Mastic (*Pistacia lentiscus*) gum and oral health: A state-of-the-art review of the literature

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Abstract

The aim of this state-of-the-art review is to provide a comprehensive overview of the various therapeutic effects of Mastic (*Pistacia lentiscus*) gum on oral health.
The search of the literature was conducted across thirteen databases for relevant publications published through May 2022 in English, Arabic, or Greek using a combination of keywords and phrases.
Out of 246 papers, the search procedure identified 14 papers for inclusion. Mastic gum displayed antibacterial and antimicrobial properties and inhibited plaque accumulation, constituting a beneficial adjuvant in caries prevention. In the treatment and prevention of periodontal diseases, *Pistacia lentiscus* essential oil provided effective antibacterial activity against a variety of periodontal bacteria as well as anti-inflammatory properties. For oral cancer, several clinical trials revealed interesting results against cell proliferation, induction of apoptosis, and regulation of intracellular signaling pathways. This indicates the potential of Mastic gum to serve as a preventive and therapeutic agent for oral mucosa inflammation and oral cancer. No notable toxic or side-effects were reported in the clinical trials reviewed. This review highlights the various beneficial effects of Mastic gum in the prevention and potential treatment of oral diseases. Further research targeting *Pistacia lentiscus* products is required in order to validate and utilize these products to prevent and to treat oral health diseases.

Keywords

Mastic gum; dental hygiene; oral health; *Pistacia lentiscus*

Introduction

Oral diseases such as dental caries, periodontal diseases, and oral cancer are major public health issues that are among the most common diseases worldwide [1]. Oral health has an impact on the overall quality of life and is linked to systemic and chronic diseases [2]. The development and progression of oral diseases are greatly influenced by oral microorganisms [1, 3-5].

Dental caries and periodontal diseases are the most common bacterial diseases of the oral cavity. In both cases, the dental biofilm is responsible for the disruption brought on by poor oral hygiene. Acidogenic gram-positive bacteria are the primary cause of dental caries (Streptococcus mutans, Actinomycetes, and Lactobacilli), whereas periodontal disorders have been associated with Anaerobic gram-negative bacteria (Actinobacillus, Porphyromonas gingivalis, Fusobacterium, and Prevotella). Inhibition of cariogenic bacteria and therapy with an anti-biofilm agent constitute two effective prophylactic treatments. The purpose is to minimize the overall amount of biofilm or specific pathogen levels. Several chemical agents with effects on bacterial metabolism and cell adhesion have been described in recent years. Some chemicals, including chlorhexidine [6-9], triclosan [10], and delmopinol [9, 11] have been shown to be effective inhibitors of biofilm growth and maturation.

Given the rising prevalence of oral diseases, bacterial resistance to antibiotics, the negative effects of certain antimicrobial agents currently used in dental care, and financial constraints in developing nations, it is necessary to offer alternative treatment and prevention options that are both safe and cost-effective. Although a number of agents are commercially accessible, they can affect the oral microbiota and cause unpleasant side effects such as diarrhea, vomiting, mucosal desquamation [12], and tooth discoloration [13]. Therefore, plant-based dentifrices, such as Miswak (*Salvadora persica*) [14-16], have lately been intensively examined as potential agents for preventing oral diseases, particularly diseases

linked to plaque, as they may have fewer adverse effects than synthetic antimicrobials. Historically, there has been widespread use of natural remedies and traditional plants to treat oral diseases. Ancient polymaths such as Herodotus, Dioscorides, and Galen cited Mastic gum in their respective works as beneficial to oral health [17]. In contemporary times, previously used plant-based dentifrice sticks made from shrubs or plants with high microbial activity have been replaced by plastic bristled toothbrushes [15, 16, 18]. Over the years, the association of plants with dental hygiene and therapeutic practices has been studied extensively [16].

Traditional medicinal plant extracts, such as cinnamon bark oil, oil of clove, and Papua mace extracts affect the development of oral pathogens, inhibit the formation of dental plaque, control bacterial adhesion to surfaces, and lessen the sign and symptoms of oral disorders. Chloroform extracts of *Drosera peltate* (Droseraceae) leaves and the ethanol extract of *Helichrysum italicum* (Compositae), *Breynia nivosa* (Euphorbiaceae), and *Ageratum conyzoides* (Asteraceae) have been utilized for their activity against oral bacteria such as *Streptococcus mutans* and *Streptococcus sobrinus*. Garlic, *Allium sativum* (Liliaceae), has been used to target gram-negative oral pathogens such as *P. gingivalis*, while *Hamamelis virginiana* (Hamamelidaceae) displayed the highest level of overall activity against a wide range of oral bacteria such as *Preveotella* species, *Porphyromonas* species, and *Actinomyces Odontolyticus*. Furthermore, Periodontopathogenic bacteria was traditionally targeted by leveraging bactericidal properties of a boiling water extract of *Coptidis rhizoma* (Ranunculaceae) spp., and *Actinomyces odontolyticus* [19].

