PHYTOCHEMICAL AND BIOLOGICAL STUDIES ON *SALVADORA PERSICA* WALL: A REVIEW

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Summary

Salvadora is an oil yielding genus belongs to the family Salvadoraceae. This genus consists of number of evergreen trees which occur in saline and non-saline habitats. Two species namely *Salvadora Persica* and *Salvadora oleoides* are identified in India so far. *Salvadora persica* is reported to have more phytoconstituents and possesses numerous biological activities as compared to the other species. It is facultative halophytes found in dry and arid regions of India (Rajasthan, Haryana, Punjab, Maharashtra and Gujarat). Traditionally the wood sticks of *S. persica* have been used for cleaning the teeth and so named toothbrush tree which possess anti-bacterial, anti-diabetic, anti-fungal, anti-cancer, anti-ulcer, anti-plaque, anti-caries, anti-plasmodial activity. The present review encloses complete updates regarding its phytoconstituents and therapeutic profile of the plant.

Keywords: Salvadoraceae, *Salvadora persica*, Miswak, Toothbrush tree, Oral hygiene, Anti-Diabetic

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Introduction

The genus, Salvadora was placed under the group, facultative halophytes, because of its occurrence in non-saline to highly saline habitats. It is a small genus of evergreen trees or shrubs distributed in tropical Africa and Asia extending up to Mascarene Island and China [1, 2]. The genus *Salvadora* belongs to the family *Salvadoraceae,* comprising of three genera (*i.e*. *Azima*, *Dobera* & *Salvadora*) and 10 species distributed mainly in the tropical and subtropical region of Africa and Asia [3]. The natural habitats are near mangroves, in saline lands, swamps, thorn shrubs, desert flood plains and grassy savannah, in seasonally wet sites and along drainage lines in arid zones. *Salvadora* species are also found near riverbanks, where ground water level is high indicating its tolerance to a wide range of water, soil and soil pH and perhaps the main reason for its widespread nativity [4, 5]. *Salvadora* genus species have a number of proven medicinal applications and almost all parts have been found to be pharmaceutically important [6, 7, 8].

Two Salvadora species are available in India [9,10,11,12].

a) *Salvadora persica* (Kharajal) Fig. no. 1
b) *Salvadora oleoides* (Meethajal) Fig. no. 2

Fig no. 1 *Salvadora Persica*

Fig no. 2 *Salvadora oleoides*

Both Salvadora species are deep rooted mesomorphic xerophytes as well as facultative halophytes with high salt tolerance [13,14,15,16] and both contains a number of constituents like terpenoids, fixed oils, steroids, alkaloids, flavanoids, saponins, tannins. Both these species grow on saline and non-saline soils. *S. persica* is more salt tolerant than *S. oleoides* [17]. It is a shrub belongs to the family Salvadoraceae [9].

Morphological Characters

It is large much branched evergreen tree with soft whitish yellow wood. Leaves somewhat fleshy, glaucous 3.8-6.3 cm to 2-3.2 cm, elliptic lanceolate or ovate, obtuse and often mucronate at the apex, base usually acute, less commonly rounded, main nerves 5-6 pairs, petioles 1.3-2.2 cm long glabrous.

Flowers greenish yellow, in axillary and terminal compound lax panicles, 5-12.5 cm long, numerous in the upper axils, pedicels 1.5-3 mm long, and bracts beneath the pedicels ovate, very caduceus. Calyx 1.25 mm long, glabrous, lobes rounded, corolla very thin, 3mm long, deeply cleft, persistent, lobes 2.5mm long oblong, obtuse, much reflexed. Stamens 4 in number, smaller than corolla, exerted. Ovary minutely pedicellate. Fruit a drupe 4-6 mm in diameter, globose, smooth, red when ripe. Seed 4 mm in diameter subglobose, smooth brown. The fruits have strong aromatic smell and taste. Bark is dull grey and deeply cracked [9].

