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Research Progress of Dental Antibacterial Materials

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Abstract

Dental caries are one of the most common diseases in the mouth and are usually repaired with dental composites. However, due to the shrinkage of dental composite resin, microleakage and repair failure lead to recurrent dental caries. Therefore, it is necessary to improve the antibacterial performance of dental resin composites. In this paper, the mechanism of common antibacterial agents and the research progress of oral adhesives in recent years are reviewed, and the development prospect of antibacterial dental resin composites is prospected.

Keywords

Composite Materials; Antibacterial Material; Oral.

1. Introduction

Dental caries is one of the most common chronic diseases in oral cavity. It is mainly caused by the corrosion of tooth hard tissues by acidic by-products produced by bacterial fermentation substances in daily diet. Its pathological formation process is complicated and long[1]. However, dental caries are not a self-healing disease and must be treated and filled with suitable materials.

Dental materials mainly consist of monomers, micro-nano fillers, coupling agents, initiators, etc[2]. However, because the polymerization process in dental composites usually leads to polymerization shrinkage, higher shrinkage rate leads to higher shrinkage stress and lower bonding efficiency, which reduces the mechanical and physical properties of the restorative materials, resulting in microleakage and repair failure[3], and further leads to recurrent dental caries, resulting in short resin service life.

Therefore, the research and development of good antibacterial, long service life, good biocompatibility of composite resin materials become the key. In order to improve dental resin composite antibacterial ability, have a lot of work, such as adding antibacterial agent (wash will taihe fluoride), integration of quaternary ammonium salt and add metal ion/oxide (zinc and silver), in order to enhance the antibacterial performance, this will help prevent dental composites and wall near the interface between the development of recurrent lesions[4]. At the same time, the antibacterial peptides, including natural antibacterial peptides and synthetic antibacterial peptides, have been studied and applied in the treatment and prevention of dental caries[5]. This paper focuses on the research progress of antibacterial mechanism and preparation methods of common dental antibacterial materials.Types of common antibacterial agents and their antibacterial mechanism.

2. Types of Common Antibacterial Agents and Their Antibacterial Mechanism

2.1. Quaternary Ammonium Salt Type Antibacterial Agent

It is generally believed that the antibacterial mechanism of quaternary ammonium salt materials is "contact killing". Quaternary ammonium compounds contain four organic groups linked to nitrogen, of which at least one substituent is a long alkyl chain. A long oleophilic alkyl chain penetrates the bacterial membrane by binding to cell wall components, resulting in leakage of bacterial cytoplasmic material, autolysis, and cell death[6].

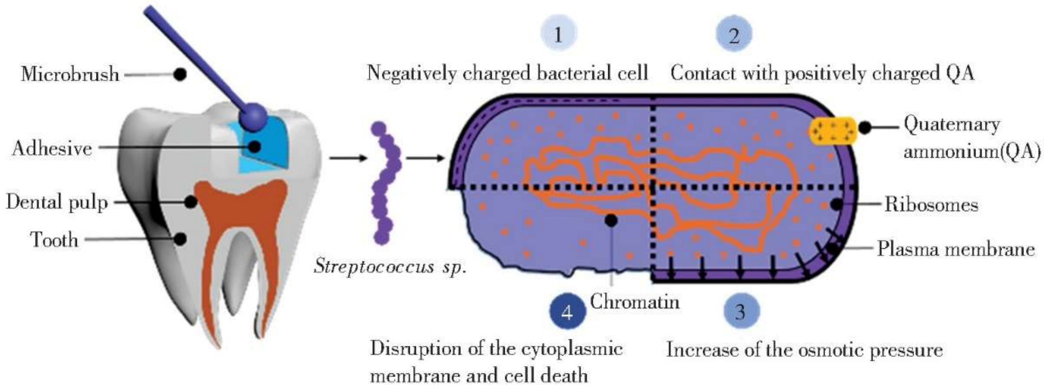

Fig. 1 [7] Antibacteria mechanism of action of the quaternary ammonium

Alkyl chain length has great influence on antibacterial activity[8]. Li[9] et al. synthesized a QAM and systematically changed the alkyl chain length to study the effect of chain length on the antibacterial effect of cured resin. As the chain length increased from 3 to 16, MIC and MBC against S. mutans decreased by 5 orders of magnitude, implying increased antibacterial activity. When the chain length was 18, the antibacterial activity decreased. However, they did not investigate chains longer than 18. The team concluded that increasing the chain length could greatly improve the antibacterial effect.

