


## **Disinfectants, antiseptics and antigingivitis/antiplaque agents**

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### **Key points**

- 1. Definitions, differences between disinfectants and antiseptics**
- 2. Types of disinfectants and antiseptics used in dentistry**
- 3. Antiplaque agents**
- 4. Antigingivitis agents**



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### **Key points of infection control program**

- 1) to reduce the numbers of pathogenic microorganisms to levels where patients' normal defense mechanisms can prevent infection
- 2) to break the cycle of infection and eliminate cross-contamination
- 3) to treat every patient and instrument as capable of transmitting infectious disease
- 4) to protect patients and health care workers from infection and its consequences

CDC - Centers of Disease Control and prevention

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- + **Disinfectants** - are used to kill or eliminate microorganisms and/or inactivate viruses on **inanimate objects and surfaces** (medical devices, instruments, equipment, walls, floors)
  
- + **Antiseptics** are used to kill or eliminate microorganisms and/or inactivate viruses on **living tissues** (intact or broken skin and mucous membranes).

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### Disinfectants vs antiseptics major differences

Disinfectants	Antiseptics
Applied to non-living surface	Applied to living tissue
Inhibit the growth of microorganism that exist on the surfaces	Kill and destroy microorganisms on living tissue
Disinfect areas that can spread germs	Reduce the risk of infections by germs
Are very toxic and injurious	Have no injurious effect on living tissue



Mycobacterium tuberculosis, cytomegalovirus, herpes simplex virus (HSV), HBV, HCV, HIV, and a number of upper respiratory tract viruses such as influenza and rhinoviruses.

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#### Ideal disinfectant criteria

- widest possible antimicrobial spectrum
- activity in the presence of organic matter (blood, saliva, sputum)
- inexpensive, odorless, effective at room temperature
- noncorrosive, nonstaining, nontoxic

#### Ideal antiseptic criteria

- selective toxicity to microorganism
- activity in the presence of organic matter (blood, saliva, sputum)

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## Disinfectants and antiseptics - mechanism of actions

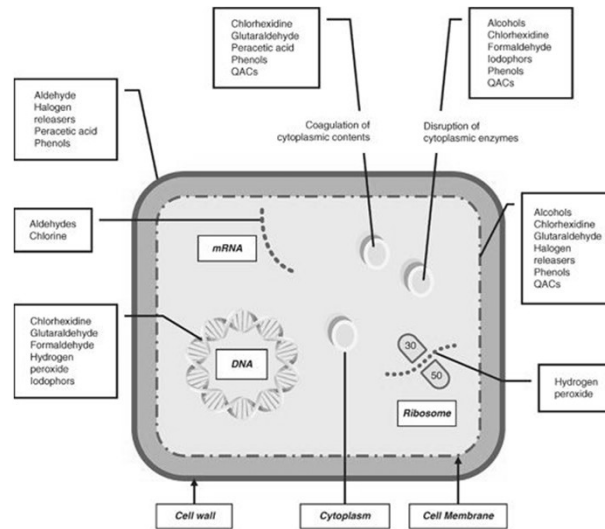


Figure 12.1 ■ Cellular targets of biocidal agents. (Adapted from Fanning S. Altered tolerance to biocides: links to antibiotic resistance? Paper presented at: International Association of Food Protection (IAFP), European Symposium on Food Safety, 2011; The Netherlands. <http://www.foodprotection.org/events/european-symposia/11Ede/Fanning.pdf>. Accessed November 15, 2012.)

