

## HOW TO DEAL WITH ORAL PATHOGENIC

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**Abstract:** The fact that bacteria are one of the most important contributors to the genesis of dental disease raises the question of how to eradicate or decrease them to acceptable levels. There are several medications and procedures for preserving oral health. New scientific and technological advancements in the field of prevention equip us with a plethora of new items to improve oral health and care. Some of them are intended for use at home, while others are intended for professional use. Modern mechanical and chemotherapeutical oral hygiene treatments seek to change the oral microbiota and contribute to healthy dental and periodontal tissue. The literature has several categories of anti-microbial agents. One of these is the grouping into groups based on chemical properties, and it is this classification that this study will adhere to. This categorization divides anti-microbial agents into cationic, anionic, non-ionic agents, enzymes, and sugar alcohols. The purpose of this research is to provide a full and comprehensive assessment of antimicrobial agents for oral hygiene, their mode of action on the bacterial cell, and the relevance and value of their use in oral prevention.

**Keywords:** antimicrobial agents, Chlorhexidine, Cetylpyridinium chloride, Benzalkonium chloride, Thymol, Fluorine, Hydrogen peroxide

### 1. INTRODUCTION

Dental caries should be viewed as a multifactorial illness caused by the interplay of three fundamental factors: the tooth surface, bacteria, and the environment. Keyes and Jordan in 1963. used three overlapping circles to symbolize those three factors: one for the host (the surface of the tooth), one for the pathogen (the qualities of the microorganisms), and one for the environment (the substrate for microorganisms). Later, a fourth dimension - time - was added to this model, which must be included in any study of the development of dental caries (Ritter, 2019).

There is no tooth decay without microorganisms. This is a commonly held belief that is supported by a number of scientifically established facts. Certain microorganisms from the oral flora can cause experimental dental caries in vitro; experimental animals raised in sterile conditions, despite a cariogenic diet, do not develop caries; and specific bacteria can be isolated from caries lesions and proven histologically and microbiologically in the caries enamel, dentin, and dental canals (Caufield et al., 2005; Caufield, 2005).

The fact that bacteria are one of the most important elements in the genesis of dental caries begs the question of whether they should be eliminated or minimized. The typological and numerical verification of microorganisms is an important requirement, and the major component in battling them is the maintenance of oral hygiene. Man has maintained oral hygiene through numerous techniques and procedures since ancient times. Today, there are a lot of tools and strategies for maintaining dental health. Every day, new scientific and technical advancements in the field of prevention make a significant number of new products for enhancing and caring for oral health available to us. Some are for personal use, while others are for professional usage (Cvikl & Lussi, 2021; Murphy 2019).

Teeth brushing is one of the most fundamental requirements for healthy teeth. Unfortunately, when compared to the outcomes of industrialized nations, the analyses and conclusions acquired in our environment are at an appalling level.

Antibiotics, caries vaccine, and enzyme inhibitors were used to treat oral microorganisms in experiments. Antibiotics had a theoretical foundation, but in practice, they did not meet expectations. Despite the enormous number of studies, the vaccine's dependability and use for human purposes remain in doubt. Sarcosinates have been found to be effective as enzyme inhibitors, despite the fact that they are not extensively employed. They have an affinity for the plaque, allowing them to stay in it longer and limit acid formation (Qiu et al., 2020; Parga et al., 2023; King, 2012; Yu et al., 2023.). Modern mechanical and chemotherapeutic oral hygiene treatments attempt to alter the oral microbiota and contribute to healthy dental and periodontal tissue.

### 2. CLASSIFICATION AND PROPERTIES OF ANTIMICROBIAL COMPOUNDS

The literature has several classifications of antibacterial agents. One of them is a categorization based on chemical characteristics, which divides antimicrobial substances into five classes. Cations are positively charged ions that have the capacity to affect bacterial membrane function, adhesion, and glucose metabolism. Anions are negatively charged ions that are capable of interfering with bacterial membrane function, glycolytic metabolism, and glucose consumption. Charged ions are believed to block membrane enzymes, resulting in decreased glucose consumption.

Some enzymes are known to inhibit bacterial adhesion, whereas others are expected to increase lysozyme activity. Polyols derived from sugar alcohols are hypothesized to impair bacterial glycolysis.

#### *Cationic antimicrobials*

Chlorhexidine, metal ions ( $Zn^{2+}$ ,  $Cu^{2+}$ ,  $Sn^{2+}$ ), Alexidine (bisbiguanide, such as chlorhexidine), Cetylpyridinium chloride, and Benzalkonium chloride (quaternary ammonium compounds), Hexetidine (synthetic hexahydropyridine), and Sanguinaria extracts (Herbal extract) are among the chemicals in this group.

