



Medicinal plants and animals of an important seasonal dry forest in Brazil

Ulysses Paulino Albuquerque^{1*}, Alanne Lucena de Brito², André Luiz Borba do Nascimento¹, Antonio Fernando Morais de Oliveira¹, Carla Mirele Tabósa Quixabeira², Diógenes de Queiroz Dias³, Eduardo Carvalho Lira², Flávia Santos Silva¹, Gyllyandeson de Araújo Delmondes³, Henrique Douglas Melo Coutinho³, Mariana Oliveira Barbosa¹, Melissa Fontes Landell⁴, Rômulo Romeu da Nóbrega Alves⁵, Washington Soares Ferreira Júnior⁶

ABSTRACT

Research performed in recent years indicates that efforts are still needed to understand the advances in the Caatinga, an important dry seasonal forest, and identify its potential for bioprospecting. These efforts are also important for pinpointing the challenges that should be addressed in future research focused on identifying new candidates for pharmacological studies in this complex region. Thus, in this review, we present the main advances of studies on plants and medicinal animals in the Caatinga region and their implications for ethnopharmacology, and we then discuss future challenges to promote the search for candidates with pharmacological potential. Based on an exploration of the available literature, we performed a critical reading of the available evidence to provide a good scenario on the studies in the region. We find that despite the large number of studies available, it is necessary to organize efforts to fill gaps in different areas of knowledge and optimize the search for new natural products.

Keywords: Ethnobotany; Ethnopharmacology; Ethnozoology; Phytotherapy; Zoototherapy

¹ Departamento de Botânica, Universidade Federal de Pernambuco, Cidade Universitária, Av. prof. Moraes Rego s/n, 50670-901, Recife, PE, Brazil.

² Departamento de Fisiologia e Farmacologia, Universidade Federal de Pernambuco, Cidade Universitária, Av. prof. Moraes Rego s/n, 50670-901, Recife, PE, Brazil.

³ Departamento de Química Biológica-DQB, Universidade Regional do Cariri – URCA, Crato, CE, Brazil.

⁴ Setor de Genética, Laboratório de Diversidade Molecular, Universidade Federal de Alagoas, Campus A. C. Simões, CEP: 57072-900, Maceió, AL, Brazil.

⁵ Departamento de Biologia, Universidade Estadual da Paraíba, Av. das Baraúnas, 351/Campus Universitário, Bodocongó, 58109-753, Campina Grande-PB, Brazil.

⁶ Laboratório de Investigações Bioculturais no Semiárido, Universidade de Pernambuco, Campus Petrolina, BR203, Km 2, s/n, CEP: 56328-903, Petrolina, PE, Brazil.

* Corresponding author. ✉E-mail address: upa677@hotmail.com

INTRODUCTION

Brazil possesses a rich diversity of fauna used for medicinal purposes (Alves *et al.* 2007, 2008a). Studies indicate that the northeast region possesses the largest volume of information on the use of medicinal fauna products (Alves and Rosa 2006 2007a, 2007b, 2007c; Alves 2009). The contribution of this information has stimulated the development of studies seeking to validate the medicinal activities of zootherapies described in ethnozoological studies in this region (Ferreira *et al.* 2010, Cabral *et al.* 2013; Oliveira *et al.* 2014; Sales *et al.* 2015).

The Caatinga of northeastern Brazil has an extensive area of 912,529 km² and represents an important ecological region since it shelters considerable biodiversity and is a semi-arid region that covers several human groups with different sociocultural characteristics (Silva *et al.* 2017a). In relation to biodiversity, recent studies have registered 4,662 species of native plants (31 endemic genera) (Queiroz *et al.* 2017), 371 native species of fish (203 are possibly endemic) (Lima *et al.* 2017), 98 species of amphibians (20 endemic) (Garda *et al.* 2017), 79 species of lizards (38 endemic) (Mesquita *et al.* 2017), 548 species of birds (67 native) (Araújo and Silva 2017) and 138 species of mammals (11 endemic species) (Carmignotto and Astúa 2017). This large diversity involves species that have adaptations to deal with low water availability environments, which is important because precipitation is concentrated in a few months and rains are irregular in the region (Silva *et al.* 2017b).

In addition to the diversity of environments and species, several human groups inhabit the region, such as “Maroon,” indigenous and rural communities, which

interact with the Caatinga biota (Albuquerque *et al.* 2017). In the last decades, many studies have investigated the interactions of people with plants and animals in Caatinga areas (Albuquerque *et al.* 2007, 2017; Melo 2017). These resources are applied to a wide variety of uses, such as medicinal, construction, food, religious, technological, fuel, etc., thus indicating the high diversity of useful species (see Albuquerque *et al.* 2007, for medicinal plants).

When considering the biological and cultural diversity of the Caatinga of northeastern Brazil as well as the variety of species indicated as medicinal, this region has an important potential for ethnopharmacological studies focused on understanding the patterns of knowledge and use of medicinal resources by human populations and identifying candidates with important pharmacological activities. To evaluate the effects of bioprospecting, several research studies have been carried out in the Caatinga environment, and their findings indicate that the plants and animals in the region have pharmacological potential for a variety of diseases (Leal *et al.* 2009; Cabral *et al.* 2013; Campos *et al.* 2014).

Some work has gone deeper in the pursuit of patterns to identify the motives associated with the choice of medicinal resources to compose local pharmacopoeias in the Caatinga (Alencar *et al.* 2010; Lucena *et al.* 2012; Alencar *et al.* 2014). These works may be promising for ethnopharmacology as they investigate the formation of local medical systems. These systems involve the set of social institutions and traditions generated from the evolution of strategies that promote the health and well-being of a given locality (Dunn 1976). To understand issues related to traditional medicines, ethnopharmacology has

accessed the knowledge present in local medical systems. However, the use of local remedies is complex, and several factors can influence the use of resources for the treatment of diseases. For example, the local significance of diseases, local norms linked to the healing process, social relations and existing institutional contexts are factors that influence the choice and evaluation of treatment efficiency (Kleinman 1978).

In this article, we present an overview of the state of the art on the medicinal animals and plants in the Caatinga and highlight ethnopharmacological, phytochemical and pharmacological advances.

1. Local medical system from the Caatinga and its relevance for ethnopharmacology

The Caatinga presents a wealth of medicinal plants. Currently, the most important checklist on the medicinal plants of the Caatinga is that produced by Albuquerque *et al.* (2007), which reported a total of 385 species of angiosperms and four species of ferns and mosses used for medicinal purposes in 21 studies conducted in the region. We used the basis of this study (Albuquerque *et al.* 2017) to make some of our considerations here. Studies on medicinal plants in the Caatinga usually present a list of medicinal plants and their uses, as well as an index to highlight the most important plants (see Medeiros *et al.* 2011a). One of the main arguments for the use of these indices is to promote the selection of plants for future pharmacological investigations. However, fewer papers were devoted to describing and testing hypotheses about how these plants fit into the complex local medical systems of the Caatinga.

A considerable amount of evidence has

been obtained from studies conducted in the Caatinga and other regions showing that the use of plants for medicinal purposes is the result of a long process of experimentation (see Medeiros *et al.* 2013; Ankli *et al.* 1999). Thus, people use certain criteria to recognize a plant as potentially effective, include it in the local pharmacopoeia, and determine the plant that will be used at the time that a disease episode occurs (see Figure 1). Organoleptic properties of plants, such as the color, shape, aroma, taste and texture, act as signs that lead to the inclusion of species in the local medicinal repertoire (Ankli *et al.* 1999; Casagrande 2000). An association can exist between people's perceptions of the taste and smell of plants and the diseases that they are used to treat, but not in all cases. In this sense, bitter taste may be a core organoleptic property used to treat the most popular diseases (see Medeiros *et al.* 2015). Only those diseases found most frequently in the lists were associated with a bitter taste, which indicates that bitter taste may be a core organoleptic property used to treat the most popular diseases.

The importance of the disease to be treated in the selection of the medical resource was highlighted in the study by Ferreira Júnior *et al.* (2016). This study indicates that diseases with similar symptoms have greater similarities to the set of medicinal plants used for their treatment. Considering this finding and that of Medeiros *et al.* (2015), people in the Caatinga choose resources with similar organoleptic characteristics for medicinal functions that are also perceived as similar. In this case, it is possible that plant characteristics are involved in the selection of medicinal resources when comparing different human groups located in different regions. The study by Salsis-Lagoudakis *et al.* (2012)

showed that human groups located in different regions select phylogenetically related medicinal plants to treat the same classes of diseases. The authors point out that human groups may have selected these plants independently based on their therapeutic efficacies. In another example, the study of Geck *et al.* (2017), which was carried out in different communities in Chiapas, Mexico, observed that the smell and taste of the plants provided important information about the humoral ("hot" or "cold") properties, thus guiding their medicinal applications. This finding may have important implications for future strategies linked to bioprospecting because it can be used to evaluate what

characteristics of plants guide the construction of medical systems and determine whether these characteristics are linked to important pharmacological activities of plants.

From the characteristics of plants that can guide their selection, it is possible that redundant plants (Albuquerque and Oliveira 2007) used to treat one or more diseases share a certain set of characteristics, such as organoleptics (e.g., bitter-tasting plants targeted for certain diseases, in Medeiros *et al.* 2015) or chemical properties. In the case of the Caatinga, medicinal plants used for the treatment of inflammation are associated with the presence of tannins (Araújo *et al.* 2008). Other studies have shown that these

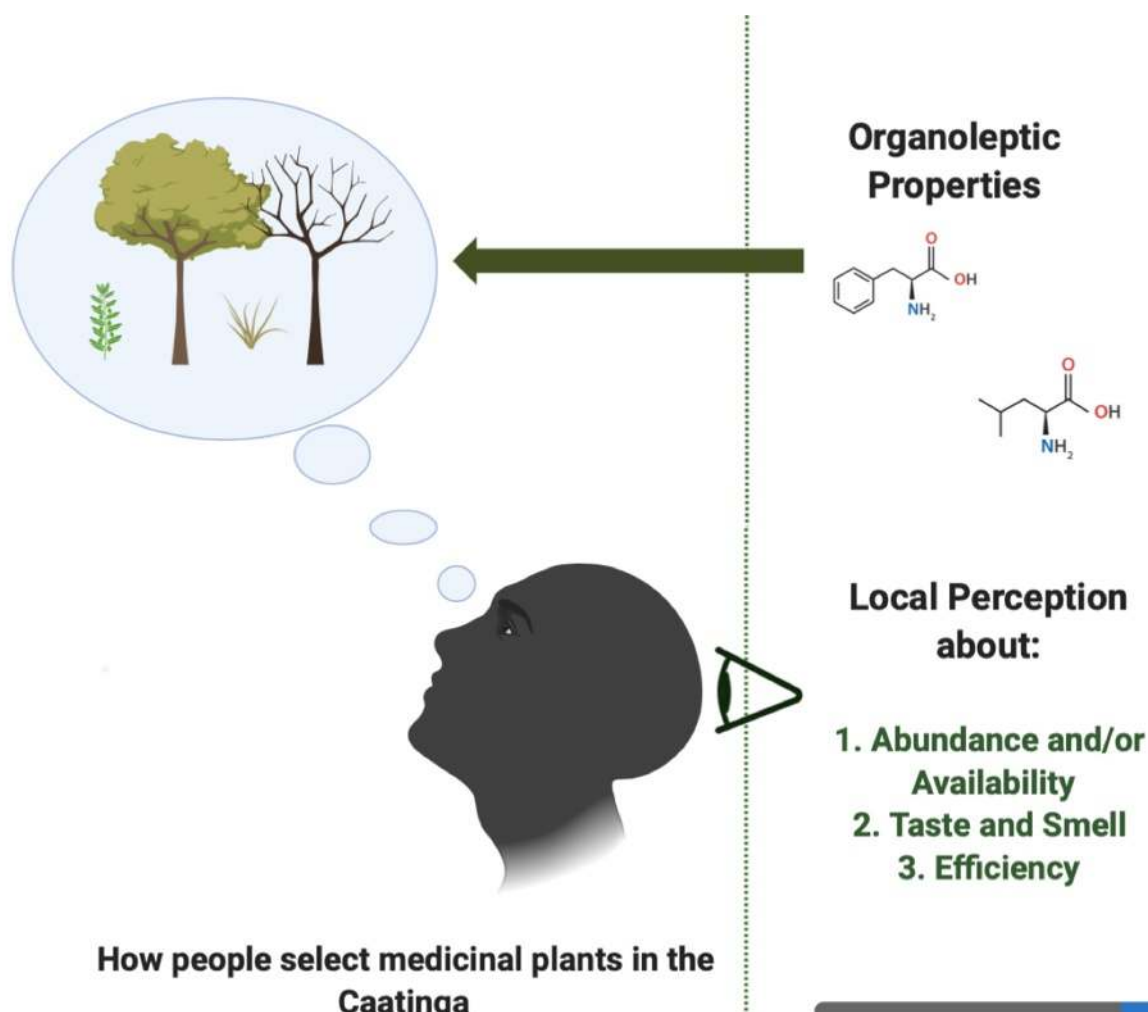


Figure 1. Some insights on how people select medicinal plants in the Caatinga.

compounds can be perceived through the astringency taste (see, for example, Dragos and Gilca 2018).

The recurrence of a disease event appears to be an important factor for structuring local medical systems. Some studies have shown that diseases considered frequent tend to be associated with a large number of medicinal plants (Santoro *et al.* 2015; Nascimento *et al.* 2016). Sousa *et al.* (2016) found that the species cited first in lists of medicinal plants are those that have been used to treat diseases that have occurred in the last year, and these plants are also considered as more important, but new studies need to be conducted to confirm or not this finding.

All of these data suggest that most studies in the Caatinga have accessed and inferred patterns concerning diseases that are most common in the local medical system. Apparently, the most relevant medical information for people is how to deal with recent and/or recurring illness events, which is interesting because it is widespread within the discourse of many authors working with medicinal plants, who consider that the most popular plants are the most relevant for bioprospecting.

In addition to the application of plants for the treatment of frequent diseases, different therapeutic modalities can also be used for these diseases. The study by Nascimento *et al.* (2018) found that the combined use of plants with medicinal products of biomedical origin can be favored in diseases with high frequency of occurrence according to local perception. An interesting example is the case of the Fulni-ô Indians, whose strategies for health management include the use of plants, visits to practitioners (local specialists), and the use of biomedical drugs (see also Soldati and Albuquerque 2012; Zamudio and Hilgert 2011). However, such

combined use can have negative consequences for people from a pharmacological point of view. Several studies have observed adverse effects when medicinal plants are given in conjunction with conventional drugs (Staines 2011; Larson *et al.* 2014; Murray *et al.* 2016). For example, plant extracts of different species may affect the expression of the CYP2D6 gene, which produces an important drug-metabolizing enzyme that may cause toxic reactions with or inhibit therapeutic effects when the extracts are administered along with conventional drugs (Feltrin *et al.* 2019). Therefore, future studies should focus on the interactions between medicinal plants native to the Caatinga and conventional drugs.

In addition to plant-drug interactions, the accumulation of distinct treatments (plants and drugs of biomedical origin) in diseases with a higher frequency of occurrence can increase the probability of maladapted information in local medical systems, i.e., the inclusion of plants that are not effective in the treatment of these diseases (Tanaka *et al.* 2009; Santoro *et al.* 2018). For example, according to the model proposed by Tanaka *et al.* (2009), diseases with higher frequencies of occurrence can increase the chance of non-effective plants being copied among pairs of people in a human group. Santoro *et al.* (2015) also explained that a greater number of species used for frequent diseases can be related to information transmission errors.

Therefore, future investigations could assess how much non-effective plants are present in local medical systems and the factors that increase the probability of insertion of these plants over time. If these transmission errors are frequent in local medical systems in the Caatinga, then caution should be exercised in the selection of medicinal plants in future studies on

bioprospecting because some of these plants cited for different uses may not be effective in the treatment of certain diseases. Moreover, future research should exercise caution when selecting plants for pharmacological evaluation by including plants prescribed for diseases that are highly frequent in a given region as a criterion.

Another important factor is that not all species known for medicinal purposes or even for a given disease are actually used by a community (Albuquerque 2006), and one plant is often used more frequently than others. Several factors may be involved in the differential use of medicinal plants (see Medeiros *et al.* 2015); therefore, different criteria have been associated with the prioritization of a medicinal plant in human groups in the Caatinga. For example, Ferreira Júnior *et al.* (2011) found that the most cited criterion for prioritizing a plant was its perceived therapeutic efficacy. In this case, a plant that is widely cited as preferred because of its perceived efficacy for a large set of diseases may be of interest for future pharmacological investigations aimed at bioprospecting (Ferreira Júnior *et al.* 2011; Albuquerque *et al.* 2014).

However, in addition to the perceived efficiency, other criteria are important in the prioritization of medicinal plants. In addition, factors such as accessibility to the resource can promote greater experimentation and learning (Molares and Ladio 2008), thus leading to greater use of these species. Cost-benefit relationships can guide the exploration of medicinal resources, in which a shorter time spent during collection demonstrates weight in the choices of human populations (Soldati and Albuquerque 2012). In environments with marked seasonality, such as the Caatinga, the temporal availability of the species may be another factor that leads to the differential

use of medicinal plants; for example, the study of Albuquerque (2006) reports the greater use of the bark of arboreal species in this region because they are found in the environment during the whole year. These environmental factors need to be taken into account since people may come to use more of a medicinal feature not for its efficiency but for its ease of collection. Many medicinal plants are transported by people to the backyards of their homes, for example, to avoid the costs associated with their collection.

In addition to plant resources, products of animal origin are frequent in Caatinga folk medicine. There is an expressive richness of species of medicinal animals used by human populations that live in the region, and these species encompass several groups of invertebrates and vertebrates (Alves *et al.* 2016a,b; Alves *et al.* 2012; Bezerra *et al.* 2013; Mendonça *et al.* 2014). Ethnozoological reviews indicate that at least 24 reptile species (Alves *et al.* 2012) and 38 mammal species (Alves *et al.* 2016a,b) are used for medicinal purposes in the region. Other groups, such as birds, amphibians and fish, are also registered as a source of medicine in the region's folk medicine (Bezerra *et al.* 2013; Santos and Alves 2016). Among invertebrates, insects stand out (Alves 2009). Curiously, medicinal species of marine origin are used in the region, and they are obtained in public markets in urban areas and are usually obtained from clandestine commercialization (Alves *et al.* 2009b). Zootherapy is also a practice employed in ethnoveterinary medicine in the region (Souto *et al.* 2011), and at least 39 animal species have been reported as source of remedies used in local ethnoveterinary medicine for the production of medicines used to treat diseases of domestic animals.

Animals are used in whole or in part, such as the feather, leg, hair, leather, tooth, lard (fat), flesh, spur, horn, scales, nail, blood, penis, bones, liver, heart, head, testicle, marrow, eye, ear, etc. Products of their metabolism, such as excreta (feces, urine) and honey, as well as materials built by animals, such as nests and cocoons, are also medicinally usable resources. Milk, blood and eggs are also part of the therapeutic arsenal. In most cases, the products are extracted after the animal's death since such raw materials are primarily obtained mainly through fishing and hunting activities, a common practice in the region (Alves *et al.* 2009a; Fernandes-Ferreira and Alves 2017). It is emphasized that slaughter is not always directly related to the medicinal use of animals. For example, in the municipality of Pocinhos, Paraíba, tejuçu (*Tupinambis merianae*) is hunted mainly for food purposes, and the by-products thereof, such as lard and tongue, are used in the elaboration of popular remedies. Another example is the rattlesnake (*Crotalus durissus*), which is an animal that poses a risk to humans and domestic "creations;" therefore, it is usually slaughtered only under precaution or control (Alves 2009), and its by-products are used in zoos. Thus, the use of medicinal products optimizes the use of slaughtered animal resources. Moura and Marques (2008) point out that a common feature in fractions of animals or even whole animals used as medicines is their uselessness for other purposes. These authors also point out that although studies on Brazilian popular zotherapy have not yet turned to the quantitative analysis of the use of leftovers or animal by-products, the practice is well documented in the lists of zotherapies used in different Brazilian states (Alves *et al.* 1990) as well as in the literature (Martínez 2013).

It is also worth noting that live animals are used in zotherapeutic practices. For example, *jabutis* (*Chelonoidis* sp.) are usually raised as pets because this practice is believed to prevent bronchitis and erysipelas among the residents of the breeder's home (Alves *et al.* 2012). Another example is recorded in the semi-arid states of Paraíba and Pernambuco, where the live song (*Cyanocorax cyanopogon*) is used in popular "sympathy" treatments for asthmatic processes in which the bird is fed with the patient's food remains (Alves *et al.* 2009b). Raw animal materials are also used in the form of amulets and in "sympathies" to prevent and treat diseases associated with unnatural causes (Alves and Rosa 2006). The interrelation between popular beliefs and zotherapy has been recorded in different localities of Brazil (Alves *et al.* 2007).

The application of remedies prepared from animal substances varies according to the nature of the disease, the purpose of use and the ingredients used. Thus, different modes of preparation and administration of zotherapeutic resources are reported (Alves 2009). Hard parts of animals, such as shells, are usually sun dried, then trodden or grated, resulting in a powder, which is then used for tea preparation or ingested along with food. Some biotherapeutic products can be used in association with medicinal plants in "*garrafadas*," a therapeutic drink that may have products derived from animals and plants that are usually soaked in cachaça (sugarcane brandy) or white wine and stored in bottles (hence the name 'bottled').

A significant portion of the fauna with medicinal value is marketed by sellers in markets and free fairs throughout the Caatinga region (Alves *et al.* 2008a,b; Alves *et al.* 2010; Alves *et al.* 2009b; Costa-Neto 1999). Trade in zotherapies involves a wide

variety of species, including whole animals (when small), although the commercialization of parts (derived from animals of medium and large size) is more common.

It is important to emphasize that some natural products (derived from plants, animals and minerals) used in traditional medicine can cause serious adverse effects and transmit zoonoses (Van Vliet *et al.* 2017), especially when considering the sanitary conditions associated with the maintenance and storage of the products (Alves *et al.* 2009b). This study, there was a significant increase in the prevalence of this disease in the Brazilian semi-arid region, which indicates the possibility of microbiological contamination and represents a potential risk to the users' health (Alves *et al.* 2007). A good example of this is "armadillos," which are hunted and used for food and medicinal purposes (Alves *et al.* 2009a; Barboza *et al.* 2016).

2. Major compounds identified in Caatinga plants

Several studies point to the great variety of secondary metabolites found in Caatinga species (see, for example, Almeida *et al.* 2011). It is believed that the synthesis of the secondary metabolites in this type of vegetation is favored by the adverse environmental conditions typical of this ecosystem that can influence the biosynthesis routes of compounds associated with plant defenses against biotic and abiotic factors (Montanari and Bolzani 2001; Almeida *et al.* 2011). Some of the key metabolites identified to date are described below and summarized in Table 1.

2.1. Alkaloids

Alkaloids are a group of heterogeneous nitrogenous secondary metabolites widely recognized for their therapeutic effects, especially on their action on the nervous system, as well as their analgesic, hallucinogenic and antitumor effects (Makkar *et al.* 2007). Several studies point to the presence of these metabolites in Caatinga plants (Almeida *et al.* 2005, Nascimento-Silva *et al.* 2011, Brandão *et al.* 2017), particularly in Apocynaceae, Erythroxylaceae and Fabaceae (Nogueira *et al.* 2014; Negreiros Neto *et al.* 2016; Ceravolo *et al.* 2018; Macedo Pereira *et al.* 2018). *Aspidosperma pyrifolium* Mart., for example, may be among the most studied species of the Caatinga in relation to their alkaloidal profile (Gilbert *et al.* 1962; Craveiro *et al.* 1983; Araújo *et al.* 2007). In *Erythroxylum pungens* O.E.Schulz (Erythroxylaceae), were identified twelve alkaloids in which one 3-(2-methylbutyryloxy)tropan-6,7-diol, showed 50% cell viability reduction against HeLa (Macedo Pereira *et al.* 2018). According to these author, edaphoclimatic features of Caatinga biome could stimulate the biosynthesis of the unusual alkaloids, e.g. tropane alkaloids.

2.2. Phenolics and Flavonoids

Flavonoids are secondary phenolic metabolites that are mainly found in high-quality vegetables, and they are responsible for conferring color to flowers and fruits and protection against UV and pathogens. In human foods, flavonoids contribute to several health benefits mainly because of their antioxidant effect (Buckingham and Munasinghe 2015). They are also known for their pharmacological importance because of their anti-inflammatory, antioxidant,

antifungal and antitumor properties, among others (Cordeiro *et al.* 2018).

