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Ethnopharmacology of Anacardiaceae R. Br. from Northeast Brazil

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ABSTRACT

Species of the Anacardiaceae are commonly used in traditional Brazilian medicine, thus, the aim of this review was to research the species of Anacardiaceae and their respective ethnopharmacological uses in Northeast Brazil. Manuscripts published from 2010 to 2019 were searched and only species with proven occurrence in the Northeast and applied in this region as medicinal were included in this study. There were analyzed 97 articles about the of 14 species. *Spondias* was the most diverse genus, with four species, followed by *Anacardium* and *Astronium*, both with three species. Most plants are used to treat diseases of the digestive, respiratory, skin and subcutaneous tissue systems, mainly for their anti-inflammatory, antibiotic, analgesic and healing properties. Ceará was the state with the highest number of species while Sergipe was the state with the lowest number of listed species and analyzed articles. *Astronium urundeuva* showed the greatest versatility of uses and the highest index of relative importance (2.0), followed by *Anacardium occidentale* and *Schinus terebinthifolia* with indexes of 1.55 and 0.86, respectively. It is noticed that the Northeastern communities preserve important knowledge about the ethnopharmacology of Anacardiaceae, and this knowledge is important to direct new ethnoecological and pharmacological studies.
Keywords: Aroeira. Medicinal plants. Pharmacological properties.

Etnofarmacologia de Anacardiaceae R. Br. no Nordeste do Brasil

RESUMO

Espécies de Anacardiaceae são comumente empregadas na medicina tradicional brasileira, assim, objetivou-se neste estudo, levantar as espécies de Anacardiaceae e seus respectivos usos etnofarmacológicos no Nordeste do Brasil. Foram consultados manuscritos publicados entre 2010 e 2019 e incluídas neste estudo apenas as espécies com ocorrência comprovada no Nordeste e aplicadas nessa região como medicinal. Foram analisados 97 artigos, revelando o uso de 14 espécies. *Spondias* foi o gênero mais diverso, com quatro espécies, seguido por *Anacardium* e *Astronium*, ambos com três espécies. A maioria das plantas são usadas no combate a doenças dos sistemas digestivo, respiratório, da pele e do tecido subcutâneo, principalmente pelas suas propriedades anti-inflamatórias, antibióticas, analgésicas e cicatrizantes. O Ceará foi o estado representado pelo maior número de espécies enquanto Sergipe foi o estado com o menor número de espécies listadas e de artigos analisados. *Astronium urundeuva* apresentou

maior versatilidade de usos e maior índice de importância relativa (2,0), seguida por *Anacardium occidentale* e *Schinus terebinthifolia* com índices 1,55 e 0,86, respectivamente. Percebe-se que as comunidades nordestinas preservam importantes saberes sobre a etnofarmacologia de Anacardiaceae, sendo esses conhecimentos importantes para direcionarem novos estudos etnoecológicos e farmacológicos.
Palavras-chave: Aroeira. Plantas medicinais. Propriedades farmacológicas.

INTRODUÇÃO

The application of plants for therapeutic purposes is one of the main practices disseminated by popular culture, and this knowledge is related not only to the medicinal uses of plants, but also their cultural significance and the sustainable management of flora resources. Wherefore, ethnobotany emerges as a tool for investigating, interpreting and retrieving this knowledge that is passed on over generations, giving rise to discussions about the potential and limitations of botanical applications in different local communities (CABALLERO, 1979; BADKE et al., 2012; STRACHULSKI; FLORIANI, 2013; CAVALCANTI; SILVA, 2014).

The Northeast Brazil has a great biological and cultural diversity, and its flora is investigated in different fields of science. In this region, studies about medicinal plants properties stand out, which seek to investigate the patterns of dissemination of traditional knowledge and the applications of plant resources with therapeutic indications, being fundamental for the adoption of conservationist behaviors (CAVALCANTI; ALBUQUERQUE, 2013; SILVA et al., 2017; GOMES et al., 2016; ALBUQUERQUE et al., 2020).

The family Anacardiaceae R. Br. covers approximately 81 genera and 800 species with tropical and subtropical distribution, including species of great economic importance, whether for their food, wood, medicinal or ornamental potential, and therefore are frequently cultivated (PICKEL, 2008; SOUZA; LORENZI, 2008; TIANLU; BARFOD, 2008; PELL et al., 2011). In Brazil, 64 species and 15 genera are recorded, being *Schinus* L. (12 species), *Spondias* L. (11 spp.), *Astronium* Jacq. (10 spp.) and *Anacardium* L. (9 spp.) the most diverse (SILVA-LUZ et al., 2020).

Phytochemical analyzes and studies on the biological activities of the compounds present in Anacardiaceae species have revealed the chemical-pharmacological potential of this group and, although important promising substances, such flavonoids, terpenes, steroids, xanthones and phenolic compounds frequently mentioned in these studies, gaps on phytochemistry of these species need more investigation (CORREIA et al., 2006).

There are records of the medicinal use of species of this group in all the regions of Brazil. North region (BATISTA; BARBOSA, 2014; VÁSQUEZ et al., 2014; FLOR; BARBOSA, 2015; FERREIRA et al., 2016; GÓIS et al., 2016), Central-West region (CUNHA; BORTOLOTTO, 2011; SOUZA et al., 2016; DAVID; PASA, 2015), Southeast region (ALBERTASSE et al., 2010; COSTA; MAYWORM, 2011; PINTO SOBRINHO et al., 2011; ALVES; POVH, 2013), South region (VENDRUSCOLO; MENTZ, 2006; MIRANDA; HANAZAKI, 2008; SILVA et al., 2015a) and in the Northeast region. Thus, this review had as main objective to list the species of the Anacardiaceae family applied in the traditional medicine of Northeast Brazil and as secondary objective it was sought to identify the relative importance of these species in the ethnopharmacology of the region from the therapeutic versatility by which these plants are used.

MATERIAL AND METHODS

The development of this review was searched articles available in the SciELO, Science Direct, PubMed and Capes Periodicals databases. The Anacardiaceae was used as the main descriptor, being combined with traditional knowledge, ethnobotany, ethnopharmacology, medicinal plants, pharmacological properties, therapeutic properties, traditional medicine, Northeast and popular use. Searches were carried out for field studies in the Brazilian Northeast, and which revealed the medicinal use of at least one species of Anacardiaceae, following the time frame from 2010 to 2019. Articles that did not accurately reveal local knowledge about the properties of plants, research with a purely pharmacological focus, bibliographic reviews and unpublished dissertations were excluded from the results.

