CLINICAL EFFECTS, USES AND APPLICATIONS OF MISWAK (SALVADORA PERSICA) ON ORAL HEALTH OVER THE LAST THREE DECADES: A SCOPING REVIEW OF LITERATURE

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Abstract
The miswak chewing sticks (*Salvadora persica*) is an effective oral care tool, and its viability is accomplished via the potential of constituent fibres to manage plaque due to friction between plant fibres and tooth surfaces, in addition to the abundance of its phytoconstituents, which are unusual in their sophistication as well as bioactivity. Previous research has unearthed that miswak has anti-plaque, anti-gingivitis, anti-cariogenic, and whitening properties, as well as improved oral health. This study adopts a systematic-descriptive method to analyse the clinical benefits, potency, limitations and disadvantages, effects, uses, and applications of miswak. Because of the combination of mechanical cleansing, enhanced salivation, and antibacterial component leaching-out, as well as other major therapeutic properties, the efficacy of adequate miswak usage can be equal to or exceed that of toothbrushes in eradicating dental plaque. However, the effectiveness of the miswak is inhibited by the configuration of its bristles (i.e., poor angulation), which limits its mechanical action concerning plaque removal. Consequently, it is essential to encourage researchers to support ongoing research into making miswak toothbrushes better at adapting to user needs and thoroughly cleaning all tooth surfaces.

Keywords: Miswak, Salvadora persica, Antibacterial, Anti-plaque, Anti-gingivitis.

Introduction

Oral hygiene has been observed by different populations in diverse ways. Plants have been utilised for centuries to promote oral hygiene and improve dental health, and this practice continues in numerous communities across the world. Chewing sticks have been connected with a cost-effective oral hygiene tool as well as other benefits such as being a jaw exerciser and generating spontaneous inducement of saliva, which is beneficial for oral hygiene in some countries where brushing with toothbrushes is uncommon.

The existence, proliferation, potent organic constituents, and usability of natural ingredients have strengthened the supposition that natural ingredients have always been the best therapeutic option, their structural variety as well as unique pharmacological activities stand them apart from synthetic medications. They are employed in both traditional and modern medicine to treat life-threatening disorders. Nonetheless, developing novel medication from natural sources is always a difficult task. The use of plants to enhance dental health and upsurge oral cleanliness, on the other hand, has a long history and is still widely utilised in different part of the Middle in East and few other Asian and African countries (1, 2).

Natural chewing stick was first employed by the Babylonians 7000 years ago, and subsequently extended to the Greek and Roman civilisations (3). In many parts of the Indian subcontinent, natural chewing sticks are made from variety of plants that consists of thin twigs of Acacia Nilotica (gum Arabic tree) and Azadirachta Indica (Neem), as well as the twigs and aerial roots of the Banyan (Ficus Religiosa) (4-6). Mangostana twigs (Garcinia Mangostana) have been utilised as chew sticks in Ghana (5). Olive (Olea Europaea) is a widely planted tree in many countries, and it can also be used to create

toothbrushes (5).

The Salvadora persica (S. persica), often known as the "toothbrush tree," is the most prevalent source of chewing sticks (1). It was estimated that around 182 plant species are being used as chewing sticks globally (7). The mechanical and chemical cleaning of oral tissues by chewing sticks is comparable to that of a toothbrush and, at times, superior. The antiplaque effectiveness of chewing sticks has been conclusively proved (8), In Arabic the word Miswak, translate as tooth cleaning stick, became a common name for S. persica due to its significant association with the oral health practice (9). S. persica (Arak tree) is a multi-branched shrub with a short trunk stem covered in smooth green leaves and a white bark that grows to a height of six metres. The oval-shaped leaves have a mustard or cress scent. In some natural settings, S. persica is a deep-rooted mesomorphic xerophyte. It can survive in harsh conditions, and dry environments, as well as tolerate saline soils (10). Furthermore, S. persica is found all over the world, including Saudi Arabia, Iraq, Egypt, , Ethiopia, Central Africa, Southwestern Africa, Mauritania, Sudan, India, Pakistan, Iran, Malaysia, and South America. (11).

The phrase "miswak" which means "natural toothbrush" is a pencil-sized stick made from various components of the Arak plant (root, twig, and stem) (12). It is available in fresh sticks which can be immediately used or dried sticks which need to be soaked in water for minutes before use to make them chewable. After that one end of the brush is nibbled until it frays and creates a brush. Like a toothbrush, the brush end is suited to scrub the teeth and gum. When used in this manner, they are referred to as "chewing sticks" or "miswak" (13, 14). Furthermore, the miswak has received a great deal of attention in the Islamic community, particularly since they established basic oral hygiene by including the miswak as a religious activity. The derivatives and historical and religious backgrounds have been adequately dealt with in the previous study (9).

The use of the miswak has been recommended before and after a meal, before going to sleep, before entering the house, during a fast, and before reciting prayers (15). As a result, it has gained popularity among Muslims worldwide. However, many studies have proved that the miswak has a therapeutic benefit for oral health as it contains antibacterial, antifungal, anti-cariogenic, and antiplaque effects (16). Moreover, the miswak extract contains a combination of silica and natural antiseptics that makes it ideally suited for tooth brushing. According to Saha S, et al., (2012) miswak can be as effective as or more effective than a conventional toothbrush at reducing plaque and gum disease (12, 17).

Several studies have reviewed the therapeutic effects, microbial activity, and application of miswak (18). The present study aims, in part, to give an insight into the benefits, applications, and potential disadvantages of using miswak around the world, as well as the various attempts at developing and expanding the use of miswak products in the last 3 decades, were also reviewed. Finally, potential study directions and priorities for the future are highlighted.

