



Nanoparticles and their Applications in Orthodontics

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Abstract

Nanoparticles (NPs) are insoluble particles smaller than 100 nm in size and the set of technologies that enables manipulation of these particles on an atomic, molecular and supra molecular scale is termed as 'Nanotechnology'. Applications of nanotechnology are being ventured in various domains including health care and have also carved their way into various specialties of dentistry. This article presents an insight into various types of nanoparticles and their application in the field of Orthodontics. The various tests performed when using nanoparticles, to detect the physical and biological properties of the new material, are also summarized for easy referral.

Keywords: Nanoparticles; Nanotechnology; Orthodontics

Abbreviations: NPs: Nano Particles; MRI: Magnetic Resonance Imaging; USP: Ultrasonic Spray Pyrolysis; NFA: Nano Sized Fluoroapatite; NFHA: Nano Fluorohydroxyapatite; PSPMA: Polymer 3-Sulfopropyl Methacrylate Potassium Salt; RMGI: Resin Modified Glass Ionomer Cement; FN: Fluoride Releasing Nanofilled Composite; AFM: Atomic Force Microscope; Bio MEMS: Biomedical Micro Electro Mechanical Systems; NEMS: Nano Electro Mechanical Systems

Scope of this Review

This article presents a brief overview on basic definitions related to field of nanotechnology, types of nanoparticles, nanotechnology and types of nanoparticles. The focus of this article is on application of nanoparticles in orthodontics. Though there are many articles published on nanodentistry, and a few on its application in orthodontics, none of them gives an overview of the various tests performed to detect the physical and biological properties of the new nanomaterials. This article provides an easy reference to a researcher who is experimenting on application of nanoparticles. The review concludes with an outlook of future scope of nanotechnology in orthodontics.

Introduction

Revolutions in the field of science and technology have given promising results in the field of material sciences and one such advancement is nanotechnology. Nanotechnology, which concerns structures at the Nano scale, is considered as a vital current technology of the 21st century based on its economic and scientific potential. Its application is being experimented in various domains in orthodontics, from surface coatings to development of novel materials.

What are nanoparticles?

British Standards Institution defines nanoparticles as those particles in which all the fields or diameters are in the nanoscale range. Whereas, nanomaterials are those material for which at

least one side or internal structure is in the nanoscale [1]. An engineered nanoparticle may be defined as any intentionally produced particle that has a characteristic dimension from 1 to 100 nm and has properties that are not shared by non-nanoscale particles with the same chemical composition [2].

What is nanotechnology?

Nanotechnology is the science of manipulating matter, measured in the billionths of a nanometer, roughly the size of two or three atoms [3].

What is nano dentistry?

It is the science and technology of maintaining near-perfect oral health through the use of nanomaterials including tissue engineering and nanorobotics [4].

Types of Nanoparticles

Nanoparticles are generally classified based on their dimensionality, morphology, composition, uniformity, and agglomeration. The various types of nanoparticles are Nano pores, Nanotubes, Quantum dots, Nano shells, Dendrimers, Liposomes, Nano rods, Fullerenes, Nano spheres, Nanowires, Nano belts, Nano rings and Nano capsules [5]. Following are some of the successfully employed nanoparticles in various uses:

Silver

Silver nanoparticles have been found to be effective against bacteria, viruses and other eukaryotes [6,7]. Successful

employment of these nanoparticles as antimicrobial agents is being done in textile industries, for water treatment, in cosmetics like in sunscreen lotions [8,9] and widely in dentistry in fabrication of new materials like cements and resins etc. Green synthesis of silver nanoparticles by plants such as *Azadirachta indica* [10], *Capsicum annuum* [11] and [12] has also been reported by various studies hence reducing their cytotoxicity.

Gold

Gold nanoparticles (AuNPs) have found application in immunochemical studies for protein identification and are also used for DNA detection and cancer diagnosis [13,14]. Nano stenciled RGD gold patterns are being used for tissue engineering.

Alloy

The structural properties of alloy nanoparticles differ from their bulk samples [15]. Silver flakes are widely used as silver has the highest electrical conductivity among metal fillers and their oxides have relatively improved conductivity [16]. The properties of bimetallic alloy nanoparticles are influenced by both metals and show better properties than ordinary metallic NPs [17].

