

# A review of the therapeutic effects of using miswak (*Salvadora Persica*) on oral health

Mohammad M. Haque, BDS, MPH, Saeed A. Alsareii, SB (Surg), JBGS.

## ABSTRACT

يُستخرج السواك من جذور شجرة الآراك، وأغصانها، وسيقانها، وقد استخدمت منذ آلاف السنين كطريقة تقليدية لتنظيف الأسنان في أجزاء كثيرة حول العالم وعلى مدى آلاف السنين. وقد أظهر عدد من الأبحاث العلمية أن سواك الآراك يمتلك تأثيراً مضاداً للبكتيريا، ومواد مضادة للفيروسات، والفطريات ومكافحة للتسوس وتجمع البلاك. وهناك بعض الدراسات التي تزعم أن السواك يحوي مواد مضادة للأوكسدة، ومواد مخففة للالتهاب، ومضادات الالتهاب. كما ويؤثر استخدام السواك تأثيراً مباشراً على تركيب اللعاب. وأكدت العديد من الدراسات السريرية أن التأثيرات الميكانيكية والكيميائية في فعالية تنظيف السواك قد تساوي وأحياناً أكبر من تأثير فرشاة الأسنان. ويهدف هذا المقال لاستعراض مختلف الآثار العلاجية لسواك الآراك على صحة الفم مما يساعد القارئ على فهم مغزى وأهمية هذا الأداة الصحية الطبيعية التقليدية.

Miswak is a traditional chewing stick prepared from the roots, twigs, and stem of *Salvadora persica* and has been used as a natural method for tooth cleaning in many parts of the world for thousands of years. A number of scientific studies have demonstrated that the miswak (*Salvadora persica*) possesses antibacterial, anti-fungal, anti-viral, anti-cariogenic, and anti-plaque properties. Several studies have also claimed that miswak has anti-oxidant, analgesic, and anti-inflammatory effects. The use of a miswak has an immediate effect on the composition of saliva. Several clinical studies have confirmed that the mechanical and chemical cleansing efficacy of miswak chewing sticks are equal and at times greater than that of the toothbrush. The present article provides a review of the various therapeutic effects of *Salvadora persica* on oral health, which will help to elucidate the significance and importance of this indigenous oral hygiene tool.

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From the Department of Preventive Dental Sciences (Haque), College of Dentistry, and the Department of Surgery (Alsareii), College of Medicine, Najran University, Najran, Kingdom of Saudi Arabia.

Address correspondence and reprint request to: Dr. Mohammad M. Haque, Department of Preventive Dental Sciences, College of Dentistry, Najran University, PO Box 1988, Najran 61441, Kingdom of Saudi Arabia. E-mail: drhaquem@gmail.com

Oral health is an integral part of overall health. Poor oral health is associated with many systemic diseases. The oral cavity is the major portal of entry, source, and site of many diseases affecting the general health status.<sup>1</sup> Well-being and quality of life, which is measured along functional, psychosocial, and economic dimensions, is related to oral health. Poor oral and craniofacial health affects diet, nutrition, sleep, psychological status, social interaction, school, and work.<sup>1</sup> Therefore, the maintenance of oral health is of vital interest and can be achieved mainly by mechanical and chemical means. The most common and modern mechanical method of tooth cleaning is the use of a toothbrush in combination with a dentifrice.<sup>2</sup> However, a wide range of methods exists to maintain and preserve oral and dental hygiene around the world. Despite the widespread use of toothbrushes and dentifrices, natural methods of tooth cleaning using chewing sticks are observed in several parts of the world.<sup>3</sup> In many traditional cultures, plastic-bristle brushes are not used. Instead, the use of herbal “chewing sticks” is common. Chewing sticks are usually taken from plants, shrubs, or trees with high anti-microbial activity.<sup>4</sup> For thousands of years, the use of plants have been closely associated with dental hygiene and therapeutic practices.<sup>5</sup> The use of chewing sticks, which can be derived from various plants, are spread throughout Asia, Africa, South America, and the Middle East, including Saudi Arabia, and throughout the Islamic countries.<sup>3,6,7</sup> Chewing sticks are known by different names in different cultures. These sticks are called ‘miswak’ in Arabic, ‘koyoji’ in Japanese, ‘qesam’ in Hebrew, ‘qisa’ in Aramaic, and ‘mastic’ in latin.<sup>8</sup> ‘Miswak’ is obtained from *Salvadora persica* and is the most extensively used plant to prepare chewing sticks.<sup>9</sup> In the Middle East, the most common

source of miswak is the Arak Tree (*Salvadora Persica*).<sup>10</sup> The Arak tree is also known as the “toothbrush tree.” The miswak is usually obtained from the roots of the Arak tree, although some sticks are also made from its twigs and stem.<sup>8,11</sup>

“Miswaq” (which has synonyms in different Arabic dialects and countries, including “miswaak,” “miswak,” “miswaki,” “meswak,” “mswaki,” “sewak,” “siwak,” and “siwaki”) is an Arabic word. The conventional meaning of miswak is ‘tooth-cleaning stick’ or “stick used on teeth and gums to clean them”.<sup>7,12,13</sup> Sticks from these plants are usually chewed or tapered on one end until they became frayed into a brush-like form, which is then used to clean the teeth in a similar manner to a toothbrush.<sup>14</sup> Most chewing sticks share a common design, although they often have different diameters<sup>3</sup> (Figure 1). During teeth and oral cleaning with miswak, a pen-like grip is used to hold the stick in one hand, and the brush-end is used with an up and down or rolling motion.<sup>15,16</sup> Two-finger and 5-finger grip techniques have been documented in the literature.<sup>17</sup> When the brush-like edge is shredded after being used several times, the stick becomes ineffective. The edge is subsequently cut off and further chewed to expose a fresh end. In this way, the stick can be used for several weeks.<sup>3,18</sup> Historically, the miswak is one of the oldest known oral hygiene tools, but it is still being used by millions of people in Africa, South America, the Middle East, and Asia.<sup>19,20</sup> Several explanations for the cleansing efficacy and the promotion of good oral health by miswak have been offered, including: (i) the mechanical effects of its fibers,<sup>3</sup> (ii) the release of beneficial chemicals, such as trimethylamine, salvadorine, mustard oil, vitamin C, resins, flavodine, saponins, sterol, and fluoride might all play an important role<sup>21</sup> or the combination of (i) and (ii). Taking into consideration the historical, religious, social, and cultural implications of the use of miswak (*Salvadora*



**Figure 1** - Typical chewing sticks (Miswaq) prepared from *Salvadora persica* of different diameters.

*Persica*) in the field of oral hygiene, the present article is an attempt to provide a comprehensive overview of the various therapeutic effects of miswak (*Salvadora Persica*) on oral health and its enormous contribution to the maintenance of oral hygiene. The existing literature was searched electronically using PubMed, and Google Scholar between the years 1968 and July 2014. The search was performed using a variety of keywords in different combinations, and only articles published in the English language were included. A manual search was also completed for relevant articles under this topic.