Methods

Research questions

The goal of this critical analysis is to examine the underlying scientific questions:

1. What are the clinical advantages of miswak (S. persica)?
2. What is the application of miswak (S. persica) in the dental field?
3. What are the limitations and disadvantages of using miswak (S. persica) in the dental field?

Design

This study adopts a systematic-descriptive method to analyse the clinical benefits, potency, limitations and disadvantages, effects, uses, and applications of miswak (S. persica) published between 1990 and May 2022. The review stems on a method proposed by the Joanna Briggs Institute (JBI) and reported using preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist (19). The research materials were sourced through electronic databases including Science Direct, PubMed, Scopus, as well as Google Scholar. The electronic search was carried out using a combination of keywords: “Natural toothbrush”, “Oral hygiene tool”, “Salvadora persica”, “siwak” or “miswak” or “chewing stick” “miswak products”, for intervention, and or ‘periodontal health’ or ‘oral disease”.

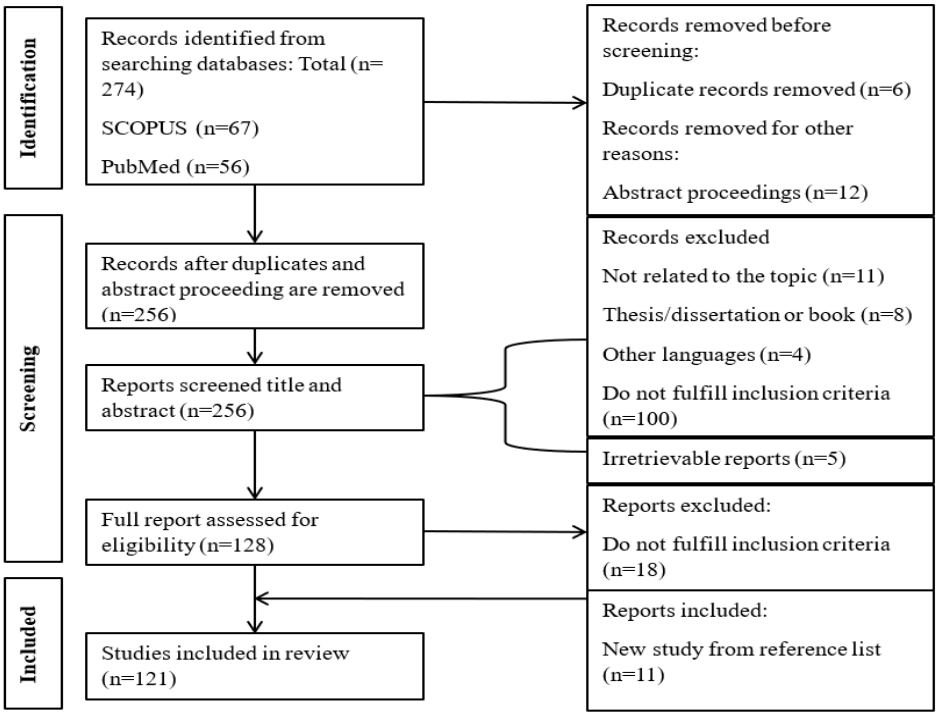
Inclusion and exclusion criteria

The study focused on research that was conducted on humans, published between the years 1990 and 2022, and written in English. Any research that had been conducted on animals or that had been published in a language other than English had been excluded.

Search strategy and selection of studies

The authors focused on articles published in Science Direct, PubMed, Scopus, and Google Scholar using various keywords as mentioned above. The included studies were scrutinised, and duplicate articles and those with only abstract proceedings were deleted. The titles and abstracts of the studies were assessed, and irrelevant or unrelated cases were excluded. Based on the inclusion criteria, the abstracts of the studies were first assessed, and the full texts of pertinent studies were examined for eligibility. Extracted data items included: authorship information, outcome data, deductions, inferences, and recommendations. The bulk of studies included in this review explore the clinical benefits advantages, disadvantages, and application of miswak in the dental field. The flowchart for selecting, screening,

and including the reviewed studies is presented in Figure 1.



Results and Discussion

Advantages of miswak

Mechanical effect of the miswak (S. persica)

The benefits of miswak in oral hygiene can be attributable to the mechanical to scrubbing role of the teeth. One of the primary reasons for cleaning teeth is the mechanical cleansing of the chewing stick as a toothbrush. The mechanical friction of miswak fibers helps in eliminating the dental plaque and simultaneously massaging the gums. In addition, the effect of miswak in plaque removal might be attributable to the considerable amount of silica identified in miswak (20). Furthermore, a miswak is often used for a longer amount of time than a contemporary toothbrush, and the buccal surfaces of the teeth are easier to reach than the lingual and proximal regions (21). The cleaning process is usually carried out for between five to ten minutes each time (22).

Mechanical action due to the tooth brushing combined with the fitting dentifrices can minimise the long-term build-up of dental plaque (23). The mechanical action of miswak can be complemented by its intrinsic chemical properties (24). Sofrata A, et al., (2011) investigated this theory based on fresh and boiled miswak to indicate chemically active and inert chewing sticks, respectively. Turesky modified the Quigley-Hein plaque index was utilised to evaluate the plaque status of both sets (12). Both chemically active and inactive miswak showed comparable efficacy towards plaque reduction which supports the hypothesis of miswak benefitting more from its mechanical effect in preference to its chemical action (25). Moreover, the stretchy and flexible feature of the fibers further enhances the mechanical effects (26). In addition, miswak is considered an easily obtainable and inexpensive oral hygiene tool that can be used by everyone regardless of economic status. Miswak up-regulates the production of calcium (22-fold) and chloride (6-fold), but inhibits the phosphate levels, resulting in pH decline (27).