The scientific name of the species (including the synonymy) followed the Brazilian Flora (2020), as well as only confirmed occurrence species for the Northeast region of Brazil were included in this work. The data contained in the investigated manuscripts were organized in spreadsheets, and the main information was extracted: studied area, medicinal indications of the mentioned species and also details about these applications, as long as they are clearly reported in the article. The properties were listed according to the medicinal uses recorded in the articles, and this information was used to determine the importance of the species, according to Bennett and Prance (2000). The Relative Importance is obtained by the formula RI= NSC + NP, where NSC is the number

of body systems and NP is the number of medicinal properties, where NSC= NSCE/NSCEV and NP= NPE/NPEV. The NSCE represents the number of body systems treated by a given species, NSCEV is the number of body systems treated by the most versatile species, NPE the number of properties attributed to a given species and NPEV the number of properties attributed to the most versatile species (CAMPOS; ALBUQUERQUE, 2021). The healing properties of the species were categorized according to the body systems listed in the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (WHO, 2021).

RESULTS AND DISCUSSION

Diversity and medicinal applications

There were analyzed 97 manuscripts revealed the use of 14 species and seven genera of Anacardiaceae in traditional medicine in Northeast Brazil (Table 1). The genus *Spondias* was the most diverse, being represented by four species, followed by *Anacardium* and *Astronium*, both with three species. The plants of this family are used in the Northeast for the treatment of many diseases, classified in 14 body systems according to the ICD-10, with 12 species applied to treat diseases of the digestive system, nine species used to for diseases in the respiratory system and seven species in the treatment of diseases of the skin and subcutaneous tissue, these being the most frequent uses, while parasitic diseases; pregnancy, childbirth and the puerperium; and diseases of the eye and adnexa had the fewest number of citations (Table 1). In a synopsis by Agra et al., (2007), which listed the plant species used as a therapeutic resource in the northeast region, 483 species belonging to 79 botanical families were recorded and Anacardiaceae was among the most diverse families, being represented by 11 species.

Table 1 – Anacardiaceae species used in traditional medicine in Northeast Brazil. Body systems according to the ICD-10.

Species	Medical use (ICD-10)	Plant part used	Northeast State	Reference
Anacardium humile A.St.-Hil.	Skin and subcutaneous tissue diseases; Respiratory system diseases.	stem bark;	CE	Silva et al., (2019)
Anacardium occidentale L.	Endocrine, nutritional and metabolic diseases; Certain infectious and parasitic	stem bark; leaf; fruit; pseudocarp	AL, BA, CE, MA, PB, PE, PI, RN, SE	Albergaria et al., (2019); Almeida et al., (2010); Almeida Neto et al., (2015); Andrade et al., (2012, 2018), Araújo; Lemos, (2015); Bandeira et al., (2018); Baptistel et al., (2014);

	diseases; Skin and subcutaneous tissue diseases; Injury, poisoning and certain other consequences of external causes; Neoplasms; Circulatory system diseases; Digestive system diseases; Genitourinary system diseases; Blood and blood-forming organs diseases and certain disorders involving the immune mechanism; Nervous system diseases; Musculoskeletal system and connective tissue diseases; Respiratory system diseases.			Bastos et al., (2018); Brito et al., (2015, 2018a); Bitu et al., (2015); Cartaxo et al., (2010); Castro et al., (2016); Cavalcante e Silva, (2014); Coelho et al., (2016); Conceição et al., (2011); Costa e Marinho, (2016), Cunha Lima et al., (2012); Dantas e Torres, (2019); Freitas et al., (2011, 2012, 2015); Gomes e Bandeira, (2012); Guerra et al., (2010); Leite et al., (2013, 2015); Lima, (2015); Lopes et al., (2016); Lós et al., (2012); Macêdo et al., (2015); Marinho et al., (2011); Medeiros et al., (2019); Nascimento e Conceição, (2011); Oliveira et al., (2010a,b, 2018); Oliveira Júnior et al., (2012); Paulino et al., (2012); Penido et al., (2016); Ribeiro et al., (2013, 2014); Rodrigues; Andrade, (2014); Santos et al., 2012, 2016, 2019a,b); Santos; Silva, (2015); Saraiva et al., (2015); Silva et al., (2012a,b, 2014, 2015b, c,d, 2016, 2019); Souza et al., (2013); Teixeira et al., (2014); Vieira et al., (2015).
Anacardium spruceanum Benth. ex Engl.	Skin and subcutaneous tissue diseases.	stem bark	MA	Rego et al., (2016)
Astronium fraxinifolium Schott	Skin and subcutaneous tissue diseases; Circulatory system diseases; Digestive system diseases; Genitourinary system diseases; Musculoskeletal system and connective tissue diseases; Respiratory system diseases.	stem bark	CE, PB, PE, PI	Baptistel et al., (2014); Cartaxo et al., (2010); Conceição et al., (2011); Macêdo et al., (2015, 2018); Saraiva et al., (2015); Silva et al., (2019)
Astronium graveolens Jacq.	Digestive system diseases.	*	PB	Bandeira et al., (2018).
Astronium urundeuva Engl.	Endocrine, nutritional and metabolic diseases; Certain infectious and parasitic diseases; Eye and adnexa diseases; Skin and subcutaneous tissue diseases; Pregnancy, childbirth and the puerperium; Injury,	stem bark; root; leaf; seed	AL, BA, CE, MA, PB, PE, PI, RN	Aguiar e Barros, (2012); Albergaria et al., (2019); Almeida et al., (2010, 2015); Almeida Neto et al., (2015); Alves et al., (2016); Andrade et al., (2018); Araújo e Lemos, (2015); Arévalo-Marín et al., (2015); Bandeira et al., (2018); Baptistel et al., (2014); Bastos et al., (2018); Bitu et al., (2015); Brito et al., (2018ª); Carneiro et al., (2016); Cartaxo et al., (2010); Cavalcanti, Silva, (2014); Cordeiro et al., (2017)

