Episode 103 – Role of Mouthrinses in Oral Care February 23, 2024

Overview
Antimicrobial mouthrinses are available over-the-counter or via prescription from oral health practitioners to help prevent various oral diseases caused by bacteria, viruses, and fungi. Fluoride mouthrinses are also widely used to improve hard tissue remineralization and prevent dental caries. Currently available antimicrobial mouthrinses may kill bacteria (bactericidal). Others may inhibit bacterial growth (bacteriostatic) and plaque biofilm formation, potentially mitigating dental caries, gingivitis, and periodontitis, plaque-induced oral diseases. There is also a resurgence of interest in preprocedural mouthrinse use, particularly since the onset of the COVID-19 pandemic. [1] [2]

A wide variety of chemical and natural antiseptic mouthrinses are available to help manage dental caries and periodontal disease as well as potentially manage or mask halitosis and whiten teeth. Mouthrinses are often used daily without the intervention of an oral health practitioner. These include chlorhexidine (CHX), fluoride, hydrogen peroxide (H_2O_2), cetylpyridinium chloride (CPC), povidone iodine (PVP-I), and essential oils (EOs). Their mode of action and potential effectiveness varies, depending on their active ingredients, concentrations, and frequency of use. [1] [2]

There is evidence commonly used mouthrinses can reduce plaque and gingivitis, with CHX being the most effective. However, many antiseptic mouthrinses appear less effective with more severe forms of periodontitis, probably because mouthrinses used alone cannot reach periodontal pocket depths where anaerobic periodontal pathogens reside. There is also evidence fluoride mouthrinses can be used successfully for dental caries management by increasing enamel remineralization. [1] [3]

Common active ingredients in mouthrinses [1] [2] [4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [14] [15] [16] [17] [18] [19] [20]

Type	Therapeutic effect	Mechanism of action	Use	Possible adverse effects*
Chlorhexidine (CHX) (bisbiguanide agent)	Broad-spectrum activity against gram-positive and gram-negative bacteria, fungi and certain viruses (e.g., herpes simplex type-1, influenza A) Dose-dependent: bacteriostatic at 0.02%-0.06%; bactericidal at >0.1%	Interacts with negatively charged microbial cell membranes, disrupts the structure spilling cell contents Penetrates the cell, condensing bacterial chromosomes and blocking DNA replication	Reduce gingivitis and plaque biofilm	Temporary taste alteration Increase calculus formation Brown staining of teeth and oral mucosa, especially the tongue Soreness, irritation, mild desquamation, ulceration, burning sensation of oral mucosa Allergic reaction (rare)
Hydrogen peroxide (H_2O_2)	Broad-spectrum antimicrobial, including anerobic bacteria. Concentrations of 0.5% virucidal to enveloped viruses (e.g., coronavirus). Carbamide peroxide (in many whitening products) breaks down in contact with water to release H_2O_2 (e.g., 10% CP converts to 3% HP and 7% urea).	Bleaching agent with strong oxidizing action that liberates oxygen free radicals and disrupts lipid microbial cell walls to kill obligate anaerobes. Foams on contact with tissues with release of water and oxygen, which may also destroy anaerobic bacteria. Tooth stains consist of compounds colour (i.e., chromogens). Bleaching mainly constitutes removal of stains by chemical degradation of chromogens. Hypothesized the whitening is attributed to reaction of H_2O_2 with chromogens.	Reduce gingivitis, bleeding scores, and tooth staining	Prolonged use has been associated with black hairy tongue. Concentrations >5% may cause soft tissue damage.
Cetylpyridinium chloride (CPC)	Broad-spectrum antimicrobial properties, including antibacterial, antifungal, and antiviral	Antibacterial by reacting with lipids and proteins of the cell membrane, leading to disorganization in its structure, leakage of cell components, disruption of cell	Reduce plaque, gingivitis, and anaerobic bacteria in plaque and saliva	Brown staining of teeth and temporary loss of taste

Type	Therapeutic effect	Mechanism of action	Use	Possible adverse effects*
(type of quaternary ammonium compound [QAC])		metabolism, inhibition of cell growth, and finally cell death. QACs also release autolytic enzymes causing lysis of the bacterial cell wall and loss of functional components. Antifungal via reverse distribution of charges on cell surface. Antiviral via disruption or detachment of viral envelope, releasing the nucleocapsid. Effects on nonenveloped viruses are less certain.		
Povidone iodine (PVP-1)	Bactericidal, viricidal, fungicidal	Release of iodine destabilizes bacterial lipid membranes and lyses proteins	Historically used to decontaminate periodontal sites before invasive procedures to reduce bacteremia risk. Investigated as possible prerinse to prevent SARS-CoV-2 transmission.	Altered thyroid function if ingested. Anaphylactic-type allergic reactions in those with iodine or shellfish allergy.
Essential oils (EOs) (e.g., eucalyptol, menthol, peppermint, clove, methyl salicylate, thymol)	Antibacterial, antifungal, antioxidant, anti-inflammatory	Antibacterial activity mainly achieved by cell membrane destruction. Increased membrane permeability may lead to vital intracellular component loss (e.g., proteins, sugars, ATP, DNA), while decreasing ATP production leading to cell damage and electrolyte leakage. Combinations of oils often used, thus difficult to ascertain which EOs are effective.	Reduce bacterial plaque biofilms, in turn, gingivitis, halitosis	Taste disturbance Rinses with alcohol should be avoided by children due to potential of accidental ingestion and it may result in relapse for those who experience alcohol use disorder. Alcohol may worsen oral dryness and mucosal pain in individuals with dry mouth or oral mucosal ulcerative disease, respectively. Alcohol-containing mouthrinses may exacerbate halitosis (common driver of mouthrinse use) by reducing saliva production. Alcohol, although used in high concentrations as an antiseptic agent for surfaces, in most

