Schinus terebinthifolius Raddi: chemical composition, biological properties and toxicity

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RESUMO: *Schinus terebinthifolius* Raddi: Composição química, propriedades biológicas, e toxicidade. *Schinus terebinthifolius* Raddi é uma planta medicinal conhecida no Brasil como "aroeira da praia", utilizada na medicina popular como antitérmica, analgésica, depurativa e no tratamento de doenças do sistema urogenital. Por outro lado, a literatura científica relata que essa planta apresenta atividade antimicrobiana, anti-inflamatória, e antiulcerogênica. Essa revisão trata das principais propriedades biológicas e efeitos toxicológicos da aroeira da praia, além de uma abordagem sistemática acerca dos compostos que já foram encontrados nessa espécie, estando a maioria deles presente nos óleos essenciais.

Palavras Chave: *Schinus terebinthifolius*, Anacardiaceae, componentes químicos, propriedades biológicas.

ABSTRACT: *Schinus terebinthifolius* Raddi is a medicinal plant known in Brazil as "aroeira da praia", which has been used in popular medicine as antipyretic, analgesic, depurative and in the treatment of diseases of the urogenital system. On the other hand, the scientific literature has reported that this plant has antimicrobial, anti-inflammatory and antiulcerogenic activity. This review addresses the main biological properties and toxicological effects of "aroeira da praia", in addition to a systematic approach of the compounds that were already found in this species, the great majority of which is present in the essential oils.

Key words: *Schinus terebinthifolius*, Anacardiaceae, chemical compounds, biological properties.

INTRODUCTION

Over the past few years, an increasing number of studies have demonstrated the large diversity of secondary metabolites present in the Anacardiaceae family, which are closely related to the biological properties of some of its species. With more than 76 genera and about 600 species (Correia et al., 2006, Corrêa, 1984), this family has been quite promising in the search for bioactive substances. From a chemical stand point, the most frequently studied genera of the Anacardiaceae family are *Mangifera, Rhus* (*Toxicodendron*), *Anacardium, Spondias*, *Lannea*, *Semecarpus*, *Schinus*, *Pistacia, Lithraea*, *Tapirirae* and *Melanorrhoea*. The genus *Schinus* (*Anacardiaceae*) is native to South America and is found mainly in the Brazilian coast (Barbosa, et al., 2007), which includes approximately 29 species (Barkley, 1957). The main species that belong to the genus *Schinus* are *S. terebinthifolius* and *S. molle*, and the former is the focus of this review.

Schinus terebinthifolius is also known as Brazilian peppertree and Florida Holly (United States); Christmas-berry (Hawaii, Guam); false pepper or faux poivrier (French Riviera); "aroeira da praia", "aroeira negra", "aroeira vermelha", "aroeira de Minas", "cor-neiba" (Brazil), "chichita" (Argentina); "copal" (Cuba) and "pimienta de Brasil" (Puerto Rico) (Morton, 1978). *S. terebinthifolius* is largely found in the Brazilian coast, and is distributed from the northeast to the south part of the country. The biological applications of this plant have been known for many years, and its properties have been described since the first edition of the Brazilian Pharmacopoeia, published in 1926. It has been used in folk medicine as anti-inflammatory, antipyretic, analgesic and as a depurative agent. In addition, *S. terebinthifolius* has been used to treat sexually transmitted diseases, uterine inflammation, urinary tract infections, skin ulcers and

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gastroduodenal disorders (Cavalher-Machado, et al., 2008, Diniz, et al., 1997, Martinez, et al., 1996). Bacchi (1986) reports the use of aroeira species in the treatment of skin, mucous membrane injuries, ulcers and infections of the respiratory, digestive and genitourinary systems

Biological properties

Schinus species are characterized by pungent-smell essential oils concentrated especially in fruits (Bendaoud, et al., 2010), which are used to treat respiratory disorders, mycosis and invasive candidal infections. According to Lima et al. (2009), these properties are attributed to the presence of high levels of monoterpenes in these species.