	poisoning and certain other consequences of external causes; Neoplasms; Circulatory system diseases; Digestive system diseases; Blood and blood-forming organs diseases and certain disorders involving the immune mechanism; Genitourinary system diseases; Nervous system diseases; Musculoskeletal system and connective tissue diseases; Respiratory system diseases.			Cordeiro e Felix, (2014); Costa e Marinho, (2016), Cunha et al., (2015); Dantas e Torres, (2019); Ferreira Junior et al., (2011); Freitas et al., (2012, 2015); Gomes et al., (2017); Leite et al., (2013, 2015); Lima, (2015); Linhares et al., (2014); Lopes et al., (2016); Lós et al., (2012); Lucena et al., (2011); Macedo et al., (2018); Marinho et al., (2011); Marreiros et al., (2015); Medeiros et al., (2019a); Nascimento et al., (2013), Nascimento e Conceição, (2011); Oliveira et al., (2010a, 2012); Paulino et al., (2012); Penido et al., (2016); Rego et al., (2016); Reis et al., (2017); Ribeiro et al., (2013, 2014); Roque et al., (2010); Santos et al., (2012, 2018a, 2019b); Santos; Silva, (2015); Saraiva et al., (2015); Silva et al., (2012b, 2015b,d, 2016, 2019); Silva; Freire, (2010); Sousa et al., (2012); Souza et al., (2016); Zank et al., (2015).
Mangifera indica L.	Endocrine, nutritional and metabolic diseases; Digestive system diseases; Respiratory system diseases.	leaf	BA, CE, MA, PB, PE, PI, RN	Almeida Neto et al., (2015); Andrade et al., (2018); Baptistel et al., (2014); Cartaxo et al., (2010); Coelho et al., (2016); Cunha Lima et al., (2012); Freitas et al., (2011); Gomes e Bandeira, (2012); Lima (2015); Linhares et al., (2015); Lopes et al., (2016); Oliveira; Rocha (2016); Nascimento e Conceição, (2011); Penido et al., (2016); Gomes e Bandeira, (2012); Rego et al., (2016); Rodrigues e Andrade, (2014); Santos et al., (2012, 2016, 2019a); Silva et al., (2012b, 2015b, 2019).
Schinopsis brasiliensis Engl.	Digestive system diseases; Genitourinary system diseases; Blood and blood-forming organs diseases and certain disorders involving the immune mechanism; Musculoskeletal system and connective tissue diseases; Respiratory system diseases	stem bark; leaf	BA, CE, PB, PE	Albergaria et al., (2019); Almeida et al., (2010); Arévalo-Marín et al., (2015); Ferreira Junior et al., (2011); Gomes e Bandeira, (2012); Marreiros et al., (2015); Ribeiro et al., (2013, 2014); Silva et al., (2014); Souza et al., (2016).
Schinus terebinthifolia Raddi	Eye and adnexa diseases; Skin and subcutaneous tissue diseases; Digestive system diseases;	stem bark; leaf	AL, BA, CE, MA, PB, PE, PI, RN, SE	Araújo et al., (2015a); Borges e Bautista, (2010); Brito et al., (2015); Cabral; Maciel, (2011); Gomes e Bandeira, (2012); Griz et al., (2017); Guerra et al., (2010); Lima et al.,

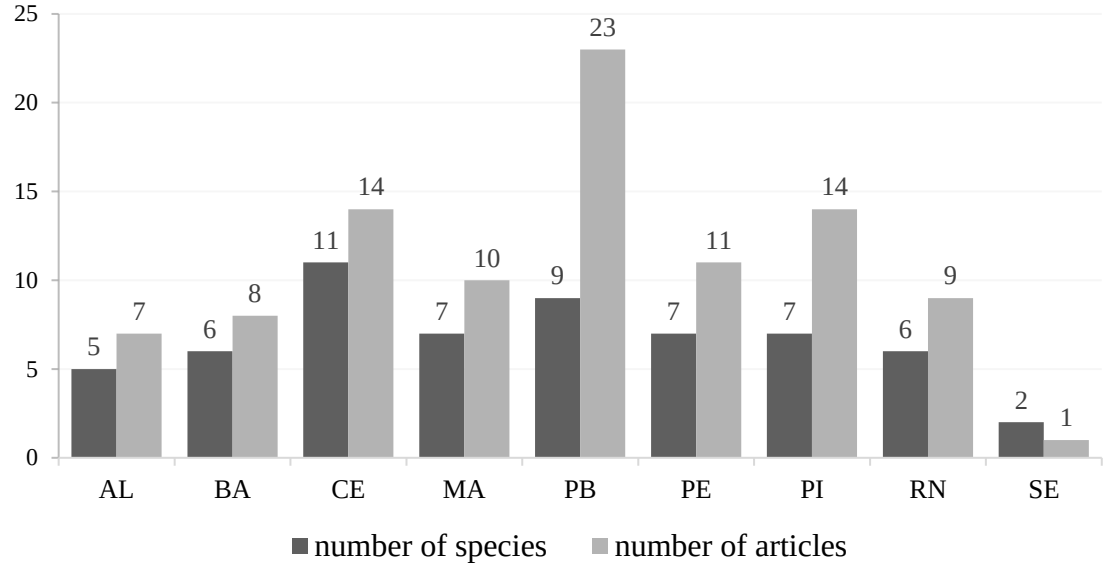
	Genitourinary system diseases; Blood and blood-forming organs diseases and certain disorders involving the immune mechanism; Musculoskeletal system and connective tissue diseases; Respiratory system diseases.			(2016); Lopes Sobrinho et al., (2018); Medeiros et al., (2019a); Oliveira et al., (2010b, 2018); Oliveira e Lucena, (2015); Reis et al., (2017); Rodrigues; Andrade, (2014); Santos et al., (2012).
Spondias dulcis Parkinson	Injury, poisoning and certain other consequences of external causes; Digestive system diseases; Respiratory system diseases.	leaf, fruit	CE	Cartaxo et al., (2010).
Spondias mombin L.	Endocrine, nutritional and metabolic diseases; Neoplasms; Circulatory system diseases; Digestive system diseases; Blood and blood-forming organs diseases and certain disorders involving the immune mechanism.	stem bark; fruit; seed	CE, PB, PI, RN	Baptistel et al., (2014); Cartaxo et al., (2010); Cordeiro e Felix, (2014); Freitas et al., (2011); Oliveira et al., (2010a).
Spondias purpurea L.	Endocrine, nutritional and metabolic diseases; Circulatory system diseases; Digestive system diseases; Respiratory system diseases.	stem bark; leaf; fruit	AL, BA, CE, MA, PI, RN	Baptistel et al., (2014); Cartaxo et al., (2010); Castro et al., (2016); Coelho et al., (2016), Freitas et al., (2012); Lopes et al., (2016); Macêdo et al., (2013); Nascimento e Conceição, (2011); Oliveira et al., (2010, 2015); Ribeiro et al., (2014); Silva et al., (2012b, 2019).
Spondias tuberosa Arruda	Digestive system diseases; Genitourinary system diseases; Blood and blood-forming organs diseases and certain disorders involving the immune mechanism; Musculoskeletal system and connective tissue diseases; Pregnancy, childbirth and the puerperium.	stem bark; root bark; leaf	AL, CE, PB, PE	Albergaria et al., (2019); Almeida et al., (2010); Almeida Neto et al., (2015); Arévalo-Marín et al., (2015); Bastos et al., (2018); Coelho et al., (2016); Ferreira Junior et al., (2011); Freitas et al., (2011, 2012); Marinho et al., (2011); Marreiros et al., (2015); Medeiros et al., (2019[a]); Oliveira et al., (2010[a]); Ribeiro et al., (2013, 2014); Saraiva et al., (2015); Silva et al., (2014); Souza et al., (2016).

