

Anti-inflammatory and wound healing properties from Caatinga plant species: how they do it? – A literature review

Propriedades anti-inflamatória e cicatrizante de espécies de plantas da Caatinga: como acontece? – Uma revisão de literatura

Propiedades antiinflamatorias y cicatrizantes de las especies de plantas Caatinga: ¿cómo lo hacen? – Una revisión de la literatura

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Abstract

Being one of the phytogeographic domains exclusively present in Brazil, the Caatinga occupies approximately 11% of the Brazilian territory and is one of the drylands with the most diversity around the world. The Caatinga is home to a floristic variety that carries a plurality of bioactive compounds capable of reversing physiological disorders. Many bioactive products from Caatinga species have anti-inflammatory and healing potential. The present review aimed to summarize the works that explored the anti-inflammatory and healing activities of plant species present in this phytogeographic domain. The articles were selected from the databases: Elsevier, Springer links, and PubMed to build the present review. In total, 39 plant species were identified, which were studied about their biological potential with

experimental assays, and we've discussed how its compounds are related to the anti-inflammatory and healing activities. Our results highlight that the most studied product obtained from those plant species is the plant extract, and still those studies aren't clear about its phytochemical profile. On the other hand, the research focused on plant oils provides a better understanding of how Caatinga plant species promote anti-inflammatory and wound healing action.

Keywords: Caatinga species; Wound healing; Anti-inflammatory; Mechanism of action.

Resumo

A Caatinga é um domínio fitogeográfico exclusivamente brasileira e ocupa uma área de aproximadamente 11% do território brasileiro, é uma das terras secas com maior diversidade no mundo. A Caatinga abriga uma variedade florística que carrega uma pluralidade de compostos bioativos capazes de reverter diversos distúrbios fisiológicos. Muitos produtos bioativos de espécies da Caatinga possuem potencial anti-inflamatório e cicatrizante. A presente revisão teve como objetivo resumir os trabalhos que exploraram as atividades anti-inflamatória e cicatrizante de espécies vegetais presentes neste domínio fitogeográfico. Os artigos foram selecionados nas bases de dados: Elsevier, Springer links e PubMed para construção da presente revisão. No total, foram identificadas 39 espécies de plantas, que foram estudadas quanto ao seu potencial biológico com ensaios experimentais, e discutimos como seus compostos estão relacionados com as atividades anti-inflamatória e cicatrizante. Nossos resultados destacam que o produto mais estudado obtido dessas espécies são os extratos vegetais. Ainda esses estudos não são claros quanto ao seu perfil fitoquímico. Por outro lado, as pesquisas com foco em óleos vegetais proporcionam uma melhor compreensão de como as espécies vegetais da Caatinga promovem ação anti-inflamatória e cicatrizante.

Palavras-chave: Espécies da caatinga; Cicatrização; Anti-inflamatório; Mecanismo de ação.

Resumen

Siendo uno de los dominios fitogeográficos exclusivamente presentes en Brasil, la Caatinga ocupa aproximadamente el 11% del territorio brasileño y es una de las tierras secas con mayor diversidad en todo el mundo. La Caatinga alberga una variedad florística que porta una pluralidad de compuestos bioactivos capaces de revertir trastornos fisiológicos. Muchos productos bioactivos de las especies de Caatinga tienen potencial antiinflamatorio y cicatrizante. La presente revisión tuvo como objetivo resumir los trabajos que exploraron las actividades antiinflamatorias y curativas de las especies vegetales presentes en este dominio fitogeográfico. Los artículos fueron seleccionados de las bases de datos: Elsevier, Springer links y PubMed para construir la presente revisión. En total, se identificaron 39 especies de plantas, las cuales se estudiaron sobre su potencial biológico con ensayos experimentales, y hemos discutido cómo sus compuestos se relacionan con las actividades antiinflamatorias y cicatrizantes. Nuestros resultados destacan que el producto más estudiado obtenido de esas especies de plantas es el extracto de plantas, y aún esos estudios no tienen claro su perfil fitoquímico. Por otro lado, la investigación centrada en los aceites vegetales proporciona una mejor comprensión de cómo las especies de plantas Caatinga promueven la acción antiinflamatoria y cicatrizante.

