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Antibacterial and Anti-cariogenic Nanoparticles Implementation in Orthodontics-A State of the Art Review

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ABSTRACT

"Nanoparticles (NPs) are defined as a sub-ionized colloidal structure composed of synthetic or semi-synthetic polymers." These materials range from 10-100nm at least in one dimension. The purpose of innovation and research about various anti-microbial and anti-caries NPs is to improve human health and life. It is challenging for individuals and dentists as the oral pathway is the most complicated, and the fortification of this channel is essential as this site is favorable for microorganisms to grow. The most significant cause of caries is a plaque attached to the tooth. This Plaque biofilm also leads to other dental (Gingival) disorders and protects microorganisms from getting destroyed by the host defense mechanism.

To overcome this problem, adhesive, cement, or acrylic resins have been incorporated with unique anti-microbial properties. These include nano-fillers and variants of apatite, i.e., hydroxyapatite, fluorohydroxyapatite and fluorapatite. We performed extensive search on bibliographic databases like pub med, google scholar, Scopus for review article on nanoparticles and its implementation in orthodontics and further compiled the necessary information from 6 related review articles into present article to elaborate the review. This research article aims to briefly define the application of anti-microbial and anti-caries NPs in dentistry, focusing on the branch of Orthodontics. NP's help to enhance antibacterial and physical properties, such as shear bond strength, and its biological and chemical properties make it more innovative.

Key words: Nanoparticles, Microorganisms, Fluorapatite

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INTRODUCTION

In the field of medicine as well as dentistry, Nanoparticles have their importance. These sub-colloidal structures are less than 100 nm in one dimension [1]. These may occur in different forms, such as grains, Nano holes, clusters, or a combination. The fundamental approach of incorporating NP's in dentistry is because they possess a larger surface area to mass ratio compared to bigger-sized particles, which helps make materials' chemical and mechanical qualities better and increases their reactivity [2]. High-charged nanoparticles (NPs) interact with the negative charges of the bacterial cell surface to produce anti-microbial activity [3]. Nowadays, antibiotic resistance is developed by many bacterial strains. To overcome this, silver, gold, etc, NP's are incorporated as they range from 1-10 nm in size and have a bactericidal effect. There are two ways to prevent biofilm formation; containing Nanoparticles entails covering the surface with NPs or mixing them with dental material to avoid additional bacteria adherence [4,5]. NP's of many inorganic and organic materials, including silver, gold, oxide particles Eg. zinc oxide (ZnO), and titanium dioxide (TiO2), because they possess broad-spectrum antibacterial properties [6]. Another mechanism used for appliances, especially orthodontic appliances, is coating the surfaces of these appliances. This is done with a fine coating of nitrogen-doped titanium dioxide. All this is done to lessen the number of microbial pathogens responsible for caries, suppress them, and lessen the decalcifications surrounding cemented orthodontic braces. Because of their ultra-small sizes, significant surface area to mass ratio for anti-microbial activity, close interaction with microbial membranes, and unique physical and chemical properties, antibacterial and anti-caries NPs seem promising. This review article emphasizes NP's anti-microbial and anti-caries

properties in orthodontics. We performed extensive search on bibliographic databases like pub med, google scholar, scopus, web of science for review articles on nanoparticles and its implementation in orthodontics and further compiled the necessary information from 6 related review articles into present article to elaborate the review. These articles' reference lists were read, and any relevant references were tracked down. Duplicate articles were removed from the list. To choose articles for full-text retrieval, titles and abstracts were screened.

Application of anti-microbial property of NP's in orthodontics

Due to orthodontic therapy, enamel demineralization occurs, which is one of the unwanted side effects [7]. Because patient wears orthodontic appliances actively and due to which level of acid-producing bacteria, including lactobacillus and staphylococci species increases which are responsible for the formation of biofilm over a tooth surface, change the oral microbiota and ultimately affect the self-cleansing ability of teeth [8-11]. Along with this, bacteria prone to caries may adhere to tooth surfaces, or there may be an interface between an orthodontic appliance and the tooth surfaces, which results in the production of a biofilm over the surfaces of the tooth and eventually decalcification or the development of white spots around brackets [12].

