The Natural Products Journal, 2017, 7, 1-7

REVIEW ARTICLE

Phytochemistry, Traditional Uses and Bioactivity of the Medicinal Plant *Schinus areira* L. (Anacardiaceae): A Review

Ana Paula Murray[a,*] and María Gabriela Murray[b]

[a]*INQUISUR-CONICET, Departamento de Química, Universidad Nacional del Sur, Av. Alem 1253, (B8000CPB) Bahía Blanca, Argentina;* [b]*INBIOSUR-CONICET, Departamento de Biología Bioquímica y Farmacia, Universidad Nacional del Sur, Bahía Blanca, Argentina*

ARTICLE HISTORY

Received: September 13, 2016
Revised: January 03, 2017
Accepted: January 16, 2017

DOI:
10.2174/2210315507666170117145728

Abstract: *Schinus areira* L. (syn. *Schinus molle* L. var. *areira* (L.) DC.) belongs to the Anacardiaceae family, native to South America, now widely distributed in temperate zones of the World, known as "aguaribay", "árbol de la pimienta", "pepper tree", "terebinto" or "pimientero". It is considered a medicinal plant in the folk medicine and it is also appreciated by its culinary properties. Its fruits are used as a spice and to prepare a popular drink named "chicha". These popular uses have stimulated a number of biological and chemical studies. This communication offers a general view of the structural characteristics of the secondary metabolites isolated from *S. areira* L., as well as their ethnomedicinal uses, biological activities and toxicological considerations.

Keywords: *Schinus*, Anacardiaceae, biological activity, secondary metabolites, traditional uses.

1. INTRODUCTION

The Twenty-nine species from the *Schinus* genus (Anacardiaceae) are distributed from Mexico to Argentina, extending from Central to South America [1-3]. In Argentine this genus is represented by 22 species, six of them endemic, which are distributed in the provinces of Corrientes, Entre Ríos, Santa Fe, Córdoba, La Pampa, Jujuy, San Juan, San Luis, Mendoza, Tucumán, Río Negro and Chubut [4-7].

Many plants belonging to this genus are known as traditional medicines for the treatment of several and diverse pathologies including rheumatism, bronchial infections, high blood pressure, ulcers, dyspepsia, menstrual disorders, gonorrhea, bronchitis, conjunctivitis, dysentery, wounds, urinary affections, gingivitis and eye infections [8]. These biological activities have encouraged many researchers to study the chemical composition and the pharmacological activities of these plants, leading to the publication of several papers reporting the isolation and identification of bioactive secondary metabolites including monoterpenes, sesquiterpenes, triterpenes, sterols, fatty acids, triterpenoids acids and flavonoids [9].

The aim of this work is to review the biological and pharmacological activities, medicinal uses and phytochemical knowledge of *Schinus areira* L. (syn. *Schinus molle* L. var. *areira* (L.) DC.). *S. areira* is commonly known as "aguaribay", "árbol de la pimienta", "pepper tree", "terebinto" or "pimientero". Native to Perú, Bolivia, Chile, Paraguay and Northern Argentina [8, 10] but now growing established in most temperate regions of the world having been distributed very early by the Spanish colonist [1, 2]. In the northwest of Argentina it is widely cultivated for the abundant production of coral-red odorific fruits which contain essential oils and piperine, and are used as condiment, to prepare a popular infusion named "aloja" or "chicha" and to obtain syrup known as "arrope" [11, 12]. Leaves, fruits, stems and bark, dried or fresh, are used to prepare infusions, ointments, cataplasms, beverages, or eye drops, which are used as purgative, diuretic, vulnerary, topic disinfectant and for the treatment of rheumatism, stomach upset, menstrual disorders, gonorrhea, bronchitis and conjunctivitis [13, 14].

Traditionally, the leaves are used as insect repellent and for its dyeing properties and the bark exudate is used as expectorant. The resin was used by the Incas for embalming corpses. Nowadays, *S. areira* is planted in rural and urban areas to provide shadow and wind protection. Its wood is used for rural buildings and for coal and regular quality firewood [8].

2. BOTANICAL DESCRIPTION AND TAXONOMIC CONSIDERATIONS

S. areira is a resin tree up to 15-20 metres high with evergreen glabrous leaves made up of 14-35 leaflets, sessiles lanceolate-linear, acute, obtusish at base, entire or less often irregularly serrulate (Fig. **1**). Axillar or terminals pendulous panicles, multiflora. Flowers are small yellowish-green, and the fruit is lilac, then dun drupe, 5-6 mm in diameter (Fig. **1**) [15].

*Address correspondence to this author at the INQUISUR-CONICET, Departamento de Química, Universidad Nacional del Sur, Av. Alem 1253, (B8000CPB) Bahía Blanca, Argentina; Tel/Fax: ++54-291-459-5187; E-mail: apmurray@uns.edu.ar

2210-3155/17 $58.00+.00

Fig. (1). *Schinus areira* L.

The genus *Schinus* presents two closely related species: *Schinus molle* L. and *Schinus areira* L. Morphologically, these species are distinguished by the number of leaflets, 5 to 31 for *S. molle*, usually opposite, lanceolate, irregularly serrate, acuminate; and 14 to 35 for *S. areira*, usually alternate, linear-lanceolate, somewhat falcate and apiculate, whole or irregularly serrate [15]. However, many authors refer to them as *Schinus molle*. Barkley [1], as well as Zuloaga [3], have pointed that the species distributed throughout the American continent and cultivated as ornamental in warm temperate regions around the World, is indeed *S. areira*, while *S. molle* has a much more limited distribution, growing wild in northeast of Argentina, Uruguay, Paraguay and south of Brazil. Anyway, since this review is focused on *S. areira*, we are including here only the references where the plants were undoubtedly classified as *S. areira*. Phytochemistry and bioactivity of *S. molle* have been reviewed elsewhere [9, 16-23].