Chemical constituents of miswak (S. persica)

The chemical components of miswak play an important part in maintaining oral health making it an effective material for dental application. Each of these elements has its own set of pharmacological and therapeutic effects. The rootbark comprises 27.06% ash and is notable for the considerable amount of chlorine present (25). The prominent phytoconstituents of S. persica include benzyl isothiocyanate which acts as a chemo-preventive agent, prevents carcinogenic and genotoxic compounds displays bactericidal activity, and has a virucidal function. Some studies quantified benzyl isothiocyanate in root extracts of S. persica by gas chromatography beside contains benzyl nitrile, carvacrol, aniline, benzaldehyde, naphthalene miswak also includes lauric, palmitic, and myristic acids, as well as phenol and furan lignin derivatives, syringins, liriodendrin, and sitosterol-O-glucopyranoside (28). Volatile oils that possess a characteristic aroma, exert antibacterial actions and stimulate the flow of saliva (29), terpenes glycosides such as salvadosides and salvadorasides, and flavonoids that exhibits cytotoxic effects (30). In addition, silica and resins present in miswak have an abrasive and protective

effect on tooth enamels against dental caries (31). Chlorine is found in the root bark of miswak which acts as a dentifrice to remove tartar. Miswak contains antimicrobial agents such as sulphate and thiocyanate (SCN). In the presence of hydrogen peroxide, SCN is oxidised by lactoperoxidase found in saliva to create hypothiocyanite (HOSCN). Hypo thiocyanate inhibits bacterial enzymes, ultimately resulting in cell damage. The strong smell and taste emanating from the sulphur compounds usually referred to as mustard plants are familiar bactericidal agents (32, 33).

Furthermore, trimethylamine and salvadorine have demonstrated significant antibacterial and gingival stimulating properties. Antifungal properties have been shown when trimethylamine, sulphur, alkaloid, and resin compounds are combined. The fibres of S. persica were morphologically and elementally analysed by Halib N, et al., (2017) as well Energy-dispersive X-ray spectroscopy (EDX) as well as scanning electron microscopy were used to discover the types of minerals within the fibres. The rhomboidal crystals are composed of calcium (Ca), sodium (Na), oxygen (O), carbon (C), sulphur (S), and potassium (K), whereas the irregular crystals containing silicon (Si), aluminium (Al), iron (Fe), as well as Ca, S, C, O, and K (34). Other research reported that the essential oil extracted from the stems of S. persica was rich in benzyl isothiocyanate (52.5%), benzyl nitrile (38.3%), carvacrol (3.3%), benzaldehyde (2.5%), aniline (0.7%) and naphthalene (0.6%) (35).

Mohamed S A, et al., (2014) looked for five different types of α-amylases: A1, A4a, A4b, A5a, and A5b in miswak. The purification method used was chromatography on a DEAE Sepharose column and a Sephacryl S-200 column, as well as gel filtration and SDS-PAGE, to figure out the molecular weight. columnresearchers found that the presence of calcium ions (Ca^{2+}) activated the enzymes, while nickel (Ni^{2+}), cobalt (Co^{2+}), and zinc (Zn^{2+}) ions either activated or inhibited the enzymes (30). Moreover, the plant fibres contain sitosterol trimethylamine, an alkaloid, chlorides, and silica (SiO_2). These studies have shown that there are a lot of salts with high levels of chlorine, a large amount of fluoride, and vitamin C (ascorbic acid). The vitamin C that typically found within plant composed of organic sulphur compounds that aid the incorporation of the antiscorbutic compounds in the body, which effectively treats spongy and bleeding gums. However, numerous studies have reported that extracts of S. persica have displayed antiplaque, anti-periodontic, anti-cariogenic, anti-inflammatory and antimycotic effects (31). The therapeutic effects of the different components of S. persica are outlined in Table 1.

Table 1: Therapeutic effects of different components of miswak

Phytocomponents	Therapeutic effect	References
Benzyl isothiocyanate (BIT)	Anticarcinogenic	(99)
	Antibacterial effects	(100)
	Virucidal effects	(101)
Beta-pinene	Antimicrobial activity	(102)
Myrcenol	Antibacterial	(103)
Sabiene	Antimicrobial activity	(104)
Silica	It has abrasive properties that eliminate dental plaque and tooth stains.	(20)
Salvadorine (Alkaloids)	Anticancer and antiplaque effects	(105)
	Anti-fungal properties	(106)
	It has antibacterial and gingival stimulating properties.	
1,8-Cineole	Antimicrobial and cytotoxic.	(105)
Salvadoraside	Anti-inflammatory.	(107)
Isoterpinolene	Antioxidant.	(99)
Tannins (Tannic acid)	Inhibition of C. albicans	(108)
	Acts as a protective layer covering the enamel of a tooth.	(109)
Essential (volatile) oils	Exert carminative & antibacterial actions and stimulate the flow of saliva (antiseptic action).	(100) (35)
Sulphur	Have bactericidal effects.	(29)
Sodium bicarbonate ($NaHCO_3$)	Acts as a mild abrasive and can be used as a dentifrice. Mild germicidal action	(110)
Calcium	Inhibits demineralisation and induces the remineralisation of enamel.	(29)
Fluoride	Anticariogenic activity and tooth remineralisation.	(29) (111)

Chloride	Inhibits the formation of calculus	(112) (113)
N-benzyl-2-phenylacetamide	Inhibits human collagen-induced platelet aggregation and has antibacterial activity against E. coli.	(114)
Trimethylamine	Has antibacterial, antiphlogistic, and gum-stimulating effects.	(115)
Flavonoids	Has cytotoxic activity.	(116)
Resins	Forms the protective covering layer over enamel, which seems to have a preventive effect against tooth cavities.	(117)
Tocopherols	Antioxidant characteristics and is as active as vitamin E.	(116)

