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A Review of Phytochemicals and Biological Studies of Schinus Molle Plants

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Abstract: Schinus molle L. belongs to the family Anacardiaceae early found as a weed in South America and later distributed in Bolivia, Brazil, Uruguay and in many others country all over the world as an ornamental plant. Various parts of this plant are used to treat a toothache, rheumatism, urinary tract and respiratory infection. The tree is popular for its pharmacological features such as antimicrobial, anticancer, anti-inflammatory, antidepressant, antioxidant and allelopathic activities. Schinus molle is also rich in various chemicals for pharmaceuticals such as sesquiterpenes, monoterpenes, essential oils, fatty acids, flavonoids and triterpenes. The aim of this report is to review the available scientific literatures published regarding the phytochemicals, biological activities and genetic characterization of Schinus molle plants.

Keywords: Biological Activities, Herbal Medicine, Phytochemicals, Schinus Molle

1. INTRODUCTION

S molle (Anacardiaceae) is pepper tree original to South America and is widely spread in tropical and subtropical parts of the globe [1]. It is planted as an ornamental plant in valleys, a public garden and along roads or as shade plant in temperate places. It is popularly known as Brazilian pepper tree, English (Mastic tree, Pink peppercorns and Peruvian pepper tree), Arabic (felfelkazib). It is distributed in Argentina, Bolivia, Brazil, Columbia and Uruguay [2]. This plant is used as traditional drugs for the treatment of analgesic, antitumoral, anti-inflammatory, rheumatism, urinary tract, respiratory infection and toothache [3] - [7].

S. molle tree is rich in various diverse bio-actives including saponins, tannins, monoterpenes flavonoids, sterols, triterpenoids, fatty acid and essential oils [3] which play an essential role in pharmaceutical properties.

To the best of our knowledge, there were no review articles described different aspects of the tree. Therefore, there is a desire need to compile a comprehensive and in-depth review article on the herbal medicinal uses, phytochemical profiling, various biological actions of Schinus molle plants. The current review will bridge the research gap, regarding phytochemical, biological activity potential and genetic studies of this plant found in many localities in Aseer region, KSA.

2. BOTANICAL DESCRIPTION

Taxonomy and Distribution

Schinus molle is a member of the Anacardiaceae family which is found in Africa, South Europe, Middle East and the subtropical areas like Peru, Brazil, Columbia, Chile, Bolivia, Ecuador, Uruguay and Argentina [2], [8]. *Taxonomic position of the tree is summarized in Table I according to Kasimala and Kasimala [8].*

Morphology

This species is highly aromatic. It is an evergreen, dioecious, branched plant that grows to 20 meters in height, the tree's

Table I: Taxonomic position of *S. Molle*

Kingdom	Plantae
Subkingdom	Tracheobionta
Super-division	*Spermatophyta*
Division	*Magnoliophyta*
Class	*Magnoliopsida*
Subclass	*Rosidae*
Order	*Sapindales*
Family	*Anacardiaceae*
Genus	*Schinus*
Species	Schinus molle *L.*

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pinnately compound leaves, with sessile alternate leaflets that measure 1.5-6 cm long by 0.2-0.8 cm wide. Flowers are small and unisexual, with yellowish white petals and borne in panicles at ends of the drooping branches. Fruits are round small, 5-8 mm diameter that turn from green to red or pink to black. Seeds are round and brown-black with 2-4 mm in diameter. Each fruit contains one or two seeds [9], [10], [2], [8]. This species can adapt to harsh extremely temperature, drought and frost conditions. It is preferred 300–60 mm rainfall. It grows in different types of soil including salinity and alkalinity and also grows at elevations up to 2,400 m [2].

Botanical synonyms

Schinus molle var. huyngan, Schinus occidentalis, Schinus areira, Schinus angustifolia, Schinus bituminosus, Schinus huigan, Schinus molle var. argentifolius, Schinus molle var. huigan, Schinus molle var. areira and Schinus angustifolia [2].

3. PHYTOCHEMICALS SCREENING

S. molle is a medical plant rich in various biologically active compounds such as monoterpenes and sesquiterpene hydrocarbons, bicyclo-germacrene, gallotannins, biflavonoids and anthocyanins [11] - [13]. The main constituents in essential oil from fruits of this plant collected in Liguria (Italy) were α-phellandrene (55.4%), β-phellandrene (15.4%) and limonene (14.3%), and in case oil of leaves were α-phellandrene (30.2%), β-phellandrene (9.6%) and limonene (9.3%), elemol (13.3%), germacrene-D (5.2%), γ-eudesmol (3.2%) and T-cadinol (4.7%) [14]. Presence of α-cadinol, α-phellandrene, limonene and β-phellandrene in oil berries and leaves were extracted using the water-distilled and analyzed by GC-MS method [15]. The main components in fruit essential oil of S. molle from Tunisia were α-phellandrene, β-phellandrene, β-pinene, p-cymene and α-pinene [16], [17], while in dried fruit oil of this plant were α-phellandrene, limonene and β-phellandrene, β-myrcene and α-pinene [18]. The chemical structures of some bioactive compounds identified from different organs of S. molle are displayed in Fig. 1.

