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Bioactivity and potential therapeutic benefits of some medicinal plants from the Caatinga (semi-arid) vegetation of Northeast Brazil: a review of the literature

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Abstract: Medicinal plants have been used in traditional medicine for several thousand years all over the world. In this sense, information from Brazilian ethnic groups on folk medicine have contributed to the discovery of pharmacological activities from various plant-derived agents potentially leading to the innovative drugs. The Caatinga (semi-arid) vegetation is a highly threatened biome, covering a vast area in northeastern Brazil and has suffered from strong human influence for many decades. Many plants species found in the Caatinga have been widely used in folk medicine and for commercial manufacturing of phytotherapeutic products. Thus, the present review aims to disseminate to the scientific community some known species of medicinal plants found in the Caatinga that have been studied and analyzed in pharmacological scientific assays. Among the species that stood out for their local importance and multiplicity of uses were: *Amburana cearensis* (umburana-de-cheiro), *Anadenanthera colubrina* (Vell.) Brenan (angico-branco), *Anacardium occidentalis* L. (cajueiro), *Bauhinia forficata* Link (mororó), *Cissus sicyoides* L. (insulina-vegetal), *Myracrodruon urundeuva* Allemão (aroeira-do-sertão) and *Zingiber officinalis* L. (gengibre). The present study shows that several herbal constituents from Caatinga plants, whose pharmacological actions have been well characterized, may be relevant candidates for future and innovative therapeutic development.

Review

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Introduction

Medicinal plants have been used in many cultures for thousands of years and information on the use of natural resources has played a vital role in the discovery of novel products from plants as chemotherapeutic agents. Brazil not only has one of the world's highest levels of biodiversity but also it has a wealth of traditional knowledge accumulated by local people who have direct access to nature and to the products of biodiversity (Albuquerque et al., 2007). In this sense, information from Brazilian ethnic groups on traditional medicine have contributed to the discovery of pharmacological activities from several plant-derived agents, which have resulted in a significant body of publications (Almeida et al., 2001; Sousa et al, 2004a; 2005; De Sousa et al., 2006; Amaral et al., 2007; Silva et al., 2007; Volpato et al., 2008; Silva et al., 2009a; Silva et al. 2009b; Morais at al., 2010). In spite of this, the current knowledge on the biodiversity of ecosystems as, for example, of the northeast region, is still very embryonic.

The Caatinga (semi-arid) vegetation is a highly threatened biome, covering a vast area in northeastern Brazil. The ecosystem of the Caatinga occupies an area of approximately 750000 km^2, accounting for about 10% of the Brazilian territory and approximately 60% of the northeast region, including parts of the states of Piauí, Ceará, Rio Grande do Norte, Paraíba, Pernambuco, Alagoas, Sergipe, Bahia, and Minas Gerais (Silva & Albuquerque, 2005). This biome is dominated by one of the few types of vegetation whose distribution is totally restricted to Brazil (Hueck 1972; Ferri 1980) and has suffered from strong human influence for many decades, resulting in the conversion of extensive areas to pasture or farm land and the intensive harvesting of wood products, especially as energy sources (Albuquerque & Andrade, 2002; Albuquerque et al., 2005).

Despite the fauna and flora are becoming greatly altered, many plants species from the Caatinga are widely known and used in folk medicine and for commercial manufacturing of phytotherapeutic products

(Albuquerque et al., 2007), although detailed studies are still needed concerning these botanical resources and the impact that intensive use might have on their availability. In this sense, the number of studies on medicinal plants from the semi-arid region of northeast Brazil has grown progressively, most of them focusing on listing plants together with their folk therapeutic indications, manner of use, and the plant parts used (Cabral & Agra, 1998; Costa-Neto & Oliveira, 2000; Almeida & Albuquerque, 2002; Almeida et al., 2006).

The present work focused on analyzing published information that intends to contribute to the identification of Caatinga resources with potential medicinal applications. Therefore, this study aims to evidence the local diversity of medicinal plants of Caatinga and disseminate to the scientific community some species that have been studied and analyzed in scientific assays highlighting species that deserve further study.

Database collection

The studies included in this review were identified primarily by using computerized literature searches of the PubMed and Lilacs databases. The selected papers (about 106) were published between 1980 and 2010. The identity of each plant was carefully checked based on the description given in the works. Only those plants whose extracts and/or isolated constituents showed clear pharmacological effects in animal models or isolated organs were included in this review.

Revised medicinal species from the Caatinga region

Concerning medicinal plants, there are few studies that enable a wider vision of the great diversity of species used by the Caatinga population for therapeutic purposes. Much of the traditional knowledge about plants, especially medicinal plants, is being lost with time, either because of the lack of studies or by the inadequate use of plant resources (Silva & Albuquerque, 2005). On the other hand, some studies show the interest of researchers on the therapeutic effects of several medicinal plants found in Caatinga. In this sense, a short list of the species covered in this work includes: *Amburana cearensis* (cumaru), *Anadenanthera colubrina* (Vell.) Brenan (angico-branco), *Anacardium occidentalis* L. (cajueiro), *Bauhinia forficata* Link (mororó), *Cissus sicyoides* (insulina-vegetal), *Myracrodruon urundeuva* Allemão (aroeira-do-sertão) and *Zingiber officinalis* L. (gengibre).