Tapirira guianensis Aubl.	Skin and subcutaneous tissue diseases.	stem bark	MA	Rego et al., (2016).

Northeast States: Al: Alagoas, BA: Bahia, CE: Ceará, MA: Maranhão, PB: Paraíba, PE: Pernambuco, PI: Piauí, RN: Rio Grande do Norte, SE: Sergipe. *Data not reported in the articles.

Analyzing the distribution of species and the number of articles in northeastern state (Figure 1), a higher incidence of records of Anacardiaceae in the traditional medicine was noticed from Ceará state (11 spp.), while in Sergipe only two species were listed, having this state the lowest number of representatives. Sergipe was also the state with the lowest number of articles analyzed, as only one article found mentioned the therapeutic application of Anacardiaceae, while most of the research included in this study was carried out in Paraíba state (23 articles), while for the other states they were found between five and seven articles. It is possible to assume that this difference among the numbers of research cannot be justified by the low diversity of medical applications of the Anacardiaceae family representatives in Sergipe, but only an indication of the need for new ethnobotanical investigations in the state, since among the 14 species listed here, 13 occur in Sergipe, according to Brazilian Flora (2020).

Figure 1 – Distribution of Anacardiaceae species used for medicinal purposes and the number of articles per state in Northeast Brazil.



Based on the number of medicinal properties and the number of treated body systems, the species with the greatest versatility of uses was *Astronium urundeuva* Engl., thus being the species with the highest index of Relative Importance (2.0), followed by *Anacardium occidentale* L. and *Schinus terebinthifolia* Raddi, with indices of 1.55 and

0.86, respectively (Table 2). Among the 14 species of Anacardiaceae listed here, only *Anacardium occidentale* and *Schinus terebinthifolia* are included in the National List of Medicinal Plants of Interest to the Unified Health System in Brazil (RENISUS), which aims to direct investigations into the curative properties of these species and disseminate the use of medicinal plants in the Brazilian population (Brazil 2009).

In a systematic review carried out by Campos and Albuquerque (2021) that focused on the determination of Conservation Priority Indicators (CPI) of native tree species used in traditional medicine in northeastern Brazil, eight representatives of Anacardiaceae were listed, being this family the third most representative. The index calculated by the authors considered, in addition to the relative importance, the inclusion of plants in RENISUS and their use as raw material for the production of medicines registered by the Brazilian Health Regulatory Agency (ANVISA). Among the 147 species surveyed by the authors, four representatives of Anacardiaceae are among the 15 species with the highest CPI values: *Anacardium occidentale*, *Schinus terebinthifolia*, *Astronium urundeuva* and *Spondias mombin* L. Campos and Albuquerque (2021) and Melo et al., (2009) emphasize that the high versatility of medical uses of *A. urundeuva* and its variety of ethnobotanical applications in northeastern Brazil, especially in the exploitation of its trunk, showing the need for priority actions aimed at the conservation of this species.

Table 2- Relative importance of Anacardiaceae species used in traditional medicine in Northeast Brazil.

Species	**NSCE**	**NSCEV**	**NSC**	**NPE**	**NPEV**	**NP**	**RI**
Anacardium humile A.St.-Hil.	2	14	0.14	2	59	0.03	0.18
Anacardium occidentale L.*	12	14	0.86	41	59	0.69	1.55
Anacardium spruceanum Benth. ex Engl.	1	14	0.07	1	59	0.02	0.09
Astronium fraxinifolium Schott	6	14	0.43	16	59	0.27	0.70
Astronium graveolens Jacq.	1	14	0.07	2	59	0.03	0.11
Astronium urundeuva Engl.	14	14	1.00	59	59	1.00	2.00
Mangifera indica L.	3	14	0.21	15	59	0.25	0.47
Schinopsis brasiliensis Engl.	5	14	0.36	20	59	0.34	0.70
Schinus terebinthifolia Raddi*	7	14	0.50	21	59	0.36	0.86
Spondias dulcis Parkinson	3	14	0.21	6	59	0.10	0.32
Spondias mombin L.	5	14	0.36	8	59	0.14	0.49
Spondias purpurea L.	4	14	0.29	11	59	0.19	0.47
Spondias tuberosa Arruda	5	14	0.36	7	59	0.12	0.48
Tapirira guianensis Aubl.	1	14	0.07	1	59	0.02	0.09

NSCE: number of body systems treated by a given species; NSCEV: the total number of body systems treated by the most versatile species; NSC: number of body systems; NPE: number of properties attributed to a given species; NPEV: total number of properties attributed to the most versatile species; NP: number of properties; RI: Relative Importance. *Presence in the RENISUS list.

Anacardium humile A.St.-Hil. is used in traditional Northeastern medicine only in the state of Ceará, for the treatment of diseases associated with the respiratory system and as a healing agent (Table 1). Only the stem bark was mentioned in its ethnopharmacological applications and, although no laboratory tests were found in the literature that evidenced the medicinal action of extracts from this plant part, some studies involving extracts from the leaves and fruits of this species were found, showing biological properties: gastroprotective (LUIZ-FERREIRA et al., 2010), hypoglycemic (URZÊDA et al., 2013), antimicrobial (MONTARANI et al., 2012; ROYO et al., 2015; MAIA et al., 2016) and anthelmintic (NERY et al., 2010). Also identified as a medicinal plant in other regions of Brazil (PINTO et al., 2013; GONÇALVES; PASA, 2015; MESSIAS et al., 2015; MESQUITA; TAVARES-MARTINS, 2018), the leaves and bark of *A. humile* has important chemical constituents, as tannins, flavonoids, alkaloids, saponins and retinoids (LUIZ-FERREIRA et al., 2008, 2010; NERY et al., 2010; ROYO et al., 2015), besides to mineral macronutrients such as K, P and Mg (PORTO et al., 2016) and vitamin C (ROCHA et al., 2013), which may be associated with its medicinal effects.