2.2. Silver Antibacterial Agent

At present, there are three hypotheses about the antibacterial mechanism of silver antibacterial agents[10]: contact action, release of reactive oxygen species (ROS) and release of Ag+. Morones et al. believed that Ag-NP could attach to the cell membrane of bacteria on the cell surface and disrupt the function of the cell membrane, penetrate the bacteria and cause leakage of cytoplasm, thus killing the bacteria. Wang[11] et al. attributed the antibacterial effect of silver nanoparticles to the increased concentration of reactive oxygen species. They suggest that reactive oxygen species cause bacterial death by inducing intracellular oxidation, membrane potential changes, and release of cell contents[11]. In contrast, Kumar[12] et al. proposed that the antibacterial activity of silver depends on Ag+, which binds closely to electron-donor groups in biomolecules containing sulfur, oxygen or nitrogen. In fact, silver can interact with H+ to release Ag+ when exposed to oxygen. This may support the Ag+ release hypothesis, whereby DNA loses its ability to replicate and cellular proteins are inactivated upon Ag+ exposure[13]. In addition, some researchers believe that Ag+ can attack proteins and cause them to denature[13, 14].

Among them, Silver nanoparticles (Ag-NP) have attracted extensive attention due to their excellent properties of broad-spectrum antibacterial, long-acting and good heat resistance, and can be used in the manufacture of antibacterial materials and products[15]. The antibacterial effect of silver nanoparticles is closely related to its particle size and particle size distribution[10]. Researchers say the antibacterial properties of silver nanoparticles often vary with different synthesis methods, as well as with reducing agents and stabilizers. Therefore, it is a great challenge to achieve size-adjustable synthesis of silver nanoparticles with large surface area and surface activity, poor stability and strong aggregation tendency [16].

2.3. Fluoride is an Antibacterial Agent

The anti-caries mechanism of fluoride adhesives mainly has two aspects: on the one hand, it inhibits demineralization and promotes remineralization, and the ability of fluoride ion (F) to inhibit enamel demineralization has been fully elucidated. In addition to bacteriostasis, F ion can also reduce the solubility of enamel and re-mineralize decalcified tooth tissue by forming fluorapatite (FAP). On the other hand, it affects the survival and metabolism of bacteria and the acidification of dental plaque.

Fluoride-releasing materials can act as a reservoir for fluoride, increasing fluoride levels in saliva, dental plaque and hard tooth tissue, thus maintaining a consistently low level of oral fluoride concentration, which is extremely beneficial for preventing dental caries. Fluoride is a release type antibacterial adhesive, and the interaction time between fluoride and dental tissue is the key. However, there are significant differences in fluorine release characteristics of fluorinated dental composite resin. To solve this problem, Jiajia Xu[17] et al. obtained imidazole salt monomer by quaternization of 1-chlorododecane and 1-vinylimidazole, and then prepared fluoride-containing salt polymerized antibacterial monomer by substitution reaction after adding silver fluoride. The release rate of antibacterial monomer was relatively slow and the antibacterial effect was very obvious.

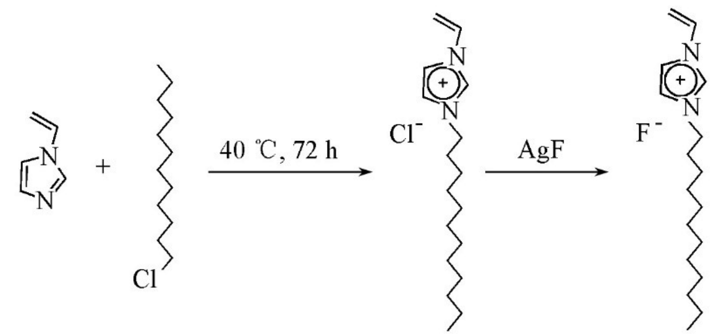

Fig. 2 [17] Synthesis routes of fluorine-containing imidazolium salt antibacterial monomer

Therefore, the control of initial explosive release and the maintenance of long-term effective release will still be the focus of future research on fluorinated dental materials, and the search for carrier materials that can be used as F-sustained release storage will become the focus of future research.

2.4. Other Types

Metal oxide antibacterial materials are also widely used, such as zinc oxide (ZnO), titanium dioxide (TiO2). Literature shows that ZnO with different morphologies has a certain effect on the antibacterial properties of composite resin[18].

