

MINI REVIEW

Chlorhexidine in Periodontics: A brief review

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ABSTRACT

Dental plaque is a complex microbial population of bacteria and salivary biomolecules on the tooth surface. Plaque control is defined as removing microbial plaque and preventing its accumulation on the tooth surface and adjacent gingival tissues to prevent the formation of calculus. Mechanical plaque control remains a primary preventive method to control dental diseases. However, the level of plaque control attained at the individual level decreases over time. As a result, to maintain proper oral health, chemical plaque must be addressed to maintain good oral health. Chlorhexidine is a cationic bisbiguanide with broad antibacterial activity against gram-positive and gram-negative bacteria, yeasts, dermatophytes, and some lipophilic viruses. In addition, it treats or prevents periodontal disease, earning it the nickname "gold standard." This article details the mechanism of action, indications, forms, and delivery systems of chlorhexidine.

Keywords: periodontal disease, chlorhexidine, chemical plaque control, mouth rinse

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INTRODUCTION

Dental plaque is the primary etiological factor in developing dental caries and gingivitis. Mechanical tooth cleaning with toothpaste is arguably the most common and potentially effective type of oral hygiene practiced by most people. Unfortunately, a significant proportion of all individuals fail to practice a high enough standard of plaque removal, resulting in gingivitis. It is prevalent and starts at a young age, most likely due to a failure to follow the recommendation to clean teeth regularly or a lack of skill with tooth-cleaning habits. In addition, mechanical plaque control is difficult, time-consuming, and sometimes ineffective in reducing or eliminating bacterial etiologic agents. As a result, the adjunctive use of chemicals is a method of overcoming deficits in mechanical tooth cleaning habits, as practiced by many people.

Chlorhexidine (CHX), with its almost 40 years of use by dental practitioners considered one of the most widely studied and efficacious compounds. In dentistry, it is primarily an antibacterial mouthwash that has significantly reduced gingival inflammation, plaque and gingival

bleeding indices². It also serves as a positive control against which other antiplaque and anti-gingivitis agents are measured.

STRUCTURE

Chlorhexidine is a bisbiguanide antiseptic- a symmetrical molecule consisting of four chlorophenyl rings and two biguanidine groups connected by a central hexamethylene bridge. It is a strong base and dicationic at pH above 3.5, with positive charges on either side of the hexamethylene bridge³. Because of its dicationic nature, it is highly reactive with anions and is helpful in its efficacy, safety, side effects and difficulty in formulating products. It is a synthetic antimicrobial in three forms digluconate, acetate (Water soluble) and hydrochloride salts (sparingly soluble). Most oral formulations and products have used digluconate salts which are manufactured at 20% v/v concentration⁴

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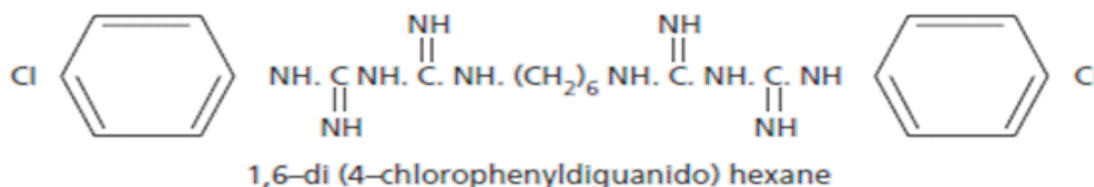
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HISTORY

It was first developed in 1940 by Imperial chemical industries and marketed as an antiseptic for skin wounds in 1954. It is widely used in medicine and surgery, particularly obstetrics, gynaecology, urology, and presurgical skin preparation.

It was used in dentistry for presurgical mouth disinfection and endodontics. Schroeder⁵ was the first to investigate plaque inhibition action in 1969. Loe and Schiott⁶ demonstrated in 1970 that twice-daily rinsing with 0.2 per cent chlorhexidine of 10ml reduced plaque and gingivitis development even without mechanical cleaning.