Palabras clave: Especies de caatinga; Cicatrización de heridas; Antiinflamatorio; Mecanismo de acción.

1. Introduction

The advancement of herbal medicine knowledge highlighted the traditional medicine as an important natural pharmaceutical alternative, especially in the countries with high biodiversity index, this popular knowledge is continuously increasing as source of information about medicinal plants and their preparations for health care (Yuan et al. 2016). The research focused on medicinal plants, in the light of traditional knowledge, revolutionized the pharmaceutical industry, increasing the possibility of developing new products for several diseases. These herbal medicines may have low costs and have few collateral effects when compared with synthetic drugs, besides that, the medicinal plants generate economy due to the productive chain, which involves several steps, from the cultivation by small farmers, to the formulation of the phytotherapy, becoming a relevant option for countries to explore their own biodiversity (Almeida et al., 2005; Vieira et al., 2016).

Caatinga is a phytogeographic domain exclusively present in Brazil, and is inserted especially in the Northeast region, occupying 11% of Brazilian territory, it's characterized by a semiarid climate, low humidity and little water resources, which is reflected in a dry and sandy soil with predominance of shrubs (Magalhaes et al., 2019). Nevertheless, one of the remarkable Caatinga property is the low and non-uniform precipitation period, which may last between 4 to 6 months, and still, due to the type of soil and high temperatures is unable to retain water, thus the Caatinga plant species only present fruits, flowers, and leaves during the raining season of the year (Dombroski et al., 2011). Due to those characteristics, the Caatinga biome is one of the

dryland with highest biodiversity around the world (Araujo et al., 2022). As a form of physiological adaptation, those plant species carry a plurality of bioactive compounds capable of reverting physiological disorders caused by pathological phenomena, and their compounds can be explored in the light of ethnopharmacological sciences (Albuquerque; Oliveira, 2007; Araujo et al., 2007; Almeida et al., 2010).

Many bioactive products from Caatinga species have anti-inflammatory and healing potential (Aquino et al., 2017; Arunachalam et al., 2019). Inflammation is characterized as a bodily biological response to an injury, or agents that cause cell damage, resulting in the release of chemokines, cytokines, and growth factors that promote the transmigration of immunologic system cells, this mechanism of action can be modulated by several factors (Sánchez-Fidalgo et al., 2013). Therefore, several molecules present in plants can, also, modulate the chemical effects caused by inflammation in different ways, acting directly on the pathways of the inflammatory process (Paiva et al., 2013). Moreover, these bioactive compounds can simply act on the inflammatory side effects, an example is the role of non-enzymatic antioxidant molecules, which decrease the level of reactive oxygen species generated in the inflammation process (Silva et al., 2010a; Silva et al., 2015; Bitencourt et al., 2019).

In addition, the healing action is a complex process involving biochemical mediator aiming to restore the tissue integrity and functionality through cell proliferation and activation of extracellular matrix components (Nascimento-Neto et al., 2015; Silva et al., 2010b). The regeneration process can be interfered by the health status of the patient, nutrition, age, and place of injury, hampering the natural healing process (Choudhary et al., 2020; Moeini et al., 2020). Thus, herbal products from Caatinga species, have biomolecules able to simulate several biological pathways involved in the tissue regeneration process, promoting, for example, angiogenesis and collagen production (Fazil; Nikhat, 2020; Cavalcanti et al., 2012).

Therefore, the present literature review aims to bring an insightful review of the Caatinga medicinal plants with activity anti-inflammatory and wound healing potential, associating the molecules present in the plant products with those biological activities. Thus, we believe that this work will stimulate research scientific proof of these biological activities of popular knowledge rooted in the Caatinga inhabitants.

2. Methodology

Study selection criteria

The present review consisted in a integrative review of Caatinga plants species with anti-inflammatory and wound healing activities. The articles were selected from the databases: Elsevier (<https://www.sciencedirect.com/>), PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), Web of Science (<https://webofknowledge.com/>) and Springer Link (<https://link.springer.com/>). The strategy adopted was to search with two or more combined keywords: wound healing, healing, inflammation, anti-inflammatory always combined with Caatinga and Brazil, like in Miranda et al. (2019).

