Study on the role of nano antibacterial materials in orthodontics (a review)

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Abstract
Nanoparticles (NPs) are insoluble particles with a diameter of fewer than 100 nanometers. Two main methods have been utilized in orthodontic therapy to avoid microbial adherence or enamel demineralization. Certain NPs are included in orthodontic adhesives or acrylic resins (fluorohydroxyapatite, fluorapatite, hydroxyapatite, SiO₂, TiO₂, silver, nanofillers), and NPs (i.e., a thin layer of nitrogen-doped TiO₂ on the bracket surfaces) are coated on the surfaces of orthodontic equipment. Although using NPs in orthodontics may open up modern facilities, prior research looked at antibacterial or physical characteristics for a limited period of time, ranging from one day to several weeks, and the limits of in vitro studies must be understood. The long-term effectiveness of nanotechnology-based orthodontic materials has not yet been conclusively confirmed and needs further study, as well as potential safety concerns (toxic effects) associated with NP size.

Keywords: anti-caries activity, antimicrobial, health risk, orthodontics, nanoparticles.

1. Introduction

Using specific nanoparticles (NPs) as antibacterial agents in dentistry and medicine has gotten a lot of press. Insoluble particles smaller than 100 nanometers are referred to be nanoparticles (Moritz and Geszke-Moritz, 2013; Melo et al., 2013; Song and Ge, 2019; Yaseen et al., 2020). NPs particles have a higher surface-to-volume ratio (per unit mass) than non-nano scale particles. This allows them to interface more intimately with microbial membranes and offer a much bigger surface area for antimicrobial action (Borzabadi-Farahani et al., 2014). Antibiotic insistence is spreading among bacteria, and microorganisms are less likely to acquire insistence on metal nanoparticles than on traditional antibiotics (Bapat et al., 2019). Such findings have rekindled interest in the usage of different nanomaterials in orthodontics.

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antibacterial agents like metallic nanoparticles (see Table 1) (Schrand et al., 2010). Metal NPs in the 110 nm size range, in particular, has been demonstrated to have the most biocidal effect against bacteria (Shkodenko et al., 2020). The antibacterial characteristics of NPs were employed in the oral cavity to inhibit microbial adherence through two main mechanisms: mixing dental materials with NPs and covering surfaces with NPs, with the ultimate goal of decreasing biofilm development (Ansarifard et al., 2021). The research on using nanoparticles in orthodontics is few. Therefore, this study summarizes research that looked at the antibacterial and anti-caries properties of NPs in orthodontics.

2. Antimicrobial Nanoparticles Usage in Orthodontics for Managing Oral Biofilm

The development of white spots, sometimes called demineralization, is a common unintended consequence of orthodontic treatment (Figure 1). During active usage of the appliance, acidogenic plaque bacteria, such as lactobacilli and mutans streptococci, might impair the self-cleaning capacity of teeth, change the oral microbiota, and raise the amounts of acidogenic plaque bacteria in saliva and dental biofilm (Roig-Vanaclocha et al., 2020; Kidd and Fejerskov, 2004; Chen et al., 2020). Demineralization or dental decay surrounding orthodontic brackets can be caused by this cariogenic biofilm (Sudjalim et al., 2007; Gorton and Featherstone, 2003). Streptococcus mutans is the major aetiological element in developing and advancing tooth decay inside such a biofilm (Kamiya et al., 2011; Lemos et al., 2019). By offering retentive regions, braces, and fixed orthodontic equipment help germs accumulate. Enamel demineralization around the brackets has been reported in 50–70% of individuals receiving fixed orthodontic appliance treatment.

The 10-mm gaps at the adhesive enamel junction have been shown to have bacterial buildup. Several techniques for reducing demineralization and white spot development during therapy have been proposed, most of which are dependent on patient compliance (Pasco et al., 2004). The use of fluoride or antimicrobial treatments, as well as mechanical plaque biofilm removal, is the mainstay (Mitwalli et al., 2021). In diverse types (i.e., incorporated into adhesives, professional application, toothpaste, mouthwash), Fluoride inhibits the caries-causing bacteria’s metabolism and boosts enamel and dentine resilience (Nayak et al., 2019). In order to regulate the oral biofilm and decrease demineralization around the brackets, certain NPs have been introduced into orthodontic adhesives because of their anti-adhesive or biocidal properties (Mobeen et al., 2021). While using NPs in traditional orthodontic equipment and adhesives, the chemical and physical characteristics mustn’t be harmed, else clinical performance will suffer (Bacela et al., 2020). Furthermore, the novel nano-adhesives’ anti-adhesive and antibacterial capabilities and their safety must be shown over a therapeutically relevant time period (George et al., 2016; Agnihotri et al., 2020). To profit from the specific features of particular NPs, orthodontic materials have been combined with NPs, or bracket surfaces have been coated with NPs thus far (Table 2). In the following, four types of examples will be shown.