Anacardium occidentale (figure 2) is generally consumed *in natura* or on processed form, and the stem bark, leaves and their fruits and pseudocarps are used in traditional Northeastern medicine in the treatment of many diseases (Table 1). This species has its medicinal use registered in all the Northeast states, mainly for its anti-inflammatory, antibiotic, antidiabetic, healing potential and for treating the symptoms of respiratory system diseases. Several studies infer the biological properties of "cashew", as antioxidant (BASKAR et al., 2019; DUANGJAN et al., 2019), anti-inflammatory (OLAJIDE et al., 2013; MIRANDA et al., 2019; SIRACUSA et al., 2020), antifungals (UDOH et al., 2019), antibacterials (AREKEMASE et al., 2019; KHATIB et al., 2020; NGOZIKA et al., 2020), antiplasmodials (GIMENEZ et al., 2019), larvicides (CARVALHO et al., 2019), anthelmintics (ALVARENGA et al., 2016), antivirals (GONÇALVES et al., 2005), gastroprotectants, (ARAÚJO et al., 2015b; CARVALHO et al., 2015; ONOJA et al., 2019), antidiabetics (DIONÍSIO et al., 2015; JAISWAL et al., 2016), antineoplastics (BARROS et al., 2020) and anxiolytics (GOMES JÚNIOR et al., 2018). The literature also reports as main secondary metabolites of *A. occidentale*: alkaloids, saponins, terpenoids phenols, steroids, volatile oils, anthraquinones, flavonoids, tannins and cardiac glycosides (figure 3) (BARCELOS et al., 2007; TCHIKAYA et al., 2011; VILAR et al., 2016; AREKEMASE et al., 2019; BASKAR et

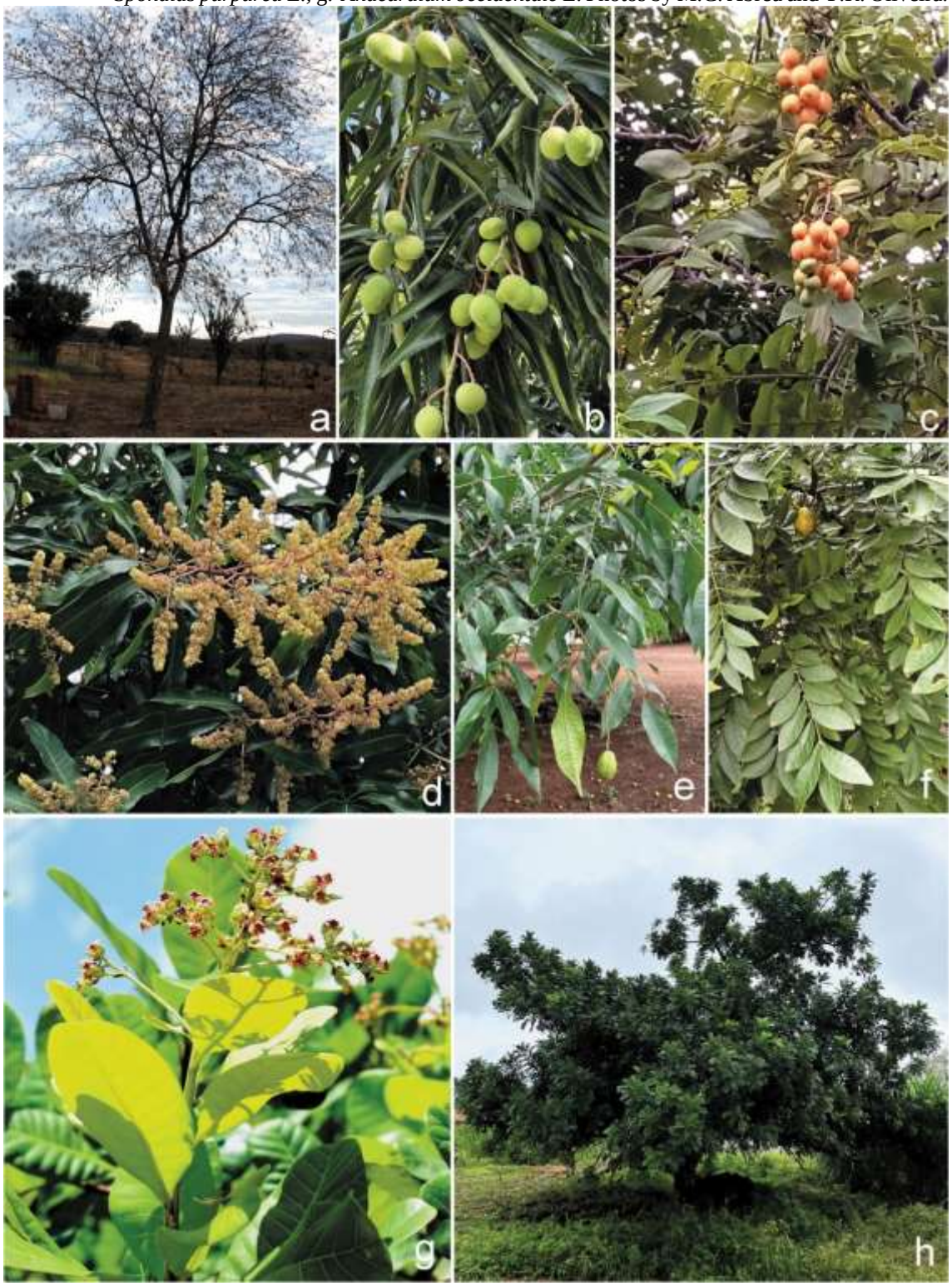
al., 2019; UDOH et al., 2019), which may, alone or in synergy, be responsible for their medicinal properties. No laboratory tests were found to investigate its therapeutic action in diseases associated with musculoskeletal tissue, specifically rheumatism, a traditional application that was only described by Bitu et al., (2015), in a study carried out in Ceará state.

Anacardium spruceanum Benth. ex Engl. was cited as medicinal only in a study carried out in the county of Cachoeira Grande, Maranhão (REGO et al., 2016), evidencing the use of the stem bark as healing, however, no laboratory tests were found that evaluate this medicinal property. There are records of *A. spruceanum* stem bark use as antineoplastic agent and against diseases of the digestive system in Amazonian communities (PEDROLLO et al., 2016).

In Neotropical savannas, Astronium species are used in folk medicine to treat allergies, inflammation, diarrhea and ulcers (RESENDE et al., 2015) and in Northeast Brazil, *Astronium graveolens* Jacq. had its medicinal use recorded only by Bandeira et al., (2018), in a study carried out in Paraiba. The form of application of this plant was not revealed in the article, but only mentioned its therapeutic purpose as an anti-inflammatory and to treat diarrhea. Vanessa et al., (2017) correlated the anti-inflammatory capacity of *Astronium graveolens* extract to its phytochemical components, such as tannins, steroids, flavonoids and other phenolic compounds, which are among the main constituents of this plant (RODRÍGUEZ-BURBANO et al., 2010; SILVA et al., 2011; HERNÁNDEZ et al., 2013; HERNANDES et al., 2014). Regarding the antibacterial power of this species, Hernández et al., (2013) attributed its performance to the monoterpenes trans-β-ocimene, α-pinene and δ-3-carene, present in its leaves.

