in the Caatinga and that many of these plants provide basic resources such as food, medicine, fodder for the most varied types of livestock, wood for construction, among others, for the survival of the populations that live in this semi-arid environment. These resources contribute considerably to improving the quality of life of these people, and the use of medicinal plants is more often the only form of medicine available in environments where some communities are installed [11].

The review presents a list of plant species from the Caatinga biome with scientifically proven anti-inflammatory activity (Table 1), highlighting the frequent use of bark for medicinal purposes. Graphic 1 illustrates the distribution of these species across botanical families, with Fabaceae standing out as the most represented (18 species), followed by Anacardiaceae (10 species).



Graphic 1. Occurrence of plant species with anti-inflammatory activity for each family

Table 1. Caatinga plant species with proven anti-inflammatory activity

Family	Species	Popular name	Habit	Used part	Method of preparation	Ref
Amaranthaceae	<i>Alternanthera brasiliana</i> (L.) Kuntz	Folha-de-papagaio; Folha-de-rubi; Folha-de-sangue	Subshrub	Flowers; Roots	Decoction; Infusion	[12]
	<i>Gomphrena demissa</i> Mart.	Capitãozinho; Ervanço	Subshrub	Roots	Decoction	[13]
Anacardiaceae	<i>Anacardium occidentale</i> L.	Cajueiro	Arboreal	Stem bark	Decoction; Infusion	[14]
	<i>Annona leptopetala</i> (R.E.Fr.) H.Rainer	Araticum; Ata-brava; Pereiro	Arboreal	Stem bark	Decoction	[15]
	<i>Astronium urundeuva</i> (M.Allemão) Engl.	Aroeira-do-sertão	Arboreal	Leaves; Stem bark	Bottled; Decoction; Maceration	[5]
	<i>Schinopsis brasiliensis</i> Engl.	Baraúna; Braúna	Arboreal	Roots; Stem bark	Decoction; Infusion	[16]
	<i>Schinus terebinthifolia</i> Raddi	Aroeira-da-praia; Aroeira-vermelha	Arboreal	Leaves; Stem bark	Infusion; Maceration	[17]
	<i>Spondias dulcis</i> Parkinson	Cajá-açu; cajá-manga	Arboreal	Leaves; Stem bark	Maceration	[18]
	<i>Spondias mombin</i> L.	Cajá; Cajarana; Cajazeira; Cajá-mirim	Arboreal	Leaves	Decoction	[19]
	<i>Spondias purpurea</i> L.	Seriguela	Arboreal	Leaves; Stem bark	Decoction	[20]
	<i>Spondias tuberosa</i> Arruda	Imbuzeiro; Umbu	Arboreal	Leaves; Resin; Roots; Stem bark; Fruits	Bottled; Decoction; Maceration	[21]
	<i>Spondias venulosa</i> (Mart. ex Engl.) Engl.	Cajá; cajazeira	Arboreal	Stem bark	Decoction	[22]

Cont. Table 1

Apocynaceae	<i>Aspidosperma pyrifolium</i> Mart. & Zucc.	Pau-pereiro; Pereiro	Arboreal	Stem bark	Decoction	[23]
	<i>Hancornia speciosa</i> Gomes	Mangaba	Arboreal	Flowers; Latex; Leaves; Stem bark	Decoction; Fresh; Infusion; Latex with water; Maceration	[24]
	<i>Himatanthus drasticus</i> (Mart.) Plumel	Janaguba	Arboreal	Leaves; Stem bark	Latex with water	[25]
	<i>Secondatia floribunda</i> A. DC.	Catuaba	Bush	Leaves; Stem bark	Decoction; Infusion; Maceration	[26]
Asteraceae	<i>Acanthospermum australe</i> (Loefl.) Kuntze	Carrapicho; Carrapicho-de-ovelha	Herbaceous	Leaves	Decoction	[27]
	<i>Achyrocline satureioides</i> (Lam.) DC.	Carrapicho-de-agulha; Macela-do-campo	Herbaceous	Leaves	Decoction; Infusion	[28]
	<i>Ageratum conyzoides</i> L.	Erva-de-são-joão; Mentrasto	Herbaceous	Leaves; Stem bark	Maceration	[29]
	<i>Porophyllum ruderale</i> (Jacq.) Cass.	Cravo-de-urubu; Couvinha	Herbaceous	Leaves	Decoction; Infusion	[30]
Bignoniaceae	<i>Handroanthus heptaphyllus</i> (Vell.) Mattos	Ipê-rosa; Pau-d'arco-roxo	Arboreal	Stem bark	Decoction	[31]
	<i>Handroanthus impetiginosus</i> (Mart. ex DC.) Mattos	Ipê-roxo; Pau-d'arco-roxo	Arboreal	Stem bark	Decoction	[32]
	<i>Handroanthus serratifolius</i> (Vahl) S.Grose	Ipê-amarelo-da-mata; Pau d'arco amarelo	Arboreal	Stem bark	Decoction	[33]
	<i>Tabebuia aurea</i> (Silva Manso) Benth. & Hook.f. ex S.Moore	Ipê-amarelo-do-cerrado; Pau d'arco	Arboreal	Stem bark	Chewing of the bark; Infusion; Maceration	[34]