2.1. Using a thin layer of nitrogen-doped TiO2 NPs to coat an orthodontic bracket

Titanium dioxide (TiO2) photocatalysis has a long history (Wold, 1993; Chen and Selloni, 2014; Cuppini et al., 2019). TiO2 NPs have higher hydrophilicity than untreated surfaces, which makes them more resistant to biofilm development. Because of remarkable aggregation caused by high surface energy, nano-sized TiO2 powder is hard to disperse, affecting its antibacterial and physicochemical characteristics directly (Teubl et al., 2015). Salehi et al. (2018) studied the antibacterial and bacterial adhesion capabilities of brackets coated with a thin coating of nitrogen-doped TiO2 NPs using visible light. TiO2 can display catalytic action in the visible light range thanks to nitrogen doping and alteration. Hydrogen peroxide (H2O2), peroxyl radicals (HO•), superoxide ions (O2•−), and Free radicals (OH) are formed as a result of the activation. These compounds react with biological components, including nucleic acids, enzymes, proteins, and lipids, through a sequence of oxidation processes, causing damage to biological cell structures while simultaneously acting as antimicrobials. This study discovered that the anti-adhesive characteristics of the material were effective against Streptococcus mutans; the coated bracket’s rate of antibacterial action against Streptococcus mutans. Such results have significance for enamel demineralization and gingivitis prevention throughout orthodontic treatment.

Table 1. Some antibacterial nanoparticles that are widely utilized.

| Nanoparticles        |
|----------------------|
| Copper (Cu/CuO)      |
| Gold (Au)            |
| Silica (SiO2)        |
| Silver (Ag)          |
| Titania (TiO2)       |
| ZnO                  |

Figure 1. After the removal of a fixed orthodontic device, white spot lesions, cavities (upper dentition), and gingival irritation (lower dentition) are produced by orthodontic biofilms.
2.3. Nanofillers or NPs (TiO$_2$, silver), being incorporated into orthodontic adhesives

The retention capacity of cariogenic streptococci was higher in orthodontic adhesives than in bracket components (Lim et al., 2008). Surface roughness may be reduced in nano-filled adhesives with smaller and more evenly dispersed filler particles, compromising bacterial adhesion. Once nano-filled adhesives were utilized for bonding orthodontic brackets in prior short-term, 24-hour in-vitro researches, shear bond strength was comparable or lower but still allowable (Bishara et al., 2007; Chalipa et al., 2013). Nanofillers lowered the adhesive’s surface roughness compared to customary orthodontic adhesives (Uysal et al., 2010; Pai et al., 2012). When silver nanoparticles were added to the mixture, nevertheless, this was not the case (Jasso-Ruiz et al., 2020). However, the long-term influence of nano-filled adhesives on enamel demineralization prevention throughout orthodontic therapy has still to be studied. Silver has long been known for its antibacterial features against cariogenic Streptococcus mutans, antibiotic-resistant strains as some viruses, protozoa, and fungi, as well as Gram-negative/affirmative bacteria (Degrazia et al., 2016; Dutra-Correa et al., 2018). Antibacterial properties were demonstrated against oral streptococci using resin composites containing silver-implanted fillers. Gonçalves et al. (2020) investigated the effects of various silver NP levels in an empirical composite adhesive comprising silica nanofillers. According to this paper, adding silver NPs to orthodontic adhesive dramatically reduced cariogenic streptococci adherence compared to typical adhesives without sacrificing physical characteristics. Sodagar et al. (2017) showed that adding TiO$_2$ NPs (1% w/w) to an orthodontic glue improved its antibacterial capabilities without affecting its physical characteristics. Adhesives containing TiO$_2$ NPs exhibited considerably greater antibacterial activity during the first 30 days, which remained consistent. When orthodontic adhesives containing additional TiO$_2$ NPs were employed, a bacterial colony count indicated no substantial changes in bacterial growth instantly or about four weeks (30 days) after the trial began.

2.4. Acrylic orthodontic materials with silver, SiO$_2$, or TiO$_2$ nanoparticles

Removable orthodontic appliances include expanders, retainers, and functional appliances. These devices are often made with cold-cure acrylic resins. Resins are mostly composed of polymethyl methacrylate (PMMA) (Rantala et al., 2003; Zafar, 2020; Poontipiriya et al., 2021). Microbial plaque attaches to acrylic resin appliances with a larger adhesion surface than normal teeth, which can contribute to cariogenic oral flora growth (Arab et al., 2021). Candida Albicans (CA) [Candida-induced stomatitis] is an erythematous infection (red areas) of the oral mucosa that can develop beneath retainers, detachable appliances, or dentures (denture stomatitis) (Ribeiro et al., 2006; Höfling et al., 2010; Rebolledo-Cobos and Sánchez-Molina, 2018; Sugio et al., 2020). Oral Candida carriage was identified in 25–75 percent of research groups, indicating that CA is an opportunistic infection. It has been introduced to the mix by adding various silver NPs into an orthodontic cement or resin-based adhesive for improved antibacterial properties. Silver nanoparticles exhibit antibacterial features against cariogenic streptococci, which are mostly composed of polymethyl methacrylate (PMMA). These materials are designed to prevent the adhesion of cariogenic bacteria and reduce oral mucosa infections. Additionally, the antibacterial effect increases with the concentration of silver NPs, which can be integrated into orthodontic adhesives to enhance their properties.