Magnetic

Magnetic nanoparticles like Fe_3O_4 (magnetite) and Fe_2O_3 (maghemite) have been actively studied for their possible use in various fields including treatment of cancer, gene therapy, DNA profiling, sorting and manipulation of stem cells, guided drug delivery systems, and magnetic resonance imaging (MRI) [18].

Copper

Due to the antibacterial and antifungal activity along with the catalytic, optical, electrical properties and application of copper nanoparticles has been quite a focus in health-related issues. Synthesis of nano-copper particles is mostly done in the micro emulsion form.

Chitosan

It is a biopolymer derived by the deacetylation of chitin, a natural polymer that occurs in exoskeleton of crustaceans. Chitosan is a positively charged particle which is soluble in acidic to neutral solution. These nanoparticles are being investigated as a potential platform for local drug delivery.

Quarternary Ammonia Nanoparticles

Quarternary poly ethylene imine nanoparticles as antimicrobials incorporated in composite resins have been developed. The hydrophobic nature and the cationic surface charge of these particles add on to their antimicrobial activity.

Zinc Compounds

These nanoparticles exhibit antibacterial, anti-corrosive, antifungal and UV filtering properties. Low toxicity and good biocompatibility make it suitable for biomedical usage. Nano Zinc can decrease biofilm formation by inhibition of the active

transport and metabolism of sugars as well as disruption of enzyme systems by displacement of magnesium ions essential for enzymatic activity of the of dental biofilms [19].

Titanium Dioxide

Nanoparticles of this compound have been used in biomaterials in order to induce antimicrobial properties. Effective catalytic effect and other properties such as white color, low toxicit, high stability and efficiency along with availability and low cost have made these nanoparticles an appropriate additive for use in dental materials [20].

Others

Nanoparticles of oxides under consideration for use include those of silica, tin, copper and tungsten trioxide.

Uses of Nanoparticles in Dentistry

Nanoparticles have been successfully used in various forms in dentistry from administering local anesthesia, simple cure of dentinal hypersensitivity to diagnosis and cure of oral cancer. Nano needles and Nano fibers have been employed for wound dressings [21]. Nanoparticles due to their property of biocidal, anti-adhesive, and delivery capabilities are being explored to prevent the formation of biofilms within the oral cavity. As nanoparticles possess a greater surface-to-volume ratio when compared with non-nanoscale particles, they can interact more efficiently with microbial membranes and provide considerably larger surface area for antimicrobial activity. Metal NPs in the size range of 1-10 nm have particularly shown the greatest biocidal activity against bacteria. Nanoparticles can be used as device coatings, as topically applied agents, and within dental materials [22,23].

Nanoparticles of Silver have been identified to be considered in dental resin composites as antimicrobial components. Low percentages of silver - zinc antimicrobial zeolites added to polymethyl methacrylate can be used for the reduction of microbial contamination of tissue conditioners, acrylic resin denture bases, and acrylic base plates of removable orthodontic appliances [24]. Incorporation of silver zeolite nanoparticles into mouth rinses and toothpastes has also been tested [25]. Small size of silver and zinc particles makes penetration through cell membranes of microbe easier, thus affecting intracellular processes resulting in higher reactivity and antimicrobial activity [26].

Nanoparticles can also be used in various restorative dental materials and procedures, including cavity liners, pit and fissure sealants, cores and buildups, indirect restorations, cements for crowns or orthodontic devices, provisional restorations, endodontic sealers, and root canal posts [27]. Nanofillers integrated in vinylpolysiloxane have been seen to produce a unique addition to siloxane impression materials that have better flow with improved hydrophilic properties and enhanced detail precision [28]. Mixing of alginate impression powders with water containing silver hydrosol can be considered to create an

impression material with an antimicrobial property, reducing microbial cross contamination to the poured stone model from the infected impression [29].

Application of Nanotechnology in Orthodontics

Nano-coatings in arch wires and brackets to reduce friction

Friction is one of the major deterrents present in alignment or retraction of teeth during orthodontic treatment. To conquer over it one method is to apply higher forces, which might lead to undesirable anchorage loss. The other alternatives are to vary the wire size and shape, altering the bracket design or coating the wire surfaces with different materials which may aid in conquering sliding resistance. These coatings have been applied either on bracket surface, or S.S. or NiTi wires. In the previous years many researchers have tried using tungsten disulfide as a surface lubricant. Naveh et al. [30] and Samorodnitzky et al. [31] reported reduced friction after coating Nickel-Titanium (NiTi) wires with nanoparticles of WS₂ in the laboratory [30].

