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Review Article

Ethnobotany, Pharmacology and Chemistry of *Salvadora persica* L. A Review

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***Salvadora persica* L., commonly known as the miswak tree, occurs in shrub savannah from northwestern India to Africa. This review discusses the current knowledge of traditional uses, chemistry, and biological effects of this species. The ethno botanical literature reveal it as a versatile medicinal plant used to treat different human and livestock ailments. Several different classes of compounds were previously isolated from various parts of *S. persica* of which the main groups are Tri-Methyamin, Salvadrin, Chloride, Fluoride, Silica, Sulfur, Mustard, Vitamin C and a small amount of Saponine Tanin. Various types of preparations, extracts and individual compounds derived from this species have been found to possess a broad spectrum of pharmacological effects as well as on different biochemical processes and physiological functions including hypoglycemic, hypocholesterolemic, and sedative, and effects in addition to be against gingival irritation. Moreover, the extracts and preparations from the plant, which are hopefully safe, exhibited various additional biological effects e.g. antimicrobial, antioxidant, antifever, anti-ulcerogenic, anti-caries, anti-periopathic activities. The results of data analysis on the chemical, pharmacological and toxicological characteristics of *S. persica* support the view that this species has beneficial therapeutic properties and indicate its potential as an effective adaptogenic herbal remedy.**

In the world today, an herbal drug is defined as a remedy derived from plants (roots, leaves, flowers, fruits, seeds) and/or other natural sources which can be used for therapeutic purposes and its active chemical constituents provide the basis for pharmaceutical synthesis. Thus confirming the economic values of various medicinal plants used in different traditional systems of medicine (Sher et al., 2010a). Ethno pharmaceutical studies have become increasingly valuable in the recent past and medicinal plants are now part of health care system. The medicinal plants conservation programs and their sustained supply are part of global health strategy (Sher and Hussain, 2009; Sher et al., 2010c). Furthermore, recent reports suggested that in some cases, synthetic antibiotic are no more effective to treat some infectious diseases because of bacterial resistance. Some drug products were found to cause health hazards if used in higher dose range. The observed bacterial resistance and undesirable side effect of certain antibiotics, led scientific community to find new antibacterial compounds from

medicinal plants or to prepare synthetic and semi-synthetic antibacterial drug products with low toxicity (Marchese and Shito, 2001; Poole, 2001). In several studies, medicinal plant extracts, plant products, and isolated phytochemical constituents showed highly significant antimicrobial activity which added more to encourage research on such potential natural drugs (Amani et al., 1998; Salvat et al., 2001).

Meswak is a product of the plant *Salvadora persica* which grows in different areas of the world including the middle east and Africa (Elvin-Lewis, 1980; Eid et al., 1990). The Miswak (*S. persica* L.), also known as tooth brush tree 4–6 m tall with a short trunk, white bark and smooth green leaves, with a life span of 25 years, belonging to the Salvadoraceae family, has been used as a brushing stick for more than 1,300 years. Because these natural tooth brushes are so commonly used in different areas of the world by millions of people, a variety of studies have been performed on the antimicrobial effect of these sticks (Al-Bagieh et al., 1994; Al-lafi, 1995).

Pharmacological studies indicated that *S. persica* L. plant possess anti-microbial, anti-plaque, aphrodisiac, alexiteric, analgesic, anti-inflammatory, anti-pyretic, astringent, diuretic and bitter stomachic activities (Galletti and Chiavari, 1993). It has great medicinal use in the treatment of nose troubles, piles, scabies, leucoderma, scurvy, gonorrhea, boils and toothache, to treat hook worm, venereal diseases, for teeth cleaning, in rheumatism, cough and asthma, to lower cholesterol plasma levels, reestablishment of the components of gastric mucosa, and as a laxative (Alali et al., 2004; Khalessi et al., 2004). It contains important phytoconstituents such as vitamin C, salvadorine, salvadourea, alkaloids, trimethylamine, cyanogenic glycosides, tannins, saponins and salts mostly as chlorides (Alali et al., 2004; Almas, 2002; Almas et al., 2005; Rajesh et al., 2009). *S. persica* seed contains about 40% oil with a fatty acid composition (lauric -20%, myristic -55%, palmitic 20% and oleic -5%) which can make an excellent soap. Radical reactions in vivo can damage life essential molecules such as nucleic acids and proteins Saez TG.et al.(1994). Phenolic compounds, particularly flavonoids, have been shown to possess an important antioxidant activity towards these radicals, which is principally based on their structural characteristics (number and position of phenolic hydroxyls, other groups, conjugation) Bors W. et al.(1990). The history and the use of miswak (tooth stick) as an oral tool as well as the biological effects of *S. persica* extracts are reviewed. Besides medicinal claims, various parts of this plant are of great ethno botanical importance and play a vital role in the livelihood of local communities (Ghazanfar, 2007; Abuzinada et al., 2005; Sher et al., 2004).