The Anacardiaceae family, which includes approximately 600 species and approximately 70 genera, includes the genus Pistacia. The species of the genus Pistacia are xerophytic evergreen or deciduous resin-bearing shrubs and trees that can reach heights of 8 to 10 meters. The resin, leaves, fruit, and aerial portions of Pistacia species have all historically

been utilized for a number of reasons. P. lentiscus is the most popular of them, and its resin has been used for up to 5000 years in various parts of the world [20].

The aim of this state-of-the-art review is to provide a comprehensive overview of the various therapeutic effects of Mastic (*Pistacia lentiscus*) gum (Figure 1) on oral health. More specifically, the effects of chewing Mastic gum, a natural resin derived from the leaves and stem of the Mastic tree, *Pistacia lentiscus*, on preventing the growth of oral pathogens, formation of dental plaque, as well as reducing the signs and symptoms of oral disorders, will be covered.

Methods

For the purpose of providing a critical survey of the contemporary literature produced in the past two decades, a synthesis of current thinking in the field of herbal interventions and plant-extracts against oral diseases would help offer new perspectives on this topic and point out areas in need of further research. Therefore, a state-of-the-art review was carried out. The literature search was conducted across six databases (Table 1) for relevant studies published up to and including March 2023 using a combination of keywords and phrases (Table 1). Publications were reviewed for topical relevance, tabulated (Table 2), and summarized. Only primary research studies that were published in English, Arabic, or Greek were included. Commentaries, letters to the editor, and grey literature were excluded in the search (Table 3). To find additional relevant publications, references from the retrieved studies were also reviewed.

Results

The search strategy produced 246 studies. After removing duplicates, the titles and abstracts of 114 papers were screened against the inclusion and exclusion criteria. In total, 15 full-text

articles were obtained and screened against inclusion criteria (Table 3), with two articles being excluded. After manually searching study reference lists, one paper was added. The search procedure ultimately identified 14 articles (Figure 2) for this review [21].

Table 4 provides an overview of all studies regarding the effects of chewing Mastic gum on oral health that were included in this review. Eight of the total studies reviewed evaluated the significant impact of chewing Mastic gum on the prevention of dental caries, with one covering the impact on periodontal diseases, four on periodontal diseases, and two on the influence of Pistacia lentiscus extract as a preventive and curative agent for oral cancer. Different types of study designs were retrieved from the research. Table 2 shows that the majority of the included studies were in vitro and in vivo experiments.

Discussion

Mastic gum is a natural, aromatic resin, yellowish-white in color and extracted from the trunk of the Mastic tree (*Pistacia lentiscus*) [22]. Also known as Chios Mastic gum, it is exclusively produced on the southern portion of the Greek island of Chios, which is located in the northern Aegean Sea, with a Protected Designation of Origin accorded by the European Union [23]. The Mastic tree has dense leaves and is a perennial cespitose tree [24]. The aromatic resin, used for a variety of purposes, has historically been obtained by cutting longitudinal incisions into the trunk and branches of the Mastic tree [24].

Pistacia resins have a long history of use in Mediterranean and Middle Eastern countries as herbal medicines and dietary supplements. Hippocrates, Dioscorides, Galenus, and Theophrastus were some of the ancient Greek doctors who advocated its usage for the treatment of numerous gastrointestinal disorders [25]. Mastic gum's primary usage

nowadays, however, is the production of the naturally bitter-tasting chewing gum used in the Mediterranean region for culinary purposes and as a food ingredient [23].

Harvested for more than 2500 years, Mastic gum finds its use in systemic as well as oral therapeutic benefits. The 15th century Spanish physician and botanist, Andrés Laguna, used it in cases of pyorrhea, while the twigs of the tree were used as toothpicks. Laguna recommended using it as a constituent in tooth cleaning agents as an infusion or a concoction as well as in breath fresheners [24]. Mastic gum was also used as an esthetic-amplifying cosmetic on skin, as well as to treat ailments and soothe menstrual symptoms. Additionally, gum of the Mastic tree was used to neutralize the foul odor caused as a result of chronic mercury poisoning. Recognizing its therapeutic value, the European Medicines Agency (EMA) has included Chios Mastic gum in the traditional herbal medicine category and has approved the use of Mastic gum for mild dyspeptic disorders, infections or minor skin lesions [23].