The stem bark of *Astronium fraxinifolium* Schott are used in traditional medicine in four Northeast states to treat ailments associated with six bodily systems. Its leaves and bark are made up of a great diversity of secondary metabolites: flavonoids, xanthones, chalcones, catechins, tannins, chlorogenic acid, rutin, quercetin and numerous derivatives of gallic acid (Figure 3) (MAIA et al., 2001; SILVA et al., 2010; MONTANARI et al., 2012; RESENDE et al., 2015). Due to its phytochemical arrangement, tests indicate that this plant has antimicrobial properties (PINTO et al., 2010; CECÍLIO et al., 2012).

Figure 2 – Anacardiaceae species cultivated in communities in Northeast Brazil. a. *Astronium urundeuva* Engl.; b,d. *Mangifera indica* L.; c. *Spondias mombin* L.; e. *Spondias tuberosa* Arruda.; f,h. *Spondias purpurea* L.; g. *Anacardium occidentale* L. Photos by M.C. Abreu and Y.R. Oliveira.

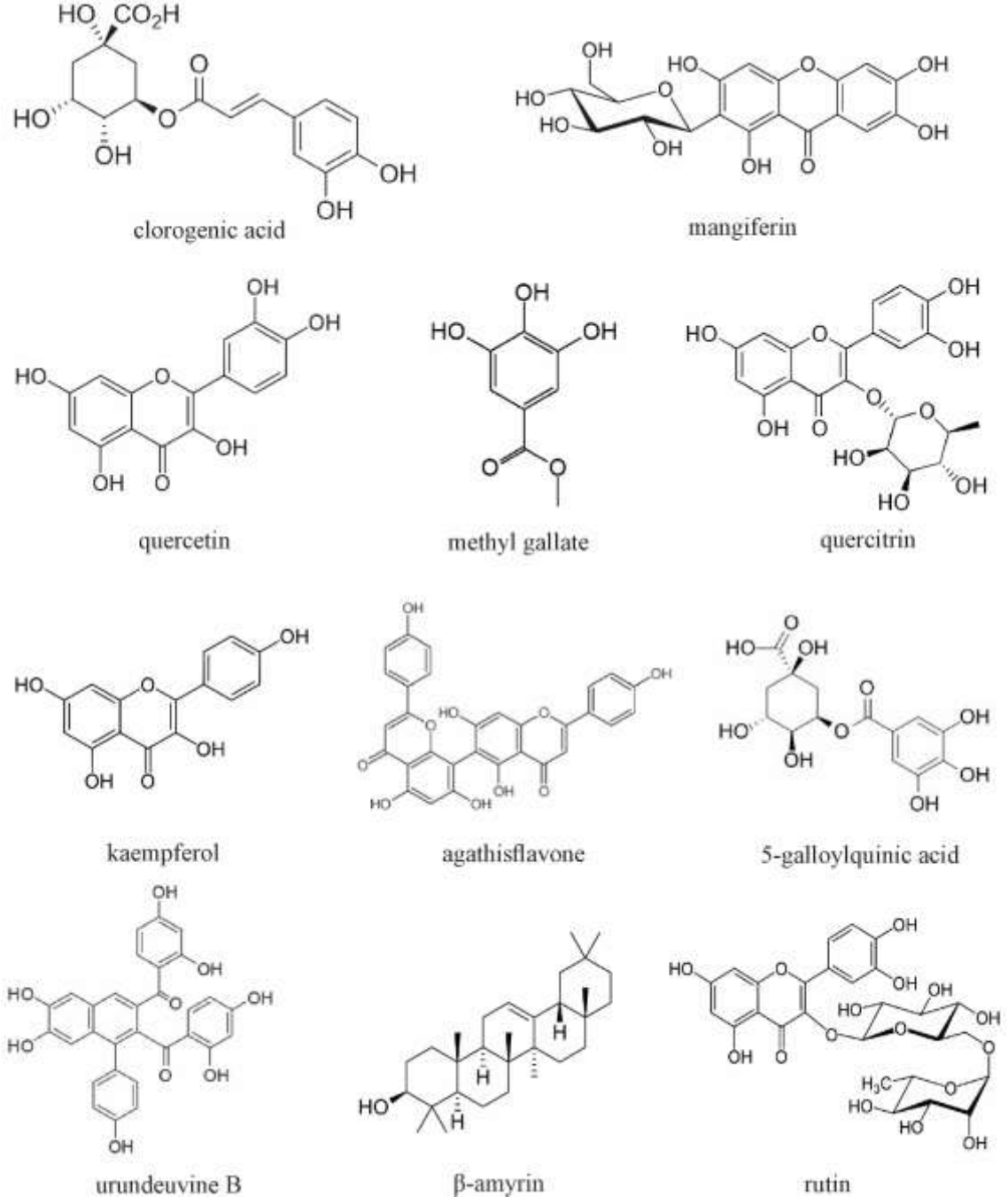


Astronium urundeuva (=*Myracrodruon urundeuva*) had its application registered in eight northeastern states, covering 14 body systems, being the species with the highest

number of indications. In Northeast Brazil, the stem bark, root, leaves and seeds are used for their properties: anti-inflammatory, antibiotic, analgesic, healing, antidiabetic, antineoplastic and against diseases associated with the digestive, respiratory and genitourinary systems. Widely used in other regions of Brazil (PASA, 2011; ALVES; POVH, 2013; PINTO et al., 2013; FERREIRA et al., 2016; DE DAVID; PASA, 2015), this species had its phytochemistry investigated in studies that revealed the presence of many secondary compounds, such as polyphenols, flavonoids, tannins, terpenoids and chalcones (CALOU et al., 2014; FIGUEIREDO et al., 2014; CECÍLIO et al., 2016; GALVÃO et al., 2018), which may be responsible for its biological properties as healing (RODRIGUES et al., 2002), antioxidant (PENIDO et al., 2017), anti-inflammatory (VIANA et al., 2003), neuroprotector (NOBRE-JÚNIOR et al., 2009), gastric anti-ulcers (SOUZA et al., 2007; GALVÃO et al., 2018), larvicide (BARBOSA et al., 2014), antibacterial (ARAÚJO et al., 2017), antifungal (OLIVEIRA et al., 2017; Almeida-APOLÔNIO et al., 2020) and antiviral (CECÍLIO et al., 2012).