Most studies on species occurring in the Caatinga have concentrated on quantifying the total flavonoid content. However, refined methods of identifying flavonoids have also been employed, such as direct flow injection-electrospray-ion trap tandem mass spectrometry (DFI-ESI-IT-MS) or even high-performance liquid chromatography with a diode-array detector (HPLC-DAD). Some studies, for example, have led to the isolation of isoquercetin, quercetin and rutin in *Caryocar coriaceum* Wittm. - Caryocaraceae (Alves *et al.* 2017), gallic acid, rutin, ellagic acid, catechin, quercetin, kaempferol and caffeic acid were identified in *Terminalia argentea* Mart. - Combretaceae (Beserra *et al.* 2018), gallic acid and hyperoside in *Spondias tuberosa* Arruda - Anacardiaceae (Cordeiro *et al.* 2018) and amentoflavone and agathisflavone in *Poincianella pyramidalis* (Tul.) LP Queiroz - Fabaceae (Pereira Gomes-Copeland *et al.* 2018). Recently, kaempferol, quercetin, isorhamnetin and myricetin were identified in *Ziziphus joazeiro* Mart. - Rhamnaceae (Andrade *et al.*, 2019).

2.3 Tannins

Tannins are phenolic compounds known especially for their astringency and ability to chemically bind to proteins, sugars and alkaloids. They present an important ecological function and are used by plants as a defense strategy against herbivores (Monteiro *et al.* 2005). Economically, they are used in the manufacture of leather products. Tannin-rich species are used in folk medicine mainly for their antidiarrheal, antiseptic, antifungal, antimicrobial, anti-inflammatory and healing effects (Mello and Santos 2001; Monteiro *et al.* 2005).

According to Almeida *et al.* (2011), tannins are one of the most investigated and most frequent compounds in the medicinal plants of the Caatinga. Species such as *Anacardium occidentale* L. (Anacardiaceae), *Anadenanthera colubrina* (Vell.) Brenan (Fabaceae), *A. falcata* (Benth.) Speg. (Fabaceae), *Caesalpinia ferrea* Mart. ex Tul. (Fabaceae), *Casearia sylvestris* var. *angustifolia* Uittien (Flacourtiaceae), *Cnidoscolus urens* (L.) Arthur and *C. infestus* Pax & K. Hoffm. (Euphorbiaceae), *Lafoensia replicata* Pohl. (Lythraceae), *Myracrodruon urundeuva* Allemão (Anacardiaceae), and *Terminalia brasiliensis* (Cambess.) Eichler (Combretaceae) are referred to as having a high amount of tannins (Araújo *et al.* 2008; Peixoto Sobrinho *et al.* 2011; Monteiro *et al.* 2014). Despite the high number of species, most tannin studies were limited to quantifying their levels in sought to correlate their presence with their therapeutic effects and their use value by local communities (Araújo *et al.* 2008; Monteiro *et al.* 2005; Siqueira *et al.* 2012; Monteiro *et al.* 2014). An exception is the study of Beserra *et al.* (2018), which have identified terminalin, corilagin, punicalin and punicalagin in the leaves of the *T. argentea*.

2.4 Volatile oils and diterpenes

Volatile oils (mono-10C and sesquiterpenes-15C) consist of a mixture of aliphatic and cyclic compounds derived from isoprene (5C). Volatile or essential oils have different functional groups in their structure, such as hydrocarbons, alcohols, aldehydes, esters, ethers and ketones, and they are mainly responsible for the odor of plants, the main function of which is to attract and/or repel herbivorous insects.

Several aromatic species are observed in Caatinga flora, and the main studies on

essential oils in this environment have focused on the chemical composition of the oils, seasonal effects on the chemical profile of the oil and the biological activity of the oil. Euphorbiaceae family, especially the genus *Croton* (Dourado *et al.* 2005; Neves and Camara 2012; Ramos *et al.* 2013; Almeida *et al.* 2014a; Carvalho *et al.* 2016; Souza *et al.* 2017; Anjos *et al.* 2018; Ribeiro *et al.* 2018), Annonaceae (Meira *et al.* 2015; Araújo *et al.* 2015a; Diniz *et al.* 2019), Verbenaceae (Neves *et al.* 2008; Souza *et al.* 2018) and Lamiaceae (Pereira *et al.* 2018) contains the largest number of studies.

Diterpenes are terpenoids with 20 carbon atoms originating biosynthetically from geranylgeranyl diphosphate (GGPP) and are classified as linear, bicyclic, tricyclic, tetracyclic, pentacyclic and macrocyclic. Diterpenes have attracted increasing attention because of their numerous biological and pharmacological activities (Lanzotti 2013). Compared with studies on volatile oils, work with diterpenes in Caatinga species is scarce and has concentrated on a few species such as *Calliandra depauperata* Benth. - Fabaceae (Pires *et al.* 2011), *Croton grewioides* Baill. - Euphorbiaceae - (Medeiros *et al.* 2011b), *Erythroxylum revolutum* Mart. - Erythroxylaceae (Oliveira 2012), and *Cnidocolus quercifolius* Pohl -Euphorbiaceae (Oliveira-Júnior *et al.* 2018).

2.5 Triterpenes and allied compounds

The triterpenes are terpenoids with 30 squalene-derived carbon atoms, generally with five ring systems. They differ from phytosteroids because they have less than 30 carbons and are usually tetracyclic. Some studies have interrogated triterpenes in Caatinga species (Silva *et al.* 2010; Barbosa

et al. 2014; Araújo Gómez *et al.* 2014; Vieira *et al.* 2016). Acids triterpenes such as betulinic, oleanolic and ursolic acids, besides lupeol, α -amyrin, β -amyrin, cycloeucaleanol, friedelin and derivatives were identified from Caatinga species (Barbosa-Filho *et al.* 1985; Silva *et al.* 2010; Vieira *et al.* 2016; Oliveira-Júnior *et al.* 2018). For phytosteroids, most of the studies have performed phytochemical screening (Peixoto *et al.* 2016; Pereira *et al.* 2017). To the best of our knowledge, phytosteroids were isolated and identified in only two studies: *Senna spectabilis* var. *excelsa* (Schrad.) H.S.Irwin & Barneby - Fabaceae (Silva *et al.* 2010) and *Pilosocereus pachycladus* F. Ritter - Cactaceae (Brito-Filho *et al.* 2017).

Saponins are glycosides which provide sugars and aglycones (sapogenins) under hydrolysis, which may be triterpene or steroidal. Studies on saponins in Caatinga species are limited, with the majority of studies only indicating the presence and absence of these metabolites (Peixoto Sobrinho *et al.* 2012; Pereira *et al.* 2016; Pereira *et al.* 2017; Cordeiro *et al.* 2018). Studies on the structural properties of saponins in the Caatinga have primarily focused on *Z. joazeiro*, a tree with stem bark rich in saponins (2-10%) that is used by local communities as detergent and phytotherapeutic (Higuchi *et al.* 1984; Ribeiro *et al.* 2013; Ribeiro *et al.* 2014) and *Manilkara rufula* (Miq.) H.J.Lam (Sapotaceae), which presents antitrichomonal activity (Vieira *et al.* 2017).

To the best of our knowledge, there are no studies focused on isolation, purification and structural elucidation of cardenolides in Caatinga species, although families such as Apocynaceae are very representative in this ecosystem.

2.6 Fatty acids and other lipids

Several Caatinga species are rich sources of fatty acids and other lipids of economic interest. Fatty acids consist of straight chain carboxylic acids found primarily in seeds in the form of triglycerides, and they are often associated with antioxidant compounds such as carotenoids, tocopherols, and tocotrienols (Gunstone 1996; Barbosa *et al.* 2019). In the Caatinga, the Euphorbiaceae, Sapindaceae and Malvaceae families stand out because of the large number of potentially oleaginous species (Pinho *et al.* 2009; Barros *et al.* 2015; Coutinho *et al.* 2015; Coutinho *et al.* 2016; Silva *et al.* 2010; Silva *et al.* 2014).

Another group of lipids studied in Caatinga plant species are those that constitute cuticular waxes, which are formed of aliphatic and cyclic constituents and cover the primary aerial surface of plants. The primary function of these waxes is to reduce water loss, especially under water stress situations, which are common in the Caatinga. Several aliphatic compounds (n-alkanes, fatty acids, primary and secondary alcohols and ketones) have been identified as well as triterpenes such as α -amyrin, β -amyrin, betulin, lupeol, epifriedelinol, ursolic acid, oleanolic acid, and betulinic acid (Oliveira *et al.* 2000; Costa Filho *et al.* 2012; Medeiros *et al.* 2017; Pereira *et al.* 2019).

3. Biological activity of medicinal plants from the Caatinga

Many of the Caatinga's plants are widely used in Brazilian traditional medicine and as phytomedicine products, and they include *Myracrodruon urundeuva* All., *Amburana cearensis* (Arr. Cam.) A.C. Sm., *Erythrina velutina* Willd., *Anadenanthera colubrina*

(Vell.) Brenan (Magalhães *et al.* 2019). The number of medicinal plants indicates the importance of this environment, and experimental approaches focused on such species have improved. To rationally explore the possible uses of this biome, its potential needs to be demonstrated scientifically. Considering the Caatinga biome, improving our knowledge about medicinal flora can provide alternatives to treating common diseases and will also serve to preserve the genetic, biological and cultural diversity. We will present below some of the main studies that have accumulated data on plants of great cultural importance in the region (see Albuquerque *et al.* 2007).

3.1 *Amburana cearensis* (Allemão) A.C. Smith

A. cearensis is a native tree commonly found in the Brazilian semi-arid region and the Caatinga biome, where it is popularly known as 'cumarú,' 'amburana-de-cheiro' or 'umburana' (Albuquerque *et al.* 2007; Leal *et al.* 2005, 2009). Its trunk bark and seeds are widely used in folk medicine for the treatment of respiratory disease, pain, worm infections, sore throat, and inflammation and as antitussive and antispasmodic agents (Bitu *et al.* 2015).

The anti-inflammatory and bronchodilator activities of *A. cearensis* were promoted by carrageenan and N-formyl-methyl-leucyl-phenylalanine (fMLP)-induced migration in rat peritoneal cavities (Leal *et al.* 2003). The crude ethanolic extract of *A. cearensis* leaves was shown to have a positive effect on ovarian cell cultures, and the antioxidant compounds could protect ovarian follicles from Reactive Oxygen Species (ROS) during in vitro culture (Barberino *et al.* 2016; Gouveia *et al.* 2016). The *A. cearensis* extract increased the rate of antrum

Table 1. Major compounds identified in Caatinga plants.

Class compounds	Species	Plant organ	Biological activity	Reference
Alkaloids				
2-Methyl-9H- β -carboline-2-ion and 2',6'-Dihydroxy-4'-methoxyacetophenone-2'-O- β -glucoside	<i>Harrisia adscendens</i> (Cactaceae)	Root	Antimicrobial	Santos et al. (2018)
3-Benzoyloxytropane; 3-(3',5'-Dimethoxy-4'-hydroxy)benzoyloxytropane; 3-(4'-Methoxy)benzoyloxytropane; 3-Phenylacetoxytropane; 3-Phenylacetoxynortropane; 3-(2-Methylbutyryloxy)tropan-6-propionyl-7-ol; 3-(2-Methylbutyryloxy)tropan-6-propionyl-7-ol; 3-(2-Methylbutyryloxy)tropan-6,7-diol; 3-(2-Methylbutyryloxy)nortropan-6,7-diol; 3-Isovaleryloxytropan-6-ol; 3-Phenyltropan-6-ol and N,N-Dimethyl-1-H-indole-3-ethanamine	<i>Erythroxylum pungens</i> (Erythroxylaceae)	Bark, root and leaf	Cytotoxicity	Macedo Pereira et al. (2018)
Usaramine and Monocrotaline	<i>Crotalaria pallida</i> and <i>Crotalaria retusa</i> (Fabaceae)	Seed	Antimicrobial	Negreiros Neto et al. (2016)
(+)-Pyrifoline; 6-Demethoxypyridifoline; (-)-Aspidofiline; (+)-Aspidospermine; Pyrifolidine; 15-Demethoxypyridifoline; Aspidofractinine and N-Formylaspidofractinine	<i>Aspidosperma pyrifolium</i> (Apocynaceae)	Stem, root and leaf	-	Araújo et al. (2007); Gilbert et al. (1962); Craveiro et al. (1983)

Anonaine; Asimilobine; Lanuginosine; Liriodenine; Pronuciferine and Stepharine	Lysicamine; and <i>Annona squamosa</i> (Annonaceae)	<i>Annona cherimola</i> Leaf	-	Rabêlo et al. (2015).
Phenolics and Flavonoids				
Kaempferol; Isorhamnetin and Myricetin	Quercetin; <i>Ziziphus joazeiro</i> (Rhamnaceae)	Leaf	Antimicrobial	Andrade et al. (2019)
Gallic acid; Rutin; Ellagic acid; Catechin; Quercetin; Kaempferol; Caffeic acid; Quinic acid; Galloylmucic acid; Quercetin xyloside; Quercetin rhamnoside; Quercetin glucoside; Caffeoyl ellagic acid; Quercetin galloyl xyloside; Quercetin galloyl glucose; Quercetin digalloyl xyloside and Quercetin digalloyl glucoside	<i>Terminalia argentea</i> (Combretaceae)	Leaf	Cytotoxicity, genotoxic and sub- chronic toxicity	Beserra et al. (2018)
Gallic acid and Hyperoside	<i>Spondias tuberosa</i> (Anacardiaceae)	Leaf	Antioxidant, antimicrobial and hemolytic	Cordeiro et al. (2018)
Amentoflavone and Agathisflavone	<i>Poincianella pyramidalis</i> (Fabaceae)	Leaf (calluses)	-	Pereira Gomes- Copeland et al. (2018)
Quercetin; and Rutin	<i>Caryocar coriaceum</i> (Caryocaraceae)	Fruit	Antioxidant, antimicrobial and antileishmanial	Alves et al. (2017)

Tannins

Terminalin; Corilagin; Punicalin and Punicalagin	<i>Terminalia argentea</i> (Combretaceae)	Leaf	Cytotoxicity	Beserra et al. (2018)
--	--	------	--------------	-----------------------

Volatile oils and diterpenes

Spathulenol; Limonene; Caryophyllene oxide; α -Pinene, (E)- β -Ocimene, Germacrene D and Bicyclgermacrene	<i>Annona vepretorum</i> (Annonaceae)	Leaf (essential oil)	Anxiolytic, sedative, antiepileptic and antidepressant	Diniz et al. (2019); Araújo et al. (2015a)
Phyllacanthone	<i>Croton quercifolius</i> (Euphorbiaceae)	Stem bark	Antimicrobial	Oliveira-Júnior et al. (2018)
<i>Ent</i> -kauran-16-ene; 13-Hydroxy-8(17); 14-Labdialene; <i>Ent</i> -kaur-16-en-3 β -ol; 3-Oxo-hydroxy-8(17); 14-Labdiene; 3,13,19-Trihydroxy-8(17); 14-Labdiene and <i>Ent</i> -kauran-16 β , 17-diol	<i>Erythroxylum revolutum</i> (Erythroxylaceae)	Aerial parts	Antimicrobial	Oliveira (2012)
7 β ,17-Dihydroxy-12-oxo-cassan-13,15-diene; Depauperatin and 15,16-Bisnor-7 β ,17-dihydroxy-12-oxo-cassan-13-ene	<i>Calliandra depauperata</i> (Fabaceae)	Root	-	Pires et al. (2011).
<i>Ent</i> -15,16-epoxy-2-oxo-3,13(16); 14-Clerodatriene and <i>Ent</i> -15,16-epoxy-20-acetoxy-2-oxo-3,13(16),14-clerodatriene	<i>Croton grewoides</i> (Euphorbiaceae)	Aerial parts	-	Medeiros et al. (2011b)

Fatty acids and other lipids				
Oleic and Paullinic acids; β -Carotene; α -Tocopherol and γ -Tocopherol	<i>Guarea guidonia</i> (Meliaceae), <i>Allophylus puberulus</i> and <i>Paullinia elegans</i> (Sapindaceae)	Seed	-	Barbosa et al. (2019)
Oleic and Eicosenoic acids	<i>Cupania racemosa</i> , <i>Paullinia pinatta</i> and <i>Serjania</i> spp. (Sapindaceae)	Seed	-	Coutinho et al. (2015)
Palmitic; Oleic and Linoleic acids	<i>Herissantia tiubae</i> and <i>Sida</i> spp. (Malvaceae)	Seed	-	Silva et al. (2010)
Palmitic and Oleic acids	<i>Anemopaegma leave</i> , <i>Pyrostegia venusta</i> and <i>Tabebuia</i> <i>impetiginosa</i> (Bignoniaceae), <i>Hippocratea volubilis</i> (Celastraceae)	Seed	-	Pinho et al. (2009)
Lupeol and Betulin	<i>Cynophalla flexuosa</i> (Capparaceae)	Leaf (cuticle)	-	Pereira et al. (2019)
Lupeol	<i>Aspidosperma</i> <i>pyrifolium</i> (Apocynaceae)	Leaf (cuticle)	-	Medeiros et al. (2017)
Ursolic Acid; <i>n</i> -Alkanes; Epifriedelinol and Lupeol	<i>Tocoyena formosa</i> , <i>Maytenus rigida</i> and <i>Didymopanax</i> <i>vinosum</i>	Leaf (cuticle)	-	Oliveira and Salatino (2000)

- not reported

formation, which was higher in follicles cultured with plant extract than the control, and it also improved the cell viability, maturation and functionality (Barberino *et al.* 2016). Several culture media have been used to improve the rate of follicular viability and growth, although ovarian culture is too expensive. The use of *A. cearensis* is an interesting economic alternative that may make in vitro culture studies cheaper and more feasible for ovine and caprine animals (Barberino *et al.* 2016; Gouveia *et al.* 2016). *A. cearensis* may represent a very important biotechnology tool.

The extract of *A. cearensis* seeds was shown to have neuroprotective and antioxidant effects in cerebellar culture cells exposed to excitotoxic damage induced by glutamate. In addition, this species attenuated oxidative stress, reducing swelling, membrane potential dissipation, ROS production and calcium influx in isolated rat brains. Moreover, it induced the preservation of astrocytes, neurons and microglia in damaged rat brains (Lima Pereira *et al.* 2017). Parkinson's disease (PD) is reproduced in animal models via the injection of 6-hydroxydopamine (6-OHDA), a hydroxylated derivative of dopamine (Blum *et al.* 2001). Its neurotoxic action leads to oxidative stress (Tiffany-Castiglioni *et al.* 1982), catecholaminergic cell line apoptosis and activates nuclear factor-kappaB (NFkB) (Oh *et al.* 1995; Blum *et al.* 2001). Amburoside A, a phenol glucoside derived from *A. cearensis*, acts as an antioxidant molecule and protects mesencephalic cells against 6-OHDA neurotoxicity (Leal *et al.* 2005).

Compounds isolated from *A. cearensis*, such as afromorsin, kaempferol, isokaempferide, amburoside A, and protocathechuic have important biological effects, (Costa-Lotufu *et al.* 2003; Lopes *et*

al. 2013; Leal *et al.* 2008). Specifically, afromorsin isolated from the extract of *A. cearensis* bark (EBAC) inhibited neutrophil degranulation, myeloperoxidase activity, TNF- α secretion, and ROS generation (Lopes *et al.* 2013). Amburoside A and isokaempferide, a flavonol, showed anti-inflammatory activity and reduced the accumulation of inflammatory cells, myeloperoxidase activity and TNF- α production without cytotoxicity (Leal *et al.* 2009). These results show that *A. cearensis* is a good source of interesting molecules for the treatment of several diseases.

3.2 *Anadenanthera colubrina* (Vell) Brenan

A. colubrina, also known as "angico," is a tree belonging to the subfamily Mimosoideae (Leguminosae), and it occurs in different biomes and predominantly in seasonal forests and riparian galleries (Mota *et al.* 2017). *A. colubrina* is an important species to local communities in the Caatinga, and it is used for timber, charcoal and firewood as well as in popular medicine (Monteiro *et al.* 2006a,b). Its products are employed to treat respiratory and lung infections, ulcerative external lesions, inflammation, diarrhea, cough, bronchitis, influenza, and toothache (Agra *et al.* 2008, 2007; Almeida *et al.* 2005; Araújo *et al.* 2008).

β -Sitosterol and β -sitosteryl linoleate were also isolated from the hexane-soluble fraction of *A. colubrina* fruits and exhibits intense antifungal effects against *Alternaria alternata* (Campos *et al.* 2014). Moreover, bufotenine, a well-studied alkaloid, has been isolated from *A. colubrina* seeds and is able to block rabies virus infection in BHK-21 cells (Vigerelli *et al.* 2014). In addition, tannins isolated from stem-bark extract from *A. colubrina* is able to impair *Pseudomonas*

aeruginosa adhesion and biofilm formation (Trentin *et al.* 2013), and strong antifungal effects were demonstrated against *Candida albicans*. This extract also demonstrated the capacity to inhibit the formation of hyphae and blastospores, thus demonstrating the susceptibility of *C. albicans* biofilm to this plant. Although *A. colubrina* did not have a strong antiproliferative effect, it was capable of diminishing tumor growth in all cell lines (Lima *et al.* 2014). The antimicrobial effects of *A. colubrina* demonstrate the possibility of developing novel antifungal and antimicrobial agents from this plant. In addition, Barbosa *et al.* (2014) evaluated several extracts of native plants from Caatinga against *Aedes aegypti* and demonstrated that an extract from the seed of *A. colubrina* was adulticidal for insects (96% died) but did not show toxicity in mammal cells.

Anti-inflammatory and antinociceptive effects of the aqueous extract of *A. colubrina* bark was demonstrated using rodent *in vivo* models. Mice subjected to acetic acid-induced writhing tests showed an improved peritoneal nociceptive response, which was partially because of the reduction of algogenic/hypernociceptive endogenous mediators, such as prostaglandins (PG), bradykinin (BK), serotonin (5-HT), and histamine (Le Bars *et al.* 2001; Santos *et al.* 2013). In addition, the hot plate test, a classical test used to evaluate the central pain process, revealed no effect of *A. colubrina* on central nociceptive pathways in mice. However, the anti-inflammatory effect of this plant was clearly demonstrated in carrageenan-induced paw edema and carrageenan peritonitis (Santos *et al.* 2013) because of a reduction in microvascular permeability and leukocyte influx and possibly because of a reduction in the formation and release of inflammatory

mediators, such as histamine, BK, 5-HT, PG, and others. The anti-inflammatory and peripheral antinociceptive effects of *A. colubrina* are consistently exerted across different pathways; however, the underlying mechanisms still need to be elucidated.

The positive effect of the hydroalcoholic extract of *A. colubrina* bark on the healing process of the skin of rats has been demonstrated. Wound treatment with this extract showed more organized granulation tissue, a higher concentration of typical fibroblasts, and greater collagen fiber and blood vessel contents (angiogenesis) at the 7th and 14th day after surgery when compared to the untreated group (Pessoa *et al.* 2012, 2015).

An interesting polysaccharide isolated from *A. colubrina* has been characterized as an immunomodulatory and antitumor molecule. A complex acidic heteropolysaccharide primarily containing galactose and arabinose (ARAGAL) was able to activate mice peritoneal macrophages in a time- and dose-dependent manner and promoted phagocytic ability and anion superoxide production (Moretão *et al.* 2003). The same research group subsequently reported that ARAGAL increased alpha tumor necrosis factor (α -TNF) levels, which is an important antitumor molecule, and killed sarcoma 180 cells both *in vitro* and *in vivo* (Moretão *et al.* 2004). Therefore, *A. colubrina* has a promising antitumor effect.

3.3 *Annona vepretorum* Mart.

A. vepretorum, which is popularly known in Brazil as “araticum,” “bruteira” and “pinha da Caatinga,” is a shrub or tree native to the Caatinga (Bomfim *et al.* 2016) that is widely used for human nutrition and medicinal purposes (Bomfim *et al.* 2016; Dutra *et al.*

2014). The leaves are used in a decoction to treat allergies, skin diseases, yeast and bacterial infections, while its roots are indicated for the treatment of bee stings and snakes bites and as a sedative, antioxidant, antimicrobial, anti-inflammatory and pain treatment (Almeida *et al.* 2014b; Bomfim *et al.* 2016; Diniz *et al.* 2013; Dutra *et al.* 2014; Silva *et al.* 2015).

In addition, the crude ethanolic extract of *A. vepretorum* exerts antinociceptive and anti-inflammatory action *in vivo* under a chemically or thermally noxious stimulus. Mice treated with *A. vepretorum* show reduced acetic acid-induced writhing (Silva *et al.* 2015). A similar positive effect was detected in a formalin test, hot plate test and tail flick test. In general, these tests assess the central and peripheral nociceptive pathways (Le Bars *et al.* 2001), and the effects were blocked by naloxone, which might indicate that the antinociceptive effects are related to opioid receptor activation by the extract. Moreover, animals treated with *A. vepretorum* had better results in histamine and carrageenan hind paw edema models and showed reduced leucocyte migration in carrageenan-induced edema than untreated mice.