***Amburana cearensis* (Allemao) A.C. Sm., Fabaceae (umburana-de-cheiro)**

Amburana cearensis A. C. Smith (syn. *Torresea cearensis* Fr. All.), Fabaceae, is a tree from Ceará State, popularly known as 'cumaru', 'amburana' or 'amburana-de-cheiro' in northeast Brazil. Its trunk bark and seeds have been traditionally used as an antispasmodic, anti-inflammatory, antitussive, and mainly for the treatment of asthma (Braga, 1976; Correa, 1984). From the trunk bark of *A. cearensis* several compounds were isolated, including protocatechuic acid, coumarin, flavonoids (isokaempferide-IKPF, kaempferol, afrormosin and 4'-methoxyfisetin) and the phenol glucosides, amburosides A and B (Canuto & Silveira, 2006; Bravo & Sauvain, 1999).

Isokaempferide (or IKPF), the main flavonoid of the trunk bark of *A. cearensis*, also isolated from other plant species (Saeidnia et al., 2005), presented antibacterial activity for *C. cucumerinum* and *B. cerus* in earlier study (Wang et al., 1989), as well as antiviral activity against type 1 poliovirus and type 15 rinovirus (De Meyer et al. , 1991). These studies corroborate, at least in part, the traditional use of *A. cearensis* in infectious respiratory diseases. Subsequently (Banskota et al., 2000), IKPF was shown to inhibit the TNF-alpha-induced cell death and the growth of tumor cell lines (Costa-Lotufo et al., 2003). Furthermore, this compound was recently found to present anti-inflammatory activity in rats and mice by researchers from our laboratory (Leal et al., 2009).

Leal et al. (2003) also demonstrated that hydroalcoholic extract (HAE), coumarin (Coum) and flavonoid fraction (FF) isolated from the trunk barks of *A. cearensis* have anti-inflammatory and smooth muscle relaxant activities. They inhibited both leucocyte and neutrophil accumulation in the carrageenan or *N*-formyl-methyl-leucyl-phenylalanine (fMLP)-induced migration in rat peritoneal cavity, and histamine- and serotonin induced increases of cutaneous vascular permeability. In the guinea-pig trachea pre-contracted with carbachol and histamine, the HAE, Coum and FF evoked relaxation in the presence of the three agonists, as well as inhibited the histamine and serotonin-induced increase of cutaneous vascular permeability. HAE and Coum also caused significant relaxation of the rat vas deferens previously contracted with adrenaline, acetylcholine or barium chloride. Results from this study suggest anti-inflammatory and bronchodilator effects of HAE, Coum and FF, justifying also the traditional uses of *A. cearensis* as anti-inflammatory and bronchodilator in the treatment of respiratory tract diseases. In addition, antinociceptive effect of the ethanolic extract was recently showed (Oliveira et al., 2009).

The literature presents some information of pharmacological studies on glucoside amburosides A, however, reports about amburosides B are scarce. Leal et al. (2005) evaluated the potential neuroprotective

properties of amburoside A on rat mesencephalic cell cultures exposure to the neurotoxin 6-hydroxydopamine (6-OHDA). The study showed that the glucoside tested, acting as an antioxidant compound, presented a significant neuroprotective effect, suggesting that this compound could provide benefits as a therapeutic agent in neurodegenerative disease such as Parkinson's. The anti-inflammatory activity of amburoside A was also showed (Leal et al., 2009) and seems to be related to an inhibition of inflammatory mediators, such as TNF-α, histamine, serotonin, prostaglandin E2, and leucocytes infiltration.

In addition, hepatoprotective effect from amburoside A was also demonstrated by Leal et al. (2008). Acute treatments of carbon tetrachloride (CCl4) intoxicated rats significantly inhibited the increase in serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. In hepatic tissues, it inhibited CCl_4-induced thiobarbituric acid-reactive substances formation, indicating a blockade of CCl_4-induced lipid peroxidation, as well as reversed the decrement in glutathione contents and restored catalase activity to normal values. The cited study related the protective effect of amburosides A to the phenolic nature of this glucoside and suggests further hepatoprotective potential from *A. cearensis* species.

Anadenanthera colubrina (Vell.) Brenan, Fabaceae (angico-branco)

The leguminous tree *Anadenanthera colubrina* (Vell.) Brenan, known in northeastern Brazil as "angico" or "angico-branco", belongs to the family Fabaceae and is widely distributed in the Caatinga. It has been used in traditional medicine to treat respiratory problems and inflammations (Delgobo et al., 1998; Maia, 2004). The seeds of *Anadenanthera peregrine* (L.) Speng., a related species, are used to prepare *yopo*, a hallucinogenic inhalant used by the "*curandeiros*" (healers) of the *Piaroa* tribe inhabiting southeastern Venezuela (Rodd, 2002).