3. PHYTOCHEMISTRY

The chemical composition of the essential oil obtained from the aerial parts of *S. areira* by hydrodistillation was determined by gas chromatography-mass spectrometry (GC-MS), for specimens collected at Bahía Blanca (Buenos Aires province, Argentina). Twenty one compounds were identified, the major ones being limonene (**1**) (28.61%), α-phellandrene (**2**) (10.11%), sabinene (**3**) (9.20%) and camphene (**4**) (9.16%) (Fig. **2**) [24]. Then, the essential oils of fruits and leaves of *S. areira* were analyzed separately. In the leaves oil forty-one compounds were determined. The main constituents were β-phellandrene (**5**) (17.57%) and α-phellandrene (**2**) (16.18%) (Fig. **2**) [25]. On the other hand, the essential oil obtained from the fruits was rich in α-phellandrene (**2**) (31.83%), β-phellandrene, (**5**) (19.95%) and β-myrcene (**6**) (19.32%) with a total of eighteen compounds identified (Fig. **2**) [25]. Similar results were obtained by Sánchez Chopa and Descamps [26], for specimens collected in the same area (Bahía Blanca city) and for essential oils obtained by hydrodistillation of leaves and fruits separately. They found that leaves were rich in α-phellandrene (**2**) (28.5%), 3-carene (**7**) (20.77%) and camphene (**4**) (10.92%), while fruits were rich in α-phellandrene (**2**) (24.82%), 3-carene (**7**) (21.35%) and β-myrcene (**6**) (19.68%) [26]. These results differed from those reported for *S. areira* specimens collected at Córdoba province, central region of Argentina, where the major components of this oil were α-pinene (**8**) (13.80 %), limonene (**1**) (12.81 %), camphene (**4**) (12.62 %) and β-caryophyllene (**9**) (11.88%) (Fig. **2**) [27]. For specimens collected at Mendoza province, west of Argentina, the composition was characterized by higher percentages of limonene (**1**) (45.95%) and α-phellandrene (**2**) (25.44%) [28].

Sabinene (**3**) (26 %), bicyclogermacrene (**10**) (14.5 %) and *E*-citral (**11**) (6.7 %) were identified as the major components in the essential oil obtained from leaves of *S. aerira* collected at Tucuman province, northwest of Argentina [29] (Fig. **2**). The essential oil obtained from fruits of *S. areira,* collected at the same location, was rich in limonene (**1**) (27.7 %), sabinene (**3**) (16.0 %) and β-phellandrene (**5**) (14.6 %) (Fig. **2**).

Leaves of *S. areira* collected in the Cuzco region, Peru (3200 m height above sea level) rendered an essential oil rich in α-phellandrene (**2**) (18.2 %), limonene (**1**) (9.4 %) and camphene (**4**) (8.4 %) [30].

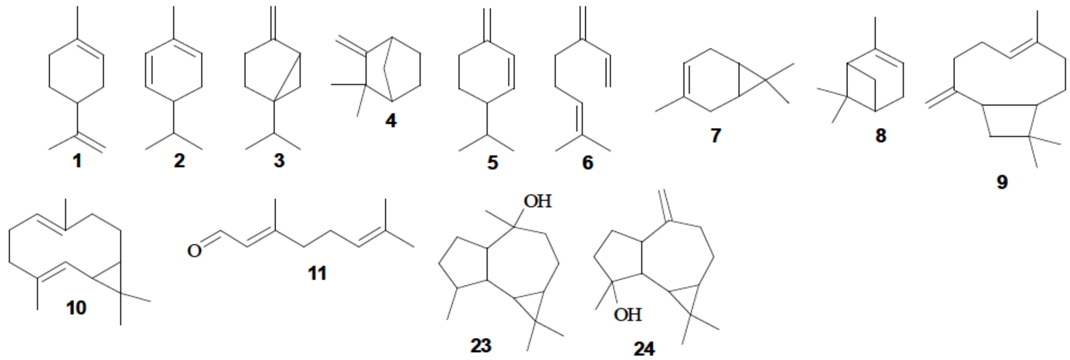


Fig. (2). Terpenes detected in *S. areira* essential oils.

The variability observed in the chemical composition of these oils can be attributed to the geographical origin (different environmental conditions). An intraspecific difference in volatile components is commonly observed in the essential oils of specimen collected from different locations.

The flavonoids quercetin-3-*O*-rhamnoside (**12**), quercetin-3-*O*-glucoside (**13**) and rutin (**14**) were detected in the leaves while the pigments cyaniding-3-*O*-galactoside (**15**), cyanidin 3-*O*-rutinoside (**16**) and peonidin 3-*O*-glucoside (**17**) were isolated from the fruits of *S. areira* (Fig. **3**) [31, 32].