Inclusion criteria and analyzed data

The inclusion criteria were complete articles, published in the beginning of 2010 until half of 2022, with scientific investigations of any Caatinga specie that have improved wound healing, healing or anti-inflammatory activity using *in vitro* and/or *in vivo* methodologies. Studies without an experimental assay, as well reviews and ethnobotanical research were excluded from our analysis. The analyzed information was plant species, type of product (oil, extract, or isolated compound) and possible mechanism of action.

3. Results and Discussion

Several studies have explored the anti-inflammatory and healing capacity of Caatinga species, most of the studied species has showed promising results, with pharmacological potential through the metabolites produced by the plants

(Bouyahya et al., 2020). The plant products used varied among essential oil, extract and isolated molecules; however, the extracts were the most common evaluated product (as seems in table 1), may be due to the fact that in popular use, the extracts are the most common preparation method (Hao and Xiao, 2020). The vegetal tissues were the most diverse, alternating among leaves, flowers, stem, roots and fruits, the prevalence was highlighted using leaves, given its abundance and less harmful action to plants health, even though the leaves aren't always available in the Caatinga plant species.

Table 1: Healing and/or anti-inflammatory action of Caatinga plant species.

Specie	Product	Activity	Chemical component	Reference
<i>Croton adamantinus</i>	Essential oil	Healing	Methyl-eugenol and 1,8-cineol	Ximenes et al., 2013
<i>Croton zehntneri</i>	Essential oil and isolated molecule	Healing	Anethole, estragole, 1,8-cineole, and trans-caryophyllene	Cavalcanti et al., 2012 Oliveira et al., 2001
<i>Croton argyrophyllus</i>	Essential oil	Anti-inflammatory	Bicyclogermacrene and spathulenol	Ramos et al., 2013
<i>Croton rhamnifolioides</i>	Essential Oil	Anti-inflammatory		Martins et al., 2017
<i>Hyptis spicigera</i>	Essential oil	Anti-inflammatory / Healing	α -pinene , 1,8-cineole, and β -pinene	Simões et al., 2017; Takayama et al., 2011
<i>Eugenia stipitata</i>	Essential oil	Anti-inflammatory	Guaiol, trans-caryophyllene, β -eudesmol, and γ -eudesmol	Costa et al., 2020
<i>Lippia gracilis</i>	Essential oil	Anti-inflammatory	thymol, p-cymene, methyl thymol, carvacrol, γ -terpinene, β -caryophyllene, 1,8-cineole, and myrcene	Mendes et al., 2010
<i>Combretum leprosum</i>	Triterpenes isolated from leaves	Healing	3 β , 6 β , 16 β -trihydroxylup-20(29)-ene	Nascimento-Neto et al., 2015
<i>Pseudobombax marginatum</i>	Extract	Anti-inflammatory	Tannins, flavonoids and free steroids	Paiva et al., 2013
<i>Croton velutinus</i>	Extract	Anti-inflammatory	Isolates derived from phenylpropanoids	Abreu et al., 2020
<i>Cnidocolus quercifolius</i>	Extract	Anti-inflammatory	Bark: coumarins, flavonoids, monoterpenes/diterpenes and naphthoquinones //Leaves: coumarins, anthracene derivatives, flavonoids, lignans and triterpenes/steroids	Gomes et al., 2014
<i>Annona vepretorum</i>	Extract	Anti-inflammatory	Phenols, steroids, terpenoids and flavonoids	Silva et al., 2015 Diniz et al., 2013
<i>Hancornia speciosa</i>	Extract	Anti-inflammatory	Rutin and chlorogenic acid	Torres-Rego et al., 2016; Bitencourt et al., 2019

