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Review

A systematic review about antibacterial monomers used in dental adhesive systems: Current status and further prospects

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ABSTRACT

Objectives. This study systematically review the literature to assess the effectiveness of antibacterial monomers incorporated into dental adhesive systems against major oral bacteria; as well as the research advances and the future prospects of this technology.

Methods. The following seven databases were screened: *MedLine (PubMed), Lilacs, Ibecs, Web of Science, Scopus, Scielo*, and *The Cochrane Library*. Furthermore, the online system Questel Orbit (Paris, France) was accessed to obtain patent data. The inclusion criteria were articles and patents that investigated the antimicrobial activity of antibacterial monomers in dental adhesive systems. Only documents written in English, Spanish or Portuguese were included.

Results. After screening, 33 studies and eight patents fulfiled all the criteria and were included. Antibacterial agents, such as QA, MDPB, DMAHM and DMADDM were found in patents, which claimed their incorporation into adhesive compositions, dental cements, composite resins. MDPB was the only antimicrobial monomer incorporated into a commercially available adhesive system, Clearfil Protect Bond™ (Kuraray Co. Ltd., Japan). All studies reported the inclusion of antimicrobial monomers in adhesive systems to be an effective dental treatment strategy.

Significance. There are potential areas to be explored with antibacterial monomers for dentistry, and their use could have important implications for future more conservative dental treatments. Although there is evidence of antibacterial activity from *in vitro* studies, clinical studies must be conducted to confirm the effectiveness of these materials in the prevention of dental pathologies.

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Contents

1. Introduction

There is a trend to use the minimally invasive dentistry approach to promote preservation of the tooth structure with conservative techniques in an effort to avoid damage to the dental pulp complex [1]. Incomplete removal of infected dentin is currently recommended, especially in clinical situations of deep carious lesions. However, viable bacteria that may be left in the dentin may lead to restorative treatment failure [2]. Moreover, restorations performed with composites accumulate more biofilm and are subject to faster degradation than those made with other materials [3–5], such as ceramics and glass ionomer cements [6]. This can lead to the formation of secondary caries, damage to the pulp and consequently lead to restoration failure [7]. Furthermore, polymerization shrinkage can result in the formation of gaps between the adhesive resin and the primed dentin, or between the adhesive resin and the hybrid layer [8], which can lead to penetration of bacteria that could cause secondary caries [9].

Several studies [10–12] indicated that self-etching adhesive systems containing acidic monomers with lower pH in their formulation may have antibacterial effect. However, this effect is limited to 24 or 48 h [10]. Therefore, materials with antibacterial effect lasting for a longer time were developed: the antibacterial-agent-releasing and non-antibacterial-agent-releasing materials [13]. The incorporation of chlorhexidine, fluoride and silver particles are considered antibacterial-agent-releasing materials, with their effect attributed to the release of antibacterial products [13,14]. Substances presented in this material are only simply dispersed in the matrix phase, and it is impossible to control the kinetics of release. Consequently, antibacterial activity decreased over the course of time. Moreover, the release of the agent may adversely influence the physical properties and result in toxic effects [15,16].

To overcome the disadvantages of these products, researchers have attempted to develop non-antibacterial-agent-releasing materials. The current trend involves the development of monomers with quarternary ammonium salts [3,17], which present relatively low toxicity and a broad antimicrobial spectrum [18]. It is reported that the quarternary ammonium (QA) is bactericidal due to three possible processes: (1) Contact of the negatively charged bacterial and positively charged QA, resulting in osmotic pressure; (2) Diffusion through the cell wall and binding to the cytoplasmic membrane; and (3) Disruption of the cytoplasmic membrane, release of cytoplasmic constituents and cell death (Fig. 1) [19–21]. Quarternary ammonium salts are able to copolymerize with other methacrylate monomers and could provide long-term antibacterial activity [1]. The following monomers with QA incorporated have been synthesized: 2-dimethyl-2-dodecyl-1-methacryloxyethyl ammonium iodine (DDMAI); 2-methacryloyloxyethyl dimethylammonium (IDMA1); 2,2-bis(methacryloxyloxyethyl dimethylammonium) (IDMA2); dimethyl amino dodecylmethacrylate (DMADDM); dimethylamino hexylmethacrylate (DMAHM); methacryloxyl ethylcetyldimethylammonium chloride (DMAE-CB); and the compound 12-methacryloyloxy dodecypyridinium bromide (MDPB). MDPB was the first antibacterial monomer incorporated into a commercially available adhesive system [22,23] Clearfil Protect Bond™(Kuraray Co. Ltd., Japan).

There is a trend toward developing dental materials with antibacterial activity, however their effectiveness in the reduction of oral bacteria has not been completely elucidated. Therefore, the aim of this systematic review was to evaluate the antimicrobial activity of dental antibacterial adhesive systems; as well as the advances in research, and future prospects for the development of antimicrobial dental materials.

2. Materials and methods

2.1. *Electronic searches*

This systematic review is described according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [24]. The literature search was carried out by two independent reviewers (ARC and WLOR) until

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