Review Article

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Nanotechnology-based materials as emerging trends for dental applications

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Abstract: Nanomaterials have unique and superior properties such as high surface area and nanoscale size, makes them highly advanced and vital for rapid diagnosis and beneficial in treatment of numerous diseases in health sector. Joint efforts from multiple disciplines have contributed to the developments of advanced nanomaterials and enabled their uses in dentistry. These advanced nanomaterials can give more promising results in diagnosis and treatment procedures compared to their conventional counterparts. This review outlines the nanomaterials available and used in dentistry and will further go into discussing the shapes and compositions of various nanomaterials relevant to dentistry. Incorporating nanoparticles in dental restorative materials can be useful for preventing and/or managing dental caries. Integrating the sciences of nanomaterials and biotechnology, nanomaterials could potentially be revolutionary in improving oral health by providing preventative and diagnostic measures; they could also have effects on repairing damaged dental tissue.

Keywords: Nanomaterials; Nano-fillers; Dental Nanocomposite; Nano-biotechnology

1 Introduction

Oral medicine is one of the most prevalent areas for the growth of nanotechnology to improve people's dental health, and therefore having the potential to improve the quality of life. Safety issues regarding the use of nanomaterials on human have been debated over years, however, research on nanomaterials has established that its use has more advantages compared to disadvantages [1]. The study of nanoscience involves a scale within a range of 1-100 nm [2]. Research in nano-biotechnology has also led to the development of environmentally friendly nanofillers using "green chemistry" [3, 4]. Nanomaterials have unique physical and chemical properties owing to their small size and large numbers, therefore an overall large surface area which have attracted much attention for its use in various dental applications [5–7].

A challenge most dentists face is to find composites that mimic the lost dentinal tissue and are capable of restoring the original dental aesthetic. The development of nanotechnology based bio-mimetic approach to replicate natural bio-material has been viewed as a newer way to create advanced nano-materials [8, 9]. Oral antibacterial materials work by breaking down or preventing the formation of biofilms on teeth surfaces in the mouth. Adding elements such as silver, gold, or titanium nanoparticles in the mixer of biomaterials can potentially improve antimicrobial properties [10]. Metallic nanoparticles (Metallic NPs) provide a large surface area which increases their anti-bacterial reach. In addition, metallic nanoparticles enhance mechanical properties such as strength and durability [11]. Inorganic Nanoparticles primarily based on metal NPs, metal oxides NPs have shown their possible use as fillers for dental nanocomposites [12, 13]. A pathogenic micro-organism such as *Streptococcus mutans* (*S. mutans*) forms colonies between the marginal gaps between the enamel and dental restorations that leads to destruction of tooth. Incorporation of such antimicrobial components into the dental restorative materials can significantly improve their efficacy [14–17].

This review focuses on the application of nanomaterials in different branches of dentistry and detailed classification of nanomaterials based on their size and shape. It has also discussed nanotechnology based possible future approaches of dental materials with highly advanced properties.

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2 Application of Nanomaterials in Dentistry

Nanomaterials have the potential to provide better control over managing of various fatal oral diseases due to their better bioavailability, efficacy and reduction in the required dose of medicine. With development of new techniques, use of nanomaterials in dentistry has made a huge impact and opened new way for various applications (Figure 1).

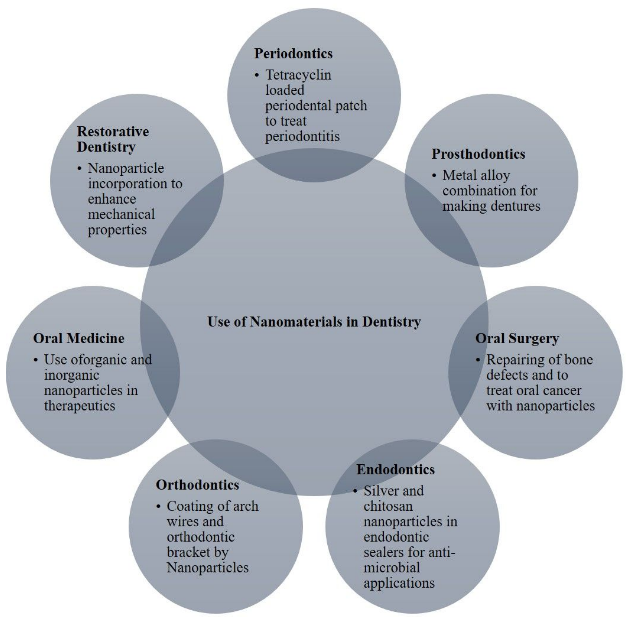

Figure 1: Various applications of Nanomaterials in Dentistry

2.1 Nanomaterials in Periodontics

Periodontics is the branch of dental science that aims exclusively on the tooth supporting structures such as gingiva, periodontal ligament, cementum, alveolar bone and mucosa, as well as diseases that affect them. Periodontal diseases affecting the hard and soft tissues around the teeth lead to gum diseases, bone loss, and in severe conditions tooth loss. Various treatments are available for the management of periodontal diseases; some of them include both medicinal treatment and surgical interventions. Medicinal treatments include drug molecules which are naturally macro-sized particles that find it challenging to penetrate the periodontal pockets. Conversely, the nanoscale sizes of nanoparticles make it easier for them to reach subgingival regions. For instance, drug delivery by inclusion of nanoparticles for treatment of periodontal treatment with Triclosan (TCS) has served as a good example [18, 19]. Tetracycline nanoparticles (Tet NPs) have been investigated for the periodontal treatment as well. The commercially available tetracycline loaded microspheres patch was marketed as Arestin® (Valeant, Bridgewater, MA, USA) and Nanogen® (Orthogen, Springfield, IL, USA). It is used by inserting a patch within the periodontal pocket which releases the drug into the affected area in a sustained manner [20]. The treatment and management of the intraosseous periodontal defects were recently evaluated with nanocrystalline-hydroxyapatite (HA) and it showed positive results [21]. In another study, nanoparticles of carbonate and apatite crystals showed effective sealing of dentinal tubules that are thought to be important for long-term treatment of dentinal hypersensitivity [22] (Table 1).

2.2 Nanomaterials in Prosthodontics

Prosthodontics deals with the diagnosis, treatment planning, complete oral rehabilitation and preservation of the normal oral function of patients with clinical conditions associated with missing teeth or oral and maxillofacial tissues using biocompatible substitutes. Natural aging process, oral diseases or trauma can affect the normal oral environment results in loss of teeth, and they need to be replaced for normal oral function. The new generation materials such as acrylic resins and dental implants have better properties and are available for numerous prosthodontic treatment procedures. Manufacturing dentures using nanoceramic material showed high strength, colour stability, and low electrical and thermal conductivity [23].

Many different metal combinations have been used for making a prosthodontic denture with titanium, cobalt-chromium and molybdenum alloys [24, 25]. Their combinations show superior mechanical properties and corrosion resistance to stainless steel or gold alloy [26, 27]. Metal nanoparticles such as hydroxyapatite NPs and titanium oxide NPs have better biological acceptance than traditional metals in fabrication of prosthodontic denture. In prosthodontics, addition of nanofillers in polymethylmethacrylate (PMMA) shows a significant increase in transverse strength, good biological compatibility, surface hardness and decreases water sorption and solubility [28, 29].

Table 1: Various applications and benefits of Nanoparticles in different disciplines of Dentistry

Discipline	Nanoparticles	Applications	Ave. size (nm)	Commercially available Nano-materials	Manufacturer	Benefits	Ref.
Periodontics	Triclosan NPs, Tetracycline NPs, HA NPs	Use in periodontal diseases, In treatment of deep periodontal pocket	5-120 nm	Nanogen® Arestin®	Orthogen, Springfield, IL, USA Valeant, Bridgewater, MA, USA	Direct access to target periodontal diseases, Rapid absorption, Non-invasive, Longer duration of action	[18–22]
Prosthodontics	ZrO_2 NPs, Al_2O_3 NPs, CoCr NPs,	Nanoapatites for bio film management on the tooth surface, Remineralisation, Nanocomposite surface coatings to prevent the pathogenic bacteria adherence	210–280 nm	Nanotech elite H-D plus, GC OPTI GLAZE color®	Zhermack, BadiaPolesine, Italy GC Corporation	Good biocompatibility, Aesthetics, High wear and corrosion resistance, Long-lasting gloss with a high discolouration resistance,	[24, 25, 28, 29, 82–84, 87–89]
Oral and Maxillofacial surgery	HA NPs, Au NPs, Carbon nanotube, Quantum-dots (QDs)	Anti-cancer drug delivery, Used as optical probes for early detection of Oral Cancer, Used as scaffolds for new bone formation Quantum-dots Alternative contrasting agents for Diagnosis of Cancer	2-50 nm	BrachySil™" deliver 32P, in clinical trial	Sivida, Boston & Perth, Australia	Nano drug delivery	[61–63, 97, 98, 118]
Conservative Dentistry and Endodontics	Au NPs, Ag NPs, ZnO NPs, QPEI NPs	Drug and gene delivery, Tissue engineering, Antibacterial agent in root canal sealers, Root canal disinfection	20 to 75 nm,	AH plus™, Epiphany, Guttaflow®.	DENTSPLY International Pentron Clinical Technologies, Wallingford, CT, USA Coltène, Altstätten, Switzerland	Significantly higheR bond strength, Exceptional dimensional stability, High biocompatibility, Anti-microbial properties	[10, 35, 37, 58, 61–63, 71, 107]
Restorative Dentistry	Ag NP, ZnO NPs, QPEI NPs, HA NPs, ACPNPs NPs	Nano particle filled restorative composite resins Remineralizing Composite resin, Nanoflled bonding agents, Nanoflled glass ionomer cements, Treatment of dental hypersensitivity	20-75 nm	Ketac™, Ketac N100, Nano-ionomers, Adper™ Single bond plus Adhesive, Filtek Supreme XT Fuji IX GP, Nano-primer, Premise™, Ceram X™	3M ESPE, St. Paul, MN, USA GC corporation, Leuven, Belgium Kerr/Sybron, Orange, CA, USA DENTSPLY International, Milford, CT, USA	Superior hardness, strength and translucency, Aesthetic appeal, Excellent colour density, High polish retention, Excellent handling properties	[21, 52, 55, 56, 59, 72, 107, 108]
Orthodontics and Dentofacial Orthopedics	Alumina NPs ZnO NPs	Coating of metal NPs on brackets and arch wires to decrease the surface irregularities and reduction in friction Metal NPs coating act as a solid lubricant film to ease sliding of orthodontics wire over bracket	150-200 nm	_	UC3M and CEOSA-EuroOrtodoncia	High strength and reduced mechanical resistance and friction between orthodontic bracket and arch wire	[39, 89]
Oral Medicine and Radiology	Silica NPs, ZrO_2 NPs, HA NPs, TiO_2 NPs Quantum dots	Therapeutic application	2–250 nm	_	_	Drug or gene carriers Targeting agents for treatment of cancer NPs against Multi Drug Resistance (MDR) cancer cells	[40, 97, 99]
Preventive Dentistry	ACPNPs, ZnO NPs, HA NPs,	Used for final rinsing of root canal treatment, Low surface tension allows NP to get to the smallest fissures and dental ducts of the system. Used directly before embedding dental fillings,	250-300 nm	NanoCare® Gold	Nano-Care, Saarwellingen, Germany	Disinfectant of deep carious region to improve composite materials, adhesion to tooth tissues, which Increases durability of dental restorations, Enhanced adhesive and Antibacterial properties	[21, 48, 51, 67]
Dental Implant	Au NPs, ZnO NPs, TiO_2 NPs, CaP NPs	Surface modifications of dental implants, CaP NP are deposited on a double acid-etched surface by Discrete Crystalline Deposition (DCD) sol-gel process	20–100 nm	Nanotite™ Nano-coated implant TiUnite	BIOMET 3i, Palm Beach Gardens, FL, USA Nobel Biocare Holding AG, Zurich, Switzerland	Soft tissue attachment and preservation of Crystal bone increased bone-to-implant contact, influences cell adhesion, stimulates maturation of osteogenic cells	[23, 43, 63, 82, 117]