Recently, Celaya *et al.* reported the presence of quercetin-3-*O*-galactoside (**18**), quercetin-3-*O*-glucoside (**13**), quercetin-3-*O*-arabinoside (**19**), quercetin-3-*O*-rhamnoside (**12**), kaempferol-3-*O*-rutinoside (**20**), 3-*O*-caffeoylquinic acid (**21**) and 5-*O*-caffeoylquinic acid (**22**) in samples of *S. areira* leaves, collected from three different locations in Jujuy province, Argentina [33]. Flavonols and hydroxycinammic acid derivatives were identified by HPLC in aqueous ethanol (70:30) extracts obtained by ultrasound assisted extraction.

4. PHARMACOLOGICAL AND BIOLOGICAL ACTIVITIES

4.1. Antioxidant Activity

The essential oils from leaves and fruits of *S. areira* were studied for their *in vitro* antioxidant activity, evaluated through its ability as free radical scavenger against the stable 2,2-diphenyl-1-picrylhydrazyl radical (DPPH). The essential oil from the leaves (IC_{50} = 38.7 ± 2.5 µg/ml, IC_{50} is the sample concentration that decreases the initial DPPH absorbance by 50%) elicited a higher activity than that from the fruits of *S. areira* (IC_{50} = 59.6 ± 3.1 µg/ml) although both oils were less effective than the reference compound butylhydroxytoluene (BHT) (IC_{50} = 17.6 ± 1.8 µg/ml [25]. A weaker antioxidant activity was observed for the essential oil obtained from leaves of *S. areira* from Peru, in the DPPH assay with IC_{50} value of 174.6 ± 12.3 µg/ml [30].

The antioxidant activity of these oils could be explained by the presence of some monoterpenes with conjugated double bonds [34], such as α-phellandrene (**2**), β-phellandrene (**5**) and β-myrcene (**6**). Also, it can be attributed to some very active minor components like sesquiterpenes bearing a *gem*-dimethylcyclopropane ring [35], such as bicyclogermacrene (**10**), globulol (**23**) and spathulenol (**24**) (Fig. **2**) [25].

The aqueous ethanol extract obtained from *S.areira* leaves also showed high antioxidant activity in the DPPH assay with an EC_{50} value of 23.3 ± 1.1 µg/ml, close to the activity of the well-known antioxidant Trolox (EC_{50} value of 36.1 ± 0.3 µg/ml). Celaya *et al.* also determined that *S. areira* leaves exhibited a free radical scavenging effect on superoxide (O2•-) and nitric oxide (NO•) radicals [33]. This antioxidant response can be attributed to the content of phenolic compounds in those samples [33].

4.2. Anticholinesterase Activity

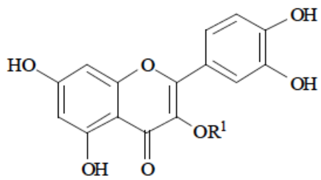
S. areira essential oils were evaluated for their *in vitro* antiacetylcholinesterase activity, taking into account that acetylcholinesterase (AChE) is an enzyme that is considered relevant in the treatment of Alzheimer's disease. The essential oil from leaves of *S. areira* was found to be more active (IC_{50} = 0.23 mg/ml, IC_{50} is the sample concentration necessary to inhibit the enzymatic activity by 50%) than the essential oil obtained from the fruits of this species (IC_{50} = 0.48 mg/ml). Both oils were found to be weak inhibitors compared with eserine, a known potent AChE inhibitor (98 % of AChE inhibition at 0.1 mg/ml) [25].

This AChE inhibition could also explain the insecticidal properties observed for these oils against several insect pests [26, 36-39].

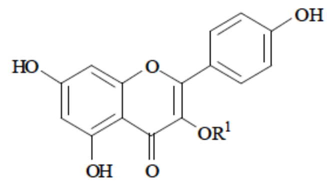
4.3. Insecticidal Activity

The use of essential oils for insect pest management has led to the development of green-pesticides as an alternative to synthetic insecticides [40, 41]. Many essential oils have shown insecticidal, fumigant, antifeedant, attractive and repellent activities against a broad spectrum of insects. *S. areira* oils are a good example of this kind of oils [26, 36-39].

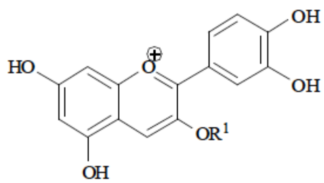
The essential oil from fruits of *S. areira* showed repellency to *Blattella germanica* (Blattodea: Blattellidae) in a choice-test arena. The response of the cockroaches to this oil differed significantly from *N*,*N*-diethyl-*m*-toluamide (DEET) at all doses tested [36]. Repellency and mortality were also observed on *B. germanica* adults treated with ethanol and petroleum ether extracts from fruits and leaves of *S. areira* [37]. All the extracts resulted to be repellent at all the



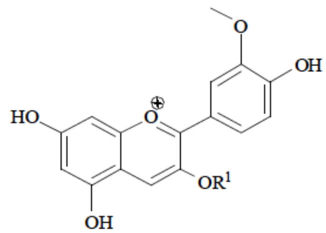
12 R^1 = α-L-rhamnopyranosyl
13 R^1 =β-D-glucopyranosyl
14 R^1 =α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranosyl
18 R^1 = β-D-galactopyranosyl
19 R^1 = α-L-arabinopyranosyl



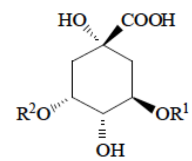
20 R^1 =α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranosyl



15 R^1 = β-D-galactopyranosyl
16 R^1 =α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranosyl



17 R^1 =β-D-glucopyranosyl



21 R^1 = caffeoyl ; R^2 = H
22 R^1 = H ; R^2 = caffeoyl

Fig. (3). Phenolic compounds present in *S. areira*

concentrations assayed and produced mortality significantly higher than the positive control.

