Antimicrobial Fillers for Dental Restorative Materials

Sharmila Jasmine, Rajapandiyan Krishnamoorthy, and Gnanasagar

Abstract Primary cause of restoration failure in dentistry is mainly due to bacterial adhesion, proliferation, colonization and formation of biofilm onto the surface of restorative materials, the so-called secondary caries. Meanwhile, biofilms also affect the longevity of the materials. Chronic denture wearers suffer from denture stomatitis due to the inability of denture base resins to prevent the colonization of fungi *Candida albicans*. Nowadays, novel strategies incorporate nanofillers such as inorganic metal ion nanoparticles and organic nanoparticles into the restorative materials to formulate improved dental materials. Nanomaterials offer a new strategy for averting and remedying dental infections. Hence it is necessary to incorporate antimicrobial nanofillers in dental restorative materials to accomplish improved antimicrobial property.

Keywords Nanomaterials · Antimicrobial fillers · Dental restorative materials · Secondary caries · Denture stomatitis

1 Introduction

Oral cavity relentlessly come across surplus of microorganisms and most of them are normal commensals. Under favourable environment, these microorganisms multiply and cause various infections and diseases. Plaque is the foremost cause of periodontitis, caries, peri-implantitis that results in failure of dental restoration (Fernandes

---

S. Jasmine (✉)
Department of Oral Maxillofacial Surgery, Rajah Muthiah Dental College and Hospital, Annamalai University, Chidambaram, India

R. Krishnamoorthy
Nanobiotechnology and Molecular Biology Research Unit, Department of Food Science and Nutrition, College of Food Science, King Saud University, Riyadh, Kingdom of Saudi Arabia

Gnanasagar
Department of Oral and Maxillofacial Surgery, Rajas Dental College, Tirunelveli, India

© Springer Nature Singapore Pte Ltd. 2021

Inamuddin et al. (eds.), *Advanced Antimicrobial Materials and Applications*,
Environmental and Microbial Biotechnology,
https://doi.org/10.1007/978-981-15-7098-8_14

et al. 2018). The combat between surgeons and bacteria is an extended war, due to the formation of biofilm. Biofilms are multicellular communities of microorganisms (bacteria, fungi and protists) that contribute to adhesion, proliferation and persistent colonization in living and non-living surfaces (Lear and Lewis 2012). The biofilm producers display unique phenotype with increased resistance to potent antimicrobials and host defence mechanism. Moreover, they form a slimy extracellular polymeric matrix (EPS) consisting of polysaccharides, proteins, lipids and DNA (Hall-Stoodley et al. 2004). They exist in a subclinical state, and upon appropriate favourable condition, they spread and cause severe infections.

2 Dental Caries

Dental caries is one of the most common, prevalent, dynamic oral disease of multifactorial origin that affects people of all age groups (Mahfouz and Esaid 2014). Primary caries occurs at the margin of the restoration due to incomplete removal of the carious lesion (Lai and Li 2012). Acid production and biofilm formation by cariogenic bacteria violate the equilibrium between demineralization and remineralization of the tooth surface. Drop in pH leads to loss in calcium and phosphate and makes the penetration deeper. The oral biofilm formation begins with the adherence of salivary pellicle (free of bacteria) on the tooth and restorative cement surface, where the acquired salivary pellicle acts as a receptor to which the adherence of microbacterium occurs (Lendenmann et al. 2000). Consequently, bacterial multiplication occurs and progresses through passive transportation of bacteria into the pellicle (Marsh 2004). Thus, results in an irreversible adhesion. Moreover, *Streptococcus mutans*, the primary inhabitant of oral cavity is capable of degrading restorative cements due to the significant esterase activity (Bourbia et al. 2013). Microleakage at the restoration-tooth interface allows microcavities, contamination and residual stresses (Venhoven et al. 1993).

Lack of interfacial integrity for a longer period would indeed predisposes to secondary caries beneath the filling material (Sakaguchi 2005) and results in restoration failure (fracture or dislodgement). Meanwhile, it is a potential cause of hypersensitivity, pulp inflammation and necrosis (Larsen and Munksgaard 1991). More specifically, matrix metalloproteinases (MMPs) present in saliva and cysteine cathepsins expressed by dentin-pulp complexes act synergistically and degrade the hybrid layer thus aid in caries progress (Nascimento et al. 2011). It has been realized that severe bacterial contamination would definitely result in treatment failure (Turner et al. 1975).

Risk factors and amenable causes for caries

- Consistency and flow rate of saliva
- Patients hygiene
- Diets rich in carbohydrates
- Mechanical and surface property of the restorative materials

- Physical and chemical property (pH and buffering capacity) of the restorative materials
- Biological property (antibacterial/antibiofilm) of the restorative materials
- Location and the extent of the caries lesion

3 Antimicrobial Agents

An Antimicrobial agent is defined as a substance or an agent that causes interference with the harmful effects of the bacteria. It inhibits the growth, mitogenesis of the microorganisms and destroys it, thus preventing microbial colony formation. On the other hand, the term bioactive is described as the biological effect of any substance that induces cell growth, proliferation and tissue formation. Meanwhile, it implies the antibacterial effect of a biomaterial to prevent infection. Dr. Larry Hench was the first to coin the term “bioactive material” (Jasmine et al. 2020).

4 Restorative Materials in Dentistry

Restorative materials used in dentistry should possess good aesthetics, superior mechanical properties and should also have excellent antimicrobial properties, thereby increasing the longevity of the restorative materials. Nowadays, innovation of new restorative materials with microbicidal activity is the current trend and a possible mean to effectively prevent and inhibit pathogenic microbial colonization on the tooth surface (Zoergiebel and Ilie 2013). Similarly, these materials should release lethal dose of antibacterial agent in a controlled manner. Some of the dental restorative materials that have incorporated various antibiotics shown to have short-term effects. Moreover, few of them encourage bacterial resistance at sub-lethal concentration and counteractively favour biofilm formation. Organic antibacterials possess greater resistance. Hence, development of metal-based antimicrobials (inorganic) have acquired significant popularity. These attractive alternates have redox properties, unique binding with minimum bacterial resistance. Despite their benefits, toxicity against human tissues should be taken into consideration and hence their therapeutic value have to be focused primarily. Metal ions with optimum properties and biocompatibility could be a better choice.

Recent studies have focused on novel strategies that incorporate nanoparticles, especially metal ions into the restorative materials with altered surface chemistry (Nguyen and Hiorth 2015). Nanomaterials offer a new strategy for averting and remedying dental infections (Magalhães et al. 2016). Nanomaterial is defined as a material which has particle size ranging from 1 nm to 100 nm in an unbound state or as an aggregate/agglomerate that has an internal or surface structure with one or more dimensions and has a specific surface of about more than 60 m^2/cm^3. Meanwhile, they possess unusual physical, biological and chemical properties that differ with different materials. Nanoparticles (NPs) exhibit increased surface area, and disperse evenly without aggregates. Incorporation of nano and microparticles into the dental materials can significantly reduce or block the microbial colonization thus improve the oral health. An important proposed strategy to be focused is the incorporation of remineralizing and antibacterial agents to reduce plaque adherence and to repair the demineralized dentin.

5 Classification of Nanoparticles

Classification of Nanoparticles

- Based on the origin
  - Organic (Natural/Artificial) (Onaizi et al 2011., Perinelli et al 2018)
  - Inorganic. (Whitesides 2003)
- Based on the structural configuration (Hall et al. 2007)
  - Carbon-based
  - Metal NP
  - Dendrimers
  - Composites
- Based on the dimension (Zhang et al. 2008)
  - Zero dimensional/ Nanoparticles
  - One dimensional/Nanorods
  - Two dimensional/films

5.1 *Organic Nanomaterials*

Organic materials are unique in structural and electronic characters. Carbon nanotubes, lipids and polymers are some of the organic types that have multifaceted applications (Hatton et al. 2008). Polymers may be of natural and synthetic origin. Natural antimicrobial fillers are Antimicrobial peptides (AMP) (Onaizi and Leong 2011) and Antimicrobial enzymes (AME) (Thallinger et al. 2013). Biopolymers are biodegradable, biocompatible and nontoxic. Sources of biopolymers are chitin, chitosan, cellulose, starch and pectin (Perinelli et al. 2018).

5.2 *Inorganic Nanomaterials*

Inorganic metal oxide NPs such as titanium oxide, zinc oxide, copper oxide, magnesium oxide and silver oxide have the ability to withstand adverse processing conditions (Whitesides 2003). Moreover, due to their tunable optical and physical properties, these NPs have attained greater attention (Makhluf et al. 2005). Restorative materials that do contain metal oxides of Ag, Hg, Cu, Ni, Zn and fluoride have a well-documented antimicrobial property (Wang et al. 2016). Acidic pH enhances the growth of aciduric and acidogenic bacteria in abundance. Hence these nanoparticles should also have cariostatic property to counteract the acidic pH caused by cariogenic bacteria to retard secondary caries. Apart from antibacterial activity, ZnO NPs has the potential of tissue regeneration.

5.2.1 Silver NPs

Silver (Ag) ions are biocompatible, less toxic, and the sustained release of ions provide a long-term antimicrobial effect (Slenters et al. 2008). With the advent of nanotechnology, AgNPs have a wide range of antimicrobial activity against bacteria and fungi species with a low bacterial resistance (Morones et al. 2005; Aziz et al. 2016; Prasad 2014, 2016, 2017). Smaller the filler size, greater the surface area, hence a high antibacterial effect is seen even with minimum quantity of incorporated filler. Thus, nanoparticles allow a greater interaction with the environmental surroundings and enhance bacterial elimination (Seil and Webster 2012). The filler shape plays important role in the production of ROS and also induces destruction of the bacteria (Pal et al. 2007). Compared to spherical shape, rods and wires exhibit more active facets. This facilitates easy penetration into the cell wall of the bacteria (Yang et al. 2009). Thus, it influences the internalization mechanism of the material. Advantages of nanoparticles are higher antibacterial activity with less influence on mechanical properties. Limitations are discoloration and agglomeration of the AgNPs (Melo et al. 2013). Development of resistant strains occurs against AgNPs due to gene mutations (Graves Jr et al. 2015). Further, they crosses the blood–brain barrier and gets accumulated in the brain (Padovani et al. 2015). AgNPs, phthalocyanine and graphite oxide composites have proven to have lasting antimicrobial activity (Gerasymchuk et al. 2016) and a promising way to prevent bacterial resistance (Karasenkov et al. 2015).

5.2.2 Zinc Oxide NPs

ZnO NPs possess a variety of shapes like nanorods, nanospheres, microspheres and microrod. These shapes or morphologies act differently against Gram-positive and Gram-negative bacterial pathogens, thus which confirms their broad-spectrum activity (Rago et al. 2014; Raghupathi et al. 2011). Size, colour and quantity of the fillers may affect the physical and mechanical properties (Sakaguchi et al. 2006). Taken these into consideration, characters such as temperature, precursor types, pH, solvents should be given importance and methods to control over it (Sirelkhatim et al. 2015). This gives restorative materials a good clinical longevity and an acceptable outcome. The important antimicrobial mechanism suggested is the production of ROS (peroxide) that favours inhibition of bacterial growth (Ranjita 2017; Zhang et al. 2007; Bhuyan et al. 2015). Comparison between micro and nanorods revealed that nanorods have superior antibacterial effect against *Staphylococcus aureus* and *Bacillus subtilis* (Rago et al. 2014). Study results of Kasraei et al. also correlated with that of Rago et al., i.e. ZnO nanoparticles inhibited *Streptococcus mutans* and *Lactobacillus* significantly. Even with the lower concentration (10% (w/w)) of ZnO, the reduction of biofilm formation is up to 80% (Sevinç et al. 2010) without affecting the mechanical properties (compressive and tensile strength) (Rastelli et al. 2012). On the other hand, it also provides a better dispersion of the filler into the composite resin (Chen et al. 2017a). Microspheres of ZnO at 5 μg/ml of concentration inhibited *S. aureus*, *S. typhimurium* and *K. pneumonia,* whereas *E. coli* at 155 μg/ml (Wahab et al. 2012).

5.2.3 Copper and Nickel Oxide NPs

Copper and nickel NPs possess broad-spectrum of antibacterial activity against a wide range of pathogenic bacteria. And also, a good alternate and inexpensive than Ag and gold NPs (Chatterjee et al. 2012; Pang et al. 2009). Hallow oxide formation through oxidation of Cu and Ni nanoparticles surface also exhibits strong antibacterial property (Ren et al. 2009; Borkow et al. 2010). Copper oxide NPs also possess antibacterial activity against Gram-positive and Gram-negative bacteria. The primary mechanisms ascribed are adsorption of metal ions and reduction reaction at the bacterial cell wall and degradation of the cytoplasm (Raffi et al. 2010; Yadav et al. 2017). Moreover, the antibacterial efficacy is based on both the concentration of NPs and the initial bacterial concentration. Being bactericidal/bacteriostatic, Cu and Ni NPs can be used in preparation of bone cements, coating for devices, sterilization, irrigation of the root canal system and in various other probable applications in the field of dentistry (Argueta-Figueroa et al. 2014). Novel nanocomposites prepared using bioglass coated with Cu NPs have significant antibacterial property with improved angiogenesis (Li et al. 2016a). However, incorporated Ti-Cu NPs as immobilized antibacterial agent in dental materials provide a long-term antimicrobicidal activity. Moreover, they have effective antibacterial and antibiofilm activity against *Porphyromonas gingivalis* and *S. mutans* (Li et al. 2016b). Optimum Cu content (5%) is indicated to maintain excellent mechanical property and a better antimicrobial property that aids in greater reduction of biofilm formation (Liu et al. 2018). By means of contact sterilization, the dissolved Cu ions tend to damage the bacteria (Cao et al. 2011). Further, they adversely affect the gene expression of extracellular polymeric substance on the MRSA (Methicillin resistant *Staphylococcus aureus*) biofilm producing bacteria. Thus, it leads to minimal adherence of the bacteria by down-regulating the production of polysaccharide intercellular adhesion and clumping factor A that disable the formation of biofilm colonies (Liu et al. 2018). Meanwhile, due to its antibacterial activity and excellent anticorrosive nature Ti-Cu alloy has the potential to be a novel dental implant material.

