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Review Article

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Pharmacological Benefits of Miswak Users and Its Impact on COVID-19 Patients – A Review

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Abstract: In the quest of vaccine/medicine for the Covid-19, a major challenge for the intact community on the Earth, the scientists are eagerly involved in the struggle to achieve a new vision in the field of drug discovery. In meantime, we have also forgotten the usage of preexisting medicinal plants and searching the treasure in the dark. To enlighten on, and to dig the hidden boon, this review paper highlights *Salvadora persica*, a miracle twig's various medicinal properties and also about major influence against the viral activities and the asymptomatic conditions in Covid-19 patients of miswak users. It also highlights the literature evidence on the isolated chemical metabolites present in the root and stem of the tree which emphasize its beneficial effects against the bacterial and viral load. This review will hopefully encourage the upcoming search to widen their research on miswak in nCoV of Covid-19 patients and the common people need to document for the regular usage of miswak with brushing the teeth, to attain its properties.

Keywords: *Salvadora persica*, drug discovery, miswak, Covid-19.

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1. INTRODUCTION

The Islamic followers have emphasized to practice the use of Miswak as a Sunnah by the Prophet for maintaining the oral hygiene[1] as the preaching says "*The implementation of the cleaning the mouth with Miswak pleases Allah*". It is a fragment of Greek o- Arab system of medicine and most traditionally used curative tree[2]. According to the literature, there are almost 180 plant species especially meant for the tooth sticks one among which is *Salvadora persica* with good medicinal values of oral hygiene[2]. They have antimicrobial, anti-inflammatory, antipyretic, analgesic, and astringent activities[3]. It is essential to kill the pathogens which enter the mouth with initial entry and upset the human body. This can overcome strongly by using aqueous extract and less active in the alcoholic and non-polar extracts. The tree "Miswak" or "Siwak" known as Arak tree, means to rub or to clean the teeth, a shrub under evergreen category with three meters in height and about 30 cm in diameter. It is called by many names in different languages like Siwak, Mastic, Koyoji, Peelu, Qesam, and Ugaai in Arabic, Latin, Japan, Urdu, Hebrew and Tamil, respectively[4].

1.1 Origin and distribution

It is famously known as the Persian toothbrush tree is broadly distributed throughout the world from the southern region like India, Iran, Iraq, Israel, Egypt, Malaysia, Pakistan to Mauritania in the west region. Also from the north region of North Africa, Sudan, Ethiopia, Central Africa. It is mainly grown in Saudi Arabia and predominantly seen in the Middle East countries. The Figure 1 states that under the report of Botanic Gardens Conservation International (BGCI) & IUCN SSC Global Tree Specialist Group. 2019, *The IUCN Red List of Threatened Species* 2019[6], *Salvadora persica* is considered in the category of least concern as it is not encountering any future threats and the above mentioned areas are the residents of this medicinal plant. So, it is available easily for its predominant usage.

Fig 1. *Salvadora persica* resident areas and distribution throughout the world…

This shrub belongs to the family of Salvadoraceae with class Magnoliopsida[7]. The leaves of this arak tree have succulent oval, thick in texture with the strong smell of mustard. These leaves have medicinal properties to cure piles, cough, asthma, rheumatism, scurvy and other diseases. The berries are red or dark purple when ripened in the tree are taken as dried and fresh. The roots are usually prepared as Miswak sticks and sometimes the stems also. The flowers are green-white which has terminal panicles 10 cm in length. The petals were 1-3 mm in length[8]. The flowers from the tree are used as laxative and stimulant. It has its beneficial effect in the treatment of leprosy and gonorrhea. The bark decoction used for stimulation of menstrual cycle and in fever condition[9].