Several reports have shown that the *Amona* genus is a source of antitumor molecules (Formagio *et al.* 2015; Tundis *et al.* 2017; Zorofchian Moghadamtousi *et al.* 2014). The antitumoral activity of *A. vepretorum* has been associated with the essential oil (EO) from the leaves, especially spathulenol. The cytotoxic effect was also evaluated in peripheral blood mononuclear cells and B16-F10 melanoma cells with promising results. Spathulenol has been reported to be active against gastric adenocarcinoma cells (Areche *et al.* 2009), and it is a good candidate as an adjuvant chemotherapy. In addition, C57BL/6 mice

inoculated with B16-F10 melanoma cells were treated consecutively for 11 days with the EO of spathulenol; *in vivo* tumor growth was inhibited by the treatment, and no toxic effects or hematological or peripheral blood biochemistry parameter changes were observed in mice (Bomfim *et al.* 2016).

Additionally, the leaf EO shows antioxidant, trypanocidal, antimalarial, antifungal properties. The antioxidant property of the EO from *A. vepretorum* (EOAV) was evaluated by two *in vitro* models, i.e., radical scavenging activity using the 1,1-diphenyl-2-picrylhydrazyl radical (DPPH) method and the β -carotene-linoleate model system, and it showed weak activity (Araújo *et al.* 2015a; Costa *et al.* 2012).

The EOAV demonstrated potent antimalarial activity against the erythrocytic stage of *Plasmodium falciparum* and a trypanocidal effect against *Trypanosoma cruzi* epimastigotes and trypomastigotes. In addition, an *in vitro* model of mouse macrophages infected with intracellular amastigotes, the chronic clinically relevant forms of *T. cruzi* showed that EOAV both significantly reduced the number of infected macrophages and the relative number of amastigotes per 100 macrophages (Meira *et al.* 2015). Trypanocidal action is mediated by plasma membrane alterations (sterol biosynthesis inhibition), severe mitochondrial swelling with a large loss of electron density from its matrix and induced necrosis (Meira *et al.* 2015). The intense trypanocidal activity could be attributed to the high concentration of bicyclogermacrene. Thus, EOAV had interesting results with low toxicity.

3.4 *Aspidosperma pyriforme* Mart.

A. pyriforme, which is popularly known as “pereiro,” “pereiro preto” or “pereiro do

sertão" (Araújo *et al.* 2007), has been used in folk medicine, such as for the relief of benign prostatic hyperplasia, diabetes, erectile dysfunction, wound healing, dizziness and inflammation (Almeida *et al.* 2019; Souza Lima and Soto-Blanco 2010; Souza Lima *et al.* 2017).

The anti-inflammatory effects of the aqueous extract of *A. pyrifolium* leaves were evaluated in carrageenan-induced and Tityus serrulatus scorpion venom-induced peritonitis models. This extract was able to prevent inflammation and reduce leukocyte migration (Souza Lima *et al.* 2017). The mechanisms involved in envenomation by *T. serrulatus* involved local leukocyte migration, sodium and potassium ions in excitable cells, nitric oxide and cytokine mediators (Martin-Eauclaire *et al.* 2018; Pucca *et al.* 2015). Thus, *A. pyrifolium* may modulate ion channels and pro-inflammatory mediator synthesis. The phytochemical profile revealed the presence of a large amount of flavonoids and phenolic derivatives in the hydroalcoholic extract of *A. pyrifolium*. Recently, the neuroprotective and antioxidant properties of this extract were demonstrated in rats (Araújo *et al.* 2018). The extract of *A. pyrifolium* seeds blocked the behavioral changes in a rat model of PD, such as apomorphine-induced rotation, motor incoordination and degeneration of dopaminergic tonus (Araújo *et al.* 2018). Araújo *et al.* (2018) showed that rats treated with *A. pyrifolium* extract presented reduced nitrite levels and lipid peroxidation in lesioned striatum. These authors also showed the reduction of TNF- α content in the striatum, thus confirming the anti-inflammatory effect of this species.

Malaria is a major parasitic infection in many tropical and subtropical regions, and it still remains one of the leading causes of death worldwide (WHO 2017, 2018).

Plasmodium vivax is the most common cause of malaria in Latin American, and it has developed resistance to the antimalarial drug Chloroquine (Rahman *et al.* 2019). Several plants have been used to treat malaria. The ethanolic crude stem-bark extract of *A. pyrifolium* showed high antimalarial activity with low in vitro toxicity (Ceravolo *et al.* 2018). The beneficial biological effects have been associated with the presence of monoterpenoid indole alkaloids, such as aspidofractinine and 15-demethoxypyrrifoline (Araújo *et al.* 2007), and another report showed that the ethanolic extract of *A. pyrifolium* leaves caused hemolysis, lethality to 1-day-old *Artemia salina* larvae, and abortion, low fetal birth weight and high toxicity in Wistar pregnant rats (de Souza Lima and Soto-Blanco 2010). Previous reports showed that embryonic death, abortion and premature birth were induced by *A. pyrifolium* in farm animals (de Souza Lima and Soto-Blanco 2010; Riet-Correa *et al.* 2012).

3.5 *Cnidoscolus quercifolius* Pohl

C. quercifolius, which is popularly named "favela" or "faveleira," is a native forage species of the Caatinga that produces latex, can be used to recover degraded areas; provide food for animal and human consumption; and as medicine, timber, and energy (de Araújo Gomes *et al.* 2014; Paredes *et al.* 2016). Considering folk medicine, *C. quercifolius* is also used to treat inflammation (Lorenzi and Matos 2002; Maia-Silva *et al.* 2012). Reports about the pharmacological effects of this species are scarce. The genus *Cnidoscolus* is used for several medicinal purposes, including as an anti-inflammatory, an antitumor agent for the genitourinary system, an antiseptic and to treat kidney infections, dermatological and

ophthalmic lesions, bruises, fractures, wounds, warts, dysentery, hemorrhage, appendicitis and rheumatism (Albuquerque *et al.* 2007; Almeida *et al.* 2005; José *et al.* 2012).

The popular use of *C. quercifolius* extract to treat inflammation is supported by its anti-inflammatory activity as demonstrated in carrageenan-induced paw edema and peritonitis inflammation models in mice. The anti-inflammatory effect of the ethanolic extract of *C. quercifolius* is at least partially because of the inhibited synthesis of inflammatory mediators including prostaglandins, histamine and neutrophils (de Araújo Gomes *et al.* 2014). The crude extract from the bark of *C. quercifolius* is efficient against *Staphylococcus epidermidis* (AM235), an important bacteria involved in severe infection, including endocarditis and sepsis, as well as routine clinical procedures, such as catheter implantation (José *et al.* 2012). However, this extract is inactive against gram-negative bacteria.

The aqueous extract of *C. quercifolius* did not present an acute toxic effect because physical, behavioral or motor changes were not observed, none of the treated animals died, and the organ weight of the treated mice did not change. However, this extract exerts a hypoglycemic effect in diabetic streptozotocin-induced mice (Lira *et al.* 2017) and has antioxidant properties (Ribeiro *et al.* 2017).

3.6 *Erythrina velutina* Willd

E. velutina is an endemic tree to the plains and riverbanks of Northeast Brazil, and it is popularly called “mulungu.” This tree is well known for its effects on the central neural system, such as sedation, insomnia, convulsions (Dantas *et al.* 2004).

The antinociceptive effect of the

hydroalcoholic extract of *E. velutina* stem bark was demonstrated by the reduction of abdominal pain induced by acetic acid independent of the opioid system in mice, and this effect was primarily caused by anti-inflammatory action (Vasconcelos *et al.* 2003). Curiously, Marchioro *et al.* (2005) showed that the ethanolic extract of *E. velutina* leaves had antinociceptive effects and was dependent on the opioid system.

The use of *E. velutina* to treat others central nervous system (CNS) disturbances has been demonstrated. The hydroalcoholic extract of *E. velutina* stem bark exerts anxiolytic-like effects in rats (Raupp *et al.* 2008; Ribeiro *et al.* 2006), anticonvulsant activity (Vasconcelos *et al.* 2007), attenuation of schizophrenia-like behavior (Dias KCF *et al.* 2019; Ximenes *et al.* 2018), antioxidant effects (Dias KCF *et al.* 2019; Silva *et al.* 2016) and neuroprotective effects against 5-6-hydroxydopamine-induced neurotoxicity (Silva *et al.* 2016) and acute cerebral ischemia (Rodrigues *et al.* 2017). In addition, the indole alkaloid hypaphorine isolated from *E. velutina* induces sleep in normal mice. Taken together, these results confirm the effect of this species on the CNS, which is reflected in the traditional knowledge of this species.

3.7 *Lippia origanoides* Kunth

L. origanoides is an aromatic shrub popularly known as “erva-do-marajó,” “alecrim-angola,” “alecrim pimenta,” “orégano,” “orégano do monte,” or “salva-do-marajó” (Brito FCR *et al.* 2018; Menezes *et al.* 2018; Raman *et al.* 2017). The leaves are used as seasoning, and its tea is used as a sedative and to treat gastrointestinal disease; infections of the throat, skin, and scalp; pain; and asthma (Menezes *et al.* 2018; Oliveira *et al.* 2014).

The ethanolic extract of *L. origanoides* leaves demonstrate an acaricidal effect against *Tetranychus cinnabarinus* and the potential for the biological control of pests (Sivira *et al.* 2011). In addition, an extract of *L. origanoides* leaves was able to inhibit the progression of aggressive breast cancer cells (Raman *et al.* 2017), which was partially associated with its ability to trigger the rapid irreversible apoptosis of cancer cells by reducing mitochondrial oxidative metabolism and ATP levels (Raman *et al.* 2018). The biological effect of this species is associated with its EO. In fact, the EO of *L. origanoides* (EOLO) has antimicrobial (Hernandes *et al.* 2017), trypanocidal (Baldissera *et al.* 2017) and insecticidal activity (Vera *et al.* 2014) because of its chemical composition, which is predominantly terpenoids compounds, including monoterpenes, such as carvacrol, p-cymene, linalool, thymol, and carvophyllene (Menezes *et al.* 2018).

In addition, EOLO has a relaxant effect on trachea smooth muscle, which is related to its ability to modulate potassium channels and soluble guanylyl cyclase (Menezes *et al.* 2018). The secondary metabolite profile of EOLO showed at least 91 different compounds of *L. origanoides* such as limonene, β -myrcene, naringenin, luteolin, quercetin, trans- β -ocimene and linalool, which are common in EO (Stashenko *et al.* 2013). In addition, this profile included well-known antimicrobial and antioxidant molecules and promoted adipose tissue proliferation (Brito FN *et al.* 2018; Stashenko *et al.* 2013). Carvacrol and thymol have been associated with the genoprotective effect of *L. origanoides* (Vicuña *et al.* 2010).

3.8 *Myracrodruon urundeuva* Allemão

M. urundeuva is a tree widely distributed in the Caatinga in the semi-arid region of Northeast Brazil. It is popularly named “*aroeira*” or “*aroeira do sertão*” and is used in folk medicine to treat gynecological infections and as an anti-inflammatory agent (Oliveira *et al.* 2017; Viana *et al.* 2003). Unfortunately, this species is threatened with extinction and has been highly exploited as a timber source and fuel (Soares *et al.* 2018).

The anti-inflammatory effect of *M. urundeuva* has been proved in several models. Enemas of *M. urundeuva* reduce the number of inflammatory cells and increased the reepithelization of tissue without fibrosis in a colitis model induced by acetic acid (Rodrigues *et al.* 2002). The aqueous extract of *M. urundeuva* leaves reduced *Streptococcus mutans* accumulation and prevented enamel demineralization and caries in rats (Crivelaro de Menezes *et al.* 2010). Matos *et al.* (2019) showed that the *M. urundeuva* extract modulates mineral bone metabolism. In addition, the ethanolic, ethyl acetate and hydroalcoholic extracts of *M. urundeuva* bark and leaves showed no hemolytic, genotoxic, mutagenic or toxic effects in rats. In addition, the *M. urundeuva* bark extract has a potential effect against *C. albicans*. These effects are associated with the presence of flavonoids and tannins (Oliveira *et al.* 2017). In addition, the chalcone-enriched fraction had a beneficial effect on periodontal disease in rats (Botelho *et al.* 2008).

Neuroprotection is another important beneficial effect of *M. urundeuva*, and this activity is associated with the antioxidant and anti-inflammatory effect of the extract, thus indicating its potential use as a tool to prevent or treat neurodegenerative states, such as PD (Calou *et al.* 2014). The chalcone-enriched fraction isolated from the *M. urundeuva* stem bark had a protective

effect on the CNS, including reduced oxidative stress and apoptotic injury induced by 6-hydroxydopamine in mesencephalic cells (Nobre-Júnior *et al.* 2009). In this context, the dimeric chalcones derived from *M. urundeuva* presents inhibitory activity against cathepsins V, which is important because this enzyme is involved in several physiological and pathological processes, including the development of neurological disorders (Niwa *et al.* 2012; Sarria *et al.* 2018).

The tannin-enriched fraction derived from the stem bark of *M. urundeuva* has both anti-inflammatory and antiulcer gastric action in mice, which is because of its antioxidant properties and presence of polyphenols (Souza *et al.* 2007). These results were confirmed in several experimental models, such as ethanol-induced gastric lesions and croton oil-induced ear edema in rats (Aguar Galvão *et al.* 2018). The antinociceptive and anti-inflammatory effects of the dimeric chalcone-enriched fraction derived from the stem-bark ethyl acetate extract of *M. urundeuva* was reported in a mouse model (Viana *et al.* 2003). Taken together, these data confirmed the traditional uses of this species.

The anthelmintic and insecticidal effects of *M. urundeuva* have been demonstrated. Recently, Soares *et al.* (2018) showed the anthelmintic activity of the extract of *M. urundeuva* seeds against *Haemonchus contortus*. An extract of the leaf and stem of *M. urundeuva* also efficiently inhibited egg hatching and larval exsheathment of *H. contortus* (de Oliveira *et al.* 2011). Moreover, lectins isolated from this species had larvicidal effects (Sá *et al.* 2009), and pentadecadienyl-phenol had insecticidal effects against *Aedes aegypti* (Souza *et al.* 2012). Taken together, the data show that *M. urundeuva* is a source of beneficial

molecules with therapeutic potential.

3.9 *Spondias tuberosa* Arruda

S. tuberosa, which is popularly known as “umbu” or “imbu,” is an endemic species to the Caatinga that is widely used as a medicinal plant for the treatment of colic, diarrhea, diabetes mellitus, menstrual disturbances, placental delivery, inflammation, renal infection, and throat afflictions, and it is also used as an antiemetic and tonic (Silva *et al.* 2012a; de Albuquerque *et al.* 2007; de Freitas Lins-Neto *et al.* 2010; Araújo *et al.* 2012). The occurrence of phenols, hydrolysable tannins, flavones, flavonoids, leucoanthocyanidins in the *Spondias* genus has been well described. Phenols, tannins, triterpenes and quinones were detected in an ethanolic extract of the inner bark (Almeida *et al.* 2005), and the flavonoid and tannin content has been quantified in a methanolic extract of the bark (Araújo *et al.* 2008). HPLC analysis of a methanolic extract of *S. tuberosa* leaves performed by Silva *et al.* (2012a) showed the occurrence of high amounts of rutin, quercetin, and ellagic acid. The chlorogenic acid, caffeic acid, rutin and isoquercitrin contents were quantified in a hydroethanolic extract of leaves from *S. tuberosa*. Although *S. tuberosa* has been extensively used in folk medicine, pharmacological studies on this species are scarce in the literature.

The anti-inflammatory activity of *S. tuberosa* extract has been demonstrated via different experimental protocols using a carrageenan-induced paw edema model as well as a peritonitis animal models (Silva Siqueira *et al.* 2016). *S. tuberosa* extract reduces the influx of neutrophils in mice paw tissues and decreases myeloperoxidase (MPO) activity and leukocyte counts in the

peritoneal fluid after carrageenan challenge (Siqueira *et al.* 2016). These effects were similar to that of dexamethasone treatment, which is a standard anti-inflammatory drug. The antibacterial activities of *S. tuberosa* extract were assayed against eight gram-negative bacteria in vitro by the agar well diffusion method (Silva *et al.* 2012a). In general, the data showed a weakly antibacterial effect of *S. tuberosa* via determination of the minimum inhibitory concentration (MIC). Although the activities of *S. tuberosa* were reduced compared with that of ciprofloxacin, a standard antibiotic, the increased resistance of microorganisms to antibiotics must be considered to promote the search for new drugs. Interestingly, the hexane extract of *S. tuberosa* leaves had a potent antifungal effect (low value of MIC₅₀) via the mitochondrial overproduction of anion superoxide and hyperpolarization of the mitochondrial membrane (da Costa Cordeiro *et al.* 2018). Recently, the antidiabetic effect of *S. tuberosa* was detailed (Barbosa *et al.* 2018). A hydroethanolic extract of the inner stem bark of *S. tuberosa* attenuated hyperglycemia and glucose oral tolerance and improved insulin sensitivity in diabetic streptozotocin-induced rats. In addition, *S. tuberosa* had important antioxidant and hepatoprotective effects in diabetic models (Barbosa *et al.* 2018).

The antioxidant activity of *S. tuberosa* has been shown in vitro (Silva *et al.* 2012a; Cordeiro *et al.* 2018) and in vivo (Barbosa *et al.* 2018). The antioxidant activity was evaluated by scavenging the radicals DPPH and 2,2-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) (ABTS^{•+}), which demonstrated a weak and moderate effect (Cordeiro *et al.* 2018). In addition, *S. tuberosa* exerted a potent in vivo antioxidant effect, reduced lipid peroxidation, improved enzymatic defense and increased the antioxidant status

in diabetic rats (Barbosa *et al.* 2018). These effects are consistent with phytochemical constitution of *S. tuberosa*.

An acute toxicity and cytotoxicity evaluation of *S. tuberosa* inner bark extract showed the absence of poisonous effects (Barbosa *et al.* 2016), which demonstrates that this species may be safely used as therapeutic alternative in the treatment of several diseases.

3.10 *Ximenia americana* L.

X. americana is a bushy or small tree popularly known as “ameixa,” and it is distributed in Africa, Asia and tropical America. In traditional medicine, the leaves and bark of *X. americana* are used in a tea to treat pain, obesity, dysmenorrhea, inflammation, wound healing, diabetes, cough, hoarseness, constipation, venereal disease, leprotic ulcer, skin diseases, malaria and osteoporosis (Diallo *et al.* 2002; Grønhaug *et al.* 2008; Le *et al.* 2012; Ogunleye and Ibitoye 2003; Bitu *et al.* 2015).

X. americana has antiviral activity against HIV-1 (Asres *et al.* 2001). In addition, this species has been used as an herbal medicine by persons living with HIV/AIDS in Africa to ameliorate HIV/AIDS-related symptoms and HIV/AIDS infection (Nagata *et al.* 2011).

The potent anticancer activity of *X. americana* aqueous extracts has also been observed (Voss *et al.* 2006b). In addition, riproximin, a type II ribosome-inactivating protein, was isolated from *X. americana* fruits and seeds and shows high selectivity for tumor cell lines (Bayer *et al.* 2012). Riproximin (RPX) was able to inhibit protein synthesis in a cell-free system and is toxic to HeLa cells. This antineoplastic effect was confirmed in vivo in a CC531 colorectal cancer rat model and in humans (Pervaiz *et*

al. 2015; Voss *et al.* 2006a). In addition, RPX induced important cytotoxic effects in the selected human breast cancer cell lines MDA-MB-231 and MCF-7 by modulating cytostatic and apoptotic pathways (Pervaiz *et al.* 2016). RPX was able to inhibit pancreatic cancer metastasis to the liver in rats bearing intraportal implanted Suit2-007 cells (Adwan *et al.* 2014).

The aqueous extract of *X. americana* elicited a potent analgesic effect on inflammatory pain but possessed a weak effect on central nociceptive pathways (Soro *et al.* 2016). These effects are related to the anti-edematogenic effect of the hydroalcoholic extract of *X. americana* on acute and chronic inflammation, which likely inhibits inflammatory mediators (Silva *et al.* 2018). Moreover, the hydroalcoholic extract of *X. americana* showed angiogenic effects and stimulated collagen synthesis to accelerate wound healing in rats (Souza Neto Júnior *et al.* 2019) and antidiabetic activity (Siddaiah *et al.* 2019). The tannin-rich extract of *X. americana* has hepatoprotective and antidiabetic properties (Sobeh *et al.* 2017). The gastroprotective effect has been confirmed in other gastric ulcer models, and this protection is mediated by sulfhydryl, nitric oxide and antisecretory activity, which is correlated with its major constituents, procyanidins B and C and catechin/epicatechin (Aragao *et al.* 2018).

In addition, the heteropolysaccharide-enriched fraction of *X. americana* bark had anti-inflammatory and analgesic effects in an experimental model of caerulein-induced acute pancreatitis, and they involved type 2 carabinoid receptors (Silva-Leite *et al.* 2018). Moreover, a polysaccharide-rich tea of *X. americana* bark protected against indomethacin-induced gastric injury mice, which was likely associated with a reduction of neutrophil infiltration (Silva Pantoja *et al.*

2018).

It is noteworthy that pharmaceutical technology has been used to improve natural products for treatment purposes; for example, a tablet of *X. americana* was developed from mucoadhesive polymers for the oral treatment of fungal infection (Almeida *et al.* 2019).

3.11 *Ziziphus joazeiro* Mart.

Z. joazeiro (Rhamnaceae) is a native tree widely distributed in northeastern Brazil (Lucena *et al.* 2008) and the Caatinga biome, where it is named “*juazeiro*.” It is used traditionally in folk medicine for treating fever, bacterial infection, general pain, gingivitis, and respiratory diseases; for topical healing; and as a hepatic and cardiac tonic; as a diuretic; and for other purposes (Brito *et al.* 2015).

The antipyretic effect of *Z. joazeiro* was demonstrated in endotoxemic rabbits (Nunes *et al.* 1987), and a low antioxidant effect was also reported based on the scavenging of the radical DPPH (Silva *et al.* 2011; Brito *et al.* 2015) and ferric reducing ability of plasma assay (Brito *et al.* 2015).

3.12 Antimicrobial activity

A great number of papers on the antimicrobial activity of plants in the Caatinga are being accumulated. Most of them are studies with crude extracts and show activities that can be considered irrelevant, since they are carried out with extracts in high concentrations. In Table 2, we present 18 plant species that showed antimicrobial activity ≤ 1000 $\mu\text{g/mL}$ against the microorganisms tested. Based on these data, most of the results were obtained with extracts at high concentrations and thus are not very interesting for future

pharmacological studies (according to Ríos and Recio 2005).

The strains that were most susceptible to extracts at ≤ 1000 $\mu\text{g/mL}$ concentrations were the Gram-positive *Staphylococcus aureus*, which was susceptible to extracts of 11 plant species; *Micrococcus luteus*, which was inhibited by the extracts of seven species; and the gram-negative *P. aeruginosa*, which was inhibited by four extracts (see Table 2). The bacteria reported as being more susceptible to extracts were also the most registered in the studies (>20 publications), with the exception of the bacteria *M. luteus*. *Escherichia coli* was the most commonly used in laboratories to test the sensitivity of plant extracts (25 publications). However, only extracts from *A. vepretorum* and *S. brasiliensis* presented good activity (≤ 1000) (Almeida *et al.* 2014b; Saraiva *et al.* 2011).

The extracts of the species that presented activities at very low concentrations ($\text{MICs} \leq 100$ $\mu\text{g/mL}$) were the methanolic extract of the leaf of *Shinopsis brasiliensis*, which presented an effect on the strains of *P. aeruginosa* and *S. aureus* at a very low concentration (31 $\mu\text{g/mL}$) (Saraiva *et al.* 2011). Additionally, the methanolic extract of *C. quercifolius* inhibited the growth of *Enterococcus faecalis*, *Enterococcus faecium*, *Lasiodiplodia theobromae*, *P. aeruginosa*, *S. epidermidis* and the fungus *Colletotrichum gloeosporioides* at concentrations of 7–62 $\mu\text{g/mL}$ (Paredes *et al.* 2016) (Table 2). Plant extracts that showed a broad spectrum of activity (≤ 1000) were those of *Buchenavia tetraphylla* (Aubl.) R.A. Howard, *Poincianella pyramidalis* (Tul) L.P. Queiroz, *Senna macranthera* (Collad.) H.S. Irwin & Barneby, and *Shinopsis brasiliensis* Engl. (Table 2).

Only a few extracts (2% of all tested extracts [$n = 174$]) inhibited fungal growth.

For this group, the most recorded species in the studies was *C. albicans*, which was more susceptible to the plant extracts (Cruz *et al.* 2007; Silva *et al.* 2011, 2012b). An aqueous extract of the leaf of *C. pyramidalis*, an aqueous extract of the bark *Z. joazeiro* and an ethanolic extract of the leaf and bark of *Z. joazeiro* presented antimicrobial action at low concentrations ranging from 6–25 $\mu\text{g/mL}$, and they also presented broad spectra of action against the fungi *C. albicans*, *Candida guilliermondii*, *Cryptococcus neoformans*, *Fonsecaea pedrosoi*, and *Trichophyton rubrum* (Cruz *et al.* 2007).

