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REVIEW ARTICLE

## The impact of oral bacteria and fungi on dental health and the therapeutic importance of meswak root: A comprehensive review

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### Abstract

**Background:** Bacteria, fungus, viruses, and other microorganisms make up the oral microbiome, a very complex ecosystem that works together to promote oral health and equilibrium. However, disruptions in the microbial equilibrium can result in oral dysbiosis, which encourages the emergence of serious dental conditions such oral candidiasis, periodontitis, and dental caries. The importance of cross-kingdom interactions between bacteria and fungi in the development of biofilms and the course of disease has been brought to light by recent developments in oral microbiology. The antibacterial, antifungal, anti-inflammatory, and plaque-reducing qualities of natural items like Meswak (*Salvadora persica*) root have garnered significant interest in addition to traditional dental hygiene procedures. Meswak root, which has long been used as a natural chewing stick, includes biologically active substances that may help maintain tooth health and prevent oral microbial colonization. These substances include fluoride, silica, sulfur compounds, alkaloids, and essential oils.

**Objective:** With a focus on microbial interactions, pathogenic mechanisms, oral biofilm formation, and their clinical consequences in contemporary dentistry, this literature review seeks to objectively assess the effects of oral bacteria and fungi on dental health. The research also examines the medicinal value of Meswak root as a natural antibacterial agent in promoting oral hygiene and managing oral infections.

**Main findings:** According to available data, periodontal pathogens like *Porphyromonas gingivalis* greatly contribute to the deterioration of periodontal tissue, while cariogenic bacteria, especially *Streptococcus mutans*, are crucial in the demineralization of enamel and the development of dental caries. It is becoming more widely acknowledged that fungi, particularly *Candida albicans*, play a significant role in oral infections and disorders linked to biofilms. Additionally, microbial pathogenicity, antibiotic resistance, and disease severity are all increased by synergistic interactions between bacterial and fungal communities. Additionally, research has shown that Meswak root inhibits a number of oral pathogens, including as *Candida albicans*, *Lactobacillus* species, and *Streptococcus mutans*, consequently lowering plaque buildup, gingival irritation, and microbial biofilm development. Meswak's natural phytochemical components may help maintain periodontal health and remineralization. Meswak root and other natural adjuncts have the potential to improve both preventative and therapeutic dental treatment, as do emerging diagnostic technologies and microbiome-targeted medications.

**Conclusion:** Both oral health and disease are significantly influenced by mouth bacteria and fungus. Comprehending the dynamics of the oral microbiome and cross-kingdom microbial interactions could aid in the creation of precision dentistry techniques as well as more

potent preventative and therapeutic measures. Meswak root's antibacterial and antifungal properties against oral microorganisms make it a useful natural supplement in oral healthcare. Improved oral hygiene, a lower incidence of disease, and better overall dental health may result from combining ancient herbal methods with contemporary dentistry procedures.

**Keywords:** Oral microbiome, Dental biofilms, Oral dysbiosis, Periodontal pathogens, *Candida albicans*, Oral microbiology

## Introduction

Oral health affects social interaction, communication, nutrition, and overall quality of life, making it a crucial part of overall health and wellbeing. Oral diseases continue to be among the most common chronic ailments in the world, impacting billions of people of all ages. The World Health Organization states that severe periodontal diseases impact a significant portion of the adult population and lead to tooth loss and functional impairment, while untreated dental caries in permanent teeth is one of the most prevalent health disorders worldwide.

The oral microbiome, which is made up of bacteria, fungus, viruses, archaea, and protozoa, is a very varied microbial ecology found in the human oral cavity. Through colonization resistance, immunological regulation, and metabolic interactions, these bacteria coexist in a balanced symbiotic relationship with the host under healthy conditions and help to preserve oral homeostasis. However, oral disorders such as dental caries, periodontal disease, peri-implantitis, and oral candidiasis can develop more readily when this ecological balance is upset, a condition known as oral dysbiosis (Lamont, et al. 2018). Natural oral hygiene products, like Meswak (*Salvadora persica*) root, have long been utilized in traditional medicine to maintain oral hygiene and prevent dental diseases in addition to contemporary oral healthcare methods. Meswak root supports oral microbial balance and dental health by containing physiologically active substances such as fluoride, silica, sulfur compounds, tannins, alkaloids, and essential oils that have antibacterial, antifungal, anti-inflammatory, and plaque-reducing qualities.

The pathophysiology of oral illnesses is significantly influenced by dental biofilms. Biofilms are organized microbial communities that cling to oral surfaces, such as teeth and mucosal tissues, and are embedded in an extracellular polymeric matrix. Biofilm-associated infections are particularly challenging to manage because these microbial communities show heightened resistance to antimicrobial drugs and host immune responses. Due to its acidogenic and aciduric characteristics, which lead to enamel demineralization, *Streptococcus mutans* has been closely linked to dental caries among the many bacterial species that live in the oral cavity (Bowen, et al. 2018). Similar to this, pathogenic anaerobic bacteria like *Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia* collectively referred to as the “red complex” are closely associated with periodontal diseases because they can cause the long-term inflammatory destruction of periodontal tissues (Hajishengallis and Lamont, 2021). According to a number of studies, Meswak root extracts exhibit inhibitory activity against periodontal and cariogenic pathogens, such as *Porphyromonas gingivalis* and *Streptococcus mutans*, which lowers plaque buildup, gingival inflammation, and bacterial adherence to tooth surfaces.

The oral mycobiome, especially fungal species in the genus *Candida*, has received more attention in recent years. While many people view *Candida albicans* as a typical commensal fungus, opportunistic overgrowth can cause oral candidiasis and accelerate the development of other oral illnesses. According to recent research, fungi actively contribute to the development of oral biofilms and work in concert with bacterial species to increase pathogenicity and antibiotic resistance (Krüger, et al. 2019). Notably, it has been demonstrated that interactions between *Streptococcus mutans* and *Candida albicans* encourage extremely virulent biofilms linked to severe early childhood caries (Falsetta, et al. 2014). It is interesting to note that meswak root has also shown antifungal activity against *Candida albicans*, indicating that it may be used as a natural supplemental treatment for oral fungal infections.