In the last few decades, studies undertaken on polysaccharides isolated from natural sources have received considerable attention for their potential role as 'biological response modifiers', in terms of immunomodulatory and anti-tumor effects (Han et al., 1999; Ooi & Liu, 2000). The *A. colubrina* is a complex branched high-arabinose heteropolysaccharide that forms an aqueous solution of low viscosity (Delgobo et al., 1998). In this sense, the immunomodulatory and anti-tumoral effects of an acidic heteropolysaccharide containing mainly galactose and arabinose (ARAGAL), isolated from the gum of the *A. colubrina* were previously studied (Moretão et al., 2003; 2004). ARAGAL presented effects on the immune system of mice, increasing the percentage of activated macrophages *in vitro* and *in vivo*, anion superoxide production by macrophages from ARAGAL-treated mice, and phagocytic activity (Moretão et al., 2003). Subsequently, the same authors (Moretão et al., 2004) showed that mice treated with ARAGAL increased peritoneal exudate cell (PEC) numbers, increased TNF-α production by peritoneal macrophages, as well as showed anti-tumoral activity against Sarcoma 180 cells in ascites or solid tumors. The results from this study suggest a possible role as a 'biological response modifier' for ARAGAL.

Several natural products have been discovered to inhibit Lipoxygenase (LO), including some flavonoids agents (You et al., 1999a; 1999b; Sadik et al., 2003). Inhibition of LO is a significant area of research due to its implication in cancer, atherosclerosis and a variety of inflammatory diseases (Steele et al., 1999; Brash, 1999). In this context, Gutierrez-Lugo et al. (2004) described the isolation and characterization of the flavonoid anadanthoflavone, together with other known compounds (alnusenol, lupenone, lupeol, betulinic acid, α-amyrin, β-amyrin, β-sitosterol, stigmasterol, apigenin, 4-hydroxybenzoic acid and cinnamic acid) from the aerial parts of *A. colubrina*, as well as their effects on human and soybean LO. Results from this report showed that anadanthoflavone was found to be active against platelet 12-lipoxygenase and human reticulocyte 15-lipoxygenase; apigenin selectively inhibited the activity of reticulocyte 15-lipoxygenase, while lupenone, lupeol and α-amyrin were found active against soybean lipoxygenase. These results may have implications with respect to possible protective effects in cancer, atherosclerosis and inflammatory diseases from some compounds of *Anadenanthera colubrina*, justifying its use in traditional medicine at least to treat inflammations problems.

Anacardium occidentale L., Anacardiaceae (cajueiro)

Anacardium occidentale L. (cashew), member of the family Anacardiaceae and presently cultivated in many regions of the world, is a tropical tree originally indigenous to Brazil, where is popularly known as "caju". The tree yields the so-called cashew apple to which the nut is attached (Barros, 1993; Konan & Bacchi, 2007; Morais et al., 2010). Although Brazil is the major exporter of cashew nut, the cashew tree is the source of many useful products, including the pseudo-fruit (cashew apple) that is used to make juices and wines (Aguiar et al., 2001). Also, the fruits, stem bark and leaves extracts have been traditionally used for the treatment of mouth and peptic ulcers, intestinal disturbances, dyspepsia, asthma, diabetes, sore throat, asthma, bronchitis and inflammatory diseases (Correia, 1984; Lorenzi & Matos, 2002; Luiz-Ferreira et al., 2008), as well as in treatment

of leishmanial ulcers due to *Leishmania (Viannia) braziliensis* (Franca et al., 1996).

The strongly vesicant cashew nut-shell liquid (CNSL) presents a high amount of anacardic acids, which are also presents in the nut and fruit juice (Toyomizu et al., 2000). Biological and pharmacological investigations carried out on these anacardic acids revealed numerous interesting activities such as parasiticidal (Cui et al, 2008; Pereira et al., 2008), anti-*staphylococcus aureus* (Kubo et al., 2003), anti-*Helicobacter pylori* (Castillo-Juárez et al., 2007), antioxidant (Trevisan et al., 2006), lipoxygenase inhibition (Kubo et al., 2008) and inhibition of NF-κB (Nuclear Factor kappa B) (Sung et al., 2008).

