Helping patients achieve optimal periodontal health is an essential goal of oral healthcare providers. Periodontal disease is a complex multifactorial process with a bacterial etiology and inflammatory progression. Much of periodontal disease is the result of the breakdown of surrounding structures caused by the host response; pathogenic bacteria initiate the inflammatory response, while chronic inflammation supports these bacteria through the production of tissue breakdown products that they use as a food source. Effective elimination of periodontal pathogens can resolve inflammation. Concurrently curtailing the host inflammatory response can eliminate periodontal pathogens from the pocket due to a decreased pathogen-friendly food supply. Because this is a cyclical process, once it has begun, the host response must be stopped or the conditions will continue to deteriorate.

The cyclic timeline of periodontal disease begins with bacterial colonization, followed by biofilm formation, then attachment, inflammation, and host response. Effective elimination of periodontal pathogens can resolve inflammation. Concurrently curtailing the host inflammatory response can eliminate periodontal pathogens from the pocket due to a decreased pathogen-friendly food supply. Because this is a cyclical process, once it has begun, the host response must be stopped or the conditions will continue to deteriorate.

Oral Rinses

Oral rinses, which are the least invasive of these therapies, are an effective proactive intervention to help break the microbiologic and inflammatory cascade that often progresses to periodontal disease. Oral rinses can be an effective and patient-friendly method of proactive intervention. They can be anti-adhesive, antiseptic, and/or anti-inflammatory. Oral rinses provide chemotherapeutic agents that compensate for the difficulty in accessing hard-to-reach-areas, poor manual dexterity, and lack of regular mechanical plaque removal. Furthermore, only 20% of the oral environment is tooth structure. The saliva, tongue, and mucosa can serve as reservoirs of periopathogenic bacteria that are routinely missed by mechanical oral hygiene tools. The public prefers mouth rinsing because of its ease of use and breath-freshening effect. Oral rinses are effective on the three mechanisms of action in different types of mouthrinses.

### TABLE 1

<table>
<thead>
<tr>
<th>Oral Rinses</th>
<th>ANTI-ADHESIVES</th>
<th>ANTISEPTICS</th>
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<td>Delmopinol HCl</td>
<td>Fixed Combination Essential Oils</td>
<td>Antioxidants</td>
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<td>Chlorhexidine</td>
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<td>Cetyl Pyridinium Chloride</td>
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**Learning Objectives**

- Discuss the etiology of periodontal disease
- Understand available proactive interventions to help prevent periodontal disease
- Describe the mechanisms of action in different types of mouthrinses

**Abstract:** Practitioners can help their patients protect their periodontal health with interventions based on an understanding of the bacterial etiology and inflammatory progression of periodontal disease. The process stages include bacterial colonization, biofilm formation, attachment, inflammation, and host response. Available therapies—both mechanical and chemotherapeutic—attempt to break the microbiologic and inflammatory cascade that often progresses to periodontal disease. Among such therapies, oral rinses are the least invasive and can be an effective and patient-friendly method of proactive intervention.
plaque hypothesis—ie, all plaque is harmful to periodontal health, and the amount of plaque must be curtailed. The currently held view is the “specific plaque” hypothesis—ie, specific microbial species create a toxic periodontal environment among otherwise harmless bacteria.4

Essentially, dental plaque formation progresses as follows: When a clean tooth contacts saliva, it is quickly covered by pellicle (glycoproteins and polysaccharides), a surface that enhances the attachment of microorganisms to the tooth, and if left undisturbed, allows for the formation of mature dental plaque. Initial colonizers are mostly non-periopathogenic, gram-positive, sugar-metabolizing bacteria. The late colonizers are protein-metabolizing anaerobes (Porphyromonas gingivalis, Tannerella forsythensis, Treponema denticola), which have been implicated in periodontal disease and breath malodor.5 Disrupting the biofilm frequently through various oral hygiene approaches keeps the biofilm in its early stage with non-periopathogenic bacteria, as the colonizers tend to appear in the same sequence.6 If not adequately controlled, dental plaque formation that begins supragingivally progresses into the sulcus. Anti-adhesive and antiseptic oral rinses stop the attachment and maturation of pathogenic biofilm that can progress to periodontal disease.