In oral microbiology research, the idea of cross-kingdom interactions between mouth bacteria and fungi has gained significant attention. Microbial colonization, pathogenicity, and disease progression are all influenced by these interactions, which include intricate communication networks, metabolic cooperation, and signaling processes. Compared to single-species biofilms, mixed-species biofilms made up of bacterial and fungal communities show improved structural stability and resistance to antimicrobial treatments (Koo, et al. 2018). As a result, it is becoming more widely acknowledged that comprehending the interactions among oral bacteria is crucial for enhancing diagnostic precision and creating focused treatment plans in contemporary dentistry. Through their broad-spectrum anti-bacterial properties, natural medicinal agents like Meswak root may offer extra advantages by preventing the formation of microbial biofilms and lowering oral pathogen colonization.

Oral microbial populations are now much better understood thanks to developments in molecular biology and sequencing technologies. The oral microbiome can be thoroughly characterized and microbial alterations linked to disease states can be identified using methods including Polymerase Chain Reaction (PCR), metagenomic sequencing, and Next-Generation Sequencing (NGS) (Wade, 2021). The development of precision dentistry techniques focused on customized prevention and treatment based on microbial profiling has also been facilitated by these technologies. In order to provide safer, more affordable, and long-lasting oral healthcare techniques, there is an increasing scientific interest in combining traditional herbal medicines, such as Meswak root, with evidence-based dental care.

## Materials and Methods

A thorough synthesis of current knowledge regarding bacterial and fungal contributions to oral health and illness is necessary given the mounting evidence regarding the function of oral microorganisms in dental diseases. With a focus on microbial interactions, pathogenic mechanisms, oral biofilm formation, and their clinical consequences in modern dentistry, this literature review attempts to objectively investigate the effects of oral bacteria and fungi on dental health. The review also emphasizes Meswak root's medicinal value as a natural antibacterial and antifungal agent that may promote oral hygiene, lessen the colonization of harmful microorganisms, and aid in the management and prevention of oral disorders.

### The oral microbiome and dental homeostasis

One of the most varied microbial ecosystems in the human body is found in the oral cavity, which is home to hundreds of bacterial and fungal species that live on the tongue, teeth, gingival tissues, saliva, and mucosal membranes. These microbes work together to create the oral microbiome, which is essential for preserving oral homeostasis and preventing pathogenic colonization (Lamont, et al. 2018). The host immune system and environmental elements like nutrition, oral hygiene, salivary composition, and antibiotic exposure constantly interact with the oral microbiome, which is a dynamic and well-organized ecological community. Meswak (*Salvadora persica*) root is one of the traditional oral hygiene methods that has been shown to support oral microbial balance and preserve oral health. Numerous bioactive substances with antibacterial and anti-inflammatory qualities found in meswak root may aid in controlling mouth microbial populations and lowering pathogenic colonization. Through balanced microbial variety and regulated microbial growth, the oral microbiome sustains a symbiotic interaction with the host under healthy conditions. By controlling local immune responses, inhibiting pathogen colonization, and preserving ecological stability within dental biofilms, beneficial bacteria support oral health (Marsh and Zaura, 2017). By offering antibacterial proteins, buffering power, and mechanical cleaning, saliva also plays a major role in maintaining dental homeostasis by controlling microbial activity and preserving physiological pH levels. In a similar vein, Meswak root's fibrous texture has been shown to increase salivary flow and offer natural cleaning benefits, promoting dental hygiene and lowering bacteria buildup on tooth surfaces. With over 700 bacterial species found in the oral cavity, bacterial communities make up the majority of the oral microbiome. Firmicutes, Actinobacteria, Proteobacteria, Bacteroidetes, and Fusobacteria are important bacterial phyla (Human Microbiome Project Consortium, 2012). *Streptococcus*, *Actinomyces*, *Veillonella*, *Neisseria*, and *Haemophilus* are common commensal genera that support oral tissue health and microbial equilibrium. On the other hand, dysbiosis and the development of oral diseases may result from changes in the microbial composition. Research has shown that Meswak root extracts exhibit antibacterial action against a number of harmful oral bacteria, such as *Porphyromonas gingivalis* and *Streptococcus mutans*, which are closely linked to periodontal disorders and dental caries. These results imply that Meswak might help keep the oral cavity's microbial balance.

The oral microbiome, also known as the oral mycobiome, includes fungi in addition to bacteria. Among the most common fungal organisms found in healthy people are *Candida* species, especially *Candida albicans* (Krüger, et al. 2019). Even though these fungi often act as commensals, immunological or environmental disruptions may promote opportunistic overgrowth and lead to mouth infections such denture stomatitis and oral candidiasis. It is interesting to note that Meswak root has shown antifungal qualities against *Candida albicans*. This could be because it contains sulfur compounds, tannins, and essential oils that prevent the growth of fungi and the production of biofilms. Meswak may therefore be a useful natural supplement for preventing opportunistic infections and managing oral fungal colonization.

Oral bacteria ecology and equilibrium depend heavily on dental biofilms. Microorganisms can attach to oral surfaces and interact through chemical signaling pathways thanks to biofilms, which are highly structured microbial communities contained inside an Extracellular Polymeric Substance (EPS) matrix (Koo, et al. 2017). Pioneer bacterial species like *Streptococcus sanguinis* and *Streptococcus gordonii*, which aid in the subsequent attachment of secondary colonizers, usually initiate early biofilm formation. Biofilms live with host tissues and preserve ecological stability in healthy oral environments without causing appreciable inflammation. According to research, Meswak root may promote plaque control and gingival health by preventing the formation of plaque biofilms by decreasing bacterial adherence and interfering with microbial deposition on tooth surfaces.

Maintaining dental health depends on host-microbiome interactions. To stop tissue damage, the innate and adaptive immune systems constantly keep an eye on oral bacteria communities and control inflammatory reactions. Immunoglobulin A (IgA), neutrophils, salivary antimicrobial peptides, and epithelial barriers all work together to regulate microbial development and preserve mucosal integrity (Moutsopoulos and Konkel, 2018). If these defense systems are disrupted, the microbial makeup may change and the growth of harmful biofilms may be encouraged. By lowering gingival inflammation and oxidative stress in the oral cavity, the anti-inflammatory and antioxidant components found in Meswak root may further enhance host defensive systems. According to the ecological plaque hypothesis, environmental changes like increased sugar intake, poor oral hygiene, smoking, and systemic diseases cause ecological changes within the microbial community that lead to oral diseases rather than the presence of particular pathogens alone (Marsh, 2003). Dental caries, gingivitis, and periodontitis can result from these ecological disruptions that favor acidogenic and proteolytic microbes. As a result, it is thought that maintaining oral microbial balance is essential to sustaining periodontal and dental health. By lowering plaque buildup, managing harmful microbes, and fostering a better mouth environment, daily use of Meswak root as a natural oral hygiene solution may help reduce these ecological disruptions.