5.2.4 Titanium Oxide NPs

Titanium and its alloys are the choice of material to be used commonly in the field of dental implants. In fact, they are biocompatible with good mechanical properties. Cell adhesive proteins that adhere on the surface of Ti implant surface proved to be the site for binding of osteoblast precursors that favours bone ingrowth and stabilization. Inappropriate intervention of these sequences by bacterial colonization results in peri-implantitis. Further apart, this has to be prevented before the integration process. Incorporation of metal NPs (Cu, Ag) into the dental implant materials permit a better control over the biofilm formation, since they acquire less resistance (Rosenbaum et al. 2017). The most commonly encountered strains are *Staphylococcus aureus* (16%), *Escherichia coli* (26%) and *Pseudomonas aeruginosa* (9%) (Von Eiff et al. 2006). Cu NPs derived TiO_2 surface when exposed in a stimulated plasma solution revealed high biocide potential against biofilm producing bacterial pathogens especially *S. aureus* and *E. coli* (Rosenbaum et al. 2017).

5.2.5 Chitosan

Chitosan is an organic bioactive compound derived naturally from chitin, an extract of seafood shells, crabs, lobsters and shrimps (Yan and Chen 2015). Being biocompatible, biodegradable and less toxic, it has shown promising results in tissue regeneration. Carboxymethylated chitosan is a derivative of chitosan exhibits extensive antimicrobial property. The major mechanism involved is, the chelation of ions, that removes the trace metals and essential nutrients that are essential for bacterial survival (Shin et al. 2005). Powdered form of this material have been used in drug delivery technology, implants and in scaffolds (Alhajj et al. 2019). In addition, BisGMA and TEGDMA monomers used for crosslinking chitosan have toxicity against pulp cells (Goldberg 2008). Furthermore, its use in composites, glass ionomer cement, denture based resins and in dental adhesives is an emerging new method. The major disadvantage is it reduces the mechanical strength of the restorative material (Takagi et al. 2003). Electrospray and electrospinning methods are used to produce microspheres and nanofibres, respectively (Chen et al. 2018). The electrospinning method incorporates calcium phosphate with chitosan microspheres and generates dibasic calcium phosphate anhydrous, a novel material with antimicrobial property. Even at the lowest concentration chitosan (0.5%) possesses antimicrobial property (Raafat and Sahl 2009). It is well established that composite loaded with chitosan exhibits strong antimicrobial potential across the restorative material without compromising its biocompatibility (Tanaka et al. 2020). The major disadvantage of chitosan is reduction in the mechanical strength of the restorative material. In addition, BisGMA and TEGDMA monomers used for crosslinking of chitosan possess toxicity against dental pulp cells.

The three main methods that render effective antibacterial activity to the dental restorative materials are

1. Release killing method.
2. Contact killing method.
3. Multirelease functional method (Cloutier et al. 2015)

Release Killing method

Local delivery of preloaded antimicrobial agents into the environment is the main mechanism of action. Examples are antibiotics and silver compounds

Advantages

1. No systemic toxicity
2. Minimal drug resistance
3. Release of high doses of antimicrobial agents over time
4. Broad spectrum antimicrobial activity (Campoccia et al. 2013).

Drawbacks

1. Inherent depletion of the reservoir source.
2. Short acting.

Contact Killing method

To evade the reservoir exhaustion of the antimicrobial agents and incorporation of antibacterial fillers into the polymers that exert their antimicrobial property through contact killing mechanism is an attractive alternate (Jia et al. 2017). Polycations, antimicrobial peptides (AMPs) (Onaizi and Leong 2011), antimicrobial enzymes (AMEs), proteolytic enzymes, polysaccharide degrading enzymes, oxidative enzymes (Thallinger et al. 2013) and chitosan are typical examples (Munoz Bonilla and Marta Fernández 2012). Also incorporation of quaternary ammonium compounds (QACs) into dental composites such as dental adhesives, glass ionomer cements (GIC), resin modified GIC, pulp capping agents, root canal sealers and acrylic resins provide a long lasting bactericide-immobilized restorative materials (Imazato 2003).

Advantages

1. Nontoxic and non-irritant
2. Long-term antibacterial property

Drawbacks

1. Bacteriostatic
2. Surface biofouling

Multirelease functional method (Responsive and Synergistic Antimicrobial Properties)

Photothermal materials based on near infrared irradiation convert light energy to thermal energy have gained increased attention owing to their distinct antimicrobial mechanism (Gharatape et al. 2016; Wang et al. 2016). Examples are gold based nanomaterials (GNPs), reduced graphene oxide (rGO) and polypyrrole nanoparticles. They cause physical destruction and penetrate the living tissues with sufficient intensity by generating local heat, thus evading resistance strains (Liang et al. 2014; Yang et al. 2009). GNPs are biocompatible and exert its antimicrobial property via surface plasmon resonance (Gharatape et al. 2016). Moreover, antimicrobial property could be further improved by surface conjugation with specific antibodies (Millenbaugh et al. 2015). The innovation of smart antibacterial surfaces is based on the "kill and release" approach that have the ability to destroy the material associated bacteria as well as eradicate dead bacteria and debris especially multidrug resistance bacteria, thus uphold long-term antimicrobial property (Qu et al. 2019). Photo therapy basically of two types—antibacterial photothermal therapy (APTT) and antibacterial photodynamic therapy (APDT). A combination of biocidal agents and phototherapy have improved antimicrobial property due to synergistic effects. Examples are gold nanorod and kanamycin against *E. coli* (Hu et al. 2013), rGO and vancomycin against multidrug resistance *E. coli* (Yang et al. 2009)

6 Mechanism of APDT action

APDT has been paid great attention in recent years owing to its potential antimicrobial activity against various oral pathogens and biofilms (Al-Shammery et al. 2019). The primary mechanism implicates interaction between photosensitizer and low energy laser that produce reactive oxygen species in the existence of oxygen (Hu et al. 2018). These agents do surface modification through different mechanisms such as disinfection, photocatalysis, photothermal lysis and photodynamic killing, thereby eliminating multidrug resistance bacteria. Based on the types of photosensitizing agents, they can be delivered through intravenous injection, topical application and oral ingestion (Konopka and Goslinski 2007).

Advantages

1. Improbable development of antimicrobial resistance
2. Prompt suppression of the contributing microbes due to oxidative changes in bacterial cell membrane (Hu et al. 2018).
3. Biopolymers and NPs hauling photosensitizers have the advantage of (1) Improved antibacterial efficiency. (2) Enhanced biocompatibility and biodegradability. (3) Reduced accumulation of photosensitizers (Zhang et al. 2016)

Drawbacks

1. Photosensitivity due to the presence of accumulated photosensitizing agents for a few days (Takasaki et al. 2009).

Materials with antimicrobial property supplemented with remineralizing and protein repellent properties come under this category. Moreover, they respond to the microenvironmental cues of the microbial infections (Wei et al. 2019). Examples are silver nanoparticles (AgNPs), amorphous calcium phosphate (NACPs), a combination of NACPs and QAM.

7 Mechanism of Action of NPs

Nanoparticles exert their antibacterial effect through interaction with the peptidoglycan of the bacterial cell wall and thereby increasing the membrane permeability (Qiu et al. 2016). In addition, NPs bind to mesosomes and impede bacterial respiration. They also inhibit DNA replication via interaction with sulphydryl groups and block signal transduction (Giannousi et al. 2014; Pal et al. 2007). The surface of NPs interacts with the transport proteins and inhibits transportation across the semipermeable membrane (Moghimi and Szebeni 2003). Further, NPs generate reactive oxygen species, dysregulate metal ion homeostasis and ATP production that are essential for cell growth and survival. This in turn causes distortion of cell membrane (Nel et al. 2006; Aziz et al. 2014, 2015). NPs mediate amino acid oxidation and produce protein bound carbonyls which results in deactivation of various enzymes (Lynch and Dawson 2008). The positively charged NPs bind to the negatively charged bacterial cell membrane and exert their antibacterial activity (Cao et al. 2018; Prasad and Swamy 2013; Swamy and Prasad 2012). Moreover, the size of nanoparticles allows them easy penetration through the bacterial membrane (Melo et al. 2013).

8 Factors Influencing the Antibacterial Property of NPs

A minimum concentration of nanofillers provide a greater release of ions without affecting the mechanical properties of the cements (Xu et al. 2011). Moreover, the components that adsorbed over the NPs, their composition and structure have a direct influence over the antibacterial activity (Olenin and Lisichkin 2011). Indeed, thick layer impedes antimicrobial activity and vice versa. Studies revealed that incorporation of NPs into polymers or coated onto biomaterials seems to have superior antimicrobial properties (Saafan et al. 2018). Moreover, it is advantageous in drug resistance microbes (Fernandes et al. 2018). Some researchers found that NPs of lower concentration do not exhibit cytotoxic effects and established a dose dependent activity. In fact, the concentration, type, form, size and distribution of the NPs influence the duration and potency of antibacterial effect.

9 Antimicrobial Fillers in Pulp Capping Agents

Pulp exposure is common as a sequalae of caries progression or due to trauma and during cavity or crown preparation (Stanley 1989). Therefore, to preserve the vitality, functional and biological activities of the exposed pulp temporarily and permanently, pulp capping procedure is being done (Haskell et al. 1978). The most commonly used pulp capping agents are calcium hydroxide (CaOH) and mineral trioxide aggregate (MTA) (Camilleri and Pitt Ford 2006). CaOH possesses high antibacterial activity through the release of hydroxyl ions in an aqueous environment (Siqueira 2001). These ions cause denaturation of proteins and damage the microorganisms cytoplasmic membrane. In addition, the alkaline pH (12.5) of the material also enhances the antibacterial effect. MTA is composed of 15–25% of silicon dioxide and 50–75% of CaOH. However, it has been shown that MTA forms silicate hydrate gel on hydration. Hence, both MTA and CaOH have similar mechanism of action (Roberts et al. 2008). Moreover, MTA discharges antimicrobial action even in anaerobic state (Reston and de Souza Costa 2009). Similarly, calcium silicate-based material otherwise called biodentine has been used for indirect pulp capping (IPT). The provisional use of biodentine seems to be beneficial in uncooperative paediatric patients in whom complete removal of caries lesion is not possible. In addition it can be used as IPT agent under dental composites and also in minimal invasive treatment. It has been investigated that biodentine has the potential to inhibit *S. mutans*, *S. gordonii* and *S. sorbinus*. The study by Deveci et al. revealed that Biodentine, Chlorhexidine (CHX) and cetrimide combination proved to have much bacterial inhibition zone of *Lactobacillus* and *S. mutans* (Deveci et al. 2019).

10 Antimicrobial Fillers in Root Canal Sealers

Root canal treatment is the chemomechanical debridement and shaping of the root canal and effective elimination of the microorganisms from them. Antibiotics, steroids and calcium hydroxide are commonly used intracanal medicaments. Despite their benefits, they may produce resistant strains and even host sensitization. Therefore, a better alternative might be nanosized metal ions such as nanomonosodium titanate and gold titanates that are much effective (Eiampongpaiboon et al. 2015). When these particles are exposed to water or while mixed up with calcium hydroxide, they occlude the dentinal tubules as well as the bacteria significantly, even at micromolar concentration (Drury et al. 2018). Due to increase in surface area to volume ratio, the ion exchange property is also more efficient (Beyth et al. 2014). Studies have proved that gold nanoparticles have the antibacterial potency against both gram-positive and gram-negative bacteria such as *Staphylococcus aureus*, *Lactobacillus casei*, *Escherichia coli* and *Pseudomonas aeruginosa* (Morim 2016).

11 Antimicrobial Fillers in Glass Ionomer Cement (GIC)

In 1969 Wilson and Kent introduced glass ionomer cement (GIC). They are frequently used material for luting, lining, fissure sealants, and also in temporary, permanent and atraumatic restorations. Composition of the conventional GIC powder is alumina, silica and calcium fluoride. In addition, Ba and Sr salts are added to impart radiopacity to the cement. The liquid of GIC contains polycarboxylic acid, tricarboxylic acid, maleic, itaconic acid and tartaric acid (Phillips and Anusavice 2013; Baig and Fleming 2015). Incorporation of tartaric acid improves the handling property and thus sufficient working time. The setting reaction of GIC is basically an acid base reaction. Among all the restorative materials, GIC is well known for their practical benefits that includes fluoride release and recharge, chemical bonding, low coefficient of thermal expansion and pleasing aesthetic quality. The inclusion of silicates and fluorides prevent caries progression. Furthermore, chelation between carboxyl group of acid polymer with the hydroxyapatite of enamel, dentin and bone enables a better chemical bond between them. The fact is that, it releases appropriate amount of fluoride that inhibit the metabolism of carcinogenic organisms, thus favouring remineralization (Wiegand et al. 2007).