HA NPs: Hydroxyapatite nanoparticles; ZrO_2 NPs: Zirconium dioxide Nanoparticles; Al_2O_3 NPs: Aluminium Oxide Nanoparticles; CoCr NPs Cobalt Chromium nanoparticles; Au NPs: Gold nanopartciles; Ag NPs: Silver nanoparticles; Zno NPs: Zinc Oxide Nanoparticles; QPEI NPs: Quaternary ammonium polyethylenimine nanoparticles; ACPNPs: Amorphous calcium phosphate Nanoparticles; TiO_2 NPs: Titanium dioxide; CaP NPs: Calcium phosphate nanoparticles.

2.3 Nanomaterials in Oral and Maxillofacial surgery

Oral and maxillofacial surgery is the branch in dentistry that focuses on treatment of oral diseases with injuries and defects in the hard and soft tissues of the oral (mouth) and maxillofacial (jaws and face) region. A number of oral diseases or trauma causes facial deformity and bone defects require surgical intervention to correct the normal facial features. Bone implants or bone forming biocompatible materials are placed orally to correct the facial appearance of the patient.

Materials with low biocompatibility cause irritation, post-operative infection and discolouration over the facial skin. Advanced nanomaterials demonstrate excellent biocompatibility and provide superior results over the traditional treatment options [30]. They can also be used as scaffolds for new bone formation due to their ability to promote the osteogenic differentiation and biomineralization of cells.

Oral cancer has become one of the most life threatening oral disease and has been considered as a major risk to human health. The biggest side effect of cancer treatment is systemic toxicity caused by chemotherapy. However, this treatment causes symptoms of burning mouth and loss of body hair. Nanotechnology can also help in reducing systemic toxicity by decreasing required amounts of anticancer drugs through precise localization and destruction of cancer cells by nanodrug delivery [31].

Localized nanodrug delivery can also help in preserving surrounding healthy tissues while targeting malignant tissue. Several studies have shown that magnetic nanoparticles could be used for the tumour targeted drug delivery therapy. They can be directly injected through intravenous route to target the tumour site tissue and due to their nano size it requires low dosage of drugs that reduces the systemic toxicity and gives the desired effect of tumour regression through precise targeting of drugs delivery [32–34].

2.4 Nanomaterials in Conservative Dentistry and Endodontics

Endodontics is the branch of dentistry associated with the biology of the normal dental pulp and the etiology and treatment of diseases and injuries of the dental pulp along with associated periradicular conditions. Micro-organisms in oral cavity can cause dental caries that lead to various endodontic procedures such as root canal treatment, one of the important reasons of the deep dental caries (Table 2).

In endodontic treatments, nanotechnology can play a major role for development of advanced endodontic materials. There are several kinds of materials required in endodontic treatments such as dental amalgum, glass inomer cements (GIC), dental composite, gutta-percha, root

Table 2: Role of Nanotechnology in Conservative Dentistry and Endodontics

NO.	Role of Nanotechnology	ADVANTAGES	Ref.
1	Treatment of dental hypersensitivity	Carbonate hydroxyapatite nanocrystals in toothpaste for blocking of dentinal tubules to treat dental hypersensitivity	[22]
2	Nano filled glass ionomer cements	Better mechanical and optical properties	[46]
3	Nano particle filled restorative composite resins	Higher filler loading , better mechanical properties, glossy surface	[43, 46, 47]
4	Nano filled bonding agents	More resistant to degradation and better bonding properties	[106]
5	Endodontic sealers	QPEI NPs nanoparticles used as filler in commercially available endodontic sealers, for instance,Guttaflow, Epiphany and AH plus for its antibacterial action	[107]
6	Remineralization of tooth structure	Combination of PVP and ACP nano fibers for remineralization of demineralized dentine in vitro	[109–111]

QPEI NPs: Quaternary ammonium polyethylenimine nanoparticles; PVP: polyvinylpyrrolidone; ACP nanofibers: Amorphous calcium phosphate nanofibres canal disinfectant and sealers. The properties of endodontic materials can be enhanced through application of nanotechnology by inclusion of anti-bacterial nanoparticles which can prevent the recurrent infection and failure of root canal treatments [35]. A recently reported study showed the inclusion of biopolymeric NPs in root canal disinfectants provided significant antibacterial activity [36]. In another study, Inclusion of QPEI (quaternary ammonium polyethylenimine) NPs improved the antibacterial activity of the root canal sealer against biofilms of (*Enterococcus faecalis*) *E. faecalis* strains [37].

2.5 Nanomaterials in Orthodontics and Dentofacial Orthopedics

Orthodontics and dentofacial orthopaedics is the field of dentistry that primarily deals with diagnosis, prevention and correction of mal-positioned teeth. The teeth should be in ideal position for the normal function of oral cavity but due to poor oral health, malocclusion, crowding of teeth or space between teeth requires orthodontic treatment.

Use of nanotechnology for orthodontic applications is in its early phase of development. Nanomaterials with advanced properties are being constantly researched and marketed by manufacturers commercially [38] Friction and mechanical resistance between orthodontic wires and bracket can be reduced by coating with nanoparticles. Nano coating of antibacterial nanoparticles in orthodontic materials can prevent the dental plaque formation around the orthodontic appliances and prevent the dental caries associated with orthodontic treatments. In 2006, Kachoei *et al.* provided evidence of reduction in friction value between arch wires and self-ligated brackets with nano coating of spherical metal nanoparticles. The nanoparticles acted as a spacers that decreases the surface irregularities, also in high load applications metal nanoparticles coating acted as a solid lubricant film that allows very low friction as well as easy sliding of orthodontics wire over bracket [39].

2.6 Nanomaterials in Oral Medicine and Radiology

Oral medicine is the speciality of dentistry that is concerned with clinical diagnosis and non-surgical management of non-dental pathologies affecting the oral and facial region. Poor oral health can leads to numerous oral diseases. Maintaining healthy oral condition requires early and accurate diagnosis of oral diseases. Nanotechnology has given an access for superior imaging and better treatment of oral diseases.

Nanotechnology based oral medicinal approaches have several benefits over the conventional approach. Nanoparticles have unpaired atoms and large surface area that tends to form strong chemical or physical bonds that generate advanced mechanical and physical properties. Organic and inorganic nanoparticles of Silica, Zirconia, HA, and Titanium dioxide have been used in oral medicine for therapeutic application [40]. Nano imaging is a newer concept for dentistry. Digital imaging are tested with Nano phosphor scintillators that rapidly emits visible light when exposed to even at very low dose of ionizing radiation. This Nano imaging technique requires very low amount of radiation to give high-quality images compared to conventional methods which can be very beneficial to dental applications [41].

2.7 Nanomaterials in Restorative Dentistry

Restorative dentistry deals with the diagnosis and management of diseases related to the teeth and their supporting structures. Advanced techniques are prerequisites for the repair and replacement of damaged tooth structures and reinstatement of tooth function and better aesthetics [42].

Nanotechnology has helped significantly for manufacturing of biocompatible and non-toxic dental restorative materials such as GIC, dental composite, dental implants and endodontic materials [43]. The resin based dental restorative materials have shown great advances in the last few years. Addition of nanoparticles in the dental composite resin matrix can significantly increase its mechanical properties, low polymerization shrinkage with high abrasion resistance and surface hardness [44, 45]. A recently reported study showed that addition of fluoro-aluminosilicate glass nanoparticles in GIC improved the mechanical and aesthetic properties [46]. Recently, Nanoionomers (Ketac™ Nano; 3M ESPE) have been marketed for clinical use [47].

2.8 Nanomaterials in Preventive Dentistry

In preventive dentistry, use of nanotechnology can help to prevent carious lesions and protect against lesion causing elements. Dental caries are initiated by early bacterial bio-films formed on the tooth surface which lead to tooth decay. Inclusion of nanoapatite particles dental restorative materials can facilitate remineralisation of damaged tooth structures [48].

Inclusion of antibacterial nanoparticles in dental nanocomposite can prevent the pathogenic bacterial adhesion on tooth surface [49]. Dentifrices containing HA nanoparticles can be used for bio-film reduction and remineralisation of enamel lesions [50, 51]. Incorporating amorphous calcium phosphate Nanoparticles (ACPNPs) in the dental composite can also facilitate remineralisation of tooth minerals [52].

3 Classification of Nanomaterials used in dentistry on the basis of Shape and Composition

Nanomaterials can be classified in various ways on the basis of their use and their composition. Here, these nanomaterials are being classified on the basis of their shape and composition. Nanomaterials with different shapes are classified in Nanoparticles, Nanotubes and Nanoplatelets.

3.1 Nanoparticles

Nanoparticles based nanomaterials include conventional and unconventional nanoparticles. Conventional nanoparticles include metallic NPs and metal oxides NP. For decades, there has been an ongoing research on the use of metallic and metal oxides NPs. Unconventional NPs (nano diamons, nanoshells and quantum dots) are the new age fillers for advanced dental materials and they can be modified easily for the application (Figure 2).

3.1.1 Metallic Nanoparticles

Metallic Nanoparticles are prepared by various processes of downgrading the bigger particles in to smaller particles up to nanoscale size. Metal nanoparticles displayed greater antibacterial activity compared to traditional metal which is currently one of the focus areas in dental research.