The diversity and function of oral microbes have been significantly better understood thanks to recent developments in molecular microbiology and sequencing technologies. Next-Generation Sequencing (NGS) and metagenomic analysis are two examples of high-throughput sequencing techniques that have made it possible to thoroughly characterize microbial communities and identify microbial signatures linked to health and disease states (Wade, 2021). These advancements have led to an increase in interest in microbiome-targeted therapy approaches that use probiotics, microbiome modulation, and precision dentistry techniques to restore oral equilibrium. Meswak root's broad-spectrum antibacterial qualities, affordability, and long history of traditional use in oral healthcare have all contributed to a rise in scientific interest in natural medicinal agents.

Overall, through intricate interactions between microorganisms, host tissues, and environmental factors, the oral microbiome plays a critical role in preserving dental homeostasis. Maintaining long-term oral health outcomes and preventing dental illnesses depend on maintaining microbial equilibrium. Through their antibacterial, antifungal, anti-inflammatory, and plaque-reducing properties, natural oral hygiene products like Meswak root may also help to preserve oral microbial equilibrium, underscoring their potential significance as supplemental tools in contemporary preventive dentistry.

## Bacterial pathogens in dental diseases

Major dental disorders, including dental caries and periodontal diseases, are largely caused by bacterial infections. Highly diverse bacterial communities that typically coexist in ecological harmony with the host can be found in the mouth cavity. However, changes in host immunity, environmental factors, and microbial composition can result in oral dysbiosis, which encourages the growth of pathogenic microorganisms that can harm oral tissues and cause chronic inflammation (Lamont, et al. 2018). Natural oral hygiene products, like Meswak (*Salvadora persica*) root, have drawn scientific interest recently because of their capacity to regulate harmful oral bacteria and maintain the oral cavity's microbial balance.

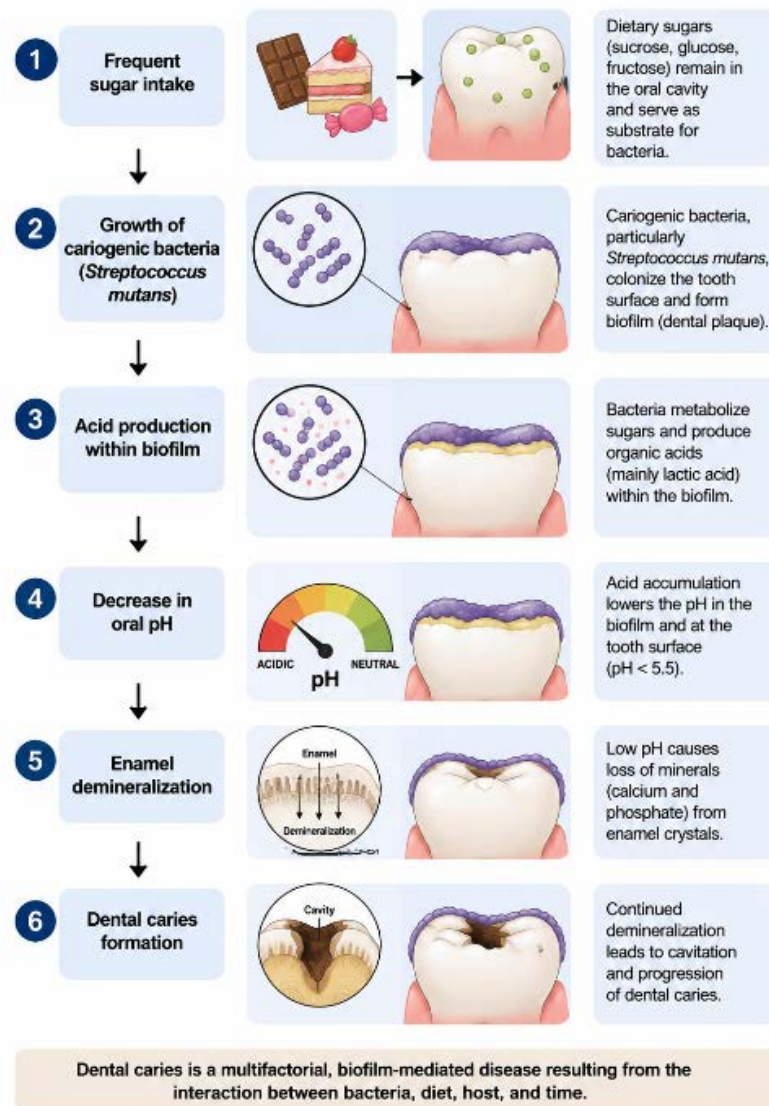
Biofilm production on tooth and gingival surfaces is closely linked to dental disorders. Because oral biofilms shield bacteria from host immune responses and antimicrobial drugs, pathogenic microorganisms are able to endure, multiply, and advance disease. Through mechanisms including acid production, toxin release, immune evasion, and tissue destruction, several bacterial species have been identified as significant contributors to oral illnesses. Research has shown that Meswak root contains physiologically active substances with antibacterial and anti-plaque properties, including fluoride, silica, sulfur compounds, tannins, alkaloids, and essential oils. These substances may lessen microbial buildup on oral surfaces, prevent biofilm formation, and interfere with bacterial adherence.

The multifactorial biofilm-mediated illness known as dental caries is typified by the gradual demineralization of dentin and tooth enamel. Because of its acidogenic and aciduric characteristics, *Streptococcus mutans* is regarded as one of the main cariogenic pathogens among the bacteria linked to the development of caries (Bowen, et al. 2018). This bacterium breaks down dietary carbohydrates, especially sucrose, into organic acids that lower the pH in the area and encourage the demineralization of enamel. Meswak root extracts have been found to have inhibitory effect against *Streptococcus mutans*, which limits bacterial colonization on tooth surfaces and lowers acid production. Meswak's natural calcium and fluoride concentration may also aid in enamel remineralization and dental caries prevention.

*S. mutans* uses glucosyltransferase enzymes to produce extracellular polysaccharides in addition to acid, which promotes bacterial adherence and stable biofilm formation on tooth surfaces (Koo, et al. 2017). The biofilm's acidic milieu speeds up the development of caries and microbial dysbiosis by favoring acid-tolerant bacteria. According to reports, meswak root contains anti-biofilm qualities that may prevent the production of extracellular polysaccharide matrices and decrease bacterial adherence, impeding the growth of cariogenic biofilms and promoting the preservation of oral hygiene.