Type	Therapeutic effect	Mechanism of action	Use	Possible adverse effects*
		Alcohol is a solvent to solubilize ingredients, a vehicle to deliver active ingredients, and enables EOs to penetrate plaque biofilm.		mouthrinses has little capacity to kill microbes because amount of ethanol present is ≤26%.
Triclosan[1] (nonionic chlorinated aromatic compound)	Synthetic antimicrobial agent with antibacterial and antifungal properties	Inhibits fatty acid biosynthetic pathway within microbial cells, disrupting lipid synthesis causing cell death	Antibacterial Found in rinses with sodium fluoride and other antiseptics (e.g., CPCs) to increase effectiveness of plaque control and reduce gingivitis.	Evidence suggests triclosan may be associated with reproductive and endocrine dysfunction, antimicrobial resistance, and toxicity in aquatic species. Clinicians must consider whether potential clinical benefits outweigh emerging risks.
Fluoride (e.g., sodium fluoride, stannous fluoride)	Dental caries prevention, remineralization, antibacterial (particularly stannous fluoride)	Remineralizes calcium hydroxyapatite structure in enamel by forming calcium fluorapatite, which is more resistant to acid attacks. The remineralization effect can reverse early decay process and create a tooth surface more resistant to decay.	Help prevent dental caries and erosion Increase remineralization Reduce tooth sensitivity	Rinses should be avoided by young children due to potential of accidental ingestion Stannous fluoride may cause yellowish-brown staining of teeth

*Nonexhaustive list

[1] Refer to Episode 100 for additional information on triclosan and antimicrobial resistance.

Mouthrinses and oral health

Antimicrobial mouthrinses purport to reduce dental plaque biofilm and thus have the potential to mitigate plaque-induced diseases, such as periodontal disease and dental caries. Mouthrinses may also play a role in managing oral conditions (e.g., halitosis, dry socket, tooth staining), protecting healthcare workers from disease transmission, and reducing healthcare-associated pneumonia.

Plaque and gingivitis

Chlorhexidine (CHX) is one of the most frequently evaluated mouthrinses. Findings from a Cochrane review by James et al. (2017) found high-certainty evidence of a large dental plaque reduction with daily use of CHX mouthrinse as an adjunct to mechanical oral hygiene procedures for 4 to 6 weeks or six months, compared to placebo, control, or no mouthrinse. There was also high-quality evidence of a moderate reduction in gingivitis in individuals with mild gingivitis. However, because the level of disease was already low, this was not considered clinically significant.

There was no evidence one concentration of CHX rinse was more effective than another. There was insufficient evidence to determine the reduction in gingivitis associated with CHX mouthrinse use in individuals with moderate or severe gingival inflammation. [6]

A meta-analysis by Hass et al. (2016) evaluating the efficacy of essential oil (EO) mouthrinses reported that EO-containing mouthrinses were more efficacious for reducing plaque and gingival inflammation than mechanical plaque control either alone (placebo) or in combination with CPC mouthrinses in individuals with gingivitis. Reductions in plaque and gingivitis were 32% and 24% higher, respectively, for EOs plus mechanical plaque control than placebo plus mechanical plaque control. However, the authors concluded the quality of the overall body of evidence was moderate to low. [21]

A meta-review of systematic reviews by Van der Weijden et al. (2015) found mouthrinse containing CHX was the first choice for plaque control in managing gingivitis, followed by EO-containing mouthrinses. [13]

Orthodontics

Andrucioli et al. (2023) evaluated the effect of CHX mouthrinses on periodontal status and extrinsic tooth staining in clients with fixed orthodontic appliances. Results showed twice weekly 0.12% CHX mouthrinse use reduced plaque, gingival, and gingival bleeding indexes when evaluated at 15, 30, and 60 days. The discolouration index increased at 30 days and was highest at 60 days. In the control group (mechanical plaque control only), no changes were observed in the plaque, gingival, gingival bleeding, or discolouration indexes at any time point evaluated. The authors concluded 0.12% CHX mouthrinse can be used twice weekly for 30 days without causing significant extrinsic tooth staining. [22]

CHX and tooth staining

For many decades, CHX has been used for oral disease management. However, reported side effects may affect client compliance. The most common side effect is tooth and tongue staining. Stain variability may be linked to extrinsic factors such as the client's diet. Numerous studies with model systems have shown dietary chromogens are partly responsible for stain. Many food items (e.g., tea, coffee, red wine) are known to stain even in the absence of CHX. The most probable cause of staining is the precipitation of anionic dietary chromogens onto adsorbed cations.[2] This means polyphenols, which are anionic and found in food substances, can react with cations adsorbed to surfaces, including cationic antiseptics such as CHX, to form a stain.