Therapeutic effects of Mastic chewing gum on systemic health

Anti-Inflammatory and anti-atherogenic properties

Chronic conditions such as inflammatory bowel disease, diabetes mellitus, cancer, and heart ailments share the common pathogenetic mechanism of inflammation. In fact, it is now widely known that a number of chronic diseases, including connective tissue and inflammatory bowel diseases, diabetes mellitus, cancer, and cardiovascular conditions share, to a lesser or larger extent, common pathogenetic processes involving inflammation.

Some studies have demonstrated the effectiveness of Mastic gum to lower the cytokines tumor necrosis factor and to have a protective effect on intestinal epithelial cells in inflammatory bowel disease [23, 26]. Mastic gum's lipid-lowering activity also suggests that

it may have cardioprotective properties [23]; the antioxidant effect and anti-inflammatory properties in unison produce Anti-atherogenic properties.

Antioxidant and anticancer Properties

Free radicals of oxygen are created by cellular metabolism, and these radicals are crucial for controlling cell signaling, differentiation, and proliferation [23]. Cancer, cardiovascular disease, and systemic inflammatory diseases are all linked to an excessive production of reactive oxygen species [23], thereby explaining the popularity of antioxidants in health products. Mastic gum down-regulates such processes, thus exhibiting antioxidant properties [23]. Mastic oil has exhibited antiproliferative and proapoptotic activity in in vivo studies, which is to be explored in further research [27]. Another study found that giving mice Mastic oil orally at a dose of 0.58 g/kg body weight/day for 13 days prevented tumor growth compared to controls [28].

Adverse Effects - Toxicity

Mastic gum has been used successfully in clinical trials, the only unremarkable side effect for humans being allergic contact dermatitis. However, animal studies have reported renal histological alterations in rats with some cytotoxicity and an increase in liver weights as well as changes in biochemical markers with use over 13 weeks, so long-term safety has yet to be investigated [23].

Therapeutic effects of Mastic chewing gum on oral health

Mastic gum possesses outstanding antibacterial and antimicrobial capabilities, according to numerous studies [29-37], as described in Table 4. Mastic gum was proven to reduce plaque building when compared to placebo gum in a study published in 2003 by Takahashi et al.

[32], demonstrating that Mastic itself has an anti-plaque formation effect, which is a significant factor for the overall quantity of Streptococci in the oral environment. Furthermore, in vitro and in vivo investigations found that chewing Mastic gum (CMG) significantly inhibits the growth of the microorganisms such as Streptococcus mutans. In this research, saliva samples were taken from participants before and after they chewed either the Mastic gum or the placebo (paraffin) gum for 15 minutes. Participants who chewed Mastic gum for 15 minutes had reduced levels of certain germs in their mouths. After 135 minutes, the bacterium levels had decreased considerably further. A placebo did not yield identical outcomes [29]. CMG has antibacterial activity against *S. mutans*, according to this study, and could be a beneficial adjuvant in caries prevention. Similar findings were confirmed by Aksoy et al. [29], who found that chewing Mastic gum reduced the total quantity of viable bacteria, *Streptococcus mutans*, and lactobacilli in saliva in orthodontic-treated patients with fixed appliances. The same authors also showed that Mastic prolongs the life of oral polymorphonuclear leukocytes by inhibiting apoptosis, implying that it may support the enhancement of natural immunity, such as the removal of microorganisms from the mouth. Previous research has also found that chewing Mastic gum improves the remineralization rate of caries-like lesions [34]. Mahalakshmi et al.[36] evaluated the antimicrobial activity of two herbal extracts (S. xanthocarpum and P. lentiscus) against three bacterial strains (S. mutans, Lactobacillus species, and A. viscosus) and found that the extracts were statistically significant against all three. This suggests that, when used appropriately, herbal extracts could be potentially used in the prevention of dental caries.

Mastic has also been demonstrated to be effective in the treatment of periodontal diseases [38-40]. When compared to popular antimicrobial treatments such as hydrogen peroxide (H2O2), studies indicated that Mastic extract prevented periodontal infections and had good effects on cell viability, implying that it might be utilized as a substitute antibacterial agent to

help prevent periodontal disease [40]. *Pistacia lentiscus* L. essential oil (PLL-EO) was studied for its antibacterial activity against a variety of periodontal Candida and bacteria, including laboratory and clinical isolates species, as well as for its anti-inflammatory effectiveness and safety. The researchers found that PLL-EO has high biocompatibility, anti-inflammatory characteristics, and antimicrobial properties against all tested species. The findings showed that by lowering inflammation, EO could be beneficial in the treatment of periodontal and Candida infections. These findings support the idea that PLL-EO might be a novel antifungal drug that reduces yeast virulence both directly and indirectly [38]. Mastic gum can also be used as a non-toxic topical therapy for bad breath and gum disease. In one study, CMG was found to totally eliminate *Porphyromonas gingivalis*, an odontogenic periopathogenic oral bacterium, suggesting that it could be utilized a non-toxic topical therapy for bad breath and gum disease [39].