Pharmacological Uses

Toothbrush and dentifrices are widely used for cleaning the teeth. The traditional toothbrush or chewing stick called 'miswak' has been used since ancient history[18]. Miswak were used by the Babylonians some 7000 years ago. They were later used throughout the Greek and Roman empires and have been used by Jews, Egyptians, and in the Islamic empires. It is believed that the precursor to the modern day toothbrush was used in Europe until about 300 years ago. Today, miswak is used in Africa, South America, Asia, and the Middle East including Saudi Arabia and throughout the Islamic countries[19]. It is also known as the Toothbrush Tree [20], Mustard Tree[21, 22], Salt Brush Gudaphala, Pilu, Jhak, Jhal, Chotapilu, Pilu or Piludi and Moti-Jal, Grape of the desert [23]. The use of wood sticks of *S. persica* for cleaning the teeth is deeply rooted in traditional Arabian medicine and it was named MISWAK (or siwak) which in Arabic means "sticks for rubbing the teeth". These chewing sticks are used for oral hygiene[24, 25]. Leaves of *Salvadora persica* have carminative, antiseptic and anti-fungal action [26]. Leaves are also used in the asthma, cough and rheumatism, virucidal activity, scurvy, piles, leprosy, hepatic disorders [27, 28]. Leaves are bitter and possess antiscorbutic, deobstruent, liver tonic, diuretic, analgesic, anthelmintic, astringent properties [28], hypoglycaemic [23, 29], anti-microbial [30], anti-bacterial [31], anti-plasmodial [32]. Because of the presence of fluoride in stems are used as traditional toothbrush or chewing stick or used as oral hygiene tool [24, 33]. Stems show anti-plaque effect more as compare to chlorhexidine gluconate [34.] Stem extracts shows anti-microbial [35], anti-caries [24], anti-spasmodial [36], anticonvulsant and sedative effects [37]. Stem bark is used as an ascarifuge and for gastric troubles. Fruits are used as carminative, diuretic, stomachic, in rheumatism [28]. The stem decoction showed hypoglycaemic effects [29]. Extract of *S. persica* shows hypolipidemic activity in rats [38]. Seeds are purgative and tonic. Seed oil is applied on the skin in rheumatism [28]. Flowers are used for de-worming, leprosy, gonorrheae. Root barks and leaves in piles and hepatic disorders [27]. Roots also possess anti-oxidant activity

[39], anti-inflammatory activity [40]. Roots and twigs also possess anti-microbial activity [41] Chlorine, trimethylamine and sulphur compounds in aqueous extract of roots of miswak tree shows anti-mycotic effect [36,42]. Antimicrobial activity of both glucosinolates: glucotropeolin and sinigrin were investigated against tooth decay microorganisms and bacterial species [43]. Aerial parts show anti-microbial [44], Anti-spasmodic, anti-arrhythmic anti-cholinergic activity [45]. Decoction of miswak tree gives anti-ulcer activity [46]. Like medicinal effects miswak tree has adverse effects on male and female reproductive system and fertility. Exposure to Miswak extract did not have much effect on female mouse fertility; although it caused a significant decrease in the relative weights of the ovary and an increase in uterine weights and exposure of male mice to miswak extract resulted in a 72% reduction in pregnancies in untreated females [47]. Extracts of S. persica and other related plants may be effective against the bacteria that are important for the development of dental plaque. Therefore, it has been claimed that miswak sticks may have antiplaque effects and may also affect the pathogenesis of periodontal diseases by reducing the virulence of periodontophathogenic bacteria [48]. Miswak contains large amount of tannic acid (Tannins). The tannins prevent the adherence of the bacteria to the teeth. It is an established fact that *Streptococcus viridians* attacking the heart valves and damaging them come from the mouth. So, the use of Miswak is a preventive measure against many diseases of the teeth, gastrointestinal tract and heart [49].

