

REVIEW ARTICLE

Nanoparticles in orthodontics, a review of antimicrobial and anti-caries applicationsALI BORZABADI-FARAHANI¹, EBRAHIM BORZABADI² & EDWARD LYNCH¹¹Warwick Dentistry, Warwick Medical School, University of Warwick, Coventry, UK, and ²Department of Electrical Engineering, Islamic Azad University, Najaf Abad Branch, Najaf Abad, Iran**Abstract**

Nanoparticles (NPs) are insoluble particles smaller than 100 nm in size. In order to prevent microbial adhesion or enamel demineralization in orthodontic therapy, two broad strategies have been used. These are incorporating certain NPs into orthodontic adhesives/cements or acrylic resins (nanofillers, silver, TiO₂, SiO₂, hydroxyapatite, fluorapatite, fluorohydroxyapatite) and coating surfaces of orthodontic appliances with NPs (i.e. coating bracket surfaces with a thin film of nitrogen-doped TiO₂). Although the use of NPs in orthodontics can offer new possibilities, previous studies investigated the antimicrobial or physical characteristic over a short time span, i.e. 24 hours to a few weeks, and the limitations of *in vitro* studies should be recognized. Information on the long-term performance of orthodontic material using nanotechnology is lacking and necessitates further investigation and so do possible safety issues (toxicity), which can be related to the NP sizes.

Key Words: nanoparticles, orthodontics, antimicrobial, anti-caries activity**Introduction**

The use of certain nanoparticles (NPs) as antimicrobial agents has attracted much attention in medicine and dentistry. Nanoparticles are considered as insoluble particles smaller than 100 nm in size [1]. Compared with non-nanoscale particles, NPs particles present a greater surface-to-volume ratio (per unit mass), interacting more closely with microbial membranes and provide considerably larger surface area for antimicrobial activity [2]. The growing numbers of bacterial strains are becoming antibiotic-resistant and bacteria are less likely to develop resistance against metal NPs [3] than conventional antibiotics. These facts have prompted a renewed interest in the use of alternative antibacterial agents such as metallic NPs (Table I). In particular, metal NPs in the size range of 1–10 nm have been shown the greatest biocidal activity against bacteria [2]. In the oral cavity, the antibacterial properties of NPs have been used through two broad mechanisms of combining dental materials with NPs or coating surfaces with NPs to prevent microbial adhesion, with the overall aim of

reducing the biofilm formation [2,4,5]. The literature on the use of NPs in orthodontics is limited and this paper provides an overview of studies that investigated the use of NPs' antimicrobial and anti-caries characteristics in orthodontics.

Applications of antimicrobial NPs for controlling oral biofilm in orthodontics

White spot formation or demineralization is a prevalent unwanted side-effect of orthodontic therapy [6]. Orthodontic appliances can affect the self-cleaning ability of teeth, alter the oral microflora and increase the levels of acidogenic plaque bacteria, i.e. mutans streptococci and lactobacilli in saliva and dental biofilm during active wear of the appliance [7–11]. In addition to saliva composition, dietary carbohydrates and oral hygiene [12,13], the adhesion of specific oral bacteria to tooth surfaces, or the interface between the orthodontic appliance and tooth surfaces, are necessary for forming cariogenic biofilms. This cariogenic biofilm can lead to dental decay [14] or demineralization around orthodontic brackets. Within such a

Table I. Some commonly used nanoparticles with antimicrobial activity [1,2].

Nanoparticles
Titania (TiO ₂)
Silver (Ag)
Gold (Au)
Silica (SiO ₂)
Copper (Cu/CuO)
ZnO

biofilm, *Streptococcus mutans* is the main aetiological factor responsible for initiation and progression of tooth decay [15,16].

Brackets and fixed orthodontic appliances facilitate bacterial accumulation by providing retentive areas [17]. It has been claimed that 50–70% of patients undergoing fixed orthodontic appliance therapy had enamel demineralization around the brackets (white spot lesions or cavities) [18]. Bacterial accumulation has been detected at the 10- μ m gaps at the adhesive–enamel junction [19]. Various strategies, which are mainly reliant on patient compliance, have been suggested to reduce demineralization and white spot formation during treatment. The mainstay is the mechanical plaque biofilm removal and the use of fluoride and/or antimicrobial agents [20,21]. The use of fluoride in various forms (i.e. mouthwash, toothpaste, professional application, incorporated into adhesives) inhibits the metabolism of the bacteria that cause caries and increase the resistance of enamel and dentine [22–25].

Due to biocidal or anti-adhesive capabilities of certain NPs, these have been incorporated into orthodontic adhesives to control the oral biofilm and reduce the demineralization around the brackets. When adding NPs to conventional orthodontic adhesives and appliances, the critical issue is that the

physical and chemical properties should not be affected adversely, leading to less than ideal clinical performance. Further, the antimicrobial and anti-adhesive properties as well as the safety of the new nano-adhesives must be ensured over a clinically relevant time span. So far, combining orthodontic materials with NPs or coating the bracket surfaces with NPs has been used to benefit from unique characteristics of certain NPs (Table II). Examples will be presented in four categories.