Several studies have suggested that *Pistacia lentiscus* extract could also be used as a preventive and curative agent for oral cancer [41, 42]. Li et al. [41] demonstrated that Chios Mastic gum induces apoptosis of YD-10B oral cancer cells by activating caspase-3, a key mediator of apoptosis, inhibits cell proliferation, and has antioxidant properties [41]. Furthermore, Choi et al. [42] claims that the Mastic shows the best outcomes in all aspects, including Xenograft model in oral cancer cells, suppression of cell proliferation, induction of apoptosis, modulation of intracellular signaling pathways, and safety [42]. Though the findings reported here are limited to mostly in vitro results, they could serve as a foundation for more comprehensive in vivo studies; additionally, the stimulation of apoptosis by Chios Mastic gum extracts suggests that they could be employed in chemotherapy alongside other anticancer medications.

Conclusion

To summarize, this review demonstrates Mastic gum's numerous beneficial effects on the prevention and treatment of oral diseases. Although the findings were encouraging, more research is necessary to further validate the effectiveness of Pistacia lentiscus products and enable their use as mouthwashes, dentifrices, and topical applications for the prevention of oral diseases in the future. Future research should involve more in-depth in vitro studies with different strains of cariogenic flora, in vivo studies, and clinical trials.

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Table 1. Electronic Databases Used with Relevant Search Period and Terms

Databases	**Search Period**	**MeSH keywords, terms, phrases, and Boolean operators**
PubMed; SCOPUS; JSTOR; ProQuest; Biomed Central; CINAHL	studies up to and including March 2023	Mastic [af]; OR mastiha [af]; OR Mastika [af]; OR tears of Chios [af]; OR *Pistacia lentiscus* [af]; AND Gum [af]; AND chewing [af]; AND Dental health [af]; oral health [af]

Table 2. Narrative summary of relevant studies (N=14)

Authors (year) [reference]	Theme	Study aim	Type of study	Study participants	Main results	Conclusion
Aksoy et al, 2006 [29]	Impact of chewing mastic gum on dental caries prevention	The objective of this study was to determine antibacterial activity of mastic chewing gum against S. mutans and mutans streptococci in vitro and in vivo conditions.	In vitro and in vivo study	• Antimicrobial activity of mastic gum was evaluated using standard S. mutans strain by disc diffusion method in vitro. Cytotoxicity effect of mastic gum on HEp-2 cells was evaluated by conventional haemocytometer using the trypan blue exclusion method. • Clinical studies were then performed on 25 periodontally healthy volunteers. The inhibitory effect of chewing mastic gum against mutans streptococci in saliva was compared to a placebo gum. Saliva samples were taken from the subjects immediately before and after chewing the mastic gum and the placebo gum for 15 min. Additional saliva samples were collected every 30 min. The samples were inoculated onto mitis salivarius-bacitracin agar and incubated for 48 h anaerobically at 37 8C. The total number of viable bacteria was then counted.	• Among tested solvents (chloroform, acetone, petroleum ether and ethanol), it was found that the acetone was found to be more convenient than the others to dissolve the mastic gum. • In the cytotoxicity assay, concentrations up to 75 mg/ml of the mastic gum were not toxic for the replication of HEp-2 cells. Thus, lower concentrations of mastic gum (20 and 50 mg/ml) were used for the experiments. • In vitro experiments, the diameters of growth inhibition zones of mastic gum were in the range 9.0—27.0 mm. • In the clinical trials, the 37% reduction in mutans streptococci counts (cfu/ml) were found just after application of mastic gum. This was the initial effect of the gum. And 48.5%, 56.7%, 62.5%, 62.1% reduction was found at 45th, 75th, 105th and 135th minutes after spiting mastic gum subsequently. All values obtained after application of mastic gum except 105th and 135th minutes applications were found statistically significant ($p < 0.05$). In contrast, paraffin gum used as placebo showed no antibacterial effect.	This preliminary study showed that mastic gum had significant antibacterial activity against S. mutans and mutans streptococci and it may be useful adjunct in the prevention of caries.
Aksoy et al, 2007 [30]	Impact of chewing mastic gum on dental caries prevention	To determine antibacterial activity of chewing mastic gum against the salivary levels of Streptococcus mutans, the total number of viable bacteria, and lactobacilli in patients undergoing therapy with fixed orthodontic appliances	In vivo study	• Saliva samples taken from the patients	• Just after chewing the mastic gum for 15 minutes, a significant decrease of total bacteria and S mutans was observed ($P < .001$). The reduction in lactobacilli was not significant at later first stage ($P > .05$). However, at the end of 135 minutes, there were significantly fewer S mutans ($P < .001$), total viable bacteria ($P < .001$), and lactobacilli ($P < .001$) in the oral cavity after chewing mastic gum than after chewing paraffin ($P < .001$). The results show that chewing mastic gum decreased the total viable bacteria, S mutans, and lactobacilli in saliva in orthodontically treated patients with fixed appliances.	Chewing mastic gum might be useful in preventing caries lesions.