Chemical Constituents

A new indole alkaloid salvadorocine has been isolated from the leaves of *Salvadora persica* [50]. Volatile oil extracted from *Salvadora persica* leaves, identified as benzyl nitrile, eugenol, thymol, isothymol, eucalyptol, isoterpinolene, and β-caryophyllene [41]. Glucotropaelin is also present [43]. Leaves contain amino-acids like alanine, asparagine, aspartic acid, glutamic acid, glutamine, methionine, phenylalanine, serine, threonine, tyrosine, and valine [51, 52, 53]. Leaves also possess the Flavanoids and flavanoid glycosides like Kaempferol, Quercetin, Kaempferol 3-α-L-rhamnosyl-7-β-xylopyranoside, isorhamnetin-3-O-robinobioside, kaempferol-3-O-robinobioside, narcissin, kaempferol-3-O-rutinoside, isorhamnetin-3-O-β-galactoside, astragalin, isorhamnetin-3-O-β-D-glucoside,isorhamnetin-3-(2,6-di-rhamnopyranosyl-galactopyranoside), Mauritanian, isorhamnetin-3-O-(2-Glc-rhamnosylrutinoside) and kaempferol 3-O-(2-Glc-rhamnosylrutinoside) [54,55,56]. Organic acids like Malic acid, citric acid, oxalic acid in major concentration and glycolic acid, succinic acid present in minor quantity [57]. Glucotropeolin is present in stems [43], β-sitosterol, β-sitosterol-3-o- β-D-glucopyranoside, octacosanol and 1-tricontanol [58]. Benzylamides are isolated and identified as butanediamide,N1,N4-bis(phenylmethyl)-2(s)-hydroxy-butanediamide,N-benzyl-2,N-benzyl-2-phenylacetamide,N-benzylbenzamide and benzourea [59]. Sodium 1-O-benzyl-β-D-glucopyranoside-2-sulfate (Salvadoside) [60], 5,5'-dimethoxylariciresinol 4,4'bis-O-β-D-glucopyranoside (Salvadoraside) two new lignin glycosides have been reported with syringin, liriodendrin and sitosterol 3-O-glucopyranoside from the stems

[61]. Sticks mainly consist of cellulose, hemicelluloses and lignin [57]. Inorganic constituent $CaSO_4$ present in major amount and Ca, Mg, Na, Ti were relatively abundant and Mn, Cu, Mo, Ni, V, Al, Fe and K are present in minor amount [62] .The flavonoids quercetin was detected in the stem of *S. persica* [54]. Chemical composition of the oil of the stem of the toothbrush was 1,8-cineole(46%),α-caryophyllene (13.4%),β-pinene(6.3%), and 9-epi-(E)-caryophyllene [63]. The existence of a new biomineral bassanite extracted from stems of *Salvadora persica* [64]. Sodium and Chloride partitioning showed their accumulation in root, bark and senescing leaves and less in immature leaves [65].Root contains essential oil [66], β-sitosterol, m-anisic acid, a new urea derivative Salvadourea [67], chloride, sulphate, thiocyanate, nitrate [68]. Benzylisothionate is also constituent of *Salvadora persica* roots may be agent for controlling oral and dental diseases [69] and also shows virucidal activity against Herpes simplex virus-1 [70].Two glucosinolates were isolated from the roots of both Egyptian and Saudi plants; Glucotropaelin sand sinigrin [54,71]. Oleic acid, linolic acid and stearic acids are also present in roots [41]. Seventeen compounds are detected from root oil by GC-MS analysis but the main are benzyl isothiocyanate (70%), limonene (9.4%) and α –pinene (8.7%) [66]. Kaempferol, quercetin, quercetrin, rutin and quercetin glucoside present in roots [54]. Root bark shows presence of alkaloids, silica, salts (mostly as chlorides), resins, Sulfur compounds and smaller amount of tannins and saponins [20]. Roots and Stems both contains thiocyanate but roots are richer in thiocyanate content as compare to stems [72]. The roots and stem extracts contained chloride, sulphate, thiocyanate and nitrate in following concentrations 4.64% and 6.84%, 19.85% and 20.1%, 0.28% and 0.38%,0.05% and 0.05% [73]. Flower and fruit reported to have rutin [54]. Seed oil shows the presence of lauric acid, myristic acid, palmitic acid [74, 75], stearic acid, oleic acid, linolic acid, malvalic acid and sterculic acid [76]. An aerial part contains β–amyrin, betulin, ursolic acid and lupeol [77]. Muscarinic antagonist Methyl Palmitate obtained from aerial parts of *S.persica* [45]. A Sulfated glycoside: Salvadoside (Sodium 1-O-benzyl-β-D-glucopyranoside-2-sulfate) isolated from *S.persica* [61]. The anti-microbial and cleaning effects of miswak have been attributed to various chemicals detectable in its extracts. These effects are believed to be due to its high content of sodium chloride and potassium chloride as well as salvadourea and salvadorine, dition to cyanogenic glycoside and benzylisothiocyanate. Thus, it has been reported that some anionic components naturally occurring in plant species exert anti-microbial activities against various bacteria [71].