**Historical and religious background.** The exact origin of mechanical devices for cleaning teeth is unknown. However, since ancient times and well before the invention of the modern toothbrush, civilized people have used some type of cleaning instrument to clean and preserve their teeth. The first early devices include the tooth stick, referred to as the toothpick, and the wood mop, twig brush, miswak, or siwak.<sup>22</sup> Toothpicks have been traced as far back as prehistoric times. They have been excavated along with other articles of toiletry in the ancient Babylonian city of Ur, which flourished in approximately 3500 BC.<sup>22</sup> The Greek sophist Alciphron in the second century BC recommended the use of a toothpick to clean the “fibrous residue” remaining between the teeth after meals. Alciphron used the Greek word ‘karpfos’ to describe the toothpick, which means ‘blade of straw’. The Romans also used toothpicks from the mastic tree (*Pistacia lentiscus*).<sup>22</sup> The historical forerunner of the modern toothbrush might be the Babylonian fiber brush, called the “chew stick,” “fiber stick,” or “fiber pencil,” which was used as early as 3500 BC. It was a wooden stick cut to 5 or 6 inches in length. One end was macerated to separate the fibers to about one quarter of an inch. The Arabs call this tool siwak or miswak.<sup>3,22</sup>

Before the emergence of Islam, people in Arab countries used miswak derived from root of the ‘Arak’ tree (*Salvadora persica*).<sup>12</sup> Miswak was used by the ancient Arabs to keep their teeth white and shiny, as white and shiny teeth were associated with beauty and attractiveness. Another possible reason for its use is its contribution to ritual purity. In the early Islamic period, the use of miswak became a part of a cultivated and elegant mode of life.<sup>8</sup> The use of miswak as a tool of basic oral hygiene has been incorporated into Islam as part of religious practice.<sup>7</sup> Islam has given an elevated status to the miswak, and its importance has been stressed in many Prophetic narratives by Muslim commentators. The Prophet Mohammad (Peace Be Upon Him) strongly recommended the use of miswak and was himself a fervent supporter of its use. According to

Muslim commentators of Prophetic narration, the use of miswak was a constant practice of Prophet Mohammad (Peace Be Upon Him) prior to sleeping, after rising, after entering the house, before and after meals, during fasting, and before recitation of prayers and reading of the holy texts. Since then, the miswak has been featured prominently in Islamic hygienic jurisprudence. In one narration, the Prophet Mohammad (Peace Be Upon Him) said, "If I had not found it hard for my followers or the people, I would have ordered them to clean their teeth with Siwak (Miwak) for every prayer".<sup>23</sup> In another narration, the Prophet Mohammad (Peace Be Upon Him) said "The Siwak is a means of purification for the mouth and a source of achieving the pleasure of Allah".<sup>24</sup> Thus, the influence of Islam on the spread and use of chewing sticks in different parts of the world is significant.<sup>25</sup> The religious and spiritual impact of the miswak probably is the principal reason why it is extensively used by Muslims all over the globe.<sup>14</sup> Today, both the traditional miswak and the modern toothbrush are used commonly in Muslim countries. Utilization of the desert plant miswak (*Salvadora persica*) is widespread in Saudi Arabia,<sup>26</sup> and young people from Saudi Arabia are increasingly combining modern and traditional oral hygiene methods.<sup>11</sup>

#### Plant description and scientific classification.

Miwak is derived from a plant species of *Salvadora persica* belonging to the family *Salvadoraceae*. The full taxonomic classification of *Salvadora persica* is given in Table 1.

*Salvadora persica*, or the Arak tree, is known in English as the "tooth brush tree." It is an upright evergreen that grows as a small tree or shrub with a crooked trunk. It is seldom more than one foot in diameter, reaching a maximum height of 3 meters. The leaves are small, rounded to ovate, slightly fleshy, thick and succulent, having a strong smell of cress or mustard. The fragrant flowers are small. The fruits are like fleshy berries; small and barely noticeable. They are edible in both fresh and dried form.<sup>13,27</sup> *Salvadora persica* is capable of surviving in extreme conditions and can tolerate very dry environments to highly saline soils.<sup>28</sup> It is widespread in arid regions, on saline lands, in coastal regions, thorn shrubs, desert flood plains, and grassy savannahs.<sup>29</sup> It is native to the Arabian Peninsula, Africa, Iraq, India, Pakistan, and Sri Lanka.

**Functions of different components of miswak on oral health.** A variety of natural bioactive components have been identified in *Salvadora persica* extracts by researchers. These constituents are considered to be essential for good oral and dental hygiene. The name

**Table 1** - The taxonomic classification of *Salvadora persica*.

Classification of <i>Salvadora persica</i>	
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Brassicales
Family	Salvadoraceae
Genus	Salvadora
Species	Persica oleoides
Binomial name	Salvadora persica

and functions of the different bioactive components are discussed in Table 2.

**Therapeutic effects of miswak on oral health. Antibacterial effects.** Much effort has focused on examining the antibacterial activity of miswak extracts against a variety of human pathogens. Several studies have shown that miswak (*Salvadora persica*) has significant antimicrobial activity against both aerobic and anaerobic bacteria. By using disc diffusion and micro-well dilution assays, Al-Bayati and Sulaiman<sup>30</sup> investigated antimicrobial activities of aqueous and methanol extracts of *Salvadora persica*. The authors used 7 isolated oral microorganisms to test the activity of the extracts: *Staphylococcus aureus*, *Streptococcus mutans*, *Streptococcus faecalis*, *Streptococcus pyogenes*, *Lactobacillus acidophilus*, *Pseudomonas aeruginosa*, and *Candida albicans*. According to both antimicrobial assays, the aqueous extract of *Salvadora persica* was active against all tested pathogens and showed more inhibitory activity than did the methanol extract, which was resisted by *Lactobacillus acidophilus* and *Pseudomonas aeruginosa*. Among all the tested pathogen, *Streptococcus species* were the most sensitive to aqueous extract and the highest inhibitory activity was seen against *Streptococcus faecalis* (zone of inhibition: 22.3 mm; minimum inhibitory concentration [MIC]: 0.781 mg/ml). Both extracts had equal antifungal activity against *Candida albicans* based on the turbidity test (MIC: 6.25 mg/ml). An in vitro study<sup>20</sup> showed that the whole miswak pieces (without extraction) embedded in agar or suspended above the agar plate had strong antibacterial effects against bacteria implicated in periodontitis and caries progression (*Streptococcus mutans*, *Lactobacillus acidophilus*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Haemophilus influenzae*). Based on their research, Sofrata et al<sup>31</sup> suggested that benzyl isothiocyanate (BITC) is the main antibacterial component of *Salvadora persica* root chewing sticks with a high killing activity against the gram-negative periodontal pathogens *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*.