3.1.1.1 Silver Nanoparticles (AgNPs)

Antibacterial properties of Silver have been known for centuries. Additionally, it has also shown to have antiviral and anti-fungal properties. The mechanism of action of silver ions by inactivation of enzymes causing failure of DNA replication and thereby leading to cell death of microorganisms [53]. Research on antibacterial properties of silver has gathered great interest for researchers. Nanotechnology has broadened opportunities for application of Silver in therapeutics. Antibacterial properties of Silver can also be used in dental materials [54]. In some of the recent publications, AgNPs have shown high antibacterial properties as a filler in dental restorative materials [55]. AgNPs also give better aesthetic results when used as a filler without affecting the mechanical properties of the dental composite [56]. A recent study had demonstrated the use of AgNPs in a dental composite reduce lactic acid formation and biofilm growth on tooth which prevent secondary caries [57]. AgNPs have been used in an endodontic sealer (Gutta-Flow Sealer) with gutta-percha powder in the form of a capsule for single use and has shown high antibacterial efficiency as well [58]. Potential of AgNPs with other bioactive agents have been studied to get dual action properties such as rem-

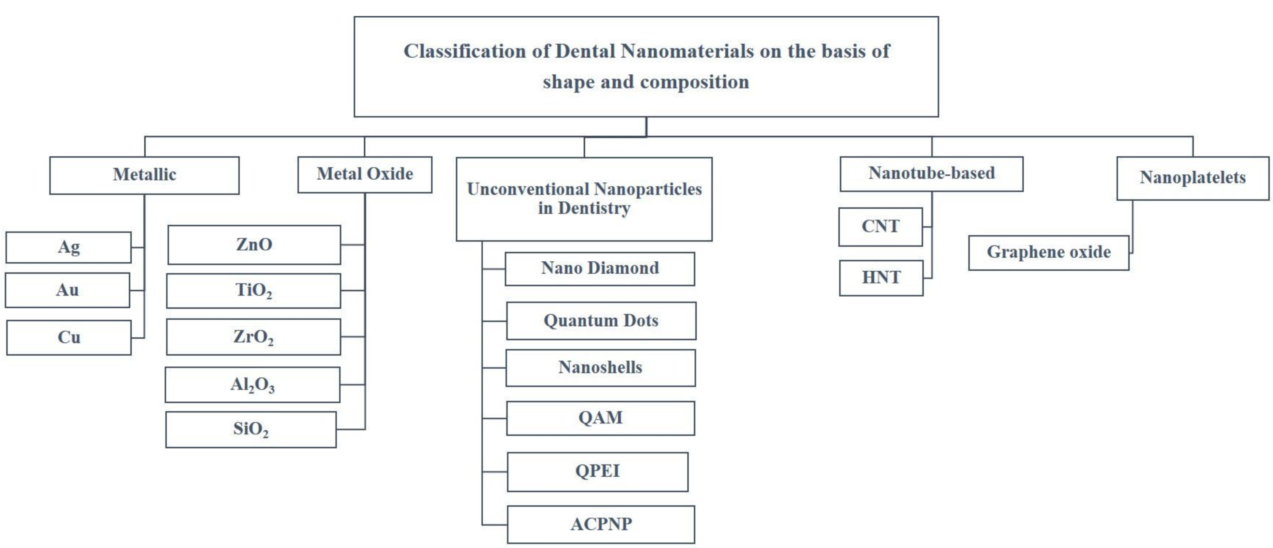

Figure 2: Classification of Dental Nanomaterials on the bases of shape and composition

ineralisation with antibacterial properties. Recently, AgNPs were used in the dental composite that shows significant increase in strength as well as antibacterial activity [59]. As reported in earlier study, a gel containing AgNPs were used against *E. faecalis* bio-film at very low concentrations in which it also showed significant antibacterial activity [60]. These dual action properties have shown high mechanical properties such as flexural strength and elastic modulus when compared with the commercially available dental composite products.

3.1.1.2 Gold Nanoparticles (AuNPs)

For decades gold has fascinated researchers for its inert and biocompatible behaviour along with antibacterial properties. In recent studies, AuNPs have been introduced as a potential nano drug delivery carrier for cancer treatment and diagnosis. Recent studies have reported synthesis of various Gold nano structures such as Gold nanospheres and nanorods can be used as photo thermal agents, contrast agents and nano drug delivery carriers [61, 62]. Heo *et al.* reported the surface immobilization of Titanium dental implants with AuNPs and used these nanocomposites as osteoinductive agents. Surface immobilization of dental implants with gold nanoparticles act as osteoinductive agents, which favours rapid formation of bone around the dental implant and maintain the nascent bone formation [63]. AuNPs has lower toxicity than other metal nanoparticles and also provides variety of ways for its synthesis such as through chemical functionalization.

3.1.1.3 Copper Nanoparticles (CuNPs)

Copper is a vital component for the metabolism of animal and plant cells. It is a trace component found in nearly every organism, and is a key component of more than 30 types of proteins. Copper produces hydroxyl radicals that causes imbalance in the cell membrane of micro-organisms which leads to leakage and cell death. CuNPs attach to carboxylic and amine groups on the microorganism surface and cause alterations that destabilize cell membranes leading to cell death [64]. The copper ions causes generation of free radicals that can change DNA replication and protein synthesis of the microorganisms [65]. According to a recent report, addition of CuNPs provides sufficient antimicrobial activity against *S. mutans* to the dental adhesives and prevents the degradation of the adhesive interface, without reduction in the mechanical properties of the formulations [66]. Metal nanoparticles with antimicrobial properties have potential to fight against bacteria and microorganism for future treatment of dental diseases.

3.1.2 Metal Oxide Nanoparticles

Metal Oxide Nanoparticles are oxides of metal particles that are more stable in the oxide form. In recent years, metal oxides nanoparticles have been broadly investigated for their act as antimicrobial agent and fillers for dentistry.

3.1.2.1 Zinc Oxide Nanoparticles (ZnO NPs)

Zinc has effective antibacterial activity at the nanoscale, their antibacterial efficiency increases significantly. When a Zinc ion makes contact with the bacterial cell membrane, it binds to the proteins and lipids causing an osmotic imbalance which increases membrane permeability and cell death [67]. Zinc NPs produce oxygen radicals and Zn^{2+} ions which increase oxidative stress and inhibit growth of microorganism [68]. ZnO NPs also have studied on cell lines of humanembryonic lung fibroblasts (HELF) [69]. They have also shown less cytotoxic effect on gastric epithelial cell lines (GES-1), which increase when administered with ascorbic acid [70]. As reported by Kasraei *et al.*, the dental composite resins containing ZnO NPs and AgNPs have presented significant antibacterial activity against *Streptococcus mutans* and *Lactobacillus* [71]. Wang *et al.* has also demonstrated that small amounts of cellulose nanocrystal /ZnO NPs combination nanohybrids have a positive influence on the mechanical and antibacterial properties of dental resin composites [72]. Use of ZnO NPs in various dental materials can be advantageous for its antibacterial properties.

3.1.2.2 Titanium Dioxide-Based Nanoparticles (TiO_2NPs)

Titanium alloys are broadly used in dentistry as a result of their excellent properties such as high strength, high corrosion resistance and good biocompatibility [73, 74]. Under exposure of ultraviolet (UV) rays, Titanium Dioxide (TiO_2) produces reactive oxygen radicals (H_2O_2 and OH^-) which causes osmotic imbalance in micro-organisms and interfere with their phosphorylation, leading to bacterial cell lysis [75]. Earlier report showed that high concentration of TiO_2 NPs causes inflammatory action on human gingival fibroblasts [76]. GIC modification with TiO_2 displays moderate biocompatibility on Oral Squamous Cell Carcinoma Cell Lines [77]. Incorporating TiO_2 nanoparticles into composite resins have shown significant antibacterial activity and caused reduction of the colony counts of Streptococcus mutans and Streptococcus sanguinis [78]. Nanoscale modification of the Titanium surface was performed with a chemical etching technique to measure proliferation of murine preosteoblastic cells in vitro and it showed better results compared to rough and smooth surfaces of pure titanium [79, 80]. There are still further research and investigations essential for potential future oral applications of TiO_2.

3.1.2.3 Zirconium dioxide Nanoparticles (ZrO_2NPs)

Zirconium dioxide (ZrO_2) has played a very important role in the manufacturing of dental materials for many years. Zirconia, also known as “ceramic steel” has superior toughness, strength, fatigue resistance, excellent wear resistance and biocompatibility. It has also shown very similar properties and colour to mimic the natural tooth thereby ensuring better aesthetics.

Zirconia nanoparticles can be prepared by using technique such as laser vaporization technique that can produce up to 20-50 nm sized nanoparticles [81]. Its biocompatibility, osseo-conductivity and tendency to reduce plaque accumulation make it an ideal choice for the manufacturing of the dental implants and coating material for dental prosthesis. ZrO_2NP can be used as a filler for the reinforcement of PMMA matrix to improve the mechanical properties [82]. Zirconia based ceramics showed even a better strength and bending resistance profile than alumina ceramics [83]. ZrO_2NP can be used as filler for dental nanocomposites to improve its mechanical properties, better aesthetics and radio opacity. The dental composites containing zirconia nanoparticles have shown enhancement in fracture toughness [84]. Addition of ZrO_2NP in GIC restorative cement has shown improvement in compressive strength and reduction in cracks within the matrix of the cements [85]. Addition of ZrO_2NPs in manufacturing of dental dentures displayed high strength, colour stability, low electrical and thermal conductivity [86].

3.1.2.4 Aluminium Oxide Nanoparticles (Al_2O_3 NP)

Aluminium oxide nanoparticles can be synthesized by various synthesis techniques like wet-chemical synthesis, mechanical ball milling, and laser ablation, exploding wire, the solution of reduction and decomposition process. Al_2O_3 NPs are highly reactive to moisture, heat, and sunlight, safety measures are essential to safeguard the material. Furthermore, Al_2O_3 NPs should be kept in vacuum and stored in a cool and dry room. Alumina ceramics as a leading example showed better aesthetics, polished surface, wear resistance, hardness, along with high biocompatibility to surrounding oral tissues. Dental materials that are lacking in mechanical strength can be made tougher through the addition of Al_2O_3 NP. Polymethylmethacrylate (PMMA) has disadvantages such as low flexural strength properties and impact strength. Addition of Al_2O_3 NP in to PMMA matrix has shown significant increase in mechanical properties of the resin and has shown improvement in the thermal properties and decrease in the water absorption and solubility [87, 88]. Orthodontic bracket made up of polysulfone incorporated with Alumina nanoparticles was introduced by UC3M in 2012, with high strength, reduced mechanical resistance and friction [89].

3.1.2.5 Silicon dioxide Nanoparticles (SiO_2NPs)

Silicon dioxide NPs is used as a filler for the dental restorative materials to improve the mechanical properties. In general dentistry, fine powder of Silica is used as polishing agent for polishing rough surface of the tooth in order to prevent food accumulation or plaque formation. SiO_2NPs, also known as silica is an oxide of silicon with the chemical formula SiO_2 and is most commonly found in nature as quartz. SiO_2 NP has increasingly been used for several biomedical and dental applications. Various drug molecules can be loaded into silica nanoparticles. SiO_2 NPs have a significant role in dentistry, due to its size, surface area, biocompatibility, low toxicity, low density and adsorption capacity [90]. Mesoporous SiO_2 can be used as blocking agent for the dentinal tubules, which upon exposure cause hypersensitivity [91]. Silica nanoparticles and hydroxyapatite (HA) nanoparticles combination have been tested on fully demineralised dentin for its effects and it has shown local increase in the concentration of calcium phosphate compounds and recovery of the mineral volume in dentin infiltrated with silica NPs [92].