Properties

Salvadora persica contains flavanoids, steroids, Glycosides and Alkaloids. Flavanoids the most common group of polyphenolic compounds [78]**.** Flavanoids are responsible for antimicrobial, antiallergic [77, 79]**,** antioxidant, antiradial [80], anti-inflammatory [81], anti-proliferative activity [82]. The core of steroids is composed of seventeen carbon atoms bonded together that take the form of four fused rings: three cyclohexane rings (designated as rings A, B, and C in the figure to the right) and one cyclopentane ring (the D ring). Steroids

are responsible for the anti-inflammatory effect [83]. Alkaloids are a group of naturally occurring chemical compounds which mostly contain basic nitrogen atoms. This group also includes some related compounds with neutral and even weakly acidic properties [84]. These compounds are used as analgesic, anesthetic, anti-tumour, anti-inflammatory, muscle relaxant, antiarrhythmic, anticholinergic [85]. A glycoside is a molecule in which a sugar is bound to a non-carbohydrate moiety, usually a small organic molecule. Glycosides play numerous important roles in living organisms. Many plants store chemicals in the form of inactive glycosides. These can be activated by enzyme hydrolysis,[which causes the sugar part to be broken off, making the chemical available for use. Many such plant glycosides are used as medications like anti-oxidant, anti-inflammatory, laxative, analgesic and heart diseases [86].

Conclusion

Salvadora is a genus of evergreen trees distributed in tropical Africa and Asia extending up to Mascarene Island and China. It belongs to the family Salvadoraceae. Over worldwide number of species are available but In India this genus has two species one is *S. persica* and *S. oleoides. S. persica* is more salt tolerant than *S.oleoides*. From the tradition time chewing sticks of *S.persica* is used as oral hygiene tool and it is also known as Toothbrush tree or miswak tree. Lots of research has been done on its anti-bacterial, anti-microbial, anti-caries, anti-plaque activity. Its extracts shows synergistic effect with other antibiotics like Tetracycline and Penicilline also. All aerial parts of *S. persica* has been ethnomedicinally used as a therapeutic agent for a variety of diseases, as we have illustrated in this article. Moreover, numerous research works have proven its uses beyond the ethnomedicinal ones in experimental animals. Numbers of Pharmaceutical preparations are also available in the market like Toothpaste, Mouthwashes, Endodontic irrigation solution. A number of secondary plant metabolites were isolated from aerial parts of *S.persica*. Despite the wide use of miswak and its containing products, its chemotherapeutic value has not been fully substantiated and the mode of action of its bioactive compounds against diseases has no yet been established. Alkaloids, flavonoids Glycosides which were isolated from this plant may be responsible for its pharmacological activities. The road ahead is to establish specific bioactive molecules, which might be responsible for these actions. Therefore the cultivation, collection, and further pharmacological exploration of *S.persica* are essential.

Preparations

Toothpaste: Some of the known commercial toothpaste produced from *Salvadora persica* plant are:

Sarkan toothpaste, Quali-meswak tooth paste, Epident toothpaste, Siwak-F toothpaste, Fluoroswak, Miswak. [30,87].

Mouthwashes: Miswak-based mouthwash can be used for reducing the plaque [88, 89]**.**

Endodontic irrigation solution: The antimicrobial activity of endodontic irrigation solution of miswak has been reported [42].

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