<i>Libidibia ferrea</i>	Extract	Anti-inflammatory	Condensed tannins (catechins) and hydrolyzable tannins (gallic acid) / Ellagic acid and gallic acid	Araújo et al., 2014; falcão et al., 2019
<i>Schinopsis brasiliensis</i>	Extract	Anti-inflammatory	Gallic acid as chemical marker	Santos et al., 2018
<i>Duguetia furfuracea</i>	Extract	Anti-inflammatory	Dicentrinone (alkaloid isolated from chloroform fraction) / Phenols, flavonoids, and flavonols	Santos et al., 2018
<i>Myracrodruon urundeuva</i>	Extract	Anti-inflammatory	Chalcones, flavonoids, and tannins / Fraction enriched in chalcone (urundeuvin A, B and C)	Galvão et al., 2018; Viana; Bandeira; Matos, 2003
<i>Jatropha gossypifolia</i>	Extract	Anti-inflammatory	C-glycosylated flavonoids (isoorientin, orientin, vitexin, and isovitexin)	Xavier-santos et al., 2018
<i>Passiflora cincinnata</i>	Extract	Anti-inflammatory	Probably flavonoids	Lavor et al., 2018
<i>Kalanchoe brasiliensis and Kalanchoe pinnata</i>	Extract	Anti-inflammatory	Flavonoid glycosides derived from patuletin and eupafolin / Flavonoids glycosides, with nucleus of quercetin, patuletin, eupafolin and kaempferol	Araujo et al., 2019
<i>Abarema cochliacarpus</i>	Extracts and Fraction of ethyl acetate, aqueous fraction and butanolic fraction from extract	Anti-inflammatory and Healing	Proanthocyanidins ((+)-catechins) / (+)-catechin, catechin dimer and epicatechin dimer / Fraction of ethyl acetate (Catechins and condensed tannin polymers), aqueous fraction (catechins) and butanolic fraction (Polymers of tannins)	Silva et al., 2010a; sánchez-fidalgo et al., 2013); Silva et al., 2010b
<i>Auxemma oncocalyx</i>	Extract	Anti-inflammatory	Quinone fraction (oncocalixone A)	Ferreira et al., 2004
<i>Tabebuia aura</i>	Extract	Anti-inflammatory	Iridoides, flavonoids, terpenes and steroids	Reis et al., 2014
<i>Sideroxylon obtusifolium</i>	Extract Isolate	Anti-inflammatory	N-methyl- (2S, 4R) - trans - 4-hydroxy-L- proline	Aquino et al., 2017
<i>Cochlospermum regium</i>	Extract	Healing	Gallic acid, rutin, myricetin, morina and kaempferol	Arunachalam et al., 2019
<i>Cratylia mollis</i>	Extract	Anti-inflammatory	pCramoll e rCramoll	Silva et al., 2015
<i>Piptadenia stipulacea</i>	Extract	Anti-inflammatory	Flavonoids	Queiroz et al., 2010
<i>Caesalpinia pyramidalis</i>	Extract	Anti-inflammatory	Rutin	Santana et al., 2012

<i>Caesalpinia pulcherrima</i>	Extract	Anti-inflammatory	Galactomannan isolated	Cunha jácome marques et al., 2019
<i>Ximenia americana</i>	Extract	Anti-inflammatory	Caffeic acid and quercitrin	Silva et al., 2018
<i>Typha domingensis</i>	Extract	Anti-inflammatory	Umbeliferona isolated	Vasconcelos et al., 2009
<i>Parapiptadenia rigida</i>	Extract	Anti-inflammatory	Condensed tannins (catechins) and hydrolyzable tannins (gallic acid)	Araújo et al., 2014
<i>Psidium guajava</i>	Extract	Anti-inflammatory	Condensed tannins (catechins) and hydrolyzable tannins (gallic acid)	Araújo et al., 2014
<i>Mansoa hirsuta</i>	Extract	Anti-inflammatory	Triterpenes	Pereira et al., 2022
<i>Mimosa pteridifolia</i>	Extract	Anti-inflammatory	Tannins, Flavonoids, Saponins	Silva et al., 2020
<i>Mimosa verrucosa</i>	Extract	Anti-inflammatory	Tannins, Flavonoids	Silva et al., 2020
<i>Mimosa tenuiflora</i>	Extract	Anti-inflammatory	Tannins, Flavonoids	Silva et al., 2020

Essential Oils and Fatty Acids. Source: Authors.

Plants essential oil production is directly related to intrinsic factors with plants genetic inherit expression, as well as extrinsic factors, such biotic and abiotic factors, which also exerts influence on gene expression, depending on the intensity of those factors (Hao; Xiao, 2020; Koyama et al., 2019). As seen in table 1, the essential oil from *Croton* generais the most studied, there is registers of 4 *Croton* species with occurrence in Caatinga biome, those species are *C. adamantinus*, *C. zehntneri*, *C. argyrophyllus* and *C. rhamnifolioides* as for other genera species, we've found reports about *Lippia gracilis*, *Hyptis spicigera* and *Eugenia stipitate*, the phytochemical analysis from those species have shown a predominance of monoterpenes and sesquiterpenes on its essential oils (table 1).