An *in vitro* study by Sarembe et al. (2022) investigated the degree of discolouration caused by various beverages during CHX treatment. The team used a scanning electron microscope to examine the effects of eleven beverages with varying pH levels and colours, including coffee and black tea with and without milk.

They exposed enamel samples from extracted human molars to artificial saliva, 0.2% CHX mouthrinse, and the beverages over 28 cycles, simulating a 14-day CHX use period. They also replicated daily teeth cleaning with water and toothpaste using a toothbrushing simulator. The dental crowns exposed to black tea and coffee showed more significant staining than those exposed to beverages diluted with milk.

Thus, adding milk to coffee and tea may be a worthy recommendation oral health practitioners can offer clients using CHX rinse. Recommending to consistently use toothpaste to brush teeth and to leave as much time as possible between mouthrinse use and eating or drinking may also reduce staining. [23]

Treatment of stage I-III periodontitis[3]

The European Federation for Periodontology (EFP) S3-Level Clinical Practice Guideline for treatment of stage I-III periodontitis states adjunctive antiseptics **may be considered**, specifically CHX mouthrinse for a limited period, in periodontitis therapy, after mechanical debridement, in specific cases. [24]

Antiseptic mouthrinse use as an adjunct to good oral self-care **may be considered** in clients with periodontitis in supportive periodontal care to help control gingival inflammation, in specific cases, as part of a personalized treatment approach. However, cost, client preference, frequency, duration of use, and possible side effects should be taken into consideration. [24]

If an antiseptic mouthrinse is being adjunctively used to control gingival inflammation in clients with periodontitis in supportive periodontal care, the guideline **suggests** using mouthrinses containing CHX, EOs, and CPC. [24]

[2] Anions and cations are negatively and positively charged ions, respectively. Because they have an opposite electrical charge, they attract each other.

[3] Refer to Episodes 49 and 50 for discussion on the EFP S3-Level Clinical Practice Guideline for treatment of stage I-III periodontitis.

Treatment of peri-implant diseases[4]
The EFP S3 level clinical practice guideline for the prevention and treatment of peri-implant diseases states in clients with peri-implant mucositis, a time-limited antimicrobial oral rinse (CHX or herbal-based) adjunctive to professional mechanical plaque removal **may be considered**. [25]

Dental caries[5]
A Cochrane review by Marinho et al. (2016) involving children and adolescents found fluoride-containing mouthrinses were associated with a large reduction in dental caries in permanent teeth. The authors were moderately certain of the size of the effect. [3]

CHX mouthrinses have been evaluated on their effectiveness in reducing cariogenic bacteria in individuals with moderate to high dental caries risk. Statistically significant differences in *Streptococcus mutans* levels during and after CHX mouthrinse use have been observed. However, there is a need for higher-quality studies of longer duration to assess whether the results translate into less dental caries development. [2] [26]

Halitosis[6]
Halitosis refers to an unpleasant or foul odour emitted from exhaled air that is unpleasant or offensive to others, which can lead to social stigma and loss of self-confidence. Halitosis may be caused by microbial degradation of amino acids into volatile sulfur compounds (VSCs), foul smelling gases. [16] [27]

A Cochrane review by Nagraj et al. (2019) found CHX mouthrinse may play a role in reducing the levels of halitosis-producing bacteria, although it found very low certainty evidence given the quality and quantity of studies. [27]

A review by Dobler et al. (2020) compared the antimicrobial activity of EOs against oral VSC-producing bacteria. Types of EOs included eucalyptol, menthol, thymol, myrtle, peppermint, clove, tea tree, lemongrass, and cinnamon. The results suggest there is considerable evidence EO mouthrinses are effective in preventing and managing halitosis. However, further research is required to establish their safety and efficacy before including them in clinical practice since only a few clinical studies have been conducted. [16]

Teeth whitening
To a large extent, the effectiveness of hydrogen peroxide (H_2O_2) containing mouthrinse on tooth whitening has been based on *in vitro* studies (e.g., colour change on extrinsically stained bovine teeth). Such laboratory-based studies may not consider dilution effects and inactivation by saliva and thus overestimate the effects compared to clinical whitening. [2] [28]

A Cochrane review by Eachempati et al. (2018) identified one clinical study with 78 participants who used a 1.5% fluoridated H_2O_2 mouthrinse (twice daily for 30 seconds

[4] Refer to Episodes 24, 46, and 84 for additional information on peri-implant diseases.
[5] Refer to Episodes 86 and 87 for detailed discussion on dental caries.
[6] Refer to Episode 67 for additional information on halitosis.

for six months) and found only weak evidence this improved the shade of the teeth compared to placebo. No other outcomes were reported. [11]

The same 2018 Cochrane review also identified one clinical study with 28 participants that compared two H_2O_2 tooth whitening systems (2% H_2O_2 prerinse and 10% H_2O_2 strips). Both the prerinse and whitening strips were used twice daily with normal toothbrushing over a one-week period. The prerinse group rinsed twice daily with 15 ml solution for 60 seconds before brushing. The strip group applied twice daily for 30 minutes. H_2O_2 whitening strips resulted in significant tooth whitening compared to H_2O_2 mouthrinse used twice daily. Tooth sensitivity and oral irritation were more common in the strip group. All adverse events were mild in severity, and no participants discontinued treatment because of these events. [11] [29]