An essential oil from the fruits of *S. terebinthifolius* was identified and investigated for its antioxidant and anticancer activities (Bendaoud et al., 2010). These authors reported a marked antioxidant and cytotoxic activities *in vitro* on human breast carcinoma. These findings suggest that the essential oil from *S. terebinthifolius* might be a promising source of active compounds for innovative therapies and/or preventive strategies against cancer. On the other hand, Roveda et al. (2010) reported the absence of antitumor activity, as well as selectivity of the essential oil from *S. terebinthifolius* on various human cancer cell lines.

Two triterpenoids isolated from *S. terebinthifolius* berries were characterized as active site-directed specific competitive inhibitors of phospholipase A2, which indicates a possible anti-inflammatory activity (Jain et al., 1995).

In addition, Morton (1978) reported that solutions obtained from leaf decoction or even from crushed dried leaves acted as an antiseptic agent when applied directly to wounds or ulcers. According to that author, this plant has also potential applications as homeopathic treatment for gout, lack of muscle tone (hyptonia), arthritis, chills, tumors, lymphatic swellings and hemoptysis. There are reports in the literature that patients suffering from rheumatism attained great relief after taking hot baths with decoction from the barks of *S. terebinthifolius*. Its juice, prepared out of pressed roots, is considered an effective alternative for the treatment of ganglionic tumors and contusions. In addition, the barks of *S. terebinthifolius* have shown satisfactory activity against fever, hemoptysis and uterine disorders. The oil extracted from the barks has also been used for the treatment of tumors and corneal diseases (Bornhausen, 2010).

To evaluate the effectiveness of medicinal herbs in the treatment of induced alveolitis in rats, Melo Junior et al. (2000) demonstrated through *in vitro* and *in vivo* studies that the ethanolic extract from *S. terebinthifolius* barks presented the best results among sixteen evaluated species. The group treated with *S. terebinthifolius* showed similar results when compared to the one treated with gentamicin, where it showed to be effective against *Enterococcus, Streptococcus viridans, Streptococcus β-hemoliticus, Bacillus corineforme*, *Staphylococcus aureus* and gram-positive bacteria present in alveolitis. Moreover, histological examination revealed an enhanced wound healing and a faster bone neoformation, when compared to the results observed in the control group.

The wound healing effect of the hydro-alcoholic extract from the bark of *S. terebinthifolius* was evaluated in surgical incisions in the bladder, stomach, abdominal wall and in colonic anastomosis in rats. It showed a favorable effect on the healing process of cystotomies and colonic anastomosis. However, it did not alter the healing process in the stomach. Besides, *S. terebinthifolius* extract did not cause any significant alteration in the macroscopic analysis of the abdominal wall but induced an increase in the maximum charge of rupture and maximum deformity of the *linea alba* in the tensiometric analysis (Coutinho et al., 2006, Lucena et al., 2006, Nunes Júnior et al., 2006, Santos et al., 2006). When the healing effect of *S. terebinthifolius* hydroalcoholic extract was evaluated on open wounds in the dorsocostal region of rats, a delayed re-epitelization was observed in these areas (Branco Neto et al., 2006). Thus, it seems that a more detailed study of the *S. terebinthifolius* healing properties needs to be addressed.

Carlini et al. (2010) reported that extracts from barks showed a marked protective effect against gastric ulcerations induced by immobilization stresses at low temperature in rats. *S. terebinthifolius* extracts were capable of raising both the pH and the volume of the gastric contents. In addition, these extracts reduced gastric hemorrhage and intestinal transit, even at the low doses of 3.4 $mg.kg^{-1}$ (1/4 of the dose used in humans). These results corroborate the popular belief that decoctions of *S. terebinthifolius* are useful for the treatment of gastric disorders.

In studies carried out by Cavalher-Machado et al. (2008), 1,2,3,4,6-pentagalloylglucose and methyl gallate, which are aromatic compounds isolated from *S. terebinthifolius*, showed important anti-allergic properties as indicated by the inhibition of edema formation, mast cell degranulation and eosinophil influx as a result of decreased production of eosinophilotactic mediators. In addition, treatment with these aromatic compounds inhibited paw edema to the same extent as the anti-allergic drug promethazine.