Moreover, the fluoride release is continuous throughout the materials life time. The linear expansion coefficient of GIC is comparable with that of the tooth. The major drawbacks of GIC are significantly reduced wear resistance, brittleness (Papacchini et al. 2005), synergism and imbibition. Resulting in dimensional changes, decrease surface wear resistance and interfacial gaps that restrict its application in the area of high occlusal load. Years of extensive research have attained considerable changes in the composition that significantly modified the mechanical and handling properties of GIC. These include resin modified GIC, fibre reinforced and bioactive GIC that incorporates of zirconia, zinc, strontium oxide, silica particles, N-vinylpyrrolidone and amino acids (Gu et al. 2005; Zoergiebel and Ilie 2013; Boyd and Towler 2005). Nowadays studies have shifted focus on the incorporation of various nanoparticles to obtain efficient bioactivity (Yli-Urpo et al. 2005). Zinc, silica, ceramics, ytterbium fluoride, titanium oxide, bioactive glass, titanium dioxide, montmorillonite clay, aluminosilicate glass, hydroxyapatite and fluoroapatite, phosphopeptide-amorphous calcium phosphate are some of the particles that are added to obtain desirable strength (Poorzandpoush et al. 2017). In general, metallic oxides such as SrO and $BaSO_4$ have been found to result in desirable mechanical properties (Moheet et al. 2019).

GIC possess chemical bonding and strong adhesion that allows them to bond on both enamel and dentin. Thus, it would be a better opportune material for posterior restoration. When increased crosslinking and polysalt bridge formation are perceived in the set cement, they improve the mechanical properties of the set cement (Oliva et al. 1996). Reinforcement of GIC with hollow and solid discontinuous glass fiber fillers increase the fracture toughness, compressive strength and flexural strength. GICs containing nanohydroxyl apatite (nHA) and fluoroapatite (FA) have improved bonding to the dentin with good mechanical properties (Moshaverinia et al. 2008). Casein phosphopeptide-amorphous calcium phosphate incorporation at 3% concentration inhibited demineralization and encouraged remineralization by enhancing calcium and phosphate release (Al Zraikat et al. 2011). Addition of 5% niobium pentoxide (Nb_2O_5) revealed bioactivity and biocompatibility (Garcia et al. 2016). Hydroxyapatite-alumina/zirconia nanocomposite (HANBG) when added to BAG improves antibacterial activity, bioactivity and also mechanical properties (Thampi et al. 2014). Inclusion of fluoroaluminosilicate glass provoked an acid base reaction with polyacrylic acid and yielded pre-reacted glass ionomer (S-PRG) filler (Ikemura et al. 2003). In turn, capable of releasing fluoride with recharge functions (Han et al. 2002). Fluoride released from the dental materials when interact with apatite of the tooth surfaces forms fluoroapatite (Feagin and Thiradilok 1979)

Addition of titanium oxide nanoparticles (TiO_2) increase the adhesiveness. TiO_2 nanotubes (TiO_2 nt) have increased surface to volume ratio. Hence, even at minimum concentration (3–5%), TiO_2 nt is stable, nontoxic, and increases the fluoride release thus have antimicrobial effects. Moreover, a better particle distribution protects the matrix effectually and increases the microhardness. Hence, an overall improvement in mechanical property of GIC to resist abrasion is essential. At a concentration of 10%, niobium pentoxide affects the interaction between powder and polyacrylic acid and negatively influence the chemical bonding of GIC to the tooth (Garcia et al. 2016). GIC appended with chlorhexidine diacetate and digluconate have bactericidal action against Streptococcus mutans and Lactobacillus acidophilus (Türkün et al. 2008).

12 Antimicrobial Fillers in Dental Composite Resins

Dental composite resins are considered to be the suitable material for tooth cavity restoration due to improved aesthetics and physical properties. The first formulated earlier composites experienced low abrasion resistance, colour instability and inadequate mechanical strength (De Gee et al. 1990). Due to extensive research, the current dental composites with good mechanical properties and excellent colour match have emerged. It is the versatile material of choice with optimal aesthetic property in all classes of direct restorative treatment (Lynch et al. 2014). Also, the wear rate is equal to that of enamel. Most of the current composites material composition is basically silane coated glass/ceramic particles dispersed in methacrylate resin that include bifunctional monomers (Chen 2010). Hardening of the material occurs through free radical polymerization, activated by visible light or initiated chemically (Stansbury 2000). It attributes to 49% of all restorations.

However, clinical studies have revealed that 74% of the failed composite restorations are due to secondary caries (SC) (Xie et al. 2011; Wiegand et al. 2007). This could be due to its surface property, release of unreacted monomers and absence of antibacterial property that accumulates more plaque and forms thick biofilm (Zhang et al. 2008). Most commonly used monomers in the conventional composites are 2,2-bis[4-(2-hydroxy-3-methacryloyloxypropoxy)phenyl]propane (BisGMA) and triethylene glycol dimethacrylate (TEGDMA). However, Bisphenol A (BPA) is used as a raw material for the synthesis of the monomer of the dental composites. After the placement of BPA based composites, trace amount of BPA was found on saliva and urine. Hence, substitution of BisGMA monomer with tris(4-hydroxyphenyl)methane triglycidyl methacrylate (TTM) is a novel approach. The advantages of TTM over BisGMA are comparable mechanical, biological properties and also the ability to photopolymerize with visible light.

Classification of Composites

Based on the filler size and the properties,

- Macrofill (10–50 μm) conventional composites-monodisperse
- Midifill (1–5 μm)
- Minifill (0.4 μm)
- Microfill (0.01–0.1 μm) homogeneous/heterogenous
- Hybrids (0.01–5 μm) polydisperse
- Microhybrid (0.01–1 μm) polydisperse
- Nanofill (0.01–0.04 μm) monodisperse
- Nanohybrid (0.01–1 μm) polydisperse

Fixing orthodontic brackets is the primary step in orthodontics and is achieved through bonding agents (Eliades 2002). In spite of their advantages like ease of application and excellent aesthetics, composite resins and dental adhesives as such are unable to hamper bacterial adhesion and demineralization. Moreover, drawbacks such as bond failure, plaque accumulation, white spots and demineralization around the brackets are unfortunately unavoidable (Allaker 2010). In earlier days, antimicrobials such as chlorhexidine, fluorides were used as effective means to prevent these drawbacks. The current trend is application of nanotechnology into the dental restorative materials to improve their properties (Leung et al. 2005; Sodagar et al. 2013). Metal nanoparticles such as Ag, Zno, Tio_2, Cuo, zirconia and magnesium oxides and hydroxyapatite have gained greater popularity among inorganic fillers. Moreover their physical, optical properties and the concentration can be tailored according to the needs. The carbon nanotubes, lipids and polymers are some of the organic NPs with the unique structural characters. Chitosan are either incorporated into the polymers or coated onto the biomaterials (Magalhães et al. 2016), due to the demonstrated broad spectrum antimicrobial properties (Saafan et al. 2018). A combination of chitosan and ZnO NPs less than 5% (Sodagar et al. 2013) of incorporation into dental composites have an potency to enhance antibacterial activity with superior mechanical properties (Mirhashemi et al. 2013). Application of TiO_2 into composite resins confers antibacterial properties. TiO_2 NPs at 1% concentration prominently inhibited *S. mutans* (Poosti et al. 2013), whereas more than 5% of TiO_2 NPs inhibited *S. mutans* and *S. sanguinis* but not on biofilm producing *L. acidophilus* (Sodagar et al. 2017).

Various methods have been used to modify the composite resins that prevent bacterial proliferation. Incorporation of low molecular weight organic or inorganic moieties including antibiotics, fluoride, iodine, zinc, QAM, chlorhexidine and silver based nanomaterials may have limitations toward antimicrobial property and mechanical property (Beyth et al. 2006). Due to the release of soluble agents, they are cytotoxic to the human tissues (Cocco et al. 2015). Inclusion of nanoparticles into dental materials have the benefit of antimicrobial property as well as remineralization of dental hard tissues (Angel Villegas et al. 2019). The composition, particle size, filler loading and the surface treatment of the antimicrobial fillers should permit release of ions even in an aqueous environment. Release of ions such as calcium, phosphate and fluoride ions have the benefits of reducing postoperative dentin hypersensitivity that enhance precipitation of hydroxyapatite crystals, better bonding of the material with tooth surface and durability (Tarle and Par 2018). However the mechanical properties such as polymerization shrinkage, shrinkage stress, elastic modulus, degradation, degree of conversion and biocompatibility should not be compromised.

Diverse research has been accomplished so far, to develop antimicrobial fillers of various types to provide the composite materials with enhanced antibacterial activity. Numerous studies have been employed on composites with added organic materials such as quaternary ammonium polyethylenimine nanoparticles, benzalkonium chloride, chlorhexidine, acrylic acid, triclosan and chitosan aminohexadecyl methacrylate. Also with additives like, quaternary ammonium dimethacrylate (QADM), 12-methacryloyloxydodecylpyridinium bromide (MDPB), dimethylaminohexadecyl methacrylate (DMAHDM), dimethyl-hexadecyl-methacryloxyethyl-ammonium iodide (DHMAI), and dimethylaminohexadecyl methacrylate that gave varying degree of success. In addition, inorganic fillers (mesoporous silica with chlorhexidine, zinc oxide and silver ions) can also be mixed with monomers. They get entrapped into polymers after polymerization and exert their antimicrobial property (Ohashi et al. 2004). Antibacterial activity of A-glass-CyCl-Ag is due to interaction of sulfadiazine with DNA and silver ion binding leads to deactivation of protein as well as expiration of the bacteria

Fluoridated glass, inorganic fluoride compounds and pre-reacted glass ionomer fillers (S-PRG) are the forms of fluoride that are incorporated with resin composites. Dental composites with S-PRG is termed as giomer. Giomer releases small amount of fluoride, and it exhibits superior optical properties and strength than conventional GIC (Garoushi et al. 2017). Moreover, inclusion of CaF_2 nanoparticles reduced mineral loss from the tooth margins. When strontium replaces Ca, it enhances the radiopacity and improves the antibacterial activity. Addition of 10–20% of monocalcium phosphate monohydrate (MCPM), tricalcium phosphate or tristrontium phosphate, help relief of residual stress by encouraging water induced expansion (Park and Ferracane 2014). This compensates the polymerization shrinkage of the composites (Aljabo et al. 2015). Nanoparticle amorphous calcium phosphate (NACP-size of 116 nm) decreased the demineralization depth of the enamel and increased the remineralization of adjacent tooth surface (Tezvergil-Mutluay et al. 2017). Also it reduced the penetration depth of the bacteria (Khvostenko et al. 2016). The ability of nanoassemblies to inhibit high bacterial load through bacterial membrane fusing, clumping and disintegration that causes significant bacterial death (Schnaider et al. 2019).

13 Bioactive Glass (BAG)

The bioactive glass was invented by Hench in 1969 (Hench et al. 2004). It is a soluble form of glass. The composition of BAG consists of $SiO_{2,}$ CaO,Na_2O and P_2O_5 in a variable concentration (Jones 2013) and can act as source of fluoride, calcium, strontium ions, and also control their release (Shahid et al. 2014). Therefore, by altering specific ingredient in a small proportion according to the particular need, it is possible to tailor BAG (Kaur et al. 2014). The BAG is capable to form apatite layer through precipitation of HA spontaneously (Jones 2013), and makes it a potential source of remineralizing ions (calcium and phosphate). BAG when exposed to water, exchanges sodium and calcium ions with the hydrogen ion of water and forms Si–OH groups (silica rich layer). During the rise in local pH, the hydroxyl ions attack Si–O–Si bonds and form $Si(OH)_4$. Then condensation of Si–OH groups occur and attract more calcium and phosphates ions (Hench 2006). Further, crystallization occurs in the form of amorphous calcium phosphate (ACP) to hydroxyl appatite (HA). It has been reported that the ability of BAG to form silicon-rich layer could serve as a template for HA precipitation. For this to happen, appropriate adjustment in hydrophilicity should be taken place (Spanovic et al. 2017). BAG increases the local pH initially and inhibits the matrix metalloprotinase activity that aids in precipitation of HA (Profeta 2014). Furthermore, it inhibits collagen degradation, upsurges the hardness of demineralized dentin. Henceforth, BAG has the ability to increase the longevity and stability of the hybrid layer by defending it from hydrolytic degradation (Tezvergil-Mutluay et al. 2017). The antimicrobial effect of BAG is mainly by the change in the local pH, in addition, direct contact toxicity also contributes to the improved effect (Chatzistavrou et al. 2014). Inclusion of 10% Al_3 to BAG improved the compressive strength without causing any adverse effect (De Caluwé et al. 2017). Incorporation of fluoride containing bioactive glass (BAG) reduces the susceptibility to SC. Monocalcium, dicalcium and tricalcium phosphates, hydroxyapatite and amorphous calcium phosphate are some of the fillers added to dental composites. Among these fillers, ACP is a direct precursor of HA (Dorozhkin 2010). When exposed to water, ACP dissolves and releases phosphates and calcium ions that subsequently transformed into HA ions (Eanes and Meyer 1977). The ACP/HA conversion is autocatalytic and forms a nuclei that progress the crystallization process (Boskey and Posner 1973). Hence, HA aids in remineralization (Skrtic et al. 2000). Pure form of ACP is unstable, thereby readily converts into HA within few hours (Pan et al. 2010).