## Results and Discussion

Actinomyces species, which are linked to root surface caries and early plaque formation, and *Lactobacillus* species, which contribute to lesion progression because to their high acid tolerance, are other bacterial species involved in dental caries (Takahashi and Nyvad, 2011). Dental caries is linked to polymicrobial interactions rather than a single pathogen alone, according to recent microbiome studies. Therefore, it is thought that preserving the general microbial balance in the oral cavity is crucial for preventing dental cavities. Meswak root's potential as a supplemental natural medicinal agent in preventive dentistry and oral healthcare management is highlighted by its broad-spectrum antibacterial action against many oral infections (Fig. 1).



**Figure 1. Mechanism of dental caries development.**

Chronic inflammatory illnesses known as periodontal diseases damage the gingiva, periodontal ligament, and alveolar bone, which are the tissues that support teeth. Pathogenic bacterial biofilms and host immune responses interact intricately to cause periodontitis, which progressively destroys tissue and causes tooth loss (Hajishengallis and Lamont, 2021). Natural oral hygiene products like Meswak (*Salvadora persica*) root have garnered a lot of attention in addition to traditional periodontal treatments because of their antimicrobial, anti-inflammatory, and plaque-reducing qualities that may promote periodontal health and microbial balance in the oral cavity.

The “red complex” bacteria, which include *Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia*, are among the most important periodontal infections (Socransky, et al. 1998). These anaerobic Gram-negative bacteria have several virulence characteristics that lead to tissue invasion, immunological dysregulation, and persistent inflammation. Meswak root extracts have been shown to have inhibitory effect against a number of periodontal pathogens, including *Porphyromonas gingivalis*, which may lessen bacterial colonization and the creation of periodontal biofilms. Despite its relatively low abundance, *Porphyromonas gingivalis* is regarded as a keystone pathogen that can change the entire microbial ecology. It generates gingipains, which are proteolytic enzymes that break down host tissues, interfere with immunological communication, and encourage dysbiosis (How, et al. 2016). Similar to how *Tannerella forsythia* increases inflammatory reactions and epithelial degradation, *Treponema denticola* contributes to periodontal deterioration through motility, tissue penetration, and protease generation. In addition to lowering gingival inflammation and enhancing the health of periodontal tissue, the bioactive components of Meswak root, such as tannins, sulfur compounds, alkaloids, and essential oils, may help inhibit the growth and virulence of these infections.

Chronic periodontal inflammation causes matrix metalloproteinases and cytokines to be released, which breaks down connective tissue and resorbs alveolar bone. Furthermore, because periodontal bacteria can spread throughout the body and cause persistent inflammation, they have been linked to systemic conditions such as rheumatoid arthritis, diabetes mellitus, and cardiovascular disease (Hajishengallis, 2015). According to reports, meswak root possesses antioxidant and anti-inflammatory properties that may help lower oxidative stress and inflammatory reactions in periodontal tissues, promoting the prevention of periodontal disease and enhancing oral health results.

Recent developments in sequencing methods have revealed more bacterial species linked to biofilm complexity and oral illnesses. Due to its function as a bridging organism that promotes coaggregation between early and late biofilm colonizers, *Fusobacterium nucleatum* has drawn special attention (Han, 2015). Additionally, this species has been connected to systemic diseases including colorectal cancer and leads to inflammatory reactions. Meswak root may restrict the colonization and interaction of bridge organisms like *Fusobacterium nucleatum* within periodontal biofilms by interfering with bacterial adhesion and biofilm maturation, according to research.

*Prevotella intermedia*, which is often linked to periodontal infections, and *Veillonella* spp., which engage in metabolic interactions within oral biofilms, are two more newly discovered oral pathogens. Through cooperative interactions with existing diseases, these bacteria may affect the severity of disease and contribute to microbial diversity. Meswak root's broad-spectrum antibacterial properties against a variety of oral microbes suggest that it could be used as a supplementary natural agent to manage polymicrobial biofilms and preserve periodontal health. Current study on the oral microbiome highlights that polymicrobial dysbiosis, not isolated bacterial infections, is the cause of oral illnesses. Disease genesis and progression are determined by the ecological interactions between microbial communities, environmental factors, and host immunity. Therefore, preventing periodontal diseases requires maintaining microbial equilibrium through good oral hygiene habits. In addition to contemporary preventative and therapeutic dentistry techniques, traditional oral care practices like the usage of Meswak root may offer extra advantages by lowering plaque buildup, preventing harmful germs, and promoting a better oral microbial habitat (Tab. 1).

**Table 1. Major bacterial pathogens associated with dental diseases.**

Bacterial species	Associated disease	Major virulence mechanisms
<i>Streptococcus mutans</i>	Dental caries	Acid production, EPS synthesis, biofilm formation
<i>Lactobacillus</i> spp.	Caries progression	Acid tolerance and acid production
<i>Actinomyces</i> spp.	Root caries	Early plaque colonization
<i>Porphyromonas gingivalis</i>	Periodontitis	Gingivapains, immune dysregulation
<i>Treponema denticola</i>	Periodontitis	Motility, tissue invasion
<i>Tannerella forsythia</i>	Periodontitis	Inflammatory stimulation
<i>Fusobacterium nucleatum</i>	Biofilm maturation	Bacterial coaggregation
<i>Prevotella intermedia</i>	Periodontal infections	Proteolytic activity

Improving dental prevention and treatment strategies requires an understanding of the pathogenic mechanisms of oral bacteria. Probiotics, biofilm disruption technologies, and precision antibacterial strategies all of which aim to restore oral microbial equilibrium rather than eradicate microorganisms indiscriminately are among the microbiome-targeted medicines that are increasingly the focus of modern research.

## Fungal communities and oral health

Fungal microbes are an essential part of the oral microbiome and have a big impact on oral health and illness. In a dynamic ecological setting marked by intricate microbial interactions and host immunological control, the oral fungus community, also known as the oral mycobiome, coexists with bacterial populations. Despite making up a lesser percentage of the oral microbiota than bacteria, fungi play a significant role in the formation of dental biofilms, microbial homeostasis, and opportunistic infections (Krüger, et al. 2019). Because of its antibacterial and antifungal qualities, which may help control oral microbial communities and promote oral health, natural oral hygiene products like Meswak (*Salvadora persica*) root have drawn more attention from scientists in recent years.