Several studies have evaluated the *in vitro* antimicrobial activity of hydroalcoholic extract or

tinctures of *S. terebinthifolius* against pathogenic microorganisms in the oral cavity. A screening study developed by Pereira et al. (2011) evaluated the susceptibility of oral pathogenic microorganisms, such as *Candida albicans, Streptococcus mutans, Staphylococcus aureus*, and *Aggregatibacter actinomycetemcomitans* to ethanol, hexane and butane extracts from *S. terebinthifolius*. The obtained results suggest that these extracts can be an efficient alternative for the treatment of infections of the oral cavity, such as stomatitis, dental cavities and periodontitis caused by *S. mutans* and *S. aureus*. Hexane and butane fractions were not effective in inhibiting the growth of *C. albicans* and *A. actinomycetemcomitans.* However, ethyl acetate fraction from leaves of *S. terebinthifolius* inhibited the growth of three *C. albicans* strains, as well as their adhesion to buccal epithelial cells at concentrations of 7.8 $\mu g.mL^{-1}$ and 15 $\mu g.mL^{-1}$, respectively (Johann et al., 2007).

According to Schmourlo et al. (2005), *S. terebinthifolius* showed bactericidal and bacteriostatic effects against *S. mutans, S. mitis, S. sobrinus, S. sanguis*e and *L. casei*, as well as antifungal properties against *C. albicans, C. tropicalis*e and *C. krusei* (Alves et al., 2009, Soares et al., 2007). Bioautography assay, which is a method to localize antibacterial activity on a chromatogram, showed that the antifungal activity was related to the apolar compounds that are present in this plant.

Recently, schinol and a new biphenyl compound (4'- ethyl – 4 – methyl – 2, 2', 6, 6'- tetrahydroxyl(1.1'- biphenyl) – 4,4'- dicarboxylate), isolated from hexane and dichloromethane fractions obtained from leaves and stems, showed marked antifungal activity against *P. brasiliensis* (MIC = 15.6$\mu g.mL^{-1}$) (Johann et al., 2010).

Santos et al. (2010) studied the fungicide effect of essential oils from *S. terebinthifolius* and *S. molle* as a possible alternative to control diseases caused by phytopathogenic fungi that affect agricultural production. The essential oils from *S. terebinthifolius* showed a pronounced fungicide effect against *Botytis ssp* isolated from "gerberas" and roses.

On the other hand, Ribas et al. (2006) showed in their studies that daily topical application of *S. terebinthifolius* extracts on chronic oral ulcers accelerated the repair of the epithelium and connective tissues. Besides, it stimulated keratinization, decreased the intensity of chronic inflammatory processes and improved collagen maturation.

Analysis of aqueous and alcoholic extracts obtained from *S. terebinthifolius* fruits showed that only the alcoholic extracts have inhibitory effect on the growth of *Staphylococcus aureus* and *Bacillus cereus*. However, no inhibitory effect on the growth of *Candida albicans, Aspergillus niger, Escherichia coli, Pseudomonas aeruginosa and Salmonella choleraesuis* were observed for both extracts (Degaspari et al., 2005).

Additional studies carried out by Amorim and Santos (2003) showed that topical applications of aroeira extracts were capable of reducing the number of pathogenic microorganisms in the vaginal microbiota. A subsequent study compared the effect of a gel containing 7.4% of *S. terebinthifolius* extract with a 0.75% metronidazole gel for the treatment of bacterial vaginosis using two groups of 140 and 137 women, aged between 18 and 40 years. The cure rate for bacterial vaginosis using *S. terebinthifolius* gel was significantly lower than that obtained with metronidazole gel, while side effects were infrequent and non-severe in both groups (Leite et al., 2011).

To verify the potential application of *S. terebinthifolius* as an antimicrobial preservative, Moura et al. (2011) compared the microbial levels of a gel containing an *S. terebinthifolius* extract with a placebo gel. When both gels were contaminated with separate inoculum of *Aspergillus niger, C. albicans*, *E. coli*, *S. aureus* and *P. aeruginosa,* no significant decrease in the microbial load was observed for *S. terebinthifolius* gel, which seems to indicate the need of adding preservatives to the products containing this plant.