Anti-Adhesive Agents
Delmopinol Hydrochloride—A recent chemotherapeutic approach for controlling plaque employs an agent that inhibits the formation of plaque while having little effect on bacteria or the balance of commensal bacteria in the oral cavity. Delmopinol hydrochloride is a surface-active agent with low antimicrobial potency.7 It interferes with biofilm matrix formation by preventing synthesis of glucan polysaccharide, the substance that keeps biofilm together and attached to oral surfaces. The adherence of primary plaque-forming bacteria is reduced, and the emerging biofilm mass is loosely adherent (Figure 1).8 The plaque can then be easily removed by the patient (Figure 2).

Delmopinol hydrochloride (0.2%) mouth rinse has shown statistically significant efficacy for reducing plaque and gingivitis.9 There is some staining, but to a lesser degree than with chlorhexidine, and it is easier to remove. Delmopinol hydrochloride is indicated for long-term daily use because it has few side effects and maintains the equilibrium of the oral ecosystem.

Antiseptic Rinses
Oral antiseptics work by causing cell death, inhibiting reproduction, or inhibiting the metabolism of microorganisms.10 They are formulated to penetrate the plaque matrix to gain access to the pathogens. (Efficacy with respect to the individual antiseptic agents is discussed below.) Effective antiseptic mouthrinse must have11: non-toxicity to oral tissues and minimal side effects; efficacy against specific pathogens; adequate bioavailability of active ingredients; stability; substantivity, ie, the ability to bind to tissue surfaces, be released slowly for continued therapeutic effect, and be resistant to dilution by saliva; and the ability to maintain ecological balance, with neither overgrowth of microorganisms nor bacterial resistance.

Three categories of antiseptic ingredients dominate the oral rinse market: essential oils, chlorhexidine, and cetyl pyridinium chloride (CPC).

Fixed Combination of Essential Oils
Essential oils (EOs) are obtained by the steam distillation of the odiferous oily portions of plant matter. They can be derived from flowers, leaves, bark, woods, roots, rhizomes, fruits, and seeds. Due to the bactericidal properties of essential oils, they are increasingly popular alternatives to synthetic chemical products.

A fixed combination of four EOs—thymol, menthol, eucalyptol, and methyl salicylate—has been in clinical use since the late 19th century. It has the longest clinical history of the antiseptic agents and minimal reported adverse effects.12 A 30-second rinse penetrates biofilm13 and provides a significant antimicrobial effect on the embedded bacteria, including periopathogens.13

The mechanism of action of use of EOs is described as follows: It causes morphological alteration of the cell surface after a 30-second exposure, which leads to cell death for specific periopathogens...
such as *Aggregatibacter actinomycetemcomitans*. It denatures protein and alters bacterial enzyme activity. It extracts bacterial endotoxins from gram-negative pathogens, and it affects the growth rate of early plaque-forming bacteria and disrupts the formation of biofilm.

EO also has anti-inflammatory effects, including inhibiting prostaglandin formation and scavenging free radicals generated by neutrophils in inflammation.

Unlike chlorhexidine and cetyl pyridinium chloride, EO has a neutral electrical change, which decreases undesirable side effects so that it does not interact with charged ions found in dentifrices and mouthrinses to decrease efficacy, it is not inhibited by proteins in blood serum that may inactivate antimicrobial agents, and it does not precipitate dietary chromogens that lead to tooth staining. However, EO has no substantivity—ie, its effect stops when the rinse is removed. But because its action is rapid, this may not be clinically significant. EO has been shown to effectively penetrate biofilm to kill bacteria, which is comparable to the action of chlorhexidine. Systematic review studies on EO with or without alcohol showed no significant difference in efficacy. Alcohol contributed no added therapeutic value.