De Lima et al. (2008) investigated whether immature cashew nut-shell liquid (iCNSL) has also antioxidant properties and measured the inhibitory activity of acetylcholinesterase (AChE). Results from this study supported a role for iCNSL in providing strong cellular antioxidant protection against hydrogen peroxide and inhibition of AChE activity. Such properties can be related to the chemical constituents of iCNSL, including anacardic acids, cardol and cardanol. Thus, it is thought that iCNSL could be pathologically important in various neurodegenerative processes, including cognitive deficits that occur during normal cerebral aging, Alzheimer's and Parkinson's disease. Also, this natural antioxidant could be better utilized in functional food formulations and may represent a cheap source of cancer chemopreventive agents. Recently, the anacardic acids from *A. occidentale* were also studied for their gastroprotective activities using the ethanol-induced gastric damage in mice as the test model (Morais et al., 2010). Results from this study suggest that these constituents afford gastroprotection principally through an antioxidant mechanism, as well as by stimulation of endogenous prostaglandins and nitric oxide, and opening of K^+ ATP channels.

Besides the nut of the *A. occidentale*, also the cashew apple juice has been reported to show several pharmacological properties such as anti-tumor (Kubo et al., 1993), antimicrobial (Kozubek et al., 2001), admirable antioxidant potential and antimutagenic properties (Melo-Cavalcante et al., 2003, 2005; Trevisan et al., 2006). Antiulcerogenic effect was also showed from plant leaf hydroethanolic extract (Konan & Bacchi, 2007), while leaf aqueous extract was demonstrated to protect against streptozotocin-induced diabetes in rats (Kamtchouing et al., 1998). Also, the stem bark is astringent and rich in tannins, which possibly supports its popular use in healing. In fact, earlier, tannins isolated from the bark of the plant were demonstrated to possess anti-inflammatory effects in some models of inflammation (Mota et al., 1985). Subsequently, this activity was described in two different models of inflammation, having reduced paw edema induced by fresh egg albumin in rats (Ojewole, 2004) and inhibited skin dye leakage in mice after subcutaneous injection of LPS (Olajide et al., 2004). More specifically, the anti-inflammatory and cicatrizing effects from the aqueous extract of *A. occidentale* were shown by the clinical evaluation of patients with skin injury or mucosa lesions such as oral or vulva erosion, uterus inflammation and body ulceration (Lopes et al., 2003). Several further investigations were carried out to determine possible mechanisms involved in anti-inflammatory properties from *A. occidentale* (Olajide et al., 2004; Vanderlinde et al., 2009).

As evidenced in the studies discussed above, several pharmacological properties from different parts of the *A. occidentale* validate its folkloric use in diverse alternative health practices. However, further potential uses of this plant are still in need of investigation.

Bauhinia forficata Link, Fabaceae (mororó)

The recognized use and potential of *Bauhinia* species to act as hypoglycemic agents have received considerable scientific attention in recent years. Aqueous extracts from *Bauhinia* species leaves, roots and stems, mainly *B. cheilantha, B. forficata, B. glabra, B. rufescens, B. splendens* and *B. ungulata,* have been widely used over time in Brazil and in other countries in the treatment of several illness, specially pain processes, infections and diabetes (Pereira et al., 2004; Macedo & Ferreira, 2004; Morais et al., 2005; Almeida et al., 2006a; Silva et al., 2006).

Leaves of the pantropical genus *Bauhinia* are popularly known in Brazil as "pata-de-vaca" (cow's hoof), due to their unique characteristic bilobed aspect (Miyake et al., 1986). *Bauhinia divaricata* aqueous extract, known in Mexico as "pezunã de vaca", showed a relatively significant hypoglycemic effect in normal mice (Gupta et al., 1980), while the *B. megalandra* species inhibited the glucose intestinal absorption (Gonzalez-Mujica et al., 2003) in rats. However, the hypoglycemic activity of *Bauhinia* species has been most extensively researched in *B. forficata*.

The *Bauhinia forficata* Link is a member of the *Caesalpinioideae* subfamily, Fabaceae, commonly found in the Caatinga. The leaves of this species, in the form of aqueous extract, are widely used as an antidiabetic herbal remedy in Brazilian folk medicine (Volpato et al., 2002; Barbosa-Filho et al., 2005; Silva et al, 2006). The first report of *Bauhinia forficata* hypoglycemic action in diabetic patients was demonstrated by Juliane (1929), and this was confirmed by a further study (Juliane, 1931). Subsequent studies were carried out to determine the constituents responsible for this activity. In this sense, numerous constituents including alkaloids, flavonoids, mucilage, essential oils and tanines were isolated from *B. forficata* (Oliveira & Saito, 1987).

Flavonoids are a class of natural products of high

pharmacological potency (Havsteen, 1983) and, among some of the constituents of *B. forficata*, most studies have examined the effects of natural flavonoids in physiological and pathological conditions of glucose metabolism, as well as in lipid peroxidation (Damasceno et al., 2004; De Sousa et al., 2004). Thus, such studies evidenced that *B. forficata* has significant antioxidant activity, beneficial in the prevention of diabetes complications associated with oxidative stress (Khalil et al., 2008).