Fungal species can coexist with other oral bacteria and host tissues in a healthy environment without producing illness. However, fungal overgrowth and pathogenicity may be encouraged by immunological dysfunction, systemic illnesses, poor dental hygiene, disruptions in microbial balance, or long-term antibiotic usage. The most common and clinically significant oral fungi linked to oral illnesses are those in the genus *Candida* (Millsop and Fazel, 2016). Regular usage of Meswak root has been linked to better oral hygiene and less microbial buildup, which may help prevent fungal overgrowth and preserve the balance of oral microbiota.

Different fungus species that colonize oral tissues, saliva, tooth surfaces, and mucosal membranes make up the oral mycobiome. *Candida*, *Cladosporium*, *Aspergillus*, *Saccharomyces*, *Fusarium*, and *Cryptococcus* are among the many fungal genera found in the oral cavity,

according to molecular sequencing technology (Ghannoum, et al. 2010). These fungi engage in intricate ecological relationships with host immune systems and bacterial populations. According to new research, Meswak root's bioactive components such as sulfur compounds, tannins, flavonoids, alkaloids, and essential oils have broad-spectrum antibacterial properties that may affect the oral cavity's bacterial and fungus populations. Age, food, dental hygiene habits, systemic health issues, smoking habits, and salivary flow all affect the composition of the oral mycobiome. Fungal populations are often kept low in healthy individuals by immune surveillance and microbial competition. Because saliva contains antimicrobial proteins, immunoglobulins, histatins, and enzymes that can prevent fungal adherence and proliferation, it plays a major role in fungal control (Moutsopoulos and Konkel, 2018). Similar to this, Meswak root's fibrous structure has been shown to increase salivary secretion and offer mechanical washing, improving oral hygiene and lowering fungus colonization.

According to recent data, fungi are not just opportunistic colonists but actively participate in oral microbial ecology. The general behavior of oral biofilms and disease susceptibility can be impacted by fungal communities through their influence on microbial signaling pathways, biofilm architecture, and food availability (Krüger, et al. 2019). By preventing microbial adherence and lowering the growth of pathogenic bacteria on oral surfaces, natural antimicrobial agents like Meswak root may aid in regulating the development of oral biofilms.

*Candida albicans* is the most researched species of oral fungus and is thought to be the main fungal pathogen in the mouth cavity. The ability of *Candida albicans* to change between yeast and hyphal forms is a dimorphic fungus that is closely linked to its pathogenicity and capacity for tissue invasion (Mayer, et al. 2013). Meswak root extracts have been shown in numerous investigations to exhibit antifungal efficacy against *Candida albicans*, possibly preventing fungal growth, adherence, and hyphal development. While *C. albicans* is frequently found in healthy people as a commensal organism, immunosuppression, diabetes mellitus, xerostomia, denture use, smoking, chemotherapy, or extended antibiotic therapy can all lead to opportunistic overgrowth. One of the most prevalent fungal infections affecting the oral mucosa, oral candidiasis, can result from such overgrowth (Millsop and Fazel, 2016). Meswak root's antifungal and anti-inflammatory qualities may help manage fungal colonization and lessen oral mucosal irritation brought on by candidal infections.

Clinical manifestations of oral candidiasis include:

- *Pseudomembranous candidiasis*
- *Erythematous candidiasis*
- *Hyperplastic candidiasis*
- *Angular cheilitis*
- *Denture stomatitis*

*Candida* biofilm growth on denture surfaces is specifically linked to denture stomatitis. Dentures' porous nature increases infection duration and resistance to antifungal therapy by promoting fungal adherence and biofilm formation (Nobile and Johnson, 2015). Meswak root extracts may reduce the incidence of denture-associated infections by interfering with fungal adherence and biofilm formation on oral surfaces and prosthetic materials, according to research.

Oral infections are increasingly being linked to non-albicans *Candida* species as *Candida glabrata*, *Candida tropicalis*, and *Candida krusei* in addition to *Candida albicans*, especially in immunocompromised people. Because some of these species show enhanced resistance to widely used antifungal drugs, they are therapeutically significant. In order to enhance oral infection management and supplement traditional antifungal treatment, natural antifungal medicines like Meswak root are being investigated as possible supplementary therapies.

A number of virulence factors that promote colonization, tissue invasion, and immune evasion are necessary for oral fungus to be harmful. Fungal adherence to oral epithelial cells, dental surfaces, and prosthetic materials *via* particular adhesion proteins called adhesins is one of the most significant processes (Mayer, et al. 2013). The yeast-to-hyphae transition seen in *Candida albicans* is another important virulence factor. Hyphal forms are more invasive and aid in tissue damage and epithelial penetration. Additionally, hyphae improve resistance to host immunological responses and biofilm development. Meswak root chemicals may decrease fungal pathogenicity and persistence by reducing fungal adherence and inhibiting biofilm development. Because extracellular polymeric matrices hinder medication penetration and shield fungal cells, oral fungal biofilms are extremely resistant to immune clearance and antifungal drugs (Nobile and Johnson, 2015). Fungi work in concert with bacterial organisms in mixed-species biofilms to increase the durability and virulence of the biofilm. Meswak root may be effective in breaking up polymicrobial biofilms and lowering microbial resistance because it has demonstrated possible anti-biofilm activity against oral bacteria.

Additionally, hydrolytic enzymes including lipases, proteases, and phospholipases that aid in tissue deterioration and inflammatory reactions are secreted by fungal pathogens. These enzymes aid in the uptake of nutrients and promote the persistence of fungi in oral tissues. Meswak root's anti-inflammatory and antioxidant qualities may lessen oxidative damage and tissue inflammation brought on by fungal infections and long-term oral inflammatory disorders.

Oral fungal infections are often associated with bacterial populations within polymicrobial biofilms rather than developing in isolation, according to recent research. Oral bacteria such as *Candida albicans* and *Streptococcus mutans* work together to increase acid production, enhance biofilm formation, and exacerbate the illness (Koo, et al. 2018). Furthermore, cross-kingdom microbial interactions might increase resistance to antimicrobial therapies and complicate clinical management. As a result, it is becoming increasingly clear that knowledge of fungal-bacterial relationships is essential for improved oral healthcare diagnostic, preventative, and treatment strategies. Meswak root is a promising natural supplement in oral healthcare that may help preserve the balance of oral microorganisms and prevent oral infections due to its antibacterial, antifungal, anti-inflammatory, and anti-biofilm properties (Tab. 2).