1.2. Scientific classification

Class : Magnoliopsida
Subclass : Dilleniidae
Order : Capparales
Family : Salvadoraceae
Genus : *Salvadora*
Species : *persica*

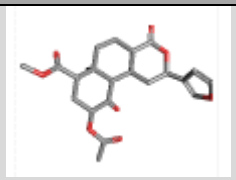
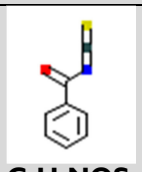
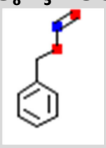
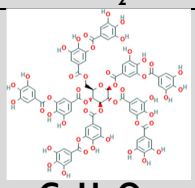
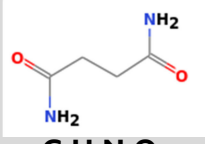
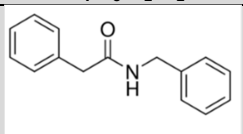
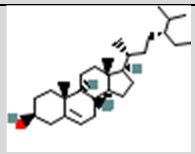
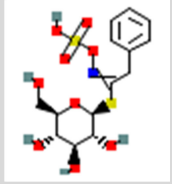
1.3 Alternative Twigs

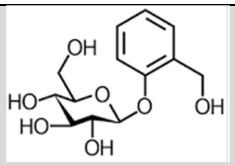
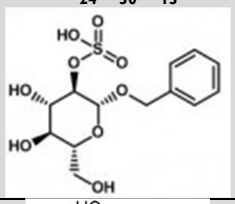
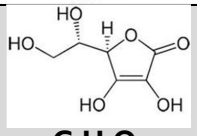
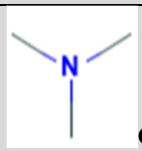
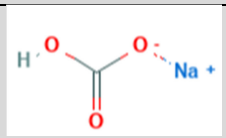
Since 7000 years ago the Babylonians were using the chewing sticks [10]. Instead of the *Salvadora persica* other plants such as *Citrus sinensis, Citrus aurantifolia* and *Azadirachta indica* namely orange, lemon and neem as common names, respectively can also be used to form the toothsticks. The oral hygiene can also be improved by using banyan and mango twigs which have an effective antimicrobial activity[11].

1.4 Artificial toothpaste Vs Miswak

Chlorhexidine and Cetylpyridinium chloride mouthwash had a maximum bactericidal activity when compared with miswak extract (50%). It proved that the alcoholic extract had more effective antibacterial effect than the aqueous extract of *Syzygium* [12].

Table 1. Pharmacological Benefits of metabolites present in the *Salvadora persica*

Chemical compounds	Structure and molecular formula	Pharmacological Benefits
Salvadorian Alkaloid and Salvadorena	 $C_{23}H_{28}O_8$	Antibacterial activity[13]
Benzyl nitrate and Benzyl isothiocyanate (Free and Bound form)	 C_8H_5NOS  $C_7H_7NO_2$	Inhibits the Gram negative Bacteria[14]
Silica and Tannin	 SiO_2	Stain and deposits remover[15]
	 $C_{76}H_{52}O_{46}$	Anti-gingivitis and Anti-plaque [15]
Chlorides and fluorides	Cl^- , F^-	Remineralization of Enamel and Anti-decay effects[15]
Essential oils	-	Buffers the pH of saliva[16]
Butanediamine	 $C_4H_8N_2O_2$	Antibacterial agents[17]
N-benzyl-2-phenylacetamide	 C15H15NO	Antimicrobial agents[17]
β sitosterol	 $C_{29}H_{50}O$	Inhibits the carcinogenic and genotoxic compounds[18]
Glucotropaeolin (Un hydrolysed product of Benzyl isothiocyanate)	 $C_{14}H_{19}NO_9S_2$	Antibacterial activity[18]

Glycosides (Salvadoside and salvadoraside)	 $C_{24}H_{30}O_{13}$ 	Bactericidal effect and stimulatory action on the gingival[19]
Vitamin C	 $C_6H_8O_6$	Tissue repair and Healing, antiscorbutic property to cure the spongy and bleeding gums[20]
Sulphur	$S^{\wedge\wedge}$	Antibacterial effect[21]
Trimethylamine	 C_3H_9N	Decreasing plaque formation antiphlogistic, antibacterial and gingiva-stimulating effects[2]
Sodium bicarbonate	 $NaHCO_3$	Mild Germicidal effect[22]
Resins	 $C_{21}H_{25}ClO_5$	Protect the enamel[23]

SOURCE and credit : https://pubchemdocs.ncbi.nlm.nih.gov/

The metabolites in the miswak is mentioned in the Table 1 are benzyl isothiocyanate, alkaloid (salvodarine), silica, sodium bicarbonate, calcium, fluoride, tannic acids, resins, essential oils and vitamin C where they contribute a strong antimicrobial action generally which get rid off the pathogens in the area where it is applied. The seed oil is applied on the wound for the snake bite [24].