**Table 2** - Bioactive components of miswak (*Salvadora persica*) and their effects on oral health.

Constituents	Function	Reference
Silica	<ul style="list-style-type: none"> <li>Acts as an abrasive material to remove plaque and stains on the teeth</li> </ul>	Khoory <sup>16</sup> Al-Lafi & Ababneh <sup>63</sup>
Tanins (Tannic acid)	<ul style="list-style-type: none"> <li>Reduces clinically detectable gingivitis               <ul style="list-style-type: none"> <li>Reduces plaque and gingivitis</li> </ul> </li> <li>Reduces <i>Candida albicans</i> counts when denture bases were treated with tannic acid</li> </ul>	Chawla <sup>52</sup> Kubota et al <sup>90</sup> Gazi et al <sup>68</sup> Kubota et al <sup>90</sup>
Resins	<ul style="list-style-type: none"> <li>Has a protective action against dental caries by forming a layer over the enamel surface</li> </ul>	Al-Lafi & Ababneh <sup>63</sup>
Alkaloids (Salvadorine)	<ul style="list-style-type: none"> <li>Have anti-fungal effects</li> <li>Have bactericidal, and stimulatory effects on gingiva               <ul style="list-style-type: none"> <li>Have cytotoxic activity</li> </ul> </li> </ul>	Noumi et al <sup>19</sup> Darmani et al <sup>91</sup>
Essential (volatile) oils	<ul style="list-style-type: none"> <li>Possess a characteristic aroma, exert carminative &amp; antibacterial actions, and stimulate the flow of saliva</li> </ul>	Rajabalian et al <sup>92</sup> Akhtar & Ajmal <sup>93</sup> Tubaishat et al <sup>53</sup>
Sulphur	<ul style="list-style-type: none"> <li>Have bactericidal effects</li> </ul>	Tubaishat et al <sup>53</sup> Mohammad & Turner <sup>94</sup>
Vitamin C	<ul style="list-style-type: none"> <li>Helps in healing, tissue repair</li> </ul>	Al Sadhan & Almas <sup>7</sup> Tubaishat et al <sup>53</sup>
Sodium bicarbonate	<ul style="list-style-type: none"> <li>Acts as a mild abrasive and can be used as a dentifrice</li> </ul>	Tubaishat et al <sup>53</sup> Mohammad & Turner <sup>94</sup>
Calcium	<ul style="list-style-type: none"> <li>Inhibits demineralization and induces the remineralization of enamel</li> </ul>	Gazi et al <sup>68</sup> Tubaishat et al <sup>53</sup>
Fluoride	<ul style="list-style-type: none"> <li>Anticariogenic activity and tooth remineralization</li> </ul>	Almas & al-Lafi <sup>10</sup> Tubaishat et al <sup>53</sup>
Chloride	<ul style="list-style-type: none"> <li>Inhibits the formation of calculus</li> </ul>	Akhtar & Ajmal <sup>93</sup>
N-benzyl-2-phenylacetamide	<ul style="list-style-type: none"> <li>Inhibits human collagen-induced platelet aggregation and has antibacterial activity against <i>Escherichia coli</i></li> </ul>	Khalil <sup>37</sup>
Benzyl isothiocyanate	<ul style="list-style-type: none"> <li>Act as chemo-preventive agents</li> <li>Prevent carcinogenic and genotoxic compounds               <ul style="list-style-type: none"> <li>Has bactericidal activity</li> <li>Has virucidal function</li> </ul> </li> </ul>	Al-Dosari et al <sup>95</sup> Attar <sup>96</sup> Al-Lafi & Ababneh <sup>63</sup> Al-Bagieh & Weinberg <sup>97</sup> Brown & Jacobs <sup>98</sup> Al-Bagieh <sup>99</sup>
Trimethylamine	<ul style="list-style-type: none"> <li>Has antibacterial, antiphlogistic, and gum-stimulating effects</li> </ul>	Hattab <sup>12</sup> Darmani et al <sup>91</sup>
Flavonoids	<ul style="list-style-type: none"> <li>Has cytotoxic activity</li> </ul>	Rajabalian et al <sup>92</sup>

The strong and rapid killing also exclusively affects gram-negative bacteria, including medically important pathogens such as *Salmonella enterica*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae*.

Poureslami et al<sup>32</sup> conducted 3 in vitro studies including: 1) in vitro evaluation of the antibacterial effects of miswak extract on selected bacteria (*Streptococcus Sanguis*, *Streptococcus salivarius*, *Eikenella corrodens*, and *Porphyromonas gingivalis*), 2) the antibacterial effects of Iranian toothpaste containing miswak extract against dental plaque in comparison with the placebo toothpaste 3) a comparison of the antibacterial effects on dental plaque between 2 toothpastes containing miswak extract (one produced in Iran and the other in Switzerland). The results of 3

studies demonstrated that miswak extract, alone or in combination with toothpaste, can affect the growth of dental plaque bacteria. Therefore, miswak extract can be used in mouth rinses and toothpastes because of its antibacterial effects. A clinical study on the immediate antimicrobial effects of a toothbrush and miswak on cariogenic bacteria was carried out by Almas and Al-Zeid.<sup>18</sup> The authors found out that the reduction of *Streptococcus mutans* was significantly greater using miswak in comparison with tooth brushing, and there were no significant differences in *Lactobacilli* reduction. Therefore, authors concluded that miswak may have an immediate antimicrobial effect and that *Streptococcus mutans* were more susceptible to the antimicrobial activity of miswak than *Lactobacilli*. Salehi & Momeni<sup>33</sup>

compared the antibacterial effects of Persica™ (Pursina Pharmaceutical Company, Tehran, Iran) mouthwash with chlorhexidine on *Streptococcus mutans* in orthodontic patients. The use of Persica™ mouthwash resulted in a significant reduction in *Streptococcus mutans* colonies, although it was not as potent as chlorhexidine. An in vivo evaluation<sup>34</sup> showed that herbal mouthwash such as Persica™ contains *Salvadora persica*, mint, and yarrow extracts can significantly decrease the *Enterococcus faecalis* and *Candida albicans* counts in the oral cavity.

Ten percent water extraction of *Salvadora persica* is an effective antimicrobial agent when utilized clinically as an irrigant in the endodontic treatment of teeth with necrotic pulps.<sup>35</sup> Based on their in vitro study, Elangovan et al<sup>36</sup> revealed that aqueous extracts of neem (*Azadirachta indica*) showed the greatest antimicrobial activity against *Streptococcus mutans*, while miswak (*Salvadora persica*) extracts showed superior antimicrobial activity against *Lactobacillus acidophilus*. The constituent of *Salvadora persica*, such as N-benzyl-2-phenylacetamide, had shown moderate antimicrobial activity against *Escherichia coli*. The activity of the extracted N-benzyl-2-phenylacetamide from the miswak at a concentration of 87µg/mL was equivalent to 20µg/mL of gentamicin.<sup>37</sup> At 50% concentration, the miswak extract was effective in inhibiting *Streptococcus mutans*, *Streptococcus sanguis*, and *Streptococcus faecalis*. At 5% and 10% concentrations, the extract was effective only against *Streptococcus faecalis*. It was concluded that miswak (*Salvadora persica*) had an antibacterial effect at higher concentrations and that there was no difference in the antibacterial effects of fresh and one-month-old Miswak.<sup>38</sup> Almas and Stakiw<sup>39</sup> evaluated the effects of fresh and 18-year-old stored miswak (*Salvadora persica*) at aqueous concentrations of 10% and 50% on 5 different microbes using a blood agar ditch method. After 48 hours of incubation at 4°C, it was found that all miswak extracts (at both 10% and 50%) had an antimicrobial effect against *Streptococcus faecalis*. However, only the 50% extract of fresh miswak had an inhibitory effect against *Streptococcus mutans*. AbdElRahman et al<sup>40</sup> assessed whether the crude extracts prepared from the roots and twigs of *Salvadora persica* inhibited the growth of some selected oral microbes (*Streptococcus mutans*, *Lactobacillus acidophilus*, *Actinobacillus actinomycetemcomitans*, *Actinomyces naeslundii*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Candida albicans*). The author used sterile distilled water, 96% ethanol, 2% acetic acid, and ethyl acetate as solvents, and found that *Streptococcus mutans* was the most susceptible strain to all extracts, while *Lactobacillus acidophilus* was resistant to all extracts except for

the root-ethanolic extract. Compared with the other solvents, the ethanolic extracts showed the strongest antimicrobial activity. Within the ethanolic extracts, the root extract was more potent than the twig extract. The stem-water extract was found to have the lowest potency. In the end, the author concluded that crude miswak extracts showed low to moderate antimicrobial activity compared with standard antimicrobial agents, such as 0.2% aqueous chlorhexidine and tea tree oil.