Terpenes can be produced in plants in different organs and need to be stored until the time of its release to ensure no volatilization of its components, being stored in most diverse plant organs, like fruits, flowers, leaves, roots and stem bark (Pichersky & Gershenzon, 2002). Terpenes are a class of secondary metabolites from the mevalonic acid and methylerythritol phosphate (MEP) pathways, and they are synthesized from primary metabolism products, like Acetyl-CoA, pyruvate and 3-phosphoglycerate (Vranová et al., 2013). The terpenes classification is due to the number of carbons on its structure, the monoterpenes possess 10 carbon atoms (C10), sesquiterpenes (C15), diterpenes (C20), triterpenes (C30), Tetraterpene (C40) (Xu et al., 2017). Due to that, there is several different compounds that can be studied and applied on pharmacological research (Bouyahya et al., 2020).

Since triterpenes are a group of secondary metabolites that have already shown biological activities such as anti-inflammatory, antinociceptive, hepatoprotective, sedative, antioxidant, antiallergic, antiangiogenic, antimicrobial and high anticancer selectivity (Silva et al., 2020).

The study performed with *L. gracilis* showed a significant difference in the production of chemical constituents of the oil, obtaining a difference of up to 10%, when it was subjected to water stress; in addition, it was guaranteeing the appearance of a new element, Carvacrol, which was not present when the plant was not under stresses (Parisotto-Peterle et al., 2020).

Carvacrol is a phenolic monoterpene present in abundance in oregano species and guarantees the characteristic aroma of the herb (Stojanović et al., 2019). Studies show its efficacy as an anti-inflammatory agent and healing by decreasing proinflammatory cytokines, COX-2, reactive oxygen species and nitrogen, in addition to ensuring an increase in cell motility which therefore will generate an efficient healing process (Avola et al., 2020).

The literature shows that *Croton* species present in Caatinga, such as *C. adamantinus*, *C. zehntneri*, *C. argyrophyllus*, share a similar chemical profile highlighting the presence of bicyclogermacrene and Caryophyllene (both sesquiterpenes), and cineole (a monoterpene) in different concentrations, still it may represent signature compounds from the genus in the Caatinga biome, and the difference in the concentration may be due to environmental influences, since the samples were studied by different researches. Bicyclogermacrene is the major component of *C. argyrophyllus* (14.6%) (Esteves et al., 2005), as for *C. adamantinus* it represents 8.06% from the oil composition, those species showed promising results *in vivo* anti-inflammatory assays, however, this compound has not been isolated for biological tests and it is suggested that the modulation of inflammation is not exclusively related to this compound, but a synergy between other compounds such as caryophyllene (Ascari et al., 2019).

Caryophyllene is present in three *Croton* species and in *E. stipitate*, and has already proven its role as an anti-inflammatory agent, being able to induce a decrease in pro-inflammatory cytokines, while increasing anti-inflammatory cytokines (Costa et al., 2020; Martim et al., 2021; Parisotto-Peterle et al., 2020), still, its healing action is not well investigated, however there was a study that suggested that the action of caryophyllene in the healing process is not direct, but rather by the attenuation of inflammation caused in the tissue, which consequently leads to cell proliferation (Stojanović et al., 2019).

Studies with *C. rhamnifolioides* (Martins et al., 2017) and *H. spicigera* (Takayama et al., 2011) explored the anti-inflammatory pathways, and the results had shown that its effect is due to the 5-lipoxygenase inhibition, impairing the formation of leukotriene B₄, leukotriene C₄, leukotriene D₄ and leukotriene E₄ in the arachidonic acid pathway, as well as the inhibition of COX, formation of PGE₂ and Tromboxane B₂. In addition, there is a block in the degranulation of the monocyte preventing the release of histamine and triggering the entire inflammatory cascade promoted by it.