The low number of active extracts against fungi may reflect the difficulty of finding active extracts for this group. Owing to the complexity of fungal cells, finding substances that are both selective against a specific target and provide a safe antifungal effect is difficult. This limitation coupled with the limited research on plants for antifungal activity compared to antibacterial activity has been a barrier in the search for new natural antifungal products. Thus, the results indicate the need for *in vitro* studies to discover new alternatives for fighting fungi.

Newman and Cragg (2016) surveyed antimicrobial sources and observed the lack of new antifungal agents obtained from natural products from 1981 to 2014. This study found that compared with antibacterial agents, antifungal agents were predominantly of synthetic origin, with 73% of the antibacterial agents obtained from natural products, while only 10% of the antifungals are from natural products. These data are of concern because of the urgent need to obtain new products since many have lost their effectiveness.

In general, in the tests evaluated by the disc-diffusion method in agar, the concentrations were very high when compared to those of the microdilution

Table 2. Native Caatinga plants with antimicrobial activity at concentrations of ≤ 1000 $\mu\text{g/ml}$.

Family/Species	Part used	Type of extract	Microorganism	Reference
Anacardiaceae				
<i>Schinopsis brasiliensis</i> Engl.	Bark	Ethanol/water 10%, 20%, 30%, 50%, 70%	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>Streptococcus oralis</i>	Silva et al. (2012c)
	Bark	Ethanol/water 30%, 50%	<i>E. faecalis</i>	Silva et al. (2012c)
	Leaf	Methanolic	<i>E. faecalis</i> , <i>E. coli</i> , <i>Klebsiella pneumoniae</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Staphylococcus saprophyticus</i> , <i>Staphylococcus sp.</i>	Saraiva et al. (2011)
Annonaceae				
<i>Annona vepretorum</i> Mart.	Leaf	Chloroform, ethanolic 95%	<i>E. coli</i>	Almeida et al. (2014b)
	Leaf	Hexane	<i>E. coli</i> , <i>Salmonella enterica</i> , <i>Serratia marcescens</i> , <i>S. aureus</i>	Almeida et al. (2014b)
Burseraceae				
<i>Commiphora leptophloeos</i> (Mart.) J. B. Gillett	Bark	Aqueous	<i>P. aeruginosa</i>	Trentin et al. (2013)
Caesalpinaceae				
<i>Poincianella pyramidalis</i> (Tul.) L.P. Queiroz	Leaf	Aqueous	<i>C. albicans</i> , <i>Candida guilliermondii</i> , <i>C. neoformans</i> , <i>F. pedrosoi</i> , <i>Trichophyton rubrum</i>	Cruz et al. (2007)
	Leaf	Aqueous	<i>Fusobacterium nucleatum</i> , <i>Porphyromonas gingivalis</i> , <i>Prevotella intermedia</i>	Alviano et al. (2008)

Combretaceae

<i>Buchenavia tetraphylla</i> (Aubl.) R.A. Howard	Leaf	Ethanollic 70%	<i>S. aureus</i> , <i>Mycobacterium smegmatis</i> , <i>Bacillus subtilis</i> , <i>M. luteus</i> , <i>Salmonella enteritidis</i> , <i>P. aeruginosa</i> , <i>Proteus vulgaris</i>	Oliveira et al. (2012)
---	------	----------------	--	------------------------

Euphorbiaceae

<i>Cnidoscopus pubescens</i> Pohl	Root	Methanollic 80%	<i>S. aureus</i>	Peixoto Sobrinho et al. (2012)
-----------------------------------	------	-----------------	------------------	--------------------------------

<i>Cnidoscopus quercifolius</i> Pohl.	Leaf, Root	Methanollic	<i>S. epidermidis</i> , <i>E. faecium</i> , <i>Lasiodiplodia theobromae</i> , <i>P. aeruginosa</i> , <i>E. faecalis</i> , <i>Colletotrichum gloeosporioides</i> .	Paredes et al. (2016)
	Bark	Methanollic 80%	<i>S. aureus</i> , <i>Staphylococcus coagulase</i> .	Peixoto Sobrinho et al. (2012)

<i>Jatropha mutabilis</i> (Pohl) Baill.	Root	Hydroalcoholic	<i>M. luteus</i>	Silva et al. (2012b)
---	------	----------------	------------------	----------------------

Fabaceae

<i>Anadenanthera colubrina</i> (Vell.) Brenan var. <i>colubrina</i>	Leaf	Hydroalcoholic	<i>S. aureus</i>	Silva et al. (2012b)
---	------	----------------	------------------	----------------------

<i>Bauhinia acuruana</i> Moric.	Leaf	Ethanollic	<i>M. luteus</i>	Silva et al. (2012b)
---------------------------------	------	------------	------------------	----------------------

<i>Libidibia ferrea</i> (Mart. exTul.) L.P. Queiroz	Fruit	Ethanollic	<i>M. luteus</i>	Silva et al. (2012b)
---	-------	------------	------------------	----------------------

	Fruit	Hydroalcoholic	<i>M. luteus</i> , <i>S. aureus</i>	Silva et al. (2012b)
--	-------	----------------	-------------------------------------	----------------------

<i>Pityrocarpa moniliformis</i> (Benth.) Luckow & R. W. Jobson	Leaf	Hydroalcoholic	<i>M. luteus</i>	Silva et al. (2012b)
--	------	----------------	------------------	----------------------

<i>Senna macranthera</i> (Collad.) H.S. Irwin & Barneby	Flower	Ethanol	<i>S. aureus</i>	Diaz et al. (2010)
	Root	Dichloromethane, ethanol	<i>S. aureus</i> , <i>Streptococcus agalactiae</i> , <i>Streptococcus bovis</i>	Andrade et al. (2015)
<i>Stylosanthes viscosa</i> Sw.	Leaf	Hydroalcoholic	<i>B. subtilis</i>	Silva et al. (2012b)
Malpighiaceae				
<i>Stigmaphyllon paralias</i> A. Juss.	Leaf	Hydroalcoholic	<i>S. aureus</i>	Silva et al. (2012b)
Myrtaceae				
<i>Eugenia brejoensis</i> Mazine	Leaf	Hydroalcoholic	<i>C. albicans</i> , <i>M. luteus</i>	Silva et al. (2012b)
Oleaceae				
<i>Ximenia americana</i> L.	Bark	Ethanol/water 10%, 20%, 30%, 50%	<i>S. aureus</i>	Silva et al. (2012c)
	Bark	Ethanol/water 30%	<i>E. faecalis</i>	Silva et al. (2012c)
	Bark	Ethanol/water 70%	<i>S. oralis</i>	Silva et al. (2012c)
Rhamnaceae				
<i>Ziziphus joazeiro</i> Mart.	Bark	Ethanol	<i>B. subtilis</i> , <i>C. albicans</i> , <i>Enterobacter aerogenes</i> , <i>E. faecalis</i> , <i>K. pneumoniae</i> , <i>M. luteus</i> , <i>M. smegmatis</i> , <i>Proteus mirabilis</i> , <i>P. vulgaris</i> , <i>S. marcescens</i> , <i>S. aureus</i> , <i>Streptococcus pyogenes</i>	Silva et al. (2011)
	Inner bark	Aqueous	<i>P. gingivalis</i>	Alviano et al. (2008)

Leaf	Ethanollic	<i>E. aerogenes</i> , <i>E. pneumoniae</i> , <i>M. luteus</i> , <i>M. smegmatis</i> , <i>P. vulgaris</i> , <i>P. aeruginosa</i> , <i>S. pyogenes</i>	K. Silva et al. (2011)
Stem	Aqueous	<i>C. albicans</i> , <i>C. guilliermondii</i> , <i>C. neoformans</i> , <i>F. pedrosoi</i> , <i>T. rubrum</i>	C. Cruz et al. (2007)

method, which is common in such studies (Braga 2016). It is reasonable that there are differences in the concentrations used for both tests, since they employed different techniques. However, excessively high amounts should be avoided to optimize the search for extracts with better activities for more detailed future studies. The extremely high doses applied in the trials have shown that there is a need to relativize the findings since they do not determine the activity of a plant. Therefore, it is suggested that new microdilution assays should be performed for the extracts that were evaluated only by diffusion, since this technique is the most recommended for determining antimicrobial activity (Alves GA et al. 2008).

4. Zoopharmacognosy and Zoopharmacology in the Caatinga

A study by Ferreira et al. (2010) indicated that research describing the chemical composition and pharmacological effects of remedies obtained from animal parts are still scarce. In the Northeast Brazil, bioprospecting has contributed to the identification and elucidation of the therapeutic effects of chemical compounds that may be present in zootherapies, which are frequently used for the empirical

treatment of different health conditions (Alves and Rosa 2005, 2006, 2007a, 2007b, 2007c; Alves et al. 2007; Cabral et al. 2013; Dias et al. 2013; Oliveira et al. 2014; Sales et al. 2015).

Reptiles and amphibians are among the most frequently studied wild species in the Caatinga in terms of their chemical compositions, especially in studies that aim to identify and/or isolate compounds present in extracts obtained from body fat and secretions (such as saliva and venom). Moreover, ethnozoology surveys have shown that reptiles are among the most commonly used animal species in folk medicine (Zhou and Jiang 2004; Mahawar and Jaroli 2006, 2008; Alves and Pereira-Filho 2007; Alves et al. 2008a, 2008b) and show that body fat stands out as one of the most commonly used products (Costa-Neto and Alves 2010; Alves and Alves 2011).

Studies performed with reptiles from the Caatinga predominantly investigate the chemical composition and pharmacological properties of secretions obtained from venomous snakes. A new bradykinin-potentiating peptide was identified and isolated (Pro-Asn-Leu-Pro-Asn-Tyr-Leu-Gly-Ile-Pro-Pro) from the venom extracted from *Crotalus durissus cascavella*. When investigated for its pharmacological

potential, the effects of this peptide were compared to that of the potentiated bradykinin peptide (BBP9a) isolated from *Bothrops jararaca* and the antihypertensive drug captopril® (Lopes et al. 2014). Studies with the *Crotalus durissus collilineatus* species have identified and isolated factors with potent central analgesic activity that possibly act on the opioid system. Gomes (2007) isolated an analgesic factor called crotamine from *C. durissus* poison; in this study, the author observed that crotamine in natura or after heat treatment (boiling at 100°C for 8 minutes) was effective at reducing algic stimuli in mice and exhibited a potency greater than morphine with a longer lasting effect. Olinda (2010) isolated an analgesic factor (Cdc factor) from *C. durissus* and observed that this substance possesses central and peripheral analgesic actions in mice, with this effect being 108% more potent than that of morphine.

Fixed oils obtained from the body fat of reptiles have shown a predominance of unsaturated fatty acids when compared to saturated fatty acids (Ferreira et al. 2010; Cabral et al. 2013). Dias et al. (2013) verified that the body fat of *Phrynosoma geoffroanus* is composed of 84.63% and 13.38% unsaturated and saturated methyl esters, respectively. Among the constituents identified in the *P. geoffroanus* fixed oil, palmitoleic and oleic acids were present in greater amounts and accounted for 58.39% and 15.7% of the extract's composition, respectively. This species displayed antifungal modifying activity against *C. albicans* strains. For lizards used as a zotherapy, fat from *Tupinambis merianae* was evaluated for its anti-inflammatory activity (Ferreira et al. 2010), and it demonstrated a reduction in inflammation in mouse ear edema models; however, analyses of the antibacterial activity of *T.*

merianae fat (Ferreira et al. 2009) and skin (Ferreira et al. 2018) did not identify antibacterial action. The fat from *Tropidurus hispidus* lizards also showed antibiotic modifying activity (Santos et al. 2015). Bioprospecting of reptile fat to determine the antibacterial and antibiotic activity modifying effects also showed that fat from *Boa constrictor*, *Spilotes pullatus* and *Crotalus durissus* snakes exhibited a synergistic effect when combined with aminoglycosides (Ferreira et al. 2009; Oliveira et al. 2014).

Oliveira et al. (2014) analyzed the chemical composition of the oil obtained from the body fat of the *Spilotes pullatus* snake and revealed the presence of 10 fatty acids that accounted for 94.97% of the extract's chemical composition. The authors observed a higher concentration of unsaturated fatty acids than saturated fatty acids (61.38% and 33.59, respectively), with the unsaturated fatty acids elaidic acid (37.26%) and linoleic acid (17.28%) and the saturated fatty acids palmitic acid (19.01%) and stearic acid (10.58%) predominating.

Extracts and decoctions of *Tropidurus hispidus*, *Tropidurus semitaeniatus*, *Ameiva ameiva*, *Tupinambis merianae*, *Iguana*, *B. constrictor* and *C. durissus* reptiles were also examined as potential antibacterial agents (Santos et al. 2012a, b; Ferreira et al. 2018.). However, modifying activity was only validated for *T. hispidus*, *T. semitaeniatus* and *A. ameiva* (Santos et al. 2012a, b). In anti-inflammatory activity validation studies using paw and ear edema models, skin decoctions from *C. durissus*, *I. iguana*, and *B. constrictor* reduced inflammation (Ferreira et al. 2014).

The *Leptodactylus* and *Rhinella* genera are among the Caatinga amphibians used in popular medicine. Cabral et al. (1926) investigated the chemical composition of fixed oils obtained from the body fat of two

species belonging to the *Leptodactylus* genus, *Leptodactylus macrosternum* Miranda-Ribeiro (1926) and *Leptodactylus vastus* Adolf Lutz (1930) and observed that the oil obtained from *L. macrosternum* contained 40% saturated fatty acids and 60% unsaturated fatty acids while the oil obtained from *L. vastus* contained 58.33% saturated fatty acids and 41.67% unsaturated fatty acids. In the aforementioned study, both species possessed common constituents, including methyl myristate, methyl pentadecanoate, methyl palmitoleate, methyl linoleate, methyl estereate and methyl 5,8,11,14-eicosatetraenoate. The authors stated that the presence of large amounts of unsaturated fatty acids in the *L. macrosternum* and *L. vastus* fixed oils was unexpected and indicated that the animals' diets potentially influencing this result since essential fatty acids are not synthesized by animals.

In the study by Sousa *et al.* (2009), the authors identified and isolated a new neutral peptide rich in glycine/leucine called leptoglycine from *Leptodactylus pentadactylus* Laurenti skin secretions. The authors observed that this peptide displayed a significant antimicrobial effect and could inhibit the growth of different gram-negative bacteria, such as *P. aeruginosa*, *E. coli* and *Citrobacter freundii*. Limaverde *et al.* (2009) isolated the protein toxin leptoxin and investigated its toxicological properties in a study performed with *L. pentadactylus* skin secretions, observing that leptoxin promotes death in mice because of acute lung edema because of an increase in lung microvascular pressure arising from direct vasoconstriction induced by this substance.

Studies with species belonging to the *Rhinella* genus have identified the presence of different saturated fatty acids, including

lauric acid, myristic acid, pentadecanoic acid, stearic acid, palmitic acid and heptadecanoic acid, and of unsaturated fatty acids, including arachidonic acid, linoleic acid, oleic acid and palmitoleic acid, in fixed oils obtained from the body fat of *Rhinella jimi* frogs (Stevaux 2002) (Sales *et al.* 2015). Moreover, the study by Sales *et al.* (2017) analyzed secretions obtained from the parotid glands of the aforementioned species and identified the presence of bufotenin, dehydro-bufotenin, marinobufagine, telocinobufagine, and bufaline. Similar constituents were also identified in venom extracted from *Bufo schneideri* Werner, namely, marinobufagine, telocinobufagine and bufaline (Freitas 2003).

Regarding wild mammals, Ferreira *et al.* (2018) evaluated the antibacterial activity of fat from *Euphractus sexcinctus* and spines from *Coendou prehensilis*, although the antibacterial action of its components was not validated. Fats from mammals and domestic fowl are also described as zootherapies used in the Caatinga biome for diseases affecting domestic animals and humans (Ferreira *et al.* 2012; Dias *et al.* 2018, Dias *et al.* 2019a, 2019b). In the study by Dias *et al.* (2019a), the antibacterial and antibiotic modifying action of fats from the mammals *Bos taurus*, *Capra hircus*, and *Ovis aries* domestic against bacteria of veterinary interest were analyzed, and these fats showed antibiotic modifying activity for terramycin, norfloxacin, amikacin, and amoxicillin. This same modifying activity was also found for fat from *Sus scrofa* domesticus (Dias *et al.* 2019b), *Gallus gallus* birds, and *Meleagris gallopavo* (Dias *et al.* 2018). For invertebrates, the modifying activity of aminoglycoside antibiotics associated with products derived from the termite *Nasutitermes corniger* was also observed (Coutinho *et al.* 2009; Coutinho *et*

al. 2010).

5. Perspectives and gaps

Although hundreds of plants occurring in the Caatinga have been identified, studies on their secondary metabolites are still limited with respect to the isolation and identification of bioactive molecules. As listed above, a large proportion of the studies are only aimed at verifying the presence of metabolites and quantifying them. Because the Caatinga is a unique ecosystem, greater partnerships with universities and research centers can provide greater insights into the phytochemistry of species occurring in the Caatinga, especially the endemic species. This collaborative effort may be important to investigate a set of questions that require the interaction of different lines of research. For example, these investigations could assess what the perceived characteristics of the medicinal plants by people (smell, taste) would be more associated with their pharmacological potential. These studies will be interesting in the future as they may benefit bioprospecting by highlighting a set of important plant characteristics from local knowledge that may be essential in finding new candidates for disease treatment. In addition, future efforts could also be directed to verify if the pharmacological potential of plants varies in response to the marked climatic seasonality of the Caatinga (see, for example, Monteiro *et al.* 2006a) and/or to the diversity of climatic conditions present in the region.

The ethnopharmacological data on zootherapeutics enable the discovery of new drugs and may also serve as a guide for the rational and sustainable use of exploited species (Alves 2009; Ferreira *et al.* 2012). Research has shown that the animal species

used for traditional medicine are threatened with extinction, and information on the biological activity of these resources may not be available (Alves and Rosa 2005, 2007c).

The treatment of human and animal diseases using animal derivatives constitute the basis of many traditional therapeutic systems and is considered relevant to science, thus necessitating a better understanding of the biological, social, cultural and economic aspects of these resources (Lev 2003; Alves and Albuquerque 2013).

Bioprospecting studies investigating the activities of fats from domestic animals that are also used as zootherapeutics were reviewed here (Dias *et al.* 2018, Dias *et al.* 2019a, 2019b). These studies have shown that fats from domestic species present the same ability to modulate antibiotic activity as the fats from wild species, which indicates that possible substitutes may be available for products from endangered species.

ACKNOWLEDGMENTS

We acknowledge the Brazilian National Council for Scientific and Technological Development (CNPq) for the research productivity grant awarded to UPA, RRNA, HDC and ML; and the contribution of the INCT Ethnobiology, Bioprospecting and Nature Conservation, certified by CNPq, with financial support from FACEPE (Foundation for Support to Science and Technology of the State of Pernambuco -Grant number: APQ-0562-2.01/17).

REFERENCES

Adwan H, Murtaja A, Kadhim Al-Tae K, Pervaiz A, Hielscher T, Berger MR (2014) **Riproximin's activity depends on gene expression and sensitizes PDAC cells to TRAIL.** *Cancer*

- Biology & Therapy 15:1185–1197. <https://doi.org/10.4161/cbt.29503>
- Agra MF, Silva KN, Basílio IJLD, Freitas PF, Barbosa-Filho JM (2008) **Survey of medicinal plants used in the region Northeast of Brazil.** *Revista Brasileira de Farmacognosia* 18:472–508. <https://doi.org/10.1590/S0102-695X2008000300023>
- Agra MF, Baracho GS, Nurit K, Basílio IJLD, Coelho VPM (2007) **Medicinal and poisonous diversity of the flora of “Cariri Paraibano.”** *Brazilian Journal of Pharmacognosy* 111:383–395. <https://doi.org/10.1016/j.jep.2006.12.007>
- Aguiar Galvão W, Braz-Filho R, Canuto KM, Ribeiro PRV, Campos AR, Moreira ACOM, Silva SO, Filho FAM, Santos SAAR, Melo Júnior JMA, Gonçalves NGG, Fonseca SGC, Bandeira MAM (2018) **Gastroprotective and anti-inflammatory activities integrated to chemical composition of *Myracrodruon urundeuva* Allemão - A conservationist proposal for the species.** *Journal of Ethnopharmacology*. 222:177–189. <https://doi.org/10.1016/j.jep.2018.04.024>
- Albuquerque UP (2006) **Re-examining hypotheses concerning the use and knowledge of medicinal plants: a study in the Caatinga vegetation of NE Brazil.** *Journal of Ethnobiology and Ethnomedicine* 2:30. <https://doi.org/10.1186/1746-4269-2-30>
- Albuquerque UP, Medeiros PM, Almeida ALS, Monteiro JM, Lins-Neto EMF, Melo JG, Santos JP (2007) **Medicinal plants of the caatinga (semi-arid) vegetation of NE Brazil: a quantitative approach.** *Journal of Ethnopharmacology* 114:325–354. <https://doi.org/10.1016/j.jep.2007.08.017>
- Albuquerque UP, Medeiros PM, Ramos MA, Ferreira Júnior WS, Nascimento ALB, Torres Avilez WM, Melo JG (2014) **Are ethnopharmacological surveys useful for the discovery and development of drugs from medicinal plants?** *Revista Brasileira de Farmacognosia* 24:110–115. <http://doi.org/10.1016/j.bjp.2014.04.003>
- Albuquerque UP, Oliveira RF (2007) **Is the use-impact on native caatinga species in Brazil reduced by the high species richness of medicinal plants?** *Journal of Ethnopharmacology* 113:156–170. <https://doi.org/10.1016/j.jep.2007.05.025>
- Albuquerque UP, Araújo EL, Castro CC, Alves RRN (2017) **People and natural resources in the Caatinga.** In: Silva JMC, Leal IR, Tabarelli M. (eds) *Caatinga: The largest tropical dry forest region in South America.* Springer, Basel, Switzerland, pp. 303–333.
- Alencar NL, Santoro FR, Albuquerque UP (2014) **What is the role of exotic medicinal plants in local medical systems? A study from the perspective of utilitarian redundancy.** *Revista Brasileira de Farmacognosia* 24:506–515. <http://doi.org/10.1016/j.bjp.2014.09.003>
- Alencar NL, Sousa Araújo TA, Amorim ELC, Albuquerque UP (2010) **The inclusion and selection of medicinal plants in traditional pharmacopoeias—evidence in support of the diversification hypothesis.** *Economic Botany* 64:68–79. <https://doi.org/10.1007/s12231-009-9104-5>
- Almeida CFCBR, Amorim ELC, Albuquerque UP (2011) **Insights into the search for new drugs from traditional knowledge: An ethnobotanical and chemical-ecological perspective.** *Pharmaceutical Biology* 49:864–873. <http://doi.org/10.3109/13880209.2010.551777>
- Almeida CFCBR, Lima e Silva TC, Amorim ELC, Maia MBS, Albuquerque UP (2005) **Life strategy and chemical composition as predictors of the selection of medicinal plants from the Caatinga (Northeast Brazil).** *Journal of Arid Environments* 62:127–142. <http://doi.org/10.1016/j.jaridenv.2004.09.020>
- Almeida J, Souza AV, Oliveira AP, Santos U, Souza M, Bispo L, Turatti ZC, Lopes N (2014a) **Chemical composition of essential oils from *Croton conduplicatus* (Euphorbiaceae) in two different seasons.** *Journal of Essential Oil Bearing Plants* 17:1137–1145. <http://doi.org/10.1080/0972060X.2014.931254>
- Almeida JRGS, Araújo CS, Pessoa CO, Costa MP, Pacheco AGM (2014b) **Atividade antioxidante, citotóxica e antimicrobiana de *Annona vepretorum* Mart. (Annonaceae).** *Revista Brasileira de Fruticultura* 36:258–264. <https://doi.org/10.1590/s0100-29452014000500030>
- Almeida L, Oshiro Júnior J, Silva M, Nóbrega F, Andrade J, Santos W, Ribeiro A, Conceição M, Veras G, Medeiros A (2019) **Tablet of *Ximenia americana* L. Developed from Mucoadhesive Polymers for Future Use in Oral Treatment of Fungal Infections.** *Polymers* 11:379. <https://doi.org/10.3390/polym11020379>