MECHANISMS OF ACTION

Woodcock (1988)⁷ examined the antibacterial effect of biguanides and related it to the mechanism of action of chlorhexidine described by Russell and Chopra (1990)⁸ and Denton (1991)⁹.

Antibacterial activity: Its antimicrobial activity is of the membrane-active type¹⁰, used to describe an antimicrobial agent that damages the inner (cytoplasmic) membrane. It binds strongly to bacterial cell membranes, increases permeability, initiates leakage and/or precipitates intracellular components. Interestingly and critically, chlorhexidine shows different effects at different concentrations; at low concentrations, the agent is bacteriostatic, whereas, at higher concentrations, the agent is rapidly bactericidal. The actual levels at which the bacteriostatic and bactericidal effects manifest themselves vary between bacterial species.¹¹

The antibacterial action of chlorhexidine is substantiated because the bacterial cell membrane is characteristically negatively charged. The cationic chlorhexidine molecule is rapidly attracted to the negatively charged bacterial cell surface, with specific and strong adsorption to phosphate-containing compounds, which alters the integrity of the

bacterial cell membrane, and chlorhexidine is attracted towards the inner cell membrane. As a result, chlorhexidine binds to phospholipids in the inner membrane, leading to increased permeability of the inner membrane and leakage of low-molecular-weight components, such as potassium ions. At this bacteriostatic (sublethal) stage, the effects of chlorhexidine are reversible; removal of excess chlorhexidine by neutralizers allows the bacterial cell to recover. This implies that the structural changes to the cytoplasmic membrane caused by low levels of chlorhexidine are minor compared with the gross damage caused by higher concentrations.

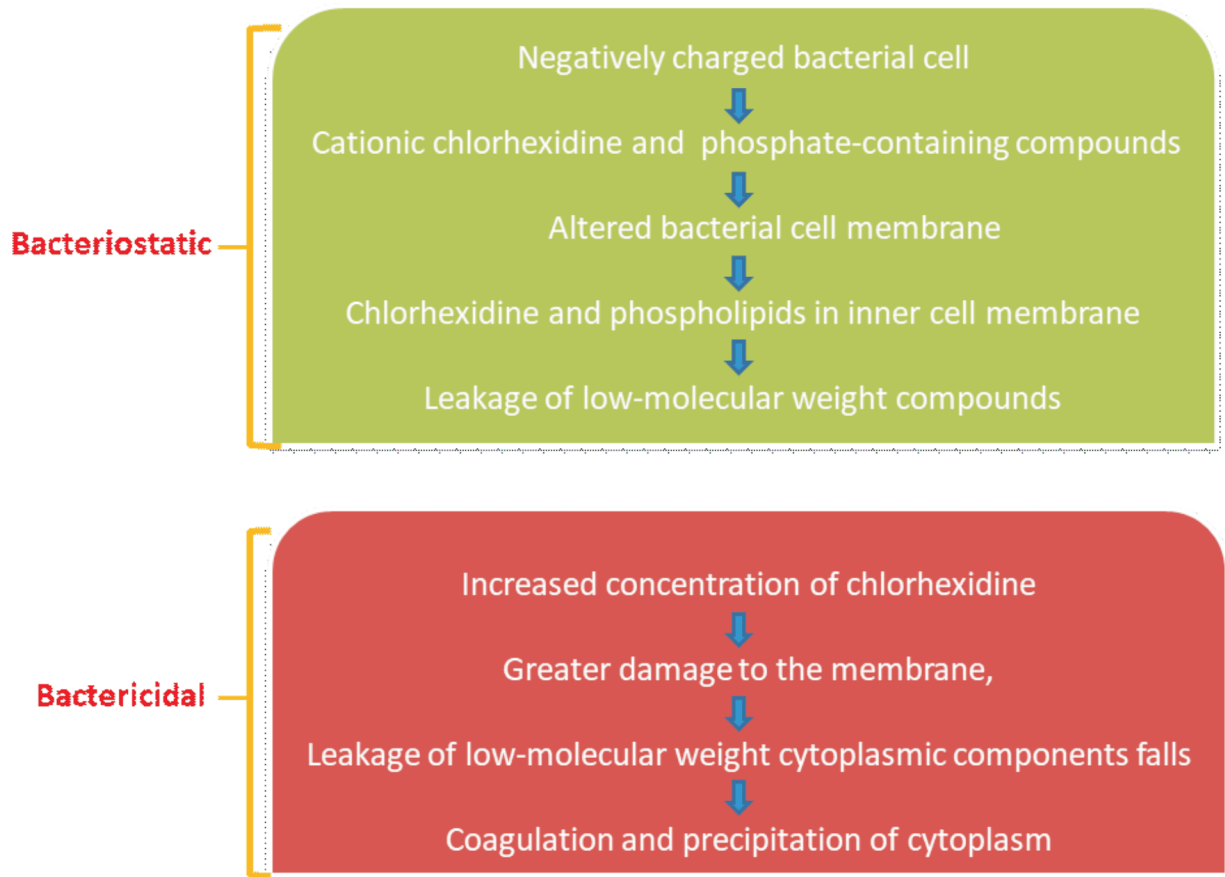
Increasing the concentration of chlorhexidine causes progressively more significant damage to the membrane, reflected in the size of the porous species lost from the cell.^{12,13} As the concentration of chlorhexidine increases, leakage of low-molecular-weight cytoplasmic components falls, reflecting the cytoplasm's coagulation and precipitation by forming phosphate complexes such as adenosine triphosphate and nucleic acids. Electron micrographs show the cytoplasm of such cells to be chemically precipitated; this bactericidal stage is irreversible.