Ethnobotanical Importance

Miswak (*Salvadora persica*) is one of the most commonly used medicinal plants for oral hygiene among global Muslim community (Sher et al., 2010c). The traditional medicinal use of *S. persica* as antimicrobial toothbrush stick for oral hygiene, and to treat gum inflammation, is a centuries old practice and a part of Greeko-Arab system of medicine (Al-Otaibi et al., 2004; Zakaria et al., 1998; Sher et al., 2010c). *S. persica* is harvested as wild, rather than cultivated, and about 80% world population use it as a natural remedy for the treatment of different diseases (Noumi et al., 2010; Sofrata et al., 2007; Monforte et al., 2002). According to Sofrata et al.in 2007, the fruits of *S. persica* are eaten in raw, cooked, or dried by the inhabitants of the sites where *S. persica* grow in abundance. Similarly, the local folks cook the leaves as a sauce and eat it with couscous or as green vegetables. The flowers of *S. persica* are found to be a good source of nectar; therefore, it is used as a honey bee plant. The local Bedouins were

found to have strong belief that the honey of *S. persica* had high medicinal value as compared to honey from other plant regions (Sofrata et al., 2007). It is worth mentioning that the leaves and young shoots of *S. persica* are used as fodder for camels, cows, goats and sheep. *S. persica* leaves make good fodder because of the high water content (15 to 36%). Moreover, it was confirmed that the leaves of this popular medicinal plant were used in animals to increase lactation in cows and improve general body weight of all animals. (Sofrata et al., 2007). Ethno-botanical evaluation of *S. persica* also reveal its significant pharmaceutical importance. Studies described that toothbrushes made from roots and small branches have been in use for over thousands of years, and currently the use of *S. persica* is more popular among Islamic communities of the world (Azaizeh et al., 2003). Toothbrushes prepared from the roots and small branches of *S. persica*, to be highly useful as maintainer of teeth (Noumi et al., 2010; Al- Khteeb et al., 1991). In Arab traditional medicine teeth cleaning with *S. persica* sticks were found to provide relief from toothache and gum inflammation, and the decoctions of *S. persica* leaves and root were successfully used as mouthwash, and in the cure of tooth/gum problems and as a remedy for joint pain, thus supporting the reports of earlier researchers (Al-Sadhan et al., 1999). It is interesting to note that decoction of *S. persica* root besides using to treat epilepsy, have been used to cure gonorrhea and skin diseases, spleen troubles, and stomach ulcer (Sanoqo et al., 1999).

Table 1. Traditional use of different parts of *Salvadora persica*

Plant Part	Nature	Traditional Use	References
Leaves	Bitter in taste, corrective, deobstruent, astringent to the bowels, tonic to the liver, pungent	Preparation of sauce, and salad, diuretic, analgesic, anthelmintic, useful in ozoena and other nose troubles, piles, scabies, leukoderma, lessening inflammation, and strengthening the teeth, scurvy and rheumatism.	*(Khatak M et al.,2010, Farooqi and Srivastava, 1968).*
Fruits	Sweet and edible	Fermented drinks, deobstruent, carminative, diuretic, lithontriptic, and stomachic , biliousness, rheumatism and snake bites.	*(Khatak M et al.,2010).*
Root / Root bark	Bitter	Tooth cleaning stick, diuretic,Vesicant, amenorrhea, stimulant, emmenagogue, gonorrhea, vesical catarrh, spleen trouble and general stomach-ache	*(Khatak M et al.,2010, Abdelrahim and Jurner 1983; Attar, 1979, Kokwaro, 1976, Ezmirly et al., 1979)*
Stem Bark	Bitter	Ascarifuge, and gastric troubles	*(Khatak M et al.,2010).*
Seeds	Sitter and sharp	Purgative, diuretic and rheumatism	*(Atassi F.,2002; Bukar A et al.,2004).*