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## Disinfectants

- ❖ **High-level disinfectants:** inactivate all microorganisms, excluding a small number of bacterial spores
- ❖ **Medium-level disinfectants:** inactivate Mycobacterium tuberculosis, vegetative forms of bacteria, most viruses and fungi, but do not inactivate all bacterial spores
- ❖ **Low-level disinfectants:** destroy most vegetative forms of bacteria (e.g., Staphylococcus species, Pseudomonas species, Salmonella species) and certain viruses (e.g., HIV, herpes virus, hepatitis B virus, hepatitis C virus) and fungi, without bacterial spores and mycobacteria

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## Disinfectants used in stomatology

### Organic:

- ❖ **Alcohols**
- ❖ **Aldehydes:** glutaraldehyde, formaldehyde, O-phthalaldehyde
- ❖ **Phenols**
- ❖ **Ethylene oxide**
- ❖ **Heterocyclic nitrogen compounds**
- ❖ **Quaternary ammonium compounds**
- ❖ **Biguanides:** chlorhexidine

### Inorganic:

- ❖ **Halogen-releasing agents:**
  - **Chlorine-releasing agents (CRA):** sodium hypochlorite
  - **Oxidizing agents:** hydrogen peroxide, potassium manganate, peracetic acid
  - **Iodine-based agents:** povidone-iodine
- ❖ **Silver nitrate**

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### Alcohols:

- **ethanol (60-80%)**
- **isopropanol (70%)**

Mechanism of action: denaturation of proteins

Spectrum: gram +, gram - bacteria, tubercle bacilli, viruses

Use: as topical antiseptics (on the skin), to dry the root canal (Et-OH 95%, isopropanol 70% + silver nanoparticles), disinfection of non-critical surface

Benefits: low cost, rapid evaporation, lack of residue

Disadvantages: ineffectiveness against many bacterial spores (not recommended for sterilizing medical and surgical materials), skin irritation

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### Why 70% alcohol is a better disinfectant than 99% alcohol against coronavirus?

A 70% alcohol can effectiveness cross over the cell membrane, thereby attacking the entire cell and killing the bacteria (CDC, 2020). The benefits of using 70% alcohol are

1. Coagulation of surface proteins proceeds at a slower pace, thereby allowing the alcohol to enter the cell.
2. 70% alcohol, being a dilution of absolute alcohol, contains water which is essential in the denaturing process of proteins.
3. Due to the concentration difference of water and alcohol on either side of the cell wall, 70% alcohol enters the cell to denature both enzymatic and structural proteins. This increases the potency of its antimicrobial properties.

Centers for Disease Control and Prevention. 2020. *Coronavirus Disease 2019 (COVID-19) – Environmental Cleaning And Disinfection Recommendations*. Available at: <<https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/cleaning-disinfection.html>>

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### Aldehydes:

- **glutaraldehyde** (2% aqueous sol. buffered to pH=7.5-8.5 with sodium bicarbonate)
- **OPA (ortho-phthalaldehyde)**
- **formaldehyde (formocresol)**

Mechanism of action: alkylation of amine and amide groups, hydroxyl groups, carboxylic nucleic acids, and proteins

Spectrum: gram +, gram - bacteria, fungi, viruses, mycobacteria (OPA)

Use: medical equipment

Benefits: wide spectrum, noncorrosive

Disadvantages: toxic and irritating effect (dermatitis, eye irritation, respiratory symptoms, headache), glutarylaldehyde is unstable at low pH, glutarylaldehyde - „cold sterilants“, glutaraldehyde - rapid loss of activity, potential carcinogenic (formaldehyde)

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**Phenols:**

- **2-phenylphenol**
- **2-benzyl-4-chlorophenol**

Mechanism of action: inactivation of enzymes and lysis of protoplasts (low concentration); denaturation of proteins (high concentration)

Spectrum: bacteria, fungi, **don't affect spores**

Use: surface disinfection

Disadvantages: not recommended for the disinfection of equipment that come in contact with skin and mucous membranes

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**Quaternary ammonium compound QACs**

(alkyl dimethyl benzyl ammonium chloride, alkyl didecyl dimethyl ammonium chloride, and dialkyl dimethyl ammonium chloride)

Mechanism of action: increase permeability of cell membrane, protoplast lysis and cell death