Limitations of whitening mouthrinse use include short contact time with the teeth and low pH mouthrinses potentially "soften" enamel and lead to increased tooth wear,[7] especially if followed by brushing. [2]

Preprocedural rinses

Aerosols and spatter are generated in oral healthcare during aerosol-generating procedures (AGPs). Oral health clinicians can be at increased risk of disease transmission through droplets on mucosae, inhalation of aerosols, or via fomites harbouring microorganisms. There are ways to mitigate and contain spatter and aerosols, which may reduce disease transmission risk. In addition to personal protective equipment (PPE) and aerosol-reducing devices (e.g., high-volume suction), it has been hypothesized that mouthrinse use by clients before oral health procedures could reduce the microbial load of aerosols generated during AGPs.

A Cochrane review by Nagraj et al. (2022) found none of the included studies measured the incidence of infection among oral health clinicians. The studies measured only a reduction in the level of bacterial contamination in aerosols. None of the studies evaluated viral or fungal contamination. There was only low to very low certainty for all findings. The authors were unable to conclude whether there is a role for preprocedural mouth rinses in reducing infection risk or the possible superiority of one preprocedural rinse over another. The review identified the need for more research that measures the effect of rinses on infectious disease risk among oral health clinicians and on contaminated aerosols at larger distances with standardized outcome measurement. [30]

Overall, the results suggest using a preprocedural mouthrinse may reduce the level of bacterial contamination in aerosols compared with no rinsing or rinsing with water. However, there was only low or very low certainty evidence, and it is not known how this reduction in contamination relates to infection risk. [30]

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. Most individuals with COVID-19 develop mild to moderate respiratory illness. Others experience severe

[7] Refer to Episode 82 for discussion on tooth wear.

symptoms and need specialist treatment and intensive care, while others may have asymptomatic infection.

COVID-19 poses a serious risk to clients and the healthcare workers treating them. The risk of infection transmission is greater when a client is undergoing an AGP. Having the client rinse with an antimicrobial mouthrinse before an AGP may be a simple and safe method to reduce the risk of infection being passed to healthcare workers through droplet transmission or direct contact. Alternatively, antimicrobial rinsing by the healthcare worker may decrease their chance of acquiring COVID-19.

Three 2020 Cochrane reviews found a lack of completed studies to advise whether antimicrobial mouthrinses used by healthcare workers or administered to clients with suspected or confirmed COVID-19 improved client outcomes and protected the healthcare workers treating them. [31] [32] [33] [34]

A systematic review and network meta-analysis by Lin et al. (2023) compared the effectiveness of different mouthrinses in reducing the viral load and infectivity of SARS-CoV-2, alleviating clinical symptoms or disease severity, and decreasing the incidence of COVID-19. The authors concluded that due to the heterogeneity of the primary studies, the effectiveness of mouthrinses in reducing viral infectivity, improving clinical symptoms, or preventing COVID-19 remains inconclusive. [35]

Dry socket

Alveolar osteitis or dry socket is a complication of dental extractions, more often involving mandibular molar teeth. It is associated with severe pain developing 2-3 days postoperatively with or without halitosis, a socket that may be partially or totally devoid of a blood clot, and increased postoperative visits. [36]

A 2022 Cochrane review found moderate certainty evidence CHX mouthrinses (0.12% and 0.2% concentrations) used before and 24 hours after extraction substantially reduced the risk of dry socket development compared with a placebo mouthrinse. [36]

Ventilator-associated pneumonia

Ventilator-associated pneumonia (VAP) is pneumonia developing in patients who have received mechanical ventilation for at least 48 hours. VAP is a potentially serious complication in patients who are already critically ill, increasing the risk of mortality. Oral hygiene care, using either a mouthrinse, gel, swab, toothbrush, or combination, together with suction of secretions, may help prevent VAP. [37]

A Cochrane review by Zhao et al. (2020) found CHX mouthrinse or gel probably reduced the incidence of critically ill patients experiencing VAP from 26% to 18% compared to placebo or usual care. However, there was no evidence of a benefit for mortality or duration of mechanical ventilation or ICU stay, although the evidence was low certainty. The review also found weak evidence povidone iodine (PVP-I) rinse was more effective than saline/placebo for the reduction of VAP. [37]

Nursing home-acquired pneumonia
Nursing home-acquired pneumonia (NHAP) is pneumonia occurring in a resident of a long-term care facility or nursing home. NHAP is one of the most common infections identified in these residents and has the highest mortality of any infection in this population. NHAP is associated with poor oral hygiene and may be caused by aspiration of oropharyngeal flora into the lung. Oral care measures to remove or disrupt oral plaque might reduce the risk of NHAP. [38]

A cluster-randomized clinical trial in which manual tooth brushing was supplemented with 0.12% CHX mouthrinse, administered twice daily, found CHX mouthrinse was ineffective for pneumonia prevention among nursing home residents. [39] [40]

Effects on oral microbiome[8]
The oral cavity hosts the second-largest and diverse microbiota after the gut, harbouring over 700 different microbial species of bacteria, fungi, archaea, viruses, and protozoa. The oral cavity is a very complex environment where different microbes preferentially colonize different ecological niches (e.g., teeth, dental implants and restorations, tongue, palate, gingiva, subgingival sulcus, tonsils, etc.). [41]