**Chlorhexidine (CHX)**

Chlorhexidine gluconate has been both a medical and surgical disinfectant since the 1950s, and has been used in the oral cavity since the 1970s. CHX binds via adsorption to surfaces in the mouth as well as the pellicle and saliva, achieving high substantivity. It is both bacteriostatic and bactericidal, depending on concentration (Figure 3).

The positively charged (cationic) CHX molecule binds strongly to the negatively charged (anionic) bacterial cell surface, altering the integrity of the cell wall. CHX then binds to the inner cell membrane, leading to increased permeability and cell damage, rupture of the cell membrane, leakage of cell contents, and eventual bacterial cell death.

CHX has a double positive charge and is, therefore, extremely interactive with anions. This helps efficacy but produces unfavorable side effects, such as the following:

- It precipitates negatively charged dietary chromogens from food and drinks (such as tea), often causing staining.
- Its efficacy may be compromised by cationic detergents (like sodium lauryl sulfate) and anionic fluoride ions found in toothpaste, so there must be a 30-minute window between using toothpaste and rinsing with CHX.
- It can cause taste alterations and nausea.
- It can enhance supragingival calculus formation.

For these reasons, CHX rinses are prescribed for short-duration therapy only, to control acute or severe bouts of periodontal disease.
CHX has a broad-spectrum effect against gram-positive and gram-negative bacteria (including many periopathogens), some fungi and yeasts (including Candida), and some viruses (including HIV). No bacterial resistance with long-term use has been reported.

By binding directly to the tooth surface, CHX occupies sites that could be used by pellicle and bacteria, thereby inhibiting early biofilm formation.\textsuperscript{28} CHX has been shown to penetrate the biofilm and kill embedded pathogens.\textsuperscript{13} Tight binding to oral structures allows it to be released slowly into the mouth and sustained for up to 12 hours, leading to high substantivity.\textsuperscript{26} Widely considered the “gold-standard” in oral rinses,\textsuperscript{23} CHX rinses are often used as a benchmark control against which new products are measured. Other chemotherapeutic agents may show either a purely immediate effect or limited persistence. CHX’s persistence is the basis of its efficacy.

CHX is especially appropriate for specific populations whose oral hygiene is compromised, such as the elderly, physically limited, and mentally handicapped. Long-term use may be appropriate in these instances.\textsuperscript{22} Formulation without alcohol has been shown to be as clinically effective in controlling plaque and gingival inflammation as the alcohol-based product.\textsuperscript{27}

**Cetyl Pyridinium Chloride**

Cetyl pyridinium chloride (CPC) is a cationic, surface-active agent with bactericidal and bacteriostatic activity against bacterial pathogens and yeast. While it is bactericidal to both gram-positive and gram-negative bacteria, it is more effective against the former. CPC has a significant inhibitory effect on plaque and gingival inflammation (Figure 4 through Figure 7).\textsuperscript{28}

The cationic CPC molecule binds to teeth and bacterial cell walls. Binding interferes with bacterial colonization on the tooth surface. CPC is effective against early colonizers in immature dental plaque, reducing the formation of mature biofilm. Binding to the bacterial surface causes disruption of bacterial cell membrane function, leakage of cytoplasmic material, and collapse of the intracellular equilibrium, leading to death of the microorganism.\textsuperscript{29}

The formulation of vehicle ingredients, preservatives, stabilizers, colors, etc, may impact the bioavailability of CPC. Rinses with 0.07% CPC in a high bioavailable, alcohol-free formulation showed significant antiplaque and antigingivitis benefits.\textsuperscript{30-32}

Side effects of CPC are due to its cationic structure. They include staining that has a similar dietary etiology to CHX but is less severe,\textsuperscript{33} and CPC can adversely interact with other charged ions in dentifrices and rinses (like CHX).