Some other reports showed the presence of α-phellandrene, limonene, β-phellandrene, elemol, α-eudesmol, caryophyllene oxide, terpin-4-ol, 1,10-di-epi-cubenol, epi-α-cadinol, 7-epi-α-eudesmol, spathulenol, 1,8-cineole and γ-cadinene, α-pinene and β-pinene were isolated from the essential oil of leaves of the tree [19] - [21]. Other previous studies with essential oils of fruits and leaves of S. molle from Tunisia showed that the chief bioactive compounds in both of the oils were limonene and β-phellendrene, α-phellendrene, myrcene and α-pinene [22], [23]. The major chemical components in the essential oil of dried aerial parts of S. molle hydrodistillation from Ethiopia were α-phellandrene, β-phellandrene, α-pinene, β-pinene, β-myrcene, β-elemene, copane, germacrene, γ-cadinene and α-humulene [24].

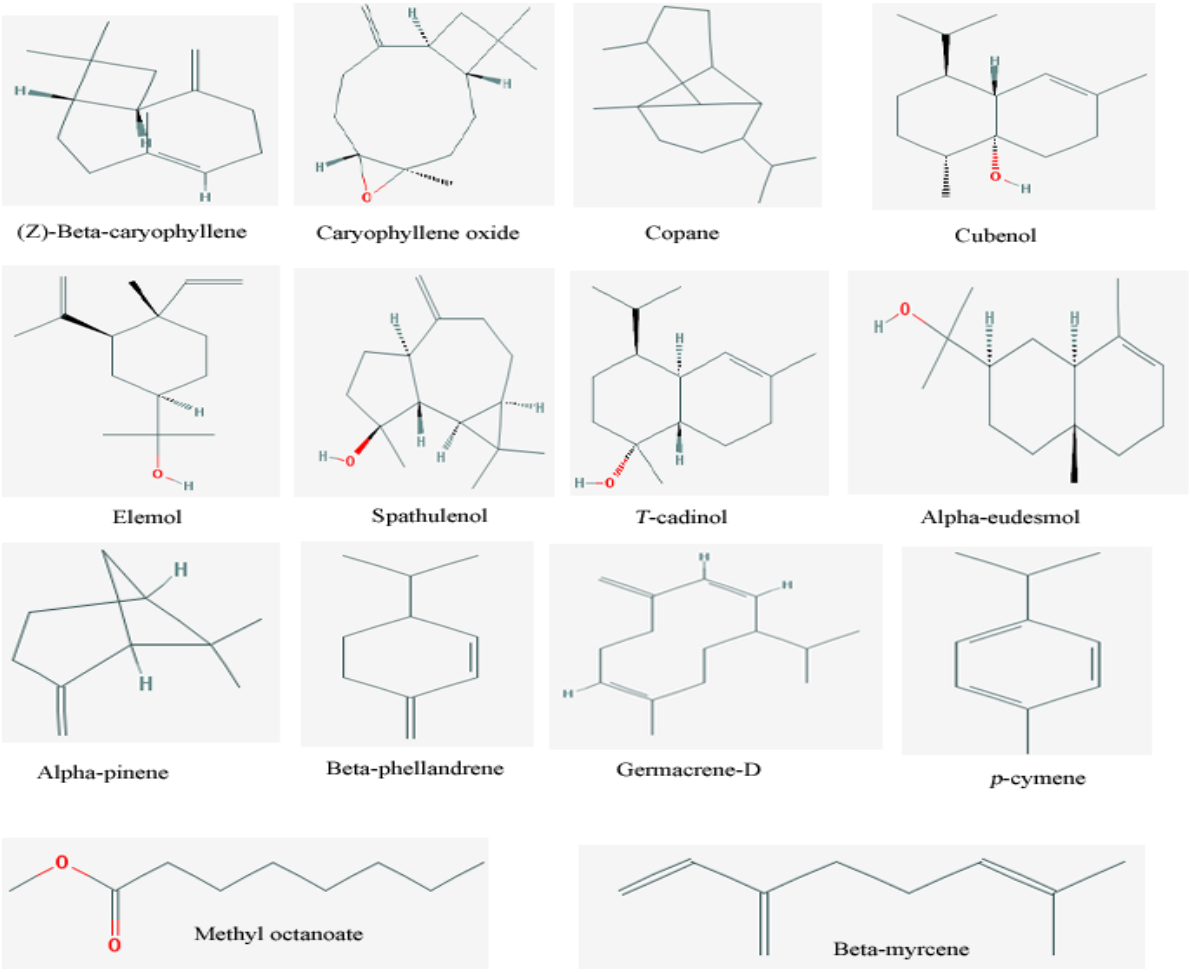

Fig.1. The chemical structures of some bioactive compounds identified from different organs of *S. molle*.

In n-hexane and petroleum ether extracts of mature fruits oil of S. molle grown in Damascus, Syria. α-phellandrene (24.86% & 22.19%), β-pinene (14.78% & 13.52%), β-phellandrene (11.02 & 10.00%), and limonene (10.58% & 9.34%) found to be main compounds in n-hexane and petroleum ether extracts, respectively [25].

The oil obtained from leaves and ripe fruit of S. molle collected from southeast Portugal were rich by monoterpenes and sesquiterpenes with α-phellandrene, limonene, β-myrcene, β-phellandrene and elemol as major compounds in leaf oil, whereas β-myrcene, limonene, α-phellandrene and β-phellandrene as main compounds in fruit oil [26]. Spathulenol, caryophyllene oxide, Cubenol, α-pinene, β-pinene and germacrene D were isolated from S. molle leaves essential oil and fruit respectively [27]. Abir et al. [28] demonstrated that α-eudesmol, elemol, β-eudesmol, spathulenol, d-limonene, 4-epi cubebol, α-eudesmol, 6-epi-shyobunol, and elemol were characterized in aerial parts of essential oil of S. molle respectively. The essential oil fruits of S. molle contained p-cymene, β-phellandrene, limonene, α-phellandrene [29], β-myrcene, δ-cadinene [30], myrcene, methyl octanoate, *(Z)-β-caryophyllene and α-pinene [31]. In a recent report, it was stated that different parts of the plant comprising oil components as myrcene,* p-*cymene, α-phellandrene and β-eudesmol [32]*.