Assessment of the free radical scavenging properties of *S. terebinthifolius* extract indicated that it presented activity against superoxide and diphenylpicrylhydrazyl (DPPH) radicals. Besides, *S. terebinthifolius* extract showed a protective effect against enzymatic and non-enzymatic lipid peroxidation in microsomal membranes of rats (Velazquez et al., 2003).

Extracts from the aerial parts of *S. terebinthifolius* exhibited an inhibitory activity against xanthine oxidase (XO) which was similar to that of allopurinol, a well known XO inhibitor. Therefore, *S. terebinthifolius* could potentially be used as a therapeutic agent for hyperuricemia, nephrolithiasis (kidney stones) and ischemic myocarditis. The XO inhibition effect seems to be due to a compound called pentagalloylglucose (1,2,3,4,6-penta-O-galloyl-P-D-glucose), which also has antiviral effect (Hayashi et al., 1989).

Chemical composition

Despite the widespread popular use as a medicinal plant, *S. terebinthifolius* has shown great potential for the development of herbal products. Although a large number of studies have evaluated the pharmacological properties of this plant, little attention has been given to the identification

TABLE 1. Chemical compounds identified in *Schinus terebinthifolius.*

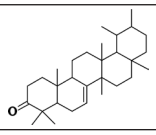
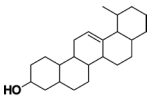
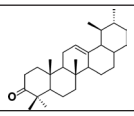
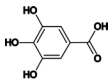
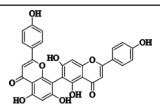
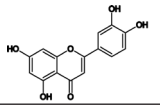
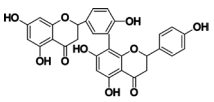
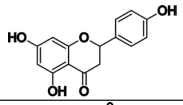
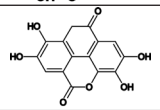
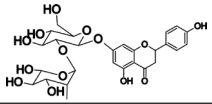
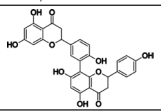
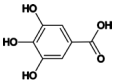
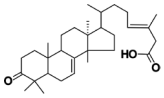
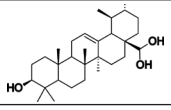
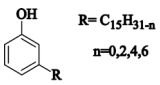
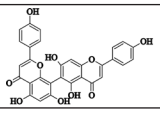
Part used	Compound	Chemical structures	Method	References
Barks	Bauerenone		Preparative Cromatography, UV, IR, NMR	(Campelo and Marsaioli, 1975)
	α-amyrin		Preparative chromatography, UV, IR, NMR	(Campelo and Marsaioli, 1975)
	α-amyrenone		Preparative chromatography, UV, IR, NMR.	(Campelo and Marsaioli, 1975)
	Gallic acid		HPLC	(Carvalho, et al., 2009)
	Agathisflavone		TLC, NMR	(Heringer, et al., 2007)
	Luteolin		TLC, NMR	(Heringer, et al., 2007)
Fruits	Tetrahydroamentoflavone		Chemical and spectral characterization	(Skopp and Schwenker, 1986)
	Apigenin		HPLC	(Degaspari, et al., 2005)
	Ellagic acid		HPLC	(Degaspari, et al., 2005)
	Naringine		HPLC	(Degaspari, et al., 2005)
	Amentoflavone		Chemical and spectral characterization	(Skopp and Schwenker, 1986)
	Gallic acid		Chemical and spectral characterization	(Skopp and Schwenker, 1986)
	Masticadienoic acid		N.D.	(Lloyd, et al., 1977)
	Ursolic acid		N.D.	(Lloyd, et al., 1977)
	Cardanol		N.D.	(Stahl, et al., 1983)
	Agathisflavone		UV, MS and NMR	(Kassem, et al., 2004)