Table 2. Nanotechnology has been utilized to improve the antibacterial and anti-caries characteristics of orthodontic materials in the past.

| Nano material used                                      | Reference                          |
|---------------------------------------------------------|------------------------------------|
| Incorporating fluorapatite or fluoroxyapatite NPs into an orthodontic adhesive | Malik et al. (2018)                |
| Nanofilled adhesive with silver nanoparticles            | Degrazia et al. (2016)             |
| Coating orthodontic bracket with a thin film of nitrogen-doped TiO$_2$ nanoparticles | Cao et al. (2013)                  |
| Nanofilled adhesive and nano-ionomer                     | Behnaz et al. (2018)               |
| Incorporating hydroxyapatite NPs into an orthodontic cement | Enan and Hammad (2013)              |
| Incorporating silver NPs into a PMMA resin               | Sodagar et al. (2017)              |
| Nanofilled adhesive                                      | Morais et al. (2015); Nayak et al. (2015); Pai et al. (2012) |
| Incorporating TiO$_2$ NPs into an orthodontic adhesive   | Toodehzaeim et al. (2018)           |
| Incorporating TiO$_2$ and SiO$_2$ NPs into a PMMA resin  | Tandra et al. (2018)               |

Nevertheless, certain crucial data on the recently improved bracket surfaces’ long-term clinical safety and effectiveness, as well as their impact on tooth bond strength, is absent.

2.2. Combining fluorapatite, fluoroxyapatite, or hydroxyapatite NPs with glass ionomer cement or resin-modified glass ionomer cement

Compared to glass ionomer cement, resin-modified glass ionomer cement (RGMICs) have a higher bond resistance while still allowing fluoride release (Godoy-Bezerra et al., 2006; Maruo et al., 2010; Pereira et al., 2013). Sharafeddin et al. (2020) investigated the impact of adding fluoroxyapatite particles (NFHA) or nanosized fluorapatite (NFA) to an RGMIC.

Fluoride levels were also substantially higher in the NFHA and NFA groups after 35 and 70 days, respectively. The optimum concentration of additional NFHA and NFA for maximal fluoride release, according to the authors, was 25 weight percent, which virtually quadrupled fluoride release after 70 days when compared to the control group. In another study, Shankar et al. (2020) investigated the impact of nano-hydroxyapatite (Nano-HA) in orthodontic banding cement in vivo. After 60 days, the methylene blue dye penetration technique was used to measure microleakage under orthodontic bands. Compared to those cemented with Nano-HA-modified glass ionomer cement, orthodontic bands cemented with regular glass ionomer cement had the greatest microleakage ratings (Heravi et al., 2019).
hypothesized that the existence of an acrylic detachable device is linked to Candida carrier status and low salivary pH levels (Majima et al., 2014). Prior to treatment, the proportion of CA carriers was lowered to 14% in one research. Similarly, as compared to tooth-borne orthodontic appliances, the tooth-tissue-borne orthodontic equipment induced greater CA proliferation (Javed et al., 2014). The rise in Candida proliferation in detachable instruments wearers may be related to safety from mechanical and natural saliva and defense system removal (Arita et al., 2005). Managing the spread of CA under detachable acrylic equipment may help to avoid orthodontic stomatitis. It’s critical to detect new ways to treat CA that have developed a resistance to antifungal medicines. Antimicrobial characteristics of NP- incorporated acrylic polymers and their usage in detachable instruments are yet in the preliminary phases of research, and in-vitro models are being used (Sultan et al., 2019; Sugio et al., 2020). After adding SiO$_2$ (1%) and TiO$_2$ (0.5%) NPs to a PMMA acrylic resin, Gad et al. (2020) investigated how the flexural strength changed. The concentration of NPs in acrylic resin has an adverse effect on the final product’s flexural strength. When silver nanoparticles were introduced to two PMMA resins’ acrylic liquid, at various silver NP concentrations, a varied influence on flexural strength was observed. Another research found that samples of PMMA with silver NP reduced CA adhesion significantly and exhibited biocompatibility, as they had no effect on proliferation/cell metabolism and did not trigger genotoxic harm to cells (to investigate this, researchers utilized micro fibroblasts and human lymphocytes). PMMA samples with silver NPs had lower flexural strength than PMMA samples without NPs once again. The restrictions of the studies stated before must be acknowledged. Some researchers didn’t test the antibacterial or safety properties of the NP- combined acrylic polymers, while others only tested biocompatibility for 24–72 hours. The citotoxicity and immunological reaction may be affected by the size of the NP. Smaller silver NPs of 3 nm, for example, have been shown to be more cytotoxic than bigger silver NPs of 25 nm. When assessing the cytotoxicity of any NP- incorporated substance, this aspect must be considered.

3. Conclusion

While the application of nanoparticles in orthodontics may open up new options, the published research only looked at antibacterial or physical characteristics for a limited period of time, such as 24 hours to a few weeks. It’s also important to acknowledge the restrictions of studies conducted mostly in vitro. Knowledge on the long-term functionality of orthodontic material created using this way is scarce. It requires investigation, as do any safety problems (toxicity) associated with the NP sizes.

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