Journal of Ayurveda & Holistic Medicine

https://jahm.co.in

eISSN-2321-1563

Review

Natural Compounds as Oral Remedies for the Treatment of Oral Diseases: A Narrative Review

[1]Swetha Mathiyazhagan, [2*]Vinitha Packirisamy

ABSTRACT:

Background: The aim of this narrative review is to inform the key role of natural products in the prevention and treatment of common oral diseases such as dental caries, gingivitis, periodontitis, oral candidiasis and oral cancer with the underlying mechanisms. Method: Reporting of this narrative review followed the Scale for the Assessment of Narrative Review Articles (SANRA) guideline. Review of the literature was conducted on PubMed, PubMed Central (PMC), Scopus, Web of Science and Google Scholar. The search period extended from January 2017 to June 2026. Eligibility criteria: English-language peer-reviewed articles studying natural compounds or phytochemicals that have experimental or clinical evidence in the prevention or treatment of oral diseases. Exclusion criteria included articles that did not provide biological outcomes or mechanisms, or that were not specific to oral diseases. Out of 800 records, 167 duplicates were removed based on the title, year of publication, author names and DOI and 43 studies were included in the qualitative synthesis after screening of titles/abstracts and full texts. Results: Natural compounds have been widely used against oral diseases through the inhibition of microbial growth and biofilm formation, inhibition of inflammatory mediators, reduction of oxidative stress via the Nrf2 pathway activation, wound healing/epithelial proliferation, antifungal effects against oral Candida spp, and apoptosis of oral cancer cells via modulation of the Bax/Bcl-2, caspases, PI3K-Akt, and VEGF signaling pathways. Nanocarriers such as nanoparticles, nanogels, hydrogels, liposomes, and mucoadhesive formulations improved the bioavailability and pharmacological activities of these six bioactive compounds. Conclusions: Multi-targeted natural products may act as a potential therapeutic approach to treating and preventing oral diseases by inducing strong anti-microbial, anti-inflammatory, anti-oxidative, anti-fungal, and anti-cancer effects. However, further experimental evidence is needed to formulate products with standardized delivery systems, pharmacokinetic studies, and well-designed clinical trials prior to the development of products with clinical use.

KEYWORDS: Epigallocatechin gallate, Natural compounds, Oral candidiasis, Oral diseases, Periodontitis.

RECEIVED ON: 29-06-2026

REVISED ON: 31-07-2026

ACCEPTED ON: 07-08-2026

Access This Article Online:

Quick Response Code:

Website Link: https://jahm.co.in

DOI Link: https://doi.org/10.70066/jahm.v14i7.2898

Corresponding Author Email: vinithap.smc@saveetha.com

CITE THIS ARTICLE AS

Swetha Mathiyazhagan, Vinitha Packirisamy. Natural Compounds as Oral Remedies for the Treatment of Oral Diseases: A Narrative Review Journal of Ayurveda and Holistic Medicine (JAHM) 2026; 14(7):102-118.

Published by Atreya Ayurveda Publications under the license CC-by-NC-SA 4.0

CC BY-NC-SA 4.0

© The Author(s). Open Access. This article is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 4.0 International License (CC BY-NC-SA 4.0). This license permits others to copy, distribute, remix, adapt, and build upon this work non-commercially, as long as appropriate credit is given to the original author and any derivative works are licensed under identical terms. For details of the license, visit https://creativecommons.org/licenses/by-nc-sa/4.0/

1. INTRODUCTION

Dental caries is the most popular oral disease and the most popular noncommunicable disease globally. It affects 3.5 billion people, with nearly 100% of the world's adults and 60%-90% of the world's school-aged children affected according to the World Health Organization (WHO). Oral diseases are a major global public health problem across the life course, for both sexes and of all socioeconomic backgrounds. [1] Dental caries, gingivitis, periodontitis, recurrent aphthous ulcers, oral candidiasis and OSCC affect oral functions, reduce quality of life, and are related to local and systemic diseases and complications. [2] Dental caries is one of the most popular chronic diseases in humans and is largely a dental biofilm-mediated disease. Biofilm-associated acidogenic bacteria metabolize dietary carbohydrates, which leads to enamel demineralization and the progression of carious lesions. [3] Periodontal diseases are chronic inflammatory conditions characterized by the progressive degeneration of the tooth-supporting structures, clinically manifesting as increased mobility and loss of teeth. Opportunistic fungal infections, such as oral candidiasis, and inflammatory lesions, such as aphthous ulcers, are frequently seen in immunocompromised individuals. Oral cancers, especially oral squamous cell carcinoma, are a meaningful cause of disease and death in much of the developing world. [4]

Standard treatments for oral disease include mechanical debridement of dental biofilm, antimicrobial mouthwashes and toothpaste, antibiotics, antifungals, corticosteroids and/or surgical approaches. Although many of these treatments are effective, the prolonged or excessive use of these conventional approaches may result in clinical adverse effects, including drug resistance, mucosal irritation, dysbiosis, dental discoloration and systemic toxicity. Long-term use of chlorhexidine-based mouth rinses is associated with side effects such as altered taste perception and staining of the teeth. The development of antibiotic-resistant micro-organisms associated with its unnecessary use is a further problem. They have thus stimulated increasing interest in alternative and adjunctive treatment modalities such as safer, economical and biocompatible approaches. [5-7]

Natural therapeutics derived from plants, herbs and apicultural products (phytochemicals such as Curcumin, Epigallocatechin gallate, Resveratrol, Xylitol and Sulforaphane; natural products such as Propolis and Aloe vera; medicinal plants such as *Azadirachta indica* have attracted researchers attention in the past few years. They have demonstrated antimicrobial, anti-inflammatory, antioxidant, wound healing, and anticancer activity, which are often exhibited in a multitargeted mechanism of action against the microbial pathogen and the host inflammatory response to infection. [8-10]

Natural compounds also have an effect on biofilm formation, a necessary step in the development of dental caries and periodontal disease. [11, 12] In addition to their antimicrobial and anti-inflammatory properties, some natural compounds have been found to have the ability to stimulate tissue regeneration as well as the healing of epithelial tissue, making them suitable for treating oral ulcers and mucosal lesions. In addition to their antifungal activity against *Candida albicans* or other forms of *Candida*, many phytochemicals are being studied for their potential to prevent and treat oral cancer through apoptosis induction, angiogenesis inhibition and modulation of cell proliferation mechanisms. [13, 14]

Given the growing popularity of integrative and preventive medicine and the attractiveness of natural products as an adjunct or alternative treatment for diverse oral conditions, an overview of the mechanisms by which natural products operate, their therapeutic applications and limitations is warranted to explain their effects and contribute to the direction of future research in oral medicine and dentistry.

2. METHODOLOGY

Review design and reporting framework: The objective of this narrative review is to summarize the evidence for natural products in preventing and treating major oral diseases, including dental caries, gingivitis, periodontitis,

oral candidiasis, oral mucosal diseases, and oral cancers. The literature search and retrieval procedure was designed according to the principles of the Scale for the Assessment of Narrative Review Articles (SANRA) to improve the methodological transparency and the reporting quality. As this study was designed as a narrative review and not as a systematic review or meta-analysis, we did not follow the protocol development process for a systematic review. However, we presented the search, screening, and selection of the studies according to the PRISMA 2020 flow diagram to ensure transparency of the literature search process.