3.1.3 Unconventional Nanoparticles in Dentistry

Fabrication of new nanoparticles are being researched for unique properties for development of advanced dental nano-materials. The prominent challenges in development of advanced dental materials are to produce strong, non-toxic and antibacterial materials by using various nanoparticles. In this respect, the field of nanotechnology enables exploring various nanoparticles to use and test for dental applications. Depending on the properties of the particles, various approaches for nanoparticle integration in dental materials have been implemented.

3.1.3.1 Nano Diamonds

Diamond is well known as the hardest natural material on earth. Nano diamonds (ND) are tiny diamonds with size well below 100 nm. Its superior surface and chemical nature makes it a very suitable candidate for use as a filler in dental nanocomposite fabrication [93]. Recently, amoxicillin loaded nano diamond Guttapercha composite (NDGP-AMC) were developed and tested for its use in root canal treatments with promising results [94]. ND incorporated PMMA had shown increase in the overall performance of fixed interim dental prostheses [95]. Nano diamonds have great potential for its use in various applications in restorative dentistry.

3.1.3.2 Quantum Dots

Quantum dots are a semi-conductive nanoparticles such as lead sulfide, zinc sulfide and indium sulfide that can emit light based on the amount and wavelength of light irradiated to them [96]. Furthermore, their semi-conductive properties can be changed under external magnetic field or light irradiation. These materials can also be used as a nanocarrier for drug or gene for therapeutic treatment [97].

The unique optical properties of quantum dots can be utilized through their conjugation with photosensitizers and targeting agents for treatment of cancer [98]. It could also be used for both diagnostic imaging and therapeutic applications. Coating them with specific substances can enhance their attachment to cancer cells. Upon attachment, radiating UV light to them initiates UV light emission and enhances the detection of oral cancers [99]. Thus, quantum dots can be used for treatment of head and neck diseases via drug delivery and correction of genetic defects. They may also play a role in prevention of oral cancer [100].

3.1.3.3 NanoShells

NanoShells are made up of dielectric core and a thin metal coating [101]. NanoShells can be used for various therapeutic applications in dentistry. The metal coating of NanoShells can be used for the destruction of oral cancer cells by stimulating it under infrared light, which generates intense heat around the NanoShells that can lead to cell death [102]. This method can also be used for various other therapeutic applications such as ligature of the vessels in controlling internal bleeding, wound healing and decreased angiogenesis. This therapeutic method can help in minimising blood loss in trauma victims that can also save nearby vital tissues. Nanoshells loaded with antibodies, proteins or other cell-targeting agents can be used for targeted drug delivery [103].

3.1.3.4 Quaternary ammonium methacrylate (QAM) Nanoparticles

Quaternary ammonium methacrylate nanoparticles can be used as fillers for restorative dental materials for their antibacterial potency. Its antibacterial mechanism of action by causing cytoplasmic leakage in the micro-organism cell wall, which causes its cell death. QAM resins and bacterial cell wall have positively and negatively charged surfaces respectively thereby favouring ionic adhesion that causes an electric imbalance in the cell membrane thus increasing the osmotic pressure and ultimately leading to cell death [104]. An interesting property of QAM resins is its ability to inhibit 3D bio-films [105]. Because of its bactericidal properties, QAM increases stress conditions, triggering apoptosis in bacteria. QAM resins have also shown effective bond strength properties with restorative dental adhesive materials, and their antibacterial ability may be useful for developing more advanced dental adhesive restorative materials [106].

3.1.3.5 Quaternary ammonium polyethyleneimine (QPEI) Nano-particles

Endodontic sealers with antibacterial properties can be very beneficial against root canal infections. QPEINPs have been used as filler in commercially available endodontic sealers, for instance, Guttaflow, Epiphany and AH plus for its antibacterial action [107]. Inclusion of QPEI NPs in resin composite have shown high antibacterial activity without any significant adverse effects on the mechanical properties [108]. Furthermore, the addition of QPEI NPs shows stability, high antibacterial potency without generating any by-products.

3.1.3.6 Amorphous Calcium Phosphate Nanoparticles (ACPNP)

Remineralisation of affected dentine or enamel can give a positive result for oral health. Addition of mineralizing agent in restorative materials can be very helpful for restoration [109]. To remove deep carious lesion, a minimal invasive technique is always used to protect pulp and preserve tooth structure [110, 111]. Incorporation of nanoparticles in restorative dental materials can serve the dual action of having antibacterial effects and remineralisation of the decayed tooth. In dental composites, the nanoparticles of amorphous calcium phosphate releases calcium and phosphate ions around the restoration during the acidic condition to maintain pH levels [112].

3.2 Nanotube Based Nanomaterials

3.2.1 Carbon Nano-tube (CNT)

Carbon nanotubes (CNTs) have excellent mechanical and electronic properties. Additionally, CNTs have been considered as a reinforcing filler in dental composites [113, 114]. Single-walled carbon Nano-tubes (SWCNT) are seamless cylinders comprised of a layer of graphene and has gathered a lot of attention as a research subject [115]. Use of SWCNT as a filler in dental resins has given satisfactory results with high flexural strength [116]. CNTs also have potential for their use as a coating material on titanium dental implants [117]. In earlier studies, CNTs were used for anti-cancer drug delivery and have shown considerable results *in vitro* and *in vivo* studies with epidermal growth factor (EGF) [118].

CNTs and carbon Nano-fibrils have been used as reinforcement fillers in various nano-materials to improve the mechanical properties [119]. Cooper *et al.* prepared the composites with different quantities of CNTs or carbon Nano-fibrils incorporated in a PMMA matrix using a dry powder mixing method. The results showed an increase in mechanical properties of composites with high impact strength [120]. In addition, An *et al.* formed alumina-CNT composites through hot-pressing technique and tested the mechanical properties of alumina-CNT composites. The results showed significant reduction in wear, and mechanical properties were enhanced significantly [121].

3.2.2 Halloysite Nano-tube (HNT)

Clay based nano materials HNTs can be a suitable alternative as a dental fillers and nano drug delivery agents for dentistry. HNTs have Nano-tubular structure with typical dimensions in Nano-metre scale. They have a natural milky white colour with high strength and elastic modulus thereby making them one of the ideal fillers for dental composite fabrication [122]. HNTs can also be loaded with antibiotic agents to develop a nano-filler with the ability to prevent the formation of oral bio-film and thereby preventing the development of secondary dental caries [123, 124].

3.3 Nanoplatelets based nanomaterials

Nanoplatelets based nanomaterials are used as nanosheets or flakes of the nanoplatelets. Graphene is a prime candidate for the nanoplatelet based nanomaterials. Graphene oxide nanoplatelets are used in dentistry for their unique properties.

3.3.1 Graphene oxide nanoplatelets

Graphene is composed of a single layer of carbon atoms arranged as a hexagonal honeycomb lattice and exhibiting unique material characteristics [125]. Use of Graphene nano-powder in dental materials has created the new opportunity for the manufacturing of dental Nano-materials [126]. Graphene as Nano-filler in dental Nano-composite has shown significant increase in mechanical properties [127]. Several studies have reported anti-bacterial properties of graphene based materials and by incorporating of it in dental materials can serve dual action of a filler and antibacterial agent [128–130].

Graphene based Nano-platelets have shown strong antibacterial activity against *Streptococcus mutans* that suggest that it can act as a key anti-bacterial agent for the dental materials [131]. Tissue engineering requires materials with very low cytotoxic effect on healthy tissues. Recent study reported that Graphene oxide (GO) with fibroin have shown no adverse effect on periodontal ligament stem cells (PDLSCs) that suggest that GO based tissue scaffolds have great potential in regenerative dentistry [132]. Graphene oxide (GO) coated Ti (GO-Ti) membranes has shown potent effects on stimulating osteogenic differentiation, superior bioactivity and enhanced new bone formation without inflammatory responses [133]. GO based substrate allowed dental pulp stem cell (DPSC) attachment, proliferation that shows high biocompatibility of graphene [134]. Graphene serves as a promising nanomaterial to improve performance of dental materials and its derivative materials can be used as high performance coating materials for dental implants.

3.4 The toxicity aspect of nanomaterials in dentistry

Now a day, nanoparticles are used for dental composites, root canal sealers, oral disease preventive drugs, prostheses and for teeth implantation. Nanomaterials further carry oral fluid or drugs, maintain oral hygiene, prevent oral disease (cancer) and hence restore oral health care up to a high extent. The use of nanomaterials in dentistry remains an area of debate due to their toxicological concern. Several nanoparticles such as metal nanoparticles i.e Gold, Silver, metal oxide nanoparticles TiO_2, Fe_2O_3 were explored for different dental applications. In a recent study, Gold nanoparticles coated dental implant showed notable os-

Table 3: The most recent patent data updates related to nanotechnology in dentistry

Patent Application Publication No.	Nanoparticles	Type of surface modification	Ave. size (nm)	Antimicrobial pathogens	Benefits	Ref.
US 20200046764A1	ZNO/GQD-PEI NPs	-	3-10 nm	*E. Coli, S. mutans*	•In dental composite, root canal sealer etc.	[135]
US 20200008909A1	Ag NPs	-	0.1-100 nm	Gram-negative and Gram-positive bacteria	•Deposition of Silver NPs on implant surface to prevent implant associated infection.	[136]
US 20190274791A1	-	Nano-pitting (Nanoscale surface roughening)	1 - 100 nm	-	•Nano-pitting of dental implant to promote osseo-integration.	[137]
US 20190151205A1	Mesoporous metal oxides NPs	-	300-1500 nm	*S. mutans*	•In dental materials and as a coating materials for dental implants.	[138]
US 20190091109A1	Graphene Nano-platelets	-	D - 20-500 nm, L - 200-3000 nm	*S. mutans*	•In dental polymer adhesive.	[139]
US 20190021333A1	Cu NPs	-	40-100 nm	*C. albicans, S. mutans, S. aureus*	•In dental prostheses to prevent and /or treat denture stomatitis and to reduce cariogenic bacteria.	[140]
US 010369089B2	FeO_2 NPs	-	1-1000 nm	Gram-negative and Gram-positive bacteria	•In dental materials to prevent biofilms formation and tooth demineralization.	[141]
US 20190183742A1	NPs containing $NaYF_4$ nanocrystals doped with Er, Yb and Tm.	-	100–200 nm	-	•In dental bonded restorations	[142]
US 20180185249A1	Chitosan polymer NPs	-	60-150 nm	*E . faecalis*	•In root canal treatment	[143]
US 00968217OB2	HAp NPs, HAp-ZnO NPs	-	50-100 nm	-	•In dental implants	[144]

E. coli: Escherichia coli; S. mutans: Streptococcus mutans; C. albicans: Candida albicans; S. aureus: Staphylococcus aureus; E. faecalis: Enterococcus faecalis; $NaYF_4$: Natriumyttriumfluorid; Er: Erbium; Yb: Ytterbium; Tm: Thulium; HAp: Hydroxyapatite; HAp-ZnO: Hydroxyapatite-Zinc Oxide; ZNO/GQD-PEI: polyethylenimine (PEI)-modified graphene quantum dot Zinc Oxide nanocomposites; Ag NPs: Silver nanoparticles; Cu NPs: Copper nanoaprtcles; FeO_2 NPs: ferrous oxide nanoparticles.

teoinductive property and found nontoxic to MG-63 cell lines [145]. Silver nanoparticles are known for their antimicrobial properties. In another study, silver nanoparticles coated with capping agent were found to be noncytotoxic on human gingival fibroblast cells (HGF-1) [146]. Recently in our study, we have used silver NPs immobilised Halloysite nanotubes for fabrication of dental resin composites and were found to be non-cytotoxic on NIH 3T3 cell lines (mouse embryonic fibroblast cell) [147]. Metal oxide nanoparticles such as TiO_2 and Fe_2O_3 were also used in fabrication of PMMA resins in past and was found to be highly biocompatible with decrease in adherence of *Candida albicans* cells [148]. In recent study, chitosan nanoparticles have been incorporated as root canal sealer for prolonging with increase antibacterial activity [149]. By controlling the relative proportion of nanoparticles in dental materials, it can be made more patient friendly for dental application. However, continual research efforts are necessary for the use of nanomaterials as well as their potential deleterious effects on human life (Table 3).