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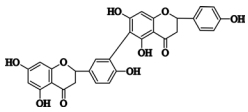
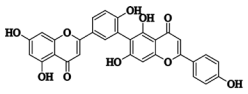
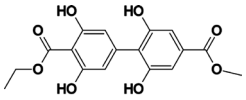
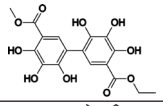
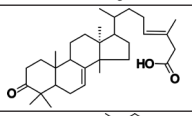
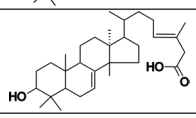
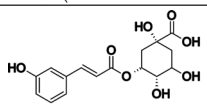
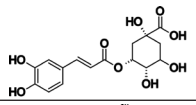
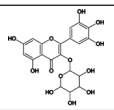
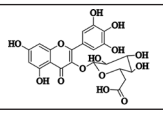
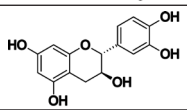
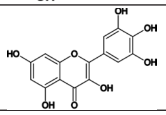
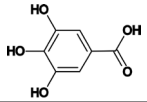
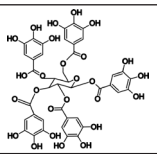
TABLE 1. Chemical compounds identified in *Schinus terebinthifolius.* *continuação...*

Part used	Compound	Chemical structures	Method	References
	Tetrahydrorobustaflavone		UV, MS and NMR	(Kassem, et al., 2004)
	Robustaflavone		UV, MS and NMR	(Kassem, et al., 2004) (Kassem, et al., 2004)
	4´-Ethyl-4-methyl-2,3´,5´,6-tetrahydroxy[1,1´-biphenyl]-4,4´-dicarboxylate		UV, MS and NMR	(Kassem, et al., 2004)
	3-Ethyl-3´-methyl-4,4´,5,5´,6,6´-hexahydroxy[1,1´-biphenyl]-3,3´-dicarboxylate		UV, MS and NMR	(Jain, et al., 1995)
	Masticadienoic acid		Physical methods and X-ray crystallography	(Jain, et al., 1995)
	3β-masticadienolic acid (schinol)		Physical methods and X-ray crystallography	(Farag, 2008)
Leaves	5-O-coumaroylquinic acid		HPLC	(Farag, 2008)
	5-O-caffeoylquinic acid (chlorogenic acid)		HPLC	(Farag, 2008)
	Myricetin 3-O-β-D-galactopyranoside		HPLC	(Farag, 2008)
	Myricetin 3-O-b-D-glucuronide		HPLC	(Farag, 2008)
	(+) Catechin		HPLC	(Ceruks, et al., 2007)
	Myricetin		NMR	(Cavalher-Machado, et al., 2008)
	Gallic acid		HPLC	(Cavalher-Machado, et al., 2008)
	Methyl gallate		HPLC	(Ceruks, et al., 2007)
			NMR	(Cavalher-Machado, et al., 2008)
	1,2,3,4,6-pentagalloylglucose		HPLC	

continua...

TABLE 1. Chemical compounds identified in *Schinus terebinthifolius.* *continuação...*

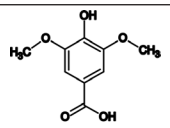
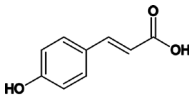
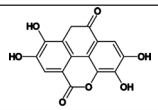
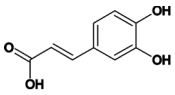
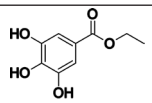
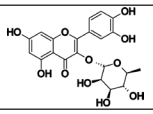
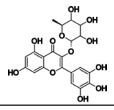
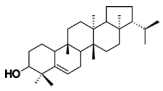
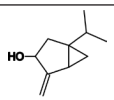
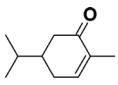
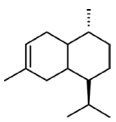
Part used	Compound	Chemical structures	Method	References
	Syringic acid		HPLC	(El-Massry, et al., 2009)
	Coumaric acid		HPLC	(El-Massry, et al., 2009)
	Ellagic acid		HPLC	(El-Massry, et al., 2009)
	Caffeic acid		HPLC	(El-Massry, et al., 2009)
	Ethyl gallate		NMR	(Ceruks, et al., 2007)
	Quercitrin		NMR	(Ceruks, et al., 2007)
	Myricetrin		NMR	(Ceruks, et al., 2007)
Essential Oil	Simiarenol		N.D.	(Lloyd, et al., 1977)
	β-cadinene		GC	(Jamal and Augusta, 2001)
	α-cadinene		GC	(Jamal and Augusta, 2001)
	Biciclogermacren		CG	(Santos, et al., 2010)
	Cis-sabinol		N.D.	(Lloyd, et al., 1977)
	Carvotanacetone		N.D.	(Lloyd, et al., 1977)
	Germacren D		CG	(Barbosa, et al., 2007)*
	α-cubebene		GC	(Lloyd, et al., 1977) (Jamal and Augusta, 2001)*(El-Massry, et al., 2009)(Bendaoud, et al., 2010)*