Similarly stainless steel wires have been coated with a composite coating of Nickel-phosphorous and fullerene-like nanoparticles of tungsten disulfide (WS₂) placed by composite electro less deposition [32]. Composite coatings of Co and fullerene-like WS₂ nanoparticles have also been tried [33]. WS₂ nanoparticles have been incorporated to Ni-W-P alloy coating and they not only reduced the coefficient of friction but also helped in improving the corrosion resistance of the coating further [34].

Considering possible toxicity of WS₂, new self-lubricating coatings, in which metals other than WS₂ have been used. Wei et al. [35] suggested use of Carbene Nitride (CN_x) coatings on stainless steel wires [35]. Similarly coatings of ZnO [36,37]. Inorganic fullerene like Molybdenum Disulfide nanoparticles [38] and diamond like carbon coating and nitro carburizing [39] have been suggested. The nanostructured DLC coating also provided excellent corrosion resistance and good elasticity when coated on S.S. wires.

Fabrication of hollow wires

Hollow wires are wires coated with NiTi/Ni-TiO₂ composite nanoparticles via the synthesis method called ultrasonic spray pyrolysis (USP). The precursor solution for the synthesis of spherical NiTi particles is prepared from an orthodontic wire with a chemical composition of Ni (amount fraction $x = 51.46\%$) and Ti ($x = 48.54\%$). A textile or polymer fiber is coated with NiTi nanoparticles via electrospinning and then the fiber is removed to produce a hollow wire for orthodontic purposes. This wire could potentially have the shape-memory and superelasticity properties, while possibly reducing the material needed for the wire production. However with the current selection of the precursors, reaction gas and collection medium, it was difficult to obtain pure NiTi particles, which were desired. For this reason, further investigation of different precursor solutions, gases and

collection media needs to be conducted [40].

Orthodontic brackets

A new material which contained polysulfone embedded with hard alumina nanoparticles was developed in the year 2012 by UC3M for making orthodontic brackets. The material innovated had the properties of strength, reduced friction and biocompatibility while maintaining the transparency of the bracket [41].

Nanoparticles application as antimicrobial agent

White spot lesions and caries are common problems encountered while undergoing orthodontic treatment due to plaque accumulation around brackets. Nitrogen doped Titanium dioxide (TiO₂), Silver (Ag), Gold (Au), Silica (SiO₂), Copper (Cu/CuO) and ZnO nanoparticles have been coated on either brackets or added to cements and bonding agents to reduce the demineralization produced as a result of orthodontic treatment.

Nitrogen doped titanium dioxide (TiO₂) brackets: Orthodontic brackets have been coated with nitrogen doped titanium dioxide. The activation of Nitrogen doped Titanium dioxide 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. Limitation of this study is that 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 [42]. TiO₂ nanoparticles of size 21±5nm have also been blended to light cure orthodontic composite paste (Transbond XT) in 1, 2, and 3%. All the three concentrations had similar antibacterial effects [43].

Fluoroapatite, fluorohydroxyapatite or hydroxyapatite NPs: Resin modified GIC has been improved by incorporating nano-sized fluoroapatite (NFA) or fluorohydroxyapatite (NFHA) particles at 25% concentration; however, this was at the cost of significant reduction in shear bond strength. The fluoride release nearly tripled after 70 days [44]. Nano-hydroxyapatite (Nano-HA) has also been added to orthodontic banding cement to prevent microleakage. This study assessed the microleakage under orthodontic bands by the methylene blue dye penetration method after 60 days [45].

Chitosan nanoparticles: Different concentrations of ZnO-NPs and CS-NPs mixture: 1%, 5% and 10% (1:1 w/w) were added to resin composite to induce antibacterial activity. It was found that Zinc NP when mixed with Chitosan NP in the ratio 10% (w/w) significantly induces antibacterial property higher than other groups [46].

Silver nanoparticles: Silver NPs have been added to composite adhesive containing silica nanofillers. 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). To increase antimicrobial activities, various concentrations of silver nanoparticles (diameter < 5 nm) have been added to the composite adhesive: 0 ppm, 250 ppm, and 500 ppm [23]. Silver and HA nanoparticles have also been added to the **primer of Transbond XT** in 1%, 5% and 10% silver concentrations. It was found that incorporation of silver/HA nanoparticles in 5% and 1% concentration maintains and increases the Shear bond strength of orthodontic adhesives, respectively, whereas increasing the amount of particles to 10% has an undesirable effect when compared to the control group [47].