Biological activities

As is summarized below, the experimental pharmacological and clinical investigations carried out during the last 32 years have shown that extract and individual compounds isolated from different parts of the plant have specific biological effects indicating it has marked adaptogenic properties including hypoglycemic effects, eliminating free radicals to prevent oxidizing pathology, and other activities. previous studies demonstrated the anti-ulcerogenic (Galati et al., 1998), hypoglycemic (Trovato et aI., 1998), hypocholesterolemic (Galati et al.,

1999) and sedative (Forestieri et aI., 1997) activities of S. *persica* aqueous extract. Many studies have demonstrated the antibacterial, anti-caries, anti-periopathic, and antifungal properties of aqueous extracts of various chewing sticks (Almas, 2002).

Antimicrobial activities

Previous studies showed that Persica extracts have antibacterial activity against cariogenic and periodontopathic bacteria and can develop periodontal health. moreover the World Health Organization recommends and encourages the use of chewing Persica sticks (miswak) as an effective oral hygiene procedure in areas where its use is traditional. WHO(1987). Several studies have described the antibacterial effects of Persica extract on cariogenic bacteria and on periodontal pathogens and a number of microbial species including bacteria, fungai, and even anti-viral testes have also been evaluated till now. A list of such microbial studies is given in Table 2.

Table 2.Reviewed list of different microbes tested for their sensitivity to *S. Persica* extract

Microbes tested using s. Persica extracts.	References
Gram positive bacteria;	Emira Noumi et al.(2011)
Staphylococcus aureus ATCC 25923, *Staphylococcus pidermidis* CIP 106510, *Micrococcus luteus* NCIMB 8166.	
Gram-negative bacteria:	
Pseudomonas aeruginosa ATCC 27853, *Salmonella typhimurium* LT2 and *P. ruginosa.*	
Fungi;	
Candida albicans, *C. dubliniensis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, *C. famata*, *C. kefyr*, *C. sake*, *C. holmii*, *C. lusitaniae*, *C. intermedia*, *C. atlantica*, *C. maritima*, *Pichia guillermondii* and *Pichia jardinii*	
Streptococcus mutans, P. aeruginosa and Streptococcus faecalis .	Salehi and Momeni, (2006), Al-Bayati and Sulaiman (2008), Almas and Stakiw (2000).
E. coli, *S. aureus*,B. *subtili,and P. aeruginosa.*	Alali (2004).
Staphylococcus aureus, S. mutans, actobacillus acifophilus, and *Pseudomonas aeruginosa.*	Hassan Sher(2011).
S. mutans and *S. aurens.*	Hussein (1992); Saleh et al., (2006).
S. pyrogenis, *S. faecalis*, *P. aeruginosa, Lactobacillus acidophilus, Candida albicans*	Suffredini et al., (2004), Al-Sabawi et al., (2007), Al-Bayati et al. (2008).
S*taphylococcus aureus.*	Zafar Ahmed et al.(2010).
Actinomyces viscosus, *Streptococcus mutans*, *Streptococcus sobrinus*, *Lactobacillus fermentum*, *Lactobacillus casei* and *Eikenella corrodens*.	Vahabi S et al.(2011).
S. mutans and *E. corrodens.*	Abdeirahman et al., (2002).
Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and Candida albicans.	Ashraf Taha Khalil(2006).
Herpes simplex virus, Streptococcus mutans,and Candida albicans.	Al-Bagieh, (1992), (1998); Al-Bagieh and Weinberg, (1988).
Haemophilus influenza.	Abier Sofrata et al (2011).
Aggregatibacter actinomycetemcomitans.	Al-Otaibi et al., (2004).
Streptococcus mutants, Streptococcus mitis and Staphylococcus.	Chawla.(1983)
Streptococcus and staphylococcus aurous.	Al-lafi, T. and Ababneh, H. (1995).
Streptococcus mutans and lacto bacilli.	Almas K, Al-Zeid Z (2004).