Almas and Al-Bagieh<sup>41</sup> reported that aqueous extracts of *Salvadora persica* bark and pulp, as well as whole miswak at a concentration of 10% and 50%, were effective against *Streptococcus faecalis*. Fifty percent aqueous extract of bark and the whole extracts of *Salvadora persica* had antimicrobial effects on *Streptococcus mutans*. However, no anti-microbial effect was observed on *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Candida albicans*. Alali et al<sup>42</sup> reported that the volatile oil of Jordanian *Salvadora persica* stems exhibits potent antibacterial activity against both Gram-positive and Gram-negative bacteria. The diameter of zones of growth inhibition was approximately 13 mm for *Escherichia coli*, 12 mm for *Staphylococcus aureus*, 3 mm for *Bacillus subtilis*, and 3.8 mm for *Pseudomonas aeruginosa* strain. Moreover, the volatile oil exhibits significant activity against resistant strains of *Pseudomonas aeruginosa* with zones of growth inhibition of approximately 2.9 mm and *Staphylococcus aureus* of 3 mm in diameter. Alireza et al<sup>43</sup> studied the effects of methanolic extracts of *Salvadora persica* on oral bacterial strains (*Staphylococcus*, *Streptococcus*, *Lactobacillus*, *Enterococcus*, and *Escherichia*) isolated from saliva. This was investigated using the agar disc diffusion and microdilution methods. The authors found that a methanolic extract of *Salvadora persica* was effective in the growth inhibition of all strains tested, although it was significantly more effective on gram-positive bacteria (6.5-12 mm) than on Gram-negative bacteria (1-8 mm).

**Antifungal effects.** Studies have indicated that Miswak (*Salvadora persica*) possesses antifungal properties. Noumi et al<sup>19</sup> showed that the diluted acetone extract of dry *Salvadora persica* stems demonstrated the highest inhibitory activity against *Candida albicans*, *Candida glabrata*, and *Candida parapsilosis* strains (with a zone of inhibition range of 10.33-15 mm) using an extract concentration of 300 mg/ml. However, methanol and ethyl acetate extracts of dry *Salvadora persica* stems were active only on one oral *Candida albicans* isolate. Other strains, such as *Pichia jadinii*, *Candida atlantica*, *Candida famata*, and *Candida maritima* were resistant to both dry and fresh *Salvadora persica* stem extracts. From this study, the authors have demonstrated that the

dried miswak has a greater antifungal activity against several *Candida strains* (both oral isolates and reference strains) than the fresh plant. These results indicate that extracts of miswak may contain compounds with therapeutic potential against different *Candida strains*, and hence, they can potentially be used as therapeutic agents. Renal transplant patients (RTPs) who used a miswak (*Salvadora persica*) for oral hygiene were found to have a significantly lower prevalence of oral candidiasis compared with other RTPs.<sup>25</sup> From their experiment, Alali et al<sup>42</sup> found that the volatile oil from Jordanian *Salvadora persica* stems had significant inhibitory effects against *Candida albicans* (with zones of growth inhibition of 16 mm) and *Trichosporon cutaneum* (with zones of growth inhibition of 12 mm). Water- and alcohol-based extract of the plant showed good antimicrobial activity against *Candida albicans*, and the diameters of the zones of growth inhibition were approximately 9 mm and 11 mm. However, Al-Bayati and Sulaiman<sup>30</sup> found that both aqueous and methanol extracts of *Salvadora persica* were active against an oral *Candida albicans* strain, with an MIC value of 6.25 mg/ml.

Al-Bagieh et al<sup>44</sup> investigated the antimycotic effect of the aqueous extract of the miswak plant roots. Various concentrations of aqueous extract of Miswak prepared with Sabouraud medium were inoculated with an oral isolate of *Candida albicans*. The authors found that at concentrations of 15% or more, the extract had a fungistatic effect for up to 48 hours. The authors suggested that this antimycotic effect was probably due to one or more of the root contents, which include chlorine, trimethylamine, alkaloid resin, and sulphur compounds. Al-Obaida et al<sup>45</sup> showed that 20% Miswak extract is an effective antifungal and antibacterial agent against *Candida albicans* and *Enterococcus faecalis*. Saadabi<sup>46</sup> reported a high antifungal activity of the *Salvadora Persica* extract against *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus niger*, and *Candida albicans*. An in vitro assessment by Paliwal et al<sup>47</sup> showed that antifungal activity of 50% ethanolic extract of *Salvadora persica* leaf against *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus xylinium* was comparable to Clotrimazole, though the extract did not show any significant activity against *Candida albicans*. The antifungal activity of solid and pulverized *Salvadora persica* was examined against reference strains and the clinical isolates of oral *Candida species* (*Candida albicans*, *Candida tropicalis*, *Candida krusei*, *Candida guilliermondii*, *Candida dubliniensis*, and *Candida glabrata*) using an agar diffusion test by Alili et al.<sup>48</sup> The authors found from this investigation that solid test specimens of *Salvadora persica* exhibited

strong antifungal activity against all *Candida species* tested, whereas pulverized *Salvadora persica* revealed no antifungal activity. Parameters such as the storage and incubation time, as well as the diameter of the sticks, influenced the level of growth inhibition. Naeini et al<sup>49</sup> had reported from an in vitro study that the alcoholic extract of *Salvadora persica* was found to have strong to moderate activity against different pathogenic *Candida species*, including *Candida albicans*, *Candida dubliniensis*, and *Candida glabrata*, whereas *Candida parapsilosis* and *Candida krusei* were shown to be resistant. Hexane, ethanol, ethyl acetate, and chloroform extracts of *Salvadora persica* had significant inhibitory effects on *Enterococcus faecalis* and *Candida albicans*. Similarly, a hexane extract of *Salvadora persica* was found to exhibit maximum antimicrobial activity against *Enterococcus faecalis* and *Candida albicans*.<sup>50</sup>

**Anti-viral effects.** The effects of BITC (a compound isolated from *Salvadora persica* root) on herpes simplex virus-1 (HSV-1) was investigated by Al-Bagieh et al.<sup>44</sup> The results of his plaque reduction assay indicated that BITC has a virucidal activity against HSV-1 at a concentration of 133 µg/ml. Thus, the authors supported the use of miswak (*Salvadora persica*) as a preventive measure for controlling oral infections.

**Anticariogenic effects.** Numerous epidemiological and laboratory research have suggested that miswak (*Salvadora persica*) has a strong anti-decay effects. A pilot and cross-sectional study by Norton and Addy<sup>51</sup> among adults in Ghana showed that the rate of plaque formation and the development, and progression of caries was less in miswak users than in those using artificial toothbrushes. It was also demonstrated in studies that miswak has anti-decay effects given its fluoride content.<sup>52,53</sup> Moreover, the hot taste of miswak plus the chewing effects of the stick can increase salivary secretion, which in turn increases its buffering capacity.<sup>12</sup> From their cross-sectional survey in Zanzibar, Petersen and Mzee<sup>54</sup> found that the caries prevalence rate was higher in urban areas than in rural areas, where the traditional use of miswak was more frequent than toothbrush use. Darmani et al<sup>55</sup> found that the aqueous extracts of miswak and derum (Walnut tree; *Juglans regia*) were both able to significantly inhibit the growth of cariogenic bacteria. Ezoddini-Ardakani<sup>56</sup> demonstrated the efficacy of miswak in preventing dental caries in a clinical trial carried out on 380 second-year high school students in the city of Yazd, Iran. Three hundred and thirty students continued the study until the end; in the case group, 174 students used miswak for one year, and in the control group, 156 students used toothbrush for one year. The training provided and number of cleaning

sessions per day were the same for 2 groups. The data showed a significant increase (55%) in the rate of dental caries for each tooth in the control group compared to the case group. The risk of dental caries for each tooth in the control group was 9.35 times more than in the case group.