The essential oil from leaves and fruits of *S. areira* were also evaluated for their repellent, toxicity and feeding deterrent properties against larvae and adults of *Tribolium castaneum* (Coleoptera: Tenebrionidae), a pest of stored and processed cereal products worldwide [38]. The leaf essential oil showed repellent effects (treated diet assay) whereas fruit essential oil was attractant. Both oils produced mortality against larvae in topical and fumigant bioassays (filter paper impregnation assay). Some alterations in nutritional physiology of the pest were observed for both oils. The methanolic extract obtained from the leaves of *S. areira* showed weak insecticidal activity against adults of *T. castaneum* when the beetles were exposed to plant extract by topical application and grain treatment [39]. In the same study, the aqueous extract resulted to be inactive.

The essential oils from *S. areira* have been analyzed in their toxicity against alates and apterous adults and sublethal effects against nymphs and adults of *Metopolophium dirhodum* (Hemiptera: Aphididae), an aphid pest commonly known as rose-grain aphid [26]. Both essential oils acted as rapid contact poisons, with more adult aphids succumbing after 1 h in the toxicity by immersion assay. In the contact toxicity assay at 24 h, the essential oil from leaves of *S. areira* was the most toxic to alate aphids, followed by oil from fruits. After 48 h exposure, no significant differences between both essential oils were observed. The oils reduced the number of offspring in a similar way in alates and apterous aphids. Compared to the control, a significant decrease in offspring number was found for both essential oils tested after 2 days of exposure and with essential oil of *S. areira* leaves no live aphids were found at days 6 and 7. Also, first-instar nymphs of *M. dirhodum* were transferred to wheat leaves treated with LC_{20} of *S.areira* oils (LC_{20} is the concentration causing 20% of mortality). All nymphs died on treated leaves with essential oil from leaves of *S. areira* [26].

In contact toxicity bioassays, the essential oils from leaves of *S. areira* showed high effect against adults of *Rhizopertha dominica* (Coleoptera: Bostrichidae), a lesser grain borer, with LD_{50} values of 0.88 mg/cm^2 [42] (LC_{50} is the concentration causing 50% of mortality). In other work from the same group, the essential oil from leaves of *S. areira* showed repellent effects on the rice weevil *Sitophilus oryzae* (Coleoptera: Curculionidae), another pest of stored grain [43]. The essential oil from fruits showed a strong feeding deterrent action. Both oils altered nutritional indices.

The essential oils from leaves and fruits of *S. areira* also exhibited moderate and high fumigant and contact toxicity on nymphs II of *Nezara viridula* (Hemiptera: Pentatomidae), a soybean pest [44]. Later, the same group reported the repellent activity against *N. viridula* adults observed for the hexanic extracts as well as the essential oils obtained from fruits and leaves of *S. areira* [45].

Recently, Gutierrez *et al.* evaluated the contact and fumigant activity of the essential oils of the leaves and fruits of *S. areira* in adults and eggs of the human head louse, *Pediculus humanus capitis* (Anoplura: Pediculidae) [46]. Both oils produced similar toxicity by fumigant activity in adults of *P. humanus capitis* with median knockdown time (KT_{50}) values of 10.8 (fruit) and 12.75 min (leaf) and no differences were found between them. After 24 h of exposure both oils were effective against medium development eggs with potent ovicidal activity (percentage of inhibition of hatch of 100 %) in the fumigant assay [46].

Leaf and fruit extracts obtained with hexane from *S. areira* produced repellent effect on first instar nymphs of *Triatoma infestans* (Hemiptera: Reduviidae), the vector of Chagas disease. Both extracts showed a higher effect than the control treatment. Ovicidal activity was observed using fruit extract and *T. infestans* eggs [47]. The hexane extract from *S. areira* fruits also showed insecticide and repellent activities on neonate larvae of *Cydia pomonella* (Lepidoptera: Tortricidae), the worm of the apple tree, together with pupae and adults malformations [48].

4.4. Allelopathic Effects

The bioassay of *S. areira* oil revealed strong inhibition of the root growth of *Zea mays* L. seedlings, showing no development of the root from 24 to 96 h of treatment. An increase in malondialdehyde values from 24 to 48 h was also observed, suggesting that lipid peroxidation was occurring [49]. This activity was attributed in part, to the high level of α-pinene in this oil (85.3 %).

4.5. Antimicrobial Activity

The antimicrobial activity of essential oils extracted from leaves and fruits of *S. areira* was investigated by Celaya *et al.* for specimens collected in Jujuy (Argentina) from over ten-year-old trees [50]. The antibacterial activity against the human pathogenic bacteria *Staphylococcus aureus* susceptible as well as methicillin resistant strain was assessed. The results showed that the limonene-rich oil extracted from the leaves and fruits have potent antibacterial effect on *S. aureus* ATCC 25923, while the α-phellandrene-rich fruit oil having a lower content of limonene showed the lowest antibacterial efficacy [50].