The healing action established by the terpenoid substance occurs in the cutaneous tissue through an increase in the deposition of extracellular matrix, stimulating an increase in fibroblasts and collagen production (Ximenes et al., 2013). The 1,8-cineole, associated with trans-anethole present in *Croton* species, promotes a potentiation in the healing process, which in turn occurs faster (Cavalcanti et al., 2012). In gastric tissue the curative action of 1,8-cineole induces an increasing of the epidermal growth factor (EGF) receptors expression, as well as an increase in COX-2 activity, which contributes to the prostaglandins synthesis that guarantees a second line of defense to replace the absence of temporary COX-1 (Takayama et al., 2011).

The essential oil from *Croton zehntneri*, presented a healing activity by reducing edema, increase in the deposition of extracellular matrix and tissue remodeling, that results in the restoration of its tissue integrity and progressive wound closure (Cavalcanti et al., 2012). Since the trans-anethole is the major compound present in *C. zehntneri*, the literature stands that the anti-inflammatory application is linked to a transformation of anethole through oxidation and epoxidation reactions in hepatic metabolism. This metabolization consists of hydroxylations in the double propenyl bond between carbons 1 and 2, which results in the most marked inhibition of the COX-2 enzyme as a main mechanism of anti-inflammatory action, just as it occurs in the standard non-steroidal anti-inflammatory drug Indomethacin (Freire et al., 2005). In addition, another study correlates the action of trans-anethole in the direct and indirect inhibition of the NF- κ B pathway by modulating the production of TNF- α and the release of NO, but there was no reduction in IL-6, which also occurs through the pathway of NF- κ B. This fact is due to the involvement of matrix metalloproteinase, matrix metalloproteinase 9 (MMP-9), that regulates several metabolic pathways, and it can activate TNF- α , but not IL-6 (Kang et al., 2013).

Triterpene 3 β , 6 β , 16 β -trihydroxylup-20 (29)-ene (TTHL) isolated from *Combretum leprosum* and showed *in vivo* healing effect. The literature shows that in the cultivation of mononuclear cells, TTHL did not induce the release of pro-inflammatory cytokines such as IL-10 and TNF- α , however in high concentrations it presented toxic effects, but without altering the functioning of the human nuclear polymerase enzyme (Lacouth-Silva et al., 2015). Due to the anti-inflammatory action, the healing process of TTHL was quite significant, since there was stimulation of angiogenesis, collagen production by fibroblasts and the migration of keratinocytes, possibly because it acts on the production of vascular endothelial growth factor (VEGF) and transforming growth factor- β (TGF- β) (Nascimento-Neto et al., 2015).

Even though *L. gracilis*, *H. spicigera* and *E. stipitate* aren't studied through the healing optics, there is evidence in the literature, that the compounds present in those species, such as Thymol, α -Pinene, and Guaiaol also induces a healing activity (Najafloo et al., 2020; García-Salinas et al., 2020; Pivetta et al., 2018). Moreover, it has antimicrobial activity (Kazemi-Pasarvi et al., 2020), antioxidant (Gursul et al., 2019), anticarcinogenesis (Li et al., 2017), and cardioprotective (El-Marasy et al., 2020). α -Pinene is effective against inflammation by suppressing activation of the MAPK/NF- κ B pathway, which consists in the inhibition of mitogen-activated protein kinases (MAPKs), and preventing extracellular signal-regulated protein kinase phosphorylation (ERK), as well, c-Jun NH2-terminal kinase (JNK). Another pathway that α -Pinene affects is the nuclear factor kappa B (NF- κ B) pathway, decreasing the levels of I κ kinase (IKK) in the cytosol and of the phosphorylated I κ B and the NF- κ B in the nucleus (Kim et al., 2015). Together, these disruptive effects in the metabolic cells can benefit for the healing activity, indicating that, besides the anti-inflammatory effect, those species may present healing activity as well.

Plant Extracts

Talking about the plant extracts, our review highlights the presence of compounds belonging to several classes, such as phenolic compounds, tannins and flavonoids, as seen in table 1. These compounds are widely found in fruits and plants and have similar therapeutic potentials, such as anti-inflammatory activity (Bai et al. 2021). It is also worth to note that, the extracts are more applied in the anti-inflammatory activity rather than wound healing activity, and we also observed that the phytochemical profile is restricted to class level.