- Almeida MLB, Freitas WES, Morais PLD, Sarmiento JDA, Alves RE (2016) **Bioactive compounds and antioxidant potential fruit of *Ximenia americana* L.** Food Chemistry 192:1078–1082.
- Almeida TS, Rocha JBT, Rodrigues FFG, Campos AR, Da Costa JGM (2013) **Chemical composition, antibacterial and antibiotic modulatory effect of *Croton campestris* essential oils.** Industrial Crops and Products 44:630–633.
- Almeida VL, Silva CG, Silva AF, Campana PRV, Foubert K, Lopes JCD, Pieters L (2019) ***Aspidosperma* species: A review of their chemistry and biological activities.** Journal of Ethnopharmacology. 231:125–140. <https://doi.org/10.1016/j.jep.2018.10.039>
- Andrade FI, Purgato GA, Maia FT, Siqueira RP, Lima S, Diaz G, Diaz MA (2015) **Chemical constituents and an alternative medicinal veterinary Herbal soap made from *Senna macranthera*.** Evidence-Based Complementary and Alternative Medicine <https://doi.org/10.1155/2015/217598>
- Alves DR, Morais SM, Tomiotto-Pellissier F, Miranda-Sapla MM, Vasconcelos FR, Silva ING, Sousa HA, Assolini JP, Conchon-Costa I, Pavanelli WR, Freire FCO (2017) **Flavonoid Composition and Biological Activities of Ethanol Extracts of *Caryocar coriaceum* Wittm., a native plant from Caatinga Biome.** Evidence-Based Complementary and Alternative Medicine <http://doi.org/10.1155/2017/6834218>
- Alves GA, Vinholis AHC, Casemiro LA, Furtado NAJC, Silva MLA, Cunha WR, Martins CHG (2008) **Estudo comparativo de técnicas de screening para avaliação da atividade antibacteriana de extratos brutos de espécies vegetais e de substâncias puras.** Quimica Nova 31:1224–1229.
- Alves RRN, Pereira-Filho GA (2007) **Commercialization and use of snakes on North and Northeastern Brazil: implications for conservation and management.** Biodiversity and Conservation 16:969–985.
- Alves RRN, Rosa IL (2005) **Why study the use of animal products in traditional medicines?** Journal of Ethnobiology and Ethnomedicine 1:1–5.
- Alves RRN, Rosa IL (2006) **From cnidarians to mammals: The use of animals as remedies in fishing communities in NE Brazil.** Journal of Ethnopharmacology 107:259–276.
- Alves RRN, Rosa IL, Santana GG (2007) **The role of animal-derived remedies as complementary medicine in Brazil.** BioScience 57:949–955.
- Alves RRN, Rosa IL (2007a) **Biodiversity, traditional medicine and public health: where do they meet?** Journal of Ethnobiology and Ethnomedicine 3:1–9.
- Alves RRN, Rosa IL (2007b) **Zootherapeutic practices among fishing communities in North and Northeast Brazil: A comparison.** Journal of Ethnopharmacology 111:82–103.
- Alves RRN, Rosa IL (2007c) **Zootherapy goes to town: The use of animal-based remedies in urban areas of NE and N Brazil.** Journal of Ethnopharmacology 113:541–555.
- Alves RRN, Lima HN, Tavares MC, Souto WMS, Barboza RRD, Vasconcellos A (2008a) **Animal-based remedies as complementary medicines in Santa Cruz do Capibaribe, Brazil.** BMC Complementary and Alternative Medicine 8:1–9.
- Alves RRN, Vieira WLS, Santana GG (2008b) **Reptiles used in traditional folk medicine: conservation implications.** Biodiversity and Conservation 17:2037–2049.
- Alves RRN (2009) **Fauna used in popular medicine in Northeast Brazil.** Journal of Ethnobiology and Ethnomedicine 5:1–11.
- Alves RRN, Mendonça LET, Confessor MVA, Vieira WLS, Lopez LCS (2009a) **Hunting strategies used in the semi-arid region of northeastern Brazil.** Journal of Ethnobiology and Ethnomedicine 5(12):1–50.
- Alves RRN, Oliveira MGG, Barboza RRD, Singh R, Lopez LCS (2009b) **Medicinal Animals as therapeutic alternative in a semi-arid region of Northeastern Brazil.** Forsch Komplementmed/Research in Complementary Medicine 16:305–312.
- Alves RRN, Oliveira MGG, Barboza RRD, Lopez LCS (2010) **An ethnozoological survey of medicinal animals commercialized in the markets of Campina Grande, NE Brazil.** Human Ecology Review 17(1):11–17.
- Alves RRN, Alves HN (2011) **The faunal drugstore: Animal-based remedies used in traditional medicines in Latin America.** Journal of Ethnobiology and Ethnomedicine 7:1–43.

- Alves RRN, Pereira Filho GA, Silva Vieira K, Souto WMS, Mendonças LET, Montenegro PFGP, Almeida WO, Vieira WLS (2012) **A zoological catalogue of hunted reptiles in the semiarid region of Brazil.** *Journal of Ethnobiology and Ethnomedicine* 8(1):27.
- Alves RRN, Albuquerque UP (2013) **Animals as a Source of Drugs: Bioprospecting and Biodiversity Conservation.** In: Alves RRN, Rosa IL (eds) *Animals in Traditional Folk Medicine.* Springer, New York, pp. 67–89.
- Alves RRN, Feijó A, Barboza RRD, Souto WMS, Fernandes-Ferreira H, Cordeiro-Estrela P, Langguth A (2016a) **Game mammals of the Caatinga biome.** *Ethnobiology and Conservation* 5:1–51.
- Alves RRN, Melo MF, Ferreira FS, Trovão DMBM, Dias TLP, Oliveira JV, Lucena RFP, Barboza RRD (2016b) **Healing with animals in a semiarid northeastern area of Brazil.** *Environment, Development and Sustainability* 18(6):1733–1747.
- Alviano WS, Alviano DS, Diniz CG, Alviano CS, Farias LM, Carvalho MA, Souza MG, Bolognese AM (2008) **In vitro antioxidant potential of medicinal plant extracts and their activities against oral bacteria based on Brazilian folk medicine.** *Archives of Oral Biology* 53: 545–552.
- Andrade JC, Silva ARP, Santos ATL, Freitas MA, Carneiro JNP, Gonçalo MIP, de Souza A, Freitas TS, Ribeiro PRV, Brito ES, Morais-Braga MFB, Coutinho HDM (2019) **UPLC-MS-ESI-QTOF characterization and evaluation of the antibacterial and modulatory antibiotic activity of *Ziziphus joazeiro* Mart. aqueous extracts.** *South African Journal of Botany* 123: 105–112. <https://doi.org/10.1016/j.sajb.2019.02.001>
- Anjos QQA, Silva SLC, Silva DC, Gualberto SA, Santos FR, Carvalho MG, Sousa DL (2018) **Chemical composition of the essential oil of the *Croton tetradenius* (Euphorbiaceae) aerial part and bioactivity on *Aedes Aegypti* (diptera: Culicidae) in relation to different collection periods.** *Periodico Tche Quimica* 15:364–379.
- Ankli A, Sticher O, Heinrich M (1999) **Yucatec Maya medicinal plants versus nonmedicinal plants: indigenous characterization and selection.** *Human Ecology* 27:557–580. <https://doi.org/10.1023/A:1018791927215>
- Aragao TP, Prazeres LDKT, Brito SA, Neto PJR, Rolim LA, Almeida JRGS, Caldas GFR, Wanderley AG (2018) **Contribution of Secondary Metabolites to the Gastroprotective Effect of Aqueous Extract of *Ximenia americana* L. (Olacaceae) Stem Bark in Rats.** *Molecules* 23:112. <https://doi.org/10.3390/molecules23010112>
- Araújo CS, Oliveira AP, Lima RN, Alves PB, Diniz TC, Almeida JRGS (2015a) **Chemical constituents and antioxidant activity of the essential oil from leaves of *Annona vepretorum* Mart. (Annonaceae).** *Pharmacognosy* 11:615–618. <https://doi.org/10.4103/0973-1296.160462>
- Araújo TAS, Almeida e Castro VTN, Solon LGS, Silva GA, Almeida MG, Costa JGM, Amorim ELC, Albuquerque UP (2015b) **Does rainfall affect the antioxidant capacity and production of phenolic compounds of an important medicinal species?** *Industrial Crops and Products* 76:550–556. <http://doi.org/10.1016/j.indcrop.2015.07.008>
- Araújo HFP, Silva JMC (2017) **The avifauna of the Caatinga: Biogeography, ecology, and conservation.** In: Silva JMC, Leal IR, Tabarelli M (eds) *Caatinga: The largest tropical dry forest region in South America.* Springer, Basel, Switzerland, pp. 181–210.
- Araújo DP, Nogueira PCN, Santos ADC, Costa RO, Lucena JD, Gadelha-Filho CVJ, Lima FAV, Neves KRT, Leal LKAM, Silveira ER, Viana GSB (2018) ***Aspidosperma pyrifolium* Mart: neuroprotective, antioxidant and anti-inflammatory effects in a Parkinson's disease model in rats.** *Journal of Pharmacy and Pharmacology* 70:787–796. <https://doi.org/10.1111/jphp.12866>
- Araújo JX, Antheaume C, Trindade RCP, Schmitt M, Bourguignon JJ, Sant'Ana AEG (2007) **Isolation and characterisation of the monoterpenoid indole alkaloids of *Aspidosperma pyrifolium*.** *Phytochemistry Reviews* 6:183–188. <https://doi.org/10.1007/s11101-006-9044-y>
- Araújo TAS, Alencar NL, Amorim ELC, Albuquerque UP (2008) **A new approach to study medicinal plants with tannins and flavonoids contents from the local knowledge.** *Journal of Ethnopharmacology* 120:72–80. <https://doi.org/10.1016/j.jep.2008.07.032>

- Araújo TAS, Almeida e Castro VTN, Amorim ELC, Albuquerque UP (2012) **Habitat influence on antioxidant activity and tannin concentrations of *Spondias tuberosa***. *Pharmaceutical Biology* 50:754–759. <https://doi.org/10.3109/13880209.2011.630673>
- Areche C, Schmeda-Hirschmann G, Theoduloz C, Rodríguez JA (2009) **Gastroprotective effect and cytotoxicity of abietane diterpenes from the Chilean Lamiaceae *Sphacele chamaedryoides* (Balbis) Briq.** *Journal of Pharmacy and Pharmacology* 61:1689–1697. <https://doi.org/10.1211/jpp/61.12.0015>
- Asres K, Bucar F, Kartnig T, Witvrouw M, Pannecouque C, De Clercq E (2001) **Antiviral activity against human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) of ethnobotanically selected Ethiopian medicinal plants.** *Phytotherapy Research* 15:62–69.
- Aye MM, Aung HT, Sein MM, Armijos C (2019) **A Review on the Phytochemistry, Medicinal Properties and Pharmacological Activities of 15 Selected Myanmar Medicinal Plants.** *Molecules* 24:293. <https://doi.org/10.3390/molecules24020293>
- Baldissera MD, de Freitas Souza C, Mourão RHV, da Silva LVF, Monteiro SG (2017) **Trypanocidal action of *Lippia alba* and *Lippia organoides* essential oils against *Trypanosoma evansi* in vitro and in vivo used mice as experimental model.** *Journal of Parasitic Diseases* 41:345–351. <https://doi.org/10.1007/s12639-016-0800-7>
- Barberino RS, Barros VRP, Menezes VG, Santos LP, Araújo VR, Queiroz MAA, Almeida JRGS, Palheta RC, Matos MHT (2016) ***Amburana cearensis* leaf extract maintains survival and promotes in vitro development of ovine secondary follicles.** *Zygote* 24:277–285. <https://doi.org/10.1017/S0967199415000179>
- Barbosa HM, Amaral D, Nascimento JN, Machado DC, Araújo TAS, Albuquerque UP, Almeida JRGS, Rolim LA, Lopes NP, Gomes DA, Lira EC (2018) ***Spondias tuberosa* inner bark extract exert antidiabetic effects in streptozotocin-induced diabetic rats.** *Journal of Ethnopharmacology* 227:248–257. <https://doi.org/10.1016/j.jep.2018.08.038>
- Barbosa-Filho JMB, Trigueiro JA, Cheriyan UO, Bhattacharyya J (1985) **Constituents of the stem-bark of *Zizyphus joazeiro*.** *Journal of Natural Products* 48:152–153. <https://doi.org/10.1021/np50037a039>
- Barbosa HM, Nascimento JN, Araújo TAS, Duarte FS, Albuquerque UP, Vieira JRC, Santana ERB, Yara R, Lima CSA, Gomes DA, Lira EC (2016) **Acute Toxicity and Cytotoxicity effect of ethanolic extract of *Spondias tuberosa* Arruda bark: hematological, biochemical and histopathological evaluation.** *Anais da Academia Brasileira de Ciências* 88:1993–2004. <https://doi.org/10.1590/0001-3765201620160041>
- Barbosa MO, Coutinho DJG, Santos J, Cordeiro RP, Muniz LR, Alves RC, Bessa CMAS, da Silva M, Oliveira MBPP, Oliveira AFM (2019) **Fatty acids, tocopherols and tocotrienols composition in seed oils of Brazilian species of Sapindaceae and Meliaceae.** *Journal of Food Science and Technology* 1–7. <http://doi.org/10.1007/s13197-019-03800-y>
- Barbosa PBBM, Oliveira JM, Chagas JM, Rabêlo LMA, Medeiros GF, Giodani RB, Silva EA, Uchôa AF, Ximenes MFFM (2014) **Evaluation of seed extracts from plants found in the Caatinga biome for the control of *Aedes aegypti*.** *Parasitology Research* 113:3565–3580. <https://doi.org/10.1007/s00436-014-4022-6>
- Barboza RRD, Lopes SF, Souto WMS, Fernandes-Ferreira H, Alves RRN (2016) **The role of game mammals as bushmeat in the Caatinga, northeast Brazil.** *Ecology and Society* 21(2):1–11.
- Barros TFS, Arriel NHC, Queiroz MF, Fernandes PD, Mendonça S, Ribeiro JAA, Medeiros EP (2015) **Fatty acid profiles of species of *Jatropha curcas* L., *Jatropha mollissima* (Pohl) Baill. and *Jatropha gossypifolia* L.** *Industrial Crops and Products* 73:106–108. <http://doi.org/10.1016/j.indcrop.2015.04.00>
- Beserra AMSS, Vilegas W, Tangerina MMP, Ascêncio SD, Soares IM, Pavana E, Damazo AS, Ribeiro RV, Martins DTO (2018) **Chemical characterization and toxicity assessment in vitro and in vivo of the hydroethanolic extract of *Terminalia argentea* Mart. leaves.** *Journal of Ethnopharmacology* 227:56–68. <http://doi.org/10.1016/j.jep.2018.08.025>
- Bezerra DMM, Araújo HFP, Alves ÂGC, Alves RRN (2013) **Birds and people in semiarid northeastern Brazil: symbolic and medicinal relationships.** *Journal of Ethnobiology and Ethnomedicine* 9:3.

- Bitu VCN, Bitu VCN, Matias EFF, Lima WP, Portelo AC, Coutinho HDM, Menezes IRA (2015) **Ethnopharmacological study of plants sold for therapeutic purposes in public markets in Northeast Brazil.** *Journal of Ethnopharmacology* 172:265–72. <https://doi.org/10.1016/j.jep.2015.06.022>
- Blum D, Torch S, Lambeng N, Nissou M, Benabid AL, Sadoul R, Verna JM (2001) **Molecular pathways involved in the neurotoxicity of 6-OHDA, dopamine and MPTP: contribution to the apoptotic theory in Parkinson's disease.** *Progress in Neurobiology* 65:135–172.
- Bomfim LM, Menezes LRA, Rodrigues ACBC, Dias RB, Gurgel Rocha CA, Soares MBP, Neto AFS, Nascimento MP, Campos AF, Silva LCRC, Costa EV, Bezerra DP (2016) **Antitumour Activity of the Microencapsulation of *Annona vepretorum* Essential Oil.** *Basic & Clinical Pharmacology & Toxicology* 118:208–213. <https://doi.org/10.1111/bcpt.12488>
- Botelho MA, Rao VS, Montenegro D, Bandeira MAM, Fonseca SGC, Nogueira NAP, Ribeiro RA, Brito GAC (2008) **Effects of a herbal gel containing carvacrol and chalcones on alveolar bone resorption in rats on experimental periodontitis.** *Phytotherapy Research* 22:442–449. <https://doi.org/10.1002/ptr.2325>
- Brandão GHA, Rigo G, Roque AA, Souza ACD, Scopel M, Nascimento CAO, Tasca T, Pereira CG, Giordani GB (2017) **Extraction of bioactive alkaloids from *Melocactus zehntineri* using supercritical fluid.** *Journal of Supercritical Fluids* 129:28–35. <http://doi.org/10.1016/j.supflu.2016.12.012>
- Brito FCR, Moura LFWG, Morais VD, Mendes ALRF, Moreira MR, Sousa VSS, Lustosa IBS, Sampaio RMM, Santos AAQA, Guedes MIF (2018) **Ethno-pharmacological studies of Brazilian Caatinga plants: a review.** *International Journal of Development Research* 8:23763–23766.
- Brito FN, Vendramin FS, Lopes CTDA, Costa MPR, Ohashi OM, Maia JGS, Ferreira LM, Silva RJK, Miranda MDS (2018) **Proliferation of human adipose tissue-derived stem cells stimulated by oil rich in thymol of *Lippia organoides*.** *Acta Cirúrgica Brasileira* 33(5):431–438. <https://doi.org/10.1590/s0102-865020180050000005>
- Brito SMO, Coutinho HDM, Talvani A, Coronel C, Barbosa AGR, Vega C, Figueredo FG, Tintino SR, Lima LF, Boligon AA, Athayde ML, Menezes IRA (2015) **Analysis of bioactivities and chemical composition of *Ziziphus joazeiro* Mart. using HPLC–DAD.** *Food Chemistry* 186:185–191. <https://doi.org/10.1016/j.foodchem.2014.10.031>
- Brito-Filho SG, Maciel JKS, Teles YCF, Fernandes MMMS, Chaves OS, Ferreira MDL, Fernandes PD, Félix LP, Cirino ICS, Siqueira-Júnior JP, Braz-Filho R, de Souza MFV (2017) **Phytochemical study of *Pilosocereus pachycladus* and antibiotic-resistance modifying activity of syringaldehyde.** *Brazilian Journal of Pharmacognosy* 27:453–458. <http://doi.org/10.1016/j.bjp.2017.06.001>
- Buckingham J, Munasinghe VRN (2015) **Dictionary of Flavonoids with CD-ROM.** 1 ed. CRC Press, Boca Raton, Florida, pp. 1199. <https://doi.org/10.1201/b18170>
- Cabral MES, Dias DQ, Sales DL, Oliveira OP, Araújo-Filho JA, Teles DA, Sousa JGG, Coutinho HDM, Costa JGM, Kerntopf MR, Alves RRN, Almeida WO (2013) **Evaluations of the antimicrobial activities and chemical compositions of body fat from the amphibians *Leptodactylus macrosternum* Miranda-Ribeiro (1926) and *Leptodactylus vastus* Adolf Lutz (1930) in the Northeastern Brazil.** *BMC Complementary and Alternative Medicine* 2013:1–7.
- Calou I, Bandeira MA, Aguiar-Galvão W, Cerqueira G, Siqueira R, Neves KR, Brito GA, Viana G (2014) **Neuroprotective Properties of a Standardized Extract from *Myracrodruon urundeuva* Fr. All. (Aroeira-Do-Sertão), as Evaluated by a Parkinson's Disease Model in Rats.** *Parkinson's Disease* 2014:1–11. <https://doi.org/10.1155/2014/519615>
- Campos VA, Perina FJ, Alves E, Sartorelli J, Moura AM, Oliveira DF (2014) ***Anadenanthera colubrina* (Vell.) Brenan produces steroidal substances that are active against *Alternaria alternata* (Fr.) Keissler and that may bind to oxysterol-binding proteins.** *Pest Management Science* 70:1815–1822. <https://doi.org/10.1002/ps.3722>

- Carvalho KS, Silva SL., de Souza IA, Gualberto SA, da Cruz RCD, dos Santos FR, de Carvalho MG (2016) **Toxicological evaluation of essential oil from the leaves of *Croton tetradenius* (Euphorbiaceae) on *Aedes aegypti* and *Mus musculus*.** Parasitology Research 115:3441–3448. <http://doi.org/10.1007/s00436-016-5106-2>
- Casagrande DG (2000) **Human taste and cognition in Tzeltal Maya medicinal plant use.** Journal of Ecological Anthropology 4:57–69. <http://doi.org/10.5038/2162-4593.4.1.3>
- Carmignotto AP, Astúa D (2017) **Mammals of the Caatinga: Diversity, ecology, biogeography, and conservation.** In: Silva JMC, Leal IR, Tabarelli M (eds) Caatinga: The largest tropical dry forest region in South America. Springer, Basel, Switzerland, pp. 211–255.
- Ceravolo IP, Zani CL, Figueiredo FJB, Kohlhoff M, Santana AEG, Krettli AU (2018) ***Aspidosperma pyriforme*, a medicinal plant from the Brazilian Caatinga, displays a high antiplasmodial activity and low cytotoxicity.** Malaria Journal 17:436. <http://doi.org/10.1186/s12936-018-2568-y>
- Cordeiro BMPC, Santos NDL, Ferreira MRA, Araújo LCC, Carvalho Júnior AR, Santos ADC, Oliveira AP, Silva AG, Falcão EPS, Correia MTS, Almeida JRGS, Silva LCN, Soares LAL, Napoleão TH, Silva MV, Paiva PMG (2018) **Hexane extract from *Spondias tuberosa* (Anacardiaceae) leaves has antioxidant activity and is an anti-Candida agent by causing mitochondrial and lysosomal damages.** BMC Complementary and Alternative Medicine 18:284. <http://doi.org/10.1186/s12906-018-2350-2>
- Costa EV, Dutra LM, Nogueira PCL, Moraes VRS, Salvador MJ, Ribeiro LHG, Gadelha FR (2012) **Essential oil from the leaves of *Annona vepretorum*: chemical composition and bioactivity.** Natural Product Communications 7(2): 265-266
- Costa Filho LO, Moura Silva MH, Almeida-Cortez JS, Silva, SI, Oliveira AFM (2012) **Foliar cuticular n-alkane of some *Croton* species from Brazilian semiarid vegetation.** Biochemical Systematics and Ecology 41:13-15. <https://doi.org/10.1016/j.bse.2011.11.005>
- Costa-Lotufo LV, Jimenez PC, Wilke DV, Leal LKAM, Cunha GMA, Silveira ER, Canuto KM, Viana GSB, Moraes MEA, Moraes MO, Pessoa C (2003) **Antiproliferative Effects of Several Compounds Isolated from *Amburana cearensis* A. C. Smith.** Zeitschrift für Naturforschung. Section C, A European Journal of Biosciences 58:675–680.
- Costa-Neto EM (1999) **Healing with animals in Feira de Santana City, Bahia, Brazil.** Journal of Ethnopharmacology 65:225–230.
- Costa-Neto EM, Alves RRN (2010) **Estado da arte da zooterapia popular no Brasil.** In: Costa-Neto EM, Alves RRN (eds) Zooterapia: os animais na medicina popular brasileira. Nupeea, Recife, Brazil.
- Coutinho DJG, Barbosa MO, Silva RM, Silva SI, Oliveira AFM (2015) **Fatty-Acid Composition of Seeds and Chemotaxonomic Evaluation of Sixteen Sapindaceae Species.** Chemistry and Biodiversity 12:1271–1280. <http://doi.org/10.1002/cbdv.201400325>
- Coutinho DJG, Barbosa MO, Souza RJC, Silva AS, Silva SI, Oliveira AFM (2016) **Biodiesel potential of the seed oils from some Brazilian native Euphorbiaceae species.** Renewable Energy 91:275–281. <http://doi.org/10.1016/j.renene.2016.01.064>
- Coutinho HDM, Almeida Filho GG, Pessoa HFL, Gadelha CA (2010) **Natural products from the termite *Nasutitermes corniger* lowers aminoglycoside minimum inhibitory concentrations.** Pharmacognosy 6:1–4.
- Coutinho HDM, Vasconcellos A, Alves RRN, Almeida Filho GG, Lima MA (2009) **Termite usage associated with antibiotic therapy: Enhancement of aminoglycoside antibiotic activity by natural products of *Nasutitermes corniger* (Motschulsky, 1855).** BMC Complementary and Alternative Medicine 9:3–5. <https://doi.org/10.1186/1472-6882-9-35>
- Craveiro AA, Matos FJA, Serur L (1983) **Alkaloids of *Aspidosperma pyriforme*.** Phytochemistry 22:1526–1528. [https://doi.org.ez16.periodicos.capes.gov.br/10.1016/S0031-9422\(00\)84061-3](https://doi.org.ez16.periodicos.capes.gov.br/10.1016/S0031-9422(00)84061-3)
- Crivelaro de Menezes TE, Delbem ACB, Brighenti FL, Okamoto AC, Gaetti-Jardim E (2010) **Protective efficacy of *Psidium cattleianum* and *Myracrodruon urundeuva* aqueous extracts against caries development in rats.** Pharmaceutical Biology 48:300–305. <https://doi.org/10.3109/13880200903122202>