Cont. Table 1

Bixaceae	<i>Cordia trichotoma</i> (Vell.) Arráb. ex Steud.	Frei-jorge	Arboreal	Stem bark	Decoction	[35]
	<i>Jacaranda jasminoides</i> (Thunb.) Sandwith	Caroba	Arboreal	Leaves; Stem bark	Decoction	[36]
Burseraceae	<i>Commiphora leptophloeos</i> (Mart.) J.B.Gillett	Imburana	Arboreal	Flowers; Stem bark	Bottled	[37]
Cactaceae	<i>Harrisia adscendens</i> (Gürke) Britton & Rose	Passa-prá-lá; Rabo-de-raposa	Arboreal	Roots	Infusion	[38]
	<i>Opuntia ficus-indica</i> (L.) Mill.	Jurumbeba; Palma; Palmatória	Arboreal	Cladodes	Fresh	[39]
	<i>Tacinga palmadora</i> (Britton & Rose) N.P.Taylor & Stuppy	Palma; Palmatória; Quipá	Arboreal	Cladodes; Roots	Decoction	[38]
	<i>Xiquexique gounellei</i> (F.A.C.Weber) Lavor & Calvente	Xique-xique	Arboreal	Roots	Decoction	[40]
Capparaceae	<i>Crateva tapia</i> L.	Pau-d'alho; Tapiá; Trapiá	Arboreal	Fruit; Leaves; Stem bark	Decoction	[41]
Caryocaraceae	<i>Caryocar coriaceum</i> Wittm.	Pequi; Piqui	Arboreal	Flowers; Fruits	Decoction	[42]
Celastraceae	<i>Monteverdia distichophylla</i> (Mart. ex Reissek) Biral	Bom-nome; Pau-doce	Arboreal	Stem bark	Decoction	[43]
	<i>Monteverdia obtusifolia</i> (Mart.) Biral	Carrancudo	Arboreal	Leaves; Stem bark	Decoction	[44]

Cont. table 1

Chrysobalanaceae	<i>Chrysobalanus icaco</i> L.	Guajiru; Guajerú	Arboreal	Roots	Maceration	[45]
Cyperaceae	<i>Rhynchospora nervosa</i> (Vahl) Boeckeler	Capim-estrela	Herb	Whole plant	Decoction	[46]
Dilleniaceae	<i>Curatella americana</i> L.	Lixeira; Sambaiba	Arboreal	Stem bark	Decoction	[47]
Euphorbiaceae	<i>Cnidoscolus quercifolius</i> Pohl	Favela; Queimadeira	Arboreal	Latex	Decoction	[48]
	<i>Cnidoscolus urens</i> (L.) Arthur	Cansanção; Urtiga-branca; Urtiga-de-boi	Arboreal	Stem bark	Decoction	[49]
	<i>Croton heliotropiifolius</i> sp.	Velame	Arboreal	Leaves	Decoction	[50]
	<i>Ricinus communis</i> L.	Mamona	Herbaceous	Leaves	Juice; Sauce	[51]
Fabaceae	<i>Abarema cochliacarpus</i> (Gomes) Barneby & J.W.Grimes	Barbatimão; Bordão-de-velho	Arboreal	Stem bark	Decoction	[52]
	<i>Amburana cearensis</i> (Allemão) A.C.Sm.	Imburana-de-cheiro	Arboreal	Fruit; Seed; Stem bark	Decoction; Infusion; Lick; Poultice soak,	[53]
	<i>Anadenanthera colubrina</i> (Vell.) Brenan	Angico	Arboreal	Flowers; Fruits; Leaves; Stem bark	Bottled; Decoction	[54]
	<i>Bauhinia forficata</i> Link	Mororó; Pata-de-vaca; Orquídea-brasileira	Bush	Flowers; Leaves; Stem bark	Decoction; infusion	[55]
	<i>Bowdichia virgilioides</i> Kunth.	Sucupira	Arboreal	Seeds; Stem bark	Bottled; Decoction	[56]
	<i>Copaifera langsdorffii</i> Desf.	Copaíba; Pau-d'óleo	Arboreal	Leaves; Resin; Seeds; Stem bark	Decoction; Fresh; Infusion; Maceration	[57]
	<i>Copaifera multijuga</i> Hayne	Copaíba	Arboreal	Fruit oil	Decoction	[58]
	<i>Dimorphandra gardneriana</i> Tul.	Fava-d'anta; Faveira	Arboreal	Fruits; Seeds; Stem bark	Decoction; Maceration	[59]
	<i>Enterolobium contortisiliquum</i> (Vell.) Morong	Orelha-de-negro; Tambor Timbaúba	Arboreal	Stem bark	Decoction	[60]
	<i>Erythrina velutina</i> Willd.	Mulungu	Arboreal	Stem bark	Bottled; Decoction	[23]