Disruption of the oral microbiome leads to dysbiosis. Microbial dysbiosis contributes to oral diseases, such as dental caries, periodontal disease, peri-implant disease, mucosal diseases (e.g., oral candidiasis), and oral cancer. Factors contributing to oral dysbiosis include salivary gland dysfunction (e.g., changes in saliva flow or composition), poor oral hygiene, gingival inflammation, lifestyle choices (e.g., dietary habits, smoking, vaping alcohol consumption), and certain drugs (e.g., antibiotics, chemotherapeutics, immunosuppressants). [12] [42] [43]

In oral health, the oral microbiome exists as a complex and diverse microbial community. To maintain oral health there needs to be a balance between commensal and pathogenic microbiota. Antimicrobial mouthrinses have long been used because of their ability to kill pathogens. Thus, the antimicrobial effect of mouthrinses on the oral microbiome can be both advantageous and deleterious, depending on whether there is a shift towards oral health, with diversity, or a shift towards disease, with a predominance of a pathogenic species as antimicrobial mouthrinses are nonspecific and can wipe out large swathes of the commensal oral microbiota. [12] [19]

<u>Chlorhexidine</u>
Chlorhexidine mouthrinses reduce plaque and gingivitis, and as per the EFP guideline, CHX may be used as an adjunct to manage periodontitis. *In vitro* studies have shown 0.01% to 0.2% CHX has a potent bactericidal effect on single species and multispecies cultures containing periodontal pathogens *Fusobacterium nucleatum, Porphrymonas gingivalis*, and *Aggregatibacter actinomycetemcomitans*. [12] [24] [44]

While this may be considered an advantage in reversing microbial dysbiosis. CHX also decreases bacterial diversity. Research in healthy individuals demonstrates certain

[8] Refer to Episode 63 for additional information on the oral microbiome.

bacterial species (e.g., *Veillonella*, *Actinomyces, Haemophilus, Rothia*, *Neisseria*) are also inhibited by CHX. These health-associated oral bacteria perform the vital function of reducing dietary nitrates to nitrite. Nearly 25% of ingested nitrate is transported, in a process referred to as the enterosalivary circuit (or nitrate-nitrite-nitric oxide pathway), to the oral cavity. Once in the mouth, oral microbes reduce nitrate to nitrite. Nitrite is then swallowed and taken into the bloodstream during digestion and converted to nitric oxide. Nitric oxide is essential to cardiovascular health as it exerts vasodilation and antihypertensive effects, contributing to the maintenance of cardiovascular health. Thus, CHX mouthrinses, due to their nonspecific antimicrobial activity, may negate the beneficial effects of nitrate-rich diets[9] mediated by the oral microbiome. [12] [19] [45] [46] [47]

A study by Bescos et al. (2020) assessed the effects of repeated use of CHX mouthrinse on the salivary microbiome in 36 orally healthy participants. Shifts in the proportions of oral microbes were found after seven days of CHX use, with a greater abundance in Firmicutes and Proteobacteria and reductions in Bacteroidetes, Saccharibacteria, SR1, and Fusobacteria. This shift was accompanied by significant reductions in salivary pH and buffering capacity and increased salivary lactate and glucose levels, which are associated with dental caries and periodontal diseases. [19] [45]

These findings add to the growing body of evidence that CHX mouthrinse use should be carefully considered. CHX could have detrimental effects on the healthy microbiome and, in turn, cardiovascular health, requiring further investigation. [45]

Hydrogen peroxide

Hydrogen peroxide (H_2O_2) is a bleaching and oxidizing agent known to be bactericidal *in vitro*. Several *in vivo* studies suggest 1.5% H_2O_2 reduces the incidence of gingivitis and bleeding scores. Currently, there appear to be no studies investigating the impact of H_2O_2 on the oral microbiome. [12]

Cetylpyridinium chloride

Cetylpyridinium chloride (CPC) is a broad-spectrum antimicrobial compound. CPC is effective in reducing plaque and the levels of anaerobic bacteria species in plaque and saliva. However, evidence from microbiome studies remains limited. One industry sponsored study reported levels of periodontal pathogens did not increase in supragingival plaque over 21 days of induction of experimental gingivitis with CPC rinsing compared to water rinsing and maintained the original biodiversity of healthy plaques. [12] [48]

Povidone iodine

Povidone iodine (PVP-I) is an antimicrobial agent via oxidation and destruction of vital cellular components, including nucleic acids, proteins, and membrane components. A concentration of 10% PVP-I rinse demonstrated appreciable bactericidal activity against

[9] Good dietary sources of nitrates include dark green leafy vegetables (e.g., spinach, kale, romaine lettuce), beets, and celery.

several periodontal pathogens (e.g., *P gingivalis, A actinomycetemcomitans, F nucleatum, Tannerella forsythia, Prevotella intermedia,* and *Streptococcus anginosus*) *in vitro*. However, the effects of PVP-I on the oral microbiome have not yet been fully described. A small one-week study involving 12 children reported reduced dental plaque accumulation without significant alterations in proportions of different bacteria within the dental plaque after topical treatment with a combination of 10% PVP-I and 5% sodium fluoride varnish. [12] [49] [50] [51]