14 Quaternary Ammonium Compounds

The development of quaternary ammonium methacrylate (QAM), and their incorporation into dental resins has promoted antimicrobial activities (Weng et al. 2018). Studies revealed that hydrophobic positively charged long polymeric alkyl chain of

QAM has the ability to penetrate the negatively charged cell membrane of the microorganisms (Skrtic et al. 2000). This enables cell membrane disruption, cytoplasmic leakage and finally death of microorganisms. Antibacterial mechanism of positively charged ammonium groups is mainly due to contact killing, and is governed by factors like chain length, number of nitrogen atoms and the nature of compound that attaches to this group. 5–10 wt% of QAMs can be used for composite resin (Liang et al. 2014). Specifically, long cationic polymers promote an increase in hydrophobicity of QAM. Hence, hydrophobicity property of QAM is directly proportional to the alkyl chain length of QAM (Tiller et al. 2001). Addition of chlorhexidine diacetate (1%) and 5% of dimethylamino-hexadecyl methacrylate (DMAHDM), a derivative of quaternary ammonium salts to self-cured resins showed significant antimicrobial action against *S. mutans* and *C. albicans* exhibits synergistic effect. These agents reduce the biofilm development without influencing the mechanical and physical properties (Campos et al. 2020).

A novel composite that consists of nanoparticles of amorphous calcium phosphate (NACP) and DMAHDM exhibited remineralizing and antimicrobial capabilities (Zhang et al. 2016). This is mainly due to the increase in CL of DMAHDM from 3 to 16 that significantly reduced the colony forming unit of microorganism and decrease the biofilm formation up to tenfold. Hence it is promising material for tooth cavity restoration. Incorporation of calcium phosphate nanoparticles along with quaternary ammonium dimethacrylate (QADM) and silver nanoparticles (Ag NP) into composites stimulated regenerative capacity and antibacterial activity (Cheng et al. 2012a).

15 Methods to Improve Mechanical Property

Zirconia particles block HA nucleation site and have the benefits of retardation of ACP conversion with improved mechanical properties (Skrtic et al. 2002). Thus it provides a long-lasting bioactive effect. Further, ACP composites when reinforced with 10% of inert glass fillers, there is an increase in mechanical properties (Marovic et al. 2014) as well as reduction in polymerization shrinkage. Thus incorporation of more inert fillers is significantly important to reduce filler/composite ratio. Also, addition of nano ACP particles is an alternative approach to increase the mechanical property with low cohesive strength that enables adequate ions release due to high surface area (Xu et al. 2011). A combination of nanoparticle amorphous calcium phosphate (NACP) and AgNP contributes to the antimicrobial property and remineralization capacity to composite material (Cheng et al. 2012b). Addition of zinc oxide particles ensures a better opacity and good antimicrobial property to the material. The primary effect of ZnO on bacteria is inhibition of the enzymes involved (Maas et al. 2017). It exhibits antibacterial activity only on the bacteria contacting it and also makes the resin weaker. To overcome this, AgNP can be mixed up along with QAMs (Zhang et al. 2013).

16 Chlorhexidine

Chlorhexidine (CHX) is a broad spectrum potent antimicrobial agent. Hence, believed as a gold standard for antibacterial application (Amin et al. 2009). Studies have shown that a gradual release into the environment leads to toxic effects to the tissues and affects the mechanical properties of the materials. Moreover, CHX is highly soluble and has poor substantivity (Bonesvoll and Gjermo 1978). It usually provides short-term antimicrobial effect and declines after a time period (Imazato 2003). The concept of Imazato et al. is "immobilized bactericide action" that means the antimicrobial monomers are not released in the environment as such, but contact inhibition takes place when the bacteria comes in direct contact with the material. Until then, it is stabilized in a carrier material (Imazato 2003). Hence, any antimicrobial agent when incorporated into a biomaterial have a finite duration of release. Thus, it has a long-lasting antibacterial effect without compromising the mechanical properties. GIC appended with chlorhexidine diacetate and digluconate have bactericidal action against *Streptococcus mutans and Lactobacillus acidophilus* (Türkün et al. 2008). Compared to these, CHX hexametaphosphate showed reduced solubility and a sustained release (Wood et al. 2015).

The DMAHDM monomer, one of the derivatives of quaternary ammonium salt along with chlorhexidine have a synergistic antimicrobial effect against *Streptococcus mutans and Candida albicans* without influencing the flexural strength, surface roughness and colour stability of the composite. Previous studies also demonstrated a synergistic effect of chlorhexidine when incorporated with other potent antifungal agents in dental materials. Recharge capacity of GIC with CHX has been recently investigated. The GIC has the ability to uptake CHX from its environment and release them in higher concentration via reversible process (Bellis et al. 2018). Matrix metalloproteinases (MMPs) present in saliva and cysteine cathepsins expressed by dentin-pulp complexes act synergistically, degrade hybrid layer and aide in caries progress (Nascimento 2011). CHX and green tea polyphenolepigallocatechin-3-gallate (EGCG) are potent inhibitors of MMP (Pallan et al. 2012). They reduced the rate of collagen degradation by preventing over activation of MMPs (Hashimoto et al. 2003). Further, these agents have the capability of inhibiting glucosyltranferases action, acid tolerance and acid production, hence the growth of cariogenic bacteria suppressed (Xu et al. 2011).

17 Antimicrobial Fillers in Dental Implants

Dental implant is a standard, recommended treatment protocol to replace, repair the lost or missing tooth structure. Peri-implant disease (PID) is the inflammation of the soft tissue around the implant, mainly due to plaque accumulation and biofilm formation (Renvert et al. 2018). PID can be of two types, peri-implant mucositis (PIM) and peri-implantitis (PI) (Berglundh et al. 2018). A high prevalence of anaerobic gram-negative organisms is associated with PIM, in addition to *S. aureus*, *S. mutans*, *E. coli*, *P. gingivalis* and *C. albicans* and can eventually progress into PI. Meanwhile, with appropriate treatment PIDs can be reversed, if not may lead to gradual bone loss and bacterial associated implant failure (Rosen et al. 2013). Hence, clinical management of PIDs is still challenging. Defensins and cathelicidins are the naturally occurring antimicrobial peptides (AMPs) that are present both in salivary and gingival secretions (Chen et al. 2017a). Further, AMPs are the key mediator in regulating microbial homeostasis normally and they establish the first line defence mechanism particularly in the gingival and periodontal disease progress (Khurshid et al. 2018). They are highly degradable by bacterial and host cell proteases.

Hence, incorporation of AMPs into engineered bioadhesive hydrogels not only protect AMPs from degradation but also deliver controlled antimicrobial activity over a period of time. Light curable gelatin methacryloyl hydrogel incorporated with AMPs gives gelatin methacryloyl antimicrobial peptide bioadhesives. Antimicrobial hydrogel bioadhesives revealed high antibacterial activity against *P. gingivalis* and are cytocompatible (Sani et al. 2019). Moreover, they create a favourable environment for the growth of migratory progenitor cells that stimulate bone regeneration. Hence, they can be used to treat PIDs. AMP coated dental implants protect against PIDs.

Titanium dioxide (TiO_2) NPs exhibits pronounced optical property, bioactivity, chemical stability and antibacterial activity. TiO_2 is most promising to have photocatalytic effect, hence when exposed to UV-A light generates electrons and holes at the valence band (Foster et al. 2011). The electrons from the valence band get excited and produce superoxide ion, whereas the holes form hydroxyl radicals (Mohammed et al. 2018). Further, production of reactive oxygen species attack the bacterial cell membrane and leads to cytoplasmic leakage (Gogniat et al. 2006). The direct contact toxic effect of TiO_2 is mainly due to photocatalytic disinfections that eventually leads to lipid peroxidation (Maness et al. 1999), protein alteration (Goulhen-Chollet et al. 2009) and DNA damage (Gogniat and Dukan 2007). TiO_2 binds to *E. coli*, causes cell disruption and lysis (Gumy et al. 2006; Carré et al. 2014). TiO_2 also possesses improved osteoinductive and osteointegration property (Li et al. 2015). The rutile TiO_2 nanorod arrays expressed potent photocatalytic antifungal and antibacterial activity against *C. albicans*, *A. actinomycetemcomitans*, *Aggregatibacter actinomycetemcomitans* and *P. gingivalis* (Jia et al. 2017). Moreover, implant surface modified with TiO_2 coating promoted adhesion and proliferation of periodontal ligament stem cells (PDLSCs) (Li et al. 2017) and also osteogenic differentiation of mesenchymal stem cells (MSCs) (Qiu et al. 2016). Anatase microspheres which is of $Ti(SO_4)$ origin, impregnated with AgNPs improved the antibacterial activity of the implant surface against *S. aureus* and *E. coli* (Weng et al. 2018). The Ag/TiO_2 combination exhibited excellent antibacterial effect due to the Schottky barrier effect and also possesses cytocompatibility with Newborn mouse calvaria-derived preosteoblastic cells (MC3T3-E1).

18 Denture Base Resins

Tooth loss or edentulism is seen in all races and across all nations of the world. An US study places the rate of edentulism of American elderly of age 65 years or more to be 19% (Dye et al. 2015), whereas 15% of UK people of the same age are edentulous (Peltzer et al. 2014). For completely edentulous people, complete dentures are still most commonly used treatment of choice. Partial dentures with acylic base plate are still used in several developing countries for partial edentulism.

Poly methyl methacrylate (PMMA) resin is the most commonly used denture base acrylic material for both types of edentulism for more than 70 years since its introduction. However, PMMA suffers from inherent drawbacks like high surface roughness, porosity and bad thermal conductor (Nandal et al. 2013). Unfortunately, these disadvantages plus its high hydrophobicity in aqueous environment do not prevent the overgrowth of a fungus *C. albicans* in chronic denture wearers. Though *C. albicans* is normally present in oral cavity as indigenous microbial flora (Cannon and Chaffin 1999), its overgrowth contributes to the clinical condition called Denture Stomatitis (DS).

19 Denture Stomatitis

DS refers to inflammatory condition of palatal mucosa corresponding to the place where the denture base remains in contact with the tissue (Dorocka-Bobkowska et al. 2010). DS is especially prevalent in elderly people with systemic diseases leading to immunocompromised status along with poor denture hygiene and xerostomia (Uzunoglu et al. 2014). *C. albicans* is not the primary pathogen as the recent reports show that DS can also be caused by other fungal species like *C. glabrata*, *C. dubliniensis*, *C. parapsilosis*, *C. krusei* and *C. tropicalis* (de Oliveira Mima et al. 2011). This has a special clinical relevance in today's time as most of the above mentioned species are resistant to common antifungal drugs (Redding et al. 2003). Bacteria like *S. mutans* and *Lactobacillus* species are also implicated in DS (Webb et al. 1998). So, prevention of such problems assumes greater importance than treatment. Keeping this in mind, a PMMA denture base with antimicrobial properties that can prevent the occurrence of DS is definitely preferable.

20 Antimicrobial Fillers in Denture Base Resins

It was found out that coating the PMMA resin with glow-discharge plasma (Zamperini et al. 2013), Mannan (Sato et al. 2013) or reactive oxygen species (ROS)-based disinfectant (Odagiri et al. 2012) could inhibit *C. albicans* but the coatings did not sustain longer in the aqueous oral environment. Thus, an external application of antimicrobial coating is of less clinical value. Incorporating the antimicrobial material as a filler into the PMMA resin is the logical next step in the research process.

The organic NPs have been primarily used to prevent the formation of secondary caries. Quaternary ammonium molecules can be combined with methacrylate monomer using silane bonds to produce quaternary ammonium methacrylate (QAMs). QAMs undergo polymerization with bisGMA (bisphenol A-glycidyl methacrylate) to produce resin polymer which is clinically useful (Gong et al. 2012). They are primarily not successfully used with PMMA denture base resin due to their inability to withstand high temperature and pressure generally required for curing the resin (Chen et al. 2017a). Though chitosan, yet another organic NPs is most abundantly available naturally, its clinical use is limited (Song and Ge 2019).

Incorporation of inorganic NPs, typically Silver (AgNPs) into the PMMA resin has stimulated a lot of research primarily due to their ability to withstand extreme environments (Arunachalam et al. 2015). Besides, they are not toxic to human tissues and equal importance is the fact that these metal fillers can be incorporated either into the powder or the liquid component of resin (Chladek et al. 2016) giving the flexibility of its usage. Their versatility lies in the fact that they can be manufactured in large-scale using variety of methods (Thomas et al. 2018). In fact, the most documented research focuses on using AgNPs into PMMA resin to produce antibacterial and antifungal denture base resin material that can be adopted clinically (Kassaee et al. 2008; Jabłońska-Stencel et al. 2018; Thomas et al. 2018; Chladek et al. 2019a, b; Jo et al. 2017; Chen et al. 2017b).

AgNPs possess broad spectrum of action covering the bacteria, fungi and viruses. The active silver ions released in the aqueous environment interact with proteins present in bacteria and cause cell lysis. In order to achieve this action, they are supplied in a variety of nanoforms and shapes like spheres, pores, capsules, tubes, shells, dendrimers or quantum dots (Şuhani et al. 2018). Kurt et al. (2017) studied the effect of adding AgNPs to PMMA denture base material in increasing concentrations and concluded that as the concentration of AgNPs increased, the antifungal activity also increased. The material was not cytotoxic to L929 mouse fibroblast cell line (Kurt et al. 2017).