Cont Table 1

Fabaceae	<i>Hymenaea courbaril</i> L.	Jatobá; Jatobá-de-boi; Jatobá-de-veado; Jatobá-do- mato	Arboreal	Fruits; Leaves resin; Stem bark	Decoction; Infusion; Maceration	[61]
	<i>Hymenaea stigonocarpa</i> Mart. ex Hayne	Jatobá-do-cerrado; Jatobá- de-veado	Arboreal	Fruits; Roots; Sap; Stem bark; Resin	Decoction; Infusion; Maceration	[62]
	<i>Libidibia ferrea</i> (Mart. ex Tul.) L. P. Queiroz.	Jucá; Pau-ferro	Arboreal	Stem bark; Fruits; Seeds	Decoction; Fresh; Infusion Maceration	[63]
	<i>Machaerium acutifolium</i> Vogel var. <i>acutifolium</i>	Bastião-de-arruda; Jacarandá-do-campo; Jacarandá-preto	Arboreal	Roots; Stem bark	Decoction	[64]
	<i>Mimosa hirsutissima</i> Mart.	Jurema-preta	Arboreal	Roots; Stem bark	Decoction	[65]
	<i>Mimosa tenuiflora</i> (Willd.) Poir.	Jurema; Jurema-preta	Bush	Stem bark	Decoction; infusion	[65]
	<i>Pterodon emarginatus</i> Vogel	Sucupira-branca; Fava-de- santo-inácio	Arboreal	Stem bark; Seeds	Decoction	[25]
	<i>Stryphnodendron rotundifolium</i> Mart.	Barbatimão	Arboreal	Stem bark	Decoction; Infusion; Maceration	[66]
Lamiaceae	<i>Rhaphiodon echinus</i> (Nees & Mart.) Schauer	Flor-de-urubu	Herb	Leaves; Roots	Decoction	[67]
Malvaceae	<i>Luehea divaricata</i> Mart.	Açoita-cavalo	Arboreal	Stem bark	Maceration	[68]
	<i>Pseudobombax marginatum</i> (A.St.-Hil., Juss. & Cambess.) A.Robyns	Embiratanha; Imbiratanha	Arboreal	Stem bark	Decoction	[69]
	<i>Sida cordifolia</i> L.	Vassourão; Malva-branca	Bush	Leaves	Infusion	[70]
Nyctaginaceae	<i>Passiflora cincinnata</i> Mart	Maracujá mochila	Arboreal	Leaves	Infusion; Maceration	[71]
	<i>Passiflora foetida</i> L.	Maracujá silvestre	Arboreal	Whole plant	Maceration	[72]
Ochnaceae	<i>Ouratea fieldingiana</i> (Gardner) Engl.	Batiputá	Arboreal	Leaves	Maceration	[73]