Hypoglycemic effect

A. Trovato et al (1998) saw hypoglycemic effects, an increase in plasma immunoreactive insulin (IRI) and an incremented oral-glucose tolerance in normal rats when treated with stem decoction of S. *persica.* In addition to the hypoglycemic effect, the decoction caused a significant decrease in mean body weights, without drastic reduction in food consumption. They hypothesized that the decoction decreases absorption from the lumen of the small intestine. Which makes it possible that the weight decrease and the hypoglycemic effect are produced by different mechanisms. According to them The ability of decoction to improve the utilization of glucose following a glucose load, may clarify the possible mechanism of hypoglycemic activity of this drug, which further may facilitate peripheral utilization of glucose, either by direct stimulation of glucose uptake or by enhanced insulin secretion. This latter effect may play a significant role in the adipose tissue.

Antiplatelet aggretion effect

The in vitro inhibitory effects of compounds butanediamide, ~, N4-bis(phenylmethyl)-2(S)-hydroxy-butanediamide (1), and N-benzyl-2-phenylacetamide (2), against human platelet aggregation induced by thrombin (0.1 U/mL) and collagen (10 p.glmL) was found by Ashraf Taha Khalil (2006). Their results showed that compound 2 exhibited a significant inhibitory effect on platelet aggregation induced by collagen. They suggested the contribution of compound 2 to the anti-inflammatory action of the crude remedy (Glitz et al., 1997) and providing a rationale for its traditional use.

Antiulcer activity

Sanogo et al. in 1999 confirmed the antiulcer activity of S. *persica* decoction using optical microscopy. Moreover, they concluded that the drug had an anti-inflammatory and antiulcer activity and the action on the surface epithelium which was cell-mediated fibroblast growth with production of collagen fibres. According to their study S. *persica* appears to strengthen the mucosal barrier which is the first line of defense against endogenous and exogenous ulcerogenic agents. They categorised it as a cytoprotective agent. They suggested that the gastric protective effect of *Salvadora* was due partly to an enhancement in the production of mucous.

Anti-oxidative property

Antioxidants are vital substances which possess the ability to protect the body from damages caused by free radical induced oxidative stress. Radical reactions in vivo can damage lifeessential molecules such as nucleic acids and proteins (Saez TG, et al 1994). Phenolic compounds, particularly flavonoids, have been shown to possess an important antioxidant activity towards these radicals, which is principally based on their structural characteristics (number and position of phenolic hydroxyls, other groups, conjugation) (Bors et al 1990). Abdalbasit Adam Mariod , et al (2001) investigated the antioxidant activity of the bark, leaves and the seed cake phenolic extracts of S. persica using the b-carotene–linoleic acid assay.they found two dominant tocopherols as γ-tocopherol, and α-tocopherol in the seed oil of S. persica. These compounds display antioxidant properties and are active as vitamin E, which makes them particularly important for human health (Ramadan & Morsel 2004). Among the other anti oxidants γ-tocotrienol, b-sitosterol followed by campesterol and stigmasterol were found by them. Among the different phytosterols, sitosterol had been most intensively investigated with respect to its beneficial and physiological effects on health. (Yang B et al 2001).