Some reports have attributed the effects of the *B. forficata* leaf extracts to the main flavonoid derivative (kaempferitrin) (Jorge et al., 2004; De Sousa et al., 2004). In fact, kaempferitrin was found to have an acute lowering effect on blood glucose in diabetic rats and to stimulate the glucose uptake percentile, as efficiently as insulin in muscle from normal rats (Jorge et al., 2004). In recent study, Tzeng et al. (2009) provided evidence of the dual effects of kaempferitrin. It improved insulin resistance by the activation of the classical insulin transduction pathway and increased adiponectin secretion. Taken together, these studies corroborate the potential of glycosylated flavonoid kaempferitrin on the pharmacological properties of *B. forficata.* Thus, as a result of several scientific investigations, evidences have reinforced the hypoglycemic efficacy of *B. forficata* species and its use as ''natural insulin'' for the control of diabetes (Miyake et al., 1986; Jorge et al., 2004; Da Cunha et al., 2010), including a study conducted by collaborators from our laboratory (Lino et al., 2004).

On the other hand, in addition to *B. forficata* antidiabetic activity, studies showed further pharmacological properties from this species. For example, an *in vitro* antitumoral activity was described and related to an unusual nitrogenated compound isolated from the leaves (Lim et al, 2006), while Oliveira et al. (2005) showed that the aqueous extract from aerial parts of *B. forficata* was able to neutralize the clotting activity induced by *Bothrops* and *Crotalus* crude venoms. This study concluded that the plant extract is also a promising source of natural inhibitors of serine-proteases involved in blood clotting disturbances induced by snake venoms.

Cissus sicyoides L., Vitaceae (insulina-vegetal)

Cissus sicyoides L., Vitaceae, a climber plant originally from the Dominican Republic, is commonly found in tropical regions, particularly in Caribbean and Brazil (Cano & Volpato, 2004). According to previous studies, it has been used in traditional medicine of some countries as a diuretic, anti-inflammatory, antidiabetic and anti-influenza agent (Carvajal et al., 1983; García et al., 2000; Cano & Volpato, 2004; Bolsoni et al., 2008). In Brazil, *C. sicyoides* is largely found in Caatinga and used in folk medicine for treatment of several diseases, such as epilepsy, stroke, gastric ulcer, abscesses, as well as it has been used widely as a popular remedy for diabetes mellitus and, for this, is locally known as "insulina-vegetal" (insulin plant) or ''cipó-pucá'' (Dey et al., 2002; Lorenzi & Matos, 2002; Agra et al., 2007).

In order to validate the popular use of the *C. sicyoides* as an antidiabetic, previous pharmacological studies have been conducted (Mori et al., 2001; Beltrame et al., 2001; Pepato et al., 2003; Viana et al., 2004). Pepato et al. (2003) administered leaf decoctions, over extended periods, to normal and streptozotocin-diabetic rats. Results showed that the treatment significantly reduced the intake of both food and fluid and the volume of urine excreted, as well as the levels of blood glucose, urinary glucose and urinary urea, in comparison with controls. The authors suggested that the *C. sicyoides* mode of action in diabetic does not resemble those of sulphonylurea or insulin but it could act in a similar way to biguanide, via inhibition of gluconeogenesis. Viana et al. (2004) showed that aqueous extract prepared from fresh leaves of the plant significantly decreased blood glucose levels in the model of alloxan-induced diabetes in rats. In addition, considering that triacylglycerides are usually increased in the serum of diabetic patients, while no changes were seen in total cholesterol levels, a significant decrease was observed in plasma triacylglyceride levels of animals. The results from these studies justify the popular use of *C. sicyoides*, pointing out to the potential benefit of the plant aqueous extract in alternative medicine, in the treatment of type 2 diabetes mellitus. Currently, the antidiabetic action of the *C. sicyoides* is in the making of clinical trials (phase II) (Santos et al., 2008) and the results obtained from this study are promising for the future use in medical clinics.

Also, considerable interest has gathered around the role of antioxidants as a means of preventing damage due to the oxidative imbalance found in diabetes (Coppey et al., 2003; Martin-Gallan et al., 2003). In this sense, similar to the observed for *B. forficate*, Khalil et al. (2008) determined the in vitro antioxidant activity of aqueous extracts from leaves of *C. sicyoides*, suggesting this species as a potential source of natural antioxidants, helpful in the prevention of diabetic complications associated with oxidative stress.

The *C. sicyoides* plant is rich in nutrients and bioactive compounds. The extracts obtained from this species have high contents of amino acids, alkaloids, steroids, terpenes, flavonoids, saponins, tannins, and phenolic compounds, and the fruits are rich in anthocyanins (Toledo et al., 1983; Otshudi et al., 2000). Thus, besides its antidiabetic action, *C. sicyoides* has been furthermore evaluated for its anticonvulsant property in Brazil, where it is also used against epilepsy (Elisabetsky et al., 1988). In fact, in the leaves of this species has been identified the presence of α-tocopherol, a compound proved to protect against pentylenotetrazol

and methylmalonate induced convulsions (Ribeiro et al., 2005) and to prevent the occurrence of epileptic foci in a rat model of posttraumatic epilepsy (Yamamoto et al., 2002). Recently, Almeida et al. (2009) demonstrated the anticonvulsant and also anxiolytic effects of a hydroalcoholic extract obtained from the *C. sicyoides* on mice, probably due to the action of α-tocopherol, flavonoid(s) and linalool present in the leaves. Taken together, the cited studies validate the folkloric use of *C. sicyoides* as anticonvulsant.