Based on the results of their study, Baeshen and Birkhed<sup>57</sup> recommended the use of fresh miswak impregnated in 0.1% sodium fluoride (NaF) or a maximum of 0.5% NaF for a day for the prevention of dental caries. The effect of fluoridated chewing sticks (Miswaks) on white spot lesions in postorthodontic patients was studied by Baeshen et al.<sup>58</sup> The authors concluded that the frequent use of a fluoridated miswak had a remineralizing effect on white spot lesions. Based on the results of their in vitro and molecular docking studies, Al-Sohaibani and Murugan<sup>59</sup> concluded that the bioactive, dual-function, anti-biofilm agents in *Salvadora persica* not only inhibit growth, but also control the colonization and accumulation of caries-causing *Streptococcus mutans*. The authors also suggested that *Salvadora persica* may offer a novel strategy to reduce the development of dental caries by inhibiting the initial adhesion and subsequent biofilm formation by cariogenic bacteria.

**Antiplatelet effects and its role in gingival & periodontal health.** Many researchers examined the effects of miswak on gingival and periodontal health. Gazi et al<sup>60</sup> observed a significant reduction in gingivitis both buccally ( $p < 0.01$ ) and lingually ( $p < 0.05$ ) after using a miswak 5 times a day compared with a conventional toothbrush. Twice-a-day brushing with a miswak produced a significant reduction in gingivitis buccally ( $p < 0.005$ ) compared with tooth brushing; however, this difference was insignificant on the lingual surfaces. These results imply that using a miswak 5 times a day may offer a suitable alternative to toothbrushing for reducing plaque and gingivitis. Darout et al<sup>61</sup> conducted a study in Sudan on 213 males, aged 20-65 years, to evaluate the periodontal status of miswak and toothbrush users. They reported that the periodontal status of miswak users in those Sudanese populations is better than that of toothbrush users. Based on the results of their study, Al-Otaibi et al<sup>62</sup> concluded that the miswak is more effective than tooth brushing for reducing plaque and gingivitis when preceded by professional instruction regarding its correct application. The use of Miswak appeared to be more effective than tooth brushing for removing the plaque from the embrasures; thus, enhancing interproximal oral health. Toothpaste containing *Salvadora Persica* miswak extract was found to be significantly more effective in

removing dental plaque when compared with Oral-B toothpaste.<sup>12</sup> Al-Lafi and Ababneh<sup>63</sup> reported that using chewing sticks twice a day on a regular basis may reduce the incidence of gingivitis and possibly dental caries. Apart from their antibacterial activity, they also inhibit formation and activity of dental plaque and can be used effectively as a natural toothbrush for teeth cleaning.

Al-Otaibi et al<sup>11</sup> showed in a single-blind, randomized, crossover study involving 15 Saudi Arabian volunteers that miswak and tooth brushing had a similar influence on the levels of subgingival microbiota, but the amount of *Aggregatibacter actinomycetemcomitans* in the subgingival plaque was significantly reduced by miswak use than toothbrushing. The authors also concluded that in case of reducing plaque and gingivitis, the use of miswak is at least as effective as toothbrushing and for the prevention or treatment of periodontal diseases, the antimicrobial effect of *Salvadora persica* is beneficial<sup>26</sup> Khalessi et al<sup>64</sup> compared the oral health efficacy of Persica™ mouthwash (containing an extract of *Salvadora persica*) with that of a placebo among a sample of healthy volunteers. The results of this double-blind, cross-over clinical trial indicate that use of Persica™ mouthwash improves the gingival health and lower the salivary carriage of cariogenic bacteria. The present study also manifested that there was no significant reduction in the accumulation of dental plaque followed by the use of Persica™ mouthwash. Another double-blinded, randomized trial<sup>65</sup> in 72 cases of moderate gingivitis showed that there was a significant reduction in the plaque index (PI), gingival index (GI), and bleeding index (BI) following the use of *Salvadora persica* extract chewing gum. Danielsen et al<sup>66</sup> examined the efficacy of brushing with chewing sticks on plaque removal on Kenyan school children, and the authors evaluated whether toothpaste has any additional effects on the removal of established dental plaque. The results showed that brushing with a chewing stick for 5 minutes resulted in a net reduction of the proportions of plaque deposit sites per child. Toothpaste added no additional effects. From their literature review, Hardie and Ahmed<sup>21</sup> stated that the plaque removing properties of miswak and conventional toothbrushes are similar. Based on the results of their study, Saha et al<sup>67</sup> concluded that miswak users exhibit a better mean gingival score compared with toothbrush and toothpaste users. The mean plaque score was lowest among the combined users of toothbrush and miswak.

**Effects on saliva.** Miswak contain chemical ingredients that may be beneficial to the maintenance of oral health. Gazi et al<sup>68</sup> conducted a study consisting of 2 experiments. In the first experiment, in order to

assess the medium term effect of Miswak on saliva, volunteers were asked to chew on an inert eliciting agent (pyrogen-free rubber) and then a piece of miswak, both for 5 minutes. There was a statistically significant increase in the calcium and chloride content in saliva produced immediately after chewing the miswak, but decreases in the phosphate and pH content, compared with the controls. For the second experiment, to assess the medium-term effect, volunteers were provided with either a miswak or a conventional toothbrush to brush 5 times a day for 2 weeks and saliva samples collected 4 hours after the last use of miswak or toothbrushing showed no significant differences in any of the components examined (calcium, magnesium, chloride, phosphate, IgA, IgG, lactate dehydrogenase, and aspartate transaminase). However, gingival and plaque indices were significantly lower after brushing with miswak. Salivary calcium promotes mineralization of tooth enamel, and chloride inhibits calculus formation. Thus, this study indicates that miswak releases substances into the saliva that could improve oral health. Calcium and chloride values were similar to those of the controls after 4 hours. Therefore, the frequent use of miswak may be necessary to maintain a favorable salivary environment. Based on the results of their investigation, Kaur et al<sup>69</sup> indicated that commercially available miswak chewing sticks, in addition to containing high amounts of calcium and chloride, may possibly release phosphate and thiocyanate into the saliva. These findings suggest that the commercially available miswak used as chewing sticks may have the potential to release substances into the saliva that could influence the state of oral health. Sofrata et al<sup>70</sup> documented the changes in plaque pH in an acidic challenge followed by rinsing with miswak extract (*Salvadora persica*). They also evaluated the effects of the miswak rinse on parotid gland secretion rate. In the present study, the authors observed that rinsing with miswak extract, compared to water rinsing, resulted in a protracted elevation in the plaque pH. At 30 minutes, there was statistically significant ( $p < 0.001$ ) difference in plaque pH between miswak extract and water rinse, and parotid gland secretion was stimulated by rinsing with miswak extract ( $p < 0.01$ ). As the miswak extract raised the plaque pH, the authors suggest that it may have a potential role in caries prevention.