In order to assess the long-lasting antimicrobial effect of AgNPs, the particles were incorporated in silver-sulfadiazine (AgSD) to form AgSD-loaded mesoporous silica nanoparticles (AgMSNs) which can release silver ions very slowly and for a prolonged duration in the aqueous medium. Besides acting as a carrier, sulfadiazine has anti-adhesive effect which is beneficial for preventing candida adhesion to oral mucosa. Jeong-Ki Jo et al. (2017) combined AgMSNs with PMMA to form a "rechargeable" resin. They found that flexural strength, hardness and anti-adhesive effects increased for up to a month (Jo et al. 2017)

Though AgNPs looks like an ideal antimicrobial filler to PMMA, it has some disadvantages. Mainly, due to its plasmon resonance effect, it imparts a dark brown colour to the final material. Obviously, it is aesthetically unacceptable in the oral cavity (Chladek et al. 2019b; Jabłońska-Stencel et al. 2018). In order to circumvent this clinical problem, AgNPs is used as silver sodium hydrogen zirconium phosphate

(SSHZP) which is white in colour and clinically acceptable. According to Jabłońska-Stencel et al. (2018), SSHZP filler concentration between 2 and 10 weight percentage (wt%) gave the best antimicrobial effect without compromising other essential mechanical properties (Jabłońska-Stencel et al. 2018).

Zirconium oxide nanoparticles (nano-ZrO_2) also have received a lot of attention for their ease of manufacturing and their efficiency (Gowri et al. 2014). Nano-ZrO_2 in various concentrations of 0% wt, 2.5% wt, 5% wt and 7.5% wt was polymerized with PMMA by Gad et al. (2017a) in their research work. The highest reduction in *C. albicans* was observed with 7.5% wt of nano-ZrO_2 (Gad et al. 2017b).

Ultrafine dispersed diamonds or detonation nanodiamonds (ND) have some eye-catching properties of high strength, chemical stability, thermal conductivity and good biocompatibility for use in biomedical applications (Mochalin et al. 2012). Mangal et al. (2019) compared ND performance with PMMA vs standard ZrO_2 with PMMA and discovered that 0.1–0.5 wt.% ND significantly improved the flexural strength, elastic modulus and surface hardness of resin and provided considerable resistance to *C. albicans* and reduction in salivary biofilm formation (Mangal et al. 2019). The same result was corroborated by Fouda et al. (2019).

Whiskers are a type of filamentary crystal, the tip of which is less than 1 nm with semi-conductive property and ability to release ROS. Silver-supported zirconium phosphate (Novaron) and Tetrapod-like zinc oxide whiskers (T-ZnOw) exhibited higher flexural strength and surface hardness and increased antibacterial activity (Chen et al. 2017a).

Glass fibres represent the architype fibre to reinforce denture base polymers due to its well known improvements in flexural strength and fatigue resistance. They were found to increase candida resistance also (Moreno-Maldonado et al. 2012; Gad et al. 2017b)

21 Antimicrobial Fillers for Other Applications

AgNPs was combined with vanadate nanowires to form silver vanadate decorated with AgNPs (β-$AgVO_3$). Ferreira et al. (2020) used silver vanadate as a filler in dental porcelain material and evaluated the mechanical and anti-microbiological properties. All the different strengths of silver vanadate increased the antimicrobial efficacy without changing hardness property (Ferreira et al. 2020).

Portland cement is a calcium silicate-based cement can be impregnated with AgNPs to form Portland cement nanocomposites. AgNPs give antimicrobial property to a bone graft and increased its bio-mechanical properties. This was confirmed by Nam (2017).

Dendrimer or Cascade polymer or Arborole is a type of nanoparticle consisting of lyophilic layer inside and lyophobic shell outside, act as drug carrier. It can be used to create different sizes and shapes of hydroxyapatite crystal to be used as a filler for dental materials (Bapat et al. 2019).

22 Conclusion

Incorporating an antimicrobial filler in restorative dental materials seems no more an option but a prerequisite for an ideal replacement material. The research for an ideal filler material which is not only antimicrobial but also augments the mechanical properties of the material is promising in some areas.

References

Al-Shammery D, Michelogiannakis D, Ahmed ZU et al (2019) Scope of antimicrobial photodynamic therapy in orthodontics and related research: a review. Photodiagn Photodyn Ther 25:456–459

Al Zraikat H, Palamara JE, Messer HH, Burrow MF, Reynolds EC (2011) The incorporation of casein phosphopeptide-amorphous calcium phosphate into a glass ionomer cement. Dent Mater 27:235–243

Alhajj N, Zakaria Z, Naharudin I, Ahsan F, Li W, Wong TW (2019) Critical physicochemical attributes of chitosan nanoparticles admixed lactose-PEG 3000 microparticles in pulmonary inhalation. Asian J Pharm Sci 15:374–384

Aljabo A, Xia W, Liaqat S, Khan MA, Knowles JC, Ashley P, Young AM (2015) Conversion, shrinkage, water sorption, flexural strength and modulus of re-mineralizing dental composites. Dent Mater 31:1279–1289

Allaker RP (2010) The use of nanoparticles to control oral biofilm formation. J Dent Res 89:1175–1186

Amin WM, Al-Ali MH, Salim NA, Al-Tarawneh SK (2009) A new form of intraoral delivery of antifungal drugs for the treatment of denture-induced oral candidosis. Eur J Dent 3:257–266

Argueta-Figueroa L, Morales-Luckie RA, Scougall-Vilchis RJ, Olea-Mejía OF (2014) Synthesis, characterization and antibacterial activity of copper, nickel and bimetallic Cu–Ni nanoparticles for potential use in dental materials. Prog Nat Sci Mater Int 24:321–328

Arunachalam A, Dhanapandian S, Manoharan C, Sivakumar G (2015) Physical properties of Zn doped TiO2 thin films with spray pyrolysis technique and its effects in antibacterial activity. Spectrochim Acta A Mol Biomol Spectrosc 138:105–112

Aziz N, Fatma T, Varma A, Prasad R (2014) Biogenic synthesis of silver nanoparticles using *Scenedesmus abundans* and evaluation of their antibacterial activity. J Nanopart, Article ID: 689419. https://doi.org/10.1155/2014/689419

Aziz N, Faraz M, Pandey R, Sakir M, Fatma T, Varma A, Barman I, Prasad R (2015) Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial and photocatalytic properties. Langmuir 31:11605–11612. https://doi.org/10.1021/acs.langmuir.5b03081

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of *Mucor hiemalis*-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Baig MS, Fleming GJP (2015) Conventional glass-ionomer materials: a review of the developments in glass powder, polyacid liquid and the strategies of reinforcement. J Dent 43:897–912

Bapat RA, Dharmadhikari S, Chaubal TV, Amin MCIM, Bapat P, Gorain B, Choudhury H, Vincent C, Kesharwani P (2019) The potential of dendrimer in delivery of therapeutics for dentistry. Heliyon 5:e02544

Bellis CA, Addison O, Nobbs AH, Duckworth PF, Holder JA, Barbour ME (2018) Glass ionomer cements with milled, dry chlorhexidine hexametaphosphate filler particles to provide long-term antimicrobial properties with recharge capacity. Dent Mater 34:1717–1726

Berglundh T, Armitage G, Araujo MG, Avila-Ortiz G, Blanco J, Camargo PM, Chen S, Cochran D, Derks J, Figuero E (2018) Peri-implant diseases and conditions: consensus report of workgroup 4 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions. J Periodontol 89:S313–SS18

Beyth N, Yudovin-Farber I, Bahir R, Domb AJ, Weiss EI (2006) Antibacterial activity of dental composites containing quaternary ammonium polyethylenimine nanoparticles against Streptococcus mutans. Biomaterials 27:3995–4002

Beyth N, Farah S, Domb AJ, Weiss EI (2014) Antibacterial dental resin composites. React Funct Polym 75:81–88

Bhuyan T, Mishra K, Khanuja M, Prasad R, Varma A (2015) Biosynthesis of zinc oxide nanoparticles from *Azadirachta indica* for antibacterial and photocatalytic applications. Mater Sci Semicond Process 32:55–61

Bonesvoll P, Gjermo P (1978) A comparison between chlorhexidine and some quaternary ammonium compounds with regard to retention, salivary concentration and plaque-inhibiting effect in the human mouth after mouth rinses. Arch Oral Biol 23:289–294

Borkow G, Zhou SS, Page T, Gabbay J (2010) A novel anti-influenza copper oxide containing respiratory face mask. PLoS One 5:e11295

Boskey AL, Posner AS (1973) Conversion of amorphous calcium phosphate to microcrystalline hydroxyapatite. A pH-dependent, solution-mediated, solid-solid conversion. J Phys Chem 77:2313–2317

Bourbia M, Ma D, Cvitkovitch DG, Santerre JP, Finer Y (2013) Cariogenic bacteria degrade dental resin composites and adhesives. J Dent Res 92:989–994

Boyd D, Towler MR (2005) The processing, mechanical properties and bioactivity of zinc based glass ionomer cements. J Mater Sci Mater Med 16:843–850

Camilleri J, Pitt Ford TR (2006) Mineral trioxide aggregate: a review of the constituents and biological properties of the material. Int Endod J 39:747–754

Campoccia D, Montanaro L, Arciola CR (2013) A review of the biomaterials technologies for infection-resistant surfaces. Biomaterials 34:8533–8554

Campos K d PL, Viana GM, Cabral LM, Portela MB, Junior RH, Cavalcante LM, Lourenço EJV, de Moraes Telles D (2020) Self-cured resin modified by quaternary ammonium methacrylates and chlorhexidine: cytotoxicity, antimicrobial, physical, and mechanical properties. Dent Mater 36:68–75

Cannon RD, Chaffin WL (1999) Oral colonization by Candida albicans. Crit Rev Oral Biol Med 10:359–383

Cao H, Liu X, Meng F, Chu PK (2011) Biological actions of silver nanoparticles embedded in titanium controlled by micro-galvanic effects. Biomaterials 32:693–705

Cao W, Yu Z, Wang X, Li Q, Xiao Y, Li P, Wang L, Ye Z, Xing X (2018) Novel resin-based dental material with anti-biofilm activity and improved mechanical property by incorporating hydrophilic cationic copolymer functionalized nanodiamond. J Mater Sci Mater Med 29:162

Carré G, Hamon E, Ennahar S, Estner M, Lett M-C, Horvatovich P, Gies J-P, Keller V, Keller N, Andre P (2014) TiO2 photocatalysis damages lipids and proteins in Escherichia coli. Appl Environ Microbiol 80:2573–2581

Chatterjee AK, Sarkar RK, Chattopadhyay AP, Aich P, Chakraborty R, Basu T (2012) A simple robust method for synthesis of metallic copper nanoparticles of high antibacterial potency against E. coli. Nanotechnology 23:085103

Chatzistavrou X, Christopher Fenno J, Faulk D, Badylak S, Kasuga T, Boccaccini AR, Papagerakis P (2014) Fabrication and characterization of bioactive and antibacterial composites for dental applications. Acta Biomater 10:3723–3732

Chen M-H (2010) Update on dental nanocomposites. J Dent Res 89:549–560

Chen J, Zhu Y, Song Y, Lin W, Zhan J, He J, Zheng J, Zhong C, Shi X, Liu S (2017a) Preparation of an antimicrobial surface by direct assembly of antimicrobial peptide with its surface binding activity. J Mater Chem B 5:2407–2415

Chen R, Han Z, Huang Z, Karki J, Wang C, Zhu B, Zhang X (2017b) Antibacterial activity, cytotoxicity and mechanical behavior of nano-enhanced denture base resin with different kinds of inorganic antibacterial agents. Dent Mater J 36:693–699

Chen Y, Xueyan M, Wang F (2018) Preparation and drug release of PVA composite nanofibers loaded chitosan microsphere. Polym Sci Ser A 60:311–321

Cheng L, Weir MD, Xu HHK, Antonucci JM, Kraigsley AM, Lin NJ, Lin-Gibson S, Zhou X (2012a) Antibacterial amorphous calcium phosphate nanocomposites with a quaternary ammonium dimethacrylate and silver nanoparticles. Dent Mater 28:561–572

Cheng L, Weir MD, Xu HHK, Kraigsley AM, Lin NJ, Lin-Gibson S, Zhou X (2012b) Antibacterial and physical properties of calcium–phosphate and calcium–fluoride nanocomposites with chlorhexidine. Dent Mater 28:573–583

Chladek G, Basa K, Mertas A, Pakieła W, Żmudzki J, Bobela E, Król W (2016) Effect of storage in distilled water for three months on the antimicrobial properties of poly (methyl methacrylate) denture base material doped with inorganic filler. Materials 9:328

Chladek G, Pakiela K, Pakiela W, Zmudzki J, Adamiak M, Krawczyk C (2019a) Effect of antibacterial silver-releasing filler on the physicochemical properties of poly(methyl methacrylate) denture base material. Materials 12:41–46

Chladek G, Pakieła K, Pakieła W, Żmudzki J, Adamiak M, Krawczyk C (2019b) Effect of antibacterial silver-releasing filler on the physicochemical properties of poly (methyl methacrylate) denture base material. Materials 12:4146