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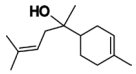
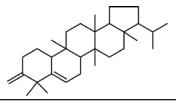
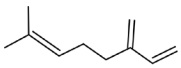
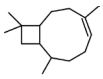
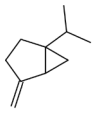
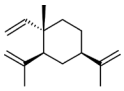
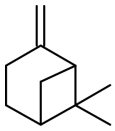
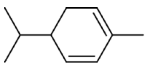
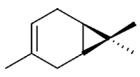
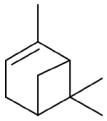
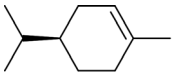
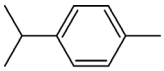
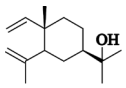
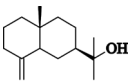
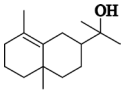
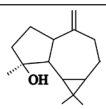
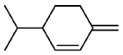
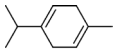
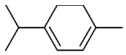
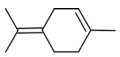
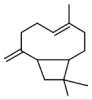
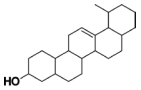
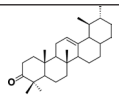
TABLE 1. Chemical compounds identified in *Schinus terebinthifolius.* *continuação...*

Part used	Compound	Chemical structures	Method	References
	α-bisabolol		GC	(Barbosa, et al., 2007)*
	Simiarenone		N.D.	(Lloyd, et al., 1977)
	Myrceno		N.D.	(Barbosa, et al., 2007)*
	Isocaryophyllene		GC	(Jamal and Augusta, 2001)*
	Sabinene		GC	(Barbosa, et al., 2007, Bendaoud, et al., 2010, Malik, et al., 1994, Pieribatestti, et al., 1981, Santos, et al., 2010)
	β-elemene		GC	(Barbosa, et al., 2007, El-Massry, et al., 2009, Jamal and Augusta, 2001)
	β-pinene		GC	(Barbosa, et al., 2007, Bauer and Brasil, 1973, Bendaoud, et al., 2010, Jamal and Augusta, 2001, Lloyd, et al., 1977, Malik, et al., 1994, Pieribatestti, et al., 1981)
	α-phellandrene		GC	(Barbosa, et al., 2007, Jamal and Augusta, 2001, Lloyd, et al., 1977, Malik, et al., 1994, Pieribatestti, et al., 1981)
	Δ-3-carene		GC	(Barbosa, et al., 2007, Jamal and Augusta, 2001, Lloyd, et al., 1977, Malik, et al., 1994, Pieribatestti, et al., 1981, Stahl, et al., 1983, Vernin and Parkanyi, 2003)
	α-pinene		GC	(Barbosa, et al., 2007, Bauer and Brasil, 1973, Lloyd, et al., 1977, Malik, et al., 1994, Pieribatestti, et al., 1981, Santos, et al., 2010, Vernin and Parkanyi, 2003)

continua...

