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](image)

### 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

<table>
<thead>
<tr>
<th>Discipline</th>
<th>Nanoparticles</th>
<th>Applications</th>
<th>Ave. size (nm)</th>
<th>Commercially available</th>
<th>Manufacturer</th>
<th>Benefits</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontics</td>
<td>ZrO NPs, Ag NPs, Au NPs, TiO NPs, HA NPs, ZnO NPs, Al NPs</td>
<td>Use in periodontal diseases, in treatment of deep periodontal pocket</td>
<td>5-300</td>
<td>NanoCare®</td>
<td>NanoCare® Gold</td>
<td>Drug delivery, improves tooth remineralization, reduces bacterial adherence</td>
<td>[1, 8-22]</td>
</tr>
<tr>
<td>Prosthodontics</td>
<td>ZrO NPs, TiO NPs, HA NPs, ZnO NPs, TiN NPs, TiC NPs</td>
<td>Nanoparticles for bio film management on the tooth surface</td>
<td>210-280</td>
<td>NanoTech Elite H-D plus, GC OPTI GLAZE color®</td>
<td>Zhermack, BadiaPolesine, Italy</td>
<td>Increased strength, reduced wear, improved aesthetics</td>
<td>[24, 25, 28, 29, 82-94, 87-89]</td>
</tr>
<tr>
<td>Oral and Maxillofacial surgery</td>
<td>HA NPs, Au NPs, Carbon nanotube, Quantum-dots (Qdots)</td>
<td>Anti-cancer drug delivery, used as scaffolds for new bone formation</td>
<td>2-50</td>
<td>NanoCare®</td>
<td>Sivoda, Boston &amp; Perth, Australia</td>
<td>Drug delivery, improved cell viability</td>
<td>[61-63, 97, 98, 118]</td>
</tr>
<tr>
<td>Conservative Dentistry and Endodontics</td>
<td>Au NPs, Ag NPs, QPEI NPs, HA NPs, ZnO NPs, Al NPs, TiO NPs, TiC NPs</td>
<td>Drug and gene delivery, tissue engineering, antibacterial agent in root canals, root canal disinfection</td>
<td>20-75</td>
<td>AH plus™, Epiphany, GuttaRelief®</td>
<td>DENTSPLY International</td>
<td>Improved bond strength, decreased risk of microbial infection</td>
<td>[10, 35, 37, 58, 61-63, 71, 107]</td>
</tr>
<tr>
<td>Restorative Dentistry</td>
<td>ZrO NPs, TiO NPs, HA NPs, QPEI NPs, AlNPs, TiC NPs, TiUnite</td>
<td>Remineralizing Composite resins, Nanofilled resins</td>
<td>20-75</td>
<td>Kava™, Kvarc 3000, Nanomax, Aduro™ Single bond plus, Filtek Supreme XT Fuji IX GP, Nano-primer, Premier™, Corp Max®</td>
<td>Kavo/Kerr/Sybron, Orange, CA, USA, DENTSPLY International, Wallingford, CT, USA, DENTSPLY International, Wallingford, CT, USA</td>
<td>Improved bond strength, increased resistance to wear, improved aesthetics</td>
<td>[21, 52, 55, 56, 79, 107, 108]</td>
</tr>
<tr>
<td>Orthodontics and Orthopedics</td>
<td>Alumina NPs, ZrO NPs, HA NPs, QPEI NPs, AlNPs, TiO NPs, TiC NPs, TiUnite</td>
<td>Coating of metal NP's on brackets and arch wires to decrease surface irregularities and reduction in friction</td>
<td>150-200</td>
<td>–</td>
<td>UCMA and CEDOS-Badtronicism</td>
<td>High strength and reduced mechanical resistance, reduced friction and wear between orthodontic bracket and arch wire</td>
<td>[39, 89]</td>
</tr>
<tr>
<td>Oral Medicine and Radiology</td>
<td>Silica NPs, ZrO NPs, HA NPs, TiO NPs, QPEI NPs, AlNPs, TiC NPs, TiUnite</td>
<td>Dental applications</td>
<td>2-200</td>
<td>–</td>
<td>–</td>
<td>Drug and gene delivery, improved cell viability</td>
<td>[60, 97, 99]</td>
</tr>
<tr>
<td>Preventive Dentistry</td>
<td>Au NPs, Ag NPs, TiO NPs, QPEI NPs, AlNPs, TiC NPs, TiUnite</td>
<td>Used for rinsing of root canal treatment, low surface tension allows NP's to get to the smallest areas and dental ducts of the system</td>
<td>250-300</td>
<td>NanoCare® Gold</td>
<td>Nano-Care, Sauerwein, Germany</td>
<td>Disinfectant of deep carious lesion to improve composite materials, decreases risk of caries, enhanced adhesion and antibacterial properties, improved cell vitality</td>
<td>[21, 48, 51, 67]</td>
</tr>
<tr>
<td>Dental Implant</td>
<td>Au NPs, Ag NPs, TiO NPs, QPEI NPs, AlNPs, TiC NPs, TiUnite</td>
<td>Surface modifications of dental implants, CaP NP are deposited on a double acid-etched surface by Discrete Crystalline Deposition (SCD) self-set process</td>
<td>20-300</td>
<td>NanoCare® Nano-coated implant, Tandem® Biomet 3i, Palm Beach Gardens, FL, USA, Nobel Biocare Holding AG, Zurich, Switzerland</td>
<td>–</td>
<td>Disinfectant of deep carious lesion to improve composite materials, decreases risk of caries, enhanced adhesion and antibacterial properties, improved cell vitality</td>
<td>[3, 43, 63, 82, 117]</td>
</tr>
</tbody>
</table>