**Antioxidant activity.** Antioxidants are vital substances that possess the ability to protect the body from damage caused by free radical-induced oxidative stress.<sup>71</sup> Exogenous and endogenous antioxidants and synthetic or natural antioxidants are all effective in preventing free radical formation by scavenging them or promoting their decomposition and suppressing

associated disorders.<sup>72</sup> Few studies have reported the antioxidant activity of Miswak (*Salvadora persica*). The antioxidant activity of the bark, leaves, and the seed cake phenolic extracts of *Salvadora persica* using the  $\beta$ -carotene-linoleic acid assay were investigated by Mariod et al.<sup>73</sup> They found 2 dominant tocopherols ( $\gamma$ -tocopherol, and  $\alpha$ -tocopherol) in the seed oil of *Salvadora persica*. These compounds display antioxidant properties and are active as vitamin E, which makes them particularly important for human health.<sup>74</sup> Among the other anti-oxidants,  $\Delta^5$ -avenasterol and beta-sitosterol, followed by campesterol and stigmasterol, were found by Mariod et al.<sup>73</sup> They also concluded that *Salvadora persica* seeds have a very high oil content (on average, 41% wt/wt) with highly saturated (~84%) fatty acids and a medium oxidative stability (~3.1 h). *Furan derivatives*, identified by Gas chromatography-mass spectrometry (GC-MS) analysis from miswak, could exhibit high antioxidant activity by scavenging 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals, (2,2'-azino-bis [3-ethylbenzo-thiazoline-6-sulfonic acid] (ABTS) radicals and reducing molybdenum (VI) to molybdenum (V). The antioxidant capacity of miswak was also attributed to the presence of antioxidant enzymes, peroxidase, catalase, and Polyphenol oxidase. At the end the authors suggested that the synergistic actions of antioxidant compounds and antioxidant enzymes make miswak a good chewing stick for cleaning teeth, oral hygiene, and food purposes.<sup>75</sup> Based on their findings, Noumi et al<sup>72</sup> support the possible use of *Salvadora persica* and walnut bark for their promising sources of potential antioxidant compounds.

**Analgesic and anti-inflammatory effects.** The extract of the *Salvadora persica* stem possess anti-inflammatory activity.<sup>76</sup> Alali and Al-Lafi<sup>77</sup> recommended that the extract of *Salvadora persica* can be used effectively as a natural tool for tooth cleaning and as a natural analgesic for the treatment of toothaches.

**Efficacy of miswak as an oral hygiene tool.** Miswak (*Salvadora persica*) is considered as an effective oral hygiene tool. Several studies were carried out to assess the cleaning effectiveness of miswak (Table 3). Ndung'u et al<sup>78</sup> studied the efficacy of plaque control by a chewing stick and a toothbrush; and concluded that in patients with severe plaque deposition, the toothbrush is more efficacious than the chewing stick for plaque control. However, for patients with moderate plaque deposits, the chewing stick is as efficacious as the toothbrush. Batwa et al<sup>79</sup> carried out a comparative study to assess plaque removal in both miswak and toothbrush users. This experimental and clinical trials revealed that miswak was as effective as tooth brushing for plaque



removal. Several clinical studies have shown that the efficacy of chewing sticks, if used appropriately, can be equal to toothbrushes in removing dental plaque. The reasons were the combined effects of mechanical cleaning, enhanced salivation, and leaching-out of antimicrobial substances.<sup>3,80</sup> Patel et al<sup>81</sup> conducted a study to compare the effects of using miswak together with tooth brushing with those of only toothbrush users on plaque levels and gingival health. The authors carried present study on the subjects diagnosed with mild to moderate chronic generalized marginal gingivitis. From the results of their

study, the authors concluded that plaque score and gingival health improve significantly when miswak and toothbrush was used together. This clearly indicates that miswak can be used aside of a toothbrush, utilizing the combined effect of the mechanical efficacy of toothbrush and the chemical effects of miswak. Malik et al<sup>82</sup> concluded that chewing sticks (Miswaak) provide parallel and at times greater mechanical and chemical cleansing of oral tissues compared with a toothbrush. This indicates that the use of miswak may effectively and exclusively replace the toothbrush.

**Table 3** - Summary of studies assessed the sensitivity of microbes against *Salvadora persica* miswak (whole and extracts).

Reference	Tested microbes	Findings
Al-Bayati & Sulaiman <sup>30</sup>	<i>Staphylococcus aureus</i> , <i>Streptococcus mutans</i> , <i>Streptococcus faecalis</i> , <i>Streptococcus pyogenes</i> , <i>Lactobacillus acidophilus</i> , <i>Pseudomonas aeruginosa</i> , and <i>Candida albicans</i>	<ul style="list-style-type: none"> <li>The aqueous extract of <i>Salvadora persica</i> showed more inhibitory activity against the tested microorganisms than the methanol extract</li> <li>The aqueous extract inhibited all isolated microorganisms, especially the <i>Streptococcus species</i> were the most sensitive</li> <li>The methanol extract was resisted by <i>Lactobacillus acidophilus</i> and <i>Pseudomonas aeruginosa</i></li> <li>The strongest antibacterial activity was observed using the aqueous extract against <i>Streptococcus faecalis</i> (zone of inhibition: 22.3 mm; minimum inhibitory concentrations [MIC]: 0.781 mg/ml)</li> <li>Both aqueous and methanol extracts had equal antifungal activity against <i>Candida albicans</i> based on the turbidity test (MIC: 6.25 mg/ml)</li> </ul>
Sofrata et al <sup>20</sup>	<i>Streptococcus mutans</i> , <i>Lactobacillus acidophilus</i> , <i>Aggregatibacter actinomycetemcomitans</i> , <i>Porphyromonas gingivalis</i> , and <i>Haemophilus influenzae</i>	<ul style="list-style-type: none"> <li>The antibacterial effect of whole (unextracted) <i>Salvadora persica</i> was most pronounced on <i>Porphyromonas gingivalis</i>, <i>Aggregatibacter actinomycetemcomitans</i>, and <i>Haemophilus influenzae</i>. It was less pronounced on <i>Streptococcus mutans</i>, and least pronounced on <i>Lactobacillus acidophilus</i></li> </ul>
Sofrata et al <sup>31</sup>	<i>Aggregatibacter actinomycetemcomitans</i> , <i>Porphyromonas gingivalis</i> , <i>Salmonella enterica</i> , <i>Pseudomonas aeruginosa</i> , and <i>Haemophilus influenzae</i>	<ul style="list-style-type: none"> <li>Benzyl Isothiocyanate (BITC) is the main antibacterial component of <i>Salvadora persica</i> root chewing sticks</li> <li>BITC had a high killing of activity against <i>Aggregatibacter actinomycetemcomitans</i> and <i>Porphyromonas gingivalis</i></li> <li>The strong and rapid killing BITC also affected <i>Salmonella enterica</i>, <i>Pseudomonas aeruginosa</i>, and <i>Haemophilus influenzae</i></li> <li><i>Streptococcus mutans</i> were more susceptible to the antimicrobial activity of <i>Salvadora persica</i> than <i>Lactobacilli</i></li> </ul>
Almas & Al-Zeid <sup>18</sup>	<i>Streptococcus mutans</i> and <i>Lactobacilli</i>	<ul style="list-style-type: none"> <li><i>Streptococcus mutans</i> were more susceptible to the antimicrobial activity of <i>Salvadora persica</i> than <i>Lactobacilli</i></li> </ul>
Salehi & Momeni <sup>33</sup>	<i>Streptococcus mutans</i>	<ul style="list-style-type: none"> <li>The use of Persica™ mouthwash in orthodontic patients resulted in a significant (<math>p &lt; 0.001</math>) reduction in the number of <i>Streptococcus mutans</i> colonies, although it was not found to be as potent as chlorhexidine</li> </ul>
Shafiei-Bafti et al <sup>34</sup>	<i>Enterococcus faecalis</i> and <i>Candida albicans</i>	<ul style="list-style-type: none"> <li>An in vivo evaluation of the herbal mouthwash Persica™ (<i>Salvadora persica</i>, mint and yarrow extracts) demonstrated significant decreases in the <i>Enterococcus faecalis</i> and <i>Candida albicans</i> counts in the oral cavity</li> </ul>
Elangovan et al <sup>36</sup>	<i>Streptococcus mutans</i> and <i>Lactobacillus acidophilus</i>	<ul style="list-style-type: none"> <li>Aqueous extracts of <i>Salvadora persica</i> showed better antimicrobial activity against <i>Lactobacillus acidophilus</i> than against <i>Streptococcus mutans</i> when compared to <i>Azadirachta indica</i> and <i>Mangifera indica</i> extracts</li> </ul>
Khalil <sup>37</sup>	<i>Escherichia coli</i>	<ul style="list-style-type: none"> <li>N-benzylbenzamide derived from the stem of <i>Salvadora persica</i> was only moderately active against <i>Escherichia coli</i> at a concentration of 87 µg/mL (which is equivalent to 20 µg/mL of gentamicin)</li> </ul>
Almas et al <sup>38</sup>	<i>Streptococcus mutans</i> , <i>Streptococcus sanguis</i> , and <i>Streptococcus faecalis</i>	<ul style="list-style-type: none"> <li>At 50% concentration, the <i>Salvadora persica</i> extract was effective in inhibiting <i>Streptococcus mutans</i>, <i>Streptococcus sanguis</i>, and <i>Streptococcus faecalis</i></li> <li>At 5% and 10% concentrations, the extract was effective only against <i>Streptococcus faecalis</i></li> </ul>
Almas & Stakiw <sup>39</sup>	<i>Streptococcus faecalis</i> and <i>Streptococcus mutans</i>	<ul style="list-style-type: none"> <li>After 48 hours of incubation at 4°C using a blood agar ditch method, fresh and 18-year-old stored <i>Salvadora persica</i> at aqueous concentrations of 10% and 50% were found to have an antimicrobial effect against <i>Streptococcus faecalis</i></li> <li>At 50% concentration, extract of fresh <i>Salvadora persica</i> had an inhibiting effect against <i>Streptococcus mutans</i></li> </ul>