Nanosilver coating process has been applied to **orthodontic brackets** placed in rat. Dental plaque, mucosal vestibular smears, saliva, and blood samples were collected from rats at various days. It is suggested that nanosilver coated orthodontic brackets, as an antibacterial agent without patient compliance, could be helpful for the prevention of white spot lesions during fixed orthodontic treatment. Since bacterial infection has been identified as one of the major causes of **titanium implant** failures, a novel antibiotic vehicle composite, TiO₂NT-PSPMA, has been synthesized via atom transfer radical polymerization; this method improved the local antibiotic concentration and prolonged its sustainable release by loading larger amounts of antibiotic into Titanium nanotubes (TiO₂ NTs) arrayed on Ti implants. Ag nanoparticles (NPs) were loaded into TiO₂ NTs with the assistance of the ionic polymer 3-sulfopropyl methacrylate potassium salt (PSPMA). This composite increased the storage of Ag NPs by employing nanotubes and using PSPMA to trap larger amounts Ag NPs. This experiment showed that the composite had a dose-dependent cell proliferation by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), indicating that the composite perhaps could be used in future to prevent implant infection [48]. Silver nanoparticles have been successfully added to PMMA to produce an antimicrobial resin without compromising on their physical properties. However, their long term effects on tissues need to be verified [49,50].

Copper: Copper NPs have been added to orthodontic adhesive at 0.0100 wt%, 0.0075 wt%, and 0.0050 wt%. Significantly higher bond strength was obtained with the orthodontic adhesive that included 0.0100 wt% of copper NPs [51].

TiO₂, SiO₂ or Silver NPs to acrylic resins: TiO₂, SiO₂ or silver NPs have been added to Cold-cure acrylic resins that are mainly made of polymethyl methacrylate (PMMA). The limitations with these studies are that some did not assess the antibacterial or safety of the NP-incorporated acrylic materials [52,53] or assessed the biocompatibility over a short period of time (24–72 h) [51,54]. The NP size may also affect the cytotoxicity and immunological response.

Zinc oxide: Zinc oxide has been added to light cured Resin modified glass ionomer to create mixtures of 13% ZnO and

23.1% Zinc oxide. It has been observed that as the concentration of Zinc oxide increases, antimicrobial activity significantly increases. Antimicrobial activity of Zinc oxide lasts for at least 1 month, albeit at lesser levels. It was also observed that as the concentration of zinc oxide increased, shear bond strength decreased. Future studies should evaluate more refined methods of adding zinc oxide in order to have less impact on the physical properties of the bonding agent. Further clinical studies are needed to assess the capabilities of zinc oxide as an intraoral antimicrobial agent [55]. Combined effect of Zinc oxide and CuO has also been studied and it has been observed that CuO and ZnO-CuO nanoparticles coated brackets have better antimicrobial effect on *S.mutans* than brackets coated with Zinc oxide or CuO alone [56].

Fluoride releasing nanoparticles: Fluoride releasing and enamel demineralization inhibition capacity of fluoride-releasing nano filled cement around orthodontic brackets has been evaluated using an artificial caries biofilm model. 4 groups: non-fluoride-releasing microfilled composite, fluoride-releasing microfilled composite, resin-modified glass ionomer cement (RMGI), and fluoride-releasing nanofilled composite (FN) were tested. Under the cariogenic exposure condition of this study, the fluoride-releasing nanofilled material had similar performance to fluoride-releasing microfilled materials. The presence of nanofillers in the fluoride releasing materials studied did not promote further benefits against caries lesion development around brackets and presented inferior demineralization inhibition than the resin modified glass ionomer material [57].

Quaternary ammonium monomer dimethyl aminododecyl methacrylate (DMADDM): In 2014, DMADDM, a recently-synthesized antibacterial monomer, was incorporated into orthodontic cement at 0%, 1.5%, 3% and 5% mass fractions and then the bond strength of brackets to enamel was measured. A microcosm biofilm model was used to measure metabolic activity, lactic acid production, and colony-forming units. DMADDM-containing orthodontic bracket cement possessed a strong antimicrobial activity when incorporating 3% of DMADDM. The anti-biofilm potency increased with increasing the DMADDM mass fraction; however, the enamel bond strength had a slight decrease at 5% DMADDM [58].