Using mesoporous silica nanoparticles as zinc carrier, Xingxing Bai team[19] synthesized zn-MSN doped mesoporous silica nanoparticles (Zn-MSN) with uniform zinc distribution, large specific surface area and well-ordered pores by solution-gel method, and applied antibacterial ion doping on MSN to dental materials for the first time. In this study, it was found that 15wt%Zn-MSNs containing zinc had the best comprehensive properties, including mechanical properties, antibacterial activity, shrinkage rate, etc. The prepared Zn-MSN is expected to be a reinforcing filler for dental resin composites.

At the same time, antimicrobial peptides are natural protein molecules with antibacterial, antiviral or antifungal activities[5], and are also widely used in the dental field.

3. Preparation of Antibacterial Adhesive

At present, there are two kinds of anti-caries adhesives: releasing anti-caries adhesives and non-releasing anti-caries adhesives [20]. Releasing-type adhesives release a certain amount of antibacterial ingredients in the process of antibacterial action [21]. However, non-release antibacterial adhesives are fixed in the polymer network by covalent bonds with antibacterial groups to avoid the gradual weakening of antibacterial properties and poor mechanical properties caused by the release of antibacterial agents, while maintaining good color stability and biological safety.

3.1. Release Type Antimicrobial Adhesive

The Heba Mitwalli [22] team incorporated calcium fluoride nanoparticles ($nCaF_2$) into the composite resin to support the release of F^- and Ca^{2+} ions, especially during cariogenic acid challenges. Recently, his team has developed a rechargeable $nCaF_2$ composite restoration on this basis, which can be repeatedly charged to release high levels of F and Ca ions for a long time and a new composite formulation containing bioactive agents $nCaF_2$ and DMAHDM. The high levels of F and Ca ion release required for potential remineralization were achieved without compromising mechanical properties.

Liyuan Zheng [23] and others combined zirconia filler and fluoride to explore its fluorine release properties. $F\text{-}ZrO_2$ powders with different fluorine content (0, 5mol%, 10mol% or 20mol%) were prepared by chemical precipitation. First, zirconium oxide octahydrate ($ZrOCl_2 \bullet 8H_2O$) was dissolved in deionized water with a concentration of 0.5mol/L, and then yttrium nitrate hexahydrate ($Y(NO_3)_3 \bullet 6H_2O$) and ammonium zirconium hexafluoride (ZrF_6NH_4) were added in sequence. completely dissolved in the above solution. After that, ammonia was added to the above solution to adjust the pH to 10, followed by drying and cooling. The amount of fluorine released increased with the increase of fluorine content, and both quantitative and qualitative analysis showed that the activity of 20% $F\text{-}ZrO_2$ powder against Streptococcus mutans exhibited the best antibacterial properties, which was consistent with the release of fluoride. Therefore, 20% $F\text{-}ZrO_2$ powder was selected as filler to develop a new composite resin.

3.2. Non-release Antimicrobial Adhesive

Most of the non-release adhesives use methyl methacrylate monomer as the adhesive system. In recent years, researchers have carried out related research work on the structural design and synthesis of this monomer. Weng [24] et al. synthesized brominated bis-methacrylate-based quaternary ammonium salt (BPDQABDMA), the structure of which is shown in Fig. 3(b).Wang [25]et al. further synthesized tetramethylammonium monomer (TMQA), whose structure is shown in Fig. 3(c).

Among them, 12-methacryloyloxydodecylammonium pyridinium bromide (MDPB) is one of the first antibacterial monomers, which has been used as an antibacterial agent in dental materials. MDPB is a polymerizable bactericide. After the resin material containing MDPB is cured, the antibacterial components in the molecule are fixed. The monomer showed antimicrobial activity in cured dental resins and in commercial self-etching systems against Streptococcus mutans.