1.5 Bactericidal effect

The strong metabolite from the oil of root extract was isolated and reported to be benzyl isothiocyanate of about 90 percent and benzyl nitrate with 10 percent which prevents the carcinogenic effect. It also has an antiviral effect against the herpes simplex virus 1 (HSV-1) with high concentration. The growth and its activity of *Streptococcus mutans* is also controlled by this metabolite benzyl isothiocyanate and differ from the action of amphicillin[25]. Also the alkaloid salvadorine was reported for its high bactericidal effect[26].According to various studies, miswak has metabolites which inhibit the plaque against the oral activity. The extracts of *Salvadora persica* has more antimicrobial activity against Aggregatibacter *actinomycetemcomitans* [27]. The miswak twigs showed inhibition zones against the bacteria such as *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Lactobacillus acidophilus* and *Haemophilus influenzae* [28]. The extract of *Salvadora persica* has antimicrobial effects against the microbes such as *E. faecalis* and *Streptococcus mutans*. Additionally, it has effect on *Prevotella intermedia* and *Treponema denticola* with critical periodontal disease. It is proved that the bacterial count in 40 samples after the miswak usage reduced less than 200 CFU/100µl. Also the ethanolic and aqueous extracts of *Salvadora persica* were found to have about 40-45% of decreased bacteria[29]. The presence of glucotropaeolin, unhydrolyzed form instant used powders of the *Salvadora persica* showed more antibacterial activity than the aqueous extract[30]. The miswak has an selective inhibition of the bacteria in the saliva such as *Eikenella corrodens, Prevotella intermedia , Capnocytophaga sputigena, Lactobacillus*

acidophilus, Streptococcus sanguis, Streptococcus salivarius, Fusobacterium nucleatum, Streptococcus oralis, and *Streptococcus mitis* etc. [31] and reported that the Sudanese population with periodontal miswak usage had recovered dental problems than the toothpaste users indicating its antibacterial effect.

1.6 Analgesic and Anti plaque effect

Miswak has an effective analgesic effect than the chemical ones. They have their thermal stimulus through skin pain receptors and proved to have a moderate pain relief in the oral pain mucosa. This analgesic effect was also tested in the toothache patient who on regular miswak usage reduced their ache[32]. The miswak users had lower cases of plaques and gingival bleeding reported. The miswak on usage increased the calcium level in the saliva inturn in remineralization of the tooth[33] and the chloride increased the inhibition of calculus formation. Dental tooth loss was reported to be very less in adults on miswak frequent usage. This proves that it has anti-carious effect[34].

1.7 Antimycotic activity and Antidiabetic activity

The aqueous extracts of the miswak had a potential to inhibit the fungi *Candida albicans* for about 36 hours with only about 15% of its concentration. Also these extracts initiates the pancreatic beta cells to prevent anti-diabetic effect in Streptozotocin induced diabetic rats[35]. *Salvadora persica* with oil of *Brassica campestris* L. (Mustard) is applied on affected areas for the treatment of ringworm. The study confirms that the patients with renal transplant on using miswak found to be lower in the oral candidiasis than the patients used with normal toothsticks [36].

1.8 Anti hyperlipidemic activity

The hypercholesterolemia induced rats found to reduce the cholesterol level by regular usage of lyophilized stem decoction of *Salvadora persica* extract. Similarly, they have a significant anti-inflammatory effect which on daily intake acts as an antiulcer agent which has proved that recovery of gastric mucosa in treated rats[37].