Use of Nanoparticles in Tissue Engineering

Nano-stenciled rgd-gold patterns

An experiment was done to analyze how restricting the size of cell-matrix adhesions affects cell morphology and behavior. Cultured fibroblasts adhere to extracellular substrates by means of cell-matrix adhesions that are assembled in a hierarchical way, thereby gaining in protein complexity and size. Using a nanostencil technique, culture substrates were patterned with gold squares of a width and spacing between 250 nm and 2 μm. The gold was functionalized with RGD peptide as ligand for cellular integrins, and mouse embryo fibroblasts were plated.

Limiting the length of cell-matrix adhesions to 500 nm or less disturbed the maturation of vinculin-positive focal complexes into focal contacts and fibrillar adhesions, as indicated by poor recruitment of $\alpha 5$ -integrin. It was found that on sub-micrometer patterns, fibroblasts spread extensively, but did not polarize. Instead, they formed excessive numbers of lamellipodia and a fine actin meshwork without stress fibers. Moreover, these cells showed aberrant fibronectin fibrillogenesis, and their speed of directed migration was reduced significantly compared to fibroblasts on 2 μ m square patterns. Interference with RhoA/ROCK signaling eliminated the pattern-dependent differences in cell morphology. Our results indicate that manipulating the maturation of cell-matrix adhesions by nanopatterned surfaces allows to influence morphology, actin dynamics, migration and ECM assembly of adhering fibroblasts. Thus in the future, the nanostencil method may offer new possibilities to control more precisely the interaction of mesenchymal cells with implant surfaces, and to influence their differentiation around the implant [59].

Nanoclay reinforced magnesium substituted E-Tcp

Advances in the field of nanotechnology presented a wide range of solutions to biological problems of high rate of microimplant failure. A nanocoating of nanoclay reinforced magnesium substituted E-TCP was placed on titanium surface to enhance the stability of orthodontic miniscrews. The nanoclay used is Na⁺-montmorillonite ("Cloisite Na⁺") powder (Southern Clay Products, TX, USA). The nanoclay suspension was prepared by dissolving clay powder in DI water under vigorous stirring for 1 week prior to use [60].

Nanosized hydroxyapatite paste/scaffolds

Biomimetically synthesized nanosized hydroxyapatite particles have been converted into an injectable paste using a neutral phosphate buffer. Synthesized system manifested a self setting behavior at 37°C in 20 min and revealed a macroporous self assembled microstructure. Stability of the injectable hydroxyapatite has been confirmed in aqueous medium as well as in human blood. These hydroxyapatite pastes can be used to fill defects in damaged bone due to any cause [61].

Titanium nanotubes with embedded silver oxide nanoparticles as biomedical coating

TiO₂ nanotube (NT) arrays have been found to significantly enhance the functions of many cell types including osteoblasts thus having promising applications in orthopedics, orthodontics, as well as other biomedical fields. TiO₂ NT arrays with Ag₂O nanoparticles embedded in the nanotube wall (NT-Ag₂O arrays) were prepared on titanium (Ti) by TiAg magnetron sputtering and anodization. Well-defined NT arrays containing Ag concentrations in a wide range from 0 to 15 % were formed. Crystallized Ag₂O nanoparticles with diameters ranging from 5 nm to 20 nm were embedded in the amorphous TiO₂ nanotube wall and this unique structure lead to controlled release of Ag

that generated adequate antibacterial activity without showing cytotoxicity. The NT- Ag₂O arrays can effectively kill *Escherichia coli* and *Staphylococcus aureus* even after immersion for 28 days, demonstrating the long lasting antibacterial ability. Furthermore, the NT- Ag₂O arrays have no appreciable influence on the osteoblast viability, proliferation, and differentiation compared to the Ag free TiO₂ NT arrays. Ag incorporation even shows some favorable effects on promoting cell spreading and can be used as a biomedical coating on devices [62].