Cont. Table 1

Olacaceae	<i>Ximenia americana</i> L.	Ameixa	Bush	Stem; Leaves; fruit peel	Decoction; Infusion; Sauce; Poultice; Roasted bark (powder)	[74]
Plantaginaceae	<i>Plantago major</i> L.	Transagem	Herbaceous	Seed; Leaves	Lick; Decoction	[75]
	<i>Scoparia dulcis</i> L.	Vassourinha; Vassoura-de- botão	Herbaceous	Leaves; Roots	Decoction; Infusion; Maceration	[76]
Portulacaceae	<i>Talinum paniculatum</i> (Jacq.) Gaertn.	Bredo	Herb	Whole plant	Infusion	[77]
Rhamnaceae	<i>Zizipus joazeiro</i> Mart.	Juazeiro	Arboreal	Between bark; Roots	Maceration; Fresh; Decoction	[78]
Rubiaceae	<i>Chiococca alba</i> (L.) Hitchc.	Caninana	Bush	Leaves; Roots	Maceration; Infusion; Decoction	[79]
	<i>Coutarea hexandra</i> (Jacq.) K. Schum.	Quina-quina	Arboreal	Roots; Stem bark	Decoction	[25]
	<i>Guettarda viburnoides</i> Cham. & Schltdl.	Angélica	Bush	Stem bark; Leaves	Decoction; Infusion	[80]
Sapindaceae	<i>Paullinia pinnata</i> L.	Mata-fome; Cururu-apé	Bindweed	Leaves	Infusion	[81]
Sapotaceae	<i>Bumelia sartorum</i> Mart.	Quixabeira	Arboreal	Stem bark	Maceration; Infusion	[82]
	<i>Sideroxylon obtusifolium</i> (Roem. & Schult.) T.D.Penn.	Quixaba Rompe-gibão	Arboreal	Whole plant	Decoction; Maceration	[83]
Turneraceae	<i>Turnera ulmifolia</i> L.	Chanana	Herbaceous	Roots	Decoction	[84]
Urticaceae	<i>Laportea aestuans</i> (L.) Chew	Urtiga-vermelha; Urtiga	Bush	Roots	Decoction	[85]
Vochysiaceae	<i>Qualea parviflora</i> Mart.	Pau-terra	Arboreal	Stem bark; Leaves; Roots	Decoction; Infusion; Maceration	[86]

DISCUSSION

Caatinga plants: Promising sources of compounds with anti-inflammatory activity

The pioneer studies of medicinal plants from the semi-arid region of Brazil were performed by the pharmacognosist Francisco José de Abreu Matos and colleagues from Federal University of Ceará State and their many publications were included in a book prepared in conjunction with the agronomist Harri Lorenzi from Santa Catarina Federal University situated in South region of Brazil and this book encompasses all Brazilian medicinal plants [87]. Many medicinal plants with anti-inflammatory activities reported from Caatinga biome are included in Table 1.

There are two main types of inflammation: acute and chronic. Acute inflammation is a quick response that occurs shortly after an injury or infection. Acute inflammation is mediated by immune system cells, such as white blood cells, which are recruited to the inflamed site. These cells release inflammatory mediators, such as histamine, prostaglandins, cytokines and chemokines, which promote the immune response and attract more defense cells to the affected area [88]. In addition, blood vessels dilate to increase blood flow, allowing more efficient arrival of defense cells and nutrients to the affected place [89].

Natural products possess anti-inflammatory activity through several mechanisms. They can inhibit the production of pro-inflammatory mediators such as cytokines (TNF- α , IL-1 β , IL-6) [90] and prostaglandins (PGE₂) [91], reducing the inflammatory response in the body. In addition, some natural products can inhibit pro-inflammatory enzymes such as cyclooxygenase (COX) [92] and lipoxygenase (LOX) [93], decreasing the production of inflammatory mediators. The antioxidant action of natural products also plays an important role, reducing oxidative stress associated with inflammation. They can also modulate the activity of immune system cells such as lymphocytes, macrophages and dendritic cells [94].

Furthermore, many natural products are capable of inhibiting inflammatory signaling pathways, such as the nuclear factor kappa β (NF- κ B) pathway [95] and the mitogen-activated protein kinase (MAPK) pathway [96]. The anti-inflammatory activity of natural products has been widely studied *in vitro*, in animal models and in clinical studies, showing effectiveness in reducing inflammation [73,97–99]. These products can be considered as alternative or complementary therapeutic options to conventional drugs in the treatment of chronic inflammatory diseases.

Various ethnomedicinal studies provide information on the use and therapeutic potential of many plants of traditional communities in the semi-arid [25]. The plants more cited which present pharmacological studies assuring this action, were selected to highlight such as *Ouratea fieldingiana* (Gardner) Engl (Batiputá), *Astronium urundeuva* (M. Allemão) Engl. (Aroeira), *Himatanthus drasticus* (Mart.) Plumel (Janaguba), *Libidibia ferrea* Mart. ex Tul. (Jucá), *Caryocar coriaceum* Wittm. (Pequi), *Hancornia speciosa* Gomes (Mangaba), *Dimorphandra gardneriana* Tul. (Faveira) and *Ximenia americana* L. (Ameixa).