Spectrum: gram-positive bacteria, are biocidal against enveloped viruses including HIV, ineffective against mycobacteria, non-enveloped viruses, spores

Use: preoperative disinfection of undamaged skin and mucous membranes and for disinfection of noncritical surfaces

Disadvantages: are affected by organic soil and they tend to cling to surfaces

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**Compounds with oxidizing properties:**

- hydrogen peroxide  $H_2O_2$
- chlorine compounds ( $HClO$ ,  $NaClO$ ,  $ClO_2$ )
- iodophors
- peracetic acid

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**Hydrogen peroxide 3%**

Mechanism of action: reactive hydroxyl radicals, DNA or RNA damage, loss of cell wall stability, cell lysis

Spectrum: bacteria and their spores (at concentration > 6%), viruses, fungi, mycobacteria

Use: 3% sol. in the endodontics, bactericidal effect by dissolving organic tissue

Benefits: broad spectrum

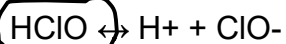
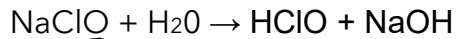
Disadvantages: is easy decomposable (light, high temp., heavy metal ions – Fe III – Fenton reaction)

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## Chlorine - Sodium chlorate NaClO

Mechanism of action: has ability to dissolve organic tissues and microbial biofilm



Spectrum: bacteria and their spores, viruses, fungi

Use: at concentration ranging from 0,5-5,25% - dental application as irrigating solution

Benefits: broad spectrum, inexpensive

Disadvantages: irritation of mucous membranes, toxic, unpleasant odor, corrodes metals such as stainless aluminum

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## Peracetic acid

Mechanism of action: denatures proteins, disrupts the cell wall permeability, and oxidizes sulfhydryl and sulfur bonds in proteins, enzymes, and other metabolites

Spectrum: gram-positive and gram-negative bacteria, fungi, viruses, mycobacteria, spores

Use: chemical sterilization of dental instruments

Benefits: broad spectrum, lacks harmful decomposition products, remains effective in the presence of organic matter, sporicidal even at low temperatures

Disadvantages: costs

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### **SPO or SOW (Super-Oxidized Water) (*Sterilox*)**

**HClO, chlorate anion, chlorine, chlorine dioxide, hydrogen peroxide, ozone**

Mechanism of action: oxidation of thiol groups in proteins, inactivation bacterial enzymes

Spectrum: bacteria, mycobacteria, viruses, fungi, and spores

Use: irrigation of canal root, disinfectant for dental unit water lines and endoscopes

Benefits: broad spectrum, nontoxic to biologic tissues

Disadvantages: antimicrobial effect is reduced in the presence of organic substances

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### **Iodophors**

**Povidone-iodine, polyvinylpyrrolidone iodine 10%**

Mechanism of action: damage cell membrane lipids, protein denaturation, coagulation of cytoplasm

Spectrum: bacteria, viruses, fungi, vegetative microorganisms

Use: surface disinfection, antiseptics of hand hygiene

Benefits: broad spectrum, nontoxic, noncorrosive, not inhibited by the presence of organic compounds

Disadvantages: require drying time on skin before becoming active

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## **Chlorhexidine gluconate**

Mechanism of action: It destroys the cell membrane, leading to cell lysis

Spectrum: aerobic and anaerobic bacteria, fungi, (incl. *Enterococcus faecalis*, *Candida albicans*)

Use: skin disinfection, oral hygiene (mouthwash), endodontic final irrigant, disinfection of surgical instruments

Benefits: antimicrobial effect can be retained for up to 12 hours or longer

Disadvantages: does not have a biocidal effect on spores and has no effect on mycobacteria, activity depends on pH and is reduced in the presence of organic matter and hard water, needs to be protected from sunlight

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## **Ethylene oxide**

Mechanism of action: alkylation of protein, DNA, and RNA, inactivation of enzymes and lysis of protoplasts (low concentration); denaturation of proteins (high concentration)

Spectrum: active against bacteria, especially gram-positive bacteria, fungi, and viruses, and also kills spores.