TABLE 1. Chemical compounds identified in *Schinus terebinthifolius.* *continuação...*

Part used	Compound	Chemical structures	Method	References
	Limonene		GC	(Jamal and Augusta, 2001, Lloyd, et al., 1977, Pieribatestti, et al., 1981, Vernin and Parkanyi, 2003)
	p-cymene		GC	(Barbosa, et al., 2007, Bendaoud, et al., 2010, Jamal and Augusta, 2001, Lloyd, et al., 1977, Pieribatestti, et al., 1981, Vernin and Parkanyi, 2003)
	Elemol		GC	(Barbosa, et al., 2007, Vernin and Parkanyi, 2003)
	β-eudesmol		GC	(Vernin and Parkanyi, 2003)
	α-cadinol		GC	(Vernin and Parkanyi, 2003)
	Y-eudesmol		GC	(Vernin and Parkanyi, 2003)
	Spathulenol		GC	(El-Massry, et al., 2009, Jamal and Augusta, 2001, Vernin and Parkanyi, 2003)
	β-phellandrene		GC	(Barbosa, et al., 2007, Lloyd, et al., 1977, Pieribatestti, et al., 1981)
	Camphene		GC	(Pieribatestti, et al., 1981)
	Y-terpinene		GC	(Pieribatestti, et al., 1981)
	α-terpinene		GC	(Pieribatestti, et al., 1981)
	Terpinolene		GC	(Lloyd, et al., 1977, Malik, et al., 1994)
	β-caryophyllene		GC	(Lloyd, et al., 1977)
	α-amyrin		N.D.	(Lloyd, et al., 1977)
	α-amyrenone		GC	(Lloyd, et al., 1977)

*coupled to Mass spectroscopy; NMR= Nuclear Magnetic Resonance; IR= Infrared; UV=Ultraviolet; N.D.= not detailed; HPLC= High Performance Liquid Chromatography; GC= Gas Chromatography.

and quantification of its chemical compounds. The vast majority of publications are restricted to the identification of compounds found in the essential oils, which are listed in Table 1. Thus, the identification of new entities that correlate with the biological properties of these species is certainly a niche that needs to be explored.

Triterpenes, phenolic lipids and biflavonoids are the most frequent substances present in the family Anacardiaceae. However, the literature reports the presence of other classes of substances, such as phenols and cinnamic acid derivatives (Correia et al., 2006). Phytochemical studies of the genus *Schinus* revealed the presence of terpenoids and fatty acids in *S. terebinthifolius* and *S. molle,* which are the main species of this genus (Lloyd et al., 1977, Terhune et al., 1974).

According to Lima et al. (2006), the chemical analysis of the ethanolic extract from the bark of *S. terebinthifolius* revealed the presence of phenols, triterpenes and anthraquinones. Positive tests for flavones, xanthones, flavonoids, free steroids, anthraquinones and triterpenes were observed when the extracts were prepared in hexane. On the other hand, ethanolic extracts from the leaves showed positive results for phenols, flavones, flavonoids, xanthones, leucoanthocyanidins, flavanones and free steroids (Lima et al., 2006).

In their studies, Jorge and Markmann (1996) demonstrated that the leaves and barks of *S. terebinthifolius* are equally rich in tannins and essential oils. Saponins, however, are restricted to the bark, where it also showed positive reactions for flavonoids, which generally have anti-inflammatory properties and might enhance the healing effect provided by the tannins.

The phytochemical study of the ethyl acetate phase coming from the ethanolic extract from leaves of *S. terebinthifolius* allowed the isolation and identification of five active compounds: ethyl gallate, myricetrin, quercitrin, methyl gallate and myricetin. Studies have suggested that these substances are responsible for the anti-free radical property observed in extracts of *S. terebinthifolius* (Ceruks et al., 2007).

Tannins are among the major compounds of *S. terebinthifolius* bark. Several biological activities such as anti-inflammatory, antibacterial, antifungal and anticancer are attributed to tannins (Matos, 1994). Basically, the biological activities of tannins are due to three properties: complexation with metal ions, antioxidant effect and ability to complex with macromolecules such as proteins and polysaccharides (Scalbert, 1991).