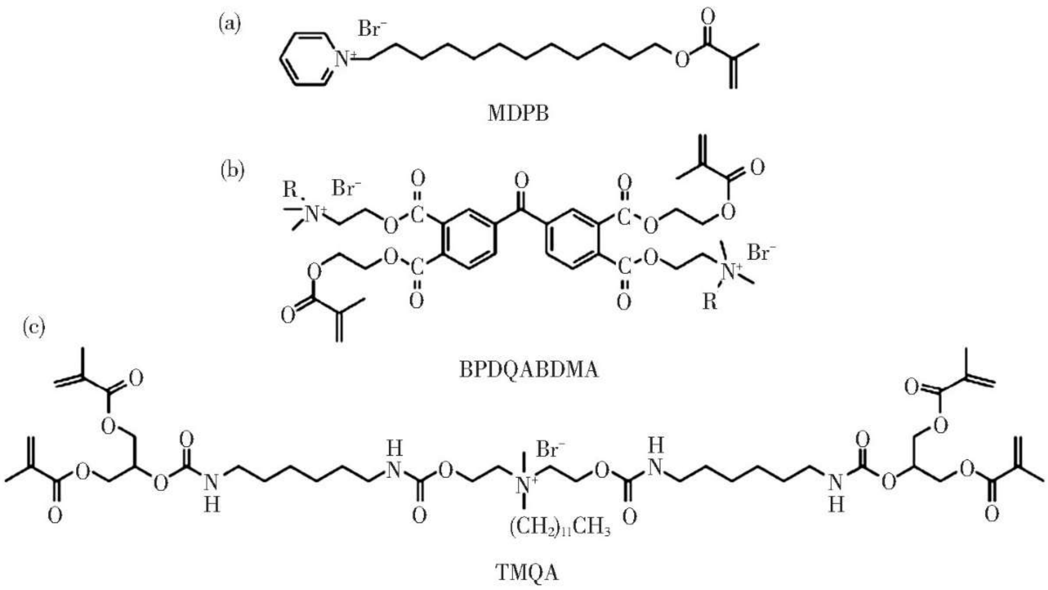

Fig. 3 The structures of (a) MDPB, (b) BPDQABDMA[24], and (c) TMQA[25]

Shuang Li [26]et al. utilized the pyridine ring in the nicotinic acid structure, which can be quaternized to form a functional group with antibacterial activity, like the antibacterial in 12-methacryloyloxy dodecylammonium pyridinium bromide (MDPB). group, 12-methacryloyloxy dodecylammonium pyridinium bromide was the first antimicrobial monomer used in dentistry. In this study, a novel quaternized pyridine dimethacrylate containing short alkyl side chains was synthesized and used to prepare antibacterial dental resin systems. The synthesis process is shown in Fig. 4.

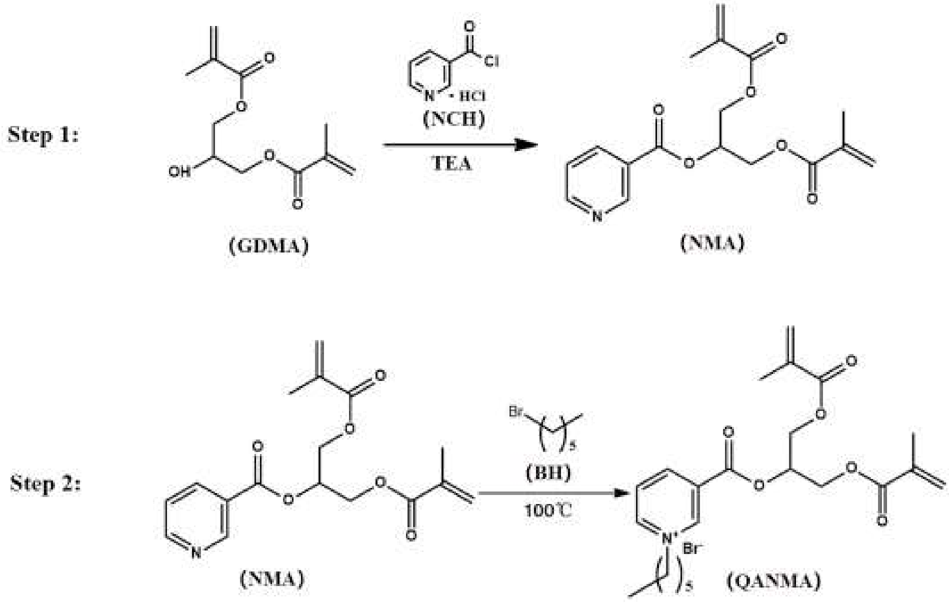

Fig. 4 [26]Synthesis route of 1,3-bis(methacryloyloxy)- propyl-carbonyl-hexylpyridinium bromide (QANMA).

4. Conclusion

Adding antibacterial agent into dental composite resin can effectively reduce the recurrence rate of dental caries. The types of antibacterial agents are diverse, mainly divided into release type and non-release type, providing a variety of choices for scientific research workers. But as well as focusing on antibacterial properties, researchers also need to consider the impact on mechanical properties, cytotoxicity, and service life. Therefore, the structure and composition of antibacterial dental composite resin still need to be further explored and studied in order to meet the long-term clinical application of the material.

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