Because of their positive charge, cations are attracted to the negatively charged bacterial cell wall. Gram-positive bacteria are more vulnerable to cations because they are more negatively charged. Mutans streptococci are Gram-positive bacteria, which makes them particularly sensitive.

#### *A) Chlorhexidine*

Chlorhexidine is the most often utilized cation compound, produced in the late 1940s. In 1954, Davies identified its actions, and in 1970, Løe and Schiøtt employed it as a plaque-inhibiting drug for the first time. It is particularly for professional purposes. Chlorhexidine molecules have both hydrophilic and hydrophobic properties. One of the benefits of chlorhexidine is its capacity to attach to oral surfaces, from which it is gradually released in bacteriostatic quantities into the saliva. Chlorhexidine can minimize plaque acid generation in these amounts. Because of these properties, chlorhexidine can have a variety of effects on cariogenic mutans streptococci. The predominant mode of action is also determined by the concentration of the chemical (Autio-Gold, 2008; Walsh et al., 2015; Ren et al., 2012; Almhöjd et al., 2023.).

Chlorhexidine can affect bacterial cells in three ways:

1. by disruption of normal bacterial membrane activities, particularly in mutans streptococci;
2. by suppression of bacterial attachment to the tooth or pellicle;
3. effect on glycolytic enzymes, resulting in decreased acid generation by the bacteria.

The use of 1% chlorhexidine gel for cleaning teeth and application in specially modified spoons yielded positive effects. When Glass ionomer cement (GIC) fillings are used in conjunction with Chlorhexidine gluconate, the amount of mutans streptococci in plaque and saliva is reduced. When used Chlorhexidine as a 0.12% alcohol or alcohol-free rinse, reduces relative microbial growth. (Slot et al, 2010). When used in the form of 1% chlorhexidine-thymol varnish - Cervitec, then chlorhexidine varnish-Chlorizon, or 3% varnish, but in specific vacuum-suited mouth guards, it had a powerful suppressive effect on mutans streptococci. *Actinomyces viscosus* levels are much lower soon after therapy in this example. When 0.4% chlorhexidine paste was used for one month, the cariogenic flora was reduced. The advantage of chlorhexidine should be stressed in immunocompromised patients and radiation patients with xerostomia and high oral levels of *Streptococcus mutans*, *Lactobacillus*, and, most importantly, *Candida*. Long-term use of chlorhexidine, most often 0.2% rinse, might result in the following adverse effects: discoloration of teeth, tongue, and prosthetic restorations, occasional sensitivity of the oral mucosa, and reversible change of taste. Low dosages of 0.06% solution are an excellent aid in long-term oral hygiene application (Ben Khadra et al., 2019). When it comes to reducing high levels of mutans streptococci, chlorhexidine is without a doubt the antibacterial agent of choice. Because of the previously described negative effects, its use must be properly supervised by a specialist, especially when it comes to youngsters.

#### *B) Metal ions*

Metal ions affect bacteria in diverse ways, chiefly through interfering with two enzymes involved in bacterial glycolysis. As a result, the bacteria produce less acid. Metal ions are incorporated into compounds with established anti-caries capabilities as commercially accessible treatments. The  $Sn^{2+}$  ion, when combined with fluorine, reduces the amount of mutans streptococci in saliva. When another chemical, such as amino fluoride, is added to this compound, these features become even more evident. In experimental mice, the combination of  $Zn^{2+}$  and Cetylpyridinium chloride lowers the number of dental cavities on smooth surfaces (Nizami, et al. 2021; Al-Hijazi, et al. 2023).

#### *C) Quaternary ammonium compounds*

##### *- Cetylpyridinium chloride (CPC)*

As an active component in oral antiseptics, CPC offers a broad antibacterial spectrum with a high bactericidal impact on Gram-positive pathogens and a fungicidal effect against yeasts. Its efficacy against Gram-negative pathogens and mycobacteria is debatable. The use of CPC in the rinses at a concentration of 0.05% leads to an immediate reduction in bacterial populations. The use of CPC at this dosage has no effect on the composition of normal oral flora or the emergence of non-oral and possibly pathogenic bacteria in the mouth. CPC has fewer residual effects than chlorhexidine, however, this results in a poorer impact against plaque and gingivitis. CPC combined with chlorhexidine and zinc lactate gives the best decrease in both anaerobic and aerobic bacteria, reducing foul breath. CPC has also been shown to be effective against oropharyngeal candidiasis (Matsuo, et al., 2019; Dimkov, et al., 2009)

- Benzalkonium Chloride (BKC)