The hydroethanolic extract of batiputá (*Ouratea fieldingiana*) is utilized for treating both topical and systemic inflammations. This extract is abundant in phenolic compounds, including flavonoids like rutin, isoquercitrin, kaempferol-3-O-rutinoside, quercetin, apigenin, and amentoflavone (Figure 3) [100]. Among the mechanisms of action investigated are effects on hypernociception, edema, and leukocyte migration. The ability to reduce the expression of oxidative markers such as MPO (myeloperoxidase) and MDA (malondialdehyde), while increasing the expression of antioxidant markers like catalase and GSH (glutathione), was observed *in vivo*. Additionally, these tests revealed an effective antinociceptive effect compared to the reference drug [73,101].

Ouratea fieldingiana fruit oil is used popularly for topic inflammation and in a pharmacological study showed anti-inflammatory action in the TPA-induced ear edema, probably the action of unsaturated fatty acids was more important in topical application, nevertheless in internal inflammation process the presence of antioxidant phenolic compounds such as kaempferol-3-O-rutinoside, apigenin, agatisflavone and amentoflavone could contribute to the high activity of the oil [102].

The compound kaempferol-3-O-rutinoside can act in the modulation of inflammatory pathways, such as inhibiting the release of inflammatory mediators and reducing the activation of inflammatory cells [103]. The biflavonoid amentoflavone revealed anti-inflammatory activity, using some important mediators of the inflammatory response, among them interleukin-1b (IL-1b) which is usually produced by monocytes and macrophages, and together with tumor necrosis factor alpha (TNF- α) [104], stimulates the production of interleukin-6 (IL-6) by smooth muscle cells and increases the expression of macrophages [105], platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF), associated with progression of the inflammatory process of atherosclerosis [106,107]. Houg and coauthors [108] report that amentoflavone inhibits prostaglandin E₂ secretion through downregulation of the inducible expression of nitric oxide

synthase and cyclooxygenase-2 (COX-2), blocking activation of the nuclear factor kappa beta (NF- κ B) pathway via phosphorylation of mitogen-activated protein kinases (MAP Kinase).

Astronium urundeuva, formerly known as *Myracrodruon urundeuva*, is popularly known as “Aroeira-do-sertão”, it is used in diabetic foot [109] and in gastrointestinal inflammations [110]. Another Aroeira species, *Schinus terebinthifolius* (Aroeira-da-praia) displays anti-inflammatory activity through the inhibition of COX-2 enzyme [17], which plays an important role in the production of pro-inflammatory prostaglandins. The main compounds responsible to combat inflammation in these plants are named as urundevines (dihydrochalcones) which structures are shown in Figure 3.

Urundevines, compounds found in the ethanolic extract of *M. urundeuva*, have demonstrated anti-inflammatory activity through several mechanisms. One of the main mechanisms of action is the selective inhibition of the enzyme cyclooxygenase (COX), especially of the COX-2 isoform [16]. COX-2 inhibition reduces the production of prostaglandins, pro-inflammatory substances, leading to a decrease in inflammation.

A component of the inflammatory response that can be modulated by urundevines is tumor necrosis factor alpha (TNF- α) [111], a pro-inflammatory cytokine. In addition, a reduction in histone deacetylase (HDAC) immunostaining was observed, an enzyme involved in the regulation of gene expression related to inflammation. This reduction suggests a potential modulating effect on inflammatory activity. Urundevines also have the ability to inhibit inflammatory signaling pathways, such as the NF- κ B pathway and the mitogen-activated protein kinase (MAPK) pathway. These pathways play a crucial role in the production of inflammatory mediators and to the reduction of the inflammatory response [112].

A widely used and commercialized plant, mainly in Ceará, Northeastern Brazil, is janaguba (*Himatanthus drasticus*), a specimen of the Apocynaceae family. Its main product is latex, which has been indicated for the treatment of cancer, inflammation and microbial infections. In pharmacological studies, *H. drasticus* latex displayed antinociceptive and anti-inflammatory activities and wound healing potential by the participation of mast cells, CD68+ and VEGF+ expressions. These actions can be associated to the compounds characterized in the Janaguba latex: a mixture of three cinnamoyl derivatives of lupeol, α -amyrin and β -amyrin [113].