Clinical activities of miswak (S. persica)

Antibacterial and antimicrobial activity

Recent in vitro investigations have demonstrated the antibacterial and antifungal characteristics of miswak against periodontal infections and cariogenic bacteria, particularly Staphylococcus aureus (S. aureus), Streptococcus mutans (S. mutans), Streptococcus faecalis (S.faecalis), Aggregatibacter actinomycetemco-mitans (A. actinomycetemcomitans), Streptococcus pyogenes (S. pyogenes), Lactobacillus acidophilus (L. acidophilus), Haemophilus influenzae (H. influenzae), Pseudomonas aeruginosa (P. aeruginosa), Porphyromonas gingivalis (P. gingivalis), and Candida albicans (C. albicans) (36-41). Extracts of S. persica as intracanal irrigant have demonstrated considerable antimicrobial activity on the oral pathogens, both in vitro and in vivo Ayoub N, et al., (2021) assessed the effectiveness of S. persica petroleum ether extract (SPE) as an intracanal bactericidal medicament for endodontic treatment against Enterococcus faecalis (E. faecalis). According to the study, SPE may effectively remove E. faecalis from the root canal, making it a viable substitute for calcium hydroxide in endodontic therapy (42). In examining three different plant extracts, S. persica, Commiphora molmol (C. molmol), and Azadirachta indica (A. indica), combined with commercially available antimicrobial agents, penicillin, tetracycline, ofloxacin, and fluconazole, on endodontic pathogens including E. faecalis, Streptococcus mitis (S. mitis), Actinomyces naeslundii (A. naeslundii), and C. albicans, The findings demonstrate the efficiency of C. molmol, A. indica, and S. persica against all endodontic experimental pathogenic bacteria (43). Other studies assess the antibacterial properties of miswak extracts in ethanol against three bacterial infections (S. aureus strain, E. faecalis strain and Klebsiella pneumoniae strain) of the oral cavity. All miswak extracts displayed potent antimicrobial activity against the three pathogens (44). According to their polarity in various solvents, miswak extracts were examined for the presence of antibacterial agents (Abhary M and Al-Hazmi A-A, (2016), the study reported that miswak contains more than one kind of antimicrobial agent that restricted the proliferation of both gram-positive and negative bacteria. Strong antimicrobial activity was observed in the aqueous extract and less activity in alcoholic and nonpolar extracts (45). The antioxidant potency evaluated in vitro antibacterial activities of S. persica extract against the three bacterial clinical isolates (P. aeruginosa, Acinetobacter baumannii and Enterobacter cloacae) using the chromatograms technique, producing inhibition zones of 20, 18 and 14, respectively. The antioxidant evaluation conducted using the DPPH (1,1-diphenyl-2-picryl-hydroxyl), free radical scavenging method, indicated that the methanol extract exhibited higher antioxidant efficiency compared to ascorbic acid (46).

Furthermore, an earlier study was conducted to analyse the antimicrobial activities against S. aureus, S. mutans, S. faecalis, S. pyogenis, L. acidophilus, P. aeruginosa, and C. albicans isolated oral pathogens through disc diffusion and micro-well dilution assays. The study reported that the aqueous extract inhibited all isolated microorganisms, particularly the Streptococcus species, with higher efficiency compared to the methanol extract, which was resisted by L. acidophilus and P. aeruginosa. The strongest antibacterial activity was noted for the aqueous extract against S. faecalis. Both aqueous and methanol extracts exhibited equivalent antifungal activity against C. albicans (46). Another study was performed to analyse the antibacterial activity of S. persica extract against bacteria (S. aureus and Streptococcus sp.) isolated from dental plaque of patients suffering from plaque-induced gingivitis. The methanol extract of S. persica exhibited a significant antibacterial effect against S. aureus and Streptococcus sp. isolates (47). Additional research was established to investigate the antibacterial activities of miswak extracts against multidrug-resistant (MDR) bacterial clinical isolates excluding oral pathogens. The miswak extract was more effective against gram-negative bacteria in comparison to that of gram-positive bacteria. The lowest minimum inhibitory concentration (MIC) value was observed for Escherichia coli (E. coli), followed by S. pyogenes, while the highest MIC value (6.25, 12.5 µg/mL) was recorded for methicillin-resistant S. aureus (MRSA), A. baumannii, and Stenotrophomonas maltophilia (S. maltophilia) (48).

Antimycotic activity

S. persica has exhibited considerable antifungal activity against several fungal species. The antimycotic activities of different solvent fractions of S. persica extract that

include acetone, ethanol, and aqueous extracts have been tested. Acetone extract has displayed the highest antifungal activity, inhibiting C. albicans, Candida glabrate (C. glabrate), Candida parapsilosis (C. parapsilosis), Candida kefyr (C. kefyr), Candida sake (C. sake), Candida atlantica (C. atlantica), Candida holmii (C. holmii), Candida krusei (C. krusei), Candida maritima (C. maritima), Pichia guilliermondii (P. guilliermondii), and Pichia jardinii (P. jardinii). The miswak reported zone of inhibitions of 11.33 ± 0.57 mm and 6 ± 0 mm for C. holmii and C. krusei, respectively (35), while other studies showed mitigative action of aqueous and methanolic extract of S. persica against C. albicans (49). The antimycotic effect was possible as a result of one or more of the root contents including chlorine, trimethylamine, alkaloid resin, and sulphur compounds.