Antiplaque Activity-

Rolla and Melsen¹⁴ postulated that the desorbed chlorhexidine inhibited plaque formation in the following ways:

1. An influence on pellicle formation by blocking the acidic groups on the salivary glycoprotein, thus reducing the protein adsorption on the tooth surface.
2. An influence on the adsorption of plaque onto the tooth surface by binding to the bacteria in sub-lethal amounts

Influenced plaque formation by precipitating the agglutination factors in saliva and displacing calcium from the plaque matrix.



SUBSTANTIVITY

The substantivity of chlorhexidine is its distinguishing feature. The ability of drugs to adsorb and bind to tissues is referred to as substantivity. Chlorhexidine binds to the pellicle as well as the saliva, and its action lasts up to 5 hours and remains in the oral cavity for more than 12 hours¹⁵

EFFICACY

It is effective against gram-positive and gram-negative bacteria, dermatophytes, viruses, fungi, and yeasts, as well as periodontal pathogens like *Streptococcus mutans*, *Porphyromonas gingivalis*, and *Prevotella intermedia*.¹⁶

PIN-CUSHION EFFECT

The positively charged end of chlorhexidine the molecule binds to the tooth surface, and the negatively charged end interacts with a bacterial membrane, which is termed a pin-cushion effect.

DELIVERY SYSTEMS

MOUTH RINSE

The application of chlorhexidine digluconate as a mouth rinse is the method most commonly documented in the literature. Chlorhexidine mouth rinses are available in 0.2% and 0.12% concentrations. 0.2% and 0.12% rinses have equal efficacy when used at appropriate similar doses. The duration of rinsing is 30 or 60 seconds, depending on the rate of antiseptic adsorption to the oral surfaces (50% of chlorhexidine binds to receptors within 15 seconds), but this varies from person to person.¹⁷ The plaque inhibiting effect of a 0.2% chlorhexidine with rinsing times of 15, 30 and 60 seconds following a 72-hour non-brushing period showed no difference¹⁸.

The ideal regimen is twice daily (morning and night), which will have a substantivity for 12 hours.