- Cruz MCS, Santos PO, Barbosa AM, Melo DLFM, Alviano CS, Antonioli AR, Alviano DS, Trindade RC (2007) **Antifungal activity of Brazilian medicinal plants involved in popular treatment of mycoses.** *Journal of Ethnopharmacology* 111:409–412.
- da Costa Cordeiro BMP, Santos ND, Ferreira MRA, Araújo LCC, Júnior ARC, Santos ADC, Oliveira AP, Silva AG, Falcão EPS, Correia MTS, Almeida JRGS, Silva LCN, Soares LAL, Napoleão TH, Silva MV, Paiva PMG (2018) **Hexane extract from *Spondias tuberosa* (Anacardiaceae) leaves has antioxidant activity and is an anti-Candida agent by causing mitochondrial and lysosomal damages.** *BMC Complementary and Alternative Medicine* 18(1):284. <https://doi.org/10.1186/s12906-018-2350-2>
- Dantas M, de Oliveira F, Bandeira S, Batista J, Silva C, Alves P, Antonioli A, Marchioro M (2004) **Central nervous system effects of the crude extract of *Erythrina velutina* on rodents.** *Journal of Ethnopharmacology* 94:129–133. <https://doi.org/10.1016/j.jep.2004.05.007>
- de Araújo Gomes LM, De Andrade TMD, Silva JC, de Lima JT, Quintans-Júnior LJ, Da Silva Almeida JRG (2014) **Phytochemical screening and anti-inflammatory activity of *Cnidioscolus quercifolius* (Euphorbiaceae) in mice.** *Pharmacognosy Research* 6:345–349. <http://doi.org/10.4103/0974-8490.138290>
- de Oliveira LMB, Bevilacqua CML, Macedo ITF, Morais SM, Machado LKA, Campello CC, Mesquita MA (2011) **Effects of *Myracrodruon urundeuva* extracts on egg hatching and larval ensheathment of *Haemonchus contortus*.** *Parasitology Research* 109:893–898. <https://doi.org/10.1007/s00436-011-2331-6>
- Diallo D, Sogn C, Samaké FB, Paulsen BS, Michaelsen TE, Keita A (2002) **Wound Healing Plants in Mali, the Bamako Region. An Ethnobotanical Survey and Complement Fixation of Water Extracts from Selected Plants.** *Pharmaceutical Biology* 40:117–128. <https://doi.org/10.1076/phbi.40.2.117.5846>
- Dias DQ, Cabral MES, Sales DL, Oliveira OP, Araújo-Filho JA, Teles DA, Sousa JGG, Coutinho HDM, Costa JGM, Kerntopf MR, Alves RRN, Almeida WO (2013) **Chemical composition and validation of the ethnopharmacological reported antimicrobial activity of the body fat of *Phrynops geoffroanus* used in traditional medicine.** *Evidence-Based Complementary and Alternative Medicine* 2013:1–4. <https://doi.org/10.1155/2013/715040>
- Dias DQ, Sales DL, Andrade JC, Silva ANP, Tintino SR, Oliveira-Tintino DM, Delmondes GA, Barbosa MO, Coutinho HDM, Ferreira FS, Rocha MFG, Navarro DMAF, Rocha SKL, Costa JGM, Alves RRN, Almeida WO (2019a) **Antibacterial and antibiotic modifying evaluation of ruminants' body fat used as zoonotherapeutics in ethnoveterinary practices in Northeast Brazil.** *Journal of Ethnopharmacology* 233:87–93.
- Dias DQ, Sales DL, Andrade JC, Silva ANP, Tintino SR, Oliveira-Tintino DM, Delmondes GA, Barbosa MO, Coutinho HDM, Ferreira FS, Rocha MFG, Navarro DMAF, Rocha SKL, Costa JGM, Alves RRN, Almeida WO (2019b) **GC-MS analysis of the fixed oil from *Sus scrofa domestica* Linnaeus (1758) and antimicrobial activity against bacteria with veterinary interest.** *Chemistry and Physics of Lipids* 219:23–27.
- Dias DQ, Sales DL, Andrade JC, Silva ANP, Tintino SR, Oliveira-Tintino DM, Delmondes GA, Rocha MFG, Costa JGM, Alves RRN, Ferreira FS, Coutinho HDM, Alves RRN, Almeida WO (2018) **Body fat modulated activity of *Gallus gallus domesticus* Linnaeus (1758) and *Meleagris gallopavo* Linnaeus (1758) in association with antibiotics against bacteria of veterinary interest.** *Microbial Pathogenesis* 124:163–169.
- Dias KCF, Almeida JC, Vasconcelos LC, Patrocínio MLV, Barbosa TM, Ximenes NC, Leitão AP de A, Louchard BO, Pimenta ATÁ, Pinto F das CL, Leal LKAM, Honório Júnior JER, Vasconcelos SMM (2019) **Standardized extract of *Erythrina velutina* Willd. attenuates schizophrenia-Like behaviours and oxidative parameters in experimental animal models.** *Journal of Pharmacy and Pharmacology* 71:379–389. <https://doi.org/10.1111/jphp.13039>
- Diaz MAN, Rossi CC, Mendonça VR, Silva DM, Ribon AOB, Aguilar AP, Muñoz GD (2010) **Screening of medicinal plants for antibacterial activities on *Staphylococcus aureus* strains isolated from bovine mastitis.** *Revista Brasileira de Farmacognosia* 20: 724–728.
- Diniz T, Araújo C, Cabral Silva J, Oliveira Júnior R, Raquel S, Quintans-Júnior L, Pereira Nunes X, Almeida JR (2013) **Phytochemical screening and central nervous system effects of ethanolic extract of *Annona vepretorum* (Annonaceae) in mice.** *Journal of Medicinal Plants Research* 7: 2729–2735.

- Diniz TC, de Oliveira Júnior RG, Medeiros MAMB, Gama e Silva M, Teles RBA, Menezes MB (2019) **Anticonvulsant, sedative, anxiolytic and antidepressant activities of the essential oil of *Annona vepretorum* in mice: Involvement of GABAergic and serotonergic systems.** *Biomedicine and Pharmacotherapy* 111:1074–1087. <http://doi.org/10.1016/j.biopha.2018.12.114>
- Dourado RCM, Silveira ER (2005) **Preliminary investigation on the volatile constituents of *Croton sonderianus* Muell. Arg.: Habitat, plant part and harvest time variation.** *Journal of Essential Oil Research* 17:36–40. <http://doi.org/10.1080/10412905.2005.9698823>
- Dragos D, Gilca M (2018) **Taste of phytochemicals: a better predictor for ethnopharmacological activities of medicinal plants than the phytochemical class?** *Journal of Ethnopharmacology* 28:129–146. <http://doi.org/10.1016/j.jep.2018.03.034>
- Dunn F (1976) **Traditional Asian medicine and cosmopolitan medicine as adaptive systems.** In: Leslie C (ed) *Asian medical systems: a comparative study.* University California Press, Oakland, California, pp. 133–158.
- Dutra LM, Bomfim LM, Rocha SLA, Nepel A, Soares MBP, Barison A, Costa EV, Bezerra DP (2014) **ent-Kaurane diterpenes from the stem bark of *Annona vepretorum* (Annonaceae) and cytotoxic evaluation.** *Bioorganic & Medicinal Chemistry Letters* 24:3315–3320. <https://doi.org/10.1016/j.bmcl.2014.06.005>
- Feltrin C, Brambila PF, Simões CMO (2019) **Development of Caco-2 cells-based gene reporter assays and evaluation of herb-drug interactions involving CYP3A4 and CYP2D6 gene expression.** *Chemico-Biological Interactions* 25:79–89. <http://doi.org/10.1016/j.cbi.2019.01.030>
- Fernandes-Ferreira H, Alves RRN (2017) **The researches on the hunting in Brazil: a brief overview.** *Ethnobiology and Conservation* 6:1–6.
- Ferreira Júnior WS, Ladio AH, Albuquerque UP (2011) **Resilience and adaptation in the use of medicinal plants with suspected anti-inflammatory activity in the Brazilian Northeast.** *Journal of Ethnopharmacology* 138:238–252. <http://doi.org/10.1016/j.jep.2011.09.018>
- Ferreira Júnior WS, Silva TG, Menezes IRA, Albuquerque UP (2016) **The role of local disease perception in the selection of medicinal plants: a study of the structure of local medical systems.** *Journal of Ethnopharmacology* 181:146–157. <http://doi.org/10.1016/j.jep.2016.01.038>
- Ferreira FS, Brito S, Ribeiro S, Almeida W, Alves RRN (2009) **Zootherapeutics utilized by residents of the community Poco Dantas, Crato-CE, Brazil.** *Journal of Ethnobiology and Ethnomedicine* 5(1):21.
- Ferreira FS, Albuquerque UP, Coutinho HDM, Almeida WO, Alves RRN (2012) **The trade in medicinal animals in Northeastern Brazil.** *Evidence-based Complementary and Alternative Medicine* 2012:1–20. <https://doi.org/10.1155/2012/126938>
- Ferreira FS, Brito SV, Costa JGM, Alves RRN, Coutinho HDM, Almeida WO (2009) **Is the body fat of the lizard *Tupinambis merianae* effective against bacterial infections?** *Journal of Ethnopharmacology* 126:233–237.
- Ferreira FS, Brito SV, Coutinho HDM, Souza EP, Almeida WO, Alves RRN (2018) **Vertebrates as a Bactericidal Agent.** *EcoHealth* 15(3):619–626.
- Ferreira FS, Brito SV, Sales DL, Alencar IR, Coutinho HDM, Souza EP, Almeida WO, Alves RRN (2014) **Anti-inflammatory potential of zootherapeutics derived from animals used in Brazilian traditional medicine.** *Pharmaceutical Biology* 52:1–8.
- Ferreira FS, Brito SV, Saraiva RA, Araruna MKA, Menezes IRA, Costa JGM, Coutinho HDM, Almeida WO, Alves RRN (2010) **Topical anti-inflammatory activity of body fat from the lizard *Tupinambis merianae*.** *Journal of Ethnopharmacology* 130:514–520.
- Formagio ASN, Vieira MC, Volobuff CRF, Silva MS, Matos AI, Cardoso CAL, Foglio MA, Carvalho JE, Formagio ASN, Vieira MC, Volobuff CRF, Silva MS, Matos AI, Cardoso CAL, Foglio MA, Carvalho JE (2015) **In vitro biological screening of the anticholinesterase and antiproliferative activities of medicinal plants belonging to Annonaceae.** *Brazilian Journal of Medical and Biological Research* 48:308–315. <https://doi.org/10.1590/1414-431x20144127>

- Freitas CIA (2003) **Estudo sobre a atividade antimicrobiana de substâncias extraídas e purificadas de secreções da pele de anfíbios**. Programa de Pós-graduação em Farmacologia (PhD Thesis). Universidade Federal do Ceará, Fortaleza-CE, Brazil, 179 p.
- Garda AA, Stein MG, Machado RB, Lion MB, Juncá FA, Napoli MF (2017) **Ecology, biogeography, and conservation of Amphibians of the Caatinga**. In: Silva JMC, Leal IR, Tabarelli M (eds) *Caatinga: The largest tropical dry forest region in South America*. Springer, Basel, Switzerland, pp. 133–150.
- Geck MS, Cabras S, Casu L, Reyes García AJ, Leonti M (2017) **The taste of heat: How humoral qualities act as a cultural filter for chemosensory properties guiding herbal medicine**. *Journal of Ethnopharmacology* 198: 499–515. <http://doi.org/10.1016/j.jep.2017.01.027>
- Gilbert B, Ferreira JM, Owellen RJ, Swanholm CE, Budzikiewicz H, Durham LJ, Djerassi C (1962) **Mass spectrometry in structural and stereochemical problems pyrifoline and refractidine**. *Tetrahedron Letters* 3:59–67. [https://doi.org/10.1016/S0040-4039\(00\)70487-4](https://doi.org/10.1016/S0040-4039(00)70487-4)
- Gomes NF (2007) **Estudo de um fator antinociceptivo de ação periférica extraído do veneno da serpente *Crotalus durissus collilineatus***. Programa de Pós-graduação em Ciências Fisiológicas (Master Science Dissertation), Universidade Estadual do Ceará, Fortaleza-CE, Brazil, 125p.
- Gomes TB, Bandeira FPSDF (2012) **The use and diversity of medicinal plants in a quilombola community in Raso da Catarina, Bahia**. *Acta Botanica Brasilica* 26:796–809. <http://doi.org/10.1590/S0102-33062012000400009>
- Gouveia BB, Macedo TJS, Santos JMS, Barberino RS, Menezes VG, Müller MC, Almeida JRGS, Figueiredo JR, Matos MHT (2016) **Supplemented base medium containing *Amburana cearensis* associated with FSH improves *in vitro* development of isolated goat preantral follicles**. *Theriogenology* 86, 1275–1284. <https://doi.org/10.1016/j.theriogenology.2016.04.068>
- Grønhaug TE, Glæserud S, Skogsrud M, Ballo N, Bah S, Diallo D, Paulsen BS (2008) **Ethnopharmacological survey of six medicinal plants from Mali, West-Africa**. *Journal of Ethnobiology and Ethnomedicine* 4:26. <https://doi.org/10.1186/1746-4269-4-26>
- Gunstone FD (1996) **Fatty Acid and Lipid Chemistry**. 1 ed. Blackie Academic & Professional, New York, USA.
- Hernandes C, Pina ES, Taleb-Contini SH, Bertoni BW, Cestari IM, Espanha LG, Varanda EA, Camilo KFB, Martinez EZ, França SC, Pereira AMS (2017) **Lippia origanoides essential oil: an efficient and safe alternative to preserve food, cosmetic and pharmaceutical products**. *Journal of Applied Microbiology* 122:900–910. <https://doi.org/10.1111/jam.13398>
- Higuchi R, Kubota S, Komori T, Kawasaki T, Pandey VB, Singh JP, Shah AH (1984) **Triterpenoid saponins from the bark of *Zizyphus joazeiro***. *Phytochemistry* 23:2597–2600. [https://doi.org/10.1016/S0031-9422\(00\)84106-0](https://doi.org/10.1016/S0031-9422(00)84106-0)
- Kleinman A (1978) **Concepts and a model for the comparison of medical systems as cultural systems**. *Social Science & Medicine* 12:85–93. [https://doi.org/10.1016/0160-7987\(78\)90014-5](https://doi.org/10.1016/0160-7987(78)90014-5)
- Laddha AP, Kulkarni YA (2019) **Tannins and vascular complications of diabetes: an update**. *Phytomedicine* 56:229–245. <https://doi.org/10.1016/j.phymed.2018.10.026>
- Lanzotti V (2013) **Diterpenes for Therapeutic use**. In: Ramawat K, Mérillon JM (eds) *Natural Products*. Springer, Berlin, Heidelberg.
- Larson EC, Hathaway LB, Lamb JG, Pond CD, Rai PP, Matainaho TK, Piskaut P, Barrows LR, Franklin MR (2014) **Interactions of Papua New Guinea medicinal plant extracts with antiretroviral therapy**. *Journal of Ethnopharmacology* 155:1433–1440. <https://doi.org/10.1016/j.jep.2014.07.023>
- Le Bars D, Gozariu M, Cadden SW (2001) **Animal models of nociception**. *Pharmacological Reviews* 53:597–652.
- Le NHT, Malterud KE, Diallo D, Paulsen BS, Nergård CS, Wangensteen H (2012) **Bioactive polyphenols in *Ximenia americana* and the traditional use among Malian healers**. *Journal of Ethnopharmacology* 139:858–862. <https://doi.org/10.1016/j.jep.2011.12.031>

- Leal LKAM, Canuto KM, Costa KCS, Nobre-Júnior HV, Vasconcelos SM, Silveira ER, Ferreira MVP, Fontenele JB, Andrade GM, de Barros Viana GS (2009) **Effects of Amburoside A and Isokaempferide, Polyphenols from *Amburana cearensis*, on Rodent Inflammatory Processes and Myeloperoxidase Activity in Human Neutrophils.** *Basic & Clinical Pharmacology & Toxicology* 104:198–205. <https://doi.org/10.1111/j.1742-7843.2008.00329.x>
- Leal LKAM, Fonseca FN, Pereira FA, Canuto KM, Felipe CFB, Fontenele JB, Pitombeira MV, Silveira ER, Viana GSB (2008) **Protective effects of amburoside A, a phenol glucoside from *Amburana cearensis*, against CCl₄-induced hepatotoxicity in rats.** *Planta Medica* 74:497–502. <https://doi.org/10.1055/s-2008-1074501>
- Leal LKAM, Júnior HVN, Cunha GMA, Moraes MO, Pessoa C, Oliveira RA, Silveira ER, Canuto KM, Viana GSB (2005) **Amburoside A, a glucoside from *Amburana cearensis*, protects mesencephalic cells against 6-hydroxydopamine-induced neurotoxicity.** *Neuroscience Letters* 388:86–90. <https://doi.org/10.1016/J.NEULET.2005.06.034>
- Leal LKAM, Nechio M, Silveira ER, Canuto KM, Fontenele JB, Ribeiro RA, Viana GSB (2003) **Anti-inflammatory and smooth muscle relaxant activities of the hydroalcoholic extract and chemical constituents from *Amburana cearensis* A. C. Smith.** *Phytotherapy Research* 17:335–340. <https://doi.org/10.1002/ptr.1139>
- Lev E (2003) **Traditional healing with animals (zootherapy): medieval to present-day Levantine practice.** *Journal of Ethnopharmacology* 85:107–118.
- Lima Pereira EP, Souza CS, Amparo J, Ferreira RS, Nunez-Figueroa Y, Gonzaga Fernandez L, Ribeiro PR, Braga-de-Souza S, Silva VDA, Costa SL (2017) ***Amburana cearensis* seed extract protects brain mitochondria from oxidative stress and cerebellar cells from excitotoxicity induced by glutamate.** *Journal of Ethnopharmacology* 209:157–166. <https://doi.org/10.1016/j.jep.2017.07.017>
- Lima RF, Alves ÉP, Rosalen PL, Ruiz ALTG, Duarte MCT, Góes VFF, Medeiros ACD, Pereira JV, Godoy GP, Melo de Brito Costa EM (2014) **Antimicrobial and Antiproliferative Potential of *Anadenanthera colubrina* (Vell.) Brenan.** *Evidence-Based Complementary Alternative Medicine* 2014:1–7. <https://doi.org/10.1155/2014/802696>
- Lima SMQ, Ramos TPA, Silva MJ, Rosa RS (2017) **Diversity, distribution, and conservation of the Caatinga fishes: Advances and challenges.** In: Silva JMC, Leal IR, Tabarelli M (eds) *Caatinga: The largest tropical dry forest region in South America.* Springer, Basel, Switzerland, pp. 97–131.
- Lima verde PT, Nascimento NRF, Evangelista JSAM, Tomé AR, Fonteles MC, Santos CF, Cardi BA, Carvalho KM (2009) **Isolation and pharmacological effects of leptoxin, a novel proteic toxin from *Leptodactylus pentadactylus* skin secretion.** *Toxicon* 54:531–538.
- Lins-Neto EMF, Peroni N, Albuquerque UP (2010) **Traditional Knowledge and Management of Umbu (*Spondias tuberosa*, Anacardiaceae): An Endemic Species from the Semi-Arid Region of Northeastern Brazil.** *Economic Botany* 64:11–21. <https://doi.org/10.1007/s12231-009-9106-3>
- Lira SM, Canabrava NV, Benjamin SR, Silva JYG, Viana DA, Lima CLS, Paredes PFM, Marques MMM, Pereira EO, Queiroz EAM, Guedes MIF (2017) **Evaluation of the toxicity and hypoglycemic effect of the aqueous extracts of *Cnidocolus quercifolius* Pohl.** *Brazilian Journal of Medical and Biological Research* 50(10). <https://doi.org/10.1590/1414-431x20176361>
- Lopes AA, Magalhães TR, Andrade Uchôa DE, Silveira ER, Azzolini AECS, Kabeya LM, Lucisano-Valim YM, Vasconcelos SMM, Viana GSB, Leal LKAM (2013) **Afrormosin, an Isoflavonoid from *Amburana cearensis* A. C. Smith, Modulates the Inflammatory Response of Stimulated Human Neutrophils.** *Basic & Clinical Pharmacology & Toxicology* 113:363–369. <https://doi.org/10.1111/bcpt.12106>
- Lopes DM, Júnior NEG, Costa PPC, Martins PL, Santos CF, Carvalho EDF, Carvalho MDF, Pimenta DC, Cardi BA, Fonteles MC, Nascimento NRF, Carvalho KM (2014) **A new structurally atypical bradykinin-potentiating peptide isolated from *Crotalus durissus cascavella* venom (South American rattlesnake).** *Toxicon* 90:36–44.
- Lorenzi H, Matos FJ (2002) **Medicinal plants in Brazil: Native and exotic cultivated.** Plantarum Institute of Flora Studies, São Paulo, Brazil.

- Lucena RFP, de Medeiros PM, Araújo EL, Alves ÂGC, Albuquerque UP (2012) **The ecological apparency hypothesis and the importance of useful plants in rural communities from Northeastern Brazil: An assessment based on use value.** *Journal of Environmental Economics and Management* 96:106–115. <https://doi.org/10.1016/j.jenvman.2011.09.001>
- Lucena RFP, Nascimento VT, Araújo EL, Albuquerque UP (2008) **Local Uses of Native Plants in an Area of Caatinga Vegetation (Pernambuco, NE Brazil).** *Ethnobotany Research and Applications* 6:3–14.
- Macedo Pereira G, Moreira LGL, Neto TDSN, Moreira de Almeida WA, Almeida-Lima J, Rocha HAO, Barbosa EG, Zuanazzi JAS, de Almeida MV, Grazul RM, Navarro-Vázquez A, Hallwass F, Ferreira LS, Fernandes-Pedrosa MF, Giordani RB (2018) **Isolation, spectral characterization, molecular docking, and cytotoxic activity of alkaloids from *Erythroxylum pungens* O.E.Shulz.** *Phytochemistry*, 155, 12-18. <http://doi:10.1016/j.phytochem.2018.07.003>
- Magalhães KN, Guarniz WAS, Sá KM, Freire AB, Monteiro MP, Nojosa RT, Bieski IGC, Custódio JB, Balogun SO, Bandeira MAM (2019) **Medicinal plants of the Caatinga, northeastern Brazil: Ethnopharmacopeia (1980–1990) of the late professor Francisco José de Abreu Matos.** *Journal of Ethnopharmacology* 237:314–353. <https://doi.org/10.1016/J.JEP.2019.03.032>
- Mahawar MM, Jaroli DP (2006) **Animals and their products utilized as medicine by the inhabitants surrounding the Ranthambhore National Park, India.** *Journal of Ethnobiology and Ethnomedicine* 2:1–5.
- Mahawar MM, Jaroli DP (2008) **Traditional zootherapeutic studies in India: a review.** *Journal of Ethnobiology and Ethnomedicine* 4(1): 17.
- Maia-Silva C, Silva CI, Hrcir M, Queiroz RT, Imperatriz-Fonseca VL (2012) **Guia de plantas: visitadas por abelhas na caatinga.** Fundação Brasil Cidadão.
- Makkar HPS, Siddhuraju P, Becker K (2007) **Alkaloids.** In: *Plant Secondary Metabolites. Methods in Molecular Biology*, Humana Press Inc., Totowa, New Jersey.
- Marchioro M, Blank MFA, Mourão RHV, Antonioli AR (2005) **Anti-nociceptive activity of the aqueous extract of *Erythrina velutina* leaves.** *Fitoterapia* 76:637–642. <https://doi.org/10.1016/j.fitote.2005.07.002>
- Martin-Eauclaire M-F, Bougis PE, Lima ME (2018) **Ts1 from the Brazilian scorpion *Tityus serrulatus*: A half-century of studies on a multifunctional beta like-toxin.** *Toxicon* 152:106–120. <https://doi.org/10.1016/j.toxicon.2018.07.024>
- Martínez GJ (2013) **Use of fauna in the traditional medicine of native Toba (qom) from the Argentine Gran Chaco region: an ethnozoological and conservationist approach.** *Ethnobiology and Conservation* 2(2): 1–43.
- Matos AA, Oliveira FA, Machado AC, Saldanha LL, Tokuhara CK, Souza LP, Vilegas W, Dionísio TJ, Santos C, Peres-Buzalaf C, Dokkedal AL, Oliveira R (2019) **An extract from *Myracrodruon urundeuva* inhibits matrix mineralization in human osteoblasts.** *Journal of Ethnopharmacology* 237:192–201. <https://doi.org/10.1016/j.jep.2019.03.052>
- Medeiros CD, Falcão HM, Almeida-Cortez J, Santos DYAC, Oliveira AFM, Santos MG (2017) **Leaf epicuticular wax content changes under different rainfall regimes, and its removal affects the leaf chlorophyll content and gas exchanges of *Aspidosperma pyrifolium* in a seasonally dry tropical forest.** *South African Journal of Botany*. 111:267–274. <http://doi.org/10.1016/j.sajb.2017.03.033>
- Medeiros PM, Ladio AH, Santos AMM, Albuquerque UP (2013) **Does the selection of medicinal plants by Brazilian local populations suffer taxonomic influence?** *Journal of Ethnopharmacology* 146:842–852. <https://doi.org/10.1016/j.jep.2013.02.013>
- Medeiros PM, Pinto BLS, Nascimento VT (2015) **Can organoleptic properties explain the differential use of medicinal plants? Evidence from Northeastern Brazil.** *Journal of Ethnopharmacology* 159:43–48. <https://doi.org/10.1016/j.jep.2014.11.001>
- Medeiros MF, Silva PS, Albuquerque UP (2011a) **Quantification in ethnobotanical research: an overview of indices used from 1995 to 2009.** *Sitientibus. Série Ciências Biológicas* 11: 211-230.
- Medeiros VM, Fernandes HMB, Sousa DF, Queiroga KF, Cabral AGS, Costa VCO, Barbosa-Filho JM, Tavares JF, Silva MS (2011b) **Diterpenos clerodanos de *Croton grewoides* Baill. (Euphorbiaceae).** 34a Reunião Anual da Sociedade Brasileira de Química, Florianópolis, SC, Brasil.