Nano-Materials as Nanofillers in Orthodontics

Nano-sized filler particles have been incorporated into the composite matrix and glass ionomer cements. Nanofillers are of two types: nanoclusters and nanoparticles [63]. Nanofillers can be prepared by techniques, such as flame pyrolysis, flame spray pyrolysis, and sol-gel processes. The addition of fillers reduced size has capacitated filler load enhancement thus reducing polymerization shrinkage and improving mechanical properties of strength. Various studies have tested the bond strength of nanocomposites and nanoionomers and have concluded that they can be used for orthodontic bonding [63-66]. Silica nanosized filler particles (10 wt%, particle diameter < 7 nm) have also been added to orthodontic adhesives [23]. Titanium dioxide and zirconia are particularly useful nanofillers, as they have very high refractive indices, and will require less weight of material than a lower refractive index material to match the refractive indices appropriately [67]. Nanozirconia has also been used in ionomer cements and provides for improved properties, including enhanced aesthetics (e.g. low visual opacity), polish retention, and radiopacity as compared to previously known glass ionomer compositions. The nanozirconia is surface modified with silanes to aid in the incorporation of the nanozirconia into ionomer compositions [68].

Enamel Remineralizing Agents

Nano particles have been used not only as antimicrobial agents but as agents for remineralization of decalcified enamel. Nano-hydroxyapatite has been introduced as nanotechnological advancement in the products for the remineralization of enamel and has been developed as a paste. Medeiros et al. [69] concluded that calcium nanophosphate forms a protective layer on the enamel surface and provides protection against erosion. Calcium nanophosphate crystals which are smaller than 100 nm, lead to improved bioactivity of the product, resulting from the increase in surface area and wet ability of HA nanoparticles. Calcium, phosphate and fluoride ions are released and organized on fluoroapatite and CaF₂ on demineralized tooth surface. In a comparative study by Carvalho et al. [70] on the effect of calcium nanophosphate and CCP-APP paste, it was concluded that calcium nanophosphate is a better remineralizing agent for eroded enamel surfaces. Thus, calcium nanophosphate could be used as a remineralizing agent after debonding of orthodontic brackets [70]. Various applications of nanoparticles in orthodontics are summarized in (Table 1).

Table 1: Various applications of nanoparticles in Orthodontics.

S.No	Application	Nanoparticle	Applied on	Tests used
1.	Surface coating to reduce friction	1.Nickel-phosphorous and tungsten disulfide (WS ₂) 2.Co + fullerene-like WS ₂ 3.Carbon Nitride (CN _x) 4.ZnO 5.Molybdenum Disulfide 6.Diamond like carbon coating and nitrocarburizing 7.Polysulfone embedded with hard alumina nanoparticles for brackets	Brackets, Niti Wires, S.S.wires	<p>To detect friction:</p> Tribological assays using ball-on-flat device. Friction tests by an Instron machine. Adhesion properties by a Raman microscope. <p>To detect Quality of coating:</p> SEM (scanning electron microscope) EDS (energy-dispersive X-ray spectrometer) Scotch-tape test Wire bending test <p>Corrosion behavior:</p> Potentiodynamic polarization test and electrochemical impedance spectroscopy Surface and cross-sectional characteristics, microhardness
2.	Fabrication of Hollow wires	NiTi/Ni-TiO ₂ composite nanoparticles	Fibers	TEM and EDX analysis(energy-dispersive X-ray spectrometer)
3.	Antimicrobial agent	1.Nitrogen doped Titanium dioxide (TiO ₂) 2.Fluorapatite, fluorohydroxyapatite or hydroxyapatite NPs 3.Zno 4.Chitosan nanoparticles 5.Silver NP 6.Cu 7.TiO ₂ NT-PSPMA 8.Nano-stenciled RGD-gold patterns 9.nanoclay reinforced magnesium substituted E-TCP 10.TiO ₂ , SiO ₂ 11.Flouride NP 12.quaternary ammonium monomer dimethyl aminododecyl methacrylate	Bracket surface Resin composite Resin modified GIC Implants Elastomeric ligatures Acrylic resins	Disc agar diffusion (DAD) test to test antimicrobial activity <p>Cytotoxicity to be checked on cell lines</p> Live and dead staining Lactate production spectroscopy <p>SEM to check uniform distribution of the nanoparticle</p> Shear bond strength on Instron machine And adhesive remnant index (ARI) scores microleakage under bands assessed by the methylene blue dye <p>Insolubility of NP</p> : atomic absorption test to check for
4.	Graft material	Injectable hydroxyapatite	Damaged/absent bone	Cytotoxicity, cell proliferation, and cell expression of osteogenic markers examined by biochemical assay and reverse transcription polymerase chain reaction.
5.	Nanofiller	Silica Zirconia(improves aesthetics) Titanium dioxide	Orthodontic adhesives	Shear bond strength and adhesive remnant index