1.9 Antioxidant activity

The miswak extract has effective antioxidant activity and its efficiency increases when it is actually taken with mint extract where about 60% of the bacteria are removed within 30 mins. It has enzymatic antioxidants such as peroxidase, catalase and polyphenoloxidase

1.10 Antiviral activity

The extract with 5-10% had shown no toxicity on *in vitro* application[38] and study proves that the Herpes simplex HSV-1 viral lesions and ganglia were reduced in the BHK (Baby Hamster Kidney) cells and in the skin of infected laboratory rats when applied with the 5% of ethanolic extract of *Salvadora persica* [39]. Also the compound Benzyl isothiocyante acts on the prevention of HSV-1 replication and cell free virus in which the roots of the *S.persica* is found to be Irrigant [40]. In his investigation when the concentration of *S.persica* extract increased the viral concentration decreased accordingly which proves that it has antiviral effect. It was also reported that the extract induces the arrest of the G2 and M phase in the A375 cells and initiates the apoptosis in this Human Melanoma cells[41].

1.11 Use of miswak in the current scenario – A Case study

World Health Organisation (WHO) has declared the Covid–19 caused by novel Coronavirus as a public emergency and a pandemic outbreak in January, 2020 and till the mid end of June, 2020 the report says about 8,393,096 active cases have been affected worldwide in which 450, 452 deaths and 4,408,937 cases were recovered whereas in India, 367,264 of total cases and 12,262 deaths with about recovery cases of 194,438 have been reported. Moreover, almost 215 countries are affected till the Mid-end of June, 2020[42]. The major precautionary measures taken by WHO are educating the public to be in social distancing, regularly washing the hands with soaps and sanitizers, using masks etc. The main mode of the infection is via the mouth and nasal tracts. By the consolidated review of literature mentioned above with various pharmacological properties of *Salvadora persica* and it can be recommended to the government to highlight the importance of usage of miswak for tooth brushing/mouthwash regularly to the public in this emergency period to get rid of the coronavirus from the mouth and to prevent the respiratory syndrome. According to the Times of India (TOI) reports dated on April 4th, 2020, that asymptomatic conditions were registered of more than 80% of the participants of the Tablighi Jamaat conference in Delhi who tested positive showed no symptoms. The attendees of the conference were from 23 states with union territory of which 4291 cases[43] which found to be asymptomatically positive where only 27 death cases were reported. On analysis ,the crude death rate was found to be 6.29 units per 1000 persons per time period. The percentage of death rate was evaluated to be 0.62% which is less than 1%. The Sunnah practice of majority people of the conference were Miswak users who have regularly undertaken the pharmacological benefits of the arak tree and as per the analysis 99% of them were found to be asymptomatic which was found to be contradictory with tag given to them as Superspreaders. Also they were the first forefront plasma volunteer donors who were negative for symptomic Covid-19 to carry out the plasma therapy in affected Covid patients. Analogous to the analysis, the reports emphasis that the virologists to study the strain and its virulence whereas the isolated samples of the participants tested positive show no signs of having symptoms and others have only mild symptoms and didn't require ventilators[44.] Therefore the regular practice of miswak usage while in tooth brushing may be the main scenario behind their asymptomatic conditions with following pharmacological properties has to be proved and paved the way for a novel stance of research on *Salvadora persica*'s impact on the Novel coronavirus.

2. CONCLUSION

The practice of using miswak (*Salvadora persica*) regularly proves its major properties of bactericidal effect and antiviral effects. We are in the era of Pandemic outbreak of COVID-19, when on regular use of the miswak stick for tooth brushing/mouthwash thereby the bacterial and viral load in the mouth is reduced to a greater extent. WHO recommends to focus on the preventive measure to be away from the coronavirus by social distancing, regularly washing the hands with Soaps and sanitizers, using Masks etc. This review paper with the literature evidence and case study

strongly recommends the government and many NGOs to continuously insist the public and also the COVID 19 patient for miswak usage regularly to get a controlled effect on this disease.

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4. CONFLICT OF INTEREST

Conflict of interest declared none.

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