Cloutier M, Mantovani D, Rosei F (2015) Antibacterial coatings: challenges, perspectives, and opportunities. Trends Biotechnol 33:637–652

Cocco AR, de Oliveira da Rosa WL, da Silva AF, Lund RG, Piva E (2015) A systematic review about antibacterial monomers used in dental adhesive systems: Current status and further prospects. Dent Mater 31:1345–1362

De Caluwé T, Vercruysse CWJ, Ladik I, Convents R, Heidi D, Martens LC, Verbeeck RMH (2017) Addition of bioactive glass to glass ionomer cements: effect on the physico-chemical properties and biocompatibility. Dent Mater 33:e186–e203

De Gee AJ, Pallav P, Werner A, Davidson CL (1990) Annealing as a mechanism of increasing wear resistance of composites. Dent Mater 6:266–270

de Oliveira Mima EG, Pavarina AC, Silva MM, Ribeiro DG, Vergani CE, Kurachi C, Bagnato VS (2011) Denture stomatitis treated with photodynamic therapy: five cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 112:602–608

Deveci C, Tuzuner T, Cinar C, Odabas ME, Buruk CK (2019) Short-term antibacterial activity and compressive strength of biodentine containing chlorhexidine/cetirimide mixtures. Niger J Clin Pract 22:227

Dorocka-Bobkowska B, Zozulinska-Ziolkiewicz D, Wierusz-Wysocka B, Hedzelek W, Szumala-Kakol A, Budtz-Jörgensen E (2010) Candida-associated denture stomatitis in type 2 diabetes mellitus. Diabetes Res Clin Pract 90:81–86

Dorozhkin SV (2010) Amorphous calcium (ortho) phosphates. Acta Biomater 6:4457–4475

Drury JL, Chen YW, Plancich BJ, Taylor-Pashow KM, Hobbs DT, Wataha JC (2018) Release of calcium ions from particulate monosodium titanates for dental mineralization applications. Am J Dent 31:42B–48B

Dye B, Thornton-Evans G, Li X, Iafolla T (2015) Dental caries and tooth loss in adults in the United States, 2011-2012. NCHS Data Brief 2015:197

Eanes ED, Meyer JL (1977) The maturation of crystalline calcium phosphates in aqueous suspensions at physiologic pH. Calcif Tissue Res 23:259–269

Eiampongpaiboon T, Chung WO, Bryers JD, Chung K-H, Chan DCN (2015) Antibacterial activity of gold-titanates on Gram-positive cariogenic bacteria. Acta Biomater Odontol Scand 1:51–58

Eliades WAB (2002) Orthodontic material: scientific and clinical aspect. Thieme Medical Publishers, New York

Feagin F, Thiradilok S (1979) Effects of magnesium and fluoride on ion exchange and acid resistance of enamel. J Oral Pathol Med 8:23–27

Fernandes GL, Delbem ACB, Do Amaral JG, Gorup LF, Fernandes RA, de Souza Neto FN, Souza JAS, Monteiro DR, Hunt AMA, Camargo ER (2018) Nanosynthesis of silver-calcium glycerophosphate: promising association against oral pathogens. Antibiotics 7:52

Ferreira I, Vidal CL, Botelho AL, Ferreira PS, da Costa Valente ML, Schiavon MA, Alves OL, Reis ACD (2020) Effect of nanomaterial incorporation on the mechanical and microbiological properties of dental porcelain. J Prosthet Dent 123:529

Foster HA, Ditta IB, Varghese S, Steele A (2011) Photocatalytic disinfection using titanium dioxide: spectrum and mechanism of antimicrobial activity. Appl Microbiol Biotechnol 90:1847–1868

Fouda SM, Gad MM, Ellakany P, Al-Thobity AM, Al-Harbi FA, Virtanen JI, Raustia A (2019) The effect of nanodiamonds on candida albicans adhesion and surface characteristics of PMMA denture base material-an in vitro study. J Appl Oral Sci 2019:27

Gad MM, Al-Thobity AM, Shahin SY, Alsaqer BT, Ali AA (2017a) Inhibitory effect of zirconium oxide nanoparticles on Candida albicans adhesion to repaired polymethyl methacrylate denture bases and interim removable prostheses: a new approach for denture stomatitis prevention. Int J Nanomedicine 12:5409

Gad MM, Fouda SM, Al-Harbi FA, Näpänkangas R, Raustia A (2017b) PMMA denture base material enhancement: a review of fiber, filler, and nanofiller addition. Int J Nanomedicine 12:3801

Garcia IM, Leitune VCB, Balbinot GDS, Samuel SMW, Collares FM (2016) Influence of niobium pentoxide addition on the properties of glass ionomer cements. Acta Biomater Odontol Scand 2:138–143

Garoushi S, Vallittu P, Lassila L (2017) Hollow glass fibers in reinforcing glass ionomer cements. Dent Mater 33:e86–e93

Gerasymchuk Y, Lukowiak A, Wedzynska A, Kedziora A, Bugla-Ploskonska G, Piatek D, Bachanek T, Chernii V, Tomachynski L, Strek W (2016) New photosensitive nanometric graphite oxide composites as antimicrobial material with prolonged action. J Inorg Biochem 159:142–148

Gharatape A, Davaran S, Salehi R, Hamishehkar H (2016) Engineered gold nanoparticles for photothermal cancer therapy and bacteria killing. RSC Adv 6:111482–111516

Giannousi K, Lafazanis K, Arvanitidis J, Pantazaki A, Dendrinou-Samara C (2014) Hydrothermal synthesis of copper based nanoparticles: antimicrobial screening and interaction with DNA. J Inorg Biochem 133:24–32

Gogniat G, Dukan S (2007) TiO2 photocatalysis causes DNA damage via Fenton reaction-generated hydroxyl radicals during the recovery period. Appl Environ Microbiol 73:7740–7743

Gogniat G, Thyssen M, Denis M, Pulgarin C, Dukan S (2006) The bactericidal effect of TiO2 photocatalysis involves adsorption onto catalyst and the loss of membrane integrity. FEMS Microbiol Lett 258:18–24

Goldberg M (2008) In vitro and in vivo studies on the toxicity of dental resin components: a review. Clin Oral Investig 12:1–8

Gong SQ, Niu LN, Kemp LK, Yiu CK, Ryou H, Qi YP, Blizzard JD, Nikonov S, Brackett MG, Messer RL, Wu CD, Mao J, Bryan Brister L, Rueggeberg FA, Arola DD, Pashley DH, Tay FR (2012) Quaternary ammonium silane-functionalized, methacrylate resin composition with anti-microbial activities and self-repair potential. Acta Biomater 8:3270–3282

Goulhen-Chollet F, Josset S, Keller N, Keller V, Lett M-C (2009) Monitoring the bactericidal effect of UV-A photocatalysis: a first approach through 1D and 2D protein electrophoresis. Catal Today 147:169–172

Gowri S, Rajiv Gandhi R, Sundrarajan M (2014) Structural, optical, antibacterial and antifungal properties of zirconia nanoparticles by biobased protocol. J Mater Sci Technol 30:782–790

Graves JL Jr, Tajkarimi M, Cunningham Q, Campbell A, Nonga H, Harrison SH, Barrick JE (2015) Rapid evolution of silver nanoparticle resistance in Escherichia coli. Front Genet 6:42

Gu YW, Yap AUJ, Cheang P, Khor KA (2005) Zirconia–glass ionomer cement—a potential substitute for Miracle Mix. Scr Mater 52:113–116

Gumy D, Morais C, Bowen P, Pulgarin C, Giraldo S, Hajdu R, Kiwi J (2006) Catalytic activity of commercial of TiO2 powders for the abatement of the bacteria (E. coli) under solar simulated light: influence of the isoelectric point. Appl Catal B Environ 63:76–84

Hall-Stoodley L, William Costerton J, Stoodley P (2004) Bacterial biofilms: from the natural environment to infectious diseases. Nat Rev Microbiol 2:95–108

Han L, Mu LI, Kazuaki N, Neamat AB, Akira O, Naoko H, Masaaki I (2002) Effect of fluoride mouth rinse on fluoride releasing and recharging from aesthetic dental materials. Dent Mater J 21:285–295

Hashimoto M, Ohno H, Sano H, Kaga M, Oguchi H (2003) In vitro degradation of resin–dentin bonds analyzed by microtensile bond test, scanning and transmission electron microscopy. Biomaterials 24:3795–3803

Haskell EW, Stanley HR, Chellemi J, Stringfellow H (1978) Direct pulp capping treatment: a long-term follow-up. J Am Dent Assoc 97:607–612

Hatton RA, Miller AJ, Silva SRP (2008) Carbon nanotubes: a multi-functional material for organic optoelectronics. J Mater Chem 18:1183–1192

Hench LL (2006) The story of Bioglass. J Mater Sci Mater Med 17:967–978

Hench LL, Xynos ID, Polak JM (2004) Bioactive glasses for in situ tissue regeneration. J Biomater Sci 15:543–562

Hu X, Yuyun Z, Zhijian H, Aditya S, Shuai H, Tao W, Wenqi L et al (2013) Gold nanorods core/AgPt alloy nanodots shell: a novel potent antibacterial nanostructure. Nano Res 6:822–835

Hu X, Huang YY, Wang Y, Wang X, Hamblin MR (2018) Antimicrobial photodynamic therapy to control clinically relevant biofilm infections. Front Microbiol 9:1299

Ikemura K, Tay FR, Kouro Y, Endo T, Masahiro Y, Miyai K, Pashley DH (2003) Optimizing filler content in an adhesive system containing pre-reacted glass-ionomer fillers. Dent Mater 19:137–146

Imazato S (2003) Antibacterial properties of resin composites and dentin bonding systems. Dent Mater 19:449–457

Jabłońska-Stencel E, Pakieła W, Mertas A, Bobela E, Kasperski J, Chladek G (2018) Effect of silver-emitting filler on antimicrobial and mechanical properties of soft denture lining material. Materials 11:318

Jasmine S, Thangavelu A, Krishnamoorthy R et al (2020) Platelet concentrates as biomaterials in tissue engineering: a review. Regen Eng Transl Med. https://doi.org/10.1007/s40883-020-00165-z

Jia L, Qiu J, Lingqian D, Li Z, Liu H, Ge S (2017) TiO2 nanorod arrays as a photocatalytic coating enhanced antifungal and antibacterial efficiency of Ti substrates. Nanomedicine 12:761–776

Jo J-K, El-Fiqi A, Lee J-H, Kim D-A, Kim H-W, Lee H-H (2017) Rechargeable microbial anti-adhesive polymethyl methacrylate incorporating silver sulfadiazine-loaded mesoporous silica nanocarriers. Dent Mater 33:e361–ee72

Jones JR (2013) Review of bioactive glass: from Hench to hybrids. Acta Biomater 9:4457–4486

Karasenkov Y, Frolov G, Pogorelsky I, Latuta N, Gusev A, Kuznetsov D, Leont'ev V (2015) Colloidal metal oxide nanoparticle systems: the new promising way to prevent antibiotic resistance during treatment of local infectious processes. IOP Conf Ser 98:012038

Kassaee MZ, Akhavan A, Sheikh N, Sodagar A (2008) Antibacterial effects of a new dental acrylic resin containing silver nanoparticles. J Appl Polym Sci 110:1699–1703

Kaur G, Pandey OP, Singh K, Homa D, Scott B, Pickrell G (2014) A review of bioactive glasses: their structure, properties, fabrication and apatite formation. J Biomed Mater Res A 102:254–274

Khurshid Z, Zafar MS, Naseem M, Khan RS, Najeeb S (2018) Human oral defensins antimicrobial peptides: a future promising antimicrobial drug. Curr Pharm Des 24:1130–1137

Khvostenko D, Hilton TJ, Ferracane JL, Mitchell JC, Kruzic JJ (2016) Bioactive glass fillers reduce bacterial penetration into marginal gaps for composite restorations. Dent Mater 32:73–81

Konopka K, Goslinski T (2007) Photodynamic therapy in dentistry. J Dent Res 86:694–707

Kurt A, Erkose-Genc G, Uzun M, Emrence Z, Ustek D, Isik-Ozkol G (2017) The antifungal activity and cytotoxicity of silver containing denture base material. Niger J Clin Pract 20:290–295

Lai G, Li M (2012) Secondary caries. In: Contemporary approach to dental caries. InTech, London

Larsen IB, Munksgaard EG (1991) Effect of human saliva on surface degradation of composite resins. Eur J Oral Sci 99:254–261

Lear G, Lewis GD (2012) Microbial biofilms: current research and applications. Horizon Scientific Press, Poole

Lendenmann U, Grogan J, Oppenheim FG (2000) Saliva and dental pellicle-a review. Adv Dent Res 14:22–28

Leung D, Spratt DA, Pratten J, Gulabivala K, Mordan NJ, Young AM (2005) Chlorhexidine-releasing methacrylate dental composite materials. Biomaterials 26:7145–7153

Li Y, Li F, Zhang C, Gao B, Tan P, Mi B, Zhang Y, Cheng H, Liao H, Huo K (2015) The dimension of titania nanotubes influences implant success for osteoclastogenesis and osteogenesis patients. J Nanosci Nanotechnol 15:4136–4142