Furthermore, several additional pharmacological properties have been evidenced from *C. sicyoides*. A previous study (Beltrame et al., 2002) showed that two compounds isolated from aerial parts of the plant (β-sitosterol and sitosterol-β-D-glucopyranoside) presented antibacterial activity, while the aqueous extract was able to contract isolated guinea-pig aortic rings by increasing the calcium entry through the membrane and mobilizing the internal calcium deposits (García et al., 1997). Aqueous extract was also shown to present cytostatic (Saenz et al., 2000), antinociceptive (Almeida et al. 2006b) and anti-inflammatory (García et al., 2000) effects. In recent study (Ferreira et al., 2008), the methanolic extract obtained from the leaves of *C. sicyoides* was evaluated for the ability to protect the gastric mucosa against injuries caused by different necrotizing agents in rodents. This extract administered by oral route significantly increased gastric volume without exerting antisecretory effect. The effect involved an increase of the defense mechanism of the gastrointestinal mucosa such as oxide nitric and sulfidryl groups that prevent and attenuate the ulcer process. Also, phytochemical evaluation demonstrated the presence of sterol ß-sitosterol (14%) and quercetin-3-*O*-β-D-rhamnoside (18%) as the majority constituents in *Cissus sicyoides* and both constituents have been reported previously as antiulcer activity (Arrieta et al., 2003). These studies corroborate the traditional use of *C. sicyoides* also for the treatment of gastric ulcer.

Zingiber officinale Roscoe, Zingiberaceae (gengibre)

Zingiber officinale Roscoe, belonging to the family Zingiberaceae, is commonly known as ginger. Originally from Southeast Asia, it was artificially introduced in South America and several countries of the African continent, and is now considered a common constituent of diet worldwide (Chemexcil, 1992; Park & Pizzuto, 2002). The underground stem or rhizome of this plant has been used as a medicine in Asian, Indian, and Arabic herbal traditions since ancient times (Nadkarni, 1976; Altman & Marcussen, 2001).

In the traditional medicine of India, Ayurveda, ginger is used extensively to block excessive clotting (in heart diseases), reduce cholesterol and fight arthritis (Sharma & Clark, 1998), while in traditional Chinese medicine it has been used extensively for more than 2500 years for headaches, colds, as well as is locally considered a pungent and warming (Grant & Lutz, 2000). In Mediterranean and Western, the plant has been used for the treatment of arthritis, rheumatological conditions and muscular discomfort (Langner et al., 1998; Sharma & Clark, 1998). In Arabian medicine, ginger is considered an aphrodisiac (Qureshi et al., 1989), while in African is considered to be a mosquito repellent (Duke & Ayensu, 1985). Also, it has also been suggested for the treatment of various other conditions, including atherosclerosis, migraine headaches, high cholesterol, ulcers, depression, and impotence (Liang, 1992).

In Brazil, the *Zingiber officinale* plant is known as "gengibre" (ginger). It is widely distributed in the Caatinga and in other regions around the country, where has been consumed as a fresh paste, dried powder, teas, preserved in sugar or in syrup, as well as is commonly found as candy (crystallized ginger). Locally, it has been used mainly as carminative, for indigestion, stomachache, diarrhea, vomit, colds, sorethroat, cough and hoarseness, as well as for the treatment of arthritis and rheumatological conditions besides several other traditional uses. Ginger rhizome is widely commercialized in Brazil due to its use in folk medicine, eating and industry, especially as raw material for manufacture of beverages, perfumes, breads, cakes, cookies and jams (Corrêa Junior et al., 1994; Palharin et al., 2008).

Numerous constituents have been reported to be present in *Z. officinale*, including volatile essential oil, tannins, flavonoids, sulphonatated compounds and pungent principles like zingerone, gingerols and shogaols (Yoshikawa et al., 1993; Ali et al., 2008). In general, flavonoids and tannins (Galvez et al. l993; Miranda et al., 1993), and recently zingerone (Chen et al., 2007), have been reported to present antidiarrhoeal activity, which has been credited to inhibition of intestinal motility and secretion (Di Carlo et al., 1993) and antimicrobial action (Lutterodt et al., 1999).