- Meira CS, Guimarães ET, Macedo TS, Silva TB, Menezes LRA, Costa EV, Soares MBP (2015) **Chemical composition of essential oils from *Annona vepretorum* Mart. and *Annona squamosa* L. (Annonaceae) leaves and their antimalarial and trypanocidal activities.** *Journal of Essential Oil Research* 27:160–168. <https://doi.org/10.1080/10412905.2014.982876>
- Melo FPL (2017) **The socio-ecology of the Caatinga: Understanding how natural resource use shapes an ecosystem.** In: Silva JMC, Leal IR, Tabarelli M (eds) *Caatinga: The largest tropical dry forest region in South America*. Springer, Basel, Switzerland, pp. 369–382.
- Mello JPC, Santos SC (2001) **Farmacognosia: da planta ao medicamento.** Simões, C.M.O., Schenckel, E.P., orgs.; Ed. UFSC. 3 ed. Porto Alegre.
- Mendonça LET, Vieira WLS, Alves RRN (2014) **Caatinga Ethnoherpetology: relationships between herpetofauna and people in a semiarid region.** *Amphibian & Reptile Conservation* 8(1):24–32.
- Menezes PMN, Brito MC, Paiva GO, Santos CO, Oliveira LM, Ribeiro LAA, Lima JT, Lucchese AM, Silva FS (2018) **Relaxant effect of *Lippia organoides* essential oil in guinea-pig trachea smooth muscle involves potassium channels and soluble guanylyl cyclase.** *Journal of Ethnopharmacology* 220:16–25. <https://doi.org/10.1016/j.jep.2018.03.040>
- Mesquita DO, Costa GC, Garda AA, Delfim FR (2017) **Species composition, biogeography, and conservation of the Caatinga lizards.** In: Silva JMC, Leal IR, Tabarelli M (eds) *Caatinga: The largest tropical dry forest region in South America*. Springer, Basel, Switzerland, pp. 151–180.
- Molares S, Ladio A (2008) **Plantas medicinales en una comunidad Mapuche del NO de la Patagonia Argentina: clasificación y percepciones organolépticas relacionadas con su valoración.** *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas* 7:149–155.
- Montanari CA, Bolzani VS (2001) **Planejamento racional de fármacos baseado em produtos naturais.** *Química Nova* 24:105–111. <http://doi.org/10.1590/S0100-40422001000100018>
- Monteiro JM, Albuquerque UP, Araújo EL, Amorim ELC (2005) **Taninos: Uma abordagem da química à ecologia.** *Química Nova* 28:892–896. <http://doi.org/10.1590/S0100-40422005000500029>
- Monteiro JM, Albuquerque UP, Lins-Neto EMF, Araújo EL, Albuquerque MM, Amorim ELC (2006a) **The effects of seasonal climate changes in the Caatinga on tannin levels in *Myracrodruon urundeuva* (Engl.) Fr. All. and *Anadenanthera colubrina* (Vell.) Brenan.** *Brazilian Journal of Pharmacognosy* 16:338–344.
- Monteiro JM, Albuquerque UP, Lins-Neto EMF, Araújo EL, Amorim ELC (2006b) **Use patterns and knowledge of medicinal species among two rural communities in Brazil's semi-arid northeastern region.** *Journal of Ethnopharmacology* 105:173–186. <https://doi.org/10.1016/j.jep.2005.10.016>
- Monteiro JM, Lins-Neto EMF, Amorim ELC, Strattmann RR, Araújo EL, Albuquerque UP (2005) **Teor de taninos em três espécies medicinais arbóreas simpátricas da Caatinga.** *Revista Árvore* 29:999–1005.
- Monteiro JM, Souza JSN, Lins-Neto EMF, Scopel K, Trindade EF (2014) **Does total tannin content explain the use value of spontaneous medicinal plants from the Brazilian semi-arid region?** *Revista Brasileira de Farmácia* 24:116–123. <http://doi.org/10.1016/j.bjp.2014.02.001>
- Moretão MP, Buchi DF, Gorin PAJ, Iacomini M, Oliveira MBM (2003) **Effect of an acidic heteropolysaccharide (ARAGAL) from the gum of *Anadenanthera colubrina* (Angico branco) on peritoneal macrophage functions.** *Immunology Letters* 89:175–185.
- Moretão MP, Zampronio AR, Gorin PA, Iacomini M, Oliveira MBM (2004) **Induction of secretory and tumoricidal activities in peritoneal macrophages activated by an acidic heteropolysaccharide (ARAGAL) from the gum of *Anadenanthera colubrina* (Angico branco).** *Immunology Letters* 93:189–197. <https://doi.org/10.1016/j.imlet.2004.03.021>
- Mota GS, Sartori CJ, Miranda I, Quilhó T, Mori FA, Pereira H (2017) **Bark anatomy, chemical composition and ethanol-water extract composition of *Anadenanthera peregrina* and *Anadenanthera colubrina*.** *PLoS One* 12:e0189263. <https://doi.org/10.1371/journal.pone.0189263>

- Moura FBP, Marques JGW (2008) **Zooterapia popular na Chapada Diamantina: uma Medicina incidental?** *Ciência & Saúde Coletiva* 13:2179–2188.
- Murray J, Picking D, Lamm A, McKenzie J, Hartley S, Watson C, Williams L, Lowe H, Delgoda R (2016) **Significant inhibitory impact of dibenzyl trisulfide and extracts of *Petiveria alliacea* on the activities of major drug-metabolizing enzymes *in vitro*: An assessment of the potential for medicinal plant-drug interactions.** *Fitoterapia* 111:138–46. <https://doi.org/10.1016/j.fitote.2016.04.011>
- Nagata JM, Jew AR, Kimeu JM, Salmen CR, Bukusi EA, Cohen CR (2011) **Medical pluralism on Mfangano Island: Use of medicinal plants among persons living with HIV/AIDS in Suba District, Kenya.** *Journal of Ethnopharmacology* 135:501–509. <https://doi.org/10.1016/j.jep.2011.03.051>
- Nascimento ALB, Lozano A, Melo JG, Alves RRN, Albuquerque UP (2016) **Functional aspects of the use of plants and animals in local medical systems and their implications for resilience.** *Journal of Ethnopharmacology* 194:348–357. <http://doi.org/10.1016/j.jep.2016.08.017>
- Nascimento ALB, Medeiros PM, Albuquerque UP (2018) **Factors in hybridization of local medical systems: Simultaneous use of medicinal plants and modern medicine in Northeast Brazil.** *PLoS ONE* 13:e0206190. <https://doi.org/10.1371/journal.pone.0206190>
- Nascimento-Silva O, Leite DS, Bernardes LA, Paiva JGA (2011) **Morphology, anatomy, and histochemistry of the leaves of *Myracrodruon urundeuva* Allemão (Anacardiaceae).** *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas* 10:56–66.
- Negreiros Neto TS, Gardner D, Hallwass F, Leite AJM, Almeida CG, Silva LM, Roque AA, Bitencourt FG, Barbosa EG, Tasca T, Macedo AJ, Almeida MV, Giordani RB (2016) **Activity of pyrrolizidine alkaloids against biofilm formation and *Trichomonas vaginalis*.** *Biomedicine and Pharmacotherapy* 83:323–329. <http://doi.org/10.1016/j.biopha.2016.06.033>
- Neves IA, da Camara CAG (2012) **Volatile constituents of two *Croton* species from Caatinga biome of Pernambuco-Brazil.** *Records of Natural Products* 6:161–165.
- Neves IA, Oliveira JCS, Camara CAG (2008) **Chemical composition of the leaf oils of *Lippia gracilis* Schauer from two localities of Pernambuco.** *Journal of Essential Oil Research* 20:157–160. <http://doi.org/10.1080/10412905.2008.9699979>
- Newman DJ, Cragg GM (2016) **Natural Products as Sources of New Drugs from 1981 to 2014.** *Journal of Natural Products* 79:629–661.
- Niwa Y, Suzuki T, Dohmae N, Umezawa K, Simizu S (2012) **Determination of cathepsin V activity and intracellular trafficking by N-glycosylation.** *FEBS Letters* 586:3601–3607. <https://doi.org/10.1016/j.febslet.2012.08.001>
- Nobre-Júnior HV, Oliveira RA, Maia FD, Nogueira MAS, Moraes MO, Bandeira MAM, Andrade GM, Viana GSB (2009) **Neuroprotective Effects of Chalcones from *Myracrodruon urundeuva* on 6-Hydroxydopamine-Induced Cytotoxicity in Rat Mesencephalic Cells.** *Neurochemical Research* 34:1066–1075. <https://doi.org/10.1007/s11064-008-9876-5>
- Nogueira PCN, Araújo RM, Viana GSB, De Araújo DP, Filho RB, Silveira ER (2014) **Plumeran alkaloids and glycosides from the seeds of *Aspidosperma pyrifolium* Mart.** *Journal of the Brazilian Chemical Society* 11:2108–2212. <http://doi.org/10.5935/0103-5053.20140204>
- Nunes PH, Marinho LC, Nunes ML, Soares EO (1987) **Antipyretic activity of an aqueous extract of *Zizyphus joazeiro* Mart. (Rhamnaceae).** *Brazilian Journal of Medical and Biological Research* 20:599–601.
- Ogunleye DS, Ibitoye SF (2003) **Studies of antimicrobial activity and chemical constituents of *Ximenia americana*.** *Tropical Journal of Pharmaceutical Research* 2(2):239–241.
- Oh YJ, Wong SC, Moffat M, O'Malley KL (1995) **Overexpression of Bcl-2 attenuates MPP+, but not 6-ODHA, induced cell death in a dopaminergic neuronal cell line.** *Neurobiology of Disease* 2:157–167.
- Olinda ACC (2010) **Estudo da atividade antinociceptiva de um novo fator extraído do veneno de *Crotalus durissus collilineatus*.** Programa de Pós-graduação em Ciências Fisiológicas (Master Science Dissertation), Universidade Estadual do Ceará, Fortaleza-CE, Brazil, 81 p.

- Oliveira Júnior RG, Ferraz CAA, Pereira ECV, Sampaio PA, Silva MFS, Pessoa CO, Rolim LA, Almeida JRGS (2019) **Phytochemical analysis and cytotoxic activity of *Cnidoscopus quercifolius* Pohl (Euphorbiaceae) against prostate (PC3 and PC3-M) and breast (MCF-7) cancer cells.** *Pharmacognosy* 5:24–28. http://doi.org/10.4103/pm.pm_6_18
- Oliveira AFM, Salatino A (2000) **Major constituents of the foliar epicuticular waxes of species from the Caatinga and Cerrado.** *Zeitschrift für Naturforschung C. A Journal of Biosciences* 55:688–692. <http://doi.org/10.1515/znc-2000-9-1003>
- Oliveira AP, Borges IV, Pereira ECV, Feitosa TA, Santos RF, Oliveira-Júnior RG, Rolim LA, Viana LGFC, Ribeiro LAA, Santos ADC, Rolim-Neto PJ, Almeida JRGS (2019) **Influence of light intensity, fertilizing and season on the cirsiliol content, a chemical marker of *Leonotis nepetifolia* (Lamiaceae).** *PeerJ* 7:61–87.
- Oliveira YLC, Silva LCN, Silva AG, Macedo AJ, Araújo JM, Correia MTS, Silva MV (2012) **Antimicrobial activity and phytochemical screening of *Buchenavia tetraphylla* (Aubl.) R. A. Howard (Combretaceae: Combretaceae).** *The Scientific World Journal* ID 849302. <https://doi.org/10.1100/2012/849302>
- Oliveira DR, Leitão GG, Fernandes PD, Leitão SG, Oliveira DR, Leitão GG, Fernandes PD, Leitão SG (2014) **Ethnopharmacological studies of *Lippia organoides*.** *Revista Brasileira de Farmacognosia* 24:206–214. <https://doi.org/10.1016/j.bjp.2014.03.001>
- Oliveira FA, Rorato VC, Almeida-Apolonio AA, Rodrigues AB, Barros AL, Sangalli A, Arena AC, Mota JS, Grisolia AB, Oliveira KMP (2017) **In vitro antifungal activity of *Myracrodruon urundeuva* Allemão against human vaginal *Candida* species.** *Anais da Academia Brasileira de Ciências* 89:2423–2432. <https://doi.org/10.1590/0001-3765201720170254>
- Oliveira OP, Sales DL, Dias DQ, Cabral MES, Araújo-Filho JA, Teles DA, Sousa JGG, Ribeiro SC, Freitas FRD, Coutinho HDM, Kerntopf MR, Costa JGM, Alves RRN, Almeida WO (2014) **Antimicrobial activity and chemical composition of fixed oil extracted from the body fat of snake *Spilotes pullatus* (Linnaeus, 1758) (Colubridae: Ophidia).** *Pharmaceutical Biology* 52:740–744.
- Oliveira SL (2012) **Fitoquímica de espécies de *Erythroxylum* do semiárido: isolamento e determinação estrutural de alcaloides tropânicos, flavonoides e diterpenos.** (PhD Thesis). Universidade Federal da Paraíba. 192p.
- Oliveira-Júnior RG, Alves Ferraz CA, Pontes MC, Cavalcante NB, Pontes M, Cavalcante NB, Araújo EC., de Oliveira AP, Picot L, Rolim LA, Almeida JRGS (2018) **Antibacterial activity of terpenoids isolated from *Cnidoscopus quercifolius* Pohl (Euphorbiaceae), a Brazilian medicinal plant from caatinga biome.** *European Journal of Integrative Medicine* 24:30–34. <http://doi.org/10.1016/j.eujim.2018.10.011>
- Paredes PFM, Vasconcelos FR, Paim RTT, Marques MMM, De Moraes SM, Lira SM, Braquehais ID, Vieira ÍGP, Mendes FNP, Guedes MIF (2016) **Screening of Bioactivities and Toxicity of *Cnidoscopus quercifolius* Pohl.** *Evidence-Based Complementary Alternative Medicine* 2016:1–9. <https://doi.org/10.1155/2016/7930563>
- Peixoto Sobrinho TJS, Castro VTNA, Saraiva AM, Almeida DM, Tavares EA, Amorim ELC (2011) **Phenolic content and antioxidant capacity of four *Cnidoscopus* species (Euphorbiaceae) used as ethnopharmacologicals in Caatinga, Brazil.** *African Journal of Pharmacy and Pharmacology* 5:2310-2316. <http://doi.org/10.5897/AJPP11.608>
- Peixoto Sobrinho TJS, Castro VTNA, Saraiva AM, Almeida DM, Tavares EA, Pisciotano MNC, Amorim ELC (2012) **Phytochemical screening and antibacterial activity of four *Cnidoscopus* species (Euphorbiaceae) against standard strains and clinical isolates.** *Journal of Medicinal Plants Research* 6:3742–3748. <http://doi.org/10.5897/JMPR11.1533>
- Peixoto RM, Lima e Silva WE, Almeida JRGS, Branco A, Costa MM (2016) **Antibacterial potential of native plants from the Caatinga biome against *Staphylococcus* spp. isolates from small ruminants with mastitis.** *Revista Caatinga* 29:758–763. <http://doi.org/10.1590/1983-21252016v29n328rc>
- Pereira Gomes-Copeland KK, da Silva Lédo A, de Almeida FTC, Moreira BO, Santos DC, Santos RAF, David JM, David JP (2018) **Effect of elicitors in *Poincianella pyramidalis* callus culture in the biflavonoid biosynthesis.** *Industrial Crops and Products* 126:421–425. <http://doi.org/10.1016/j.indcrop.2018.10.038>

- Pereira JR, Queiroz RF, Siqueira EA, Brasileiro-Vidal AC, Sant'ana AEG, Silva DM, Affonso PRAM (2017) **Evaluation of cytogenotoxicity, antioxidant and hypoglycemic activities of isolate compounds from *Mansoa hirsuta* D.C. (Bignoniaceae).** *Anais da Academia Brasileira de Ciências* 89:317–331.
- Pereira EJP, do Vale JPC, da Silva PT, Lima J dos R, Alves DR, Costa PS, Rodrigues THS, Menezes JESA, Morais SM, Bandeira PN, Fontenelle ROS, Santos HS (2018) **Circadian Rhythm, and Antimicrobial and Anticholinesterase Activities of Essential Oils from *Vitex gardneriana*.** *Natural Product Communications* 13:635–638. <https://doi.org/10.1177/1934578X1801300528>
- Pereira JV, Freire IA, Castilho AR, Cunha MG, Alves HS, Rosalen PL (2016) **Antifungal potential of *Sideroxylon obtusifolium* and *Syzygium cumini* and their mode of action against *Candida albicans*.** *Pharmaceutical Biology* 54:2312–2319. <http://doi.org/10.3109/13880209.2016.1155629>
- Pereira S, Figueiredo-Lima K, Oliveira AFM, Santos MG (2019) **Changes in foliar epicuticular wax and photosynthesis metabolism in evergreen woody species under different soil water availability.** *Photosynthetica* 57:192–201. <http://doi.org/10.32615/ps.2019.013>
- Pervaiz A, Adwan H, Berger MR (2015) **Riproximin: A type II ribosome inactivating protein with anti-neoplastic potential induces IL24/MDA-7 and GADD genes in colorectal cancer cell lines.** *International Journal of Oncology* 47:981–990. <https://doi.org/10.3892/ijo.2015.3073>
- Pervaiz A, Zepp M, Adwan H, Berger MR (2016) **Riproximin modulates multiple signaling cascades leading to cytostatic and apoptotic effects in human breast cancer cells.** *Journal of Cancer Research and Clinical Oncology* 142:135–147. <https://doi.org/10.1007/s00432-015-2013-3>
- Pessoa WS, Estevão LRM, Simões RS, Barros MEG, Mendonça FS, Baratella-Evêncio L, Evêncio-Neto J (2012) **Effects of angico extract (*Anadenanthera colubrina* var. *cebil*) in cutaneous wound healing in rats.** *Acta Cirúrgica Brasileira* 27:655–670. <https://doi.org/10.1590/s0102-86502012001000001>
- Pessoa WS, Estevão LRM, Simões RS, Mendonça FS, Evêncio-Luz L, Baratella-Evêncio L, Florencio-Silva R, Sá FB, Evêncio-Neto J (2015) **Fibrogenesis and epithelial coating of skin wounds in rats treated with angico extract (*Anadenanthera colubrina* var. *cebil*).** *Acta Cirúrgica Brasileira* 30:353–358. <https://doi.org/10.1590/s0102-865020150050000007>
- Phillips O, Gentry AH (1993) **The useful plants of Tambopata, Peru: I. Statistical hypothesis tests with a new quantitative technique.** *Economic Botany* 47:15–32. <https://doi.org/10.1007/BF02862203>
- Pinho RS, Oliveira AFM, Silva SI (2009) **Potential oilseed crops from the semi-arid region of northeastern Brazil.** *Bioresource Technology* 100:6114–6117. <http://doi.org/10.1016/j.biortech.2009.06.010>
- Pires AML, Pessoa ODL, Silveira ER, Braz-Filho R (2011) **Diterpenos cassanos de *Calliandra depauperata*.** 34a Reunião Anual da Sociedade Brasileira de Química, Florianópolis, SC, Brasil.
- Pucca MB, Peigneur S, Cologna CT, Cerni FA, Zoccal KF, Bordon KCF, Faccioli LH, Tytgat J, Arantes EC (2015) **Electrophysiological characterization of the first *Tityus serrulatus* alpha-like toxin, Ts5: Evidence of a pro-inflammatory toxin on macrophages.** *Biochimie* 115:8–16. <https://doi.org/10.1016/j.biochi.2015.04.010>
- Queiroz LP, Cardoso D, Fernandes MF, Moro MF (2017) **Diversity and evolution of flowering plants of the Caatinga domain.** In: Silva JMC, Leal IR, Tabarelli M (eds) *Caatinga: The largest tropical dry forest region in South America*. Springer, Basel, Switzerland, pp. 23–63.
- Rabêlo SV, Costa EV, Barison A, Dutra LM, Nunes XP, Tomaz JC, Oliveira GG, Lopes NP, Santos MFC, Almeida JR (2015) **Alkaloids isolated from the leaves of *atemya* (*Annona cherimola* x *Annona squamosa*).** *Brazilian Journal of Pharmacognosy* 25:419–421. <http://dx.doi.org/10.1016/j.bjp.2015.07.006>
- Rahman K, Khan SU, Fahad S, Chang MX, Abbas A, Khan WU, Rahman L, Haq ZU, Nabi G, Khan D (2019) **Nano-biotechnology: a new approach to treat and prevent malaria.** *International Journal of Nanomedicine* 14:1401–1410. <https://doi.org/10.2147/IJN.S190692>

- Raman V, Aryal UK, Hedrick V, Ferreira RM, Fuentes Lorenzo JL, Stashenko EE, Levy M, Levy MM, Camarillo IG (2018) **Proteomic Analysis Reveals That an Extract of the Plant *Lippia organoides* Suppresses Mitochondrial Metabolism in Triple-Negative Breast Cancer Cells.** *Journal of Proteome Research* 17:3370–3383. <https://doi.org/10.1021/acs.jproteome.8b00255>
- Raman V, Lorenzo JLF, Stashenko EE, Levy M, Levy MM, Camarillo IG (2017) ***Lippia organoides* extract induces cell cycle arrest and apoptosis and suppresses NF-κB signaling in triple-negative breast cancer cells.** *International Journal of Oncology* 51:1801–1808. <https://doi.org/10.3892/ijo.2017.4169>
- Ramos JMO, Santos CA, Santana DG, Santos DA, Alves PB, Thomazzi SM (2013) **Chemical constituents and potential anti-inflammatory activity of the essential oil from the leaves of *Croton argyrophyllus*.** *Brazilian Journal of Pharmacognosy* 23:644–650. <http://doi.org/10.1590/S0102-695X2013005000045>
- Raupp IM, Sereniki A, Virtuoso S, Ghislandi C, Cavalcanti e Silva EL, Trebien HA, Miguel OG, Andreatini R (2008) **Anxiolytic-like effect of chronic treatment with *Erythrina velutina* extract in the elevated plus-maze test.** *Journal of Ethnopharmacology* 118:295–299. <https://doi.org/10.1016/j.jep.2008.04.016>
- Ribeiro BD, Barreto DW, Coelho MAZ (2014) **Recovery of saponins from jua (*Ziziphus joazeiro*) by micellar extraction and cloud point preconcentration.** *Journal of Surfactants and Detergents* 17:553–561. <https://doi.org/10.1007/s11743-013-1526-5>
- Ribeiro BD, Coelho MAZ, Marucho IM (2013) **Extraction of saponins from sisal (*Agave sisalana*) and juá (*Ziziphus joazeiro*) with cholinium based ionic liquids and deep eutectic solvents.** *European Food Research and Technology* 237:965–975. <https://doi.org/10.1007/s00217-013-2068-9>
- Ribeiro MD, Onusic GM, Poltronieri SC, Viana MB (2006) **Effect of *Erythrina velutina* and *Erythrina mulungu* in rats submitted to animal models of anxiety and depression.** *Brazilian Journal of Medical and Biological Research* 39:263–270. <https://doi.org/S0100-879X2006000200013>
- Ribeiro PPC, Silva DML, Assis CF, Correia RTP, Damasceno KSFSC (2017) **Bioactive properties of faveleira (*Cnidocolus quercifolius*) seeds, oil and press cake obtained during oilseed processing.** *PLoS One* 12:e0183935. <https://doi.org/10.1371/journal.pone.0183935>
- Ribeiro SM, Bonilla OH, Lucena EMP (2018) **Influência da sazonalidade e do ciclo circadiano no rendimento e composição química dos óleos essenciais de *Croton* spp. da Caatinga.** *Iheringia - Serie Botanica* 73:31–38. <http://doi.org/10.21826/2446-8231201873104>
- Riet-Correa F, Medeiros RMT, Schild AL (2012) **A review of poisonous plants that cause reproductive failure and malformations in the ruminants of Brazil.** *Journal of Applied Toxicology* 32:245–254. <https://doi.org/10.1002/jat.1754>
- Ríos JL, Recio MC (2005) **Medicinal plants and antimicrobial activity.** *Journal of Ethnopharmacology* 100:80–84.
- Rodrigues FTS, Sousa CNS, Ximenes NC, Almeida AB, Cabral LM, Patrocínio CFV, Silva AH, Leal LKAM, Honório-Júnior JER, Macedo D, Vasconcelos SMM (2017) **Effects of standard ethanolic extract from *Erythrina velutina* in acute cerebral ischemia in mice.** *Biomedicine & Pharmacotherapy* 96:1230–1239. <https://doi.org/10.1016/j.biopha.2017.11.093>
- Rodrigues LV, Ferreira FV, Regadas FSP, Matos D, Viana GSB (2002) **Morphologic and morphometric analyses of acetic acid-induced colitis in rats after treatment with enemas from *Myracrodruon urundeuva* Fr. All. (Aroeira do Sertão).** *Phytotherapy Research* 16:267–272. <https://doi.org/10.1002/ptr.841>
- Sá RA, Santos NDL, Silva CSB, Napoleão TH, Gomes FS, Cavada BS, Coelho LCBB, Navarro DMAF, Bieber LW, Paiva PMG (2009) **Larvicidal activity of lectins from *Myracrodruon urundeuva* on *Aedes aegypti*.** *Comparative Biochemistry & Physiology Part C: Toxicology and Pharmacology* 149:300–306. <https://doi.org/10.1016/j.cbpc.2008.08.004>