**Table 2. Major oral fungal species and associated oral diseases.**

Fungal species	Associated oral conditions	Major virulence factors
<i>Candida albicans</i>	Oral candidiasis, denture stomatitis	Hyphal formation, biofilm production, adhesins
<i>Candida glabrata</i>	Opportunistic oral infections	Antifungal resistance
<i>Candida tropicalis</i>	Oral candidiasis	Biofilm formation
<i>Candida krusei</i>	Immunocompromised-associated infections	Drug resistance
<i>Aspergillus</i> spp.	Rare oral fungal infections	Tissue invasion
<i>Cryptococcus</i> spp.	Opportunistic oral lesions	Capsule-mediated immune evasion

Fungal communities are increasingly recognized as major contributors to oral disease pathogenesis and biofilm complexity. Improved understanding of the oral mycobiome may support the development of microbiome-based diagnostics, targeted antifungal therapies, and personalized approaches in preventive and restorative dentistry.

### Cross-kingdom interactions in oral biofilms

The intricate ecological ties that exist between microorganisms from several biological kingdoms, especially bacteria and fungi, within oral biofilms are referred to as cross-kingdom interactions. These interactions are essential for microbial colonization, biofilm formation, pathogenicity increase, and disease progression in the oral cavity. Recent developments in oral microbiology have shown that dynamic polymicrobial communities with cooperative and synergistic interactions between microorganisms are more likely to cause oral disorders than isolated pathogens alone (Lamont, et al. 2018). Because of their potential to disrupt microbial interactions, prevent biofilm development, and maintain oral microbial balance, natural oral hygiene treatments like Meswak (*Salvadora persica*) root have garnered increasing scientific attention.

Oral biofilms are highly organized microbial ecosystems that are embedded in Extracellular Polymeric Substances (EPS) and affixed to tooth and mucosal surfaces. Microorganisms are shielded by these biofilms from host immunological responses, antimicrobial treatments, and environmental stresses. Microbial behavior and pathogenicity are influenced by the physical contacts, metabolic cooperation, and communication pathways that bacteria and fungi use to communicate inside these biofilms (Koo, et al. 2018). Tannins, sulfur compounds, flavonoids, alkaloids, and essential oils are among the bioactive substances found in Meswak root that have shown antibacterial and anti-biofilm properties. These compounds may disrupt microbe adhesion and lessen the structural stability of oral biofilms.

*Candida albicans* and *Streptococcus mutans* are two of the most well-researched instances of cross-kingdom contact in the oral cavity. Strong synergistic connections between these microbes greatly increase their pathogenicity and biofilm production. In order to promote fungal adherence and stabilize mixed-species biofilms, *S. mutans* generates glucosyltransferase enzymes that can synthesize extracellular glucans from dietary sucrose (Falsetta, et al. 2014). According to research, Meswak root extracts may prevent *Candida albicans* and *Streptococcus mutans* from growing and adhering, which could lessen the development of highly dangerous mixed-species biofilms. In exchange, *Candida albicans* increases microbial biomass and provides structural support for biofilm architecture. In children with Early Childhood Caries (ECC), in particular, this interaction produces dense, highly acidogenic biofilms that can speed up enamel demineralization and worsen dental cavities (Koo, et al. 2018). Meswak root's anti-cariogenic qualities, such as its inherent fluoride content and antibacterial activity, may aid in lowering acid generation, preventing microbial colonization, and bolstering enamel defense against demineralization.

Mixed bacterial-fungal biofilms are more metabolically active and produce more acid than single-species biofilms, according to experimental research. Additionally, these polymicrobial communities show greater resistance to mechanical removal and antimicrobial treatments, making disease management more difficult and raising the risk of recurrence. By preventing microbial aggregation and restricting the build-up of extracellular polysaccharides, meswak root has shown potential anti-biofilm properties that could enhance plaque reduction and lessen biofilm persistence.

Several communication pathways that control microbial cooperation and pathogenicity are involved in cross-kingdom microbial interactions. Quorum sensing, a microbial communication method mediated by signaling molecules that regulate gene

expression based on microbial population density, is one important mechanism (Krüger, et al. 2019). Quorum sensing chemicals, such as farnesol, control the growth of hyphae and the production of biofilms in fungi like *Candida albicans*. These fungal signaling pathways can be influenced by bacterial species, changing the shape and virulence of fungi. Similar to this, bacterial proliferation, adhesion, and metabolic activity inside oral biofilms can be impacted by fungal metabolites. According to new research, Meswak root's natural phytochemicals may disrupt microbial signaling pathways and prevent microbial communication that is necessary for biofilm growth and pathogenicity.

Biofilm production is further strengthened by physical interactions between fungus and bacteria. Bacterial attachment and colonization are facilitated by adhesion molecules on fungal hyphae, resulting in highly ordered microbial networks inside the biofilm matrix (Jenkinson and Lamont, 2005). Meswak root's fibrous texture also acts as a natural mechanical cleanser, perhaps reducing plaque buildup and physically disrupting bacteria adherence on dental and mucosal surfaces.

When compared to mono-species infections, mixed bacterial-fungal biofilms are linked to higher pathogenicity and more serious oral illnesses. Oral bacteria and fungus work in concert to accelerate tissue invasion, prolong inflammation, and boost resistance to antimicrobial treatments (Nobile and Johnson, 2015). Cross-kingdom biofilms cause increased acid generation and quick enamel degradation in dental caries. Polymicrobial biofilms in periodontal disorders trigger heightened inflammatory reactions that cause alveolar bone resorption and connective tissue deterioration. Similarly, mixed biofilm growth on prosthetic surfaces is closely linked to denture stomatitis and oral candidiasis. Meswak root's antibacterial, antifungal, and anti-inflammatory properties may help manage these polymicrobial infections and lessen the severity of the illness.

Crucially, polymicrobial biofilms show significant resistance to traditional antimicrobial treatments because of a variety of defense mechanisms, including as decreased drug penetration, modified microbial metabolism, and cooperative stress reactions. In many oral disorders, this resistance leads to treatment failure and recurring infections. As a result, Meswak root and other natural therapeutic agents are becoming more popular as supplemental methods for controlling resistant oral biofilms and enhancing oral hygiene results.