Benzalkonium chloride is recognized as an adjuvant antibacterial agent by the United States Pharmacopoeia. Many toothpastes and mouthwashes contain it as the primary antibacterial ingredient. Benzalkonium Chloride is a potent biological agent with a somewhat lengthy duration of action. Acts on bacteria, viruses, fungi, and protozoa. Bacterial spores are thought to be resistant. Depending on the concentration, solutions are bacteriostatic or bactericidal. Gram-positive bacteria have a higher sensitivity than Gram-negative bacteria. The activity of BKC is unaffected by pH, however, it rises dramatically at higher temperatures and over longer periods of time. (McDonnell & Hansen, 2020; Dimkov, et al., 2016)

D) *Sanguinaria*

Sanguinaria is an alkaloid derived from the plant *Sanguinaria canadensis* and is found in the mouthwash Viadent (Perioguard in the UK). Sanguinaria is present in kinds of toothpaste and mouthwashes, however, research on its efficacy is mixed. (Croakera et al., 2017)

*Anionic antimicrobials*

The principal anionic agents are fluoride-containing compounds. This category also includes sodium lauryl sulfate. Anionic agents fight for positively charged ligands (bonds) with negatively charged microorganisms. As a result, bacterial adhesion is inhibited. Ligands are protein structures found in the pellicle. Hydroxyapatite can also function as a ligand.

E) *Fluorine*

Fluoride ions have been utilized since 1940 due to their well-documented anti-caries properties, which mostly relate to the demineralization/remineralization process. Fluoride-containing compounds also have antibacterial capabilities, as they reduce the levels of salivary cariogenic germs and impact bacteria in various ways, depending mostly on fluoride concentration.

Effects of fluoride on bacteria include:

- The normal function of the membrane in bacteria is influenced.
- Fluoride has an effect on positively charged glycolytic enzymes. Enzyme activity is lowered or inhibited, resulting in less acid output from the bacterium.
- Glucose absorption is limited at lower pH levels. This is due to the decreased function of the membrane gradient for  $H^+$ , which affects one of two types of glucose uptake channels.

Fluoride-containing rinses combined with another antimicrobial ingredient can help prevent dental cavities, particularly in youngsters having fixed orthodontic treatment, who require significantly more oral care due to difficult teeth cleaning. The effects of these rinses with combination formulae are less when compared to chlorhexidine, but the absence of adverse effects is an essential factor in evaluating the indications for their usage (Cavazana, et al., 2012). Several studies have been conducted to evaluate the effects of fluoride on oral microorganisms. The most important finding shows that while the ionic form of fluorine, or  $F^-$ , cannot traverse the cell wall and membrane, it can readily enter cariogenic bacterial cells in its unaltered form, such as HF. When the pH of the plaque drops as a result of bacterial acid production, part of the fluorine in the plaque mixes with hydrogen ions to generate HF, which rapidly diffuses into the cell, effectively drawing additional HF from the outside. When HF enters the cell, it dissociates, acidifying the cell and releasing fluoride ions, which inhibit bacterial enzyme function. Fluoride ions, for example, inhibit enolase, an enzyme required by bacteria to digest carbohydrates (Zhang, et al., 2022).

F) *Sodium lauryl sulfate*

This chemical is commonly used as a surfactant in commercial toothpastes. Sodium lauryl sulfate is used to emulsify and clean surfaces. It has a great affinity for protein molecules and acts as a denaturing agent. Sodium lauryl sulfate is a protein degrader that can cause epithelial desquamation (Modesto, et al., 2000).

*Nonionic antimicrobials*

The agents in this class are phenol derivatives. They have both hydrophilic and hydrophobic characteristics and have a wide range of activity on Gram-positive and Gram-negative bacteria. The agents in this class have the following mechanisms of action: breakdown of the bacterial cell wall, inhibition of bacterial enzymes, and extraction of bacterial lipopolysaccharides. This action reduces or inhibits glucose absorption, resulting in minimal or no acid generation. A higher concentration damages the membrane and induces bacteriolysis. The most important representatives of this group are Listerine and triclosan. Triclosan is a free-of-charge substance, while Listerine is a mixture of thymol and eucalyptol, which are essential oils. Listerine has emerged as a legitimate therapeutic treatment for the reduction of plaque-induced oral illnesses in recent years. When diverse bacteria are exposed to Listerine for 30 seconds, they exhibit well-defined morphological changes on their cell surfaces, resulting in cell integrity loss. Triclosan is manufactured under the brand Irgasan DP 300 by the American corporation Ciba Specialty Chemicals, as well as by many other producers outside the United States. Triclosan has found widespread

use in personal care products such as kinds of toothpaste, deodorants, soaps, antiperspirants, body washes, detergents, dishwashing detergents, cosmetic and antimicrobial creams, and lotions due to its bacteriostatic activity against broad spectrum of Gram-positive and Gram-negative bacteria (De Farias et al., 2023). They have been utilized as antiseptics in the mouth since the late 1980s. To improve triclosan's efficiency, a surface protective layer - a copolymer - is added, like in Colgate Total® toothpaste.

