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Therapeutic polymers for dental adhesives: Loading resins with bio-active components

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ABSTRACT

Objectives. Many recent adhesives on the market exhibit reasonable clinical performance. Future innovations in adhesive materials should therefore seek out novel properties rather than simply modifying existing technologies. It is proposed that adhesive materials that are "bio-active" could contribute to better prognosis of restorative treatments.

Methods. This review examines the recent approaches used to achieve therapeutic polymers for dental adhesives by incorporating bio-active components. A strategy to maintain adhesive restorations is the focus of this paper.

Results. Major trials on therapeutic dental adhesives have looked at adding antibacterial activities or remineralization effects. Applications of antibacterial resin monomers based on quaternary ammonium compounds have received much research attention, and the loading of nano-sized bioactive particles or multiple ion-releasing glass fillers have been perceived as advantageous since they are not expected to influence the mechanical properties of the carrier polymer.

Significance. The therapeutic polymer approaches described here have the potential to provide clinical benefits. However, not many technological applications in this category have been successfully commercialized. Clinical evidence as well as further advancement of these technologies can be a driving force to make these new types of materials clinically available.

1. Incorporation of QAC-based resin monomers

Quaternary ammonium compounds (QACs) are a group of cationic antimicrobials widely used for numerous industrial and pharmaceutical purposes [1]. In 1994, to develop non-agent-releasing antibacterial dental resins, Imazato et al. combined alkylpyridinium, a type of QAC, with a methacrylate group, and successfully synthesized a novel dental resin monomer, 12-methacryloyloxydodecylpyridinium bromide (MDPB) [2] (Fig. 1). While the QAC group is responsible for the antibacterial activity of MDPB, the methacrylate group allows for copolymerization with other conventional monomers. Since antibacterial monomers are immobilized in the resin matrix and do not leach out after curing,

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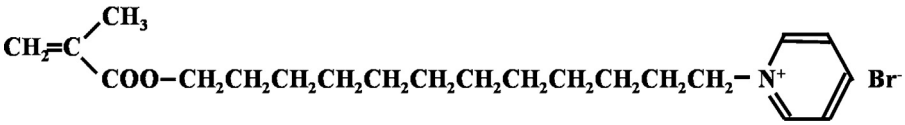

Fig. 1 – QAC-based antibacterial monomer MDPB.

incorporating these monomers imposes no negative influences on the mechanical properties of the carrier material [2]. Without releasing these active agents, QAC-based resinous materials can exhibit stable and long-term antibacterial effects [2].

1.1. *Antibacterial effects*

Experimental antibacterial adhesive systems were first prepared by incorporating MDPB into the primer of commercial self-etching adhesive Liner Bond 2 [3]. Since then, the antibacterial activity of this prototype has been investigated and confirmed by a number of in vitro studies. Based on the findings of this experimental material, Clearfil Protect Bond, employing a 5% MDPB-containing primer, was developed and commercialized (sold as Clearfil SE Protect in USA and Clearfil Mega Bond FA in Japan).

Before curing, the MDPB-containing primer can kill bacteria rapidly because of the bactericidal activity of unpolymerized MDPB. It can thereby act as a cavity disinfectant. When the primer containing MDPB was kept in direct contact with planktonic bacteria, all bacteria were killed within 30 s [3–5]. It is noteworthy that the Clearfil Protect Bond primer was able to penetrate a 500-μm-thick dentin block [6] and eradicate caries-related species inside the dentin [7]. In vivo studies using beagle dogs found that the MDPB-containing primer could also inactivate *Streptococcus mutans* in the cavity [8]. Since residual bacteria are one of the primary causes of secondary caries, the cavity-disinfecting effects of the MDPB-containing primer may improve the outcomes of restorative treatments of caries lesions.

After curing, MDPB-containing resins can inhibit the growth of bacteria that comes into contact with the material, thereby acting as a so-called "contact inhibitor" (Fig. 2). When *S. mutans* was incubated in contact with the cured primer/adhesive surface containing MDPB, the number of viable bacteria was significantly reduced [9,10]. However, materials containing MDPB only exhibited bacteriostatic, rather than bactericidal effects, against the contacting bacteria. Two possible reasons for the reduction in antibacterial activity after curing have been proposed; (i) the movement of the immobilized molecules is limited, and (ii) the density of the QAC group of MDPB exposed on the outer surface is not high enough to kill bacterial cells.

MDPB-containing adhesives have been suggested to be effective in root caries arrestment and dental pulp preservation. This is attributed to their lesion-disinfecting effects and bacteriostatic functionality on contact with bacteria after curing. In a *S. mutans*-induced artificial root caries model, a MDPB-containing adhesive completely prevents lesion progress [11]. As for pulp preservation, it has been confirmed using beagle dog models that the antibacterial primer containing MDPB can kill bacteria in the cavity, thus maintaining pulp vitality and primary odontoblastic function in infected, non-exposed and exposed cavities [8,12].

Besides MDPB, several other QAC monomers have been developed that can be utilized in resinous dental materials. Methacryloxylethyl cetyl dimethyl ammonium chloride (DMAE-CB, Fig. 3), synthesized by Chen's group, provided a commercial etch and rinse adhesive with stable antibacterial activities that does not damage the bonding capacity [13,14]. In recent years, significant efforts have been devoted to developing QAC monomers with improved properties. For instance, QAC monomers with two methacrylate groups have been synthesized to enhance the polymerization capacity [15–17] (Fig. 4). Antibacterial monomers with radio-opacity have also been developed using iodine as a counter ion [18,19] (Fig. 5).

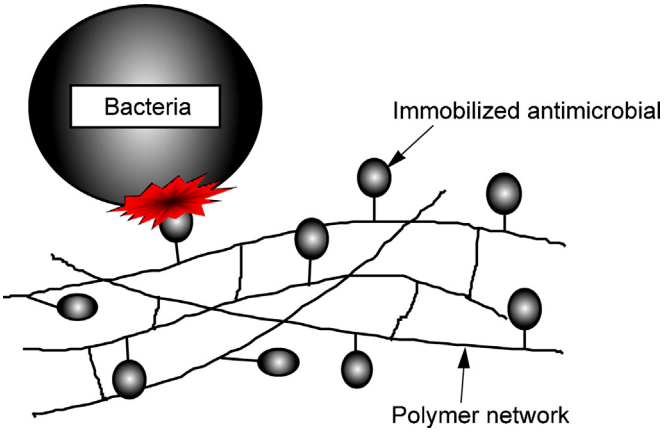

Fig. 2 – Antimicrobial immobilized in a polymer network by copolymerization of the antibacterial monomer with conventional methacrylate monomers; contact inhibition of bacteria.