In orthodontics, composite is used as an adhesive substance to adhere brackets to the tooth surface. Unfortunately, the bracket may debond, and due to plaque formation, demineralization around the bracket occurs mainly during fixed orthodontic treatment in 50% to 75% of patients [13-15]. To overcome this, patient is educated on oral hygiene maintenance, and mechanical therapy is provided to remove biofilm. Still, a long-term treatment method is needed with anti-adhesion and antibacterial properties. A study showed that the incorporation of NPs in adhesive materials, for Eg. Composite resin and resin modified glass ionomer cement (RMGIC), acts as an anti-adhesive material and has antibacterial properties that prevent the accumulation of plaque [16,17]. According to research by Sodagar, et al. eliminating cariogenic microorganisms enhances the anti-microbial characteristics and shear bond strength of silver (Ag)/hydroxyapatite non-fillers [18]. In the case of orthodontic elastomeric modules for Eg. Ligatures which are allied by Ag NP which releases silver ions that affect the adhesion of the most common etiological pathogen, i.e., Streptococcus mutants, and inhibit bacterial action around wires and brackets [19]. The advantages of adding Ag are biocompatibility of the materials and have no ability for mutation and cytotoxicity. Also, these materials show a delayed type of hypersensitivity and negligible irritation to the mucosa and do not affect the shear bond strength of the material [20]. The incorporation of TiO2 NP shows suitable antibacterial properties but weakens the shear bond strength [21]. Because of its excellent fluoride ion release, RMGIC is a commonly used NP in orthodontic appliances [22,23]. There are four potential approaches for including NPs in dental materials used in orthodontics to enhance their anti-microbial and anti-caries effects:

A thin coat of nitrogen-doped titanium dioxide (TiO2) over the surface of orthodontic brackets: Because of the high biocompatibility and chemical stability of TiO2 NP these are used widely on orthodontic brackets. It has a wavelength of <385 nm, and due to this, it becomes strongly oxidative upon illumination. It shows Photocatalytic reaction by utilizing visible light by doping or surface modifications of TiO2 NP [24,25]. Upon activation in visible light, hydrogen peroxide, superoxide ions, peroxyl radicals, and free radicals of the OH type are released. A series of oxidation reactions occurs through which chemicals metabolize biological substances, including lipids, enzymes, and nucleic acids. Still, there is a significant increase in antibacterial properties by incorporating TiO2 into orthodontic adhesives without disturbing mechanical properties Eg. shear bond strength [26,27]. High antibacterial and high adhesive properties are made possible by a fine layer of Titanium dioxide NP deposited on the orthodontic bracket compared to the typical oral microbial flora [25]. TiO2-coated orthodontic appliances are costly and time-consuming process. Therefore, a fine film of nitrogen-doped TiO2 is implemented in orthodontic appliances to give long-term (90 days) success rates and antibacterial properties against Streptococcus mutants [28]. Nitrogen-doped TiO2 has high hydrophilicity, and due to this, it resists the formation of plaque over the tooth surface around brackets [2].

Combination of glass ionomer cement (GIC) or RMGIC with fluorapatite, fluorohydroxyapatite, or hydroxyapatite NPs: Orthodontic brackets are adhered to tooth surface using a variety of types of cement. One of them is glass ionomer cement bonded to the tooth surfaces with brackets, but it has a limitation of low bond strength [29]. To overcome this issue, some modifications are done in GIC. RMGIC is used instead of GIC because of high bond strength compared to GIC, and it releases fluoride, which shows anti-microbial properties [30]. According to Lin, et al. [31], it is due to adding nano-sized fluorapatite of flurohydroxyapatite into RMGIC. However, there has been a noticeable decline in shear bond strength, which is unsuitable for cementing orthodontic braces. Maximum shear strength is measured a day after cement application, necessitating a lengthy clinical experiment. Also, more time is required to release fluoride in cases with the addition of nano-sized fluorapatite (NFA) or flurohydroxyapatite (NFHA), that is, 35 and 75 days, respectively [31]. An in-vivo study by Enan, et al. [32], they found that orthodontic bands modified by nano-hydroxyapatite into GIC have shown less microleakage than conventional GIC.