Coating orthodontic bracket with a thin film of nitrogen-doped TiO₂ NPs

Photocatalysis of titanium dioxide (TiO₂) has been well known [2]. Compared with unmodified surfaces, the TiO₂ NPs tend to resist the formation of surface biofilms through increased hydrophilicity [2,26]. The nano-sized TiO₂ powder is difficult to disperse due to the strong aggregation resulting from high surface energy, which directly affects its antimicrobial and physiochemical properties [27].

Cao et al. [27] used brackets coated with a thin film of nitrogen-doped TiO₂ NPs and reported on the antimicrobial and bacterial adhesive properties against normal oral pathogenic bacteria through visible light. The nitrogen doping and modification enable TiO₂ to exhibit catalytic activity within the visible-light region. The activation leads to the formation of OH• free radicals, superoxide ions (O₂•), peroxy radicals (HO₂•) and hydrogen peroxide (H₂O₂). These chemicals, through a series of oxidation reactions, react with biological molecules such as lipids, proteins, enzymes and nucleic acids, damage biological cell structures, but also exert antimicrobial activity. Good anti-adhesive properties against *Streptococcus mutans* were observed in this study [27]; the rate of antimicrobial activity of the coated bracket against *Streptococcus mutans*,

Table II. Examples of previously used nanotechnology to enhance antimicrobial or anti-caries properties of orthodontic materials.

Reference	Nano material used	Study type
Bishara et al. [37]	Nanofilled adhesive	<i>In-vitro</i>
Ahn et al. [36]	Nanofilled adhesive with silver nanoparticles (NPs)	<i>In-vitro</i>
Uysal et al. [39]	Nanofilled adhesive and nano-ionomer	<i>In-vitro</i>
Lin et al. [30]	Incorporating fluorapatite or fluorohydroxyapatite NPs into an orthodontic adhesive (RMGIC)	<i>In-vitro</i>
da Silva et al. [38]	Nanofilled adhesive	<i>In-vitro</i>
Pai et al. [40]	Nanofilled adhesive	<i>In-vitro</i>
Poosti et al. [47]	Incorporating TiO ₂ NPs into an orthodontic adhesive	<i>In-vitro</i>
Sodagar et al. [55]	Incorporating silver NPs into a PMMA resin	<i>In-vitro</i>
Cao et al. [27]	Coating orthodontic bracket with a thin film of nitrogen-doped TiO ₂ nanoparticles	<i>In-vitro</i>
Sodagar et al. [54]	Incorporating TiO ₂ and SiO ₂ NPs into a PMMA resin	<i>In-vitro</i>
Enan and Hammad [32]	Incorporating hydroxyapatite NPs into an orthodontic cement (GIC)	<i>In-vivo</i>

Lactobacillus acidophilus, *Actinomyces viscosus* and *Candida albicans* were 95%, 91%, 69% and 99%, respectively [27]. These findings have implications in the prevention of enamel demineralization and gingivitis during orthodontic treatment. However, some important information on the long-term clinical performance and safety of the newly modified bracket surfaces as well as the effects on the bond strength to teeth are missing.

Combining glass ionomer cements or resin-modified glass ionomer cements with fluorapatite, fluorohydroxyapatite or hydroxyapatite NPs

Compared with glass ionomer cements (GICs) that offer a relatively lower bond strength with teeth when used for bracket bonding [28], resin-modified glass ionomer cements (RMGICs) present with stronger bond strength while maintaining some ability to release fluoride [29]. Lin et al. [30] assessed the effect of incorporating nano-sized fluorapatite (NFA) or fluorohydroxyapatite (NFHA) particles into a RMGIC. The fluoride release of the RMGIC improved by incorporating NFA or NFHA; however, this was at the cost of significant reduction in shear bond strength, which remained at the lower boundaries of the recommended range for orthodontic brackets [31]. The findings of shear bond strength (SBS) were obtained after 24 h and longer-term trials are needed to test the long-term clinical performance. The fluoride releases after 35 and 70 days were also significantly higher in groups that had NFA or NFHA, respectively [30]. The authors stated that, compared with the control group, the optimal concentration of added NFA and NFHA for maximum fluoride release was 25 wt.%, which nearly tripled fluoride release after 70 days.

In another study, Enan and Hammad [32] assessed the *in-vivo* effect of adding nano-hydroxyapatite (Nano-HA) to orthodontic banding cement. This study assessed the microleakage under orthodontic bands, which was assessed by the methylene blue dye penetration method after 60 days. Orthodontic bands cemented with conventional GIC showed the highest microleakage scores in comparison with those cemented with Nano-HA-modified GIC [32].