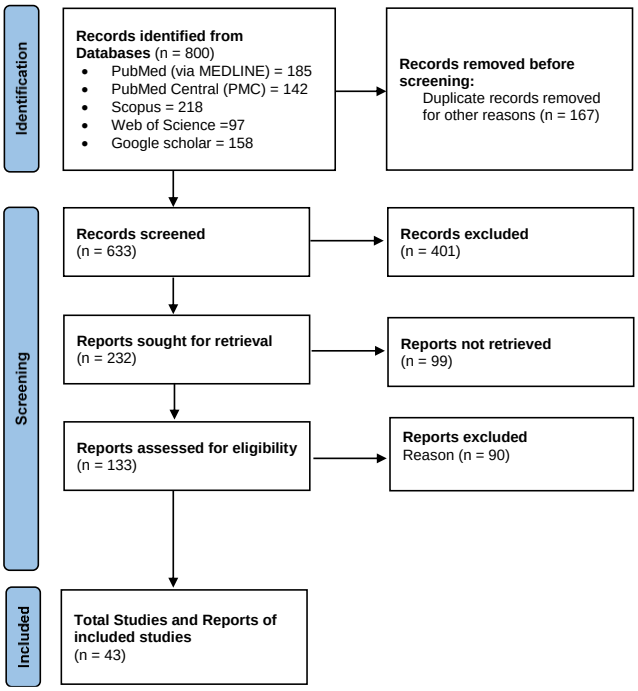

Figure 1. PRISMA flow chart depicts the literature search and study selection process

Literature Search Strategy: We searched PubMed, PubMed Central (PMC), Scopus, and Web of Science (WOS) databases for literature searches, and additionally searched Google Scholar for other relevant publications and studies that may not have been captured through the database searches. The literature search was performed for studies published from January 2017 to June 2026. The search strategy was instituted using controlled vocabulary terms and free-text (keyword) terms associated with natural products, phytochemicals, oral diseases, and their related therapeutic applications. Boolean operators AND and OR were used to combine the search terms, which increased the sensitivity and specificity of the retrieved articles.

The terms searched for were natural compounds, natural products, phytochemicals, plant-derived compounds, herbal medicines, oral diseases, dental caries, periodontitis, gingivitis, oral candidiasis, oral cancer, oral therapeutics, oral microbiome, and oral inflammation. The search strings, used filters, and total number of records extracted from each database are detailed in Table 1 for reproducibility purposes.

Study identification and screening process: In total 800 records were identified from electronic database searches and screening the reference lists of the included articles; these records were imported into a reference management software (Mendeley) and de-duplicated. Duplicates were identified based on matching using the article title, author details, year & journal or DOI. These detections were automated but subsequently manually checked for their accuracy: whether the identified records represented duplicates or multiple records of the same publication. After removing 167 duplicate records, screening of the results was conducted.

A total of 633 titles and abstracts were then screened, and any publication that was unrelated to oral diseases, did not investigate natural products, or lacked adequate scientific quality was removed from the next stages. Out of the 232 full text articles retained, 189 studies were excluded because of a lack of experimental data, mechanistic information, therapeutic relevance to oral disease management, methodological descriptions, or biological activity data pertaining to antimicrobial effects, antibiofilm properties, anti-inflammatory, antioxidant, antifungal, wound healing, or anticancer activity. Ultimately, 43 studies were included in the qualitative synthesis of this narrative review. The identification and selection of studies is provided in Figure 1 using a PRISMA 2020 flow diagram.

Table 1. Literature search strategy used for the review

Database	Search Terms Used	Filters Applied	Results Retrieved	Notes
PubMed (MEDLINE)	("Natural compounds" OR phytochemicals OR "natural products" OR "herbal medicines") AND ("Oral diseases" OR "Dental caries" OR periodontitis OR gingivitis OR "oral cancer" OR "oral candidiasis")	English language; Publication years 2017-2026; Peer-reviewed articles	185	Title/Abstract/Keywords.
PubMed Central (PMC)	("Natural products" OR "Plant-derived compounds" OR phytochemicals) AND ("Oral health" OR "Oral therapeutics" OR "Dental diseases" OR "Oral disorders")	English language; Publication years 2017-2026; Free full-text articles	142	Title/Abstract/Keywords
Scopus	TITLE-ABS-KEY ("Curcumin" OR "Epigallocatechin gallate" OR Resveratrol OR Propolis OR Xylitol OR Eugenol OR Sulforaphane OR phytochemicals) AND ("Oral disease management" OR "Oral microbiome" OR "Oral inflammation" OR "Dental diseases")	English language; Publication years 2017-2026; Peer-reviewed articles	97	Title/Abstract/Keywords
Web of Science	TS= ("Oral candidiasis" OR "Oral cancer" OR periodontitis OR "Dental caries") AND ("Natural compounds" OR phytochemicals OR "plant-derived compounds")	Language: English; Years: 2017-2026; Publication type: peer-reviewed articles	Language: English; Years: 2017-2026; Publication type: peer-reviewed articles	Title/Abstract/Keywords
Google Scholar	("Natural compounds for oral diseases" OR "Phytochemicals in dentistry" OR "Oral health natural products")	English Language years 2017 to 2026	158	Additional relevant studies

Study identification and screening process: In total 800 records were identified from electronic database searches and screening the reference lists of the included articles; these records were imported into a reference management software (Mendeley) and de-duplicated. Duplicates were identified based on matching using the article title, author details, year & journal or DOI. These detections were automated but subsequently manually checked for their accuracy: whether the identified records represented duplicates or multiple records of the same publication. After removing 167 duplicate records, screening of the results was conducted.

A total of 633 titles and abstracts were then screened, and any publication that was unrelated to oral diseases, did not investigate natural products, or lacked adequate scientific quality was removed from the next stages. Out of the 232 full text articles retained, 189 studies were excluded because of a lack of experimental data, mechanistic information, therapeutic relevance to oral disease management, methodological descriptions, or biological activity data pertaining to antimicrobial effects, antibiofilm properties, anti-inflammatory, antioxidant, antifungal, wound healing, or anticancer activity. Ultimately, 43 studies were included in the qualitative synthesis of this narrative review. The identification and selection of studies is provided in Figure 1 using a PRISMA 2020 flow diagram.

Eligibility criteria: To minimize selection bias, predefined inclusion criteria were utilized. Publications from 2017 to June 2026 were included if they were in the English language and were either peer-reviewed original articles, clinical trials, systematic reviews, or meta-analyzes related to the effects of natural products and natural ingredients on oral health. Eligible trials were those using naturally derived compounds or phytochemicals, such as curcumin, epigallocatechin gallate (EGCG), resveratrol, xylitol, eugenol, sulforaphane, propolis, and bioactive natural molecules, in

the treatment of oral disease, including dental caries, gingivitis, periodontitis, oral candidiasis, oral mucosal disorders, and oral cancer.

Studies were included if they presented experimental data (either in vitro, in vivo or clinical) and at least one of the following biological activities: antimicrobial, antibiofilm, antifungal, anti-inflammatory, antioxidant, wound healing, or anticancer activity. Studies describing the mechanism of action through the investigation of molecular pathways, oxidative stress, inflammatory mediators, microbial virulence factors, or apoptosis mechanisms were also considered for inclusion in this study.

Exclusion criteria: Studies not published in the English language were excluded, as were conference abstracts, editorials, letters to the editor, dissertations, book chapters, or other non-peer-reviewed articles. Studies that did not focus on diseases of the oral cavity, or only investigated synthetic drugs, dental materials or medical devices, were also excluded from the review. Additional exclusion criteria included studies without experimental validation, quantitative biological data, and adequate methodological information and mechanistic interpretation, as well as duplicate studies (with an equivalent sample size) without explicit indication of the sample size and experimental procedures.

Quality assessment of included studies: While this review is a narrative review, the authors have critically assessed the methodological quality and strength of evidence of each included study. These included the clarity of the experimental design, control used, description of the biological model, experimental replicability, the validity of the outcome measurements, and the mechanistic studies available. Studies with established experimental methodology, appropriate controls, biological activity, biological assay validation and molecular mechanistic validation provided greater evidence than studies where these criteria were not satisfied. This qualitative categorization set the stage for a balanced synthesis of the literature in which the range of biological effects was considered in terms of their methodological robustness.