Addition of silver, TiO2, or other NP's into orthodontic adhesives: Patient cooperation is continuously required during orthodontic treatment to maintain oral hygiene. Therefore, nowadays, many clinicians focus on treatment without much patient compliance because orthodontic

brackets, as well as adhesive material used to bond it, can accumulate plaque on the tooth surface, which ultimately leads to demineralization of enamel around it or the formation of white spots over tooth surface which prone to decay. Numerous strategies are used to combat this, including brushing with fluoride toothpaste [27], cementing brackets using anti-microbial cementing materials, a thin layer of a remineralizing agent over orthodontic brackets or wires, mouth rinses with the addition of anti-microbial agents, etc. [33]. But all these approaches show limited results in research. Due to the invention of nanotechnology in dentistry, specific nanoparticles are incorporated into these adhesives, increasing the antibacterial and mechanical properties and the biological and chemical properties of parent adhesives [34]. It prevents bacterial adhesion on the tooth surface and around the brackets and adhesive material and further demineralization of enamel. Many kinds of literature showed that incorporating nano-fillers into adhesives decreases the demineralization of enamel without arbitration in the physical properties of parent material, such as shear bond strength [35]. Compared with conventional orthodontic adhesives, adhesives incorporating nano-fillers tend to reduce the roughness of materials used for surface adhesion, except for silver NP. Ahn examined the effectiveness of adding various concentrations of silver nanoparticles to orthodontic adhesives. As a result, he found that silver shows a marked reduction in the adhesion of streptococcus mutants to the tooth surface and adhesives because of its highest anti-microbial property.

Incorporation of silver, Silicon dioxide (SiO2), and TiO2 into acrylic orthodontic materials: Removable orthodontic appliances are fabricated using cold-cure acrylic resin, mainly polymethyl methacrylate (PMMA). When acrylic resin is used as a part of orthodontic treatment, microbial flora adheres more readily on and around it than natural teeth [36]. Due to this, different clinical conditions can be seen beneath the denture; for Eg., Candida-induced stomatitis is of utmost priority. The prevalence of candida albicans inflammation is more common in acrylic denture wearers than in routine oral flora, according to other literature on candida albicans role in acrylic materials [36,37]. Sodagar investigated the changes in strength properties following the inclusion of various NP's into acrylics, such as silver, TiO2, SiO2, etc. A different concentration of NPs adversely affects the flexural strength of the final material. Another study showed that acrylic resin incorporated with silver nano-fillers has marked resistance to candida albicans. It prevents adherence of candida albicans beneath the dentures and has higher biocompatibility [38]. TiO2 shows antibacterial properties and other advantages such as white color, high stability, cost-effectiveness, and less toxicity [38,39]. Therefore, it serves as appropriate material for incorporation into orthodontic acrylic materials (Table 1).

Criteria for selection of literature of review is that after searching the articles related to current topic of review article, most of them which are added in table 1 were relevant in adding the essential information to enhance the importance of topic and to make it more purposeful. Also, nano particles like silver, silica dioxide, titanium dioxide and their effect on orthodontic treatment has been clearly mentioned along with their advantages specially in the field of orthodontics.

According to Ali Borzabadi Farahani, et al. this study aimed to combine orthodontic materials with addition of NP's or coating surfaces with NPs to inhibit bacterial growth. He found that addition of silver NP's to PMMA resins resulted in flexural strength variations at different concentrations of NP's [40]. Certain NPs have been added to orthodontic adhesives to regulate the oral flora and lessen demineralization around the brackets because of their biocidal or anti-adhesive properties. Furthermore, the efficacy of new nano-adhesives must be guaranteed over a clinically appropriate duration, together with their antibacterial and anti-adhesive capabilities. So far, NPs have been added to orthodontic materials or coated on the surface of brackets to take advantage of specific NPs' special qualities.

According to Alberto, this study is mainly focused on the materials used in orthodontic treatment such as, orthodontic elastomeric ligatures, orthodontic bands and orthodontic mini screws. It also focused on how to reduce the frictional forces in orthodontics. Earlier researches assessed capability of relationship between elastomeric ligatures and a material that has potential ability to reduce the cariogenic activity of white spot forming micro-organisms i.e. silver nanoparticles, in spite of altering mechanical properties of material

Table 1: Literature review.

Author (Year)	Aim	Finding
Ali Borzabadi, et al. [40]	The overall aim of incorporating Nanoparticles in orthodontics is to decrease plaque formation.	After incorporation of NPs into orthodontic materials shows antibacterial properties, physical properties, and biological and chemical properties.
Alberto, et al. [41]	Describe the most current and well-known advancements in orthodontic nanotechnology.	Incorporating Nanoparticles into orthodontics helps partially solve limitations of dental materials and technical procedures.
Mandall, et al. [42]	Aspire to assess the efficiency of several adhesives used in orthodontics	According to this study, there is no clear evidence about which adhesive should be used in orthodontics.
Iris Xiaoxue Yin, et al. [43]	The aim of this study is that they focus on the antibacterial properties of Ag NPs in dentistry.	The incorporation of Ag NPs into orthodontic materials enhances the anti-microbial as well as physical properties.
Wenjing, et al. [44]	Studies the creation, uses, and underlying workings of anti-microbial nanoparticles in dentistry.	Antimicrobial NPs have a broad utility in dentistry; however, they may be impacted by concentration, kind, shape, and other aspects.
Ranjeet, et al. [45]	Studied the impact of adding Ag nanoparticles to multiple biologic materials in various other dental applications will be discussed.	AgNPs prevent biofilm formation on composite surfaces, preventing microleakage and secondary caries.