Use: sterilization of medical devices (plastics that are sensitive to high temperature and moisture)

Benefits: effectively sterilizes and does not damage the device (incl. sensitive to high temperature and moisture)

Disadvantages: environmental pollution, toxic (skin burns, mutagenic and cancerogenic action)

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<b>Antimicrobial spectrum of different disinfectants and antiseptics</b>							
<b>Agent</b>	<b>Gram + bacteria</b>	<b>Gram - bacteria</b>	<b>Bacterial spores</b>	<b>Tubercle bacilli</b>	<b>HBV</b>	<b>HIV</b>	<b>Fungi</b>
<b>Halogens</b>	+	+	±	±	+	+	+
<b>Aldehydes</b>	+	+	+	+	+	+	+
<b>Phenols</b>	+	+	-	+	-	+	+
<b>Alcohols</b>	+	+	-	+	±	+	±
<b>Chlorhexidine</b>	+	+	-	-	-	+	±
<b>Surface-active agents anionic</b>	+	-	-	-	-		-
<b>Surface-active agents cationic</b>	+	±	-	-	-		+
<b>Oxidizing agents</b>	+	+	+	+	+	+	+
<b>Heavy metals</b>	+	±	-	-	±		+

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<b>Characteristics of common disinfectants</b>		
<b>Agents</b>	<b>Activity</b>	<b>Liabilities</b>
<b>Chlorine dioxide</b>	Rapid disinfection activity; can be used for sterilization with 6 hr of exposure	Corrosive; activity greatly reduced in the presence of protein and organic debris; requires good ventilation
<b>Glutaraldehyde</b>	As 2%-3.2% immersion preparation, broad-spectrum antimicrobial activity; sporicidal after 10 hr of contact; long use life	Very irritating to skin and mucous membranes; allergenic with repeated exposures
<b>Hypochlorite</b>	Rapidly acting, broad-spectrum bactericidal, sporicidal, virucidal disinfectant	Irritating to skin; corrosive; can degrade some plastics
<b>Iodophors</b>	Rapidly acting, broad-spectrum bactericidal disinfectant; residual antimicrobial activity remains on surface after drying	Corrosive to some metals; may discolor some surfaces; inactivated by hard water
<b>Phenols</b>	Broad-spectrum antimicrobial activity; effective in presence of detergents	Can degrade plastics; irritating to skin and eyes; inactivated by hard water and organic debris

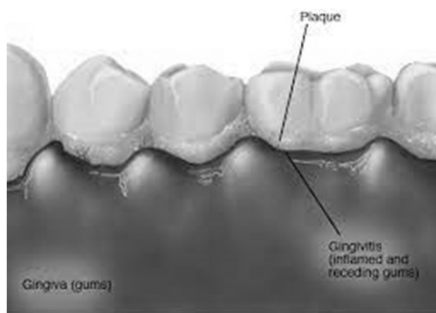
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### Miscellaneous Uses of Disinfectants and Antiseptics

Agent	Formulation (weight/volume)	Use
<b>Alcohol</b>	70%	Solvent and adjuvant for other agents; prevention of bedsores
<b>Parachlorophenol</b>	Variable	Root canal debridement
<b>Phenol</b>	0,5%-1,4%	Relief of sore throat
<b>Eugenol</b>	Variable	Relief of pulpal pain
<b>Guaiacol</b>	Variable	Relief of pulpal pain
<b>Sodium hypochlorite</b>	5% solution	Root canal debridement
<b>Iodine solution</b>	8%-9% iodine	Plaque-disclosing solution
<b>Povidone-iodine</b>	Solution with 1% available iodine	Plaque-disclosing solution
<b>Formaldehyde</b>	4% (10% formalin)	Fixative for tissue biopsy specimen
<b>Hydrogen peroxide</b>	3% 30%	Wound cleaning Tooth bleaching

