

Nanotechnology Used FOR Antibacterial Activity IN Novel Composite Restorations: A Review

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Abstract: Application of nanotechnology in dental composites can enhance properties like bringing anticariogenic potential, incorporate antibacterial property and even provide remineralization of demineralized enamel. We will explore recent thoughts, present applications, and succeeding aspects of nanoparticles mixed into composite restorative materials to enhance antibacterial properties as a beneficial technique for dental caries treatment in this review. We will also emphasise the hypothesised antibacterial mechanism by incorporating a variety of components into nanostructures, such as polylysine, chlorhexidine, various quaternary ammonium compounds, silver particles, and triclosan, to achieve the required antibacterial potential. These nanostructured materials have great potential in decreasing the antibiofilm accumulation and decrease the streptococcus count.

Keywords: composite resins, antibacterial activity, nanotechnology

1. INTRODUCTION

Composite is the most popular and adaptable material for filling cavities in teeth. It has many advantages but still consists of certain drawback related to mechanical properties, micro leakage and shrinkage during the process of polymerization which will causes fracture or recurrent caries. Various modifications have been experimented to increase the biological as well the mechanical properties, especially wrt antibacterial property[1]. Adding an antibacterial element to a composite can be done in three ways: packaging the inorganic antibacterial agent, directly adding the organic agent, or utilising a polymeric antibacterial agent. Based on the type of agent they can also be classified as organic or inorganic antibacterial agent[1] (figure 1). Below are some antibacterial agents which have been added at nanoscale into composites to bring out the desired antibacterial potential.

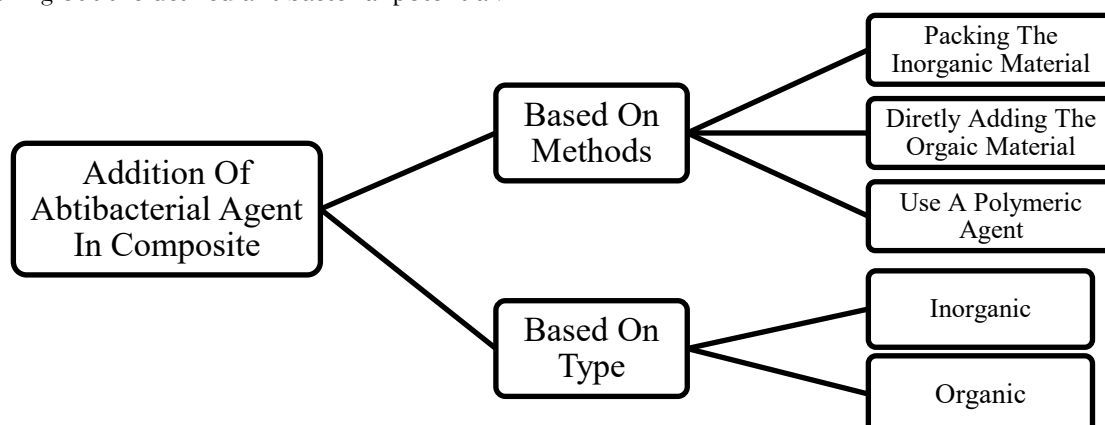


Figure: 1 Methods of adding antibacterial agent into composite

1. FLUORIDE

The antibacterial action of fluoride is by making itself resistant to cariogenic bacteria by forming fluorapatite crystals. This action is enhanced by use of nanotechnology. When calcium fluoride nanoparticles are added into composite it resists the acidic challenge caused by cariogenic bacteria [2]. In a study done by Mitwalli et al the incorporation of calcium fluoride nanoparticles showed the ability to reduce biofilm acid production and reduce secondary caries formation [2]. In another study nanoparticles of fluoride when doped with silver particles and added to composite, proved that there was 30 % reduction of bacterial growth and the natural morphology of fluorapatite was maintained[3]. Even when nanoparticles of fluoride were added with other antibacterial agent like chlorhexidine, calcium phosphate into composite resins it showed reduced biofilm formation with reduction in bacterial colony forming units and enhanced anticaries action[4], proving dual effects of composite.