CPC binds strongly to tooth structure and biofilm, giving it good substantivity, although to a lesser degree than CHX.\textsuperscript{17}

**Efficacy of Antiseptic Rinses**

In a systematic literature review,\textsuperscript{34} CHX, CPC, and EO were all determined to have beneficial antiplaque and antigingivitis effects when used long-term in conjunction with mechanical oral hygiene tools. CHX had the most consistent results. CHX has been shown to be more effective than EO in plaque reduction, but is comparable in antigingivitis properties.\textsuperscript{25}

**Anti-Inflammatory Pro-Healing Rinses**

In the healthy periodontium, the innate response attempts to eliminate foreign bodies and is protective against injury or infection.\textsuperscript{36} Periodontal disease results from the body’s failure to turn off its inflammatory response to infection. The result is chronic maladaptive inflammation.\textsuperscript{37} This produces an environment that exudes a rich source of nutrients such as degraded host proteins, which are specifically what pathogenic bacteria need for survival and growth. Bacterial pathogens continue to exploit this environmental change, leading to more bacteria, more inflammation, bone resorption, and a perfect niche space (deeper periodontal pockets) where the entire process can continue undisturbed.\textsuperscript{38}

As shown in Figure 8 and Figure 9, in chronic unresolved inflammation, cellular and molecular responses to bacterial challenges involve constant adjustment and regulatory feedback.\textsuperscript{29} Neutrophils and other cells secrete cytokines, which promote the release of matrix metalloproteinases (MMPs)—proteolytic enzymes, including collagenases, implicated in normal bone remodeling.\textsuperscript{35} Tissue destruction is not unidirectional, so it is constantly being adjusted by host-bacterial interactions.\textsuperscript{39} Alveolar bone destruction is the result of the uncoupling of the normally tightly coupled processes of bone resorption and formation.\textsuperscript{39} Prostaglandin production plays a role in alveolar bone resorption.

The inappropriate host response is the major contributing factor for chronic maladaptive periodontal disease: A deficient host response initiates the chronic condition, and a too-vigorous response leads to further tissue breakdown.\textsuperscript{41}

Emerging data suggest that periodontal pathogens that are present in low numbers use inflammation to provide an environment to foster their growth. Control of inflammation may actually return the composition of a pathologic biofilm to a healthy one. The implication is that the pathologic biofilm is a result of periodontal inflammation, as well as being the cause of periodontal inflammation.

Anti-inflammatory rinses, which are newer products in the oral rinse category, attempt to break this pathologic cycle. They are marketed under two major classifications of ingredients: antioxidants and botanicals (essential oils). There is some overlap, but they are discussed separately for clarity.

**Antioxidants**

A free radical is an atom or group of highly reactive atoms that have one or more unpaired electrons. They are formed as intermediates during normal biochemical reactions. When they are generated in excess or not controlled, radicals can damage cells. Radicals of
most concern in biological systems are derived from oxygen and are known as reactive oxygen species (ROS). ROS are generated by neutrophils in host defense to kill invading pathogens, thus raising the level of ROS during inflammation. Antioxidants neutralize damaging free radicals that produce disease states.

There is promising new research on topical application of anti-oxidants on oral tissue to promote gingival healing. Dental manufacturers have incorporated antioxidants into toothpastes, mouthrinses/mouthwashes, lozenges, gels, oral sprays, breath fresheners, and other dental products for the control of gingival and periodontal diseases. There are potential beneficial clinical effects, but due to the inherently unstable nature of antioxidants, simply adding an antioxidant to an oral preparation may not produce an effective agent.

Patients with periodontal disease have a reduced level of gingival and serum antioxidants. It is not yet clear whether the lower level of antioxidants contributes to the cause of periodontitis or whether the antioxidant level is reduced as a result of increased action in neutralizing free radicals.

In vitro studies have shown antioxidants to have a beneficial effect on fibroblast migration and proliferation during gingival healing or periodontal repair. Fibroblasts are critical in the healing process. Their collagen deposition restores tissue strength, integrity, and structure.