Mangifera indica is a plant rich in bioactive compounds and its use in folk medicine is widespread throughout the world. In Brazil, it is used as therapeutic resource in seven states of Northeast as anti-inflammatory, analgesic, and antipyretic. Widely investigated, the phytochemistry of *Mangifera indica* reveals in its composition the presence of flavonoids, phenols, carotenoids, tannins, saponins, coumarins, steroids, terpenoids and alkaloids (LAULLOO et al., 2018; Ameen et al., 2019; CHIRAYATH et al., 2019; DE SILVA et al., 2019; MANZUR et al., 2019; MURALIDHARA et al., 2019; NAVARRO et al., 2019; UMAMAHESH et al., 2019; YU et al., 2019; GÓMEZ-MALDONADO et al., 2020; NIVEDHA et al., 2020; VILLANUEVA et al., 2020). Laboratory tests indicate that leaf extracts of this species have properties antineoplastic (ANOOP et al., 2017; BAI et al., 2018; OLASEHINDE et al., 2018; VELDERRAIN-RODRÍGUEZ et al., 2018), anti-inflammatory (KHUMPOOK et al., 2018; PAN et al., 2018; TOLEDO et al., 2019), antidiabetics (SALEEM et al., 2019; BOAS et al., 2020), immunostimulants (KUMOLOSASI et al., 2018), antimicrobials (ANAND et al., 2015; LAULLO et al., 2018; OLASEHINDE et al., 2018; MAZLAN et al., 2019; OLUSOLA et al., 2019; CARRILLO-TOMALÁ et al., 2020), anthelmintics (ROBIYANTO et al., 2018) and antioxidants (DE SILVA et al., 2019; PATARAKIJAVANICH et al., 2018; UDEM et al., 2018).

Figure 3 – Chemical structure of some secondary metabolites found in Anacardiaceae species.



Chemical compounds according to Viana et al., (2003), Johann et al., (2010), Moura (2014), Silva (2016) and Galvão et al., (2018).

Schinopsis brasiliensis had its medicinal indication reported in four states (Table 1), with the stem bark and leaves used mainly as an analgesic and for digestive system problems, such as heartburn, gastritis, and diarrhea. Its use was also revealed in the fight for Genitourinary system diseases (cystitis, urethritis and prostate problems) and of the musculoskeletal system (rheumatism, sciatica and gout). Some laboratory trials tested extracts from these plant organs, revealing its potential has antineoplastic (LUZ et al.,

2018), antinociceptive and anti-inflammatory (SANTOS et al., 2018b), antibacterial (Saraiva et al., 2013; FORMIGA-FILHO et al., 2015; LIMA-SARAIVA et al., 2017) and antivirals (CECÍLIO et al., 2012).

Schinus terebinthifolia had its use reported in all states of Northeast, for the treatment of problems associated with seven body systems. The stem bark and its leaves are mainly used as an anti-inflammatory, healing and for disorders in the integumentary, respiratory and digestive systems. Therapeutic uses of this plant against menstrual disturbances, skin diseases (erysipelas) and the discomfort caused by conjunctivitis have also been recorded. Chemically are registered as components of *S. terebinthifolia*: phenolic compounds, flavonoids, alkaloids, monoterpenes and saponins (SANTANA et al., 2012a; FEUEREISEN et al., 2014, 2017; GLÓRIA et al., 2017; TLILI et al., 2018; OLIVEIRA et al., 2018; OLIVEIRA et al., 2020). Extracts from the leaves and bark of this plant have revealed its potential as anti-inflammatory (CAVALHER-MACHADO et al., 2008; FREIRES et al., 2013; ROSAS et al., 2015; GLÓRIA et al., 2017), antineoplastic (SANTANA et al., 2012b), antibacterial (ELSHAFIE et al., 2016; ROCHA et al., 2019), antifungal (JOHANN et al., 2010; BIASI-GARBIN et al., 2016), antiviral (NOCCHI et al., 2016), healing (SANTOS et al., 2013; ESTEVÃO et al., 2015, 2017; KOMATSU et al., 2019), photoprotective (BULLA et al., 2015), analgesic (SHEID et al., 2018) and antidiabetic (ROCHA et al., 2019).

Spondias species are commonly used in traditional medicine around the world to treat stomach pain, diarrhea, diabetes, anemia and infections (SAMEH et al., 2018). In Northeastern Brazil, *Spondias dulcis* was mentioned only by Cartaxo et al., (2010), in Ceará, describing the use of stem bark, leaves and fruits as an antiseptic and to treat diseases of the integumentary, digestive and respiratory systems. This species is frequently used as food in Brazil (LORENZI et al., 2006; BARRETO; SPANHOLI, 2019), and its medicinal use has been described in other Brazilian communities (GONÇALVES; PASA, 2015; FERREIRA et al., 2016). Chemically, saponins, steroids, alkaloids, tannins, flavonoids and terpenoids are part of its composition, which may be responsible for its antioxidant and antimicrobial effects (ISLAM et al., 2013; PERERA et al., 2016; ZOFOU et al., 2019).

Spondias mombin is native from southern Mexico to southeastern Brazil and is also found in Africa and Asia (MITCHELL; DALY, 2015). In northeastern Brazil, the stem bark, fruits and seeds of this species are used especially as an analgesic,

antineoplastic and for diseases in the digestive system. There are also records of the use of this plant in the postoperative recovery of patients and in the treatment of disorders associated with the blood and cardiovascular system. In laboratory tests, extracts from the fruits showed gastroprotective activity (BRITO et al., 2018b), attenuated the cardiac remodeling process induced by exposure to tobacco smoke in rats (LOURENÇO et al., 2018), and also fought strains of Streptococcus mutans (D'ANGELIS et al., 2020), while the seed extract reduced total glucose in diabetic rats (IWEALA; OLUDARE, 2011) and the bark extract acted against Mycobacterium turbeculosis (OLUGBUYIRO et al., 2013). Although the *S. mombin* leaves was not recorded in this study, tests indicate antibacterial (BRITO et al., 2018c; WAMBA et al., 2018), antidiabetic (GOODIES et al., 2015), uterine contraction-inducing (PAKOUSSI et al., 2018) and antioxidants (OJO et al., 2018) from compounds extracted from this organ. This plant is frequently cited in the treatment of malaria in several indigenous groups in the Amazon (CARABALLO et al., 2004; RUIZ et al., 2011; FERREIRA et al., 2015) and also in Africa (IDOWU et al., 2010; KOUDOUVO et al., 2011; TRAORÉ et al., 2013; YETEIN et al., 2013), and its phytochemistry has been extensively investigated, revealing terpenes, phenols, tannins, saponins, flavonoids, alkaloids and sterols as important constituents of the various parts of this plant (HAMANO; MERCADANTE, 2001; VASCO et al., 2008; TIBURSKI et al., 2011; ASUQUO et al., 2013; LOURENÇO et al., 2018).