4 Conclusion

The merger of nanotechnology with dentistry would improve the quality of current treatment procedures and patient care. It can provide novel method for synthesis of dental materials which increases efficacy, accuracy and speed of treatment while decreasing costs. Research in nanotechnology can effectively benefit the further growth of new techniques for early diagnosis and treatment of oral malignant diseases. Further research on nanotechnology and antimicrobial materials has the potential of improving therapeutics in dentistry. An extensive amount of research in the development of highly advanced, restorative nanomaterials is essential for its success in dentistry. In clinical practice, it is essential to have adequate clinical data is available before new material is used clinically. This review article sheds light on the potentials and capabilities of nanotechnology in the dental field. In the near future, this technology may become the core of dental and medical science and accurate steps in this technique can bring about favorable social, economic and healthier oral health outcomes for people.

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References

[1] Fayaz, A. M., K. Balaji, M. Girilal, R. Yadav, P. T. Kalaichelvan, and R. Venketesan. Biogenic Synthesis of Silver Nanoparticles and Their Synergistic Effect with Antibiotics: A Study against Gram-Positive and Gram-Negative Bacteria. *Nanomedicine: Nanotechnology, Biology and Medicine*, Vol. 6, No. 1, 2010, pp. 103–109.

[2] Bruins, M. R., S. Kapil, and F. W. Oehme. Microbial Resistance to Metals in the Environment. *Ecotoxicology and Environmental Safety*, Vol. 45, No. 3, 2000, pp. 198–207.

[3] Beveridge, T. J., M. N. Hughes, H. Lee, K. T. Leung, R. K. Poole, I. Savvaidis, et al. Metal-Microbe Interactions: Contemporary Approaches. *Advances in Microbial Physiology*, Vol. 38, 1996, pp. 177–243.

[4] Kim, J. S., E. Kuk, K. N. Yu, J.-H. Kim, S. J. Park, H. J. Lee, et al. Antimicrobial Effects of Silver Nanoparticles. *Nanomedicine: Nanotechnology, Biology and Medicine*, Vol. 3, No. 1, 2007, pp. 95–101.

[5] Dastjerdi, R. and M. Montazer. A Review on the application of inorganic nano-structured materials in the modification of textiles: Focus on anti-microbial properties. *Colloids and Surfaces B: Biointerfaces*, Vol. 79, No. 1, 2010, pp. 5–18.

[6] Khodashenas, B. and H. R. Ghorbani. Synthesis of silver Nanoparticles with different shapes. *Arabian Journal of Chemistry*, Vol. 12, No. 8, 2019, pp. 1823–1838.

[7] Khan, I., K. Saeed, and I. Khan. Nanoparticles: Properties, Applications and Toxicities. *Arabian Journal of Chemistry*, Vol. 12, No. 7, 2019, pp. 908–931.

[8] Chahal, S., A. Kumar, and F. S. J. Hussian. Development of Biomimetic Electrospun Polymeric Biomaterials for Bone Tissue Engineering. A Review. *Journal of Biomaterials Science, Polymer Edition*, Vol. 30, No. 14, 2019, pp. 1308–1355.

[9] Adams, L. K., D. Y. Lyon, and P. J. Alvarez. Comparative Eco-Toxicity of Nanoscale TiO_2, SiO_2, and ZnO Water Suspensions. *Water Research*, Vol. 40, No. 19, 2006, pp. 3527–3532.

[10] Juan, L., Z. Zhimin, M. Anchun, L. Lei, and Z. Jingchao. Deposition of silver nanoparticles on titanium surface for antibacterial effect. *International Journal of Nanomedicine*, Vol. 5, 2010, p. 261–267.

[11] Tjong, S. C. Novel nanoparticle-reinforced metal matrix composites with enhanced mechanical properties. *Advanced Engineering Materials*, Vol. 9, No. 8, 2007, pp. 639–652.

[12] Schabes-Retchkiman, P. S., G. Canizal, R. Herrera-Becerra, C. Zorrilla, H. B. Liu, and J. A. Ascencio. Biosynthesis and characterization of Ti/Ni bimetallic nanoparticles. *Optical Materials*, Vol. 29, No. 1, 2006, pp. 95–99.
[13] Gong, P., H. Li, X. He, K. Wang, J. Hu, W. Tan, S. Zhang, and X. Yang. Preparation and antibacterial activity of Fe_3O_4@ Ag nanoparticles. *Nanotechnology*, Vol. 18, No. 28, 2007, id. 285604.
[14] Barot, T., D. Rawtani, P. Kulkarni, C. M. Hussain, and S. Akkireddy. Physicochemical and biological assessment of flowable resin composites incorporated with farnesol loaded halloysite nanotubes for dental applications. *Journal of the mechanical behavior of biomedical materials*, Vol. 104, 2020, id. 103675.
[15] Ju-Nam, Y. and J. R. Lead. Manufactured nanoparticles: An overview of their chemistry, interactions and potential environmental implications. *Science of the Total Environment*, Vol. 400, No. 1–3, 2008, pp. 396–414.
[16] Ahmad, Z., R. Pandey, S. Sharma, and G. K. Khuller. Alginate nanoparticles as antituberculosis drug carriers: formulation development, pharmacokinetics and therapeutic potential. *Indian Journal of Chest Diseases & Allied Sciences, Vol. 48, No. 3, 2006, p. 171.*
[17] Monteiro, D. R., L. F. Gorup, A. S. Takamiya, A. C. Ruvollo-Filho, E. R. de Camargo, and D. B. Barbosa. The growing importance of materials that prevent microbial adhesion: Antimicrobial effect of medical devices containing silver. *International Journal of Antimicrobial Agents*, Vol. 34, No. 2, 2009, pp. 103–110.
[18] Arcos, D., A. Lopez-Noriega, E. Ruiz-Hernandez, O. Terasaki, and M. Vallet-Regi. Ordered mesoporous microspheres for bone grafting and drug delivery. *Chemistry of Materials*, Vol. 21, No. 6, 2009, pp. 1000–1009.
[19] Piñón-Segundo, E., A. Ganem-Quintanar, V. Alonso-Pérez, and D. Quintanar-Guerrero. Preparation and characterization of triclosan nanoparticles for periodontal treatment. *International Journal of Pharmaceutics*, Vol. 294, No. 1-2, 2005, pp. 217–232.
[20] Khurshid, Z., M. Zafar, S. Qasim, S. Shahab, M. Naseem, and A. AbuReqaiba. Advances in nanotechnology for restorative dentistry. *Materials*, Vol. 8, No. 2, 2015, pp. 717–731.
[21] Chitsazi, M. T., A. Shirmohammadi, M. Faramarzie, R. Pourabbas, and A. N. Rostamzadeh. A Clinical Comparison of Nano-Crystalline Hydroxyapatite (Ostim) and Autogenous Bone Graft in The Treatment Of Periodontal Intrabony Defects. *Medicina Oral, Patologia Oraly Cirugia Bucal*, Vol. 16, 2011, pp. 448–453.
[22] Vano, M., G. Derchi, A. Barone, and U. Covani. Effectiveness of nano-hydroxyapatite toothpaste in reducing dentin hypersensitivity: A double-blind randomized controlled trial. *Quintessence International*, Vol. 45, No. 8, 2014, pp. 703-711.
[23] Wang, W., S. Liao, Y. Zhu, M. Liu, Q. Zhao, and Y. Fu. Receptor-mediated drug delivery Systems targeting to glioma. *Journal of Nanomaterials*, Vol. 6, No. 1, 2015, id. 3.
[24] Tang, N., Y. P. Li, S. Kurosu, H. Matsumoto, Y. Koizumi, and A. Chiba. Interfacial reactions between molten Al and a Co–Cr–Mo alloy with and without oxidation treatment. *Corrosion Science*, Vol. 53, No. 12, 2011, pp. 4324–4326.
[25] Tang, N., Y. Li, Y. Koizumi, S. Kurosu, and A. Chiba. Interfacial reaction between Co–Cr–Mo alloy and liquid Al. *Corrosion Science*, Vol. 75, 2013, pp. 262–268.
[26] Tang, N., Y. Li, Y. Koizumi, and A. Chiba. Effect of nitriding treatment on corrosion behaviour of Co–Cr–Mo alloy in liquid Al. Corrosion Science, Vol. 78, 2014, pp. 244–250.
[27] Lombardo, G. H., R. S. Nishioka, R. O. Souza, S. M. Michida, A. N. Kojima, A. M. Mesquita, et al. Influence of surface treatment on the shear bond strength of ceramics fused to cobalt-chromium. *Journal of Prosthodontics*, Vol. 19, No. 2, 2010, pp. 103–111.
[28] Jasim, B. S. and I. J. Ismail. The effect of silanized alumina nano-fillers addition on some physical and mechanical properties of heat cured polymethyl methacrylate denture base material. *Journal of Baghdad College of Dentistry*, Vol. 26, No. 2, 2014, pp. 18–23.
[29] Li, Y., B. Zhao, S. Xie, and S. Zhang. Synthesis and properties of poly (methyl methacrylate)/montmorillonite (PMMA/MMT) nanocomposites. *Polymer International*, Vol. 52, No. 6, 2003, pp. 892–898.
[30] Foster, B. L., M. S. Ramnitz, R. I. Gafni, A. B. Burke, A. M. Boyce, J. S. Lee, et al. Rare bone diseases and their dental, oral, and craniofacial manifestations. *Journal of Dental Research*, Vol. 93, No. 7, Supplement, 2014, pp. 7S–19S.
[31] Huber, F. -X., O. Belyaev, J. Hillmeier, H. -J. Kock, C. Huber, P. -J. Meeder, et al. First histological observations on the incorporation of a novel nanocrystalline hydroxyapatite paste OSTIM® in human cancellous bone. *BMC Musculoskeletal Disorders*, Vol. 7, No. 1, 2006, id. 50.
[32] Malik, A., T. Tahir Butt, S. Zahid, F. Zahid, S. Waquar, M. Rasool, et al. Use of magnetic nanoparticles as targeted therapy: Theranostic approach to treat and diagnose cancer. *Journal of Nanotechnology*, Vol. 2017, 2017, id. 1098765.
[33] Zhengli, X. and S. Jiao. Application of nanotechniques and nanomaterials in oral medicine. *Chinese Journal of Dental Materials and Devices*, Vol. 4, 2009.
[34] Yu, K., M. Liu, H. Dai, and X. Huang. Targeted drug delivery systems for bladder cancer therapy. *Journal of Drug Delivery Science and Technology*, Vol. 56, 2020, id. 101535.
[35] Shrestha, A. and A. Kishen. Antibacterial nanoparticles in endodontics: A review. *Journal of Endodontics*, Vol. 42, No. 10, 2016, pp. 1417–1426.
[36] Fan, W., D. Wu, T. Ma, and B. Fan. Ag-loaded mesoporous bioactive glasses against enterococcus faecalis biofilm in root canal of human teeth. *Dental Materials Journal*, Vol. 34, No. 1, 2015, pp. 54–60.
[37] Kesler Shvero, D., N. Zaltsman, E. I. Weiss, D. Polak, R. Hazan, and N. Beyth. Lethal bacterial trap: Cationic surface for endodontic sealing. *Journal of Biomedical Materials Research Part A*, Vol. 104, No. 2, 2016, pp. 427–434.
[38] Aitken, R. J., M. Q. Chaudhry, A. B. A. Boxall, and M. Hull. Manufacture and use of nanomaterials: Current status in the UK and global trends. *Occupational Medicine*, Vol. 56, No. 5, 2006, pp. 300–306.
[39] Kachoei, M., F. Eskandarinejad, B. Divband, and M. Khatamian. The effect of zinc oxide nanoparticles deposition for friction reduction on orthodontic wires. *Dental Research Journal*, Vol. 10, No. 4, 2013, pp. 499-505.
[40] Tay, C. Y., W. Fang, M. I. Setyawati, S. L. Chia, K. S. Tan, C. H. L. Hong, et al. Nano-hydroxyapatite and nano-titanium dioxide exhibit different subcellular distribution and apoptotic profile in human oral epithelium. *ACS Applied Materials & Interfaces*, Vol. 6, No. 9, 2014, pp. 6248–6256.
[41] Sahoo, S. K., S. Parveen, and J. J. Panda. The present and future of nanotechnology in human health care. *Nanomedicine: Nanotechnology, Biology and Medicine*, Vol. 3, No. 1, 2007, pp. 20–31.