Biria et al, 2014 [31]	Impact of chewing mastic gum on dental caries prevention	The aim of this study was to assess the effects of three types of mastic gums on the level of Mutans streptococci, Lactobacilli and pH of the saliva	In vivo study	Forty-two students in the age range of 20-30 years were divided into three parallel groups; each of them separately used pure mastic gum, xylitol mastic gum and probiotic mastic gum for three weeks. Number of microorganisms and pH of the saliva were assessed before and after the intervention.	• Level of Mutans streptococci showed a significant reduction compared to its base-line value in all three groups (P<0001 for all). • Salivary Lactobacillus count increased in the groups using pure and xylitol mastic gums but decreased in the group using probiotic type, albeit these changes were only significant in the group using probiotic mastic gum (P<0.001). • Use of pure and xylitol mastic gums increased the pH of the saliva but not significantly. In the group using probiotic mastic gum, the pH of the saliva decreased significantly (P=0.029).	Three weeks use of all mastic gums resulted in a significant drop in the number of Mutans streptococci in the saliva. However, the drop in the saliva pH due to the use of probiotic mastic gum is not in favour of dental health.
Biria et al, 2009 [34]	Impact of chewing mastic gum on dental caries prevention	This study carried out to compare the effect of mastic gum and a xylitol chewing gum on remineralization of caries-like lesions.	Cross-over, single blinded, in situ study,	Fifteen 20-30 years of age healthy volunteers with no evidence of progressive periodontal disease and no untreated dental caries participated in the study.	• The decrease in demineralized surfaces in both groups was statistically significant (Mastic gum: P=0.018, xylitol gum: P<0.001). The difference of average decrease between the two groups, however, was not statistically significant (P>0.05).	Chewing both mastic gum and xylitol chewing gum improved the remineralization of caries-like lesions but their effects were similar.
Karygianni et al, 2019 [35]	Impact of chewing mastic gum on dental caries prevention and periodontal disease	The aim of this study was to investigate the antimicrobial potential of five natural constituents of Olea europaea (oleuropein, maslinic acid, hydroxytyrosol, oleocanthal, oleacein) and three compounds of Pistacia lentiscus (24Z isomasticadienolic acid, oleanolic acid, oleanonic aldehyde) against ten representative oral bacterial species and a Candida albicans strain	Vitro study	Five natural constituents of Olea europaea (oleuropein, maslinic acid, hydroxytyrosol, oleocanthal, oleacein) and three compounds of Pistacia lentiscus (24Z isomasticadienolic acid, oleanolic acid, oleanonic aldehyde) against ten representative oral bacterial species and a Candida albicans strain.	• Among all O. europaea-derived constituents, maslinic acid was the most active (MIC = 4.9–312 μgmL− 1, MBC = 9.8–25 μgmL− 1) one against oral streptococci and anaerobic pathogenic bacteria (Porphyromonas gingivalis, Fusobacterium nucleatum, Parvimonas micra), while oleuropein, hydroxytyrosol, oleocanthal and oleacein showed milder, yet significant effects against P. gingivalis and F. nucleatum. • Among all P. lentiscus compounds, oleanolic acid was the most effective one against almost all microorganisms with MIC values ranging from 9.8 μgmL− 1 (P. gingivalis) to 625 μgmL− 1 (F. nucleatum, P. micra). In the presence of 24Z-isomasticadienolic acid, a mean inhibitory concentration range of 2.4 μgmL− 1 to 625 μgmL− 1 was observed for strict anaerobia. The MIC value for 24Z-isomasticadienolic acid was estimated between 39 μgmL− 1 (Streptococcus sobrinus, Streptococcus oralis) and 78 μgmL− 1 (Streptococcus mutans). All tested compounds showed no effects against Prevotella intermedia.	Maslinic acid and oleanolic acid exerted the most significant inhibitory activity against the tested oral pathogens, especially streptococci and anaerobic oral microorganisms.
Karygianni et al, 2014 [37]	Impact of chewing mastic gum on periodontal disease	To examine the antimicrobial impact of Mediterranean natural extracts on	Vitro study	Five different extracts from Olea europaea, mastic gum, and Inula viscosa were tested against ten bacteria and one Candida albicans	• The screened extracts were found to be active against each of the tested microorganisms. O. europaea presented MIC and MBC ranges of 0.07–	Overall, extracts from O. europaea, mastic gum, and I. viscosa were active against the tested oral pathogens,