Additionally, recent research indicates that oral polymicrobial biofilms may affect systemic health through microbial dispersion and chronic inflammatory pathways. Mixed-species biofilm-associated oral pathogens have been connected to lung infections, diabetes mellitus, heart disease, and poor pregnancy outcomes (Hajishengallis, 2015). Meswak root may help maintain oral health and lessen systemic issues related to oral microbial dysbiosis by lowering pathogenic microbial colonization and managing persistent oral inflammation (Tab. 3).

**Table 3. Major cross-kingdom interactions in oral biofilms.**

Microorganisms involved	Type of interaction	Clinical impact
<i>Streptococcus mutans</i> + <i>Candida albicans</i>	Synergistic biofilm formation	Severe dental caries
<i>Candida albicans</i> + <i>Porphyromonas gingivalis</i>	Enhanced inflammation	Periodontal tissue destruction
<i>Fusobacterium nucleatum</i> + <i>Candida</i> spp.	Biofilm stabilization	Persistent oral infections
Oral bacteria + fungal biofilms	Increased antimicrobial resistance	Treatment failure

Understanding cross-kingdom interactions within oral biofilms is essential for advancing preventive and therapeutic strategies in modern dentistry. Targeting microbial communication pathways, biofilm architecture, and polymicrobial cooperation may provide innovative approaches for controlling oral diseases and improving long-term oral health outcomes.

Maintaining oral health and managing biofilm-associated dental disorders require therapeutic and preventive measures that target oral bacteria. Due to the strong correlation between microbial dysbiosis and complex polymicrobial biofilms and oral diseases like dental caries, periodontitis, and oral candidiasis, modern dental management increasingly prioritizes methods targeted at restoring microbial balance rather than eradicating microorganisms indiscriminately (Marsh and Zaura, 2017). Innovative antimicrobial treatments, biofilm-targeted interventions, microbiome modulation methods, and preventive clinical procedures have all been made possible by developments in oral microbiology and biofilm research. Traditional natural oral hygiene products, like Meswak (*Salvadora persica*) root, are becoming more widely acknowledged for their antimicrobial, antifungal, anti-inflammatory, and anti-biofilm qualities in addition to contemporary therapeutic methods, making them useful supplementary tools in preventive dentistry.

One of the main methods for managing oral bacterial and fungal infections is still conventional antibiotic therapy. While antifungal medications are routinely administered for oral candidiasis and fungal infections associated with dentures, antibiotics are often used to treat severe periodontal infections and odontogenic abscesses.

Common antibacterial agents used in dentistry include:

- Amoxicillin
- Metronidazole

- Clindamycin
- Doxycycline

These substances aid in lowering the bacterial load and inhibiting periodontal infections including *Treponema denticola* and *Porphyromonas gingivalis* (Slots, 2017). On the other hand, overuse or improper use of antibiotics can lead to antimicrobial resistance and disruption of the good oral flora. Natural antimicrobial medicines like Meswak root, which has shown inhibitory action against cariogenic and periodontal infections without appreciably upsetting oral microbial balance, are therefore gaining popularity.

Antifungal medications commonly used for oral fungal infections include:

- Nystatin
- Fluconazole
- Clotrimazole
- Miconazole

By compromising the integrity of fungal cell membranes or preventing ergosterol synthesis, these substances target fungal infections, especially *Candida albicans* (Millsop and Fazel, 2016). However, a rising clinical problem is the rise in resistance among non-*albicans Candida* species. Meswak root extracts have been proven in numerous studies to have antifungal qualities against *Candida albicans* and other oral fungal species, indicating their potential utility as an additional natural therapy for managing oral fungal infections and lowering the production of fungal biofilms.

Additionally, antiseptic mouthwashes are crucial for controlling oral microbes. Because of its broad-spectrum antibacterial action and extended substantivity, chlorhexidine gluconate is regarded as one of the most efficient antiseptic agents for lowering plaque deposition and gingival inflammation (James, et al. 2017). Preventive dentistry also makes extensive use of cetylpyridinium chloride formulations and mouthwashes based on essential oils. In a similar vein, Meswak root has long been utilized as a natural chewing stick and oral hygiene tool. While its bioactive ingredients support antibacterial activity, gingival inflammation reduction, and dental hygiene maintenance, its fibrous structure offers mechanical plaque removal.

Modern therapeutic approaches increasingly concentrate on interrupting microbial communication routes and biofilm architecture since oral bacteria are typically found within biofilms. The goal of biofilm-targeted treatments is to increase antibiotic penetration while decreasing bacteria pathogenicity. According to research, Meswak root may restrict the development of plaque biofilms and lessen microbial buildup on oral surfaces by interfering with microbial adherence and extracellular polysaccharide production.

Photodynamic Treatment (PDT), which combines photosensitizing drugs with particular light wavelengths to produce reactive oxygen species capable of killing microbial cells within biofilms, is one promising strategy (Cieplik, et al. 2018). PDT is being researched more and more as an adjuvant treatment for periodontitis and oral candidiasis since it has demonstrated efficacy against both bacterial and fungal oral infections.

Innovative approaches to oral healthcare have also included nanotechnology-based treatments. Silver, zinc oxide, and chitosan nanoparticles are examples of nanoparticles with antibacterial qualities that can more successfully penetrate biofilm matrix than traditional treatments (Besinis, et al. 2014). To improve antibacterial activity, these substances can be added to dental materials, coatings, and mouth rinses. In order to increase the antibacterial and anti-biofilm performance of dental products based on nanotechnology, future research may examine the integration of phytochemicals obtained from Meswak.

Another developing field of study is enzyme-based biofilm disruption treatments. Extracellular Polymeric Substances (EPS) can be broken down by enzymes, which may degrade the structure of biofilms and make them more vulnerable to antimicrobial therapy. By further decreasing microbe adhesion and biofilm durability, natural chemicals derived from Meswak root may enhance these treatments.

The development of microbiome-centered treatments that attempt to restore ecological balance rather than just eradicate bacteria has been prompted by growing knowledge of the oral microbiome. When taken in sufficient quantities, probiotics live microorganisms offer health advantages and may help preserve oral microbial balance (Devine and Marsh, 2009).

Numerous probiotic strains have shown promise in lowering cariogenic bacteria, inhibiting periodontal pathogens, and enhancing gingival health, especially *Lactobacillus* and *Bifidobacterium* species. Through competitive adhesion, bacteriocin synthesis, and host immune response regulation, probiotics may prevent harmful bacteria. By preventing pathogenic overgrowth and maintaining beneficial microbial populations, natural dental hygiene techniques employing Meswak root may further promote microbial balance.