Natural Compounds in Dental Caries Management: Dental caries is a multifactorial disease driven by biofilm formation that results in demineralization of enamel and dentin due to organic acid production by cariogenic bacteria. Although many different bacteria are involved with caries, *Streptococcus mutans* is the organism most associated with the initiation and propagation of caries, due to its ability to produce acid, adhere to tooth enamel, and form extracellular polysaccharides. While customary preventive agents, including fluoride application, pit and fissure sealants, and antimicrobial mouth rinses, have considerably reduced caries incidence, concerns regarding potential adverse effects of fluoride toxicity, antimicrobial resistance, and microbiome disruption have driven the need to investigate biocompatible alternatives that could replace customary caries prevention methods. This has led to a natural product-based approach as a promising strategy for the prevention and treatment of dental caries (Figure 2). [15]

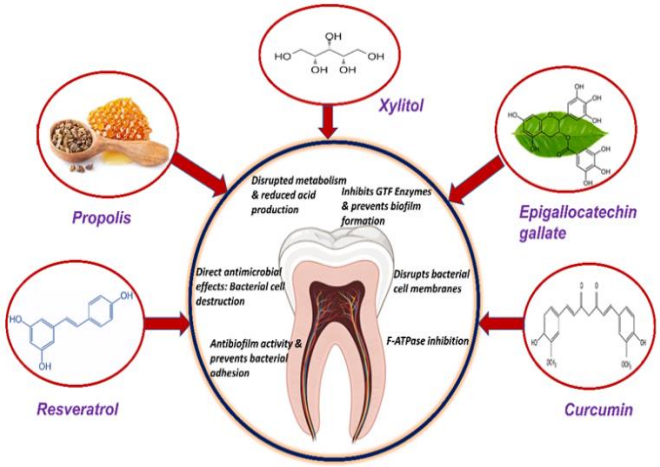

Figure 2. Schematic illustration of natural compounds used in dental caries management and their mechanisms of action against *Streptococcus mutans*.

Xylitol: Xylitol, a naturally occurring sugar alcohol, is found in a number of fruits, in birch wood, and has been studied extensively. Xylitol is not a fermentable sugar, but one of a number of carbohydrates that *S. mutans* does not use to produce acid. Instead, xylitol inhibits the bacterium's

energy metabolism and attachment to enamel. The frequent chewing of xylitol chewing gum has been shown to reduce salivary levels of *S. mutans*, and reduce dental plaque and caries levels in children and adults. Xylitol chewing gum also increases saliva flow. The increase in saliva increases the buffering capacity of the saliva, or ability to neutralize the acidity in the mouth. [16, 17]

Epigallocatechin gallate: Epigallocatechin gallate (EGCG) is another important phytochemical noted for its dental caries preventive properties and is the dominant catechin in green tea. The antibacterial and anti-biofilm activity of EGCG may result from EGCG's ability to inhibit glucosyltransferase (Gtf) enzymes, which are responsible for producing a sticky, viscous, extracellular glucan. These glucans are necessary for the adhesion of bacteria and the formation of dental biofilm; by interfering with these processes, EGCG may reduce dental plaque formation and the proliferation of acidogenic bacteria. Additionally, EGCG's antioxidant properties may help reduce oxidative stress within the oral cavity, with proposed benefits on the periodontal complex in addition to its caries-preventive effects. [8, 18]

Propolis: Propolis is a mixture of resinous, waxy, and balmy substances collected from exudates of trees and plants by *Apis mellifera*. Propolis is widely studied for its bioactive potential. It is rich in flavonoids and phenolic acids, and has inhibitory effects on cariogenic bacteria like *Streptococcus mutans* and *Lactobacillus spp.* It damages bacterial cytoplasmic membranes, inhibits some bacterial enzymes, and reduces acidogenesis. Besides its antimicrobial action, propolis may help remineralize enamel because of the minerals and bioactive components it contains. Clinical trials with varnishes, mouthrinses, and toothpaste containing propolis have shown a reduction in plaque index and bacteria counts. [19-21]

Curcumin: Curcumin is the active ingredient of turmeric (*Curcuma longa*). Due to a wide variety of anti-microbial, anti-inflammatory, and antioxidant properties, curcumin has attracted great interest in oral health research. The cariostatic properties of curcumin have been attributed to its antimicrobial effects associated with inhibition of the growth of caries-inducing bacteria including *Streptococcus mutans*. This effect is accomplished via disruption of bacterial membranes, inhibition of F-ATPases that confer acid resistance in acidogenic bacteria, and inhibition of glucosyltransferases (GTFs) that synthesize extracellular polysaccharides (EPS) in bacteria. These virulence factors play an important role in bacterial adhesion and biofilm formation on the enamel surface. [12, 22, 23]

Resveratrol: Another naturally occurring stilbene-based polyphenol called resveratrol has received interest as an anticaries agent. It is found mainly in *Vitis vinifera*, some other berries, and *Arachis hypogaea* (groundnut). In addition to its cardioprotective and anti-aging effects, resveratrol also shows antimicrobial and antibiofilm activity against oral microorganisms. [24]

Some secondary metabolites in nature have, in addition to their antibacterial characteristics, a role in enamel remineralization. Polyphenols, which are secondary metabolites in plants,

have been shown to improve the deposition of calcium and phosphate ions on the surface of demineralized tooth enamel. Natural compounds have also been studied in combination with low-dose fluoride to promote remineralization while simultaneously reducing side effects associated with each agent.

The mechanistic basis of their anticariogenic properties is multidimensional, including the inhibition of bacterial adhesion in the oral cavity, prevention of acid production, reduction of glucan formation, impairment of pre-formed biofilm development, free radical scavenging, as well as the enhancement of the protective role of saliva. Many natural products are selective against pathogens, thus sparing the oral flora unlike broad-spectrum synthetic antimicrobials and keeping the ecological balance of the oral cavity. [12, 25]

Despite promising antimicrobial and antibiofilm activities, evidence for xylitol, EGCG, curcumin, and propolis remains inconsistent. While *in vitro* studies show strong activity

Streptococcus mutans and biofilm formation, clinical outcomes vary because of differences in formulations, dosages and study designs. Therefore, further well-designed randomized clinical trials are needed to confirm their long-term effectiveness in caries prevention. [12]

Natural therapies for gingivitis and periodontitis: Chronic inflammatory diseases around teeth are gingivitis and periodontitis. Gingivitis is defined as a reversible inflammatory reaction of the gingival tissues to a local irritating factor. Periodontitis is the progressive destruction of periodontal ligament fibers and of alveolar bone, which will eventually lead to the loss of teeth if the condition is not treated. The most common primary aetiological agents in these conditions are microbial biofilms containing Gram-negative anaerobic bacteria including *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*. However, the pathogenesis of the conditions is largely influenced by an exaggerated host inflammatory response and oxidative stress. Common adjunctive medications include scaling and root planning (SRP), antimicrobial mouth washes (such as chlorhexidine) and systemic or local antibiotics. Long term adjunctive therapy may be associated with side effects, drug resistance, and changes in the oral microbiome. Hence, the use of natural products as adjunctive therapy or alternatives has gained importance for their intrinsic anti-inflammatory, antimicrobial and antioxidant properties. [26, 27]

Curcumin is one of the most widely studied phytochemicals for periodontal treatment. Curcumin has anti-inflammatory characteristics that block the activation of nuclear factor-kappa B (NF-κB) and prevent the release of inflammatory mediators such as TNF-alpha, IL-1β, and IL-6. Within the periodontal tissues, they are involved in connective tissue breakdown and bone resorption. Curcumin seems to inhibit MMP activity and therefore, can slow collagen degradation caused by these proteinases. A number of studies suggest curcumin gel used as an adjunct to SRP results in a more meaningful decrease in the gingival index, plaque index, probing depth, and bleeding on probing compared to SRP alone. Curcumin is believed to have antioxidant properties that may help neutralize reactive oxygen species and reduce periodontal tissue destruction. [8, 28]

Another phytotherapeutic in the management of periodontal diseases is *Azadirachta indica*. Neem extracts have been shown to have a broad-spectrum bactericidal activity against periodontal pathogens, and also to inhibit plaque formation. Bioactive compounds like nimbidin and azadirachtin are responsible for inhibiting bacterial adhesion and colonization. [29, 30] Resveratrol has been proposed as an adjunctive treatment for periodontal disease. It is a strong antioxidant that is able to lessen the oxidative stress in inflamed periodontal tissues.