4.6. Anti-Inflammatory Activity

The activity of aqueous extracts obtained from the leaves and branches of *S. areira* on inflammation and the effect on superoxide anion production in mice macrophages were assayed by Davicino *et al*. [51]. Aqueous extracts were prepared by soaking herbs in cold water (cold extract), boiling water (infusion), and simmering water (decoction). Authors observed that cold extract exhibited an anti-inflammatory activity in carrageenan-induced inflammation and ear edema assays in mice, although it was not as active as indomethacin. Also, this extract significantly decreased the tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) levels in serum and in the supernatant of macrophages. On the other hand, decoction and infusion showed pro-inflammatory activity suggesting that the temperature of extraction affects the chemical composition of those extracts which, in turn, alters the bioactivity of them. Cold extract increased the production of superoxide anion in peritoneal macrophages. All the extracts did not significantly affect the macrophage viability after 24 h of incubation [51].

4.7. Toxicity Assessment

Due to the wide range of biological activities reported for *S. areira*, several attempts have been made to evaluate the safety/toxicity of this plant, concerning its essential oils as well as the organic and aqueous extracts that have been studied. That includes preliminary assays with invertebrates and more complete studies with rats and rabbits.

The essential oil of *S. areira* leaves exhibited biotoxicity in a brine shrimp assay with *Artemia persimilis*. After 48 h of exposure, 100% of mortality was observed for *S. areira* at 100 μg/ml [24].

To evaluate toxicity of ethanolic extracts from fruits of *S. areira* in rats, the plant extract was added to the diet at 2 g/kg body weight/day during 1 day (acute toxicity) and at 1 g/kg body weight/day during 14 days (subacute toxicity). Behavioral and functional parameters were assessed 7 days after the end of the exposure. Finally, histopathological examinations were conducted on several organs. An increase in the arousal level was observed in both exposures. Also, the landing foot splay parameter increased in the experimental group after acute exposure. Only the subacute exposure produced a significant increase in the motor activity in the open field. All these changes disappeared after 7 days. None of the exposures affected the different organs evaluated. The authors suggest that ethanolic extracts from *S. areira* should be relatively safe to use as insecticide [52].

In order to study the safety of *S. areira* extracts the effects of subchronic exposure to ethanolic extracts from leaves and fruits in mice were evaluated [53]. Plant extracts were added to the diet at 1g/kg body weight/day for 90 days. At the end of the exposure, behavioral and functional parameters in a functional observational battery and motor activity in an open field were assessed. Also, several biochemical and histopathological studies were realized. The exposure to extract from leaves produced an increase in the number of rearings in the open field and of urine pools in the functional observational battery. On the other hand, the exposure to extract from fruits produced an increase in the neutrophil count and a decrease in the lymphocyte count and in the total cholesterol levels. None of the exposures affected the different organs evaluated. This study suggests that subchronic exposure to ethanolic extracts from leaves and fruits of *S.areira* should be potentially useful in the treatment of lipid pathologies and safe to use [53].

Taking into account that *S. areira* is known for its topical use as wound healer, antiseptic, for skin disorders and as repellent and insecticide, the acute dermal exposure to ethanolic and hexanic extracts from leaves of *S. areira* was studied in rats [54]. A single dose of 2 g/kg of body weight of these extracts was applied on the shaved skin of male and female rats. After 24 h of exposure, the patch was removed and any sign of irritation was recorded. Slight signs of erythema and edema were observed, but they disappeared after 48 h. The exposure to the hexanic extract produced an increase in activity parameters, rearing and arousal assessed in the functional observational battery, which reversed after 14 days. The ethanolic extract caused an increase in locomotor activity, reflected in a higher number of rearings performed in the open field in the evaluation carried out on Day 14. No histopathological alterations were detected in the analyzed organs.

Taking into account that the *S. areira* oils could be used as a pediculicide product [46], Gutiérrez *et al*. considered important to evaluate the potential adverse effects that these might cause on the human skin. For that, they choose an animal model using New Zealand albino rabbits, performing dermal corrosion/irritation tests. That study demonstrated that none of the EOs tested (fruits and leaves) caused irritating or corrosive effects on rabbit skin although the applied doses were larger than those that could be used in pediculicide products [46].

Bigliani *et al*. studied the effects of *S. areira* essential oils obtained from leaves and flowers, on hemodynamic functions in rabbits, as well as myocardial contractile strength and airways inflammation associated to bacterial endotoxin lipopolysaccharide (LPS) in mice [27]. This study showed the important properties of this oil on lung with significant inhibition associated to LPS, which was assessed in mice bronchoalveolar lavage fluid and evidenced by stability of the percentage of alveolar macrophages, infiltration of polymorphonuclear leukocytes and tumor necrosis factor-α concentration, and without pathway modifications in conjugated dienes activity. Morbidity or mortality, macroscopic morphology and lung/body weight index were unaffected by the administration of the *S. areira* oil. The *ex vivo* analysis of isolated hearts demonstrated the negative inotropic action of the oil in a mice model. In rabbits the oil changed in the hemodynamic parameters, such as a reduction of systolic blood pressure [27].

CONCLUSION

The genus *Schinus* is widespread all over America, Europe and Africa, and many species of this genus have been used as traditional herbal medicines. *S. areira* in particular is popularly used for culinary purposes and as a medicinal plant. The toxicological studies conducted so far in animal models, indicate that the use of the extracts of this plant maybe safe. Similar results were observed for the topical use of the essential oils. Nevertheless, further studies are needed in order to establish the safety of the essential oils and extracts for humans. So far, the phytochemical studies of *S. areira* are scarce. Many volatile secondary metabolites such as mono- and sesquiterpenes, and some flavonoids and phenolic compounds have been reported for this species. Taking into account that *S. areira* has shown interesting and diverse bioactivities, a more complete phytochemical study, including the different organs of the plant and diverse experimental conditions for the metabolites extraction, is desirable.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

The authors thank Universidad Nacional del Sur (grant number 24/Q071) for the financial support. A.P.M. and M.G.M are Research Members of the National Research Council of Argentina (CONICET).