Libidibia ferrea is used in ethnomedicine to treat many problems related to inflammation such as stomach pain, injury, internal wounds, insect bites, throat inflammation, gastritis, influenza, uterine inflammation, footcracks, cough, ulcer, back pain, inflammation of internal and external organs, bone pain, bone fracture [114]. In a wound healing study of *L. ferrea*, it was observed the modulation of TNF- α , IL-1 β , NO and TGF- β , controlling the inflammatory phase and attenuating hypernociception. Anti-inflammatory activity could also occur via negative modulation, e.g., in carrageenan-induced paw edema, using the following mediators: bradykinin, nitric oxide, histamine, serotonin, and PGE2 [115]. In the *L. ferrea* bark, ellagic and gallic acids were characterized [116].

Caryocar coriaceum also contains gallic and ellagic acids and the flavonoids quercetin and rutin, among others, being used to combat asthma, bronchitis, whooping cough, colds, and anti-inflammatories [117]. Gallic acid regulates pro-inflammatory pathways, as the signaling pathway of nuclear factor kappa B (NF- κ B) [115].

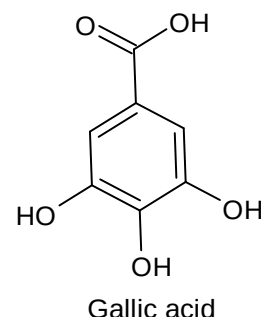
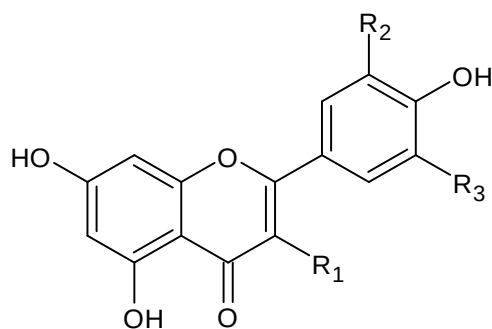
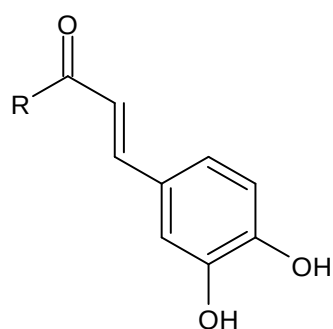
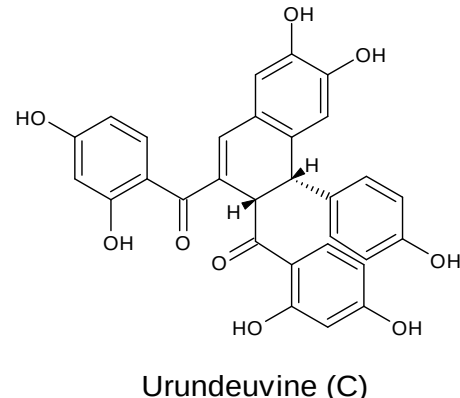
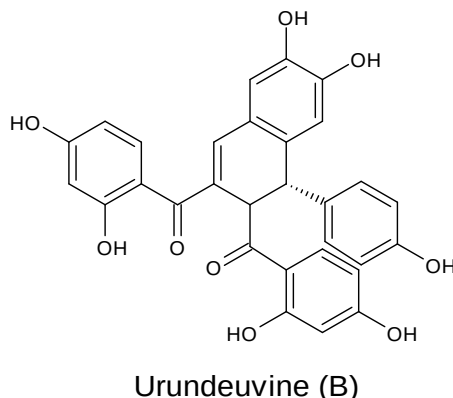
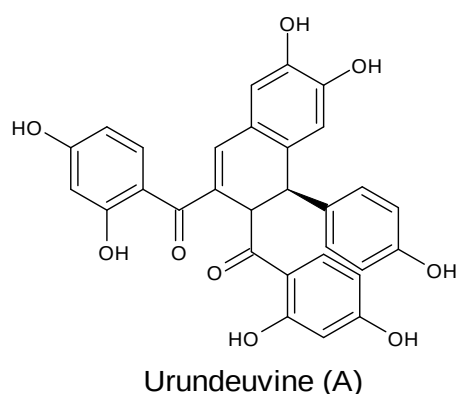
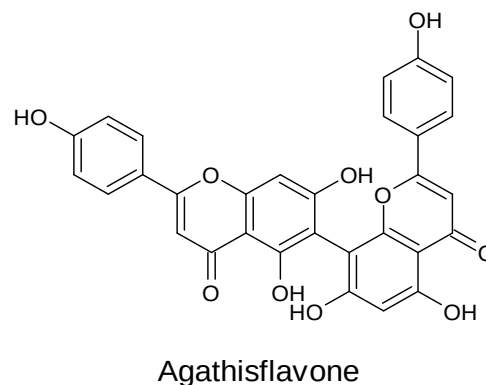
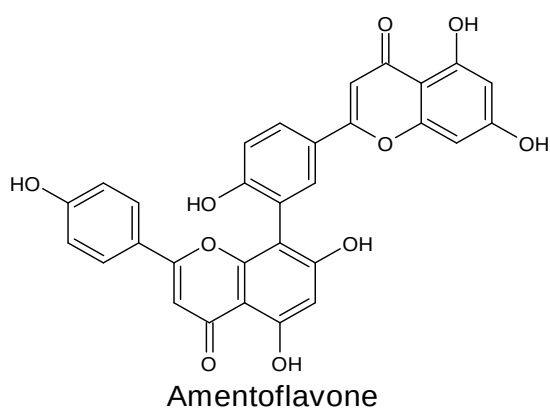
Handroanthus heptaphyllus, *H. impetiginosus*, *H. serratifolium* and *H. aurea* called Pau d'Arcos have lapachol as their main constituent, a naphthoquinone isolated from several species of plants of the Bignoniaceae family, easily found in the North and Northeast regions of Brazil. This compound is known for its anti-cancer, anti-inflammatory, analgesic, antibiotic, anti-trypanosome, anti-malaria, and anti-ulcerogenic properties. This medicinal plant potently reduces pro-inflammatory cytokine responses in primary human lymphocytes [118].