2. ZINC OXIDE

Zinc is nontoxic, stable antibacterial agent which acts by preventing the proliferation of bacteria[5]. Nanoparticles of zinc when coupled with copper and fluoride ions and added to composite showed to have antibacterial and remineralization properties, indicating their potential as multifunctional dental materials [6] However in a study done by Xingxing et al shows Zn doped mesoporous silica nanoparticles when added to composite resins for restorative purpose improved the mechanical property of the material and exhibited antibacterial effects[7].

3. CHLORHEXIDINE

CHX is bactericidal (kills microorganisms) and bacteriostatic (prevents their growth when present in small concentrations). Incorporating CHX into composites has a negative impact on their mechanical properties. As a result, mesoporous silica nanoparticles were used to encase the CHX and maintain mechanical characteristics[8]. The pH of composites containing nanoparticles and CHX was found to be 6.5, which is higher than the 5.5 critical pH. This outcome in 10-20 fold reduced the bacterial motion when compared to composites lacking nanoparticles. [9]. This is also supported by a study done by Tejas et al where chlorhexidine loaded halloysite nanotube based (HNTCHX) newly formulated dental composite were successfully prepared. They were subjected to check mechanical, biological and cytotoxic activity, these newly formulated HNT/CHX dental composite displayed nontoxicity, enhanced mechanical activity and showed good antimicrobial action[10]. In another study CHX was added with nanoparticles of ACP into composites where they exhibited dual property of remineralization and antibacterial action[11].

4. QUATERNARY AMMONIUM COMPOUNDS

Nanoparticles of quaternary ammonium compounds (QAC) were added to a resin composite utilising nanotechnology and showed strong and wide antibacterial activity against salivary bacteria. [12]. After 6 and 12 months, the composite's anti-biofilm effect comprising QAM was proved to be sustained. After 12 months, there was no discernible difference in anti-biofilm action as the water-aging time was extended. [12,13]. Of late, a novel antibacterial monomer, dimethylaminohexadecyl methacrylate (DMAHDM), was discovered and integrated into dental resins, demonstrating powerful antibacterial capabilities without impairing the resin's mechanical properties [12]. QAC are also added with several other antibacterial agents like silver nanoparticles [13], chlorhexidine, along with remineralizing agents like titanium oxide ,nanoparticles of calcium phosphate[13] and calcium fluoride[2] into composite. Together it exhibits good remineralization, antibacterial action and reduces the biofilm formation.

5. SILVER PARTICLES

Silver (Ag), the next antibacterial agent, possesses antibacterial, antifungal, and antiviral effects. Silver's antibacterial process involves inactivating critical enzymes and reducing bacteria's ability to reproduce DNA, causing cell damage. The inclusion of Ag micro particles to resin dental composite can enhance surface hydrophobicity, which brought about fewer adhering streptococci on composite surfaces and a higher ratio of dead and inactive cells. Because of advances in nanotechnology, silver's cosmetic problem has been resolved [14]. Ag nanoparticles (NAg) exhibit antimicrobial properties as well. In comparison to other metal ions, Hernández et al [15] discovered that NAg require low doses to suppress the development of the *S. mutans* strain because of large surface area to mass ratio. In a study done by Keskar et al showed that when silver nanoparticles were added with nanoparticles of ACP it showed dual benefits of antibacterial as well as remineralization process [16].

6. TRICLOSAN

Triclosan was first introduced in 1972 as an effective antibacterial agent. It is frequently utilised in the manufacture of dental care products such as toothpaste & mouthwash due to its wide range of action and low toxicity.[17]. TCN when incorporated in resin-based materials it showed significant leachability, resulting in a quick loss of antibacterial characteristics. To solve this problem, TCN is placed in nanotubes, that are special "vehicles" which allow an antibacterial medicine to be delivered more slowly and more precisely [18]. Another study done by de Paula et al showed that when triclosan was added to resin composite it would reduce biofilm formation and bacterial adhesion[17]. These same results were confirmed by a de Souza Araujo et al where triclosan monomer caused molecular and cellular level destruction of *S.mutans* indicating a reduction of their virulence [19].