REFERENCES

[1] Barkley, F.A. A study of *Schinus* L. *Lilloa*, **1957**, *28*, 1-110.

[2] Dimitri, M.J. *Enciclopedia Argentina de Agricultura y Jardinería,* ACME: Buenos Aires, Argentina, **1988**.

[3] Zuloaga, F.O.; Morrone, O.; Belgrano, M.J. *Catálogo de Plantas Vasculares del Cono Sur. Vol. II*, Missouri Botanical Garden Press: St. Louis, Missouri, USA, **2008**.

[4] Marino, G.D.; Pensiero, J.F. Catálogo de árboles y arbustos de la Provincia de Santa Fe. *Com. Mus. Prov. Cs. Nat. «Florentino Ameghino»*, **2006**, *12*, 1-28.

[5] Zuloaga, F.O.; Morrone, O. *Catálogo de las Plantas Vasculares de la República Argentina II. Monographs in Systematic Botany from the Missouri Botanical Garden. Vol. 74,* Missouri Botanical Garden Press: St. Louis, Missouri, USA. **1999**.

[6] Steibel, P.E.; Troiani, H.O.; Williamson, T. Agregados al catálogo de las plantas naturalizadas y adventicias de la provincia de La Pampa, Argentina. *Rev. Fac. Agronom-UNLPam,* **2000**, *11*, 75-90.

[7] Martínez Carretero, E. Anacardiaceae. *Multequina 18*, **2009**. http://www.redalyc.org/articulo.oa?id=42812317010 Accessed 9.09.16

[8] Demaio, P.; Karlin, U.O.; Medina, M. *Árboles nativos del centro de Argentina*, Ed. L.O.L.A.: Buenos Aires, Argentina, **2002**.

[9] Murray, A.P.; Rodriguez, S.A.; Alza, N.P. Chemical Constituents and Biological Activities of Plants from the Genus *Schinus.* In *Recent Progress in Medicinal Plants*; J.N. Govil Ed.; Studium Press LLC: Houston, TX, USA, **2012**, Vol. 32, pp. 261-287.

[10] Hurrell, J.A.; Ulibarri, E.A.; Delucchi, G.; Pochettino, M.L. Plantas Aromáticas condimenticeas. In *Biota Rioplatense,* J.A. Hurrell Ed.; L.O.L.A.: Buenos Aires, Argentina; **2008**, Vol. XIII, pp. 168-169.

[11] Pochettino, M.L. Diferenciación de los frutos de "molles" de importancia etnobotánica en el noroeste argentino. *Notas del Mus. La Plata, Bot.,* **1988**, *21*, 158-167.

[12] Múlgura, M.E. Anacardiaceae. Anacardiáceas In *Flora de San Juan, República Argentina,* R. Kiesling Ed.; Estudio Sigma: Buenos Aires, Argentina, **2003**, Vol. II, pp. 86-90.

[13] Barboza, G.E.; Cantero, J.J.; Nuñez, C.O.; Ariza Espinar, L. *Flora Medicinal de la Provincia de Córdoba (Argentina). Pteridofitas y antofitas silvestres o naturalizadas,* Ed. Museo Botánico: Córdoba, Argentina, **2006**.

[14] Gupta, M.P. *270 Plantas Medicinales Iberoamericanas,* Ed. CYTED: Bogotá, Colombia, **1995**.

[15] Muñoz, J.D. Anacardiaceae. In *Flora Fanerogámica Argentina;* Hunziker, A.T. Ed. Buenos Aires, Argentina, **2000**, Part 65, pp.1-28.

[16] Mendonça Rocha, P.M.; Rodilla, J.M.; Díez, D.; Elder, H.; Guala, M.S.; Silva, L.A.; Pombo, E.B. Synergistic Antibacterial Activity of the Essential Oil of Aguaribay (*Schinus molle* L.) *Molecules,* **2012**, *17,* 12023-12036.

[17] Leite, S.R.R.F.; Amorim, M.M.R.; Sereno, P.F.B.; Leite, T.N.F.; Ferreira, J.A.C.; Ximenes, R.A.A. Randomized clinical trial comparing the efficacy of the vaginal use of metronidazole with a Brazilian pepper tree (*Schinus*) extract for the treatment of bacterial vaginosis. *Braz. J. Med. Biol. Res.*, **2011**, *44*, 245-252.

[18] Hayouni, E.A.; Chraief, I.; Abedrabba, M.; Bouix, M.; Leveau, J.Y.; Mohammed, H.; Hamdi, M. Tunisian *Salvia officinalis* L. and *Schinus molle* L. essential oils: their chemical compositions and their preservative effects against *Salmonella* inoculated in minced beef meat. *Int. J. Food Microbiol*., **2008**, *125*, 242-251.

[19] Yueqin, Z.; Recio, M.C.; Máñez, S.; Giner, R.M.; Cerdá-Nicolás, M.; Ríos J.L. Isolation of two triterpenoids and a biflavanone with anti-Inflammatory activity from *Schinus molle* fruits. *Planta Med*., **2003**, *69*, 893-898.