Li J, Dong Z, Lv F, Yu Q, Ma H, Yin J, Yi Z, Liu M, Chang J, Chengtie W (2016a) Preparation of copper-containing bioactive glass/eggshell membrane nanocomposites for improving angiogenesis, antibacterial activity and wound healing. Acta Biomater 36:254–266

Li M, Zheng M, Zhu Y, Xia H, Yao M, Chu X, Wang X, Yang K, Yang M, Yu Z (2016b) Toward a molecular understanding of the antibacterial mechanism of copper-bearing titanium alloys against Staphylococcus aureus. Adv Healthc Mater 5:557–566

Li Z, Qiu J, Ling Qian D, Lu J, Liu H, Ge S (2017) TiO2 nanorod arrays modified Ti substrates promote the adhesion, proliferation and osteogenic differentiation of human periodontal ligament stem cells. Mater Sci Eng 76:684–691

Liang X, Söderling E, Liu F, He J, Lassila LVJ, Vallittu PK (2014) Optimizing the concentration of quaternary ammonium dimethacrylate monomer in bis-GMA/TEGDMA dental resin system for antibacterial activity and mechanical properties. J Mater Sci Mater Med 25:1387–1393

Liu R, Tang Y, Zeng L, Zhao Y, Zheng M, Sun Z, Xiang L, Ren L, Yang K (2018) In vitro and in vivo studies of anti-bacterial copper-bearing titanium alloy for dental application. Dent Mater 34:1112–1126

Lynch I, Dawson KA (2008) Protein-nanoparticle interactions. Nano Today 3:40–47

Lynch CD, Opdam NJ, Hickel R, Brunton PA, Gurgan S, Kakaboura A, Shearer AC, Vanherle G, Wilson NHF (2014) Guidance on posterior resin composites: academy of operative dentistry-European section. J Dent 42:377–383

Maas MS, Alania Y, Natale LC, Rodrigues MC, Watts DC, Braga RR (2017) Trends in restorative composites research: what is in the future? Braz Oral Res 31:e55

Magalhães A-P-R, Francine-Couto LM, Alves C-RD-R-S, Estrela A, Estrela C, Carrião M-S, Bakuzis A-F, Lopes L-G (2016) Silver nanoparticles in resin luting cements: antibacterial and physiochemical properties. J Clin Exp Dent 8:e415

Mahfouz M, Esaid AA (2014) Dental caries prevalence among 12–15 year old Palestinian children. Int Sch Res Notices 2014:785404

Makhluf S, Dror R, Nitzan Y, Abramovich Y, Jelinek R, Gedanken A (2005) Microwave-assisted synthesis of nanocrystalline MgO and its use as a bacteriocide. Adv Funct Mater 15:1708–1715

Maness P-C, Smolinski S, Blake DM, Huang Z, Wolfrum EJ, Jacoby WA (1999) Bactericidal activity of photocatalytic TiO2 reaction: toward an understanding of its killing mechanism. Appl Environ Microbiol 65:4094–4098

Mangal U, Kim J-Y, Seo J-Y, Kwon J-S, Choi S-H (2019) Novel poly (methyl methacrylate) containing nanodiamond to improve the mechanical properties and fungal resistance. Materials 12:3438

Marovic D, Tarle Z, Hiller K-A, Müller R, Rosentritt M, Skrtic D, Schmalz G (2014) Reinforcement of experimental composite materials based on amorphous calcium phosphate with inert fillers. Dent Mater 30:1052–1060

Marsh PD (2004) Dental plaque as a microbial biofilm. Caries Res 38:204–211

Melo MAS, Weir MD, Rodrigues LKA, Xu HHK (2013) Novel calcium phosphate nanocomposite with caries-inhibition in a human in situ model. Dent Mater 29:231–240

Millenbaugh NJ, Baskin JB, DeSilva MN, Elliott WR, Glickman RD (2015) Photothermal killing of Staphylococcus aureus using antibody-targeted gold nanoparticles. Int J Nanomed 10:1953–1960

Mirhashemi AH, Bahador A, Kassaee MZ, Daryakenari G, Ahmad-Akhoundi MS, Sodagar A (2013) Antimicrobial effect of nano-zinc oxide and nano-chitosan particles in dental composite used in orthodontics. J Med Bacteriol 2:1–10

Mochalin VN, Shenderova O, Ho D, Gogotsi Y (2012) The properties and applications of nanodiamonds. Nat Nanotechnol 7:11

Moghimi SM, Szebeni J (2003) Stealth liposomes and long circulating nanoparticles: critical issues in pharmacokinetics, opsonization and protein-binding properties. Prog Lipid Res 42:463–478

Mohammed FH, Niazy MA, El-Sharkawy DA (2018) The antibacterial activity of titanium dioxide nanoparticles incorporated into resin composite restoration (in vivo study). Al-Azhar Dent J Girls 5:173–180

Moheet IA, Luddin N, Rahman IA, Kannan TP, Ghani NRNA, Masudi SM (2019) Modifications of glass ionomer cement powder by addition of recently fabricated nano-fillers and their effect on the properties: a review. Eur J Dent 13(3):470–477

Moreno-Maldonado V, Acosta-Torres LS, Barceló-Santana FH, Vanegas-Lancón RD, Plata-Rodríguez ME, Castano VM (2012) Fiber-reinforced nanopigmented poly (methyl methacrylate) as improved denture base. J Appl Polym Sci 126:289–296

Morim S (2016) Antibacterial efficacy of gold-titanate nanoparticles as an intracanal medicament. MSD Thesis. University of Washington

Morones JR, Elechiguerra JL, Camacho A, Holt K, Kouri JB, Ramírez JT, Yacaman MJ (2005) The bactericidal effect of silver nanoparticles. Nanotechnology 16:2346

Moshaverinia A, Ansari S, Moshaverinia M, Roohpour N, Darr JA, Rehman I (2008) Effects of incorporation of hydroxyapatite and fluoroapatite nanobioceramics into conventional glass ionomer cements (GIC). Acta Biomater 4:432–440

Munoz Bonilla A, Marta Fernández G (2012) Polymeric materials with antimicrobial activity. Prog Polym Sci 37:281–339

Nam KY (2017) Characterization and antimicrobial efficacy of Portland cement impregnated with silver nanoparticles. J Adv Prosthodont 9:217–223

Nandal S, Ghalaut P, Shekhawat H, Gulati MS (2013) New era in denture base resins: a review. Dent J Adv Stud 1:136–143

Nascimento FD, Minciotti CL, Geraldeli S, Carrilho MR, Pashley DH, Tay FR, Nader HB, Salo T, Tjäderhane L, Tersariol ILS (2011) Cysteine cathepsins in human carious dentin. J Dent Res 90:506–511

Nel A, Xia T, Mädler L, Li N (2006) Toxic potential of materials at the nanolevel. Science 311:622–627

Nguyen S, Hiorth M (2015) Advanced drug delivery systems for local treatment of the oral cavity. Ther Deliv 6:595–608

Odagiri K, Sawada T, Hori N, Seimiya K, Otsuji T, Hamada N, Kimoto K (2012) Evaluation of denture base resin after disinfection method using reactive oxygen species (ROS). Dent Mater J 31:443–448

Ohashi S, Saku S, Yamamoto K (2004) Antibacterial activity of silver inorganic agent YDA filler. J Oral Rehabil 31:364–367

Olenin AY, Lisichkin GV (2011) Metal nanoparticles in condensed media: preparation and the bulk and surface structural dynamics. Russ Chem Rev 80:605

Oliva A, Ragione FD, Salerno A, Riccio V, Gianpaolo T, Cozzolino A, Salvatore D'A, Pontoni G, Zappia V (1996) Biocompatibility studies on glass ionomer cements by primary cultures of human osteoblasts. Biomaterials 17:1351–1356

Onaizi SA, Leong SS (2011) Tethering antimicrobial peptides: current status and potential challenges. Biotechnol Adv 29:67–74

Padovani GC, Feitosa VP, Sauro S, Tay FR, Durán G, Paula AJ, Durán N (2015) Advances in dental materials through nanotechnology: facts, perspectives and toxicological aspects. Trends Biotechnol 33:621–636

Pal S, Tak YK, Song JM (2007) Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the gram-negative bacterium Escherichia coli. Appl Environ Microbiol 73:1712–1720

Pallan S, Araujo MVF, Cilli R, Prakki A (2012) Mechanical properties and characteristics of developmental copolymers incorporating catechin or chlorhexidine. Dent Mater 28:687–694

Pan H, Liu XY, Tang R, Hong Yao X (2010) Mystery of the transformation from amorphous calcium phosphate to hydroxyapatite. Chem Commun 46:7415–7417

Pang H, Lu Q, Li Y, Gao F (2009) Facile synthesis of nickel oxide nanotubes and their antibacterial, electrochemical and magnetic properties. Chem Commun 2009:7542–7544

Papacchini F, Goracci C, Sadek FT, Monticelli F, Garcia-Godoy F, Ferrari M (2005) Microtensile bond strength to ground enamel by glass-ionomers, resin-modified glass-ionomers, and resin composites used as pit and fissure sealants. J Dent 33:459–467

Park JW, Ferracane JL (2014) Water aging reverses residual stresses in hydrophilic dental composites. J Dent Res 93:195–200

Peltzer K, Hewlett S, Yawson AE, Moynihan P, Preet R, Wu F, Guo G, Arokiasamy P, Snodgrass JJ, Chatterji S, Engelstad ME, Kowal P (2014) Prevalence of loss of all teeth (edentulism) and associated factors in older adults in China, Ghana, India, Mexico, Russia and South Africa. Int J Environ Res Public Health 11:11308–11324

Perinelli DR, Fagioli L, Campana R et al (2018) Chitosan-based nanosystems and their exploited antimicrobial activity. Eur J Pharm Sci 117:8–20

Phillips RW, Anusavice KJ (2013) Phillips' science of dental materials. Elsevier, London

Poorzandpoush K, Omrani L-R, Jafarnia SH, Golkar P, Atai M (2017) Effect of addition of Nano hydroxyapatite particles on wear of resin modified glass ionomer by tooth brushing simulation. J Clin Exp Dent 9:e372

Poosti M, Ramazanzadeh BA, Zebarjad M, Javadzadeh P, Naderinasab M, Shakeri MT (2013) Shear bond strength and antibacterial effects of orthodontic composite containing TiO2 nanoparticles. Eur J Orthod 35:676–679

Prasad R (2014) Synthesis of silver nanoparticles in photosynthetic plants. J Nanopart, Article ID: 963961. https://doi.org/10.1155/2014/963961

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer International Publishing, Cham. ISBN 978-3-319-42989-2

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd., Singapore. ISBN 978-3-319-68423-9

Prasad R, Swamy VS (2013) Antibacterial activity of silver nanoparticles synthesized by bark extract of *Syzygium cumini*. J Nanopart. https://doi.org/10.1155/2013/431218

Profeta AC (2014) Dentine bonding agents comprising calcium-silicates to support proactive dental care: origins, development and future. Dent Mater J 33:443–452

Qiu J, Li J, Wang S, Ma B, Zhang S, Guo W, Zhang X, Tang W, Sang Y, Liu H (2016) TiO2 nanorod array constructed nanotopography for regulation of mesenchymal stem cells fate and the realization of location-committed stem cell differentiation. Small 12:1770–1778

Qu J, Huang Y, Lv X (2019) Crisis of antimicrobial resistance in China: now and the future. Front Microbiol 10:2240

Raafat D, Sahl H-G (2009) Chitosan and its antimicrobial potential–a critical literature survey. Microb Biotechnol 2:186–201

Raffi M, Mehrwan S, Bhatti TM, Akhter JI, Hameed A, Yawar W, Masood Ul Hasan M (2010) Investigations into the antibacterial behavior of copper nanoparticles against Escherichia coli. Ann Microbiol 60:75–80

Raghupathi KR, Koodali RT, Manna AC (2011) Size-dependent bacterial growth inhibition and mechanism of antibacterial activity of zinc oxide nanoparticles. Langmuir 27:4020–4028

Rago I, Chandraiahgari CR, Bracciale MP, De Bellis G, Zanni E, Guidi MC, Sali D, Broggi A, Palleschi C, Sarto MS (2014) Zinc oxide microrods and nanorods: different antibacterial activity and their mode of action against Gram-positive bacteria. RSC Adv 4:56031–56040

Ranjita RM (2017) Metal nanoparticles in pharma, 1st edn. Springer, Berlin

Rastelli ANS, Jacomassi DP, Faloni APS, Queiroz TP, Rojas SS, Bernardi MINÊB, Bagnato VS, Hernandes AÔC (2012) The filler content of the dental composite resins and their influence on different properties. Microsc Res Tech 75:758–765

Redding SW, Kirkpatrick WR, Saville S, Coco BJ, White W, Fothergill A, Rinaldi M, Eng T, Patterson TF, Lopez-Ribot J (2003) Multiple patterns of resistance to fluconazole in Candida glabrata isolates from a patient with oropharyngeal candidiasis receiving head and neck radiation. J Clin Microbiol 41:619–622

Ren G, Hu D, Cheng EWC (2009) Int J Antimicrob Agents 33:587–590

Renvert S, Rutger Persson G, Pirih FQ, Camargo PM (2018) Peri-implant health, peri-implant mucositis, and peri-implantitis: case definitions and diagnostic considerations. J Clin Periodontol 45:S278–SS85