**Table 3** - Summary of studies assessed the sensitivity of microbes against *Salvadora persica* miswak (whole and extracts) (cont'd).

Reference	Tested microbes	Findings
AbdElRahman et al <sup>40</sup>	<i>Streptococcus mutans</i> , <i>Lactobacillus acidophilus</i> , <i>Actinobacillus actinomycetemcomitans</i> , <i>Actinomyces naeslundii</i> , <i>Porphyromonas gingivalis</i> , <i>Prevotella intermedia</i> , and <i>Candida albicans</i>	<ul style="list-style-type: none"> <li>Crude extracts were prepared from the roots and twigs of <i>Salvadora persica</i> using different solvents (sterile distilled water, 96% ethanol, 2% acetic acid, and ethyl acetate)</li> <li>The ethanolic extracts showed the strongest antimicrobial activity, and the ethanolic root extracts was more potent than the ethanolic twig extracts <ul style="list-style-type: none"> <li>The stem-water extract was found to have the least effect</li> </ul> </li> <li><i>Streptococcus mutans</i> was the most susceptible strain to all extracts, while <i>Lactobacillus acidophilus</i> was resistant to all extracts except for the root-ethanolic extract</li> </ul>
Almas & Al-Bagieh <sup>41</sup>	<i>Streptococcus faecalis</i> , <i>Streptococcus mutans</i> , <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , and <i>Candida albicans</i>	<ul style="list-style-type: none"> <li>Aqueous extracts of <i>Salvadora persica</i> bark, pulp, and the entire plant at concentrations of 10% and 50% were effective against <i>Streptococcus faecalis</i></li> <li>50% aqueous extract of bark and whole extracts of <i>Salvadora persica</i> had an antimicrobial effect on <i>Streptococcus mutans</i> <ul style="list-style-type: none"> <li>No anti-microbial effect was observed on <i>Staphylococcus aureus</i>, <i>Staphylococcus epidermidis</i>, and <i>Candida albicans</i></li> </ul> </li> </ul>
Alali et al <sup>42</sup>	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Pseudomonas aeruginosa</i> , <i>Candida albicans</i> , and <i>Trichosporon cutaneum</i>	<ul style="list-style-type: none"> <li>The volatile oil of Jordanian <i>Salvadora persica</i> stems exhibited potent antibacterial activity against both gram-positive and gram-negative bacteria (the diameters of the zones of growth inhibition were approximately 13 mm for <i>Escherichia coli</i>, 12 mm for <i>Staphylococcus aureus</i>, 3 mm for <i>Bacillus subtilis</i> and 3.8 mm for <i>Pseudomonas aeruginosa</i>)</li> <li>The volatile oil also exhibited significant activity against resistant strains of <i>Pseudomonas aeruginosa</i> with a diameter of the zones of growth inhibition of approximately 2.9 mm and <i>Staphylococcus aureus</i> of 3 mm</li> <li>Volatile oil from <i>Salvadora persica L</i> stems produced significant growth inhibition in <i>Candida albicans</i> and <i>Trichosporon cutaneum</i></li> <li>The aqueous extract of <i>Salvadora persica L</i> showed weak antifungal activity against <i>Candida albicans</i>, but the alcohol extract showed strong antifungal activity against <i>Candida albicans</i></li> </ul>
Alireza et al <sup>43</sup>	<i>Staphylococcus</i> , <i>Streptococcus</i> , <i>Lactobacillus</i> , <i>Enterococcus</i> , and <i>Escherichia</i>	<ul style="list-style-type: none"> <li>The growth of all tested bacterial genera was significantly (<math>p &lt; 0.05</math>) inhibited in the presence of methanol extracts from <i>Salvadora persica</i></li> <li>A methanolic extract of <i>Salvadora persica</i> exhibited a stronger antibacterial activity against gram-negative (6.5-12 mm) than gram-positive (1-8 mm) bacteria</li> <li>The methanolic extract was most effective when its concentration was 400 mg/ml <ul style="list-style-type: none"> <li>The diluted acetone extract of dry <i>Salvadora persica</i> stems demonstrated the highest inhibitory activity against some <i>Candida albicans</i>, <i>Candida glabrata</i>, and <i>Candida parapsilosis</i> strains (with a zone of inhibition range of 10.33-15 mm) at an extract concentration of 300 mg/ml</li> </ul> </li> <li>Methanol and ethyl acetate extracts of dry <i>Salvadora persica</i> stems were active only on one oral <i>Candida albicans</i> isolate</li> <li>Other strains, such as <i>Pichia jadinii</i>, <i>Candida atlantica</i>, <i>Candida famata</i>, and <i>Candida maritima</i> were resistant to both dry and fresh <i>Salvadora persica</i> stem extracts</li> </ul>
Noumi et al <sup>19</sup>	<i>Candida albicans</i> , <i>Candida glabrata</i> , <i>Candida parapsilosis</i> , <i>Pichia jadinii</i> , <i>Candida atlantica</i> , <i>Candida famata</i> , and <i>Candida maritima</i>	<ul style="list-style-type: none"> <li>The aqueous extract of <i>Salvadora persica</i> had a fungistatic effect for up to 48 hours against <i>Candida albicans</i> (oral isolate) at concentrations of 15% and above</li> </ul>
Al-Bagieh et al <sup>44</sup>	<i>Candida albicans</i>	<ul style="list-style-type: none"> <li>20% Miswak extract was completely effective in inhibiting the growth <i>Candida albicans</i> after 1, 6, and 24 hours of exposure</li> <li>20% Miswak extract was ineffective in inhibiting the growth of <i>Enterococcus faecalis</i> and a mixture of <i>Enterococcus faecalis</i> and <i>Candida albicans</i> after one hour of exposure, but was completely effective in inhibiting their growth after 6 and 24 hours of exposure</li> </ul>
Al-Obaida et al <sup>45</sup>	<i>Candida albicans</i> and <i>Enterococcus faecalis</i>	<ul style="list-style-type: none"> <li>Methanol, chloroform and aqueous extracts of <i>Salvadora persica</i> inhibited the growth of <i>Aspergillus fumigatus</i>, <i>Aspergillus flavus</i>, <i>Aspergillus niger</i> and <i>Candida albicans</i></li> </ul>
Saadabi <sup>46</sup>	<i>Aspergillus fumigatus</i> , <i>Aspergillus flavus</i> , <i>Aspergillus niger</i> , and <i>Candida albicans</i>	<ul style="list-style-type: none"> <li>The potency of 50% ethanolic leaf extract of <i>Salvadora persica</i> were comparable with Clotrimazole in case of <i>Aspergillus niger</i>, <i>Aspergillus flavus</i>, <i>Aspergillus xylinium</i>, whereas the activity of the same extract against <i>Candida albicans</i> were found to be far less than Clotrimazole</li> </ul>
Paliwal et al <sup>47</sup>	<i>Aspergillus niger</i> , <i>Aspergillus flavus</i> , <i>Aspergillus xylinium</i> , and <i>Candida albicans</i>	