It decreases the production of inflammatory cytokines and osteoclast differentiation, which may lead to a reduction in alveolar bone loss. Further research has suggested that the mechanisms by which resveratrol may protect against periodontitis progression could be through inhibition of osteoclastogenesis by suppression of receptor activator of nuclear factor kappa-B ligand (RANKL) expression. [8, 24]

The antimicrobial and wound healing properties of propolis have been widely studied. Rich in flavonoids and phenolic compounds, propolis has been shown to inhibit growth of the bacterium *Porphyromonas gingivalis* and other perio-pathogenic bacteria. It is known to have fibroblast-stimulating and collagen metabolic effects, which has led to claims of promoting tissue regeneration. Gels and mouthrinses with propolis have been used as an adjunct to SRP therapy, with studies showing important reductions in periodontal pocket depth and clinical attachment gain. [31]

The active ingredients of essential oils, e.g. Eugenol, have an effect in periodontal therapy due to their antibacterial and analgesic (i.e. numbing) action. Eugenol has been shown to effectively dissolve bacterial cell membranes and relieve pain in inflamed gingival tissues. Green tea catechins such as Epigallocatechin gallate can also inhibit bacterial proteases and the production of inflammatory mediators. [10, 12, 32]

Natural bioactive compounds exert a variety of pharmacological effects on periodontal diseases such as antibacterial activity, prevention of biofilm formation, reduction of the expression and release of inflammatory mediators, reduction of oxidative stress, and modulation of the host immunologic response. Bone resorption is inhibited by these compounds and they exhibit bone-renewing activities. They also inhibit alveolar bone loss seen in periodontitis. Unlike most synthetic antimicrobials that target the bacteria, many natural antimicrobials also have host-modulatory properties that may act on some aspects of the periodontitis inflammatory process.

Although natural compounds have shown potential effects in reducing gingival inflammation and periodontal pathogens, clinical outcomes remain inconsistent. Variations in study design, treatment protocols, and follow-up periods contribute to these differences. Therefore, current evidence supports their use as adjunctive therapies rather than replacements for conventional periodontal treatment. [25]

Natural Compounds in Oral Candidiasis: Most oral candidiasis is caused by *Candida albicans*, but non-albicans *Candida* species such as *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, and *C. krusei* can also cause the disease. Contributing factors include immunosuppression, dentures, diabetes, infants, and antibiotics. Clinically, it presents with pseudomembranous, erythematous, hyperplastic and angular cheilitis forms. Standard antifungal therapy consists of nystatin, clotrimazole, and fluconazole. Long-term usage can result in resistance, recurrence, mucosal irritation, and systemic side effects. These issues have prompted investigations into the use of natural products as a safer, and possibly more effective, treatment strategy for oral candidiasis (Figure 3). [33, 34]

Eugenol is a natural phenolic organic compound derived from clove oil, and the most studied natural antifungal agent in dentistry, causing disintegration in fungal membranes. Eugenol may also interfere with ergosterol biosynthesis, which is required for fungal growth and viability, and can act as an analgesic and anti-inflammatory agent to alleviate the effects of candidiasis on mucosal lesions. It is commonly used in gels, mouthrinses, and denture cleaning products.

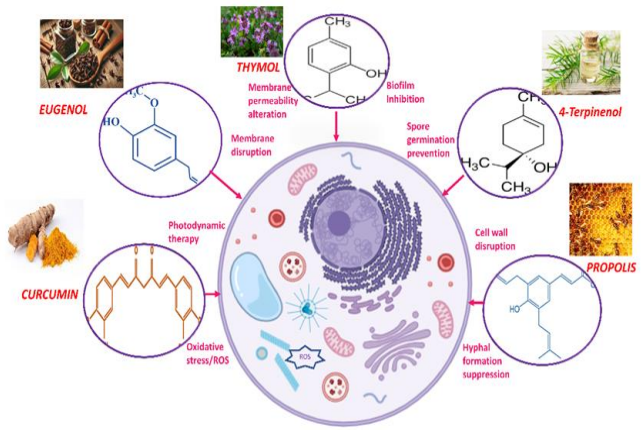

Figure 3. Mechanisms of natural compounds against *Candida* species in oral candidiasis.

Another antifungal agent, thymol, is a phenolic compound naturally occurring in thyme oil. Thymol has a broad antifungal spectrum with a mechanism of action that may involve membrane damage and enzyme inhibition. It modifies the membrane properties, inhibiting transfer of nutrients inside the cell and killing the cell. Studies show that thymol mouthwashes reduce *Candida* in the mouth and on dentures. Thymol also has antioxidant and anti-inflammatory properties that promote the repair of the mucosa.

Melaleuca alternifolia essential oil (tea tree oil) is antifungal. Its active ingredient, terpinen-4-ol, blocks fungal hyphae by interfering with their functional membranes and prevents germination of the spores. Tea tree oil is highly inhibitory to planktonic cells and biofilm growth of *C. albicans*. Biofilm-associated candidiasis (such as denture stomatitis infections) is notoriously resistant to antifungal agents, making the discovery of natural antibiofilm agents highly desirable. Tea tree oil should instead be carefully diluted and used in formulated preparations to avoid mucosal irritation. [32]

Propolis extracts have powerful antifungal activity on oral *Candida* spp. The active components are flavonoids and phenolic acids which cause damage to the fungal cell wall

and inhibit hyphal growth. By inhibiting its hyphal transformation it would thus reduce the organism's ability to invade epithelium and its virulence, and promote wound healing and re-epithelization and can be useful in the management of the erythematous or ulcerated lesions of the mucosa. [31]

Antifungal photodynamic therapy has also been studied with the polyphenol Curcumin, which acts as a photosensitizer and generates reactive oxygen species that have specific toxicity for fungus cells on blue light activation. It has been shown to decrease the amount of *Candida* biofilm on denture acrylics without affecting the surrounding tissue. Curcumin also has anti-inflammatory effects by inhibiting NF-κB signaling pathways, which may alleviate inflammation of the mucosa. [35, 36]

Natural antifungals have diverse modes of action including alterations to membrane integrity, inhibition of ergosterol biosynthesis, the disruption of hyphal growth and biofilm formation, the induction of oxidative stress, and immunomodulation. Unlike synthetic antifungals which generally affect a single cellular target, many natural antifungals have multiple molecular targets, which may offer a strategy for avoiding resistance development in relevant fungal pathogens. Although eugenol, thymol, tea tree oil, propolis, and curcumin exhibit promising antifungal activity in laboratory studies, clinical evidence remains limited and inconsistent. [35] Standardized clinical trials are needed to validate their safety and therapeutic efficacy in oral candidiasis.

Natural Compounds in Oral Cancer Prevention and Adjunct Therapy: Oral cancer usually means oral squamous cell carcinoma (OSCC); this is a meaningful public health burden in many countries where use of tobacco, alcohol and betel quid are popular. Despite advances in surgery, radiotherapy, and chemotherapy, the 5-year survival rate has not improved substantially due to late-stage presentations, recurrences, and metastases. Therapeutic strategies like surgery, radiation therapy and chemotherapy are associated with mucositis, xerostomia, impaired immunity and systemic toxicity, side effects called severe adverse effects of treatment. These disadvantages have prompted researchers to look into natural compounds and their use as potential adjuvant chemopreventive agents against oral cancer. [37]

Among these phytochemicals, Curcumin has been studied extensively for its anticancer effects by modulation of multiple molecular pathways, and thus it may have broad-spectrum efficacy. Curcumin was shown to affect transcription factors like NF-κB, AP-1, and STAT3 that are involved in inflammation, cell proliferation and survival of cancer cells. In an experimental model of oral squamous cell carcinoma, curcumin was shown to induce apoptosis through the activation of a caspase cascade, and by increasing the Bax/Bcl-2 ratio. It also inhibited the expression of cyclin D1, and caused cell cycle arrest in the G1/S transition. It suppresses angiogenesis by downregulating VEGF, and also suppresses the tumor metastasis due to inhibition of MMPs expressions. Therefore, due to its anti-inflammatory and antioxidant properties, curcumin may exert a chemopreventive effect against malignancy in OPMDs like leukoplakia and oral submucous fibrosis. [38]

Another important polyphenol that possesses strong antiproliferative activity against oral cancer cell lines through cell cycle arrest and apoptosis induction is epigallocatechin gallate (EGCG). EGCG inhibits the signaling pathway of epidermal growth factor receptor (EGFR), which is overexpressed in many OSCC cases. Angiogenesis is inhibited and oxidative DNA damage is reduced, suggesting a role in chemoprevention. Epidemiological studies link regular green tea consumption with a reduction in risk of certain oral cancers, but these associations may not be conclusive. Very large clinical trials are needed to confirm any possible association. [18]

Resveratrol has more strong anticancer activity, and modulates a number of intracellular signaling pathways, including PI3K/Akt and MAPK signaling pathways, leading to decreased tumor cell proliferation and increased apoptosis.