		oral microorganisms. Five different extracts From Olea europaea, mastic gum, and Inula viscosa were tested against ten bacteria and one Candida albicans strain.		strain. The extraction protocols were conducted according to established experimental procedures. Two antimicrobial assays—the minimum inhibitory concentration (MIC) assay and the minimum bactericidal concentration (MBC) assay—were applied.	10.00mgmL−1 and 0.60–10.00mgmL−1, respectively. The mean MBC values for mastic gum and I. viscosa were 0.07–10.00mgmL−1 and 0.15– 10.00mgmL−1, respectively. • Extracts were less effective against C. albicans and exerted bactericidal effects at a concentration range of 0.07–5.00mgmL−1 on strict anaerobic bacteria (Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, and Parvimonas micra). • Ethyl acetate I. viscosa extract and total mastic extract showed considerable antimicrobial activity against oral microorganisms and could therefore be considered as alternative natural anti-infectious agents.	especially Gram-negative anaerobic bacteria, and could therefore be considered as alternative natural anti-infectious agents which could be used against periodontitis.
Mahalakshmi et al, 2019 [36]	Impact of chewing mastic gum on dental caries prevention	To Evaluate the Antimicrobial properties of Solanum xanthocarpum and Pistacia lentiscus extracts on cariogenic oral microbial flora.	Vitro study	The antimicrobial properties of Solanum xanthocarpum and Pistacia lentiscus extracts on cariogenic oral microbial flora (streptococcus mutans, lactobacillus, actinomyces viscosus) by different culture techniques to estimate the zone of inhibition (well diffusion method) and minimum inhibitory concentration (tube dilution method).	• The antimicrobial efficacy of Solanum xanthocarpum and Pistacia lentiscus on test bacteria were analyzed using kurskal wallis test and values of 0.003 and 0.002 were obtained respectively, since the p values were less than 0.005, indicating that both herbal products possess statistically significant antimicrobial properties.	The antimicrobial effects of the herbal extracts were almost on par with commercially available allopathic agents like chlorhexidine on oral cariogenic microbes. The efficacy should be further validated in a large-scale study and can be utilized for caries prevention in the form of mouth rinses, dentifrices and topical application in the future.
Takahashi et al, 2003 [32]	Impact of chewing mastic gum on dental caries prevention	The aim of the present study was to assess the extent to which mastic chewing gum might prevent bacterial growth in saliva and inhibit plaque accumulation and gingival inflammation against a placebo,	A double blinded, Randomized study.	Twenty dental students (16 males, 4 females, mean age 25.9 years) enrolled in the Meikai University School of Dentistry volunteered for this study. In the first trial, after mechanical toothbrushing, the inhibitory effect of mastic gum on bacteria in saliva following its use was compared to a placebo gum. Saliva samples were collected at the end of 1, 2, 3, and 4 hours. In the second trial, the effects of mastic gum on de novo plaque formation on tooth surfaces and gingival inflammation were evaluated over a 7-day period without mechanical oral hygiene following random use of either mastic or placebo chewing gum. The degree of plaque accumulation and gingival	• The total number of bacterial colonies was significantly reduced during the 4 hours of chewing mastic gum compared to the placebo gum ($P < 0.05$, Student t test). The mastic group showed a significantly reduced plaque index (2.69 ± 0.29 versus 3.15 ± 0.24; $P = 0.001$, Student t test) and gingival index (0.44 ± 0.15 versus 0.66 ± 0.23, $P = 0.021$, Student t test) compared to the placebo group.	These results suggest that mastic chewing gum is a useful antiplaque agent in reducing the bacterial growth in saliva and plaque formation on teeth.