6.	Enamel remineralizing agents	Nano-hydroxyapatite Calcium nanophosphate Fluoride	Paste	Surface microhardness (SMH) measurements Surface examination by scanning electron microscope
7.	Fabrication of brackets	Hard alumina nanoparticles embedded in polysulfone	Brackets	SX-ray diffraction for compositional changes Surface examination by colorimeter, scanning electron microscope (SEM), and atomic force microscope Fundamental material properties

Future Applications of Nanotechnology

Nanorobots in orthodontics

Nanorobotics centers are self-sufficient machines which are functional at the nanoscale. The nanorobot design consists of a biocompatible glycocalyx-coated diamondoid material with molecular sorting rotors and a robot arm (telescoping manipulator) [71]. Different nanorobot molecule types are distinguished by a series of chemotactic sensors and their functioning is controlled by a stimulator. Nanorobots may be used for manipulation of tissues directly at nano level and research has begun on the use of nanorobotics for medical applications like drug delivery, management of aneurysms and tumors. The theory of use of such nanorobots could be extended to dentistry and orthodontics in distant future, where nanorobots with specific motility mechanisms would navigate through periodontium to remodel it directly allowing accelerated orthodontic tooth movement.

Nanoindenter

A nanoindenter coupled with atomic force microscope (AFM) is used to evaluate nanoscale surface characteristics of bio-materials. They have also been used to evaluate mechanical properties such as hardness, elastic modulus, yield strength, fracture toughness, scratch hardness and wear properties by nano indentation studies [72].

Bio Mems/nems for orthodontic tooth movement

Biomedical Microelectromechanical systems (Bio MEMS) can be defined as the science and technology of operating at the microscale level for biological and biomedical applications, which may or may not include any electronic or mechanical functions. The MEMS micromachined elements include gears, motors and actuators with linear and rotary motion for applications to biological systems. Nanoelectromechanical systems (NEMS) are devices integrating electrical and mechanical functionality on the nanoscale level. It has been proposed that microfabricated biocatalytic fuel cells (enzyme batteries) can be used to generate electricity to aid orthodontic tooth movement. An enzymatic microbattery when placed on the gingiva near the alveolar bone might be a possible electrical power source for accelerating orthodontic tooth movement. However, there are several issues like soft tissue biocompatibility, effect of food with different

temperature and pH range on the output of such microfabricated enzyme battery that need to be addressed. It is expected that the MEMS/NEMS based system will be applied over the next few years to develop biocompatible powerful biofuel cells, which can be safely implanted in the alveolus of the maxilla or mandible to enhance orthodontic tooth movement [73,74].

Nano LIPUS devices

Ultrasound is a form of mechanical energy that is transmitted through and into biological tissues as an acoustic pressure wave at frequencies above the limit of human hearing, is used widely in medicine as a therapeutic, operative, and diagnostic tool [75,76]. LIPUS has been reported to enhance bone growth into titanium porous-coated implants [77] and bone healing after fracture [78,79] and after mandibular distraction osteogenesis [80] and has also stimulated mandibular cartilaginous growth [81]. Another application of this technique is to reduce root resorption during orthodontic treatment. Based on their observation that LIPUS can promote dental tissue formation in rabbits, El Bialy et al. [82] concluded that it may be used to treat root resorption. The unit will be easily mounted on a bracket or even a plastic removable crown. An energy sensor can also be used that will ensure the LIPUS power is reaching the target area of the teeth roots within the bone.

Smart brackets with nanomechanical sensors

The concept of a smart bracket with integrated sensor system for 3D force and moment measurement has recently been published. Nanomechanical sensors can be fabricated and be incorporated into the base of orthodontic brackets in order to provide real-time feedback about the applied orthodontic forces. This real-time feedback allows the orthodontist to adjust the applied force to be within a biological range to efficiently move teeth with minimal side effects [83,84] (Table 1).

Conclusion

A lot of research is being focused on the application of nanotechnology in orthodontics. Though much of the research has taken place in the labs, gradually *in vivo* studies are making their way. Biosafety of nanoparticles and materials is a subject of concern, demanding focus on further studies of the toxic effects of nano-particles to ensure their ethical usage in the oral cavity.

The future in orthodontic treatment will benefit enormously through nanotechnology should all the current attempts succeed to its clinical application at a reasonable cost to the orthodontist and patients.

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