It has been reported to act as an inhibitor of epithelial cell to mesenchymal transition (EMT), a process responsible for tumor invasion and metastases. In addition, resveratrol has antioxidant properties and is able to protect normal cells, but it may cause oxidative stress and cell death in cancer cells. [39]

As a bioactive compound in cruciferous vegetables, sulforaphane is one of the most strong chemopreventive agents, due to modulation of Nrf2 and subsequent induction of phase II detoxifying enzymes, such as glutathione S-transferase and quinone reductase. These enzymes also play an important role in neuroprotection against carcinogens, apoptosis induction and inhibition of histone deacetylase (HDAC) activity in neoplastic cells. Their activities play important roles in epigenetic regulation. Preclinical studies indicate that sulforaphane may inhibit tumor growth and prevent malignization. [10, 40]

Cytotoxic effects from propolis on oral carcinoma cells have been reported, attributed to flavonoid and phenolic components of propolis. Propolis induces apoptosis and reduces tumor cell proliferation and tumor-promoting inflammatory mediators. Propolis may also be able to improve immune responses, contributing to the antitumor effects. [19, 32]

Natural products have also been studied as protective agents against some of the damages associated with standard cancer therapies. For example, curcumin and propolis have been studied in preventing chemotherapy- and radiotherapy-induced oral mucositis. Their anti-inflammatory and wound healing properties can reduce pain and ulcer severity, and improve healing.

The following table (Table 2) summarizes the current knowledge on natural compounds that have been tested against various oral conditions in in vitro, in vivo, and/or clinical studies. Sources and pharmacological activity of the products are presented in Table 3. Natural compounds demonstrate promising anticancer activities in preclinical studies, however, clinical evidence remains limited and inconsistent. Therefore, these compounds should be regarded as adjunctive chemopreventive agents until validated by clinical trials.

3. DISCUSSION

Mechanisms of Action of Natural Oral Therapeutics: Natural products that are active in the prevention or treatment of oral disease exert their effect through a plurality of biological mechanisms, rather than acting solely on a single target as is the case with most single-target synthetic drugs. This multi-targeted action of phytochemicals or bioactive natural products is helpful in application against complex oral diseases like caries, periodontitis, candidiasis and oral cancer (Figure 4).

Table 2: Summary of experimental and clinical evidence supporting the role of natural compounds in oral health applications

Study type	Natural compound / intervention	Disease model / sample,	Major findings	Reference
Observational studies	Green tea catechins (Epigallocatechin gallate, EGCG)	Human observational studies analyzing green tea consumption and the risk of oral cancer	how that habitual green tea consumption may lower the risk of some oral cancers; however, these studies are inconclusive and large clinical studies must be conducted to confirm the association.	[18]
In vitro models	Curcumin	Periodontal inflammation models and oral squamous cell carcinoma cell models	Inhibits activation of NF-κB, decreases inflammatory cytokines (TNF-α, IL-1β, IL-6), decreases MMP activity, induces apoptosis via cleavage of activated caspases, regulates expressed proteins such as increased Bax/Bcl-2 ratio, inhibited cyclin D1 and inhibits angiogenesis by inhibiting VEGF.	[8, 28, 38]
In vitro studies	*Azadirachta indica*	antibacterial properties	inhibits their ability to adhere and form plaque due to	[29, 30]

	(Neem extract)	against periodontal bacteria	its bioactive compounds, such as nimbidin and azadirachtin	
In vitro studies	Resveratrol	periodontal inflammatory models and oral cancer cell models	Reduces oxidative stress, suppresses pro-inflammatory cytokines, and inhibits osteoclast differentiation. Modulates PI3K/Akt and MAPK signaling pathways which are associated with tumor progression	[8, 24, 39]
In vitro studies	Propolis	Periodontal organisms, Candida species, and oral cancer cells	Antimicrobial and anti-fungal activity with antimicrobial activity involving damage to microbial membranes, inhibition of Porphyromonas gingivalis, limitation of Candida hyphal formation, induction of apoptosis, and inhibition of tumor cell proliferation	[19, 31, 32]
In vitro studies	Eugenol	Periodontal pathogens and Candida albicans models	acts by disrupting microbial membranes, interference with fungal ergosterol biosynthesis and anti-microbial; also analgesic and anti-septic effects on inflamed gingival tissue	[10, 12, 32]
In vitro studies	Thymol	*effects of thymol on Candida albicans and biofilms*	interferes with fungal membranes and transport of nutrients, and decreases survival and biofilm viability	[32]
In vitro studies	*Melaleuca alternifolia* (Tea tree oil)	*Candida albicans planktonic cells and biofilms*	terpinene-4-ol can disrupt fungal membranes, inhibit hyphal growth, and reduce biofilm mass	[32]
In vitro studies	Curcumin-mediated photodynamic therapy	*Candida albicans biofilms on acrylic denture surface Photosensitizer*	production of reactive oxygen species upon exposure to blue light leads to inhibition of biofilm formation without causing major damage to the tissue.	[35, 36]
Animal studies	Curcumin	Experimental oral squamous cell carcinoma models	curcumin can inhibit tumor growth through induction of apoptosis, cell-cycle arrest, inhibition of inflammatory pathways and angiogenesis, and preventing metastasis.	[38]
Animal studies	Sulforaphane	Experimental carcinogenesis models	Activating Nrf2 signaling, it induces phase II detoxification enzymes including glutathione-S-transferases and quinone reductase. It has been shown to have chemopreventive properties	[10, 40]
Animal models	natural bioactive compounds, periodontal tissue inflammation, oxidative stress	Experimental periodontal disease models	osteoclast activity, and alveolar bone destruction due to experimental periodontal disease are reduced by the effect of antimicrobial and host modulation	[8, 24]

Table 3. Natural compounds for oral diseases treatment

Oral Disease	Natural Compound	Source	Mechanism of Action	Reported Benefits
Dental Caries	Xylitol	Birch wood, fruits	Reduces *Streptococcus mutans* adhesion and inhibits acid production	Decreases dental caries incidence

	Epigallocatechin gallate (EGCG)	Green tea	Inhibits bacterial growth, glucosyltransferase activity, and biofilm formation	Reduces plaque formation and cariogenic activity
	Propolis	Bee-derived product	Exhibits antimicrobial activity and promotes enamel remineralization	Lowers cariogenic bacterial load and supports oral health
Gingivitis	Curcumin	Turmeric (*Curcuma longa*)	Anti-inflammatory activity through inhibition of NF-κB signaling and oxidative stress reduction	Reduces gingival inflammation, bleeding, and gingival index
	Allicin	Garlic (*Allium sativum*)	Exhibits antibacterial activity against periodontal anaerobic pathogens	Reduces periodontal pathogen load
	Neem	Neem leaves (*Azadirachta indica*)	Antimicrobial and anti-inflammatory effects; inhibits plaque-forming bacteria	Decreases plaque accumulation and gingival inflammation
Oral Ulcers	Aloe vera	Aloe leaves (*Aloe barbadensis*)	Promotes epithelial regeneration, wound healing, and reduces inflammation	Accelerates ulcer healing and reduces pain
	Honey	Bee-derived product	Antimicrobial activity and stimulation of tissue regeneration	Promotes ulcer healing and decreases lesion duration
	Glycyrrhizin	Licorice root (*Glycyrrhiza glabra*)	Anti-inflammatory activity and mucosal protective effects	Soothes oral lesions and reduces discomfort
Oral Candidiasis	Thymol	Thyme oil (*Thymus vulgaris*)	Disrupts fungal cell membrane integrity and inhibits biofilm formation	Suppresses *Candida albicans* growth
	Eugenol	Clove oil (*Syzygium aromaticum*)	Antifungal, antimicrobial, and analgesic activity	Reduces fungal burden and oral pain
	Terpinen-4-ol	Tea tree oil (*Melaleuca alternifolia*)	Causes fungal membrane disruption and inhibits adhesion	Supports adjunctive management of candidiasis
Oral Cancer	Sulforaphane	Cruciferous vegetables (broccoli, cabbage)	Induces apoptosis, activates detoxification enzymes, and modulates oxidative stress pathways	Exhibits anti-proliferative and chemopreventive effects
	Resveratrol	Grapes and berries	Antioxidant, anti-inflammatory, and anti-angiogenic activity	Inhibits tumor progression and cancer cell proliferation