[42] Mount, G. J. Minimal intervention dentistry: Rationale of cavity design. *Operative Dentistry*, Vol. 28, No. 1, 2003, pp. 92–99.

[43] Hua, Y., L. Gu, and H. Watanabe. Micromechanical analysis of nanoparticle-reinforced dental composites. *International Journal of Engineering Science*, Vol. 69, 2013, pp. 69–76.

[44] Hojati, S. T., H. Alaghemand, F. Hamze, F. A. Babaki, R. Rajab-Nia, M. B. Rezvani, et al. Antibacterial, physical and mechanical properties of flowable resin composites containing zinc oxide nanoparticles. *Dental Materials*, Vol. 29, No. 5, 2013, pp. 495–505.

[45] Turssi, C. P., J. L. Ferracane, and L. L. Ferracane. Wear and fatigue behavior of nano-structured dental resin composites. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 78, No. 1, 2006, pp. 196–203.

[46] Moshaverinia, A., S. Ansari, Z. Movasaghi, R. W. Billington, J. A. Darr, and I. U. Rehman. Modification of conventional glass-ionomer cements with N-vinylpyrrolidone containing polyacids, nano-hydroxy and fluoroapatite to improve mechanical properties. *Dental Materials*, Vol. 24, No. 10, 2008, pp. 1381–1390.

[47] Uysal, T., A. Yagci, B. Uysal, and G. Akdogan. Are nano-composites and nano-ionomers suitable for orthodontic bracket bonding? *The European Journal of Orthodontics*, Vol. 32, No. 1, 2010, pp. 78–82.

[48] Reynolds, E. C. Calcium phosphate-dased remineralization systems: Scientific evidence? *Australian Dental Journal*, Vol. 53, No. 3, 2008, pp. 268–273.

[49] Reynolds, E. C. Remineralization of enamel subsurface lesions by casein phosphopeptide-stabilized calcium phosphate solutions. *Journal of Dental Research*, Vol. 76, No. 9, 1997, pp. 1587–1595.

[50] Hannig, M., and C. Hannig. Nanomaterials in Preventive Dentistry. *Nature nanotechnology*, Vol. 5, No. 8, 2010, pp. 565–569.

[51] Arafa, M. G., H. A. Mousa, and N. N. Afifi. Preparation of PLGA-chitosan based nanocarriers for enhancing antibacterial effect of ciprofloxacin in root canal infection. *Drug Delivery*, Vol. 27, No. 1, 2020, pp. 26–39.

[52] Toledano, M., R. Osorio, E. Osorio, A. L. Medina-Castillo, M. Toledano-Osorio, and F. S. Aguilera. Ions-modified nanoparticles affect functional remineralization and energy dissipation through the resin-dentin interface. *Journal of the Mechanical Behavior of Biomedical Materials*, Vol. 68, 2017, pp. 62–79.

[53] Samuel, U. and J. P. Guggenbichler. Prevention of catheter-related infections: The potential of a new nano-silver impregnated catheter. *International Journal of Antimicrobial agents*, Vol. 23, 2004, pp. 75–78.

[54] Yoshida, K., M. Tanagawa, S. Matsumoto, T. Yamada, and M. Atsuta. Antibacterial activity of resin composites with silver-containing materials. *European Journal of Oral Sciences*, Vol. 107, No. 4, 1999, pp. 290–296.

[55] Bürgers, R., A. Eidt, R. Frankenberger, M. Rosentritt, H. Schweikl, G. Handel, et al. the anti-adherence activity and bactericidal effect of microparticulate silver additives in composite resin materials. *Archives of Oral Biology*, Vol. 54, No. 6, 2009, pp. 595–601.

[56] Yoshida, K., M. Tanagawa, and M. Atsuta. Characterization and inhibitory effect of antibacterial dental resin composites incorporating silver-supported materials. *Journal of Biomedical Materials Research A*, Vol. 47, No. 4, 1999, pp. 516–522.

[57] Cheng, L., M. D. Weir, H. H. Xu, J. M. Antonucci, N. J. Lin, S. Lin-Gibson, et al. Effect of amorphous calcium phosphate and silver nanocomposites on dental plaque microcosm biofilms. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 100, No. 5, 2012, pp. 1378–1386.

[58] Punia, S. K., P. Nadig, and V. Punia. An in vitro assessment of apical microleakage in root canals obturated with gutta-flow, resilon, thermafil and lateral condensation: A stereomicroscopic study. *Journal of Conservative Dentistry: JCD*, Vol. 14, No. 2, 2011, pp. 173-177.

[59] Weir, M. D., L. C. Chow, and H. H. Xu. Remineralization of demineralized enamel via calcium phosphate nanocomposite. *Journal of Dental Research*, Vol. 91, No. 10, 2012, pp. 979–984.

[60] Wu, D., W. Fan, A. Kishen, J. L. Gutmann, and B. Fan. Evaluation of the antibacterial efficacy of silver nanoparticles against enterococcus faecalis biofilm. *Journal of Endodontics*, Vol. 40, No. 2, 2014, pp. 285–290.

[61] Pourjavadi, A., M. Bagherifard, and M. Doroudian. Synthesis of micelles based on chitosan functionalized with gold nanorods as a light sensitive drug delivery vehicle. *International Journal of Biological Macromolecules*, Vol. 149, 2020, pp. 809–818.

[62] Alkilany, A. M., L. B. Thompson, S. P. Boulos, P. N. Sisco, and C. J. Murphy. Gold nanorods: Their potential for photothermal therapeutics and drug delivery, tempered by the complexity of their biological interactions. *Advanced Drug Delivery Reviews*, Vol. 64, No. 2, 2012, pp. 190–199.

[63] Heo, D. N., W. -K. Ko, H. R. Lee, S. J. Lee, D. Lee, S. H. Um, et al. Titanium dental implants surface-immobilized with gold nanoparticles as osteoinductive agents for rapid osseointegration. *Journal of Colloid and Interface Science*, Vol. 469, 2016, pp. 129–137.

[64] Ruparelia, J. P., A. K. Chatterjee, S. P. Duttagupta, and S. Mukherji. Strain specificity in antimicrobial activity of silver and copper nanoparticles. *Acta Biomaterialia*, Vol. 4, No. 3, 2008, pp. 707–716.

[65] Kishen, A., Z. Shi, A. Shrestha, and K. G. Neoh. An investigation on the antibacterial and antibiofilm efficacy of cationic nanoparticulates for root canal disinfection. *Journal of Endodontics*, Vol. 34, No. 12, 2008, pp. 1515–1520.

[66] Gutiérrez, M. F., P. Malaquias, V. Hass, T. P. Matos, L. Lourenço, A. Reis, et al. The role of copper nanoparticles in an etch-and-rinse adhesive on antimicrobial activity, mechanical properties and the durability of resin-dentine interfaces. *Journal of Dentistry*, Vol. 61, 2017, pp. 12–20.

[67] Aydin Sevinç, B., and L. Hanley. Antibacterial activity of dental composites Containing zinc oxide nanoparticles. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 94, No. 1, 2010, pp. 22–31.

[68] Srakaew, V., P. Ruangsri, K. Suthin, P. Thunyakitpisal, and W. Tachaboonyakiat. Sodium-phosphorylated chitosan/zinc oxide complexes and evaluation of their cytocompatibility: An approach for periodontal dressing. *Journal of Biomaterials Applications*, Vol. 27, No. 4, 2012, pp. 403–412.

[69] Yuan, J. -H., Y. Chen, H. -X. Zha, L. -J. Song, C. -Y. Li, J. -Q. Li, et al. Determination, characterization and cytotoxicity on HELF cells of ZnO nanoparticles. *Colloids and Surfaces B: Biointerfaces*, Vol. 76, No. 1, 2010, pp. 145–150.

[70] Wang, Y., L. Yuan, C. Yao, L. Ding, C. Li, J. Fang, et al. A combined toxicity study of zinc oxide nanoparticles and vitamin C in food additives. *Nanoscale*, Vol. 6, No. 24, 2014, pp. 15333–15342.