Anti-cariogenic properties

Dental caries can be treated, and the tooth structures restored using glass ionomer cement and dental varnishes. Nonetheless, the effectiveness of restoration is dependent on the deterrence of more bacterial colonisation to the caries site and improved remineralisation of the enamel surface. Miswak is reported to have the three minerals (fluoride, phosphate, and calcium) of the hydroxyapatite crystal that comprise the teeth structure, indicating its ability to improve dental caries restoration (50). Further report that studied the remineralisation efficacy of teeth varnishes introduced with chitosan, miswak, and propolis on damaged enamel. Chitosan and miswak were shown to have significantly higher remineralisation than the control varnish, thus, indicating the potential of miswak in the remineralisation of damaged enamel (51). Furthermore, Mustafa M, et al., (2016) assessed the decayed-missing-filled (DMF) index of 240 school students across a period of two years. The incidence of dental caries was observed to be substantially higher in non-users of miswak than in users, suggesting the potential efficacy of miswak for dental caries prevention (52).

Several laboratory studies have reported that miswak extract has a strong antibacterial effect against bacterial species isolated from dental caries (53,54) and the anti-decay effect of miswak has been attributed to its fluoride content (29). This explains the higher prevalence rate of caries in urban areas than in rural areas, where the traditional use of miswak was more common (55). In a clinical trial conducted on selected high school students in the city of Yazd, Iran, Ezoddini-Ardakani F, (2010) discovered that aqueous extracts of miswak had the potential to prevent dental caries. (56). Other researchers advised the utilisation of fresh miswak impregnated in 0.1% sodium fluoride (NaF) or a maximum of 0.5% NaF for a day to avert the formation of dental caries, in an attempt to investigate the effect of fluoridated chewing sticks (miswak) on white patch lesions in post-orthodontic patients, the study concluded that the frequent use of a fluoridated miswak enabled the remineralisation of white spot lesions (57). Similarly, an additional study has reported that S. persica can inhibit growth, as well as control the colonisation and build-up of caries because of its bioactive, dual-function, anti-biofilm agents, thus preventing the formation of Streptococcus mutans (S. mutans). They further claimed that S. persica can slow the progression of tooth caries by inhibiting the initial adhering and subsequent generation of biofilm by cariogenic bacteria (58).

Whitening properties

The whitening action of miswak was ascribed to the abrasive action of silica and mineral crystals. Tooth discolouration was frequently taken care of using abrasive materials composed of hydrated silica, aluminium oxide, dehydrated calcium phosphate, calcium carbonate, and perlite. Consequently, the silica in miswak can function as a natural abrasive (59). Halib N, et al. (2017) investigated the whitening ability of miswak on tea and coffee-stained premolar teeth. The different concentrations of miswak extract showed no significant difference in whitening effect in comparison to that of commercially available whitening toothpaste (34). Nonetheless, another study demonstrated a higher decrease in staining index when probiotic and miswak spray was combined and used compared to the control, although the disparity had no statistical significance (60).

Anti-plaque properties

Miswak plays a role in the prevention of plaque, given that S. persica consists of an antimicrobial agent that restrict the formation of different plaque-causing bacteria or microbes (61). The formation of plaque via the build-up of a significant quantity of pathogens on enamel accounts for dental caries, which subsequently results in several periodontal diseases. The antiplaque effect of miswak against oral microbes is due to the occurrence of tannins (25). Another experiment reported the activity of S. persica against dental caries, gingivitis, and plaque (57). However, a different study investigated the decline in occurrences of periodontal diseases in children using miswak. The clinical studies concluded that S. persica is a viable alternative strategy to maintaining good oral hygiene, thus preventing the growth and proliferation of bacteria and fungi, which, while simultaneously preventing the rise of periodontal disorders, can implicitly regulate the development of plaque and tooth cavities (32). The usage of the miswak led to significantly lower plaque ($P<.001$) and gingival ($P<.01$) indices as compared to tooth brushing. Image analysis of the plaque distribution showed a significant difference in the reduction of plaque between the miswak and toothbrush periods ($P<.05$). It was concluded that miswak is more effective than toothbrushing for reducing plaque and gingivitis when preceded by professional instruction in its correct application. The

miswak appeared to be more effective than toothbrushing for removing plaque from the embrasures, thus enhancing interproximal health (62).

Miswak is capable of considerably reducing plaque, buccal and lingual gingivitis more than brushing with a conventional toothbrush, although the effect might not be very obvious with lingual surfaces. In addition, miswak exhibits a higher reduction of A. actinomycetemcomitans in subgingival plaque (24, 63). Combining the benefits of miswak with those of a regular toothbrush is more successful than either method alone. However, as compared to just using a regular toothbrush, the debris index shows that utilising miswak (either alone or in conjunction with a regular toothbrush) is much more effective (64). The therapeutic effects of miswak are summarised in Table 2.