Incorporating nanofillers or NPs (silver, TiO₂) into orthodontic adhesives

Orthodontic adhesives demonstrated higher retaining capacity for cariogenic streptococci than bracket materials [33]. The nano-filled adhesives with smaller and more uniformly distributed filler particles may present with decreased surface roughness that compromises bacterial adhesion [34–36]. Previous short-term (24 h) *in-vitro* studies reported comparable [36–38] or lower and still acceptable [39,40] shear bond strength, when nano-filled adhesives were used

for bonding orthodontic brackets. Compared with conventional orthodontic adhesives, using nanofillers reduced the surface roughness of adhesive [36]; however, this was not true when silver NPs was added to this mixture. Nonetheless, evaluating the long-term effect of nano-filled adhesives on prevention of enamel demineralization during orthodontic therapy, particularly around brackets and beneath orthodontic bands, has yet to be investigated.

Silver has been recognized for its antimicrobial activity against Gram-positive/negative bacteria, fungi, protozoa, some viruses, and antibiotic-resistant strains [41–44] as well as cariogenic *Streptococcus mutans* [45]. Resin composites containing silver ion-implanted fillers presented with antibacterial characteristics against oral streptococci [46]. Ahn et al. [36] examined the effect of adding different concentrations of silver NPs to an experimental composite adhesive containing silica nanofillers. Based on this study, addition of silver NPs significantly reduced the adhesion of cariogenic streptococci to orthodontic adhesive relative to conventional adhesives, without compromising physical properties (shear bond strength). Similarly, Poosti et al. [47] demonstrated that incorporating TiO₂ NPs (1% w/w) into an orthodontic adhesive enhanced its antibacterial effects without compromising the physical properties. Adhesives with added TiO₂ NPs showed a significantly higher antibacterial activity [47], which remained steady for the initial 30 days. Bacterial colony count also revealed no significant difference in bacterial growth immediately and 30 days after starting the experiment when orthodontic adhesives with added TiO₂ NPs were used [47].

Adding TiO₂, SiO₂ or silver NPs to acrylic orthodontic materials

Cold-cure acrylic resins that are mainly made of polymethyl methacrylate (PMMA) are widely used for fabrication of removable orthodontic appliances such as expanders, retainers and functional appliances. Compared with natural teeth, microbial plaque adheres to acrylic resin appliances with a wider adhesion area [48], which can lead to development of cariogenic oral flora. *Candida*-induced stomatitis [*Candida Albicans* (CA)] is also an inflammation of oral mucosa characterized by erythema (red areas), particularly in the palatal mucosa [49,50] that at times occurs beneath dentures (denture stomatitis), removable appliances or retainers.

CA is an opportunistic pathogen and oral *Candida* carriage is found in 25–75% of study populations [51]. A relationship between the presence of an acrylic removable appliance and *Candida* carrier state as well as low salivary pH levels was suggested [51,52]. In one study, the prevalence of CA carriers before treatment with removable appliance was 39%; this was increased to 79% after 9 months and after treatment

was reduced to 14% [52]. In similar fashion, the tooth-tissue-borne orthodontic appliances promoted more CA proliferation, compared with the tooth-borne appliances [53]. The increase in *Candida* proliferation in removable appliance wearers is perhaps due to protection from natural and mechanical removal of the saliva and the defensive system [51].

Controlling the CA proliferation under the acrylic removable appliances can potentially prevent the development of orthodontic stomatitis. Finding alternative therapies to eliminate CA, which shows tolerance to conventional antifungal drugs [50], is essential. Studies of antimicrobial properties of NP-incorporated acrylic materials and their use in removable appliances are in early stages and limited to *in-vitro* models. Sodagar et al. [54] studied the changes of the flexural strength of a PMMA acrylic resin after adding TiO₂ (0.5%) and SiO₂ (1%) NPs. Incorporating NPs into acrylic resin adversely affected the flexural strength of the final product and this effect was correlated with the concentration of NPs [54]. However, when silver NPs were added to the acrylic liquid of two PMMA resins, a variable effect on the flexural strength was observed at different concentration of silver NPs [55]. Another study reported that samples of PMMA with silver NP showed significant reduction of CA adherence and presented with a biocompatible behaviour in that they did not affect cell metabolism/proliferation or cause genotoxic damage to cells (mouse fibroblasts and human lymphocytes were used to test this) [56]. Yet again, flexural strength of the PMMA with added silver NPs were inferior compared with PMMA samples without NPs [56].

Studies mentioned earlier have limitations that should be recognized. Some did not assess the antibacterial or safety of the NP-incorporated acrylic materials [54,55] or assessed the biocompatibility over a short period of time (24–72 h) [56]. The NP size may also affect the cytotoxicity and immunological response. For instance, it has been reported that smaller silver NPs (3 nm) are more cytotoxic than larger particles (25 nm) [57]. This factor needs careful attention when cytotoxicity of any NP-incorporated material is assessed.

Conclusion

Although the use of NPs in orthodontics could offer new possibilities, reported studies investigated the antimicrobial or physical characteristic over a very short time span, i.e. 24 h to a few weeks. Further, the limitations of studies carried out mainly under *in vitro* conditions should be recognized. Information on the long-term performance of orthodontic material using this technology is lacking and needs further investigation and so do possible safety issues (toxicity), which can be related to the NP sizes.

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