4. Herbal Medicine Uses

In traditional systems of drugs, various organs of the tree such as fruits, barks and leaves are used to treat a variety of illnesses due to the presence of effective substances. It was found that leaf juice of the plant used to cure fever, rheumatism, ophthalmia, digestive, respiratory, urinary, menstrual disorders, wound, cough, and eyes problems.

The resin isolated from the bark used to cure digestive disorders. The bark extract has been used to treat diarrhea and depressant and used as astringent [2], [33],[34], [35]. Herbal medicinal uses of the plant are summarized in Table II.

Table II: Some medicinal uses of *S. Molle*

Part	Medicinal use	Reference
Leaves	Fever, rheumatism, ophthalmia, digestive, respiratory, urinary, menstrual disorders, wound, cough, eyes problems, diuretic	[36], [2], [33], [34], [35]
Bark	Diarrhea and depressant	[2], [33], [34], 35]
Fruits	Antihypertensive, wounds, diuretic, and haemorrhoids, get rid of gases and digestive activating	[19]
Whole plant	Antiseptic, cardiotonic, stimulant, tonic, antihemorrhagic, toothache, central depressant and analgesic	[34], [3]

5. Biological Properties

The enormous medicinal value is attributed to a broad spectrum of bioactive compounds such as alkaloids, flavonoids, phenols, saponins, tannins and sterols which are responsible for various biological properties of different parts of the tree [6] as shown in Table III.

Antimicrobial Properties

The essential oil prepared from the fresh leaves of S. molle was investigated by Gundidza [36] for antimicrobial activity. The results show that Escherichia coli, Alcaligenes faecalis, Pseudomonas aeruginosa, Beneckea natriegens, Enterobacter aerogenes, Proteus vulgaris, Alternaria alternate, Acinetobacter calcoacetica, Klebsiella pneumoniae, Leuconostoc cremoris, Citrobacter freundii, Aspergillus ochraceus, Fusarium culmorum, Brochothrix thermosphacata, Clostridium sporogenes, Aspergillus parasiticus, Bacillus subtilis and Serratia marcescens presented considerable activity to the essential oil. Fuselli et al. [37] stated that aerial parts of the plant were efficient against Paenibacillus larvae larvae, a causal factor of American foulbrood in honey bees.