Due its spasmolytic actions, the efficacy of ginger against motion or sea sickness was evidenced in several early studies (Grontved et al., 1988; Holtmann et al., 1989; Stewart et al., 1991), as well as it was showed as an antiemetic in nausea and vomiting induced by chemotherapy in a randomized, cross-over and double blind study (Sontakke et al., 2003). In addition to these reports, Geiger (2005) showed that a 5% solution of essential oil of ginger is an effective post-operative nausea and vomiting prevention when administered preoperatively, concurrently with conventional therapies, to general anaesthesia patients at high risk for post-operative nausea and vomiting, with increased patient satisfaction and less expense to patients and hospital.

Recently, ginger capsules were effective for decreasing nausea and vomiting during pregnancy (Ozgoli et al., 2009). The authors suggest that a daily total of 1000 mg of ginger in a capsule preparation can be suggested by care providers as a means of decreasing pregnancy nausea and vomiting in women who tend to herbal medicines. In addition, in isolated guinea pig ileum, several compounds in ginger have been shown to have anti-serotonin (5-hydroxytryptamine) effects (Yamahara et al., 1989; Huang et al., 1991). These early studies suggest that, at least in part, the anti-emetic action of either ginger or some of its constituents may be mediated centrally via 5-HT3 receptors, as these constituents have small molecular weights and could easily cross the blood brain barrier.

A number of studies shows that some constituents present in ginger may exert cancer preventive effects. The oleo resin from the root of ginger contains [6]-gingerol (the majority pharmacologically active component) and lesser amounts of a structurally related vanilloid, [6]-paradol. Previous studies suggest that both compounds suppress proliferation of human cancer cells through the induction of apoptosis (Lee & Surh, 1998; Lee et al., 1998) and were found to exert inhibitory actions on the viability of human HL-60 (promyelocytic leukemia) cells (Lee & Surh, 1998). [6]-Paradol and other structurally related derivatives like [10]-paradol, [3]-, [6]- and [10]-dehydroparadol, induced apoptosis in an oral squamous carcinoma cell line through a caspase-3-dependent mechanism (Keum et al., 2002), while [6]-gingerol was able to inhibit the growth of human colorectal cancer cells (Bode, 2003). It was found that gingerol inhibited the growth of *H. pylor*i strains *in vitro* and this activity may contribute to its chemopreventive effects against colon cancer (Mahady et al., 2003). This anti- *H. pylori* action was further confirmed by Mahady et al. (2005) and Nostro et al. (2006). Recently, Weng et al. (2010) demonstrated that [6]-shogaol and [6]-gingerol exerted anti-invasive activity against human hepatocarcinoma cells.

Since tumor promotion is closely linked to inflammation and oxidative stress (Fang et al., 2009), many herbs and spices are known to possess antioxidant and anti-inflammatory properties that are believed to contribute to their anticarcinogenic and antimutagenic activities (Chung et al., 2001; Wang et al., 2007). In fact, gingerol, shogaol, paradol and other structurally related substances in ginger were found also to possess considerable antiinflamatory activity (Flynn et al., 1986; Kiuchi et al., 1982; 1992; Nurtjahja-Tjendraputra et al., 2003), while more than fifty antioxidants (mainly [6]-gingerol) isolated from the rhizomes were showed (Aeschbach et al., 1994; Chung et al., 2001; Masuda et al., 2004).

The antiinflammatory-like substances from ginger were found to inhibit prostaglandin and leukotriene biosynthesis through suppression of 5-lipoxygenase or prostaglandin synthetase. However, it is established that neither ginger nor its constituents produce the gastrointestinal adverse effects that are usually produced by the conventional non steroidal antiinflammatory drugs as a result of prostaglandin inhibition (Konturek et al., 2005). In fact, the cytoprotective and gastric anti-ulcer effect of ginger have been showed experimentally in early studies in rats (Yamahara et al., 1988; Wu et al., 1990). Recently, data provides evidence for the potential ulcer-preventive ability of phenolics in ginger aqueous extract and addresses the probable mode of action through the inhibition of gastric H^+, K^+-ATPase and *Helicobacter pylori* growth (Siddaraju et al., 2007; Nanjundaiah et al., 2009).

Thus, ginger and many of its chemical constituents have been shown, in numerous experimental and clinical studies, to be useful in combating several health disturbances, providing evidences to explain the actions of folk medicines in terms of conventional biochemistry and pharmacology.

Myracrodruon urundeuva Allemão, Anacardiaceae (aroeira-do-sertão)

Myracrodruon urundeuva Allemão, Anacardiaceae, a medicinal plant known as 'aroeira-do-sertão', is a prominent species in the regional Caatinga vegetation and very popular in the Northeastern of Brazil. Locally, it has been used in folk medicine as an anti-inflammatory agent in the treatment of gynaecological and gastrointestinal problems, as well as in skin and mucous lesions cicatrization process. Decoction, infusion in water, syrup and intimate soaps are some of the manners of popular use (Matos et al., 2001; Monteiro et al., 2006).