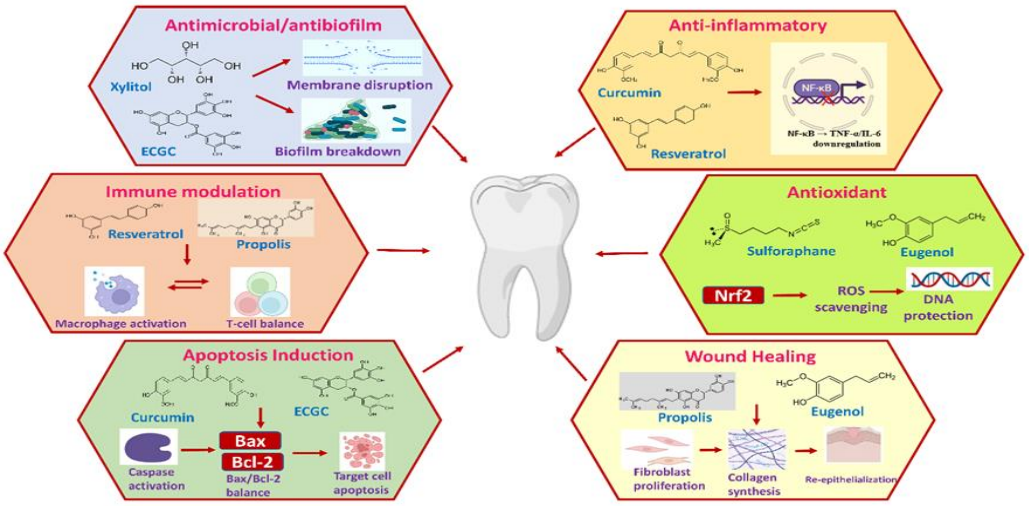

Figure 4. Overview of the multifaceted mechanisms of natural compounds in oral disease prevention and therapy.

Antimicrobial and Antibiofilm Activity: One of the major approaches is the inhibition of microbial proliferation and biofilm formation. Dental caries and periodontitis constitute biofilm-related infections caused by microorganisms such as *Streptococcus mutans*, *Porphyromonas gingivalis* and *Candida albicans*.

Epigallocatechin gallate, curcumin, eugenol and propolis can exert antimicrobial effects by disrupting microbial cellular membranes and by inhibition of glucosyltransferases and quorum sensing. This can prevent bacterial adhesion, extracellular polysaccharide production, and biofilm maturation. Furthermore, some natural compounds have selective activity against pathogen microorganisms, thus sustaining the balance of oral flora. [33]

Inhibition of inflammatory mediators such as TNF-α, IL-6, and NF-κB: Inflammation is paramount in periodontal diseases, oral mucosal lesions and the progression of cancer. Natural compounds have been employed as modulators of these signaling pathways.

Other examples include Resveratrol and Curcumin, which inhibit the activation of the transcription factor nuclear factor-kappa B (NF-κB) which upregulates pro-inflammatory cytokines (e.g., TNF-α and IL-6). Inhibition of NF-κB signaling has been reported to reduce inflammatory cell infiltration, collagen degradation, and alveolar bone resorption in periodontitis. The inflammatory damage is also decreased by reducing COX-2 and inducible nitric oxide synthase (iNOS). [33, 41]

Antioxidant Free Radical Scavenging: Oxidative stress plays an important role in the tissue destruction in periodontal diseases and carcinogenesis. ROS generated during the chronic inflammation can cause damage to the lipids, proteins, and DNA. Polyphenols including Epigallocatechin gallate, Resveratrol and Sulforaphane neutralize free radicals and up-regulate the endogenous antioxidant defense system. For example, sulforaphane induces phase II detoxifying enzyme expression, for example glutathione S-transferase, through the activation of the Nrf2 (Nuclear factor (erythroid-derived 2) like 2) pathway. The antioxidant action protects periodontal tissues from oxidative damage and decreases DNA damage responsible for malignant transformation. [14]

Modulation of host immune responses: The immunomodulatory effects of natural products can regulate macrophage polarization, cytokine levels, and T-cell activity. These compounds can restore normal host immune homeostasis. For example, propolis has been shown to promote phagocytic activity and tissue repair, while curcumin has been involved in the regulation of the Th1/Th2 immune response. This is especially useful in chronic inflammatory conditions such as periodontitis and recurrent aphthous ulcers. [42]

Malignant Cells Apoptosis Inducing Agents: The natural compounds used in the chemoprevention and adjuvant treatment of oral cancer exert their anticancer effects through induction of oral cancer cell apoptosis with little or no toxicity toward adjacent normal cells. Curcumin, resveratrol, and sulforaphane induce apoptosis through the intrinsic and extrinsic pathways, activating caspases, altering the Bax/Bcl-2 ratio, and inhibiting the PI3K/Akt pathway. Inhibition of angiogenesis and metastasis occurs due to downregulation of vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMPs), impeding tumor growth and metastasis. [40, 41]

Promotion of Wound Healing and Epithelial Regeneration: Natural agents stimulate the proliferation of fibroblasts and collagen production and re-epithelialization of mucosal wounds and tissue repair in the oral cavity, and also exert potential use in the management of oral ulcers and therapy-induced mucositis, like propolis and curcumin, not only due to their anti-inflammatory and antimicrobial properties but also due to their antioxidant activity. [43]

Limitations: Natural molecules display a positive biological activity that could be exploited for the prevention and treatment of oral diseases. Nonetheless, many limitations interfere with their immediate use. Their efficacy depends on chemical, extraction, formulation and immunological

characteristics, as well as biological availability. Numerous phytochemicals have been screened for antimicrobial, antioxidant, anti-inflammatory, and anticancer activities with promising results in vitro. However, very little is known of the mechanism of action and the bio-activity of phytochemicals in the dynamic multi-factorial oral cavity through saliva, microflora, and host interaction. The current evidence is mainly based on in vitro studies and animal studies with limited clinical evidence that shows the safety and efficacy of phytochemicals in the long term. Lack of formulation standardization, bioactive compound concentrations, and toxicity, pharmacokinetics, stability, and drug-drug interactions with customary prescribed oral agents need further study. Natural compounds possess multipotent biological activities, but the mechanisms underlying some of the identified clinical activities are not completely understood. This review attempted to characterize whether the observed biological activities are suggestive of their therapeutic applications, without claiming clinical use through medically validated pathways. An additional limitation of the current literature is the considerable heterogeneity in experimental methodologies, natural product standardization, outcome measures and reporting quality, which complicates direct comparison among studies and limits the ability to draw definitive conclusions regarding clinical efficacy.

Future Research Priorities: Further investigations are needed to close the divide between in vitro studies and clinical application of natural products in oral health. Clinical trials are needed to consider the therapeutic utility, optimal dosage, safety, and long-term benefits of natural products in the management of dental caries, periodontal diseases, oral candidiasis, oral mucosal diseases, and oral cancer. Research into standardized medicines with defined active ingredients may enable better reproducibility and clinical results. In the future, formulations using drug delivery systems such as nanoparticles, liposomes, hydrogels and mucoadhesive systems may be used to improve solubility, stability and bioavailability of some natural products. In any case, future studies investigating the interplay of natural products with the oral microbiome are needed to determine if these natural products selectively inhibit pathogenic microbes while permitting the growth of commensal microbes. Characterization of pharmacokinetics, toxicology, and underlying molecular mechanism(s) for each natural product is also needed. Combination strategies involving natural products together with preventive and therapeutic interventions combined with multidisciplinary approaches integrating the fields of dentistry, pharmacology, molecular biology, and clinical practice will be essential to translate promising natural products into evidence-based oral healthcare products.

4. CONCLUSION

Natural products can potentially be used for oral applications due to potential antimicrobial, antibiofilm, anti-inflammatory, antioxidant, wound healing, and anticancer properties. There is evidence that phytochemicals may be useful adjuncts for treating oral conditions, but most studies are preclinical with the efficacy not yet verifiable in clinical population studies, and therefore should still be considered preliminary candidates for oral applications. Well-designed clinical trials are needed to determine their efficacy, safety, standardization and application in oral health practice.