**Botanicals (Essential Oils)**

While harnessing the antimicrobial properties of plant matter is not new, the concept of using the anti-inflammatory and healing (not only the antimicrobial) properties of botanicals is now being explored in new oral rinses. The ideal anti-inflammatory rinse is one that targets pro-inflammatory cytokines and enzymes involved in oral inflammation and tissue destruction.

A botanical rinse has been formulated with three botanical extracts at specific ratios that are antimicrobial and anti-inflammatory and promote tissue repair. The concept is to help modulate the host inflammatory response and break the inflammation cycle. The anti-inflammatory and tissue repair properties of the botanical extracts have been demonstrated in multiple bioassays during product development. The bioassays showed inhibition of inflammatory cytokines and their tissue-destructive products (prostaglandin, MMPs); tissue-healing products (collagen, growth factors) produced by fibroblasts were increased.

The three herbs are: centella asiatica (gotu kola), which has been shown to increase effective collagen and is used in wound healing; sambucus nigra, which inhibits the pro-inflammatory properties of two periodontal pathogens (*P. gingivalis* and *A. actinomycetemcomitans*); and echinichia purpurea, which has antiviral, antibacterial, and anti-cytotoxic effects.

The botanical rinse has demonstrated an ability to reduce gingival inflammation. A study on managing post-surgical inflammation around implants found the rinse clinically equivalent to 0.12% CHX in controlling plaque, but more effective than CHX in reducing inflammation at implant sites and areas of surgical incision.

**Water?**

The ideal rinse would have no side effects and be cost effective and readily available. Water is such an agent. When used as a rinse it has no clinical effect; when it is delivered via a pulsating device and controlled pressure such as a water flosser, it demonstrates significant efficacy.

Extensive research on one water flosser demonstrates consistent benefits on gingival and periodontal health. The effects are broad-based, impacting the inflammatory cycle from plaque formation and adhesion to the host inflammatory response. One of the significant advantages of water flossing versus rinsing is the

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**Fig 4 through Fig 7.** The positively charged cetyl pyridinium chloride (CPC) binds to the bacterial surface (Fig 4) to cause disruption of bacterial cell membrane function (Fig 5), leakage of cytoplasmic material (Fig 6), and bacterial cell death (Fig 7). (Images courtesy of Procter & Gamble. Reprinted from the Journal of Contemporary Dental Practice, 2005;6(1), with permission.)
ability to reach subgingivally and interdentally. Agents delivered via rinsing can penetrate the sulcus approximately 2 mm, whereas water or an antimicrobial agent delivered via a water flosser can remove bacteria in deeper pockets (up to 6 mm).64 Recently, water flossing was compared to using string floss in five separate studies and consistently demonstrated superior reductions in bleeding, gingivitis, and plaque removal.60-64

Daily oral irrigation with the water flosser showed efficacy comparable to the administration of minocycline in patients with moderate to severe periodontitis. Both maintenance programs were effective in reducing clinical signs of periodontitis and in preventing the recolonization of periopathogenic bacteria after scaling and root planing.65

The mechanical action of the water jet disrupts biofilm and prevents bacterial recolonization. The hydrodynamic action has no side effects and does not potentiate the development of resistant strains, as can occur with antimicrobial drugs such as minocycline.65 Pulsating oral irrigation produces a qualitative change in subgingival plaque.