Table 2: Studies on the therapeutic benefits of miswak

Effects of S. persica	Findings	Articles
Antibacterial and antifungal	Antibacterial activity of methanol and aqueous extract from S. persica and Commiphora gileadensis against 5 different bacteria including S. mutants, L. Casei, S. aureus, S. salivarius, S. epidermidi, F. nucleatum.	(41)
	Effectiveness of ethanol extracts of S. persica stem against Gram negatives (E. coli, Salmonella enterica, K. pneumonia, P. aeruginosa and Proteus vulgaris) The Gram-positives (S. aureus, S. epidermidis and B. cereus) strains.	(118)
	The antibacterial activity of hexan was found to be superior to that of an ethanol extract of S. persica against monospecies biofilms established on orthodontic brackets.	(119)
	S. persica hexane extracts were reported to have antibacterial action against S. aureus, P. aeruginosa, and C. albicans at high and low concentrations, but miswak alcoholic extract had no inhibitory effect against the same microorganisms.	(120)
	Evaluated the antimicrobial effects of ethanol, methanol, and ethanol/methanol extracts of miswak S. aureus strain KKU-020, Enterococcus faecalis strain KKU-021 and K. pneumoniae strain KKU-022 of the oral cavity.	(44)
	Miswak extract was found highly significant against fungus like C. albicans	(121)
	Reported zone of inhibitions of 11.33 ± 0.57 mm and 6 ± 0 mm for C. holmii and C. krusei, respectively.	(35)
Mechanical effect	Both chemically active and inactive miswak showed comparable efficacy towards plaque reduction.	(12)
	A miswak can be usually utilised for a longer duration compared to a modern toothbrush, and it can reach the buccal surfaces of the teeth with less difficulty compared to the lingual and proximal surfaces.	(21)
	The stretchy and flexible feature of the fibres in S. persica further enhances its mechanical effects.	(25)
Anti-cariogenic	Investigated the remineralisation efficacy of teeth varnishes incorporated with chitosan, miswak, and propolis on damaged enamel. Chitosan and miswak showed significantly higher remineralisation than the control varnish.	(49)
Whitening properties	Reported a higher decrease in staining index when a combination of probiotic and miswak spray was used compared to the control, although the disparity had no statistical significance.	(60)
	Different concentrations of miswak extract showed no significant difference in whitening effect compared to the commercial whitening toothpaste.	(34)

Anti-plaque	Investigated the decline in occurrences of periodontal diseases in children using S. persica and concluded that S. persica is successful in maintaining good oral hygiene, by indirectly controlling the formation of plaque and dental caries.	(39)

Salivation promotion of the miswak (S. persica)

Another possible reason why the miswak is so important for oral health is that chewing miswak sticks increases salivation, which raises calcium and chloride content while lowering the pH and phosphate levels. Calcium stimulates the mineralisation of dental enamel, whereas chloride inhibits calculus formation (65). A study found that the miswak extract stimulated parotid gland secretions and increased plaque pH within 30 minutes of washing the oral cavity with the miswak extract. Exaggerating the saliva secretions and raises the pH of the plaque, hence preventing dental cavities (66). In addition, the Bawazeer T M, et al. (2016) study examined the effectiveness of aqueous extracts of S. persica (AESP) as dissolution inhibitors for acid eroded enamel in caries-free, non-erupted human premolar teeth. The outcome showed the aqueous extracts of S. persica protect human tooth enamel against citric acid solutions. Most of the protection comes from the "shielding" effect of the polymers, which form right away on the surface of the enamel of a person's teeth after AESP therapy (67).

Application of miswak

Extensive research on the potency and efficacy of miswak has confirmed its usefulness in tooth decay prevention, even when used in the absence of any other tooth-cleaning techniques. Consequently, there are several existing and potential uses for miswak. For example, the use of miswak extract chewing gum may advance oral or periodontal health by lowering plaque, bleeding, and gingival indices (68). This is critical because chronic illnesses such as diabetes mellitus and renal problems (which are frequently treated with immunosuppressive medications) are known to be vulnerable to oral candida infection since these conditions impair a patient's immune response. The applications are elaborated on below.

a) Miswak chewing stick

Miswak was shown to be a more effective antibacterial toothbrush than commercial toothpaste, particularly toothpaste with fluoride, and it was found to be safe for use (69). In addition, the miswak chewing stick remains an effective anti-plaque agent in comparison to that of a toothbrush (70). This superiority of miswak over the conventional technique was established by a study done by Saha S, et al., (2012) among 297 individuals in Lucknow, India. In their study, they showed that the mean plaque index (PI) was significantly lesser in persons that utilised the combination of miswak and toothbrush, followed by miswak only users, with a toothbrush only users showing the highest mean PI (17). Another study reports that when fluoride was added to miswak chewing sticks, there was no noticeable alteration in plaque reduction between the miswak and conventional toothbrushes, as compared with or without fluoride. Nonetheless, the rate of plaque reduction was found to be similar for both miswak and conventional toothbrushes (71). In other performed experimental and clinical trials to comparatively assess plaque removal in both miswak and toothbrush users, it was revealed that miswak shows similar effectiveness to a toothbrush for plaque removal (72).

One study compared the effects of using miswak combined with the conventional toothbrush and the use of only toothbrushes on plaque levels and gingival health. The clinical subjects had mild to moderate chronic generalised marginal gingivitis. They found that plaque score and gingival health were significantly enhanced when miswak was combined with a toothbrush, which indicated that miswak can be utilised solely without a toothbrush since it combines the mechanical efficacy of a toothbrush and the chemical properties of miswak (20). The efficacy of appropriate use of chewing sticks can be equal to toothbrushes in removing dental plaque due to the combined effects of mechanical cleaning, improved salivation, and leaching-out of antimicrobial substances (61).

b) Miswak toothpaste

Miswak-incorporated toothpaste is currently prevalent in the market. To determine its applicability as toothpaste, miswak-incorporated toothpaste was compared with other herbal toothpaste, like the tea tree oil-incorporated toothpaste, in randomised controlled trials with 24 healthy people in a single-blind crossover arm. The study revealed that the miswak toothpaste reduced plaque much more than the tea tree oil toothpaste (73).

In another study performed in the triple-blind, parallel arm, randomised controlled trial (RCT) of 330 healthy youngsters, the researchers examined the effectiveness of miswak-infused toothpaste versus fluoridated toothpaste in reducing plaque. They found that toothpaste with miswak was much better at getting rid of plaque than regular fluoridated toothpaste (74).