Essential oils

Numerous essential oils (EOs) used in mouthrinses have demonstrated antimicrobial effects against oral pathogens. EOs are also reported to reduce plaque and bleeding scores when used as an adjunct to tooth brushing. *In vitro*, an EO blend was able to eradicate *Staphylococcus aureus* and *Streptococcus* biofilms on hydroxyapatite discs to a greater extent than CHX. However, there appear to be no studies investigating the effects of various EOs on the oral microbiome *in vivo*. [12]

Alcohol

Alcohol (ethanol) is found in many mouthrinses. Alcohol acts as a solvent to solubilize the ingredients and a vehicle to deliver active ingredients in mouthrinses. Alcohol can decrease the abundance of commensal bacteria in heavy alcohol consumers and increase the abundance of *Actinomyces, Leptotrichia, and Neisseria* (some of these genera contain oral pathogens). However, alcohol in most mouthrinses has little capacity to kill microbes because the amount of ethanol present is 26% or less. In addition, no studies have reported the effects of mouth rinsing on oral microbiome communities. [12] [19] [52]

Sodium fluoride

Sodium fluoride mouthrinses offer anticariogenic and remineralization properties. Currently, the effects of different concentrations of sodium fluoride mouthrinse on the oral microbiome are unknown. [12]

Effect on the mycobiome

Communities of fungal species within the oral cavity are referred to as the oral mycobiome. *Candida spp*, as commensals, form an important part of a balanced microenvironment on oral hard and soft tissues. However, many other fungal species may exist in a healthy oral microbiome (e.g., *Malassezia spp, Caldosporium*, *Aspergillus*). [12]

Candida spp may predominate during oral dysbiosis, leading to oral disease (e.g., oral candidiasis and denture-associated stomatitis). *In vitro* studies have shown 0.2% CHX can inhibit *C. albicans* growth and can also be fungicidal. However, there is insufficient information on the effects of different antimicrobial mouthrinses on the oral mycobiome *in vivo*. More research is required in this area. [12] [53] [54]

Effect on the virome

The oral microbiome also contains viruses, known as the oral virome, comprising RNA or DNA, being either single-stranded or double-stranded. Research has revealed

bacteriophages constitute the vast majority of viruses in the healthy oral cavity. Bacteriophages, also known as phages, are viruses that infect and replicate only in bacterial cells. The oral virome may also contain some eukaryotic viruses (e.g., herpes simplex virus, cytomegalovirus, Epstein-Barr virus, human coronavirus, SARS-CoV-2).

It is expected that enveloped viruses are more prone to inactivation by mouthrinses compared to nonenveloped viruses due to the membrane-disrupting mechanism of action of most antiseptic mouthrinses used in vitro. Generally, much less is known about the effects of antiseptic mouthrinses on the oral virome compared to the oral bacteriome. More research is needed to assess the effects of mouthrinses on the virome, particularly when oral viral loads lead to clinical signs of disease. [12]

Antimicrobial resistance[10]
Research has shown no significant changes in bacterial sensitivity, overgrowth of potentially opportunistic organisms, or other adverse changes in the oral microbial flora following the use of CHX mouthrinse 0.12% for six months. Three months after use was discontinued, the number of bacteria in plaque had returned to pretreatment levels, and the sensitivity of plaque bacteria to CHX remained unchanged. [55]

However, studies over the last few decades have reported CHX resistance in different bacterial species, but at concentrations well below those used in the clinical setting. Meanwhile, studies of *in vitro* CHX-adapted bacteria have reported cross-resistance between CHX and other antimicrobials. While clinical studies to support the hypothesis of CHX cross-resistance with antibiotics are currently lacking, it is important oral health practitioners understand that appropriate clinical use of CHX should be oral disease specific. [56] [4]

Current literature is ambivalent on the clinical significance of developing resistance to CPC. In addition, it is unclear whether the oral cavity is a potential reservoir for horizontal gene transfer that will increase resistance to CPC and other antibiotics through co-resistance. Studies investigating shifts in bacterial, fungal, and viral populations or acquisition and transfer of antimicrobial resistance amongst oral microbes are lacking. Considering the current limitations of the available literature, it is recommended to limit mouthrinses to specific indications and periods of use supported by appropriate evidence. [12]

Mouthrinses and systemic conditions
There is some emerging data on the potential association between antimicrobial mouthrinse and systemic conditions, such as cardiovascular disease (CVD), diabetes, and Alzheimer's disease.

Cardiovascular disease[11]
Several reports suggest antimicrobial mouthrinses may impact cardiovascular health. The underlying mechanisms between mouthrinses and CVD are not yet fully elucidated.

[10] Refer to Episode 100 for discussion on antimicrobial resistance.
[11] Refer to Episodes 79, 80, and 81 for detailed discussion on cardiovascular disease.