GELS

The concentrations of chlorhexidine gels available are 1%, 0.2%, and 0.12%. A 1% chlorhexidine gel product is available and is used along with the toothbrush/ in trays. Distribution of the gel in a toothbrush is poor, and trays are effective in plaque and gingivitis control¹⁹

SPRAYS

They are available in concentrations of 0.1 and 0.2 %. It has been demonstrated that 0.2 % revealed a small dose of 2mg on the tooth surface, producing plaque inhibition comparable to rinse. They are beneficial for people with disabilities. Sprays are directed at the tooth, which reduces the dose while potentially improving taste.²⁰

TOOTH PASTE

Chlorhexidine is challenging to formulate in toothpaste²¹. In 1993 Yates et al. showed that chlorhexidine toothpaste with /without fluoride was superior to the control product. Still, there was increased staining and supragingival calculus formation. 0.12% of chlorhexidine with one part per million of fluoride has antiplaque effects similar to chlorhexidine mouthwash. 1% chlorhexidine used as slurries and rinsed twice daily for one minute causes a significant reduction in the plaque and gingival scores. The different modes of application should be adapted to the individual patient's needs.

VARNISH

Varnish formulation is used in the prevention of root caries.²²

CHEWING GUM

It contains 20mg of chlorhexidine diacetate. It is advised to chew two pieces twice per day for 10 minutes. Chewing gum containing chlorhexidine may be helpful for short-term plaque control. In the long run, if found to be equally effective, chlorhexidine-containing chewing gum may support oral hygiene routines for hospitalized and geriatric patients, xerostomia cases, and others at high caries risk. Routine use of chlorhexidine-containing chewing gum may also include situations in which mechanical hygiene measures or mouth rinses are impractical, but chewable antiplaque agent appears appealing.²³

CHLORHEXIDINE CHIP

Perio Chip is a small, orange-brown, rectangular chip with

one end rounded for insertion into periodontal pockets. Each PerioChip weighs about 6.9 mg is a 5 ×4 ×0.3 mm film containing 2.5 mg of chlorhexidine gluconate in a biodegradable matrix of hydrolysed gelatine cross-linked with glutaraldehyde. Glycerine and purified water are also included in PerioChip.²⁴

Chlorhexidine local drug delivery

Periochip (2.5mg Chlorhexidine)

Periocol CG (2.5mg Chlorhexidine)

Chlosite (1.5% Chlorhexidine)

INDICATIONS

1. As an adjunct to oral hygiene: Chlorhexidine improves gingival health through plaque control. It overcomes the deficiencies of mechanical plaque control. Duration for adjunctive use is not established. The recommendation of the manufacturer is Four weeks.
2. Post oral surgery, including periodontal surgery/root planning: It is used to reduce bacterial load post-surgery and prevent plaque formation when mechanical plaque control is difficult. It improves healing and reduces discomfort. It can be used post-treatment immediately and till oral hygiene is reinstituted.²⁵
3. Patients with jaw fixation: Oral hygiene is challenging when jaws are immobilized by methods such as IMF (intermaxillary fixation). Chlorhexidine has been shown to reduce markedly the bacterial load, which tends to increase during jaw immobilization, and improve plaque control¹⁹
4. In physically and mentally handicapped- They rely on caregivers; - Sprays are especially appropriate for such patients²⁶
5. Medically compromised individuals predisposed to infection: Chlorhexidine is an effective antiseptic agent but most useful when combined with antifungal drugs such as nystatin / amphotericin b, nitroimidazole
6. High caries risk patients: Chlorhexidine rinses or gels can considerably reduce the Streptococcus mutans counts in caries-prone individuals. Additionally, and interestingly, chlorhexidine appears synergistic with sodium fluoride and combining chlorhexidine and

fluoride rinses appears beneficial to such at-risk individuals²¹. Sodium monofluorophosphate, on the other hand, reduces the effect of chlorhexidine and probably vice versa¹⁹