Chemical fractionation studies revealed that the *M. urundeuva* ethyl acetate extract has two main fractions, one rich in chalcones and the other one rich in tannins. Chalcones are biosynthetic precursors of flavonoids and together to other biogenetically related compounds are collectively called flavonoids. Tannins can be classified as hydrolysable and condensed and, as flavonoids, they are polyphenols, which act as astringents that shrink tissues and contract structural proteins in the skin and mucosa. It has been shown that both fractions are involved with the pharmacological activity of the plant (Viana et al., 1997; 2003).

Dimeric chalcones isolated from bark showed analgesic effects and anti-inflammatory activity in several experimental models of inflammation (Viana et al., 2003; Araico et al., 2007). Many of chalcones derivatives have been found to be also antioxidant (Miranda et

al., 2000), molluscicidal (Adewunmi et al., 1987) and antimicrobial (Nielsen et al., 2004). In addition to these pharmacological actions, in recent study carried out by researchers from our laboratory (Nobre-Junior et al., 2009), a chalcone-enriched fraction isolated from the stem bark of *M. urundeuva* presented neuroprotective action on 6-hydroxydopamine (6-OHDA)-induced neuronal cell death, in rat mesencephalic cells. The authors suggested that the anti-oxidative properties of chalcone-enriched fraction could partly explain its neuroprotective effect. In this sense, the fraction was able to completely reverse the drastic increase in thiobarbituric acid reactive substances formation induced by 6-OHDA, besides decreasing the 6-OHDA-induced nitrite formation.

The tannin fraction from *M. urundeuv*a was also found to possess analgesic and anti-inflammatory pharmacological effects in several experimental tests conducted by collaborators from our laboratory (Viana et al., 1997). The antinociceptive effect was not reversed by the opioid antagonist naloxone, pointing to the noninvolvement of the opioid system in the antinociception, and suggesting a peripheral action. Also, similarly to aspirin, the response in the formalin test 2nd phase was more sensitive to inhibition by tannin fraction, suggesting that it acts through the inhibition of prostaglandin synthesis. In addition, an antioedematogenic effect in rat paw oedema induced by both carrageenan and dextran models was also observed in the cited study. Subsequently (Souza et al., 2007), anti-inflammatory and antiulcer effects from tannin-enriched fraction were credited to its antioxidant action, known to be present in polyphenols, including tannins.

As referred above, in Northeast Brazil *M. urundeuva* has been commonly used as antiinflammatory agent for the treatment of gastrointestinal diseases. In this sense, Rodrigues et al. (2002) showed the effects of *M. urundeuva,* in the form of enemas prepared from the stem bark, on several morphologic and morphometric parameters after acetic acid-induced colitis in rats. Results evidenced that animals treated with *M. urundeuva* showed complete epithelial tissue regeneration, while in the controls chronic inflammatory exudate persisted and tissue regeneration occurred through fibrosis. It is possible that the antiinflammatory properties of tannin fraction isolated from the plant stem barkthese are, at least in part, responsible for the decrease in oedema and inflammatory exudate and also for the complete epithelial regeneration.

In addition, a recent study evaluated the effect of a topical herbal gel from *Lippia sidoides* and *Myracrodruon urundeuva* (5%) (aroeira-do-sertao) in experimental periodontal disease in rats (Botelho et al., 2007). The authors showed that the combined gel treatment preserved alveolar bone resorption and demonstrated anti-inflammatory and antibacterial activities in experimental periodontitis. In a more recent report, Crivelaro de Menezes et al. (2010) evaluated the influence of *M. urundeuva aqueous* extracts on *S. mutans* counts and dental enamel micro-hardness of rats submitted to a cariogenic challenge. The authors concluded that the extract tested had a significant effect on *S. mutans* in oral biofilm of the rats, decreasing *S. mutans* accumulation and enamel demineralization. In fact, *M. urundeuva* is considered a hardwood, very dense, elastic and resistant to microorganisms and termites and, therefore, studies were conducted in order to evaluate its antimicrobial activity against bacteria and fungi that attack plants, including woods. In this sense, a lectin isolated from heartwood was showed to inhibit Gram-negative and Gram-positive bacteria and was more effective than antifungal Cercobin (a recognized systemic fungicide) in growth inhibition of phytopathogenic fungi (Sá et al., 2009), corroborating the antimicrobial potential of this species.

Taken together, scientific studies about pharmacological properties from *M. urundeuva* validate its extensive traditional use in the treatment of gynecological conditions, skin and mucous lesions and gastrointestinal disturbances, as well as evidence further therapeutic potential from this plant and their constituents.

Final Considerations

Although an expressive number of medicinal plant species from the Caatinga region is known and used in folk medicine, detailed studies of their pharmacological and biological activity are still needed. On the other hand, the native and introduced species or their active constituents revised in the present study demonstrated potential targets for future use as a dietary supplement or as a drug therapy. In this sense, we suggest that these species and compounds be examined for a wider range of pharmacological activities. Therefore, the Caatinga region should be of high conservation priority and thus research efforts should be directed to the sustainable management of those species integrated with vegetation management in disturbed areas.

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