The ethanolic extract of fruit proved to be effective against Salmonella enteritidis, K. pneumonia, Listeria monocytogenes, Staphylococcus aureus, P. aeruginosa, Bacillus cereus and E. coli [38].

Significant antimicrobial activity was observed for hexane extract from dried fruits of S. molle against Streptococcus peneumoniae (MIC=62.5 mg/ml) [39]. Oil extracted from leaves inhibited growth of Escherichia coli, Streptococcus pyogenes, Staphylococcus aureus and Candida albicans [19], [20]. The leaf extract of the two Schinus spp. proved to be effective on some of the fungi tested [40]. Inhibitory effect of the growth of Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Enterococcus faecalis, Candida albicans, Listeria monocytogenes, Pseudomonas morgani, Klebsiella pneumoniae, Salmonella anatum, Salmonella enteritidis was reported for essential oil of dried fruit of S. molle [16]. The essential oil of S. molle fruits collected in Tunisia showed inhibition activity against Salmonella typhymurium, Bacillus subtilis, Escherichia coli and Bacillus cereus but they do not any changes against Candida albicans [18]. Pérez-López et al. [30] demonstrated the antimicrobial efficacy of essential oil prepared from the fruit of S. molle against Streptococcus pneumonia, a causal factor of respiratory ailments.

Rocha et al. [41] reported that the crude extract essential oil from fruits and leaves of S. molle has the largest activity against Staphylococcus aureus, a potent/mild activity against Escherichia coli and mild/low activity against Pseudomonas aeruginosa. Scopel et al. [34] found that CO2, CO2/water and CO2/ethanol extracts of leaves and twings of S. molle exhibited antimicrobial activity against Escherichia coli, while supercritical CO2/water exhibited activity against Micrococcus luteus. Petroleum ether extract of dried mature fruit oil of S. molle showed maximum activity against Botrytist cinerea at dose 1000 ppm [25]. The essential oil of leaves and ripe fruit of S. molle were investigated for antibacterial and antifungal activity. The results exhibited that oil of leaf gave the highest effect against Staphylococcus epidermidis, Staphylococcus aureus and Enterococcus faecalis, and in case of fruit essential oil gave the largest

effect against Staphylococcus aureus and Enterococcus faecalis and they have the least effect against Pseudomonas aeruginosa, Proteus mirabilis and Salmonella enteritidis serovar Typhimurium. Both oils revealed that similar activity against (Aspergillus spp.) and Fusarium oxysporum, whereas essential oil of leaf was the only one which was active against (Rhizophus spp.) [26]. Inhibition of Staphylococcus aureus and Bacillus subtilis were observed by Malca-García et al. [43] for terebinthene and pinicolic acid were isolated from the bark resin of S. molle.

Anticancer Properties

In a study carried out by Ruffa et al. [4], methanolic extracts of S. molle showed activities against a human hepatocellular carcinoma cell line, Hep G2. Another study proved that essential oil of S. molle leaves showed the highest activity against leukemic and breast carcinoma cell lines by using a mechanism related to apoptosis [21]. It was observed that essential oils of fruits of S. molle gave anticancer activity on human breast cancer cells (MCF-7) [17]. The leaf oil of the plant has been reported to be effective against Ehrlich ascites carcinoma cell lines, leukemic cell line K562 and NCI-ADR/RES [44], [20]. Terebinthene was identified from the bark resin of S. molle found to be cytotoxic activity on a human colon carcinoma HCT-116 cells [43]. In Egypt, p-cymene, myrcene, limonene, α-phellandrene were isolated from the essential oil of different parts of this tree showed significant actions in numerous cell lines including hepatocellular (HepG-2), breast (MCF-7) and human colon (HCT-116) [32].

Allelopathic Properties

Many of plants contain on a range of allelo-constitutes which inhibited growth neighboring weeds. These substances could be used as natural herbicides [45], [20]. Zahed et al. [22] discovered that the essential oil of fruits and leaves of the S. molle displayed activity against wheat germination and radicle elongation. Water and ethanolic leaves extracts of S. molle under several kinds of pruning resulted in various elongation of root between the two extracts tested [46]. According to Simionatto et al. [20], S. molle has been presented to inhibit seed germination and seedling growth of weeds such as Allium cepa and Lactuca sativa.

Toxicity Properties

It was observed that fruit and leaf essential oils from S. molle offered potent toxicity on Artemia salina and weak toxicity on Swiss mice [26]. Bras et al.[47] indicated that hexanic and ethanolic extracts from leaves of S. molle var. areira presented acute dermal exposure in the rat. on the other hand, ethanolic extracts of fruits have been pointed as acute and subacute toxic in rat [48].