- Sales DL, Morais-Braga MFB, Santos ATL, Machado AJT, Araújo-Filho JA, Dias DQ, Cunha FAB, Saraiva RA, Menezes IRA, Coutinho HDM, Costa JGM, Ferreira FS, Alves RRN, Almeida WO (2017) **Antibacterial, modulation activity of antibiotics and toxicity from *Rhinella jimi* (Stevaux, 2002) (Anura: Bufonidae) glandular secretions.** *Biomedicine & Pharmacotherapy* 92:554–561.
- Sales DL, Oliveira OP, Cabral MES, Dias DQ, Kerntopf MR, Coutinho HDM, Costa JGM, Freitas FRD, Ferreira FS, Alves RRN, Almeida WO (2015) **Chemical identification and evaluation of the antimicrobial activity of fixed oil extracted from *Rhinella jimi*.** *Pharmaceutical Biology* 53:98–103.
- Santoro FR, Ferreira Júnior WS, Araújo TAS, Ladio AH, Albuquerque UP (2015) **Does plant species richness guarantee the resilience of local medical systems? A perspective from utilitarian redundancy.** *PLoS One* 10:e0119826. <https://doi.org/10.1371/journal.pone.0119826>
- Santoro FR, Nascimento ALB, Soldati GT, Ferreira Júnior WS, Albuquerque UP (2018) **Evolutionary ethnobiology and cultural evolution: opportunities for research and dialog.** *Journal of Ethnobiology and Ethnomedicine* 14:1. <https://doi.org/10.1186/s13002-017-0199-y>
- Santos CAB, Alves RRN (2016) **Ethnoichthyology of the indigenous Truká people, Northeast Brazil.** *Journal of Ethnobiology and Ethnomedicine* 12(1): 1–12.
- Santos GID, Lemos EL, Fernandes AC, Rocha WRV, Catão RMR, Braz-Filho R, Tavares JF, Fachine IM, Alves HS (2018) **Phytochemical study of *Harrisia adscendens*.** *Revista Brasileira de Farmacognosia* 28:298–302. <http://dx.doi.org/10.1016/j.bjp.2018.04.011>
- Santos IJM, Coutinho HDM, Matias EFF, Costa JGM, Alves RRN, Almeida WO (2012a) **Antimicrobial activity of natural products from the skins of semiarid living lizards *Ameiva ameiva* (Linnaeus, 1758) and *Tropidurus hispidus* (Spix, 1825).** *Journal of Arid Environments* 76:138–141.
- Santos IJM, Leite GO, Costa JGM, Alves RRN, Campos AR, Menezes IRA, Freita FRV, Nunes MJH, Almeida WO (2015) **Topical anti-inflammatory activity of oil from *Tropidurus hispidus* (Spix, 1825).** *Evidence-based Complementary Alternative Medicine* 2015:1–7. <https://doi.org/10.1155/2015/140247>
- Santos IJM, Matias EFF, Santos KKA, Braga MFBM, Andrade JC, Souza TM, Santos FAV, Sousa ACA, Costa JGM, Menezes IRA, Alves RRN, Almeida WO, Coutinho HDM (2012b) **Evaluation of the antimicrobial activity of the decoction of *Tropidurus hispidus* (Spix, 1825) and *Tropidurus semitaeniatus* (Spix, 1825) used by the traditional medicine.** *Evidence-based Complementary and Alternative Medicine* 2012:1–6. <https://doi.org/10.1155/2012/747969>
- Santos JS, Marinho RR, Ekundi-Valentim E, Rodrigues L, Yamamoto MH, Teixeira SA, Muscara MN, Costa SK, Thomazzi SM (2013) **Beneficial effects of *Anadenanthera colubrina* (Vell.) Brenan extract on the inflammatory and nociceptive responses in rodent models.** *Journal of Ethnopharmacology* 148:18–222. <https://doi.org/https://doi.org/10.1016/j.jep.2013.04.012>
- Saslis-Lagoudakis CH, Savolainen V, Williamson EM, Forest F, Wagstaff SJ, Baral SR, Watson MF, Pendry CA, Hawkins JA (2012) **Phylogenies reveal predictive power of traditional medicine in bioprospecting.** *PNAS* 109(39):15835–15840. doi:10.1073/pnas.1202242109
- Saraiva AM, Castro RHA, Cordeiro RP, Sobrinho TJSP, Castro VTNA, Amorim ELC, Xavier HS, Pisciotto MNC (2011) **In vitro evaluation of antioxidant, antimicrobial and toxicity properties of extracts of *Schinopsis brasiliensis* Engl. (Anacardiaceae).** *African Journal of Pharmacy and Pharmacology* 5:1724–1731.
- Sarria ALF, Silva TL, Oliveira JM, Oliveira MAR, Fernandes JB, Silva MFGF, Vieira PC, Venancio T, Alves Filho EG, Batista JM, Guido RVC (2018) **Dimeric chalcones derivatives from *Myracrodruon urundeuva* act as cathepsin V inhibitors.** *Phytochemistry* 154:31–38. <https://doi.org/10.1016/j.phytochem.2018.06.009>
- Siddaiah M, Souris K, Janapati Y, Vasanth Kumar P (2019) **Phytochemical Screening and Anti Diabetic Activity of Methanolic Extract of Leaves of *Ximenia americana* in Rats.** *International Journal of Innovative Pharmaceutical Research* 2(1):78–83.

- Silva Pantoja Pd, Assreuy AMS, Silva RO, Damasceno SRB, Mendonça VA, Mendes TS, Morais JAV, de Almeida SL, Teixeira AÉEA, de Souza MHL, Pereira MG, Soares PMG (2018) **The polysaccharide-rich tea of *Ximenia americana* barks prevents indomethacin-induced gastrointestinal damage via neutrophil inhibition.** *Journal of Ethnopharmacology* 224:195–201. <https://doi.org/10.1016/j.jep.2018.05.041>
- Silva Siqueira EM, Félix-Silva J, Araújo LML, Fernandes JM, Cabral B, Gomes JADS, Araújo Roque A, Tomaz JC, Lopes NP, Fernandes-Pedrosa MF, Giordani RB, Zucolotto SM (2016) ***Spondias tuberosa* (Anacardiaceae) leaves: profiling phenolic compounds by HPLC-DAD and LC-MS/MS and in vivo anti-inflammatory activity.** *Biomedical Chromatography* 30:1656–65. <https://doi.org/10.1002/bmc.3738>
- Silva ARA, Morais SM, Marques MMM, Oliveira DF, Barros CC, Almeida RR, Vieira ÍGP, Guedes MIF (2012a) **Chemical composition, antioxidant and antibacterial activities of two *Spondias* species from Northeastern Brazil.** *Pharmaceutical Biology* 50:740–746. <https://doi.org/10.3109/13880209.2011.627347>
- Silva AG, Silva LCN, Filho CMB, Araújo DRC, Silva JFV, Arruda IR, Araújo JM, Correia MTS, Macedo AJ, Silva MV (2012b) **Antimicrobial activity of medicinal plants of the Caatinga (semi-arid) vegetation of NE Brazil.** *Current Topics in Phytochemistry* 11:81–94.
- Silva MS, Brando DO, Chaves TP, Formiga Filho AL, Costa EM, Santos VL, Medeiros AC (2012c) **Study bioprospecting of medicinal plant extracts of the semiarid northeast: Contribution to the control of oral microorganisms.** *Evidence-based Complementary and Alternative Medicine* ID 681207. <https://doi.org/10.1155/2012/681207>
- Silva ACO, Oliveira AFM, Santos DYAC, Silva SI (2010) **An approach to chemotaxonomy to the fatty acid content of some *Malvaceae* species.** *Biochemical Systematics and Ecology* 38:1–4. <http://doi.org/10.1016/j.bse.2010.10.006>
- Silva AH, Fonseca FN, Pimenta ATÁ, Lima MS, Silveira ER, Viana GSB, Vasconcelos SMM, Leal LKAM (2016) **Pharmacognostical Analysis and Protective Effect of Standardized Extract and Rizonic Acid from *Erythrina velutina* against 6-Hydroxydopamine-Induced Neurotoxicity in SH-SY5Y Cells.** *Pharmacognosy* 12:307–312. <https://doi.org/10.4103/0973-1296.192200>
- Silva BAFd, Costa RHS, Fernandes CN, Leite LHI, Ribeiro-Filho J, García TR, Coutinho HDM, Wanderley AG, de Menezes IRA (2018) **HPLC profile and antiedematogenic activity of *Ximenia americana* L. (Olacaceae) in mice models of skin inflammation.** *Food and Chemical Toxicology* 119:199–205. <https://doi.org/10.1016/j.fct.2018.04.041>
- Silva CG, Marinho MG, Lucena MFA, Costa JGM (2015) **Ethnobotanical survey of medicinal plants in the caatinga area in the community of sitio Nazaré, Milagres, Ceará, Brazil.** *Revista Brasileira de Plantas Medicinais* 17:133–142. http://doi.org/10.1590/1983-084X/12_055
- Silva FO, Oliveira IR, Silva MG, Braz-Filho R (2010) **Constituintes químicos das folhas de *Senna spectabilis* (DC) Irwin & Barneby var. *excelsa* (Schrad.) Irwin & Barneby.** *Química Nova* 33:1874–1876. <http://dx.doi.org/10.1590/S0100-40422010000900010>
- Silva JC, Araújo CS, Lima-Saraiva SRG, Oliveira-Júnior RG, Diniz TC, Wanderley CWS, Palheta-Júnior RC, Mendes RL, Guimarães AG, Quintans-Júnior LJ, Almeida JRGS (2015) **Antinociceptive and anti-inflammatory activities of the ethanolic extract of *Annona vepretorum* Mart. (Annonaceae) in rodents.** *BMC Complementary Alternative Medicine* 15:197. <https://doi.org/10.1186/S12906-015-0716-2>
- Silva SI, Oliveira AFM, Negri G, Salatino A (2014) **Seed oils of Euphorbiaceae from the Caatinga, a Brazilian tropical dry forest.** *Biomass and Bioenergy* 69:124–134. <http://doi.org/10.1016/j.biombioe.2014.07.010>
- Silva TCL, Almeida CCB, Veras Filho J, Peixoto Sobrinho TJS, Amorim ELC, Costa EP, Araújo JM (2011) **Atividades antioxidante e antimicrobiana de *Ziziphus joazeiro* mart. (Rhamnaceae): avaliação comparativa entre cascas e folhas.** *Revista de Ciências Farmacêuticas Básica e Aplicada* 32(2):193–199.
- Silva JMC, Leal IR, Tabarelli M (2017a) **Caatinga: The largest tropical dry forest region in South America.** Springer, Basel, Switzerland.
- Silva JMC, Barbosa LCF, Leal IR, Tabarelli M (2017b) **The Caatinga: Understanding the Challenges.** In: Silva JMC, Leal IR, Tabarelli M (eds) *Caatinga: The largest tropical dry forest region in South America.* Springer, Basel, Switzerland, pp. 3–19.

- Silva-Leite KESd, Girão DKFB, Freitas Pires A, Assreuy AMS, de Moraes PAF, Cunha AP, Ricardo NMPS, Criddle DN, de Souza MHL, Pereira MG, Soares PMG (2018) ***Ximenia americana* heteropolysaccharides ameliorate inflammation and visceral hypernociception in murine caerulein-induced acute pancreatitis: Involvement of CB2 receptors.** *Biomedicine & Pharmacotherapy* 106:1317–1324. <https://doi.org/10.1016/j.biopha.2018.07.067>
- Siqueira CF, Cabral DL, Peixoto Sobrinho TJ, Amorim EL, Melo JG, Araújo TA, Albuquerque UP (2012) **Levels of tannins and flavonoids in medicinal plants: evaluating bioprospecting strategies.** *Evidence-Based Complementary and Alternative Medicine* ID 434782. <https://doi.org/10.1155/2012/434782>
- Sivira A, Sanabria M, Valera N, Vásquez C (2011) **Toxicity of ethanolic extracts from *Lippia organoides* and *Gliricidia sepium* to *Tetranychus cinnabarinus* (Boisduval) (Acari: Tetranychidae).** *Neotropical Entomology* 40:375–379. <https://doi.org/10.1590/s1519-566x2011000300011>
- Soares AMS, Oliveira JTA, Rocha CQ, Ferreira ATS, Perales J, Zanatta AC, Vilegas W, Silva CR, Costa-Júnior LM (2018) ***Myracrodruon urundeuva* seed exudates proteome and anthelmintic activity against *Haemonchus contortus*.** *PLoS One* 13:e0200848. <https://doi.org/10.1371/journal.pone.0200848>
- Sobeh M, Mahmoud MF, Abdelfattah MAO, El-Beshbishy HA, El-Shazly AM, Wink M (2017) **Hepatoprotective and hypoglycemic effects of a tannin rich extract from *Ximenia americana* var. *caffra* root.** *Phytomedicine* 33:36–42. <https://doi.org/10.1016/j.phymed.2017.07.003>
- Soldati GT, Albuquerque UP (2012) **A new application for the optimal foraging theory: the extraction of medicinal plants.** *Evidence-Based Complementary and Alternative Medicine* 2012:364564. <http://doi.org/10.1155/2012/364564>
- Soro TY, Zahoui OS, Nene-Bi AS, Traore F (2016) **Analgesic activity of the fractions of the aqueous extract of *Ximenia americana* (Linné) (Olacaceae).** *International Journal of Pharmacology and Toxicology* 4:1. <https://doi.org/10.14419/ijpt.v4i1.5513>
- Sousa DCP, Soldati GT, Monteiro JM, Araújo TAS, Albuquerque UP (2016) **Information Retrieval during Free Listing Is Biased by Memory: Evidence from Medicinal Plants.** *PLoS One* 11:e0165838. <https://doi.org/10.1371/journal.pone.0165838>
- Sousa JC, Berto RF, Gois EA, Fontenele-Cardi NC, Honório-Júnior JERK, Richardson M, Rocha MFG, Camargo AACM, Pimenta DC, Cardi BA, Carvalho KM (2009) **Leptoglycin: A new Glycine/Leucine-rich antimicrobial peptide isolated from the skin secretion of the South American frog *Leptodactylus pentadactylus* (Leptodactylidae).** *Toxicon* 54: 23–32.
- Souto WMS, Mourão JS, Barboza RRD, Alves RRN (2011) **Parallels between zootherapeutic practices in Ethnoveterinary and Human Complementary Medicine in NE Brazil.** *Journal of Ethnopharmacology* 134(3):753–767.
- Souto WMS, Barboza RRD, Fernandes-Ferreira H, Magalhães-Júnior AJC, Monteiro JM, Abichacra EA, Alves RRN (2018) **Zootherapeutic uses of wildmeat and associated products in the semiarid region of Brazil: general aspects and challenges for conservation.** *Journal of Ethnobiology and Ethnomedicine* 14(60):1–16.
- Souza AVV, Santos US, Carvalho JRS, Barbosa BDR, Canuto KM, Rodrigues THS (2018) **Chemical composition of essential oil of leaves from *Lippia schaueriana* Mart. collected in the caatinga area.** *Molecules* 23:2480. <https://doi.org/10.3390/molecules23102480>
- Souza Lima M, Oliveira Bitencourt M, Furtado A, Torres-Rêgo M, Siqueira E, Oliveira R, Rocha HO, Rocha KF, Silva-Júnior A, Zucolotto S, Fernandes-Pedrosa M (2017) ***Aspidosperma pyriforme* Has Anti-Inflammatory Properties: An Experimental Study in Mice with Peritonitis Induced by *Tityus serrulatus* Venom or Carrageenan.** *International Journal of Molecular Sciences* 18:2248. <https://doi.org/10.3390/ijms18112248>
- Souza Lima MCJ, Soto-Blanco B (2010) **Poisoning in goats by *Aspidosperma pyriforme* Mart.: Biological and cytotoxic effects.** *Toxicon* 55:320–324. <https://doi.org/10.1016/j.toxicon.2009.08.004>

- Souza Neto Júnior JC, Estevão LRM, Ferraz AA, Simões RS, Vieira MGF, Evêncio-Neto J (2019) **Ointment of *Ximenia americana* promotes acceleration of wound healing in rats.** *Acta Cirúrgica Brasileira* 34(3). <https://doi.org/10.1590/s0102-865020190030000007>
- Souza SMC, Aquino LCM, Jr ACM, Bandeira MAM, Nobre MEP, Viana GSB (2007) **Anti-inflammatory and antiulcer properties of tannins from *Myracrodruon urundeuva* Allemão (Anacardiaceae) in Rodents.** *Phytotherapy Research* 21:220–225. <https://doi.org/10.1002/ptr.2011>
- Staines SS (2011) **Herbal medicines: adverse effects and drug-herb interactions.** *Journal of the Malta College of Pharmacy Practice* 17:38–42.
- Stashenko EE, Martínez JR, Cala MP, Durán DC, Caballero D (2013) **Chromatographic and mass spectrometric characterization of essential oils and extracts from *Lippia* (Verbenaceae) aromatic plants.** *Journal of Separation Science* 36:192–202. <https://doi.org/10.1002/jssc.201200877>
- Tanaka M, Kendal JR, Laland KN (2009) **From traditional medicine to witchcraft: why medical treatments are not always efficacious.** *PLoS One* 4:e5192. <https://doi.org/10.1371/journal.pone.0005192>
- Tiffany-Castiglioni E, Saneto RP, Proctor PH, Perez-Polo JR (1982) **Participation of active oxygen species in 6-hydroxydopamine toxicity to a human neuroblastoma cell line.** *Biochemical Pharmacology* 31:181–188.
- Trentin DS, Silva DB, Amaral MW, Zimmer KR, Silva MV, Lopes NP, Giordani RB, Macedo AJ (2013) **Tannins Possessing Bacteriostatic Effect Impair *Pseudomonas aeruginosa* Adhesion and Biofilm Formation.** *PLoS One* 8:e66257. <https://doi.org/10.1371/journal.pone.0066257>
- Tundis R, Xiao J, Loizzo MR (2017) ***Annona* species (Annonaceae): a rich source of potential antitumor agents?** *Annals of the New York Academy of Sciences* 1398:30–36. <https://doi.org/10.1111/nyas.13339>
- Van Vliet N, Moreno J, Gómez J, Zhou W, Fa JE, Golden C, Alves RRN, Nasi R (2017) **Bushmeat and human health: Assessing the Evidence in tropical and sub-tropical forests.** *Ethnobiology and Conservation* 6:1–45.
- Vasconcelos SMM, Lima NM, Sales GTM, Cunha GMA, Aguiar LMV, Silveira ER, Rodrigues ACP, Macedo DS, Fonteles MMF, Sousa FCF, Viana GSB (2007) **Anticonvulsant activity of hydroalcoholic extracts from *Erythrina velutina* and *Erythrina mulungu*.** *Journal of Ethnopharmacology* 110:271–274. <https://doi.org/10.1016/j.jep.2006.09.023>
- Vasconcelos SMM, Oliveira GR, Carvalho MM, Rodrigues ACP, Silveira ER, Fonteles MMF, Sousa FCF, Viana GSB (2003) **Antinociceptive activities of the hydroalcoholic extracts from *Erythrina velutina* and *Erythrina mulungu* in mice.** *Biological and Pharmaceutical Bulletin* 26:946–949.
- Vera SS, Zambrano DF, Méndez-Sánchez SC, Rodríguez-Sanabria F, Stashenko EE, Luna JED (2014) **Essential oils with insecticidal activity against larvae of *Aedes aegypti* (Diptera: Culicidae).** *Parasitology Research* 113:2647–2654. <https://doi.org/10.1007/s00436-014-3917-6>
- Viana GSB, Bandeira MAM, Matos FJA (2003) **Analgesic and antiinflammatory effects of chalcones isolated from *Myracrodruon urundeuva* Allemão.** *Phytomedicine* 10:189–195. <https://doi.org/10.1078/094471103321659924>
- Vicuña GC, Stashenko EE, Fuentes JL (2010) **Chemical composition of the *Lippia origanoides* essential oils and their antigenotoxicity against bleomycin-induced DNA damage.** *Fitoterapia* 81:343–349. <https://doi.org/10.1016/j.fitote.2009.10.008>
- Vieira PB, Silva NLF, Silva GNS, Silva DB, Lopes NP, Gnoatto SCB, Silva MV, Macedo AJ, Bastida J, Tasca T (2016) **Caatinga plants: natural and semi-synthetic compounds potentially active against *Trichomonas vaginalis*.** *Bioorganic and Medicinal Chemistry Letters* 26:2229–2236. <http://doi.org/10.1016/j.bmcl.2016.03.061>
- Vieira PB, Silva NLF, Menezes CB, Da Silva MV, Silva DB, Lopes NP, Macedo AJ, Bastida J, Tasca T (2017) **Trichomonocidal and parasite membrane damaging activity of bidesmosic saponins from *Manilkara rufula*.** *PLoS One* 12. <https://doi.org/10.1371/journal.pone.0188531>

- Vigerelli H, Sciani JM, Jared C, Antoniazzi MM, Caporale GMM, Silva ACR, Pimenta DC (2014) **Bufotenine is able to block rabies virus infection in BHK-21 cells.** *Journal of Venomous Animals and Toxins including Tropical Diseases* 20(1):45. <https://doi.org/10.1186/1678-9199-20-45>
- Voss C, Eyol E, Berger MR (2006a) **Identification of potent anticancer activity in *Ximenia americana* aqueous extracts used by African traditional medicine.** *Toxicology and Applied Pharmacology* 211:177–187. <https://doi.org/10.1016/j.taap.2005.05.016>
- Voss C, Eyol E, Frank M, von der Lieth CW, Berger MR (2006b) **Identification and characterization of riproximin, a new type II ribosome-inactivating protein with antineoplastic activity from *Ximenia americana*.** *FASEB Journal* 20:1194–1196. <https://doi.org/10.1096/fj.05-5231fje>
- World Health Organization (2017) **World Malaria Report 2017.** WHO, Geneva, Switzerland.
- World Health Organization (2018) **World Malaria Report 2018.** WHO, Geneva, Switzerland.
- Ximenes NC, Santos Júnior MA, Vasconcelos GS, Dias KCF, Jucá MM, Silva AH, Leal LKAM, Viana GSB, Sousa FCF, Vasconcelos SMM (2018) **Ethanol extract of *Erythrina velutina* Willd ameliorate schizophrenia-like behavior induced by ketamine in mice.** *Journal of Complementary and Integrative Medicine* 16. <https://doi.org/10.1515/jcim-2018-0038>
- Zhou Z, Jiang Z (2004) **International trade status and crisis for snake species in China.** *Conservation Biology* 18:1386–1394.
- Zorofchian Moghadamtousi S, Karimian H, Rouhollahi E, Paydar M, Fadaeinasab M, Abdul Kadir H (2014) ***Annona muricata* leaves induce G1 cell cycle arrest and apoptosis through mitochondria-mediated pathway in human HCT-116 and HT-29 colon cancer cells.** *Journal of Ethnopharmacology* 156:277–289. <https://doi.org/10.1016/j.je>

Received: 20 August 2019
Accepted: 20 February 2020
Published: 19 March 2020