				inflammation were compared between the 2 groups (n = 10).		
Talib & Esra, 2013 [33]	Impact of chewing mastic gum on dental caries prevention	To evaluate the antibacterial effect of mastic gum against the most common aerobic oral bacteria and emphasized on oral streptococci.	Experiment	10 persons (males and females of 18-60 years old) were randomly assigned to chew mastic gum (1.5 gm for 45 minutes). Mouth washes were collected before and after gum chewing. The two mouth washes were diluted (10-1 – 10-6) and cultivated aerobically for 24 hours at 37C0 on BHI agar for total bacterial count and on MSF agar for counting the oral streptococci.	• The results showed that the total bacterial count for staphylococci, Neisseria and oral streptococci on BHI agar and MSF agar for oral streptococci after mastic chewing were highly reduced and arrived at more than 5 grades according to statistical analysis.	Chewing of mastic gum daily and for many hours may be useful in controlling dental caries, and dental plaque. It is good for general and oral hygiene; it protects teeth, and other organs from systemic inflammation caused by oral bacteria.
Koychev et al, 2017 [40]	Mastic gum and periodontal diseases	Antimicrobial properties of mastic extract on commensal and pathogenic oral bacteria, as well as its possible cytotoxic effect toward cells of epithelial and mesenchymal origin, were evaluated in comparison to the common antimicrobial agents hydrogen peroxide (H2O2) and chlorhexidine digluconate (CHX).	Vitro study	Oral and periodontal pathogens (P. gingivalis, S. mutans, S. oralis, A. actinomycetemcomitans, F. nucleatum, P. intermedia, and P. nigrescens) were treated with different concentrations of mastic extract, 3 % H2O2 and 0.2 % CHX, and then evaluated with an agar diffusion test.	• Mastic extract led to significantly (P ≤0.016) increased inhibition of the tested periodontal pathogens compared with H2O2. No effect of mastic extract was observed on Streptococcus mutans. • Mastic extract showed beneficial effects on cell viability because viability values of tested cells were significantly (P ≤0.016) lower for cells treated with CHX and H2O2 compared with mastic extract–treated cells after stimulation for 2, 4, and 6 hours.	The present data demonstrate mastic extract's inhibition of periodontal pathogens, as well as beneficial effects on cell viability, compared with H2O2, suggesting that it could be considered an alternative antibacterial agent in the prevention of periodontal disease.
Milia et al, 2020 [38]	Mastic gum and periodontal diseases	This study assessed the antimicrobial capacity of Pistacia lentiscus L. essential oil (PLL-EO) toward a wide range of periodontal bacteria and Candida.	Vitro study	PLL-EO was screened by gas chromatography/mass spectrometry. The minimal inhibitory concentration (MIC) was determined. The anti-inflammatory activity was measured by cyclooxygenase (COX-1/2) and lipoxygenase (LOX) inhibition, while the antioxidant capacity was determined electro-chemically and by the MTT assay. The WST-1 assay was used to ascertain cytotoxicity toward four lines of oral cells.	• According to the concentrations of terpens, PLL-EO is pharmacologically active phytocomplex. MICs against periodontal bacteria ranged between 3.13 and 12.5 g/ml, while against Candida sp. they were between 6.25 and 12.5g/mL. Oxidation by COX-1/2 and LOX was inhibited by 80% and 20% g/mL of the oil, respectively. Antioxidant activity seemed negligible, and no cytotoxicity arose.	PLL-EO exhibits a broad-spectrum activity against periodontal bacteria and Candida, with an interesting dual inhibitory capacity toward COX-2 and LOX inflammatory enzymes, and without side effects against oral cells.
Sterer, 2006 [39]	Mastic gum and periodontal diseases	The purpose of the present report is to test the antimicrobial activity of mastic gum methanolic extract (MME) against P. gingivalis	Vitro study	The antimicrobial effect of mastic gum against Porphyromonas gingivalis, a known odontogenic periopathogenic oral bacterium, was tested using the agar diffusion test.	• Results showed that mastic extracts produced inhibition zones up to 40% in diameter of the inhibition zones created by chlorhexidine, without showing any signs of hemolysis. Chlorhexidine, on the other hand, produced large hemolytic zones, which may be an indication for its potential	These results suggest that mastic gum may be used as a potential nontoxic local agent in treating oral malodor and gum disease.

		as compared with the chemical agent chlorhexidine.			harmfulness. Negative control discs impregnated with methanol alone did not cause bacterial inhibition, indicating that the methanol evaporated. completely during the discs' drying process.	
Li et al, 2011 [41]	Oral cancer and Pistacia lentiscus extract	The purpose was to investigate Chios mastic gum (CMG) extract as a potential anti-tumor agent for oral squamous cell carcinoma in vitro	Vitro study	• Chios mastic gum (CMG) extracts were obtained from Mastic Korea • Cell culture / Human oral squamous carcinoma YD-10B cell lines were derived from oral cancer research institute • Paclitaxel (Taxol, Bristol-Myers Squibb, Canada) was used as the control.	• MTT assay suggested that both CMG and Taxol inhibited the proliferation of YD-10B cells in a time and dose-dependent manner. • 10μg/mL of CMG and 50μg/mL of Taxol caused fragmentation of the genomic DNA at 24 hours. • 10μg/mL of CMG and 50μg/mL of Taxol caused cleavage of procaspase-3 in western blot analysis.	CMG extracts and Taxol inhibited growth and induced apoptosis of YD-10B oral cancer cells in vitro and CMG extracts had greater antitumor potency than Taxol.
Choi et al, 2022 [42]	Oral cancer and Pistacia lentiscus extract	This study aimed to examine the preventive and therapeutic effects of the supercritical extracts of Momordica charantia Linn., Pistacia lentiscus, and Commiphora myrrha on oral inflammation and oral cancer.	Vitro study	Mixed extract samples (MPC-1–4) of natural plants, Momordica charantia Linn., Pistacia lentiscus, and Commiphora myrrha, were prepared according to their respective extraction methods.	• As a result of the cell proliferation inhibition experiment, all samples decreased the proliferation of oral cancer cell MC3 and HN22 cells in a concentration-dependent manner ($p < 0.01$). The survival rates of MPC-4 and MPC-1 were about 50% and about 80%, respectively, showing a difference according to the extraction method. • In flow cytometry results, early apoptosis and late apoptosis of MPC-4 were 26.9% and 18.1%, respectively, indicating that apoptosis induction was the most effective. Although the induction effect was shown in other samples, the result was lower than that of MPC-4. • As a result of confirming the regulation of the signaling pathway, it was confirmed that the expression of cleaved caspase 3 and Bak regulatory genes increased in a concentration-dependent manner in MC3 and HN22 cells ($p < 0.01$), thus inducing apoptosis in oral cancer cells. • As a result of safety and Xenograft model experiments, it was found that MPC-4 had no toxicity to oral administration.	MPC-4 showed the best results in all aspects, such as inhibition of cell proliferation, induction of apoptosis, regulation of intracellular signaling pathways, safety, and Xenograft model in oral cancer cells.