Phenolic compounds are chemical structures that have hydroxyls and aromatic rings, in simple or polymer forms, which give them a strong antioxidant action. In addition, it is described in the literature with several other biological actions: anticarcinogenic, anti-inflammatory, antimicrobial, among others. These compounds constitute a very diverse group of phenols, among them, flavonoids, phenolic acids, tannins, and tocopherols stand out as the most common phenolic antioxidants from natural sources, in free form or linked to sugars (glycosides) and proteins. They are bioactive substances and typically occur in small concentrations in food and have beneficial health effects (Souza et al., 2018; Moraes et al., 2019; Rasera et al., 2020)

One example of phenolic compound is the gallic acid, an important phenolic acid found in natural sources. In addition to its antioxidant action, it is described in the literature with several biological activities, one of them is anti-inflammatory activity. Studies report that the anti-inflammatory action of this compound is related to the interference in the functioning of polymorphonuclear leukocytes (PMNs). Its action eliminates superoxide anions, inhibits the release and activity of myeloperoxidase, interferes in the NADPH-oxidase formation and activity, as well as its action inhibits the production of pro-inflammatory cytokines, such as IL-6 and TNF- α (Singh et al., 2004; Kim et al., 2006; Badhani et al., 2015; Gao, 2019). These studies confirm the therapeutic potential of gallic acid, which may represent several mechanisms of action of several phenolic compounds, and its importance in inflammatory processes, which in turn is strongly present in Caatinga plant extracts.

The flavonoids represent one of the most important and diversified phenolic groups among products of natural origin. Its structural diversity can be attributed to the level of oxidation and variations in the basic carbon skeleton, promoted by reactions of alkylation, glycosylation or oligomerization. Several biological activities are attributed to this class of polyphenols

and one of them is anti-inflammatory activities. According to studies, the anti-inflammatory action of flavonoids acts by modulating cells involved with inflammation, such as inhibiting the proliferation of T lymphocytes and the production of pro-inflammatory cytokines (TNF- α and IL-1), as well modulating the activity of enzymes from the arachidonic acid pathway, such as phospholipase A2, cyclooxygenase and lipoxygenase, in addition to the modulating of nitric oxide-forming enzyme, and the induced nitric oxide synthase (iNOS). (Reginato et. al., 2015). These studies report the mechanism of action of flavonoids and confirm that this natural substance has great therapeutic potential, especially in inflammatory processes.

The tannins are commonly defined as soluble polyphenolic compounds, and when in contact with water, and this gives it the ability to precipitate proteins. This compound is described in the literature with several biological properties, one of which is the anti-inflammatory action. The anti-inflammatory mechanism of action of tannins is often related to the inhibition of NO, TNF- α and production of IL-6 through its ability to precipitate proteins, thus affecting functions but also due to the ability to bind to proteins and other macromolecules, tannins can show toxic effect (Liu et. al., 2015; Costa et. al., 2020). Thus, these studies confirm the anti-inflammatory action of tannins through its mechanism of action.

Even though inflammatory diseases are the basis of several pathologies, an adequate and universal therapy for their treatment has not been found yet. Based on the studies cited above, plants compounds present themselves as a promising therapeutic alternative for inflammatory processes, in addition to their beneficial effects on health species (Moraes et al., 2019; Rasera et. al., 2020). It is worth to note that, only five research were carried out evaluating the healing process since the beginning of the last decade 10 years, using ulcer healing methodologies, and both authors associated the healing process with the anti-inflammatory effect from extracts compounds.

4. Conclusion

Caatinga species are studied in the light of anti-inflammatory process, which is the foundation of several disease, since even the two studies involving the influence of plant extracts with healing process is explained due to their capacity of modulating inflammation pathways, indicating that those species may be studied about the healing process as well. Moreover, we noticed that extracts and isolated compounds from extracts are more frequently studied rather than essential oils and fatty acids from fixed oils. It may be due to the Caatinga plant species particularity of fructification and blooming only in a few months during the year, and those organs, are the most common source to obtain oils, and since leaves and bark are available most part of the year, especially the bark, thus is more common to obtain extract and infusion from those organs, still, the chemical characterization from the plant extracts demands more research to better understand the mechanism of action behind the molecules.

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