Hancornia speciosa fruit extract was evaluated for its anti-inflammatory activity using several animal models exposed to different inflammatory agents [119]. Rutin and chlorogenic acid were identified in the extract as the main secondary metabolites [120]. In addition, the extract as well as rutin and chlorogenic acid significantly inhibited the xilol-induced ear edema also reduced the cell migration in both carrageenan-induced peritonitis and zymosan-induced air pouch models. Reduced levels of cytokines were also observed [24].

Dimorphandra gardneriana, popularly known as fava d'anta, is a plant widely distributed in the Brazilian Cerrado, occurring also in the Chapada do Araripe, located in the South of the state of Ceará. Its fruits are exploited to obtain rutin and quercetin, both are bioflavonoids with several pharmacological activities studied, for supplying the pharmaceutical industry. The extraction of *D. gardneriana* is an important source of income, especially for residents of communities surrounding the extraction region. However, uncontrolled extraction threatens this species to extinction [121].

Rutin, known for its antioxidant, anti-inflammatory, cytoprotective and gastroprotective properties, was used in the treatment of intestinal mucositis, a condition marked by inflammatory and/or ulcerative processes in the gastrointestinal tract resulting from cell and tissue damage induced by treatment with 5-fluorouracil (5-FU), mitigating the inflammatory response by reducing MPO activity, intestinal mastocytosis and COX-2 expression [122].

The antinociceptive and anti-inflammatory effects of the ethanolic extract, fractions and epicatechin (XM-Catechin) isolated from the ethanolic extracts of *Ximenia americana* L. bark were evaluated using *in vivo* models such as writhing induced by acetic acid, formalin test, hot plate test, zymosan-induced peritonitis and *in vitro* cyclooxygenase inhibition assay. The results indicate that the extract, fractions and XM-Catechin present antinociceptive and anti-inflammatory responses. According to the results of cyclooxygenase inhibition assays, these effects are attributed to the inhibition of both COX-1 and COX-2 [74].