Table 3. PICOS Criteria for Inclusion and Exclusion of Studies

Parameter	Inclusion Criteria	Exclusion Criteria
Population	All eligible study participants included	N/A
Publication date	Up to and including March 2023	N/A
Intervention type	Any oral health-based outcome study that employs the use of Mastic gum as part of the study	Interventions that did not incorporate the use of Mastic gum in the study
Comparators	N/A	N/A
Outcomes of Interest	All oral health-based outcomes	Non-oral health related outcomes
Study Type	Experimental intervention studies with quantitative outcomes	All other study designs
Language	English, Arabic, Greek	All other languages
Study Type	Any peer-reviewed primary research studies In-vivo studies In-vitro studies	Non peer-reviewed articles Commentaires Narratives Communications Non-intervention based studies White papers Grey literature Similar article types Conference Abstracts

Abbreviations
N/A – Not applicable

Table 4. Summary of Studies on the Effect of Mastic on Oral Health Outcomes

Therapeutic effect of Mastic gum on oral health outcomes	References	Summary of findings
Mastic gum's potential for preventing dental caries.	Aksoy et al. 2006 [29] Aksoy et al. 2007 [30] Biria et al. 2009 [34] Biria et al. 2014 [31] Karygianni et al. 2019 [36] Mahalakshmi et al. 2019 [37] Takahashi et al. 2003[32] Talib & Esra. 2013 [33]	• Mastic gum possess antibacterial and antimicrobial properties. • Chewing mastic gum reduces plaque formation and inhibits the growth of Streptococcus mutans, a bacteria associated with dental caries. • Chewing Mastic gum reduces the total quantity of viable bacteria in saliva and supports natural immunity. • Chewing mastic gum improves the remineralization rate of caries-like lesions. • Herbal extracts like S. xanthocarpum and P. lentiscus have antimicrobial activity against bacterial strains associated with dental caries and could potentially help prevent them.
Mastic gum's potential to treat periodontal diseases	Karygianni et al. 2014 [35] Karygianni et al. 2019 [36] Koychev et al. 2017 [41] Milia et al. 2020 [39] Sterer. 2006 [40]	• Mastic gum has been shown to be effective in the treatment of periodontal diseases. • Mastic gum extract is a potential substitute for antimicrobial agents such as hydrogen peroxide in preventing periodontal infections. • Pistacia lentiscus L. essential oil (PLL-EO) has high biocompatibility, anti-inflammatory characteristics, and antimicrobial properties against all tested species of periodontal Candida and bacteria. • Mastic gum can be used as a non-toxic topical therapy for halitosis and gum disease as it can eliminate Porphyromonas gingivalis, an odontogenic periopathogenic oral bacterium.
Mastic gum's potential for preventing and treating oral cancer	Li et al. 2011 [42] Choi et al. 2022 [43]	• Mastic gum extract could be used to prevent and treat oral cancer • Mastic gum induces apoptosis (cell death) of oral cancer cells and inhibits cell proliferation • Mastic gum possess antioxidant properties • Mastic gum has been shown to suppress cell proliferation, induce apoptosis, modulate intracellular signalling pathways, and safety • Mastic gum extracts could be employed in chemotherapy alongside other anticancer medications • The findings are limited to mostly in vitro results and further in vivo studies are needed

Figure 1. Mastic (*Pistacia lentiscus*) gum

Figure 2. Flow Diagram