enhancing the quality of orthodontic treatment. It is highly cytotoxic to variety of micro-organisms. The exact etiology is not known but it may be due to synthesis of DNA and denaturation of enzymes of respiratory cycle. It is advantageous because it has less toxicity and high biocompatibility. In order to prevent the initiation of demineralization, orthodontic bands cementing with antimicrobial NP's has been incorporated. Orthodontic Mini screws are primarily used for anchorage control and development of force to get the desired results. Several researches have examined the osseointegration and strength of mini screws modified by TiO2 nano tube arrays. It enhances the surface roughness and wettability. According to orthodontic therapy, these current modifications are incentive for future purpose [41]. The core objective of orthodontic therapy is to organize it in a coordinated and safe manner. Scientific and technical constraints on dental materials and techniques frequently prevented this from happening, but science and nanotechnology have slightly overcome these constraints and improved patient care along the clinical pathway. To create materials that are completely safe and biocompatible, more research is required.

According to Mandall, et al. this research aims to examined effectiveness of various orthodontic adhesive materials on bonding purpose. It is carried out to overcome the crisis of debonding of brackets which is responsible for treatment prolongation which ultimately results in decalcification of enamel due to fixed orthodontic treatment. As a result of this research there is no straight forward proof for appropriate use of type of orthodontic adhesive material during fixed appliance therapy mainly due to inappropriate design and reporting of existing trails [42].

According to Iris Xiaoxue Yin, this study aims to study the antibacterial and anti-caries mechanism, safety and possible uses of silver NP's in orthodontic treatment. Result showed that there is no exact known mechanism of silver NP's but probably it may be due to release of Ag ions through Ag NP's which helps to kill the bacteria's. This improves the antibacterial and mechanical characteristic of orthodontic materials [43]. The potential toxicity of AgNP is still unclear in terms of its clinical importance. Additional research is required as there is lack of clinical proof.

Acording to Wenjing Song, et al. various studies concentrated on antibacterial characteristics of NP's and showed excellent antibacterial properties in drug resistant bacteria. This study focused on the application, development and the related mechanisms of antibacterial NP's in the field of orthodontics. Development of multipurpose orthodontic cement incorporated with NP's shows superior antibacterial properties which can prevent accumulation of plaque on adhesive cements and in and around the brackets. As a result this study demonstrate that NP's have broad perspective in the field of orthodontics [44]. The inclusion of copper oxide (CuO) and (CuO-ZnO) NPs had a higher antibacterial action and control than ZnO NP groups, according to the proof. The incorporation of AgNPs into orthodontic retainers exhibited a potent antibacterial impact on S. mutans during the debonding stage in vivo.

According to Ranjeet, et al. this review concentrated on effect of addition of silver NP's in orthodontic materials in dentistry. Ag-NP loaded band cement incorporated with silver NP's which showed superior antibacterial properties and prevents enamel decalcification without altering the mechanical properties of cement [45]. AgNP inclusion reduces the formation of biofilm on composite surfaces, preventing microleakage and secondary caries. It helps in improving adhesion between dentine and biomaterial, changing the bond strength, and the mechanical characteristics of restorative materials.

CONCLUSIONS

In this review article, antibacterial and anti-caries properties of NP's are explored. Our results illustrate that although NPs have a powerful antibacterial effect, other parameters such as concentration, kind, and form can affect how antimicrobial they are. Overall literature studied in this review article has shown that nanoparticles have immense importance in the field of orthodontics. Orthodontics provides a novel implementation of different NPs in various aspects of treatment offered by an orthodontist. NP's help to enhance antibacterial and physical properties, such as shear bond strength, and its biological and chemical properties to make it more innovative. It increases the bond strength between orthodontic materials and tooth surface, making it resistant to cariogenic bacteria and preventing white spot lesion formation. In order to understand the precise mechanism, more studies are necessary to clarify the unique antibacterial mechanism and toxicity.

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