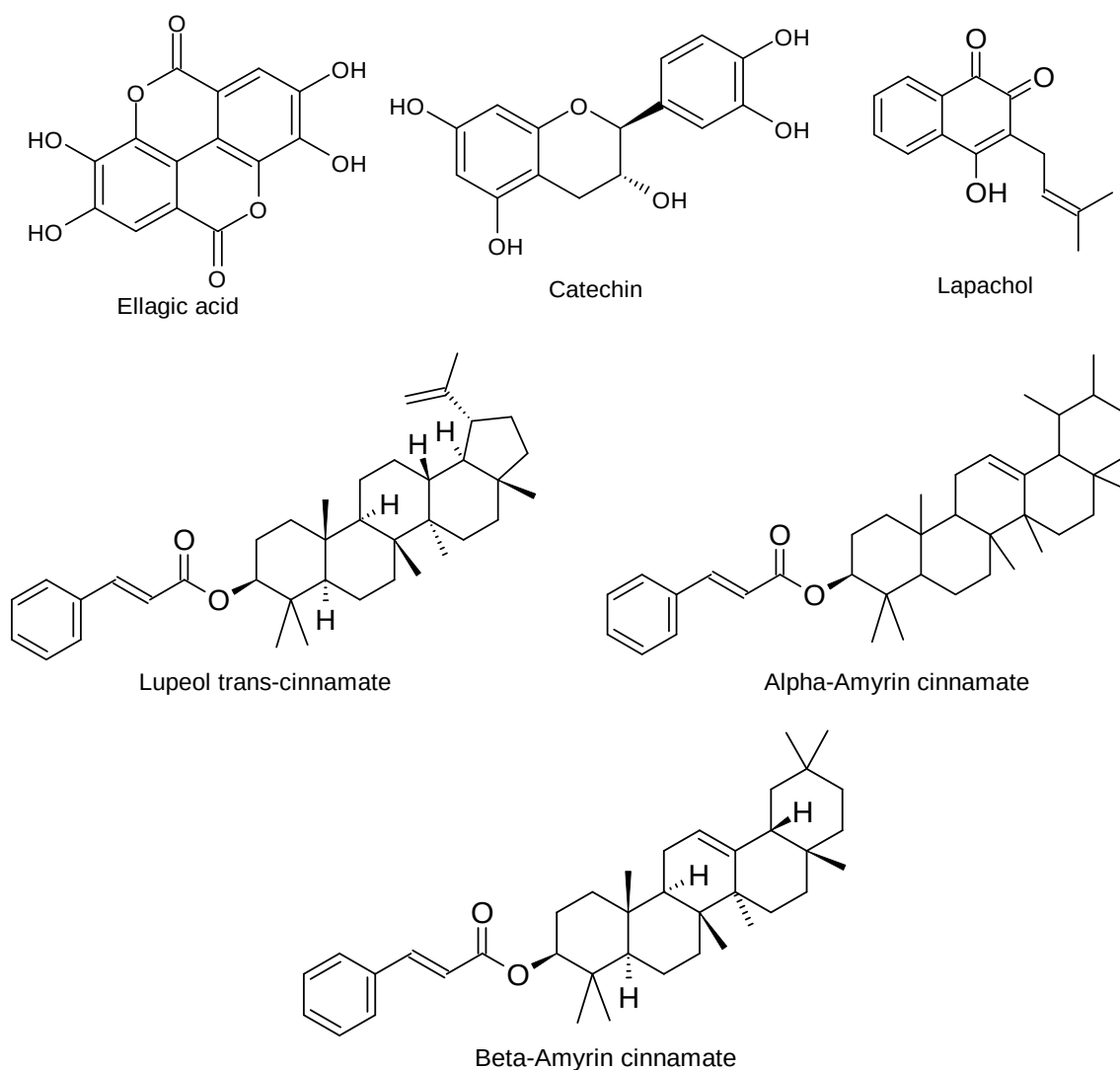


Figure 3. Structure of the major compounds cited in the text

Carrying out an ethnobotanical survey in the semi-arid northeast, we observed that the bark of plants is the most commonly used part in the preparation of medicines, especially due to environmental influences, seasonal climate variations and regional cultural characteristics. This preference is intrinsically linked to the availability of the plant part used. Such factors, together with the limitation of presence throughout the year, play a crucial role in choosing the species or part of the plant for a specific therapeutic treatment [9]. This trend is confirmed in Table 1, which lists plant species from the Caatinga biome with proven anti-inflammatory activity and highlights the frequent use of bark as the primary medicinal part. Additionally, Graphic 1 reflects the botanical families most represented among these species, with Fabaceae and Anacardiaceae standing out, suggesting a correlation between cultural use patterns and the pharmacological potential identified in scientific studies.

CONCLUSION

Plants found in the Caatinga biome are promising sources of bioactive compounds with anti-inflammatory properties, with the Fabaceae family being the most reported, with the largest number of reported species. The part of the plants most widely used for medicinal purposes is the bark, since Caatinga plants are caducifolious.

The natural defense mechanisms developed by these plants to face the extreme conditions of the Caatinga environment give them the ability to produce compounds with therapeutic properties, such as phenolic compounds, which are also antioxidants and protect the plant against UV solar radiation, which has a high incidence as it is close to the equatorial region. These compounds have the potential to reduce the inflammatory response, helping to mitigate inflammatory processes associated with various diseases. Furthermore, the sustainable exploitation of these plants can pave the way for the development of new medicines and therapies that contribute to human health and well-being.

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