Spondias purpurea was recorded in ethnobotanical studies of six states, being used as a medicine mainly in the treatment of diseases of the digestive system. Its fruit, due to its pleasant aroma and flavor, is often consumed *in natura* and as juice (AUGUSTO et al., 2012). In Northeast Brazil, the fruit is also used for its therapeutic properties, as well the stem bark and leaves. Originating from Central America and disseminated through Mexico, the Caribbean and South America (POPENOE et al., 1979), *S. purpurea* has antibacterial activity evidenced in some laboratory tests (ROSAS-PIÑÓN et al., 2012; SANTOS et al., 2017), as well investigations are found that reveal the antioxidant property of its fruits (ZIELINSKI et al., 2014; VILA-HERNÁNDEZ et al., 2017; MUÑIZ et al., 2018) and the gastroprotective activity of leaf extracts (ALMEIDA et al., 2017). Although some secondary metabolites of relevant pharmacological interest, such as anthocyanins, anthraquinones, phenols, flavonoids and tannins, are part of the chemical composition of the stem bark and its fruits (OMENA et al., 2012; ELUFIOYE; BERIDA,

2018), there are not many studies that individually relate these compounds to the likely curative effects of this vegetable (ELUFIOYE; BERIDA, 2018).

Spondias tuberosa is native to the Brazilian Northeast and its medicinal use has been registered in six states, being applied the stem and root bark, leaves and fruits as an analgesic, appetite stimulant, abortifacient and against diseases associated to blood and the musculoskeletal, digestive and genitourinary systems. Among the species listed in this study, only *Astronium urundeuva* and *Spondias tuberosa* were cited with abortifacient properties, and umbu was registered for this purpose only by Oliveira et al., (2010), in a survey carried out in 21 rural communities in the county of Oeiras, in Piauí. Phenols, tannins, anthocyanins, anthraquinones, saponins and triterpenes are part of the composition of *S. tuberosa* (SILVA et al., 2011; OMENA et al., 2012). The studies by Siqueira et al., (2016) and Barbosa et al., (2018) revealed, respectively, the anti-inflammatory activity of leaf compounds and a hepatoprotective action of the stem bark in the treatment of diabetes. Furthermore, it's recognized the antioxidant power of extracts obtained from the fruits and bark (ALMEIDA et al., 2011; ZIELINSKI et al., 2014) and antimicrobial, from the leaf and stem bark (SILVA et al., 2011; COSTA et al., 2013; CORDEIRO et al., 2020).

In Brazil, *Tapirira guianensis* is used in traditional medicine as an expectorant syrup, analgesic, in the treatment of childhood oral candidiasis and skin problems (FONSECA-KRUEL; PEIXOTO 2004; MARONI et al., 2006; SOUZA; FELFILI, 2006; COELHO-FERREIRA, 2009). In Brazilian Northeast, this species had its use recorded only in the state of Maranhão for the treatment of skin and subcutaneous tissue diseases. Roumy et al., (2009) identified the presence of alkyl polyol derivatives in the bark extract of *T. guianensis*, including a mixture of biologically active molecules against amastigotes of *Leishmania amazonenses* and strains of bacteria that cause skin diseases, corroborating the ethnopharmacological application of this species in state of Maranhão.

Species of unproven occurrence for Northeast Brazil

The research revealed the use of three species of Anacardiaceae with proven occurrence for Brazil, but not for the Northeast region according to Brazilian Flora 2020: *Anacardium parvifolium* Ducke, *Lithraea brasiliensis* Marchand and *Schinus molle* L. These species were not included in the results of this research because they have a restricted geographic distribution in Brazil and their medical uses were reported in a few

articles. *Anacardium parvifolium* (=*Anacardium tenuifolium* Ducke) had its anti-inflammatory use revealed only by Madaleno (2011) in a survey carried out based on the ethnobotanical knowledge of farmers in the capital of the state of Maranhão. In Brazil, this species occurs only in the state of Amazonas, and there are no investigation studies on its anti-inflammatory capacity.

Lithraea brasiliensis is popularly known as "aroeira" and occurs naturally in areas of Restinga and Ombrophilous Forest in the South and Southeast regions of Brazil (SILVA-LUZ; PIRANI, 2015), and its medicinal use is reported in some communities in these regions for the treatment of wounds, diarrhea and cholesterol (AMORIM 2009; GIORDANI et al., 2013). In the Northeast, this species was only recorded by Oliveira and Rocha (2016) in a rural community in the state of Maranhão, revealing the stem bark use as an anti-inflammatory. Studies involving this species have demonstrated its antineoplastic potential in human cancer cells (MONKS et al., 2002; LOPES et al., 2003).

Popularly known as "aroeira", *Schinus molle* L. was mentioned for its medicinal use in only two articles carried out in the states of Ceará (TEIXEIRA et al., 2014) and Bahia (ÂNGELO; RIBEIRO, 2014), highlighting the stem bark use as healing, anti-inflammatory and against gastritis. In Brazil, this species occurs only in the Southern states, being applied in ethnobotanical and ethnoecological uses (GOMES et al., 2016). Extracts from the bark of *S. molle*, according to Salazar-Aranda et al., (2011), showed antimicrobial activity for *Enterococcus feacalis*, *Staphylococcus aureus* and species of the genus *Candida*. No laboratory tests were found that investigated the anti-inflammatory or healing capacity of compounds from *Schinus molle* bark. However, other parts of this plant, especially leaves and fruits, are commonly used in traditional medicine in other regions of the world (RUFFA et al., 2002; SILVA-JUNIOR et al., 2015; RIBEIRO et al., 2019), and it's been reported their potential has an anti-inflammatory (YUEQUIN et al., 2003; TAYLOR et al., 2016), anticancer (RUFFA et al., 2002; BENDAOUD et al., 2010; GARZOLI et al., 2019; OVIDI et al., 2019) and antimicrobial (ELSHAFIE et al., 2016; DELGADO-ALTAMIRO et al., 2017; PRADO et al., 2018).

CONCLUSION

Anacardiaceae species are commonly used in traditional Northeastern medicine, mainly as anti-inflammatory, analgesic, healing and to treat diseases associated with the digestive and respiratory system. It is concluded that Northeastern communities hold

important knowledge about the ethnopharmacology of Anacardiaceae species, and this knowledge is important empirical bases that can direct new research associated with the conservation of widely exploited species. The literature also shows the phytochemistry of some of these species reveals that these plants have substances of important medical relevance in their chemical composition and can, in isolation or in synergy, exert healing activities, which need to be better investigated, and may also direct the search for new bioactive compounds.

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