Reston EG, de Souza Costa CA (2009) Scanning electron microscopy evaluation of the hard tissue barrier after pulp capping with calcium hydroxide, mineral trioxide aggregate (MTA) or ProRoot MTA. Aust Endod J 35:78–84

Roberts HW, Toth JM, Berzins DW, Charlton DG (2008) Mineral trioxide aggregate material use in endodontic treatment: a review of the literature. Dent Mater 24:149–164

Rosen P, Clem D, Cochran DL, Froum S, McAllister B, Renvert S, Wang HL (2013) Peri-implant mucositis and peri-implantitis: a current understanding of their diagnoses and clinical implications. J Periodontol 84:436–443

Rosenbaum J, Versace DL, Abbad-Andallousi S, Pires R, Azevedo C, Cénédese P, Dubot P (2017) Antibacterial properties of nanostructured Cu–TiO 2 surfaces for dental implants. Biomater Sci 5:455–462

Saafan A, Zaazou MH, Sallam MK, Mosallam O, El Danaf HA (2018) Assessment of photodynamic therapy and nanoparticles effects on caries models. Open Access Macedon J Med Sci 6:1289

Sakaguchi R (2005) Review of the current status and challenges for dental posterior restorative composites: clinical, chemistry, and physical behavior considerations. Summary of discussion from the Portland Composites Symposium (POCOS) June 17-19, 2004, Oregon Health & Science University, Portland, Oregon. Dent Mater 21:3–6

Sakaguchi RL, Powers JM, Craig S (2006) Restorative dental materials. Mosby, St. Louis

Sani ES, Lara RP, Aldawood Z, Bassir SH, Nguyen D, Kantarci A, Intini G, Annabi N (2019) An antimicrobial dental light curable bioadhesive hydrogel for treatment of peri-implant diseases. Matter 1:926–944

Sato M, Ohshima T, Maeda N, Ohkubo C (2013) Inhibitory effect of coated mannan against the adhesion of Candida biofilms to denture base resin. Dent Mater J 32:355–360

Schnaider L, Ghosh M, Bychenko D, Grigoriants I, Ya'ari S, Antsel TS, Matalon S, Sarig R, Brosh T, Pilo R (2019) Enhanced nanoassembly-incorporated antibacterial composite materials. ACS Appl Mater Interfaces 11:21334–21342

Seil JT, Webster TJ (2012) Antimicrobial applications of nanotechnology: methods and literature. Int J Nanomedicine 7:2767

Sevinç A, Berdan A, Hanley L (2010) Antibacterial activity of dental composites containing zinc oxide nanoparticles. J Biomed Mater Res B Appl Biomater 94:22–31

Shahid S, Hassan U, Billington RW, Hill RG, Anderson P (2014) Glass ionomer cements: effect of strontium substitution on esthetics, radiopacity and fluoride release. Dent Mater 30:308–313

Shin S-Y, Park H-N, Kim K-H, Lee M-H, Choi YS, Park Y-J, Lee Y-M, Young K, Rhyu I-C, Han S-B (2005) Biological evaluation of chitosan nanofiber membrane for guided bone regeneration. J Periodontol 76:1778–1784

Siqueira JF (2001) Strategies to treat infected root canals. CDA 29:825–838

Sirelkhatim A, Mahmud S, Seeni A, Kaus NHM, Ann LC, Bakhori SKM, Hasan H, Mohamad D (2015) Review on zinc oxide nanoparticles: antibacterial activity and toxicity mechanism. Nano-Micro Lett 7:219–242

Skrtic D, Antonucci JM, Eanes ED, Eichmiller FC, Schumacher GE (2000) Physicochemical evaluation of bioactive polymeric composites based on hybrid amorphous calcium phosphates. J Biomed Mater Res 53:381–391

Skrtic D, Antonucci JM, Eanes ED, Brunworth RT (2002) Silica-and zirconia-hybridized amorphous calcium phosphate: Effect on transformation to hydroxyapatite. J Biomed Mater Res 59:597–604

Slenters TV, Hauser-Gerspach I, Daniels AU, Fromm KM (2008) Silver coordination compounds as light-stable, nano-structured and anti-bacterial coatings for dental implant and restorative materials. J Mater Chem 18:5359–5362

Sodagar A, Bahador A, Khalil S, Shahroudi AS, Kassaee MZ (2013) The effect of TiO2 and SiO2 nanoparticles on flexural strength of poly (methyl methacrylate) acrylic resins. J Prosthodont Res 57:15–19

Sodagar A, Akhoundi MSA, Bahador A, Jalali YF, Behzadi Z, Elhaminejad F, Mirhashemi AH (2017) Effect of TiO2 nanoparticles incorporation on antibacterial properties and shear bond strength of dental composite used in Orthodontics. Dent Press J Orthodont 22:67–74

Song W, Ge S (2019) Application of antimicrobial nanoparticles in dentistry. Molecules 24:1033

Spanovic N, Par M, Marovic D, Sever EK, Gamulin O, Tarle Z (2017) Development of experimental bioactive composites with reduced water sorption. In: 3rd international congress of the school of dental medicine. University of Zagreb, Zagreb

Stanley HR (1989) Pulp capping: conserving the dental pulp—can it be done? Is it worth it? Oral Surg Oral Med Oral Pathol 68:628–639

Stansbury JW (2000) Curing dental resins and composites by photopolymerization. J Esthet Restor Dent 12:300–308

Şuhani MF, Băciuț G, Băciuț M, Şuhani R, Bran S (2018) Current perspectives regarding the application and incorporation of silver nanoparticles into dental biomaterials. Clujul Med 91:274

Swamy VS, Prasad R (2012) Green synthesis of silver nanoparticles from the leaf extract of *Santalum album* and its antimicrobial activity. J Optoelectron Biomed Mater 4(3):53–59

Takagi S, Chow LC, Hirayama S, Eichmiller FC (2003) Properties of elastomeric calcium phosphate cement–chitosan composites. Dent Mater 19:797–804

Takasaki AA, Aoki A, Mizutani K, Schwarz F, Sculean A, Wang CY et al (2009) Application of antimicrobial photodynamic therapy in periodontal and peri-implant diseases. Periodontol 51:109–140

Tanaka CB, Lopes DP, Kikuchi LNT, Moreira MS, Catalani LH, Braga RR, Kruzic JJ, Gonçalves F (2020) Development of novel dental restorative composites with dibasic calcium phosphate loaded chitosan fillers. Dent Mater 36:551–559

Tarle Z, Par M (2018) Bioactive dental composite materials. Med Sci 45:83–100

Tezvergil-Mutluay A, Seseogullari-Dirihan R, Feitosa VP, Cama G, Brauer DS, Sauro S (2017) Effects of composites containing bioactive glasses on demineralized dentin. J Dent Res 96:999–1005

Thallinger B, Prasetyo EN, Nyanhongo GS, Guebitz GM (2013) Antimicrobial enzymes: an emerging strategy to fight microbes and microbial biofilms. Biotechnol J 8:97–109

Thampi VVA, Prabhu M, Kavitha K, Manivasakan P, Prabu P, Rajendran V, Shankar S, Kulandaivelu P (2014) Hydroxyapatite, alumina/zirconia, and nanobioactive glass cement for tooth-restoring applications. Ceram Int 40:14355–14365

Thomas R, Snigdha S, Bhavitha KB, Babu S, Ajith A, Radhakrishnan EK (2018) Biofabricated silver nanoparticles incorporated polymethyl methacrylate as a dental adhesive material with antibacterial and antibiofilm activity against Streptococcus mutans. Biotech 8:404

Tiller JC, Liao C-J, Lewis K, Klibanov AM (2001) Designing surfaces that kill bacteria on contact. Proc Natl Acad Sci 98:5981–5985

Türkün LSE, Türkün M, Rul FE, Ates M, Brugger S (2008) Long-term antibacterial effects and physical properties of a chlorhexidine-containing glass ionomer cement. J Esthet Restor Dent 20:29–44

Turner JE, Moore DW, Shaw BS (1975) Prevalence and antibiotic susceptibility of organisms isolated from acute soft-tissue abscesses secondary to dental caries. Oral Surg Oral Med Oral Pathol 39:848–857

Uzunoglu E, Bicer AZY, Dolapci I, Dogan A (2014) Biofilm-forming ability and adherence to poly-(methyl-methacrylate) acrylic resin materials of oral Candida albicans strains isolated from HIV positive subjects. J Adv Prosthodont 6:30–34

Venhoven BAM, De Gee AJ, Davidson CL (1993) Polymerization contraction and conversion of light-curing BisGMA-based methacrylate resins. Biomaterials 14:871–875

Villegas A, Natalia MJSC, Ajá MS, Rocca DM, Becerra MC, Molina GF, Palma SD (2019) Novel antibacterial resin-based filling material containing nanoparticles for the potential one-step treatment of caries. J Healthc Eng 2019:8

Von Eiff C, Arciola CR, Lucio M, Becker K, Campoccia D (2006) Emerging Staphylococcus species as new pathogens in implant infections. Int J Artif Organs 29:360–367

Wahab R, Mishra A, Soon-Il Y, Hwang IH, Mussarat J, Al-Khedhairy AA, Kim Y-S, Shin H-S (2012) Fabrication, growth mechanism and antibacterial activity of ZnO micro-spheres prepared via solution process. Biomass Bioenergy 39:227–236

Wang D, Lin Z, Wang T, Yao Z, Qin M, Zheng S, Wei L (2016) Where does the toxicity of metal oxide nanoparticles come from: the nanoparticles, the ions, or a combination of both? J Hazard Mater 308:328–334

Webb BC, Thomas CJ, Willcox MDP, Harty DWS, Knox KW (1998) Candida-associated denture stomatitis. Aetiology and management: a review: Part 1. Factors influencing distribution of candida species in the oral cavity. Aust Dent J 43:45–50

Wei G, Sun F, Liu F, Cao L, Yang J, Chen Y (2019) Antimicrobial resistance surveillance and prediction of gram-negative bacteria based on antimicrobial consumption in a hospital setting: a 15-year retrospective study. Medicine (Baltimore) 98:e17157

Weng S, Xu Z, Liu G, Guan Y, Wu F, Luo Y (2018) Synthesis, characterization, antibacterial activity in dark and in vitro cytocompatibility of Ag-incorporated TiO 2 microspheres with high specific surface area. J Mater Sci 29:50

Whitesides GM (2003) The 'right' size in nanobiotechnology. Nat Biotechnol 21:1161–1165

Wiegand A, Buchalla W, Attin T (2007) Review on fluoride-releasing restorative materials—fluoride release and uptake characteristics, antibacterial activity and influence on caries formation. Dent Mater 23:343–362

Wood NJ, Jenkinson HF, Davis SA, Mann S, O'Sullivan DJ, Barbour ME (2015) Chlorhexidine hexametaphosphate nanoparticles as a novel antimicrobial coating for dental implants. J Mater Sci Mater Med 26:201

Xie D, Weng Y, Guo X, Zhao J, Gregory RL, Zheng C (2011) Preparation and evaluation of a novel glass-ionomer cement with antibacterial functions. Dent Mater 27:487–496

Xu HHK, Moreau JL, Sun L, Chow LC (2011) Nanocomposite containing amorphous calcium phosphate nanoparticles for caries inhibition. Dent Mater 27:762–769

Yadav L, Tripathi RM, Prasad R, Pudake RN, Mittal J (2017) Antibacterial activity of Cu nanoparticles against *E. coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Nano Biomed Eng 9(1):9–14. https://doi.org/10.5101/nbe.v9i1.p9-14

Yan N, Chen X (2015) Sustainability: don't waste seafood waste. Nature 524:155–157

Yang H, Liu C, Yang D, Zhang H, Xi Z (2009) Comparative study of cytotoxicity, oxidative stress and genotoxicity induced by four typical nanomaterials: the role of particle size, shape and composition. J Appl Toxicol 29:69–78

Yli-Urpo H, Lassila LVJ, Närhi T, Vallittu PK (2005) Compressive strength and surface characterization of glass ionomer cements modified by particles of bioactive glass. Dent Mater 21:201–209

Zamperini CA, de Lima Carneiro H, Rangel EC, Cruz NC, Vergani CE, Machado AL (2013) In vitro adhesion of Candida glabrata to denture base acrylic resin modified by glow-discharge plasma treatment. Mycoses 56:134–144

Zhang L, Jiang Y, Ding Y, Povey M, York D (2007) Investigation into the antibacterial behaviour of suspensions of ZnO nanoparticles (ZnO nanofluids). J Nanopart Res 9:479–489

Zhang L, Gu FX, Chan JM, Wang AZ, Langer RS, Farokhzad OC (2008) Nanoparticles in medicine: therapeutic applications and developments. Clin Pharmacol Therap 83:761–769

Zhang K, Li F, Imazato S, Cheng L, Liu H, Arola DD, Bai Y, Xu HHK (2013) Dual antibacterial agents of nano-silver and 12-methacryloyloxydodecylpyridinium bromide in dental adhesive to inhibit caries. J Biomed Mater Res Pt B 101:929–938

Zhang K, Cheng L, Weir MD, Bai Y-X, Xu HHK (2016) Effects of quaternary ammonium chain length on the antibacterial and remineralizing effects of a calcium phosphate nanocomposite. Int J Oral Sci 8:45–53

Zoergiebel J, Ilie N (2013) Evaluation of a conventional glass ionomer cement with new zinc formulation: effect of coating, aging and storage agents. Clin Oral Investig 17:619–626