[20] Marzouk, M.S.; Moharram, F.A.; Haggag, E.G.; Ibrahim, M.T.; Badary, O.A. Antioxidant flavonol glycosides from *Schinus molle. Phytother. Res.,* **2006**, *20*, 200-205.

[21] Díaz, C.; Quesada, S.; Brenes, O.; Aguilar, G.; Cicció, J.F. Chemical composition of *Schinus molle* essential oil and its cytotoxic activity on tumour cell lines. *Nat. Prod. Res.,* **2008**, *22*, 1521-1534.

[22] Machado, D.G.; Bettio, L.E.B.; Cunha, M.P.; Santos, A.R.S.; Pizzolatti, M.G.; Brighente, I.M.C.; Rodrigues, A.L.S. Antidepressant-like effect of rutin isolated from the ethanolic extract from *Schinus molle* L. in mice: evidence for the involvement of the serotonergic and noradrenergic systems. *Eur. J. Pharmacol.,* **2008**, *587*, 163-168.

[23] Machado, D.G.; Kaster, M.P.; Binfaré, R.W.; Dias, M.; Santos, A.R.S.; Pizzolatti, M.G.; Brighente, I.M.C.; Rodrigues, A.L.S. Antidepressant-like effect of the extract from leaves of *Schinus molle* L. in mice: Evidence for the involvement of the monoaminergic system. *Prog. Neuropsychopharmacol. Biol. Psychiatry,* **2007**, *31*, 421-428.

[24] Murray, A.P.; Frontera, M.A.; Tomas, M.A.; Mulet, M.C. Gas Chromatographic-Mass Spectrometry Study of the Essential Oils of *Schinus longifolia* (Lindl.) Speg., *Schinus fasciculata* (Griseb.) I.M. Jhonst. and *Schinus areira* L. *Z. Naturforsch. C,* **2005**, *60*, 25-29.

[25] Murray, A.P.; Vela Gurovic, M.S.; Rodriguez, S.A.; Murray, M.G.; Ferrero, A.A. Acetylcholinesterase inhibition and antioxidant activity in essential oils from *Schinus areira* L. and *Schinus longifolia* (Lindl.) Speg. *Nat. Prod. Comm.,* **2009**, *4*, 873-876.

[26] Sánchez Chopa, C.; Descamps, L.R. Composition and biological activity of essential oils against *Metopolophium dirhodum* (Hemip-

tera: Aphididae) cereal crop pest. *Pest Manag. Sci.,* **2012**, *68*, 1492-1500.

[27] Bigliani, M.C.; Rossetti, V.; Grondona, E.; Lo Presti, S.; Paglini, P.M.; Rivero, V.; Zunino, M.P.; Ponce, A.A. Chemical compositions and properties of *Schinus areira* L. essential oil on airway inflammation and cardiovascular system of mice and rabbits. *Food Chem. Toxicol.,* **2012**, *50*, 2282-2288.

[28] Wannaz, E.D.; Zygadlo, J.A.; Pignata, M.L. Air pollutants effect on monoterpenes composition and foliar chemical parameters in *Schinus areira* L. *Sci. Total Environ.,* **2003**, *305*, 177-193.

[29] Sampietro, D.A.; Belizan, M.M.E.; Terán Baptista, Z.P.; Vattuone, M.A.; Catalán, C.A.N. Essential Oils from *Schinus* Species of Northwest Argentina: Composition and Antifungal Activity. *Nat. Prod. Comm.,* **2014**, *9*, 1019-1022.

[30] Solis-Quispe, L.; Tomaylla-Cruz, C.; Callo-Choquelvica, Y.; Solís-Quispe, A.; Rodeiro, I.; Hernández, I.; Fernández, M.D.; Pino, J.A. Chemical composition, antioxidant and antiproliferative activities of essential oil from *Schinus areira* L. and *Minthostachys spicata* (Benth.) Epl. grown in Cuzco, Peru. *J. Essent. Oil Res.*, **2016**, *28*, 234-240.

[31] Graziano, M.N.; Seguí, M.; Coussio, J.D. Estudio de los flavonoids presents en plantas argentinas. *J. Argent. Chem. Soc.,* **1967**, *55*, 235-237.

[32] Rahman, A.U.; Tomas, M.A.; Frontera, M.A. Anthocyanins from fruits of *Schinus molle* var. *areira* (Aguaribay). *J. Argent. Chem. Soc.,* **1974**, *62*, 169-170.

[33] Celaya, L.S.; Viturro, C.I.; Silva, L.R. Moreno, S. Natural antioxidants isolated from *Schinus areira* leaves by ultrasound-assisted extraction. *IJFS*, **2016**, *5*, 167-179.

[34] González-Burgos, E; Gómez-Serranillos, M.P. Terpene Compounds in Nature: A Review of Their Potential Antioxidant Activity. *Curr. Med. Chem.*, **2012**, *19*, 5319-5341.

[35] Durán-Peña, M.J.; Botubol Ares, J.M.; Hanson, J.R.; Collado, I.G.; Hernández-Galán, R. Biological activity of natural sesquiterpenoids containing a *gem*-dimethylcyclopropane unit. *Nat. Prod. Rep.,* **2015**, *32*, 1236-1248.