8. POLYLYSINE

A more recent antibacterial agent is polylysine which is widely used as a broad antimicrobial agent[20]. Polylysine causes electrostatic adsorption on the outer bacterial membrane, resulting in cytoplasm disarray and bacterial cell death[21]. Polylysine has been added into composite more recently. In addition, adding polylysine to composites with CaPO_4 can boost apatite crystallization on their surfaces when replicated bodily fluid is applied. As a result, polylysine may improve the remineralization potential of composites[20]. However in a study done by Kangwankai et al where polylysine was added with calcium phosphate it helped in apatite precipitation and reduced the surface roughness upon wear[22]. Its antibacterial activity was confirmed by Nikos et al where composite containing polylysine [23] drastically reduced cariogenic bacterial count. Further studies are yet to be conducted with the role of nanotechnology in the use of polylysine.

9. CONCLUSION

These resin-based composites incorporated with antibacterial agents can prevent formation of caries, reduce biofilm formation and improve some of the drawbacks of composite materials. This novel approach in composite materials will enable a less aggressive approach and more conservative tooth preparation. However, more research into the role of nanotechnology with the inclusion of antibacterial compounds is needed. As a result, this composite will benefit children, anxious patients, and underdeveloped areas with few dental facilities.

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REFERENCES:

- [1] Wu Z, Xu H, Xie W, Wang M, Wang C, Gao C, Gu F, Liu J, Fu J. Study on a novel antibacterial light-cured resin composite containing nano-MgO. *Colloids and Surfaces B: Biointerfaces*. 2020 Apr 1;188:110774.
- [2] Mitwalli H, Balhaddad AA, AlSahafi R, Oates TW, Melo MA, Xu HH, Weir MD. Novel CaF_2 nanocomposites with antibacterial function and fluoride and calcium ion release to inhibit oral biofilm and protect teeth. *Journal of Functional Biomaterials*. 2020 Sep;11(3):56.
- [3] Anastasiou AD, Nerantzaki M, Gounari E, Duggal MS, Giannoudis PV, Jha A, Bikiaris D. Antibacterial properties and regenerative potential of Sr^{2+} and Ce^{3+} doped fluorapatites; a potential solution for peri-implantitis. *Scientific reports*. 2019 Oct 9;9(1):1-1.
- [4] Cheng L, Weir MD, Xu HH, Kraigsley AM, Lin NJ, Lin-Gibson S, Zhou X. Antibacterial and physical properties of calcium-phosphate and calcium-fluoride nanocomposites with chlorhexidine. *Dental materials*. 2012 May 1;28(5):573-83.
- [5] Amjadi S, Emaminia S, Davudian SH, Pourmohammad S, Hamishehkar H, Roufegarinejad L. Preparation and characterization of gelatin-based nanocomposite containing chitosan nanofiber and ZnO nanoparticles. *Carbohydrate polymers*. 2019 Jul 15;216:376-84.
- [6] Matsuda Y, Okuyama K, Yamamoto H, Fujita M, Abe S, Sato T, Yamada N, Koka M, Sano H, Hayashi M, Sidhu SK. Antibacterial effect of a fluoride-containing ZnO/CuO nanocomposite. *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms*. 2019 Nov 1;458:184-8.
- [7] Bai X, Lin C, Wang Y, Ma J, Wang X, Yao X, Tang B. Preparation of Zn doped mesoporous silica nanoparticles (Zn-MSNs) for the improvement of mechanical and antibacterial properties of dental resin composites. *Dental Materials*. 2020 Jun 1;36(6):794-807.
- [8] Zhang JF, Wu R, Fan Y, Liao S, Wang Y, Wen ZT, Xu X. Antibacterial dental composites with chlorhexidine and mesoporous silica. *Journal of dental research*. 2014 Dec;93(12):1283-9.
- [9] Chang JC, Hurst TL, Hart DA, Estey AW. 4-META use in dentistry: a literature review. *The Journal of prosthetic dentistry*. 2002 Feb 1;87(2):216-24.