[71] Kasraei, S., L. Sami, S. Hendi, M.-Y. AliKhani, L. Rezaei-Soufi, and Z. Khamverdi. Antibacterial properties of composite resins incorporating silver and zinc oxide nanoparticles on streptococcus mutans and lactobacillus. *Restorative Dentistry & Endodontics*,

Vol. 39, No. 2, 2014, p. 109.
[72] Wang, Y., H. Hua, W. Li, R. Wang, X. Jiang, and M. Zhu. Strong antibacterial dental resin composites containing cellulose nanocrystal/zinc oxide nanohybrids. *Journal of Dentistry*, Vol. 80, 2019, pp. 23–29.
[73] Özcan, M. and C. Hämmerle. Titanium as a reconstruction and implant material in dentistry: Advantages and pitfalls. *Materials*, Vol. 5, No. 9, 2012, pp. 1528–1545.
[74] Chaturvedi, T. P. An overview of the corrosion aspect of dental implants (titanium and its alloys). *Indian Journal of Dental Research*, Vol. 20, No. 1, 2009, pp. 91-98.
[75] Gogniat, G. and S. Dukan. TiO_2 photocatalysis causes DNA damage via fenton reaction-generated hydroxyl radicals during the recovery period. *Applied and Environmental Microbiology*, Vol. 73, No. 23, 2007, pp. 7740–7743.
[76] Garcia-Contreras, R., M. Sugimoto, N. Umemura, M. Kaneko, Y. Hatakeyama, T. Soga, et al. Alteration of metabolomic profiles by titanium dioxide nanoparticles in human gingivitis model. *Biomaterials*, Vol. 57, 2015, pp. 33–40.
[77] Padovani, G. C., V. P. Feitosa, S. Sauro, F. R. Tay, G. Durán, A. J. Paula, et al. Advances in dental materials through nanotechnology: Facts, perspectives and toxicological aspects. *Trends in biotechnology*, Vol. 33, No. 11, 2015, pp. 621–636.
[78] Sodagar, A., M. S. A. Akhoundi, A. Bahador, Y. F. Jalali, Z. Behzadi, F. Elhaminejad, et al. Effect of TiO_2 nanoparticles incorporation on antibacterial properties and shear bond strength of dental composite used in orthodontics. *Dental press journal of orthodontics*, Vol. 22, No. 5, 2017, pp. 67–74.
[79] Meng, W., Y. Zhou, Y. Zhang, Q. Cai, L. Yang, and B. Wang. Effects of hierarchical micro/nano-textured titanium surface features on osteoblast-specific gene expression. *Implant dentistry*, Vol. 22, No. 6, 2013, pp. 656–661.
[80] Dorkhan, M., T. Yücel-Lindberg, J. Hall, G. Svensäter, and J. R. Davies. Adherence of human oral keratinocytes and gingival fibroblasts to nano-structured titanium surfaces. *BMC Oral Health*, Vol. 14, No. 1, 2014, pp. 1–9.
[81] Lohbauer, U., A. Wagner, R. Belli, C. Stoetzel, A. Hilpert, H. D. Kurland, et al. Zirconia nanoparticles prepared by laser vaporization as fillers for dental adhesives. *Acta Biomaterialia*, Vol. 6, No. 12, 2010, pp. 4539–4546.
[82] Enomoto, K., Y. Ichijo, M. Nakano, M. Kikuchi, A. Narumi, S. Horiuchi, et al. Unique hydrophobization and hybridization via direct phase transfer of ZrO_2 nanoparticles from water to toluene producing highly transparent polystyrene and poly(methyl methacrylate) hybrid bulk materials. *Macromolecules*, Vol. 50, No. 24, 2017, pp. 9713–9725.
[83] Wang, J., and R. Stevens. Zirconia-toughened alumina (ZTA) ceramics. *Journal of Materials Science*, Vol. 24, No. 10, 1989, pp. 3421–3440.
[84] Chan, K. S., D. P. Nicolella, B. R. Furman, S. T. Wellinghoff, H. R. Rawls, and S. E. Pratsinis. Fracture toughness of zirconia nanoparticle-filled dental composites. *Journal of Materials Science*, Vol. 44, No. 22, 2009, pp. 6117–6124.
[85] Souza, J. C., J. B. Silva, A. Aladim, O. Carvalho, R. M. Nascimento, F. S. Silva, et al. Effect of zirconia and alumina fillers on the microstructure and mechanical strength of dental glass ionomer cements. *Open Dentistry Journal*, Vol. 10, No. 1, 2016, pp. 58–68.
[86] Gad, M. M., A. Rahoma, A. M. Al-Thobity, and A. S. ArRejaie. Influence of incorporation Of ZrO_2 nanoparticles on the repair strength of polymethyl methacrylate denture bases. *International Journal of Nanomedicine*, Vol. 11, 2016, pp. 5633–5643.
[87] Jasim, B. S. and I. J. Ismail. The effect of silanized alumina nanofillers addition on some physical and mechanical properties of heat cured polymethyl methacrylate denture base material. *Journal of Baghdad College of Dentistry*, Vol. 26, No. 2, 2014, pp. 18–23.
[88] Safarabadi, M., N. Khansari, and A. Rezaei. An experimental investigation of HA/AL_2O_3 nanoparticles on mechanical properties of restoration materials. *Engineering Solid Mechanics*, Vol. 2, No. 3, 2014, pp. 173–182.
[89] Llorente, A., B. Serrano, J. Baselga, G. Gedler, and R. Ozisik. Nanoindentation and wear behavior of thermally stable biocompatible polysulfone–alumina nanocomposites. *RSC Advances*, Vol. 102, No. 102, 2016, pp. 100239–100247.
[90] Hamouda, I. M. Current perspectives of nanoparticles in Medical and dental biomaterials. *Journal of Biomedical Materials Research*, Vol. 26, 2012, pp. 143–151.
[91] Yu, J., H. Yang, K. Li, J. Lei, L. Zhou, and C. Huang. A novel application of nanohydroxyapatite/mesoporous silica biocomposite on treating dentin hypersensitivity: An in vitro study. *Journal of Dentistry*, Vol. 50, 2016, pp. 21–29.
[92] Besinis, A., R. van Noort, and N. Martin. Infiltration of demineralized dentin with silica and hydroxyapatite nanoparticles. *Dental Materials*, Vol. 28, No. 9, 2012, pp. 1012–1023.
[93] Chu, Y. Q., Y. Tong, T. L. Zhang, F. L. Huang, and X. Z. Wang. Synthesis of nanodiamond reinforced dental composite resins and their mechanical properties. *Fullerenes, Nanotubes and Carbon Nanostructures*, Vol. 20, No. 4–7, 2012, pp. 628–632.
[94] Lee, D. K., S. V. Kim, A. N. Limansubroto, A. Yen, A. Soundia, C. Y. Wang, et al. Nanodiamond-Gutta percha composite biomaterials for root canal therapy. *ACS Nano*, Vol. 9, No. 11, 2015, pp. 11490–11501.
[95] Protopapa, P., E. Kontonasaki, D. Bikiaris, K. M. Paraskevopoulos, and P. Koidis. Reinforcement of a PMMA resin for fixed interim prostheses with nanodiamonds. *Dental Materials Journal*, Vol. 30, No. 2, 2011, pp. 222–231.
[96] Ozkan, M. Quantum dots and other Nanoparticles: What can they offer to drug discovery? *Drug Discovery Today*, Vol. 9, No. 24, 2004, pp. 1065–1071.
[97] Ge, J., Q. Jia, W. Liu, M. Lan, B. Zhou, L. Guo, et al. Carbon dots with intrinsic theranostic properties for bioimaging, red-light-triggered photodynamic/photothermal simultaneous Therapy in vitro and in vivo. *Advanced Healthcare Materials*, Vol. 5, No. 6, 2016, pp. 665–675.
[98] Yaghini, E., A. M. Seifalian, and A. J. MacRobert. Quantum dots and their potential biomedical applications in photosensitization for photodynamic therapy. *Future Nanomedicine,* Vol. 4, No. 3, 2009, pp 353-363.
[99] Wang, Y. and L. Chen. Quantum dots, lighting up the research and development of nanomedicine. *Nanomedicine: Nanotechnology, Biology and Medicine*, Vol. 7, No. 4, 2011, pp. 385–402.
[100] Kanaparthy, R. and A. Kanaparthy. The changing face of dentistry: Nanotechnology. *International Journal of Nanomedicine*, Vol. 6, 2011, pp. 2799–2804.
[101] Loo, C., A. Lowery, N. Halas, J. West, and R. Drezek. Immunotargeted nanoshells for integrated cancer imaging and therapy. *Nano Letters*, Vol. 5, No. 4, 2005, pp. 709–711.
[102] El-Sayed, I. H., X. Huang, and M. A. El-Sayed. Selective laser photo-thermal therapy of epithelial carcinoma using anti-EGFR antibody conjugated gold nanoparticles. *Cancer Letters*, Vol. 239,