[36] Sánchez Chopa, C.; Alzogaray, R.; Ferrero, A.A. Repellency assays with *Schinus molle* var. *areira* (L.) (Anacardiaceae) essential oils against *Blattella germanica* L. (Blattodea: Blattellidae). *BioAssay*, **2006**, *1*, 1-3.

[37] Ferrero, A.A.; Sánchez Chopa, C.; Werdin González, J.O.; Alzogaray, R.A. Repellence and toxicity of *Schinus molle* extracts on *Blattella germanica*. *Fitoterapia,* **2007**, *78*, 311-314.

[38] Descamps, L.; Sánchez Chopa, C.; Ferrero, A.A. Activity of *Schinus areira* (Anacardiaceae) essential oils against the grain storage pest *Tribolium castaneum*. *Nat. Prod. Comm.,* **2011**, *6*, 887-891.

[39] Padín, S.B.; Fusé, C.; Urrutia, M.I.; Dal Bello, G.M. Toxicity and repellency of nine medicinal plants against *Tribolium castaneum* in stored wheat. *B. Insectol.,* **2013**, *66*, 45-49.

[40] Mossa, A.T.H. Green Pesticides: Essential Oils as Biopesticides in Insect-pest Management. *J. Environ. Sci. Technol.*, **2016**, *9*, 354-378.

[41] Pavela, R. History, Presence and Perspective of Using Plant Extracts as Commercial Botanical Insecticides and Farm Products for Protection against Insects – a Review. *Plant Protect. Sci.*, **2016**, *52*, 229-241.

[42] Benzi, V.; Murray, A.P.; Ferrero, A.A. Insecticidal and insect-repellent activities of essential oils from Verbenaceae and Anacardiaceae against *Rhizopertha dominica*. *Nat. Prod. Comm.,* **2009**, *4*, 1287-1290.

[43] Benzi, V.; Stefanazzi, N.; Ferrero, A.A. Biological activity of essential oils from leaves and fruits of pepper tree (*Schinus molle* L.) to control rice weevil (*Sitophilus oryzae* L.). *Chil. J. Agr. Res.,* **2009**, *69*, 154-159.

[44] Werdin González, J.O.; Murray, A.P.; Ferrero, A.A. Bioactividad de aceites esenciales de *Schinus molle* var. *areira* (Anacardiaceae) en ninfas II de *Nezara viridula* (Hemiptera: Pentatomidae). *Bol. San. Veg. Plagas,* **2008**, *34*, 367-375.

[45] Werdin González, J.O.; Gutiérrez, M.M.; Ferrero, A.A. Repellency Assays with Plant Extracts and Essential Oils from *Schinus molle* var. *areira* (L) (Anacardiaceae) and DEET against *Nezara viridula* L. (Hemiptera: Pentatomidae). *BioAssay,* **2011**, *6*, 1-4.

[46] Gutiérrez, M.M.; Werdin González, J.O.; Stefanazzi, N.; Bras, C.; Ferrero, A.A. The potential application of plant essential oils to control *Pediculus humanus capitis* (Anoplura: Pediculidae). *Parasitol. Res.,* **2016**, *115*, 633-641.

[47] Ferrero, A.A.; Werdin González, J.O.; Sánchez Chopa, C. Biological activity of *Schinus molle* on *Triatoma infestans*. *Fitoterapia,* **2006**, *77*, 381-383.

[48] Chirino, M.; Cariac, M.; Ferrero, A.A. Actividad insecticida de extractos crudos de drupas de *Schinus molle* L. (Anacardiaceae) sobre larvas neonatas de *Cydia pomonella* L. (Lepidoptera: Tortricidae). *Bol. San. Veg. Plagas,* **2001**, *27*, 305-314.

[49] Scrivanti, L.R.; Zunino, M.P.; Zygadlo, J.A. *Tagetes minuta* and *Schinus areira* essential oils as allelopathic agents. *Biochem. Sys. Ecol.,* **2003**, *31*, 563-572.

[50] Celaya, L.S.; Alabrudzińska, M.H.; Molina, A.C.; Viturro, C.I.; Moreno, S. The inhibition of methicillin-resistant *Staphylococcus aureus* by essential oils isolated from leaves and fruits of *Schinus areira* depending on their chemical compositions. *Acta Biochim. Pol.,* **2014**, *61*, 41-46.

[51] Davicino, R.; Mattar, A.; Casali, Y.; Anesini, C.; Micalizzi, B. Different activities of *Schinus areira* L.: anti- inflammatory or pro-inflammatory effect. *Immunopharmacol. Immunotoxicol.,* **2010**, *32*, 620-627.

[52] Ferrero, A.A.; Minetti, A.; Bras, C.; Zanetti, N. Acute and subacute toxicity evaluation of ethanolic extract from fruits of *Schinus molle* in rats. *J. Ethnopharmacol.,* **2007**, *113*, 441-447.

[53] Bras, C.; Domínguez, S.; Codón, S.; Minetti, A.; Ferrero, A.A Consequences of subchronic exposure to ethanolic extract from fruits and leaves of *Schinus molle* var. *areira* L. in mice *J. Ethnopharmacol.,* **2010**, *132*, 321-327.

[54] Bras, C.; Gumilar, F.; Gandini, N.; Minetti, A.; Ferrero, A.A. Evaluation of the acute dermal exposure of the ethanolic and hexanic extracts from leaves of *Schinus molle* var. *areira* L. in rats. *J. Ethnopharmacol.,* **2011**, *137*, 1450-1456.