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### Antiplaque/ antigingivitis agents



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#### Dental biofilm:

- Bacteria 70%: gram positive rods, cocci
- Organic components: lipids, proteins, polysaccharides
- Inorganic matrix: calcium, phosphorus ions



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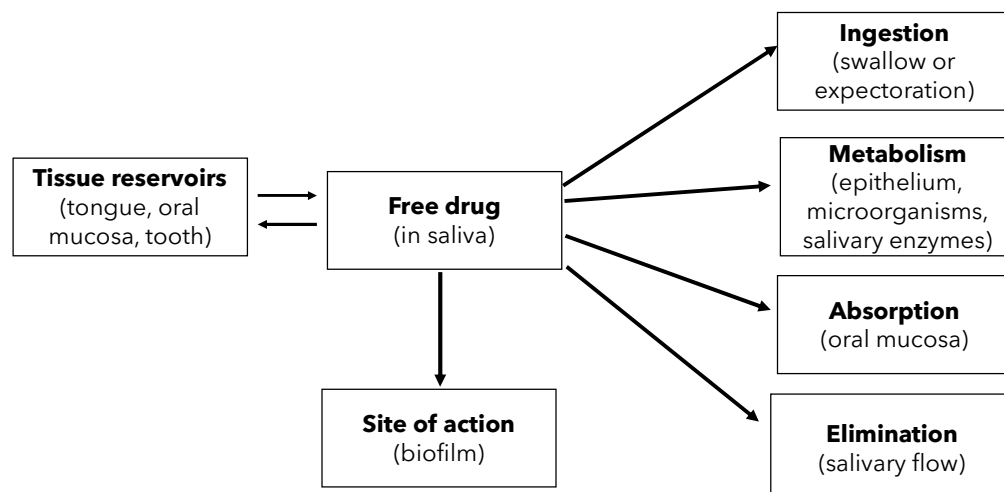
## Gingivitis - etiology

- + Streptococcus
- + Fusobacterium
- + Actinomyces
- + Veillonella
- + Treponema
- + Bacteroides
- + Capnocytophaga
- + Eikenella



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## Drug pharmacokinetics in the oral cavity



**Substantivity:** the time that a drug is in contact with a particular substrate in the oral cavity.

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## Ideal properties of antiplaque agents

- + **Efficacy** - nontoxic, nonallergenic, nonirritating
  - + **Stability** - statistically and clinically meaningful reduction of plaque and gingivitis
  - + **Specificity**: affects only the pathogenic flora
  - + **Substantivity** - binds to and releases slowly from the tooth surface
  - + No induced drug resistance
  - + Acceptable taste
  - + Low cost
- No such perfect antiplaque agent exists today 😊

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## Antiplaque and antigingivitis agents

### Chlorhexidine (0,03-0,2%)

**Mechanism of action:** binds to anionic groups on the bacterial surface, probably the phosphate groups of teichoic acid in gram-positive bacteria and the phosphate groups of lipopolysaccharides in gram-negative bacteria.

**Use:** mouth infections or ulcers, gum disease, denture care (> 12 Yo)

**Side effects** (occasionally): yellow-brown stains on the teeth, anterior restorations, dorsum of the tongue, supragingival calculus formation, persistent aftertaste or disturbed taste sensation, rare but serious allergic reaction.

**Advantages:** low level of local toxicity

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## Antiplaque and antigingivitis agents

### Nonionic bisphenols - triclosan (0,2%; 0,3%)

**Mechanism of action:** binds to membrane targets interfering with transport mechanisms, inhibits the enzyme enoyl-acyl carrier protein reductase, which results in a reduction of type II bacterial fatty acid synthesis and lipid synthesis, ↓ prostaglandins production

**Use:** gingival inflammation

**Side effects** (occasionally): allergy, bacterial resistance, ↓ thyroid hormones ??

**Advantages:** broad spectrum, low level of local toxicity, antiinflammatory effect, bacteria resistance to antibiotics??