Thymol has a substantially higher germicidal activity than phenol. It is only soluble in water at a ratio of 1:1000, but it is considerably more soluble in organic solvents like ethanol and glycerol. Thymol can be found in disinfectants and antiseptics. It is also available as a prescription for some mouthwashes, however, triclosan and Listerine dominate in this category. The optimum pH for action is between 4 and 9.

#### *Enzyme antimicrobial agents*

There are many enzymes that exhibit antimicrobial activity in in vitro testing by breaking the link in the lucan, resulting in a decrease in the buildup of dental plaque. Some tests with enzyme pastes had anti-plaque outcomes, whereas others did not. Some toothpastes and mouthwashes contain enzymes such as amyloglycosidase and glucose oxidase as extra components (Pleszczyńska, et al., 2017).

#### *Sugar alcohols as antimicrobial agents*

Sugar alcohols are not "antimicrobials" in the same way as rinses are, but because they operate on bacteria in a similar way, we have included them in this classification. They are present in chewing gums, lozenges, toothpastes, and saliva replacements, accounting for 30-60% of the total. They are primarily a mixture of hexitol and pentitol, with the most prevalent being xylitol, sorbitol, and, to a lesser extent, mannitol.

In terms of cariogenicity, xylitol is non-cariogenic since it is not fermented by oral bacteria, but sorbitol can be slowly fermented by mutans streptococci while causing no pH reduction. Sugar alcohols are popular nowadays due to the widespread use of chewing gums that contain them. Chewing gum with xylitol or sorbitol has two benefits. On the one hand, salivary stimulation and increased salivary flow result in rinsing of plaque from the teeth and part of the bacteria, neutralization of acids, and washing away carbohydrates. Chewing gums containing sorbitol or xylitol, on the other hand, have a direct effect on the bacterial cell (Dhar, 2016). Some research stresses the superiority of sorbitol in decreasing dental plaque and caries incidence, while others highlight the superiority of xylitol. Some research looks at the effect of a xylitol-sorbitol combination on plaque and the quantity of mutans streptococci (Nasseripour, et al., 2021). Sugar alcohols can cause gastrointestinal difficulties if consumed in significant amounts, however, the concentration in chewing gum is quite minimal and cannot cause such problems. The World Dental Federation (FDI) has acknowledged Wrigley USA's Extra® and Orbit® sugar-free chewing gums as the first to provide substantial dental health advantages.

#### *Hydrogen peroxide*

Although hydrogen peroxide does not fit into this classification, it should be noted as an essential antimicrobial agent since it has a wide variety of antibacterial qualities and has been used in routine dentistry practice for many years. Also known as Hydrogenium peroxydatum, it is a transparent liquid that has been utilized in aqueous solutions or in conjunction with salts for over 70 years. It is commonly utilized in cariology, endodontics, and periodontology. It includes 2.8 to 3.2% hydrogen peroxide as Hydrogenii peroxydi solutio diluta and 28-31% hydrogen peroxide as Hydrogenii peroxydi solutio concentrata. The most significant medicinal function of hydrogen peroxide is its ability to kill bacteria. It oxidizes organic compounds, such as amino, amido, and other protein groups that are bacterial poisons, until they are completely degraded. Hydrogen kills anaerobic microbes by releasing nascent oxygen. It also works to reduce bacterial adhesion. As a 3% solution, hydrogen peroxide has a modest bactericidal action and lowers gingivitis and plaque indices. The bactericidal action rises as the concentration increases. The combination of H<sub>2</sub>O<sub>2</sub> and sodium bicarbonate (NaHCO<sub>3</sub>) inhibits the growth of some facultative Gram-negative bacteria. By eliminating the soft deposits first, the therapeutic impact of hydrogen is increased, its disintegration happens more slowly, and its activity is more gradual. It possesses hemostatic, mechanical, decolorizing, and deodorant properties in addition to a bactericidal action (Zhu & Kreth, 2012). In terms of hydrogen peroxide side effects, research has revealed that after 6 years of daily usage of 3% H<sub>2</sub>O<sub>2</sub>, occasional transitory irritating effects occur only in a small number of participants with pre-existing ulceration or when large amounts of saline solutions are administered concurrently. Some animal investigations have revealed that 30% H<sub>2</sub>O<sub>2</sub> has a cocarcinogenic impact, as opposed to 3% or less, when such an effect is not found (Marshall, et al. 1995).

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