No. 1, 2006, pp. 129–135.
[103] Mercado, N., P. Bhatt, V. Sutariya, F. L. E. Florez, and Y. V. Pathak. Application of nanoparticles in treating periodontitis: Preclinical and clinical overview. In: *Surface Modification of Nanoparticles for Targeted Drug Delivery,* Y. V. Pathak, Ed. Springer International Publishing, Cham, pp. 467–480.
[104] Li, F., M. D. Weir, J. Chen, and H. H. K. Xu. Effect of charge density of bonding agent containing a new quaternary ammonium methacrylate on antibacterial and bonding properties. *Dental Materials*, Vol. 30, No. 4, 2014, pp. 433–441.
[105] Hoque, J., P. Akkapeddi, C. Ghosh, D. S. S. M. Uppu, and J. Haldar. A biodegradable polycationic paint that kills bacteria in vitro and in vivo. *ACS Applied Materials & Interfaces*, Vol. 8, No. 43, 2016, pp. 29298–29309.
[106] Cheng, L., M. D. Weir, K. Zhang, D. D. Arola, X. Zhou, and H. H. K. Xu. Dental primer and adhesive containing a new antibacterial quaternary ammonium monomer dimethylaminododecyl methacrylate. *Journal of Dentistry*, Vol. 41, No. 4, 2013, pp. 345–355.
[107] Abramovitz, I., N. Beyth, G. Weinberg, A. Borenstein, D. Polak, D. Kesler-Shvero, et al. In vitro biocompatibility of endodontic sealers incorporating antibacterial nanoparticles. *Journal of Nanomaterials*, Vol. 2012, 2012, id. 858073.
[108] Beyth, N., Y. Houri-Haddad, L. Baraness-Hadar, I. Yudovin-Farber, A. J. Domb, and E. I. Weiss. Surface antimicrobial activity and biocompatibility of incorporated polyethylenimine nanoparticles. *Biomaterials*, Vol. 29, No. 31, 2008, pp. 4157-4163.
[109] Selwitz, R. H., A. I. Ismail, and N. B. Pitts. Dental caries. *The Lancet*, Vol. 369, No. 9555, 2007, pp. 51–59.
[110] White, J. M. and W. S. Eakle. Rationale and treatment approach in minimally invasive dentistry. *Journal of the American Dental Association (1939)*, Vol. 131 Supplement 1, 2000, pp. 13S-19S.
[111] Ericson, D., E. Kidd, D. McComb, I. Mjör, and M. Noack. Minimally invasive dentistry - concepts and techniques in cariology. *Oral Health & Preventive Dentistry*, Vol. 1, 2003, pp. 59–72.
[112] Xu, H. H. K., J. L. Moreau, L. Sun, and L. C. Chow. Nanocomposite containing amorphous calcium phosphate nanoparticles for caries inhibition. *Dental Materials*, Vol. 27, No. 8, 2011, pp. 762–769.
[113] Li, X., W. Liu, L. Sun, K. E. Aifantis, B. Yu, Y. Fan, et al. Resin composites reinforced by nanoscaled fibers or tubes for dental regeneration. *BioMed Research International*, Vol. 2014, 2014, id. e542958.
[114] Wang, S. -F., L. Shen, W. -D. Zhang, and Y.-J. Tong. Preparation and mechanical properties of chitosan/carbon nanotubes composites. *Biomacromolecules*, Vol. 6, No. 6, 2005, pp. 3067–3072.
[115] Ajayan, P. M. Nanotubes from carbon. *Chemical Reviews*, Vol. 99, No. 7, 1999, pp. 1787–1800.
[116] Wang, W., F. Watari, M. Omori, S. Liao, Y. Zhu, A. Yokoyama, et al. Mechanical properties and biological behavior of carbon nanotube/polycarbosilane composites for implant materials. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, Vol. 82B, No. 1, 2007, pp. 223–230.
[117] Park, J. E., I.-S. Park, M. P. Neupane, T.-S. Bae, and M.-H. Lee. Effects of a carbon nanotube-collagen coating on a titanium surface on osteoblast growth. *Applied Surface Science*, Vol. 292, 2014, pp. 828–836.
[118] Bhirde, A. A., V. Patel, J. Gavard, G. Zhang, A. A. Sousa, A. Masedunskas, et al. targeted killing of cancer cells in vivo and in vitro with EGF-directed carbon nanotube-based drug delivery. *ACS Nano*, Vol. 3, No. 2, 2009, pp. 307–316.
[119] Lv, L., X. Han, L. Zong, M. Li, J. You, X. Wu, and C. Li. Biomimetic hybridization of kevlar into silk fibroin: Nanofibrous strategy for improved mechanic properties of flexible composites and filtration membranes. *ACS Nano*, Vol. 11, No. 8, 2017, pp. 8178–8184.
[120] Cooper, C. A., D. Ravich, D. Lips, J. Mayer, and H. D. Wagner. Distribution and alignment of carbon nanotubes and nanofibrils in a polymer matrix. *Composites Science and Technology*, Vol. 62, No. 7, 2002, pp. 1105–1112.
[121] An, J.-W., D.-H. You, and D.-S. Lim. Tribological properties of hot-pressed alumina–CNT composites. *Wear*, Vol. 255, No. 1, 2003, pp. 677–681.
[122] Chen, Q., Y. Zhao, W. Wu, T. Xu, and H. Fong. Fabrication and evaluation of bis-GMA/TEGDMA dental resins/composites containing halloysite nanotubes. *Dental Materials*, Vol. 28, No. 10, 2012, pp. 1071–1079.
[123] Lvov, Y. and E. Abdullayev. Functional polymer–clay nanotube composites with sustained release of chemical agents. *Progress in Polymer Science*, Vol. 38, No. 10, 2013, pp. 1690–1719.
[124] Avani, F., S. Damoogh, F. Mottaghitalab, A. Karkhaneh, and M. Farokhi. Vancomycin loaded halloysite nanotubes embedded in silk fibroin hydrogel applicable for bone tissue engineering. *International Journal of Polymeric Materials and Polymeric Biomaterials*, Vol. 69, No. 1, 2020, pp. 32–43.
[125] Pan, Y., H. Zhang, D. Shi, J. Sun, S. Du, F. Liu, et al. Highly ordered, millimeter-scale, continuous, single-crystalline graphene monolayer formed on Ru (0001). *Advanced Materials*, Vol. 21, No. 27, 2009, pp. 2777–2780.
[126] Sava, S., A. Tonea, B. Stanca, C. Alb, C. Sarosi, and D. Dudea. The study of new composites with graphene used in dentistry. *Studia Universitatis Babes-Bolyai, Chemia*, Vol. 60, 2015.
[127] Sarosi, C., A. R. Biris, A. Antoniac, S. Boboia, C. Alb, I. Antoniac, et al. The nanofiller effect on properties of experimental graphene dental nanocomposites. *Journal of Adhesion Science and Technology*, Vol. 30, No. 16, 2016, pp. 1779–1794.
[128] Hu, W., C. Peng, W. Luo, M. Lv, X. Li, D. Li, et al. Graphene-based antibacterial paper. *ACS Nano*, Vol. 4, No. 7, 2010, pp. 4317–4323.
[129] Ji, H., H. Sun, and X. Qu. Antibacterial applications of graphene-based nanomaterials: Recent achievements and challenges. *Advanced drug Delivery Reviews*, Vol. 105, 2016, pp. 176–189.
[130] Das, M. R., R. K. Sarma, R. Saikia, V. S. Kale, M. V. Shelke, and P. Sengupta. Synthesis of silver nanoparticles in an aqueous suspension of graphene oxide sheets and its antimicrobial activity. *Colloids and Surfaces B: Biointerfaces*, Vol. 83, No. 1, 2011, pp. 16–22.
[131] Rago, I., A. Bregnocchi, E. Zanni, A. G. D'Aloia, F. D. Angelis, M. Bossu, et al. antimicrobial activity of graphene nanoplatelets against Streptococcus Mutans. Presented the 2015 IEEE 15th *International Conference on Nanotechnology* (IEEE-NANO), 2015.
[132] Rodríguez-Lozano, F. J., D. García-Bernal, S. Aznar-Cervantes, M. A. Ros-Roca, M. C. Algueró, N. M. Atucha, et al. Effects of composite films of silk fibroin and graphene oxide on the proliferation, cell viability and mesenchymal phenotype of periodontal ligament stem cells. *Journal of Materials Science: Materials in Medicine*, Vol. 25, No. 12, 2014, pp. 2731–2741.
[133] Park, K. O., J. H. Lee, J. H. Park, Y. C. Shin, J. B. Huh, J.-H. Bae, et al. Graphene oxide-coated guided bone regeneration membranes with enhanced osteogenesis: spectroscopic analysis and animal

study. *Applied Spectroscopy Reviews*, Vol. 51, No. 7–9, 2016, pp. 540–551.

[134] Rosa, V., H. Xie, N. Dubey, T. T. Madanagopal, S. S. Rajan, J. L. P. Morin, et al. Graphene oxide-based substrate: Physical and surface characterization, cytocompatibility and differentiation potential of dental pulp stem cells. *Dental Materials*, Vol. 32, No. 8, 2016, pp. 1019–1025.

[135] Liu J., S. H. Jianzhen, J. Ma, H. Liu and J. Li. Preparation of high-performance antimicrobial agent based on ZnO/GQD-PEI nanocomposites. U.S. Patent No. 16/439,408, 2020.

[136] Fu, C., E. Ajami, H. B. Wen, O. S. Sanchez. Methods of depositing silver nanostructures on to implant surfaces. U.S. Patent No. 16/502,781, 2020.

[137] Mayfield, R. L., and R. W. Towse. Method and system for selecting surface finishes. U.S. Patent No. 16/222,231, 2019.

[138] Stewart, C. A., B. D. Hatton, and Y. Finer. Highly loaded metal oxide materials by self-assembly for extended biologically active molecule release in medical and dental applications. U.S. Patent No. 16/301,773, 2019.

[139] Sarto M. S., A. Polimeni, D. Uccelletti, M. Bossu, A. Bregnocchi, C. R. Chandraiahgari, et al. Process for the production of antimicrobial dental adhesives including graphene and relative product thereof. U.S. Patent No. 10/610,461, 2020.

[140] llardo, C. M. C., S. A. C. Hernandez, L. F. M. Lopez, and J. P. G. Rojas. Preparation process of dental and orthopedic acrylic materials with antimicrobial properties using copper nanoparticle technology. U.S. Patent No. 16/067,053, 2019.

[141] Koo, H., L. Gao, D. Cormode, and P. Naha. Iron oxide nanoparticles and methods of use thereof. U.S. Patent No. 10/369,089, 2019.

[142] Giannini, M., R. R. Pacheco, F. A. Rueggeberg, J. R. S. Montero, E. D. Martinez, A. F. G. Flores, et al. Fluorsecent nanoparticle compositions for dental bonded restorations. U.S. Patent No. 16/228,014, 2019.

[143] Kishen, A. and A. Shrestha. Multi-functional micro and nanoparticles for use in root canal therapies. U.S. Patent No. 15/932,180, 2018.

[144] Malshe, A. P. and W. Jiang. Nanostructured hydroxyapatite coating for dental and orthopedic implants. U.S. Patent No. 9/682,170, 2017.

[145] Jadhav, K., R. Hr, S. Deshpande, S. Jagwani, D. Dhamecha, S. Jalalpure, K. Subburayan, et al. Phytosynthesis of gold nanoparticles: Characterization, biocompatibility, and evaluation of its osteoinductive potential for application in implant dentistry. *Materials Science and Engineering: C*, Vol. 93, 2018, pp. 664–670.

[146] Niska, K., N. Knap, A. Kędzia, M. Jaskiewicz, W. Kamysz, and I. Inkielewicz-Stepniak. Capping agent-dependent toxicity and antimicrobial activity of silver nanoparticles: An in vitro study. Concerns about potential application in dental practice. *International Journal of Medical Sciences*, Vol. 13, No. 10, 2016, pp. 772–782.

[147] Barot, T., D. Rawtani, and P. Kulkarni. Physicochemical and biological assessment of silver nanoparticles immobilized halloysite nanotubes-based resin composite for dental applications. *Heliyon*, Vol. 6, No. 3, 2020, id. e03601.

[148] Acosta-Torres, L. S., L. M. López-Marín, R. E. Núñez-Anita, G. Hernández-Padrón, and V. M. Castaño. Biocompatible metal-oxide nanoparticles: Nanotechnology improvement of conventional prosthetic acrylic resins. *Journal of Nanomaterials*, Vol. 2011, 2010, id. e941561.

[149] Del Carpio-Perochena, A., A. Kishen, A. Shrestha, and C. M. Bramante. Antibacterial properties associated with chitosan nanoparticle treatment on root dentin and 2 types of endodontic sealers. *Journal of Endodontics*, Vol. 41, No. 8, 2015, pp. 1353–1358.