Chemical composition

Several different classes of compounds were previously isolated from various parts of S. persica. The plant has proved to contain trimethylamine, related to urea alkaloids, sulphur monocline, organic sulphur compounds *β-sitosterol* and small amounts of saponins (Ezmirly et al., 1979; Hegnauer, 1973; Mansour et al., 1986; Oliver Bever, 1986; Robinson, 1983). Five lignane glycosides were isolated from stems of *Salvadora persica* (Kamel et al., 1992). One of the earlier photochemical reports reveal that its seed contains 40% oil with a fatty acid composition (lauric -20%, myristic -55%, palmitic 20% and oleic -5%) which can make an excellent soap. Three lignan glycosides were isolated from the stems of this species (Kamel et al., 1992). Whereas an indole alkaloid was reported in the leaves (Malik et al., 1987). Salvadourea, (m-MeOC6H4CH2NH)2CO, has been reported in the roots (Ray et al, 1975). Moreover It contains important phyto-constituents such as, vitamin C,salvadorine, salvadourea, alkaloids, trimethylamine, cyanogenic glycosides, tannins, saponins and salts mostly as chlorides (Alali et al., 2004; Almas, 2002; Almas et al., 2005; Rajesh et al., 2009). A partial review of the list of chemicals extracted by different researchers is given in Table-3.

Table 3.Review of compounds/metals extracted from *S.persica*.

Compound /metal	Plant parts	References
N t,N4-Bis(phenylmethyl)-2(s)-hydroxy.butanediamide , N-Benzyl.2.phenylacetamide, N-Benzylbenzamide, Benzyl urea	stem	*Ashraf Taha Khalil (2006)*
octacosanol, 1-triacantanol, β-sitosterol, and β-sitosterol-3-O-β-d-glucopyranoside	stem	*Jain M. et al (2004)*
Cu, Ni, Mn, V, Ti, and Mo	leaf	*Raj KP et al (1979), Almas K.(2001)*
α- and β-thujones, camphor, cineole, β-cymene, limonene, β-myrcene, borneol, linalool, and bornyl acetate and nonvolatile fraction contained humulene, caryophyllene, β-santatol, and farnesol	seed	*Hyson JM (2003)*
Benzyl isothiocyanate , benzyl nitrile , carvacrol, benzaldehyde , aniline and naphthalene.	Stem,root	*Emira Noumi.et al.(2011), AI-Bagieh et aL, (1992)*
Benzyl Nitril, Isotymol,thymol ,eugenol , β-caryophyllene , eucalyptol, and isoterpinolene	stem	*Alali and Al-Lafi (2003)*
1,8-cineole , α-caryophyllene ,β-pinene and 9-epi-(E)- caryophyllene.	stem	*Alali et al (2004).*
Rutin and Quercetin	Root	*AbdeI-Wahab et al., (1990)*

Conclusion

Literature review revealed that a great number of pharmacological and phytochemical studies carried out during last 32 years have demonstrated the vast medicinal potential of *S. persica*, especially its marked adaptogenic effect. Various types of preparations, extracts and individual compounds derived from this species have been found to possess various pharmacological effects on several organs such as the teeth, blood, and reproductive systems (Darmani.et al. 2003) as well as on different biochemical processes with some other biological actions e.g. antioxidant, Antiplatelet aggretion effect, and anti-ulcer activities, indicates marked adaptogenic properties of the plant. Moreover, some other biological activities including antimicrobial, and antiplaque effects have been reported for extracts or individual compounds of *S. persica.* Among several classes of biologically active compounds identified in *S. persica*, Cl- (Chloride), SO- (Sulphate), SCN-

(Thiocyanate) and NO- (Nitrate). are assumed to be its main active principle, responsible for the majority of the pharmacological effects. However, other components described in this review such as volatile oils, flavonoids, alkaloids, steroids, terpenoids, saponins, and carbohydrates (Abdillahi et al., 2010; Garboui et al., 2009; Kamil et al., 1999) may, to some degree, augment the pharmacological effects of the plant. The data summarised above, together with the low toxicity potential of the plant, strongly support the view that the *S. persica* has beneficial therapeutic properties indicating its potential as an effective adaptogenic antiseptic herbal remedy. However, further studies are needed to understand the complex pharmacological action and full phytochemical profile of the plant. Clarification of the chemical composition and biological actions of the essential oil, together with verification of inconsistent results regarding reproduction and sexual function (Darmani et al. 2003) and detailed investigation of the anti-microbial and anti plaque property, antioxidant potential , hypoglycemic effects or Antiulcer activity suggest the most up-to-date challenges for the future research of *S. persica.*

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