Abbreviations

AP-1 :Activator Protein-1
Bax :Bcl-2-associated X Protein
Bcl-2 :B-cell Lymphoma 2
C. albicans:Candida albicans
COX-2 :Cyclooxygenase-2
DNA :Deoxyribonucleic Acid
EGCG :Epigallocatechin Gallate
EGFR :Epidermal Growth Factor Receptor
EMT :Epithelial-to-Mesenchymal Transition
EPS :Extracellular Polymeric Substances (or Extracellular Polysaccharides)
GTF :Glucosyltransferase
HDAC :Histone Deacetylase
IL :Interleukin
IL-1β :Interleukin-1 Beta
IL-6 :Interleukin-6

iNOS :Inducible Nitric Oxide Synthase
MAPK :Mitogen-Activated Protein Kinase
MEDLINE:Medical Literature Analysis and Retrieval System Online
MMP :Matrix Metalloproteinase
NF-κB :Nuclear Factor Kappa B
Nrf2 :Nuclear Factor Erythroid 2-Related Factor 2
OPMDs :Oral Potentially Malignant Disorders
OSCC :Oral Squamous Cell Carcinoma
PI3K :Phosphoinositide 3-Kinase
PI3K/Akt :Phosphoinositide 3-Kinase/Protein Kinase B Signaling Pathway
PMC :PubMed Central
PRISMA :Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RANKL :Receptor Activator of Nuclear Factor Kappa-B Ligand
ROS :Reactive Oxygen Species
SANRA :Scale for the Assessment of Narrative Review Articles
SRP :Scaling and Root Planning
STAT3 :Signal Transducer and Activator of Transcription 3
TNF-α :Tumor Necrosis Factor Alpha
TS :Topic Search (Web of Science search field)
VEGF :Vascular Endothelial Growth Factor
WHO :World Health Organization
WOS :Web of Science

Authors Details:

[1]Department of Community Medicine, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Thandalam, Chennai- 602105.

[2*]Assistant professor, Department of Community Medicine, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Thandalam, Chennai- 602105.

Authors Contribution:

Conceptualization and clinical management: SM
Data collection and literature search: SM, VP
Writing – original draft preparation: VP
Reviewing & editing: VP
Approval of final manuscript: All authors

Declaration of Generative AI

The authors declare this manuscript was written without the use of generative artificial intelligence tools. All the content, including text generation, data analysis and references was developed and reviewed by the author without assistance from AI technologies.

Conflict of Interest – The authors declare no conflicts of interest.

Source of Support – The authors declare no source of support.

Additional Information:

Authors can order reprints (print copies) of their articles by visiting: **https://www.akinik.com/products/2281/journal-of-ayurveda-and-holistic-medicine-jahm**

Publisher's Note:

Atreya Ayurveda Publications remains neutral with regard to jurisdictional claims in published maps, institutional affiliations, and territorial designations. The publisher does not take any position concerning legal status of countries, territories, or borders shown on maps or mentioned in institutional affiliations.

REFERENCES:

1. Wu J, Chen J, Lv C, Zhou L. Global, regional, and National levels and trends in burden of dental caries and periodontal disease from 1990 to 2035: result from the global burden of disease study 2021. BMC oral health. 2025 May 29;25(1):844. https://doi.org/10.1186/s12903-025-06108-w2
2. Banihashem Rad SA, Esteves-Oliveira M, Maklennan A, Douglas GV, Castiglia P, Campus G. Oral health inequalities in immigrant populations worldwide: a scoping review of dental caries and periodontal disease prevalence. BMC public health. 2024 Jul 23;24(1):1968. https://doi.org/10.1186/s12889-024-19354-4
3. Heidari F, Heboyan A, Rokaya D, Fernandes GV, Heidari M, Banakar M, Zafar MS. Postbiotics and dental caries: a systematic review. Clinical and Experimental Dental Research. 2025 Feb;11(1):e70114. https://doi.org/10.1002/cre2.70114
4. Baskar G, Palaniyandi T, Viswanathan S, Wahab MR, Surendran H, Ravi M, Sivaji A, Rajendran BK, Natarajan S, Govindasamy G. Recent and advanced therapy for oral cancer. Biotechnology and Bioengineering. 2023 Nov;120(11):3105-15. https://doi.org/10.1002/bit.28452
5. Fiorillo L. Chlorhexidine gel use in the oral district: A systematic review. Gels. 2019 Jun 11;5(2):31. https://doi.org/10.3390/gels5020031
6. Deus FP, Ouanounou A. Chlorhexidine in dentistry: pharmacology, uses, and adverse effects. International dental journal. 2022 Jun 1;72(3):269-77. https://doi.org/10.1016/j.identj.2022.01.005
7. Sooampon S, Jirojvanichakorn C, Ratanapakorn T, Harnleulomviboon A, Phowan T, Ayuthaya BI. Antibacterial activity and randomised controlled trial of chlorhexidine-coated floss on gingival bleeding. International Dental Journal. 2025 Apr 1;75(2):1292-301. https://doi.org/10.1016/j.identj.2024.09.017
8. Hashim NT, Babiker R, Chaitanya NC, Mohammed R, Priya SP, Padmanabhan V, Ahmed A, Dasnadi SP, Islam MS, Gismalla BG, Rahman MM. New insights in natural bioactive compounds for periodontal disease: advanced molecular mechanisms and therapeutic potential. Molecules. 2025 Feb 10;30(4):807. https://doi.org/10.3390/molecules30040807
9. Saleh MM, Darwish ZE, El Nouaem MI, Fayed NA, Mourad GM, Ramadan OR. The potential preventive effect of dietary phytochemicals In Vivo. BDJ open. 2023 Jul 18;9(1):30. https://doi.org/10.1038/s41405-023-00157-5
10. Parasakthi M, Sanjeev K. Sulforaphane as a preventive agent in Oral Cancer-A Systematic Review. Oral Oncology Reports. 2024 Jun 1;10:100429. https://doi.org/10.1016/j.oor.2024.100429