The water flosser has an impact on the host inflammatory response, as evidenced by decreased proinflammatory cytokines in the gingival crevicular fluid.65 Studies have shown decreased reactive oxygen species generation in diabetic patients, signifying decreased inflammatory activity.66

A water flosser has also demonstrated the ability to deliver an antimicrobial agent into the periodontal pocket. When compared to rinsing with the agent, the water flosser showed better effects on the reduction of bleeding, gingivitis, and pathogenic bacteria.65 Studies have shown significant periodontal improvements in patients with orthodontic appliances,62 implants,64 gingivitis,66 diabetes,66 crown and bridge,68 and those in periodontal maintenance programs.58,59

Conclusion
There are many tools available, both mechanical and chemotherapeutic, to maintain periodontal health. Oral rinsing and water flossing are patient-friendly, minimally invasive ways to proactively control the complex inflammatory cycle. Oral healthcare providers must understand the pathogenic cycle, the needs of the patient, and the specifics of the oral rinses. With this knowledge, clinicians are able to counsel their patients on maintaining good periodontal health for life.

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Oral Rinses for a Proactive Intervention Approach to Periodontal Health

Fay Goldstep, DDS

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<table>
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<tr>
<th>1. Effective elimination of periodontal pathogens:</th>
<th>6. Due to their bactericidal properties, what are increasingly popular alternatives to synthetic chemical products?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. is best achieved only with the use of antioxidants.</td>
<td>A. chlorhexidine (CHX) rinses</td>
</tr>
<tr>
<td>B. can resolve inflammation.</td>
<td>B. anti-adhesives</td>
</tr>
<tr>
<td>C. will accelerate inflammation.</td>
<td>C. matrix metalloproteinases (MMPs)</td>
</tr>
<tr>
<td>D. enhances the attachment of microorganisms to the tooth.</td>
<td>D. essential oils</td>
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<tr>
<th>2. Oral rinses provide what type of agents, which compensate for difficulty in accessing hard-to-reach areas and poor manual dexterity?</th>
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<tbody>
<tr>
<td>A. molecular</td>
<td>A. substantivity</td>
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<tr>
<td>B. mechanical</td>
<td>B. bioavailability</td>
</tr>
<tr>
<td>C. chemotherapeutic</td>
<td>C. stability</td>
</tr>
<tr>
<td>D. &quot;non-specific&quot;</td>
<td>D. antigingivitis effects</td>
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<tr>
<th>3. When a clean tooth contacts saliva, it is quickly covered by:</th>
<th>8. The formulation of vehicle ingredients, preservatives, stabilizers, and colors may impact the what of CPC?</th>
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<tbody>
<tr>
<td>A. mature dental plaque.</td>
<td>A. substantivity</td>
</tr>
<tr>
<td>B. protein-metabolizing anaerobes.</td>
<td>B. bioavailability</td>
</tr>
<tr>
<td>C. cetyl pyridinium chloride (CPC).</td>
<td>C. stability</td>
</tr>
<tr>
<td>D. pellicle.</td>
<td>D. antigingivitis effects</td>
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<tr>
<th>4. Delmopinol hydrochloride interferes with biofilm matrix formulation by preventing synthesis of:</th>
<th>9. Anti-inflammatory rinses are marketed under which two major classifications of ingredients?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. glucan polysaccharide.</td>
<td>A. antioxidants and botanicals</td>
</tr>
<tr>
<td>B. glycoproteins.</td>
<td>B. anti-adhesives and antiseptics</td>
</tr>
<tr>
<td>C. plaque-forming bacteria.</td>
<td>C. fixed combination essential oils and CHX</td>
</tr>
<tr>
<td>D. non-periopathogenic bacteria.</td>
<td>D. CHX and CPC</td>
</tr>
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<tr>
<th>5. Effective antiseptic mouthrinse must have:</th>
<th>10. One of the advantages of water flossing versus rinsing is the ability to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. non-toxicity to oral tissues.</td>
<td>A. cause cell death.</td>
</tr>
<tr>
<td>B. adequate bioavailability of active ingredients.</td>
<td>B. reach subgingivally and interdentally.</td>
</tr>
<tr>
<td>C. the ability to be released slowly for continued therapeutic effect.</td>
<td>C. prevent synthesis of glucan polysaccharide.</td>
</tr>
<tr>
<td>D. all of the above</td>
<td>D. all of the above</td>
</tr>
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