**Table 3** - Summary of studies assessed the sensitivity of microbes against *Salvadora persica* miswak (whole and extracts) (cont'd).

Reference	Tested microbes	Findings
Alili et al <sup>48</sup>	<i>Candida albicans</i> , <i>Candida tropicalis</i> , <i>Candida krusei</i> , <i>Candida guilliermondii</i> , <i>Candida dubliniensis</i> , and <i>Candida glabrata</i>	<ul style="list-style-type: none"> <li>The volatile compounds of solid test specimens of <i>Salvadora persica</i> exhibited strong antifungal activity against all <i>Candida</i> species tested, whereas pulverized <i>Salvadora persica</i> showed no antifungal activity</li> <li>Storage and incubation time, as well as the diameter of the sticks, may play an important role for the strength of this antifungal activity</li> </ul>
Nacini et al <sup>49</sup>	<i>Candida albicans</i> , <i>Candida dubliniensis</i> , <i>Candida glabrata</i> , <i>Candida parapsilosis</i> , and <i>Candida krusei</i>	<ul style="list-style-type: none"> <li>The alcoholic extract from <i>Salvadora persica</i> showed the highest zone of growth inhibition for the <i>Candida albicans</i> strain, followed by the <i>Candida dubliniensis</i> with diameters of the zones of growth inhibition of 10 mm and <i>Candida glabrata</i> strains with 7 mm. In contrast, <i>Candida parapsilosis</i> and <i>Candida krusei</i> were not susceptible</li> </ul>
Balto et al <sup>50</sup>	<i>Enterococcus faecalis</i> and <i>Candida albicans</i>	<ul style="list-style-type: none"> <li>The hexane, ethanol, ethyl acetate, and chloroform extracts of <i>Salvadora persica</i> had significant inhibitory effects on <i>Enterococcus faecalis</i> and <i>Candida albicans</i></li> <li>The hexane extract of <i>Salvadora persica</i> was found to exhibited maximum antimicrobial activity against <i>Enterococcus faecalis</i> and <i>Candida albicans</i></li> <li>No significant effects were observed for the methanol-soluble, methanol-insoluble, and water extracts</li> </ul>
Al-Bagieh <sup>99</sup>	Herpes simplex virus type 1	<ul style="list-style-type: none"> <li>The plaque reduction assay indicated that benzylisothiocyanate has a virucidal activity against herpes simplex virus type 1 at a concentration of 133 µg/ml</li> </ul>
Al-Sohaibani & Murugan <sup>59</sup>	<i>Streptococcus mutans</i>	<ul style="list-style-type: none"> <li><i>Salvadora persica</i> contains bioactive anti-biofilm agents with dual functionalities in growth inhibition and Quorum sensing (QS) regulator interaction, which not only inhibit growth, but also control the colonization and accumulation of caries-causing <i>Streptococcus mutans</i></li> </ul>

**Disadvantages of miswak use.** There are some disadvantages associated with the use of miswak. Eid et al<sup>83</sup> examined the relationship between Miswak and gingival recession. The authors found that miswak users had significantly more sites with gingival recession than with the toothbrush users. Furthermore, the severity of the recession was significantly more pronounced in the miswak users than with the toothbrush users. Johansson et al<sup>84</sup> analyzed the possible factors influencing the occurrence of occlusal tooth wear in a young Saudi population. The result of the present study shown that increased occlusal wear found to correlate significantly with bruxism, pen- and nail-biting habits, use of miswak, and high intake of fruit juices. Eid and Selim<sup>85</sup> examined the influence of miswak on gingival health and periodontal health. The authors reported the use of miswak is a possible factor to gingival recession and may influence the periodontal health. Agrawal et al<sup>86</sup> demonstrated that miswak (*Salvadora persica* L) users exhibited good oral hygiene and a favorable gingival index score, but they also had higher gingival recession scores, which may influence their periodontal health. According to Agbor & Azodo,<sup>87</sup> chewing stick users were less likely to have visited the dentist and experience mouth odor, but were more likely to report oral health problems than the non-users among adult Muslim's inhabitants of Banyo in the Adamawa region of Cameroon.

Miswak and toothbrushes have different designs, but similar functions. In contrast to the conventional toothbrush, the bristles of the miswak are situated along the long axis of its handle. As a result, there is reduced access to the lingual surfaces or the interdental spaces, but the facial surfaces of the teeth can be reached more easily.<sup>88</sup> Thus, it may not be possible for miswak users to access all surfaces of the dentition easily. On the other hand, the angulation of a toothbrush allows the user to reach distal tooth surfaces, particularly on the posterior teeth, with greater ease.

In conclusion, this present review clearly highlights the many beneficial effects of *Salvadora persica* (Miwak) on oral disease prevention and health promotion. Strong evidence from the available descriptive and experimental studies support the view that *Salvadora persica* (Miwak) can be a potent oral hygiene tool, not only due to its excellent mechanical plaque-removing efficiency, but for its broad range of biological properties. The use of miswak is associated with health, social and cultural norms, and religious beliefs. The World Health Organization has recommended and encouraged the use of these sticks as a tool for oral hygiene in areas where their use is effective and customary.<sup>89</sup> This recommendation is also consistent with the principles of the Primary Health Care Approach that focus on prevention, community participation, and the use of appropriate technology. To obtain optimum oral health

and hygiene, miswak (*Salvadora persica*) can be used alone or as an adjunct to a traditional toothbrush. Hence, miswak use should be encouraged and promoted based on scientific knowledge of its numerous therapeutic effects on oral health, easy availability, popularity, and low cost. However, achieving the optimum effects of miswak (*Salvadora persica*) depends on its regular use with proper, and effective techniques.

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