Other researchers employed a double-blind, parallel arm, randomised controlled trial of 66 non-smoking patients with gingival inflammation in their clinical investigation. In people with mild to moderate gingivitis, the efficacy of

a miswak extract-containing toothpaste was compared to that of an established herbal Parodontax® and conventional Colgate® toothpaste. According to the findings, patients with gingivitis can safely use a toothpaste containing miswak extract, which has a similar impact to herbal toothpaste (75). Moreover, chewing sticks provide comparable and at times greater mechanical and chemical cleansing of oral tissues than a conventional toothbrush, indicating that the use of miswak may effectively and exclusively replace the conventional toothbrush (61).

c) Miswak mouthwash and chewing gum

Mouthwash is effective for the removal of plaque (76). However, the conventional mouthwash contains chlorhexidine, a cationic chemical agent that is potent against plaque, which is reported to cause several side effects that include teeth discolouration, oral mucosal irritation, and horrid taste after its use (77). This has prompted the need for natural alternative mouthwash formulation.

In a double-blind (RCT) Niazi F H, et al., (2018) performed a study of 80 people getting orthodontic treatment. The results showed that the mouthwash made from miswak was much more effective at getting rid of plaque than the two chemical ingredients (78).

An investigation assessed the effectiveness of miswak (ethanol and aqueous) extracts on periodontal pathogens. The chlorhexidine (Oradex) mouthwash was used as a positive control, and distilled water served as a negative control mouthwash. Eikenella corrodens (E. corrodens), S. constellatus, S. sanguis, and S. salivarius were among the examined biofilm microorganisms. The results revealed that the miswak ethanol extract has a greater antibacterial effect against periodontal pathogenic microorganisms. Consequently, it is a suitable alternative to commercial mouthwash for decreasing and preventing periodontal pathogenic bacteria (79).

Another study found no variation in plaque levels between the groups using miswak and chlorhexidine mouthwash. Fixed orthodontic treatment for four months was the subject of a single-blind RCT in which 54 participants were enrolled. Both miswak and chlorhexidine were more effective at getting rid of plaque than a placebo mouthwash. This suggests that miswak can be used as an alternative mouthwash in orthodontic patients instead of chlorhexidine mouthwash (80). In addition, evaluate the efficacy of plaque reduction following the use of an electronic toothbrush with miswak mouthwash. It was found that the combination of miswak mouthwash and an electronic toothbrush significantly decreased plaque in 72 orthodontic patients with at least two areas of gingival expansion, compared to the use of only an electronic toothbrush (81). The investigation by Almas K, et al., (2005), obtained eight commonly used non-alcohol mouthwashes that were commercially available in the Middle East (Saudi Arabia), namely (Corsodyl®, Alprox®, Oral-B® advantages, Florosept®, Sensodyne®, Aquafresh®, Betadine®, and Emoform-F®) and 50% miswak extract against seven microorganisms. The result revealed the miswak extract had mild antimicrobial activity against S. mutans (82). Other studies compared the effectiveness of commercially available herbal mouthwash containing S. persica extracts to that of a placebo. Compared to pre-treatment values, the S. persica mouthwash enhanced gingival health and decreased the carriage rate of cariogenic bacteria in the research. The placebo (vehicle control) also dramatically improved gingival health. Neither S. persica nor placebo decreased dental plaque accumulation (83). In different research, 24-hours plaque re-growth, double-blinded randomised controlled crossover trial was carried out where a miswak (roots of S. persica (7.82 mg) extracts/1 ml distilled water) and green tea (0.25mg) mixture mouthwash was compared with chlorhexidine mouthwash. The miswak and green tea combination mouthwash displayed a considerably higher reduction in plaque build-up compared to the placebo and chlorhexidine mouthwash (21).

Miswak-flavoured chewing gum has also been manufactured. Amoian B, et al., (2010) studied miswak chewing gum with or without tooth scaling. There was no statistically significant difference in plaque reduction across the groups that rinsing with 15 ml of combination twice daily (68).

d) Miswak varnish

The miswak-containing varnish was effective in enamel remineralisation. In an in vitro study, the ions released from different varnishes were assessed to compare the remineralising potential of alcohol and freeze-dried aqueous miswak extracts, propolis ethanolic extract, and chitosan nanoparticles in the presence and absence of 5% NaF to 5% NaF varnish. Seventy sound-extracted primary molars were mesiodistally divided. Each of the equal halves of enamel and dentin was varnished with acid-resistance varnish. Surface microhardness specimens were implanted in polymethyl methacrylate, then enamel was sanded flat and manually polished with aqueous silicon carbide slurries up to 4000 grit and subjected to enamel lesion formation via immersion in a demineralising solution. The results showed the chitosan-nanoparticles and miswak-containing varnishes were most effective in remineralising enamel lesions, probably due to the release of F^{-}, Ca^{++}, and $PO4^{--}$ ions compared to NaF varnish, which released F^{-} only. (49).

Other researchers evaluated the effects of miswak extract varnish on S. mutans levels in saliva and plaque in orthodontic patients compared to a varnish containing chlorhexidine. A random study of 75 female orthodontic patients, ages 14 to 20, was followed for three months and the gingival bleeding index (GBI) and plaque index (PI) statuses were tested. The results demonstrated that

miswak varnish can be a suitable natural alternative for chlorhexidine varnish as an anti-cariogenic agent when used monthly (84).