- [10] Barot T, Rawtani D, Kulkarni P. Development of chlorhexidine loaded halloysite nanotube based experimental resin composite with enhanced physico-mechanical and biological properties for dental applications. *Journal of Composites Science*. 2020 Jun;4(2):81.
- [11] Yang Y, Xu Z, Guo Y, Zhang H, Qiu Y, Li J, Ma D, Li Z, Zhen P, Liu B, Fan Z. Novel core-shell CHX/ACP nanoparticles effectively improve the mechanical, antibacterial and remineralized properties of the dental resin composite. *Dental Materials*. 2021 Apr 1;37(4):636-47.
- [12] Zhou W, Peng X, Zhou X, Weir MD, Melo MA, Tay FR, Imazato S, Oates TW, Cheng L, Xu HH. In vitro evaluation of composite containing DMAHDM and calcium phosphate nanoparticles on recurrent caries inhibition at bovine enamel-restoration margins. *Dental Materials*. 2020 Oct 1;36(10):1343-55.
- [13] Cheng L, Zhang K, Zhou CC, Weir MD, Zhou XD, Xu HH. One-year water-ageing of calcium phosphate composite containing nano-silver and quaternary ammonium to inhibit biofilms. *International journal of oral science*. 2016 Sep;8(3):172-81.
- [14] Arjmand N, Boruziniat A, Zakeri M, Mohammadipour HS. Microtensile bond strength of resin cement primer containing nanoparticles of silver (NAg) and amorphous calcium phosphate (NACP) to human dentin. *The journal of advanced prosthodontics*. 2018 Jun;10(3):177.
- [15] Hernández-Sierra JF, Ruiz F, Pena DC, Martínez-Gutiérrez F, Martínez AE, Guillén AD, Tapia-Pérez H, Castañón GM. The antimicrobial sensitivity of *Streptococcus mutans* to nanoparticles of silver, zinc oxide, and gold. *Nanomedicine: Nanotechnology, Biology and Medicine*. 2008 Sep 1;4(3):237-40.
- [16] Keskar M, Sabatini C, Cheng C, Swihart MT. Synthesis and characterization of silver nanoparticle-loaded amorphous calcium phosphate microspheres for dental applications. *Nanoscale Advances*. 2019;1(2):627-35.
- [17] de Paula AB, Taparelli JR, Alonso RC, Innocentini-Mei LH, Puppini-Rontani RM. Synthesis and application of triclosan methacrylate monomer in resin composites. *Clinical oral investigations*. 2019 Feb;23(2):965-74.
- [18] Cunha DA, Rodrigues NS, Souza LC, Lomonaco D, Rodrigues FP, Degrazia FW, Collares FM, Sauro S, Saboia V. Physicochemical and microbiological assessment of an experimental composite doped with triclosan-loaded halloysite nanotubes. *Materials*. 2018 Jul;11(7):1080.
- [19] de Souza Araújo IJ, de Paula AB, Bruschi Alonso RC, Taparelli JR, Innocentini Mei LH, Stipp RN, Puppini-Rontani RM. A novel Triclosan Methacrylate-based composite reduces the virulence of *Streptococcus mutans* biofilm. *Plos one*. 2018 Apr 2;13(4):e0195244.
- [20] Jia H, Zeng X, Cai R, Wang Z, Yuan Y, Yue T. One-pot synthesis of magnetic self-assembled carrageenan- ϵ -polylysine composites: A reusable and effective antibacterial agent against *Alicyclobacillus acidoterrestris*. *Food Chemistry*. 2021 Oct 30;360:130062.
- [21] Shih L, Shen MH, Van YT. Microbial synthesis of poly(ϵ -lysine) and its various applications. *Bioresource technology*. 2006 Jun 1;97(9):1148-59.
- [22] Kangwankai K, Sani S, Panpisut P, Xia W, Ashley P, Petridis H, Young AM. Monomer conversion, dimensional stability, strength, modulus, surface apatite precipitation and wear of novel, reactive calcium phosphate and polylysine-containing dental composites. *PloS one*. 2017 Nov 14;12(11):e0187757.
- [23] Lygidakis NN, Allan E, Xia W, Ashley PF, Young AM. Early polylysine release from dental composites and its effects on planktonic *Streptococcus mutans* growth. *Journal of Functional Biomaterials*. 2020 Sep;11(3):53.