7. Recurrent oral ulceration: Mouthwashes and gels reduce incidence, duration and severity of oral ulceration by lowering contamination of ulcers
8. Removable and fixed orthodontic appliance wearers: Plaque control in the early stages of orthodontic appliance therapy may be compromised, and chlorhexidine can be prescribed for the first 4-8 weeks. Additionally, chlorhexidine has been shown to reduce the number and severity of traumatic ulcers during the first four weeks of fixed orthodontic therapy
9. Chlorhexidine has been recommended in the treatment of candidal infections; however, it is less effective in the therapeutic mode, and it is more advantageous to treat dentures stomatitis with specific anticandidal drugs and then employ chlorhexidine to prevent recurrence. It is also used as denture soak.
10. Preoperative rinse and Irrigation: It markedly reduces the bacterial load and contamination of the dental office. When used as an irrigant, it reduces bacteremia
11. In Implant dentistry: Conventional SRP cannot be readily applied to implants as to natural teeth; therefore, antiplaque rinse is vital in implant maintenance.
12. Long stay hospital patients-because oral health deteriorates due to medical conditions, physical state, and medication chlorhexidine can prove to be useful.

SIDE EFFECTS

Following are the side effects.

1. Brown discolouration of the teeth, tongue dorsum and restoration²⁷
2. Unpleasant taste and taste perturbation with salt taste being preferentially affected
3. Oral mucosal erosion idiosyncratic reaction, which is concentration dependent. Dilution of 0.2% formulation to 0.1% but rinsing with the whole volume resolves this problem
4. Rarely mucosal erosions are seen.
5. Unilateral/bilateral parotid swelling is rare; the

explanation is not available

6. Supragingival calculus formation is increased increased precipitation onto the tooth surface, thereby increasing the pellicle thickness and precipitation of inorganic salts on the pellicle layer
7. Bitter taste is difficult to mask.
8. When pocket depth increases, it is ineffective because it does not reach/penetrate the pocket, making it ineffective for periodontitis.²⁸

Chlorhexidine staining

The mechanism proposed for chlorhexidine staining can be debated.

The following are suggested:

1. Degradation to release parachloraniline appears not to occur on storage or as a result of a metabolic process. However, alexidine, a related bisbiguanide, does not have a parachloraniline group yet causes similar staining.
2. Catalysis of Maillard's reaction a non-enzymatic browning reaction (Maillard reaction) leading to the formation of brown pigmented substances known as melanoidins. a response that can be catalyzed by a high-pH substance such as chlorhexidine.²⁹
3. Protein denaturation and metal sulphide formation (Erikson 1982 and Nordbo 1982)²⁹-produced by chlorhexidine with the interaction of exposed sulphides radicals with metal ions are only theoretically possible this does not take into account similar staining produced by other antiseptics and metal ions
4. Precipitation of anionic dietary chromogens by cationic antiseptics and polyvalent metal ions-provides the possible explanation thus locally bound antiseptics /metal ions on the teeth and mucosa can react with the polyphenols in the diet (gallic acid, polyphenol derivatives and tannins) cause stain

ANTI-DISCOLORATION SYSTEM [ADS]:³⁰

Researchers have investigated the possibility of reducing and/or eliminating pigmentation

associated with the use of chlorhexidine-based products by adding antioxidants such as essential oils, peroxyborate,

polyvinylpyrrolidone, sodium metabisulphite, or ascorbic acid - by interrupting the Maillard reaction and interfering with the pigmentation reaction caused by the reduction of Fe III to Fe II, thereby avoiding the reaction between Fe III and SH groups. One of the most severe issue with these agents is the possibility of interfering with chlorhexidine's activity. The scarcity of studies prevents a definitive conclusion.

CONCLUSION

Chlorhexidine is the most effective chemical plaque control agent, with numerous clinical applications in periodontics. Its broad antimicrobial spectrum is a boon for overall oral health. As a result of chlorhexidine's effective antibacterial properties, it is a viable option for use in all periodontal procedures with few undesirable side effects.

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Conflict of Interest: None

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