However, there is accumulating evidence it may be related to the impact of antimicrobial mouthrinses on the oral microbiome. For example, studies have shown antimicrobial mouthrinses may lead to adverse effects on blood pressure control in both healthy adults and those with hypertension. CHX use, in particular, has been found to cause a shift in the oral microbiome leading to a possibly unfavourable decline in salivary nitrite concentration. [57]

The systemic health benefits of regular exercise are well documented. Post-exercise hypotension is a common physiological phenomenon leading to lower blood pressure after intense exercise. Cutler et al. (2019) investigated whether the nitrate-reducing activity of oral bacteria is a key mechanism to trigger post-exercise hypotension.

For the study, 23 adults with good oral health ran on a treadmill for 30 minutes on two separate occasions and then monitored for 2 hours. On each occasion, the participants rinsed with either 0.2% CHX rinse or placebo (mint-flavoured water) at 1, 30, 60, and 90 minutes after exercise cessation. The results showed an average reduction in systolic blood pressure of –5.2 mmHg one hour after exercise with water rinsing. However, when participants rinsed with CHX mouthrinse, the average decrease in systolic blood pressure after one hour was –2 mmHg.

Based on these findings, the researchers recommend healthcare professionals should pay attention to the oral environment when recommending physical activity to reduce high blood pressure. [58]

However, other studies did not find any change in blood pressure related to antimicrobial mouthrinse use. A long-term study over almost 19 years by Janket et al. (2023) showed a profound reduction in risk of cardiovascular mortality of 51% with good oral self-care, and this effect did not differ with additional mouthrinse use. Adding mouthrinse did not help beyond the benefits of good brushing and flossing. [59]

Diabetes[12]

Most mouthrinses contain antibacterial ingredients, which could impact oral microbes critical for nitric oxide formation and, in turn, predispose to metabolic disorders, including diabetes. Joshipura et al. (2017) evaluated the association between baseline mouthrinse use and the development of prediabetes/diabetes over a 3-year follow-up. The results of this longitudinal study found daily mouthrinse use (irrespective of its constituents) was associated with increased risk of developing prediabetes/diabetes. [60]

However, a bidirectional relationship between diabetes and periodontitis has been reported, and mouthrinse use is known to reduce periodontal pathogens. Matayoshi et al. (2024) investigated the effects of mouthrinse use on the numbers of red complex species (e.g., *P. gingivalis, T. denticola,* and *T. forsythia*) and HbA1c levels[13] in participants with type 2 diabetes.

[12] Refer to Episodes 91, 93, and 94 for detailed discussion on diabetes.

[13] Hemoglobin A1C (HbA1c), also referred to as A1C, is an estimate of the average levels of blood glucose over the last three months.

The researchers found the number of red complex species significantly decreased in younger or male participants who used mouthrinse. HbA1c levels significantly decreased in younger participants or participants with higher HbA1c levels who used mouthrinse. The results suggest mouthrinse use reduces the number of red complex species and improves the hyperglycemic status in individuals with type 2 diabetes, especially younger people. [61]

Alzheimer's disease[14]
Multiple animal and human studies have demonstrated an association between periodontitis and dementia. Antimicrobial mouthrinse use to prevent or control periodontal disease may help attenuate Alzheimer's disease progression. However, there is currently insufficient evidence to support or refute this notion. [57]

However, mouthrinse use may be a simple means for individuals with Alzheimer's disease (or their caregivers) to reduce the oral bacterial and fungal load and lessen the risk of oral plaque-induced diseases, especially when mechanical plaque removal becomes challenging. [57]

Mouth rinses and oral cancer[15]
Alcohol consumption is a known risk factor for potentially malignant and malignant disease of the oral mucosa. The risk of oral cancer has been shown to increase by 6.4-fold in nonsmokers who drink alcohol heavily, compared with a risk of 2.1-fold for smokers who do not drink alcohol. There have been suggestions alcohol in many available mouthrinses (with amounts up to 26%) may increase the risk of oral cancer, but at present, the evidence is limited and conflicting. [57] [62]

There are several clinical benefits of mouthrinse use. However, these benefits need to be balanced against the potential risk of oral cancer. If mouthrinse use is required long term, nonalcohol mouthrinses should be recommended. However, there is an obvious need for research to assess ideal nonalcohol mouthrinses or new alternatives. [57]

Alternate mouthrinses
Alternate or "natural" mouthrinses are gaining popularity and are preferred by some. Thus, oral health practitioners need to be aware of available alternative mouthrinses. Types of alternate mouthrinses include charcoal, seaweeds, probiotics, and oil pulling. [63]

<u>Charcoal</u>
Mouthrinses containing activated charcoal are widely available online and in health food stores, often in combination with other agents such as peppermint, coconut oil, and tea tree oil or with antimicrobial constituents, such as CHX and CPC. There is some evidence charcoal in toothpaste may enhance enamel whitening *in vitro*.[16] However, there appear to be no studies investigating the effects of charcoal mouthrinse on

[14] Refer to Episode 29 for conversation on Alzheimer's disease and oral health.
[15] Refer to Episodes 76, 77, and 78 for detailed discussion on oral cancer.
[16] Note *in vitro* studies have shown activated charcoal-based toothpastes have a high abrasive potential that may be detrimental to the hard tissues of the teeth. [74] [75]

plaque, gingivitis, or oral bacteria and viruses *in vivo* associated with oral disease. Thus, oral health practitioners should be cautious about the efficacy of charcoal mouthrinses presently. [63] [64]