HA NPs: Hydroxyapatite nanoparticles; ZrO NPs: Zirconium dioxide nanoparticles; Au NPs: Gold nanoparticles; Ag NPs: Silver nanoparticles; ZnO NPs: Zinc oxide nanoparticles; TiO NPs: Titanium dioxide; Al NPs: Aluminum nanoparticles; QPEI NPs: Quaternary ammonium polyethyleneimine nanoparticles; ACPNPs: Amorphous calcium phosphate nanoparticles; TiN NPs: Titanium nitride; TiC NPs: Titanium carbide; 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 anti-cancer 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 ionomer cements (GIC), dental composite, gutta-percha, root

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

QPEI NPs: Quaternary ammonium polyethyleneimine 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*) 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 diamonds, 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](image-url)
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 Zn²⁺ ions which increase oxidative stress and inhibit growth of microorganism [68]. ZnO NPs also have studied on cell lines of human embryonic 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 (TiO₂ NPs)
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 (TiO₂) produces reactive oxygen radicals (H₂O₂ 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 TiO₂ NPs causes inflammatory action on human gingival fibroblasts [76]. GIC modification with TiO₂ displays moderate biocompatibility on Oral Squamous Cell Carcinoma Cell Lines [77]. Incorporating TiO₂ 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$_2$ NPs)
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 prostheses. ZrO$_2$ NP can be used as a filler in 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$_2$ NP 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$_2$NP in GIC restorative cement has shown improvement in compressive strength and reduction in cracks within the matrix of the cements [85]. Addition of ZrO$_2$ NPs in manufacturing of dental dentures displayed high strength, colour stability, low electrical and thermal conductivity [86].

3.1.2.4 Aluminium Oxide Nanoparticles (Al$_2$O$_3$ 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$_2$O$_3$ NPs are highly reactive to moisture, heat, and sunlight, safety measures are essential to safeguard the material. Furthermore, Al$_2$O$_3$ 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$_2$O$_3$ NP. Polymethylmethacrylate (PMMA) has disadvantages such as low flexural strength properties and impact strength. Addition of Al$_2$O$_3$ 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$_2$ NPs)
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$_2$ NPs, 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 den-
tal 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 nanomaterials 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 TiO₂, Fe₂O₃ 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

<table>
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<tbody>
<tr>
<td>US 20200046764A1</td>
<td>Ag NPs</td>
<td></td>
<td>0.1-100 nm</td>
<td><em>E. Coli, S. mutans</em></td>
<td>In dental composite, root canal sealer etc.</td>
<td>[135]</td>
</tr>
<tr>
<td>US 20200008909A1</td>
<td>ZNO/GQD-PEI NPs</td>
<td>Nano-pitting (Nanoscale surface roughening)</td>
<td>1 - 100 nm</td>
<td><em>Gram-negative and Gram-positive bacteria</em></td>
<td>Deposition of Silver NPs on implant surface to prevent implant associated infection.</td>
<td>[136]</td>
</tr>
<tr>
<td>US 20190274791A1</td>
<td>-</td>
<td></td>
<td></td>
<td><em>E. coli, S. mutans</em></td>
<td>In dental composite, root canal sealer etc.</td>
<td>[137]</td>
</tr>
<tr>
<td>US 20190151205A1</td>
<td>Mesoporous metal oxides NPs</td>
<td>-</td>
<td>300-1500 nm</td>
<td><em>S. mutans</em></td>
<td>In dental materials and as a coating materials for dental implants.</td>
<td>[138]</td>
</tr>
<tr>
<td>US 20190021333A1</td>
<td>Cu NPs</td>
<td>-</td>
<td>40-100 nm</td>
<td><em>C. albicans, S. mutans, S. aureus</em></td>
<td>In dental prostheses to prevent and/or treat denture stomatitis and to reduce cariogenic bacteria.</td>
<td>[140]</td>
</tr>
<tr>
<td>US 010369089B2</td>
<td>FeO₂ NPs</td>
<td>-</td>
<td>1-1000 nm</td>
<td><em>Gram-negative and Gram-positive bacteria</em></td>
<td>In dental materials to prevent biofilms formation and tooth demineralization.</td>
<td>[141]</td>
</tr>
<tr>
<td>US 20190183742A1</td>
<td>NPs containing NaYF₄ nanocrystals doped with Er, Yb and Tm.</td>
<td>-</td>
<td>100-200 nm</td>
<td>-</td>
<td>In dental bonded restorations</td>
<td>[142]</td>
</tr>
<tr>
<td>US 20180185249A1</td>
<td>Chitosan polymer NPs</td>
<td>-</td>
<td>60-150 nm</td>
<td><em>E. faecalis</em></td>
<td>In root canal treatment</td>
<td>[143]</td>
</tr>
<tr>
<td>US 009682170B2</td>
<td>HAp NPs₄, HAp-ZnO NPs</td>
<td>-</td>
<td>50-100 nm</td>
<td>-</td>
<td>In dental implants</td>
<td>[144]</td>
</tr>
</tbody>
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*E. coli: Escherichia coli; S. mutans: Streptococcus mutans; C. albicans: Candida albicans; S. aureus: Staphylococcus aureus; E. faecalis: Enterococcus faecalis; NaYF₄: 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 nanoparticles; FeO₂ 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$_2$O$_3$ 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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Data availability statement: Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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