To compare the effects of fluoride varnishes, propolis-based chitosan varnish, and S. persica varnish on S. mutans and Lactobacilli count, ElSayed M, et al., (2020) randomly selected 48 children who were enrolled in the study, and the designated varnishes were applied to all the teeth of subjects in all the three groups and followed up for 6 months. The results showed that both S. mutans and Lactobacillus bacteria were affected by all-natural varnishes, but the S. persica varnish was the most effective (85).

e) Miswak containing glass ionomer cement

The miswak incorporation in glass ionomer cement improved restoration survivability after atraumatic restorative treatment (ART) approach. Throughout an in vivo investigation, 35 children between the ages of six and nine with 60 first permanent molar teeth were enrolled, to assess the therapeutic efficacy and in vivo antibacterial effect of adding chlorhexidine gluconate (CHX) or aqueous of miswak to conventional glass ionomer cement (GIC). The result demonstrated a more effective reduction in bacterial counts by combining glass ionomer with either CHX or miswak inhibits the growth of caries under restorations in young permanent molars (86).

Another study examined the impact of introducing CHX and miswak extract to GIC as a restorative material in early childhood caries (ECC). They discovered that aqueous extracts of miswak and 1% chlorhexidine digluconate were equally efficient against S. mutans and S. sobrinus, rather than the conventional anhydrous GIC which was the least effective (87). Hence, miswak can be used as an alternative herbal antibacterial agent against S. mutans and S. sobrinus to improve anhydrous GIC (88). Moreover, the addition of 0.25 % miswak and 1.25 % propolis might increase the fluoride-releasing capacity of the studied GIC (89).

f) Endodontic irrigation solution

The removal of bacterial contaminants is crucial to the effectiveness of root canal therapy, and this is accomplished with the use of a root canal chemical irrigant like sodium hypochlorite, which has the drawbacks of being irritating to periapical tissues, staining the instruments, scorching the surrounding tissues, etc. According to the research, 10% of miswak water extraction is a powerful antibacterial agent when employed in a clinical setting as an irrigant in the endodontic treatment of teeth with necrotic pulp (90). In other research the antibacterial activity of Azadirachta indica (neem) and S. persica (miswak) extracts against E. faecalis was investigated. 50 single-rooted teeth exhibited size 40 K-file apical canal enlargements. In 3 ml of brain-heart broth, each root was autoclaved. Following E. faecalis infection in the root canal, samples were split into five categories depending on solution type: normal saline group, NaOCl solution group, neem leaf extract group, miswak extract group , and a combination of NaOCl and neem leaf extract group. Miswak extract has the least antibacterial activity against E. faecalis. However, the combining herbal and synthetic chemicals can enhance antibacterial activity (91).

In vitro antimicrobial effects of 1%, 5%, 10%, 15%, and 20% alcoholic extract of miswak, 5.25% sodium hypochlorite, 0.2% chlorhexidine, and normal saline revealed that all concentrations of miswak extract, sodium hypochlorite, and chlorhexidine had a significant antimicrobial effect against aerobic and anaerobic bacteria recovered from teeth with necrotic pulps, whereas the best antibacterial action was seen at a concentration of 15% of miswak extract (92).

The addition investigation involved 40 infected primary teeth where the children were separated into four groups of 10. As an irrigating solution, Group 1 received 3% sodium hypochlorite; Group 2 received 12.5% alcoholic extract of miswak; Group 3 received 11% alcoholic extract of propolis; and Group 4 received 0.9% saline. They used sodium hypochlorite's antibacterial activity as the gold standard to compare the antimicrobial properties of propolis and miswak. Depending on the statistics, it appears that miswak may be a suitable natural alternative to sodium hypochlorite, whereas propolis performed similarly to the placebo (normal saline) (93).

Limitations and disadvantages of miswak use

Despite the benefits and therapeutic effects of miswak demonstrated in several types of study, its use is limited by a variety of constraints. Miswak users showed significantly greater rates of gingival recession than toothbrush users (94). In addition, higher occlusal wear, tooth abrasion, gingival recession, and indications of soft tissue damage were shown to be substantially correlated with miswak usage (95). Although miswak users displayed good dental hygiene and a favourable gingival index score (96, 97). Furthermore, according to a study carried out on the Muslim populace of Banyo in the Adamawa area of Cameroon. The miswak users were less prone to dentist visitations and mouth odour but were more likely to report oral health problems than the non-users among adults (98). Moreover, contrary to the usual toothbrush, the bristles of the miswak are positioned along the long axis of its handle, which reduces access to the lingual surfaces or the interdental spaces, although the facial surfaces of the teeth are more accessible. Therefore, it may be impossible for miswak users to easily reach all surfaces of the teeth. In contrast, the angulation of a conventional toothbrush enables the user to easily access distal tooth surfaces, especially on the posterior teeth. Overall, the miswak mechanical action in plaque removal

is limited by the way its bristles are arranged (i.e., they are not angled). In addition, both the brushing method and its application are unfamiliar to most of the populace. As a result, improper usage of a miswak toothbrush raises the risk of tooth wear and gingival recession.

Conclusion

This focuses on the key significant effects of miswak on oral hygiene, oral disease prevention, as well as health promotion. Because of its outstanding chemo-mechanical plaque-removing efficacy and wide range of phytochemicals, available descriptive studies and experimental research support the notion that miswak could be a beneficial dental hygiene solution. The clinical effects of miswak, which include anti-bacterial, anti-fungal, anti-plaque, anti-gingivitis, anti-cariogenic, and whitening properties, were comprehensively reviewed. Despite all of the miswak properties, most people are unfamiliar with the brushing method and its application resulting in improper usage of a toothbrush, which raises the risk of tooth wear and gingival recession. Modern science and technology are being used to design modern doses in order to reap the greatest clinical advantages from miswak toothbrushes to be easier to use and more familiar to the public, given their broad catalogue of benefits and therapeutic effects on oral health.

Acknowledgement

This work was supported by the Ministry of Higher Education, Malaysia, through Fundamental Research Grant Scheme (FRGS)(FRGS/1/2021/SKK0/USM/03/9).

Competing interests

The authors have no conflict of interest by any circumstances by other secondary bodies.

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