Seaweed

Seaweed is found in seawater and freshwater. It is rich in bioactive molecules (e.g., polysaccharides, polyphenols, peptides) and omega-rich oils. Several *in vitro* studies have shown extracts from different types of seaweeds possess antibacterial activity against *S mutans* and *P gingivalis.* Red algae extract was shown to be effective *in vitro* to enhance dental enamel mineralization. However, more research, especially clinical studies, is required to investigate the potential benefits of seaweed extracts in mouthrinse formulations for managing oral diseases. [63]

Probiotics[17]

Probiotics are live bacteria administered to the host to orchestrate a healthy microbiome. Probiotic mouthrinses contain living microbes (*Lactobacillus, Bifidobacterium, Bacillus, Saccharomyces*) that can rebalance the oral microbiome, promote beneficial bacteria, and compete with pathogenic bacteria. Evidence on the effectiveness of probiotics as a mouthrinse is limited. Studies have been conducted on probiotic mouthrinse use for managing periodontal disease, halitosis, and dental caries. However, research on the overall impact of probiotics on the oral microbiome and oral health remains limited. More comprehensive laboratory methods are required to understand the effectiveness of probiotics in improving oral health. [12] [63]

Oil pulling[18]

Oil pulling is traditional folk remedy that has been practised in India and southern Asia for centuries. The practice involves swishing or “pulling” a tablespoon of edible oil (e.g., coconut, sesame, olive, sunflower) through the teeth and mouth for anywhere from 1-5 minutes to up to 20 minutes or more. [65]

Reported side effects from oil pulling include lipid pneumonia associated with oil aspiration and nausea from accidentally swallowing the oil. More trial data is required to provide evidence of other possible side effects. Consideration should be given to spitting out the oil into a tissue before disposing to avoid oil build up and drain pipe blockage. [66] [67] [68] [69]

A systematic review by Woolley et al. (2020) assessed oil pulling with coconut oil in improving oral health and oral hygiene. The authors noted the data were insufficient for conclusive findings, the quality of studies was mixed, and the risk of bias was high. The review highlighted the lack of high-quality evidence in the literature. Consequently, it is difficult to determine the actual benefits of oil pulling with coconut oil on oral health. More well-designed randomized control trials (RCTs) are required to determine its impact. [70]

[17] Refer to Episode 63 for additional information on probiotics and the oral microbiome.
[18] Refer to Episode 89 for discussion on oil pulling.

Raja et al. (2021) conducted a systematic review of RCTs to determine the oral health effects of oil pulling. The authors concluded the quality of evidence was low to recommend oil pulling as an adjunct to other conventional oral hygiene methods, as most of the included studies had a high or unclear risk of bias. [71]

A meta-analysis by Peng et al. (2022) investigated the effect of oil pulling on oral health. Nine RCTs (344 participants) were included in the study. The included studies varied in their risk of bias. Although the included articles were RCTs, four studies were considered low-quality after risk of bias assessment.

Results showed salivary bacterial colony counts were significantly reduced in the oil pulling group compared to water or CHX control group. There was no significant difference between the two groups in plaque index (PI) and gingival index (GI) scores. Limitations of this systematic review included the small number of studies, and three studies were by the same author, which may introduce biases in outcome assessment.

The authors concluded oil pulling may have possible benefits in reducing salivary bacterial colony count. However, oil pulling had no significant effect on PI outcome and GI scores. Therefore, more evidence from well-designed, large-scale RCTs is needed to confirm these results. [72]

A systematic review and meta-analysis by Jong et al. (2023) found probable benefit of oil pulling in improving gingival health. CHX remained superior in reducing the amount of plaque compared to oil pulling. However, there was very low certainty in the evidence on the beneficial effect of oil pulling intervention. Therefore, oil pulling in oral healthcare cannot be recommended for clinical use until further evidence of greater certainty supports this regimen. [73]

Overall, no reliable studies demonstrate oil pulling reduces dental caries, whitens teeth, or improves oral health. Thus, oil pulling should not replace conventional self-care practices (e.g., brushing and interdental cleaning). [65]

Take home messages

- There is evidence many mouthrinses appear to be effective as adjuncts in some areas of oral care. Evidence for mouthrinse effectiveness is emerging in many areas, including alternate mouthrinses. There will be more evidence to confirm or refute mouthrinse effectiveness, the more they are widely studied.
- There appears to be evidence of mouthrinse effectiveness in reducing plaque, irrespective of the mouthrinse used. This is important, considering most oral diseases are plaque-related. Currently, most evidence relates to the use of CHX. In particular, there is considerable evidence regarding the effectiveness of mouthrinses as an adjunct to conventional oral self-care for preventing gingivitis and improving gingival health.
- Mouthrinses may be ineffective without tooth brushing, interdental cleaning, and professional biofilm removal.

- Mouthrinses may play a role in masking or managing halitosis. However, managing the underlying cause of halitosis is essential, such as through nonsurgical periodontal therapy if halitosis is associated with periodontal disease.
- Mouthrinses have the potential to cause dysbiosis of the oral microbiome. Thus, oral health practitioners should advise antiseptic mouthrinses that maintain a healthy, balanced, and diverse microbiome when used to manage microbial-induced oral disease.
- Mouthrinses target specific oral conditions and generally should not be used by clients with good oral health.

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