The search for antimicrobial substances in plants has been the subject of many studies since the discovery of penicillin. Alkaloids, flavonoids, isoflavonoids, tannins, coumarins, glucosides, terpenes, polyacethylenes and essential oils are originated from various metabolic routes. These substances are important in the defense mechanisms of the plant against fungi, bacteria, virus, parasites, insects, mollusks and superior animals (Calixto et al., 2001).

The essential oils from *S. terebinthifolius* contain α-and β-pinene, Δ^3-carene, limonene, α- and β-phellandrene, *p*-cymene and terpinolene as the main compounds, in addition to minor amounts of mono- and triterpene alcohols, sesquiterpene hydrocarbons and ketones. Bark and leaf extracts have shown to contain triterpenes and triterpene acids, respectively (Lima et al., 2006). The major constituents in the essential oils extracted from the fruits of *S. terebinthifolius* collected in Dourados – MS, Brazil were: α-pinene (22.56%), sabinene (15.78%), Z-salvene (10.69%), β-pinene (10.52%), α-funebrene (8.82%) and limonene (5.52%) (Table 1) (Roveda et al., 2010).

Toxicity

It has been reported that when people inhale for a long time the aromatic balsam that exudes from the trunk of *S. terebinthifolius*, eruptions resembling those of measles or scarlet fever appear on the skin. On the other hand, this sap seems to be vesicant when applied to people suffering from rheumatic pain. In addition, frequent contacts with wood-cutters produce lesions resembling second-degree burns, severe itching and exudation of a yellowish fluid. Ingestion of unripe or ripe fruits by children can cause reactions like vomiting, rash and swelling of the hands, arms and face (Morton, 1978).

A toxicological research through the somatic segregation assay was carried out in aqueous or alcoholic extracts of *S. terebinthifolius* used in folk medicine in Cuba. The study demonstrated that alcoholic extracts from *S. terebinthifolius* did not present any genotoxic effect on *Aspergillus nidulans*. Although it is necessary to confirm the results through well validated tests performed in mammalian cells, it probably indicates the absence of potential risks in inducing cancer and other genetic disorders in individuals under treatment with this plant (Ruiz et al., 1996). *Evaluating the* genotoxic potential of *S. terebinthifolius extract in an in vitro assay, Carvalho et al. (2009) observed that although the extract did not cause a direct break in the DNA structure, it showed potential to cause oxidative damage to DNA, as well as bacterial mutation.*

In addition, Varela-Barca et al. (2007) showed that flavonoid-enriched fractions of *S. terebinthifolius* stem barks were capable of breaking phosphodiester bonds in DNA, generating lesions that could potentially lead to mutations. Chromatographic

and spectral analysis helped support the hypothesis that flavonoids are the compounds involved in the oxidative damage.

Amorim and Santos (2003) showed that a gel of *S. terebinthifolius* can be used for the treatment of bacterial vaginosis in non-pregnant women, showing an 84% cure rate. However, the presence of alkyl phenols in preparations based on aroeira materials can cause allergic reactions on the skin and mucous membranes, which seems to indicate that the use of these products requires caution (Lorenzi and Matos, 2008).

On the other hand, results obtained by Lima et al. (2009) showed that the oral administration of dried extracts from *S. terebinthifolius* barks during 45 days in Wistar rats of both genders did not induce any toxic effect. No significant changes were observed in biochemical and hematological index, as well as in anatomic and histopathological characteristics of the animals. Therefore, the absence of acute and subacute toxicity of the plant extracts corroborates its safety.

Frequently used in culinary, the fruit of *S. terebinthifolius* has proven to be innocuous. The LD_{50}, calculated after oral and intra-peritoneal administration to mice, was estimated to be 5.0 $g.Kg^{-1}$ and 3.5 $g.Kg^{-1}$, respectively, which suggests that *S. terebinthifolius* fruits do not offer any risk for human use (Pires et al., 2004).

FINAL CONSIDERATIONS

Since its widespread popular use as a medicinal plant, *S. terebinthifolius* has shown great potential for the development of new herbal products. Although many studies have evaluated the biological properties of this plant, little has been done to identify and characterize its chemical constituents, which is certainly a niche that needs to be further explored.

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