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## Antiplaque and antigingivitis agents

### Phenolic compounds

(thymol, chlorothymol, menthol, eucalyptol)

**Mechanism of action:** inhibition of bacterial enzymes

**Use:** as combination of thymol 0,064%, menthol 0,042%, eucalyptol 0,092% - as an adjunct to brushing and flossing

**Side effects** (occasionally): allergy

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## Antiplaque and antigingivitis agents

### Surface-active compounds:

- anionic: sodium lauryl sulfate
- cationic : quaternary ammonium compounds
- nonionic: polysorbate

### Quaternary ammonium compounds - cetylpyridinium chloride

**Mechanism of action:** inactivation of membrane-associated enzymes, damage to the membrane

**Use:** as mouth rinses (greater activity against gram+ than gram- bacteria)

**Side effects** (occasionally): oral ulceration and discomfort and a mild burning sensation of the tongue

**Disadvantages:** are inactivated by the presence of organic matter; by low pH; and by anionic compounds, soaps, metallic ions, unpleasant taste

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## Antiplaque and antigingivitis agents

### Fluorides

(Sodium fluoride, monofluorophosphate, stannous fluoride)

**Mechanism of action:** poor antibacterial properties, inhibition of glycolysis in plaque bacteria glucose transport into cells (at high concentration)

**Use:** for caries prevention (tablets, gel, mouthwashes), professional use, stannous fluoride more effective agent

**Side effects:** (overdosage) stomach discomfort, nausea, vomiting, neurological symptoms

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## Antiplaque and antigingivitis agents

### Oxygenating agents

(hydrogen peroxide, perborates)

**Mechanism of action:** release molecular oxidase

**Use:** reduction of plaque formation and gingivitis (mouth rinse)

**Side effects:** (occasionally) oral ulcerations

### Morpholino compounds

(delmopinol 0,2%)

**Mechanism of action:** acts as a cationic surfactant and prevents the attachment and the adherence of plaque bacteria to the tooth surface.

**Use:** reduction of plaque formation and gingivitis (mouth rinse)

**Side effects:** modest staining of tooth and tongue, transient anesthesia of the tongue, disruption of taste, and infrequent mucosal soreness and erosion

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## Antiplaque and antigingivitis agents

### Photodisinfection

Photodynamic disinfection is a nonantibiotic therapy for the treatment of a broad spectrum of bacterial, fungal, and viral infections.

#### **Mechanism of action:**

1. Methylene blue is added to the subgingival biofilm where it selectively binds to periodontal pathogens.
2. the excitation of methylene blue with a nonthermal diode laser at a wavelength of 670 nm. Highly reactive oxygen species are released and inactivate bacterial virulence factors and disrupt selectively the bacterial membranes of a wide range of periodontal pathogens.

**Use:** disinfection of roots and furcation areas, periodontitis

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<b>Active agents</b>	<b>Concentration</b>	<b>Pharmacologic action</b>	<b>Effect on plaque</b>	<b>Effect on gingivitis</b>
<b>Chlorhexidine</b>	0,12	Disrupts cell membranes; precipitates intracellular proteins	↑↑↑	↑↑↑
<b>Delmopinol</b>	0,2	Prevents attachment and adherence of bacteria to tooth surface	↑↑	↑
<b>Stannous fluoride</b>	0,45	Suppresses select bacterial enzymes and alters bacterial aggregation	↔	↑↑
<b>Thymol</b>	0,06	Suppresses bacterial enzymes	↑	↑
<b>Triclosan</b>	0,3	Inhibits enoyl-acyl carrier protein reductase; reduces type II bacterial fatty acid synthesis and lipid synthesis	↑↑	↑↑