In oral healthcare, prebiotics and synbiotics are also being studied more and more. While synbiotics mix probiotics and prebiotics to improve microbial balance and therapeutic effects, prebiotics specifically promote the growth of beneficial microorganisms. Through focused ecological manipulations, emerging microbiome engineering techniques seek to specifically alter oral microbial ecosystems.

These tactics could be significant future paths for customized oral healthcare and precision dentistry.

In order to preserve oral microbial balance and lower the prevalence of oral illnesses, preventive dentistry is still essential. Controlling bacteria formation and breaking up dental biofilms require good oral hygiene habits. Fluoride-containing toothpaste greatly lowers dental plaque and encourages enamel remineralization when used on a daily basis. By removing plaque from places that toothbrushes cannot reach, dental floss and interdental cleaning tools can lower the risk of periodontal disease and gingival inflammation. Meswak root's mechanical cleaning and antibacterial properties may enhance plaque control when used as an additional oral care aid.

Another important preventive tactic is dietary change. Frequent eating of sugary meals and fermentable carbohydrates raises the risk of caries by fostering the growth of acidogenic bacteria. Oral microbial stability is significantly influenced by cutting back on sugar consumption and maintaining a balanced diet (Moynihan and Kelly, 2014). Additionally, Meswak root's natural fluoride, silica, calcium, and mineral content may improve enamel and prevent demineralization.

Frequent dental checkups allow for the early detection and treatment of oral conditions before significant tissue damage takes place. Effective methods for lowering the burden of illness include professional cleaning, the use of fluoride varnish, fissure sealants, and oral health education. Maintaining oral health and lowering vulnerability to periodontal infections and fungal overgrowth are also greatly aided by quitting smoking and managing systemic diseases, including diabetes.

In general, ecological management of the oral microbiota and destruction of pathogenic biofilms are becoming more and more important in contemporary therapeutic and preventive approaches. Meswak root's antibacterial, antifungal, anti-inflammatory, antioxidant, and anti-biofilm properties make it a viable natural adjunct in oral healthcare, complementing both traditional therapies and cutting-edge technologies. Improved dental cleanliness, decreased microbial dysbiosis, and better long-term oral health outcomes could result from combining evidence-based modern dentistry with traditional herbal treatments (Tab. 4).

**Table 4. Therapeutic and preventive strategies for oral microbial diseases.**

Strategy	Target	Clinical purpose
Antibiotics	Periodontal bacteria	Infection control
Antifungal agents	Candida species	Oral candidiasis treatment
Chlorhexidine mouthwash	Oral biofilms	Plaque reduction
Photodynamic therapy	Bacteria and fungi	Biofilm destruction
Nanoparticles	Resistant biofilms	Enhanced antimicrobial activity
Probiotics	Oral dysbiosis	Microbial balance restoration
Fluoride therapy	Enamel surfaces	Caries prevention
Oral hygiene practices	Dental plaque	Prevention of biofilm accumulation

Contemporary oral healthcare increasingly emphasizes preventive and microbiome-based approaches for managing oral diseases. Integrating antimicrobial therapies with biofilm disruption technologies, probiotics, and preventive clinical practices may improve long-term treatment outcomes and support the development of personalized dentistry strategies.

## Conclusion

In order to preserve oral health and control microbial equilibrium in the oral cavity, the oral microbiome is essential. Communities of bacteria and fungi coexist in a highly dynamic ecological setting where healthy physiological processes and defense against pathogenic invasion are facilitated by balanced microbial interactions. On the other hand, disruptions in the microbial balance can result in oral dysbiosis, which encourages the emergence of serious dental conditions such oral candidiasis, periodontitis, and dental caries. Natural oral hygiene products like Meswak (*Salvadora persica*) root have drawn more scientific attention in addition to contemporary preventive and therapeutic methods because of their potential to preserve oral microbial balance and promote oral health through antimicrobial and anti-inflammatory properties.

According to available data, fungi, especially *Candida albicans*, play a major role in opportunistic infections and biofilm-associated oral diseases, while bacterial pathogens, such as *Streptococcus mutans* and *Porphyromonas gingivalis*, are closely linked to cariogenic and periodontal processes. Crucially, interactions between bacteria and fungi across kingdoms increase microbial virulence, biofilm stability, inflammatory responses, and antibiotic resistance, which exacerbates disease severity and complicates therapy. Meswak root has been demonstrated in numerous studies to have broad-spectrum antibacterial and antifungal qualities against significant oral pathogens such as *Candida albicans*, *Porphyromonas gingivalis*, and *Streptococcus mutans*. Fluoride, silica, sulfur compounds, tannins, alkaloids, and essential oils are some of its bioactive components that may lessen microbial colonization, prevent the formation of biofilms, and promote periodontal and dental health.

Understanding of oral microbial diversity, microbial communication routes, and disease-associated dysbiosis has been increased thanks to developments in molecular microbiology and sequencing technologies. Probiotics, biofilm-targeted medicines, photodynamic therapy, and precision dentistry techniques that attempt to restore ecological balance rather than eradicate bacteria indiscriminately have all emerged as a result of these discoveries. Because of its antibacterial, antifungal, antioxidant, and anti-biofilm qualities, natural medicinal agents like Meswak root have received more attention as supplementary treatments in oral healthcare. Controlling microbial biofilms and lowering the prevalence of oral disorders worldwide continue to depend on preventive oral healthcare. The cornerstones of maintaining long-term oral health continue to be good oral hygiene habits, dietary changes, early diagnosis, and routine dental care. Through both mechanical washing and antibacterial actions, traditional oral hygiene methods utilizing Meswak root may further contribute to plaque control and mouth cleanliness. Meswak's natural phytochemicals help lower gingival inflammation and bacteria buildup, and its fibrous texture aids in the elimination of plaque. To assist the creation of novel and more successful clinical interventions in contemporary dentistry, future research should concentrate on tailored microbiome modulation, targeted antimicrobial medicines, and a deeper investigation of fungal-bacterial interactions. Further clinical and molecular research on Meswak root's therapeutic potential may also shed light on the plant's potential as a natural, safe, and affordable adjunct in oral healthcare, both therapeutic and preventive.

Integrating traditional herbal remedies such as Meswak with evidence-based dental practices may contribute to improved oral hygiene, reduced oral disease burden, and enhanced long-term oral health outcomes.

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