Anti-Inflammatory Properties

According to Yuequin et al. [5] the biflavanone, chamaesjasmin, triterpenes 3-epi-isomasticadienolalic acid and isomasticadienonalic acid were separated from fruits S. molle. All these chemicals decreased the chronic model of inflammation, while only isomasticadienonalic acid was action on the phospholipase A2 -induced mouse paw edema. On the other hand, dichloromethanol extract from the seed of S. molle was characterized by mast icatrienonate and isomast icadienonic, which gave effective effects on rat models [49].

Table III: Some bioactive compounds found in S. Molle.

Compounds	Source	Biological action	Reference
Terebinthene	Bark resin	Antibacterial and cytotoxic activity	[43]
Pinicolic acid	Bark resin	Antibacterial activity	[43]
1,8-cineole	Oil of leaf	Allelopathic activity	[20]
α-phellandrene	Stem,flower, leaf, fruit and oils	Anticancer and antifungal activities	[32], [25]
Biflavanone, chamaesjasmin, triterpenes, 3-epi-isomasticadienolalic acid and isomasticadienonalic acid chamaesjasmin, triterpenes,	Fruits	Anti-Inflammatory activity	[5]
terpin-4-ol	Oil of leaf	Allelopathic activity	[20]
δ-cadinene	Oil of fruit	Antimicrobial activity	[30]
Limonene	Stem,flower, leaf and fruit oils	Anticancer activity	[32]
α-pinene	Fruit oil	Antifungal activity	[25]
p-cymene	Stem, flower, leaf and fruit oils	Anticancer activity	[32]
Myrcene	Stem, flower, leaf and fruit oils	Anticancer activity	[32]
α-humulene	Oil leaf	Cytotoxic activity	[20]
Caryophyllene oxide	Oil leaf	Cytotoxic activity	[20]

Antidepressant Properties

The work conducted by Machado et al. [7], [50] found that the hexanic and ethanolic extracts of S. molle leaves generated antidepressant activity in tail suspension test in mice.

Insecticidal And Repellent Properties

It was demonstrated that volatile extracts leaves of this species showed repellent and feeding deterrent influences against Musca domestica L. [51]. In another work, hexanic extracts from fruits and leaves of Schinus molle var areira exhibited repellent activity against neonate larvae of Cydia pomonella [52]. Ferrero et al. [6] stated that hexanic extracts of S. molle of fruits and leaves showed significant repellent on Triatoma infestans. According to Ferrero et al. [53], petroleum ether and ethanol extracts of S. molle leaves and fruits were proved to generated significant repellent activity on Blattella germanica.

Another study by Abdel-Sattar et al. [54] confirmed that essential oils of S. molle leaf and fruits gave insecticidal and insect repellent properties against two insect species: Trogoderma granarium and Tribolium castaneum. In the study of water and ethanolic extracts of S. molle leaves were studied by Huerta et al. [55] for toxicity and repellency properties against adult Xanthogaleruca luteola both extracts gave effectively. Also, the water extract showed feeding completely, but ethanol extract did not any changes.

Antioxidant Properties

Hosni et al. [18] examined essential oil extracted from fruits of S. molle showed very low action. A study presented by Martins et al. [26] found that essential oils prepared from the fruits and leaves of S. molle expressed higher action by using the β-carotene/linoleic acid technique, while those by using the DPPH free radical technique showed low action. It was illustrated that the methanol extract and essential oil of fruit from S. molle displayed the strongest properties assessed by ABTS assay [28]. A recent work by Eryigit et al. [29] reported that essential oil from fruits of S. molle showed lower activity. Tlili et al. [56] showed that fruits of S. molle had risen antioxidant activity.

5. Genetic Studies

Only two research on genetic diversity of S. molle has been mentioned. Among nine populations of S. molle examined in the Brazilian Pampa. Amplified fragment length polymorphism markers showed less genetic diversity, clear genetic structure and significant fine-scale spatial genetic structure at short distances [57]. In Saudi Arabia, the degree of variations in DNA fingerprints associated with a slight altitudinal change of S. molle using three various markers evaluated by Al-Andal et al. [58]. Random amplified polymorphic DNA (RAPD), mixed RAPD and inter-simple sequence repeat markers depicted different degrees in their capacity to recognize the diversifications among seven populations of S. molle.

6. Conclusion

The chemical investigation of S. molle has detected many secondary metabolites with significant biological and pharmaceutical properties. This work recommends the need for further investigations regarding the toxicological aspects to develop safe and cheap therapeutic drugs. Nevertheless, there are only few genetic and antidepressant studies carried out on this species. So, further studies should be conducted in the future.

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