11. Tzimas K, Antoniadou M, Varzakas T, Voidarou C. Plant-derived compounds: A promising tool for dental caries prevention. Current Issues in Molecular Biology. 2024 May 26;46(6):5257-90. https://doi.org/10.3390/cimb46060315
12. Kashi M, Varseh M, Hariri Y, Chegini Z, Shariati A. Natural compounds: new therapeutic approach for inhibition of Streptococcus mutans and dental caries. Frontiers in Pharmacology. 2025 Apr 1; 16:1548117. https://doi.org/10.3389/fphar.2025.1548117
13. Anwar MA, Sayed GA, Hal DM, Hafeez MS, Shatat AA, Salman A, Eisa NM, Ramadan A, El-Shiekh RA, Hatem S, Aly SH. Herbal remedies for oral and dental health: a comprehensive review of their multifaceted mechanisms including antimicrobial, anti-inflammatory, and antioxidant pathways. Inflammopharmacology. 2025 Mar;33(3):1085-160. https://doi.org/10.1007/s10787-024-01631-8
14. Zhao W, Zhang Y, Chen J, Hu D. Revolutionizing oral care: Reactive oxygen species (ROS)-Regulating biomaterials for combating infection and inflammation. Redox Biology. 2025 Feb 1; 79:103451. https://doi.org/10.1016/j.redox.2024.103451
15. Spatafora G, Li Y, He X, Cowan A, Tanner AC. The evolving microbiome of dental caries. Microorganisms. 2024 Jan 7;12(1):121. https://doi.org/10.3390/microorganisms12010121
16. Janakiram C, Kumar CD, Joseph J. Xylitol in preventing dental caries: A systematic review and meta-analyses. Journal of natural science, biology, and medicine. 2017 Jan;8(1):16. https://doi.org/10.4103/0976-9668.198344
17. Umai D, Kayalvizhi R, Kumar V, Jacob S. Xylitol: bioproduction and applications-a review. Frontiers in Sustainability. 2022 Feb 15;3:826190. https://doi.org/10.3389/frsus.2022.826190
18. Capasso L, De Masi L, Sirignano C, Maresca V, Basile A, Nebbioso A, Rigano D, Bontempo P. Epigallocatechin gallate (EGCG): pharmacological properties, biological activities and therapeutic potential. Molecules. 2025 Jan;30(3):654. https://doi.org/10.3390/molecules30030654
19. Ayad AS, Benchaabane S, Daas T, Smagghe G, Loucif-Ayad W. Propolis stands out as a multifaceted natural product: meta-analysis on its sources, bioactivities, applications, and future perspectives. Life. 2025 May 9;15(5):764. https://doi.org/10.3390/life15050764
20. Martinello M, Mutinelli F. Antioxidant activity in bee products: A review. Antioxidants. 2021 Jan 7;10(1):71. https://doi.org/10.3390/antiox10010071
21. Heidrich D, Fortes CB, Mallmann AT, Vargas CM, Arndt PB, Scroferneker ML. Rosemary, castor oils, and propolis extract: activity against Candida albicans and alterations on properties of dental acrylic resins. Journal of Prosthodontics. 2019 Feb;28(2):e863-8. https://doi.org/10.1111/jopr.12746
22. Inchingolo F, Inchingolo AD, Latini G, Trilli I, Ferrante L, Nardelli P, Malcangi G, Inchingolo AM, Mancini A, Palermo A, Dipalma G. The role of curcumin in oral health and diseases: a systematic review. Antioxidants. 2024 May 28;13(6):660. https://doi.org/10.3390/antiox13060660
23. Li B, Pan T, Lin H, Zhou Y. The enhancing antibiofilm activity of curcumin on Streptococcus mutans strains from severe early childhood caries. BMC microbiology. 2020 Sep 16;20(1):286 https://doi.org/10.1186/s12866-020-01975-5
24. Radeva L, Yoncheva K. Resveratrol—A promising therapeutic agent with problematic properties. Pharmaceutics. 2025 Jan 19;17(1):134. https://doi.org/10.3390/pharmaceutics17010134
25. Kamarehei F, Mehdiabadi M, Naderi F. Antibacterial effects of natural compounds on biofilm formation of Streptococcus mutans. Clinical and Experimental Dental Research. 2022 Dec;8(6):1426-33. https://doi.org/10.1002/cre2.673
26. Sczepanik FS, Grossi ML, Casati M, Goldberg M, Glogauer M, Fine N, Tenenbaum HC. Periodontitis is an inflammatory disease of oxidative stress: We should treat it that way. Periodontology 2000. 2020 Oct;84(1):45-68. https://doi.org/10.1111/prd.12342
27. Malcangi G, Inchingolo AM, Casamassima L, Trilli I, Ferrante L, Inchingolo F, Palermo A, Inchingolo AD, Dipalma G. Effectiveness of herbal medicines with anti-inflammatory, antimicrobial, and antioxidant properties in improving oral health and treating gingivitis and periodontitis: A systematic review. Nutrients. 2025 Feb 21;17(5):762. https://doi.org/10.3390/nu17050762
28. Kumbar VM, Peram MR, Kugaji MS, Patil S, Kambimath M, Magennavar S, Hussain M, Bhat KG, Paranjape R. Antimicrobial and antibiofilm activity of curcumin against oral pathogens: Potential for periodontal treatment. The Microbe. 2025 Jun 1;7:100355. https://doi.org/10.1016/j.microb.2025.100355
29. Pradhan Y, Devkota HP, Ali A. Potential Role of Medicinal Plants and their Phytochemicals against Plaque forming Oral Microbiota. Biosciences Biotechnology Research Asia. 2024 Jul 1;21(2):371-89. http://dx.doi.org/10.13005/bbra/3232
30. Gawish AS, ElMofty MS, Jambi S, Felemban D, Ragheb YS, Elsayed SA. Phytotherapy in periodontics as an effective and sustainable supplemental treatment: a narrative review. Journal of Periodontal & Implant Science. 2023 Dec 11;54(4):209. https://doi.org/10.5051/jpis.2301420071\
31. Amalia NR, Budhy TI, Ridwan RD, Rianti D, Bramantoro T, Luthfi M, Ramadhani NF, Pramusita A, Putranti NA, Nugraha AP, Situmorang PC. Propolis nanoemulsion extract from celebes stingless bee (Tetragonula biroi) phytochemistry and antibacterial analysis to periodontopathogen bacteria. Journal of Oral Biology and Craniofacial Research. 2025 May 1;15(3):576-84. https://doi.org/10.1016/j.jobcr.2025.03.013
32. Almehyawi MH, Basyoni DM, Alsibaie RB, Alhussini KH, Lashkar RM, Alla RK, Shammas M, Alotaibi GM. Natural products used as disinfectants in prosthodontics and oral implantology: a narrative

review. Journal of Exploratory Research in Pharmacology. 2025 Jun 30;10(2):49-61. https://doi.org/10.14218/JERP.2025.00016

33. Nosratzehi T, Nosratzehi F. The role of curcumin in perspectives of oral-healthcare: Medicinal Plants - International Journal of Phytomedicines and Related Industries. 2021 June; 13(2):221-228. https://doi.org/10.5958/0975-6892.2021.00025.3
34. Vila T, Sultan AS, Montelongo-Jauregui D, Jabra-Rizk MA. Oral candidiasis: A disease of opportunity. Journal of fungi. 2020 Jan 16;6(1):15. https://doi.org/10.3390/jof6010015
35. Dias LD, Blanco KC, Mfouo-Tynga IS, Inada NM, Bagnato VS. Curcumin as a photosensitizer: From molecular structure to recent advances in antimicrobial photodynamic therapy. Journal of Photochemistry and Photobiology C: Photochemistry Reviews. 2020 Dec 1 ;45:100384. https://doi.org/10.1016/j.jphotochemrev.2020.100384
36. Warakomska A, Kępa M, Fiegler-Rudol J, Latusek-Kotyczka K, Skaba D, Wiench R. In Vitro Antifungal Efficacy of Blue-Light Photodynamic Therapy with Curcumin andRiboflavin Formulation Activated by 450 nm Diode Laser Against Candida albicans Biofilm on Titanium Implants. Pharmaceutics. 2025 Nov 7;17(11):1437. https://doi.org/10.3390/pharmaceutics17111437
37. Eloranta R, Vilén ST, Keinänen A, Salo T, Qannam A, Bello IO, Snäll J. Oral squamous cell carcinoma: effect of tobacco and alcohol on cancer location. Tobacco induced diseases. 2024 Jun 18;22:10-8332. https://doi.org/10.18332/tid/189303
38. Amaroli A, Panfoli I, Bozzo M, Ferrando S, Candiani S, Ravera S. The bright side of curcumin: a narrative review of its therapeutic potential in cancer management. Cancers. 2024 Jan;16(14):2580. https://doi.org/10.3390/cancers16142580
39. Guo K, Feng Y, Zheng X, Sun L, Wasan HS, Ruan S, Shen M. Resveratrol and its analogs: potent agents to reverse epithelial-to-mesenchymal transition in tumors. Frontiers in Oncology. 2021 Apr 16;11:644134. https://doi.org/10.3389/fonc.2021.644134
40. Jiang X, Liu Y, Ma L, Ji R, Qu Y, Xin Y, Lv G. Chemopreventive activity of sulforaphane. Drug design, development and therapy. 2018 Sep 11:2905-13. https://doi.org/10.2147/DDDT.S100534
41. Koushki M, Amiri-Dashatan N, Ahmadi N, Abbaszadeh HA, Rezaei-Tavirani M. Resveratrol: A miraculous natural compound for diseases treatment. Food Science & Nutrition. 2018 Nov;6(8):2473-90. https://doi.org/10.1002/fsn3.855
42. Meng T, Xiao D, Muhammed A, Deng J, Chen L, He J. Anti-inflammatory action and mechanisms of resveratrol. Molecules. 2021 Jan 5;26(1):229. https://doi.org/10.3390/molecules26010229
43. Ferreira AS, Macedo C, Silva AM, Delerue-Matos C, Costa P, Rodrigues F. Natural products for the prevention and treatment of oral mucositis—a review. International Journal of Molecular Sciences. 2022 Apr 15;23(8):4385. https://doi.org/10.3390/ijms23084385