Dental Medicine Nanosystems: Nanoparticles and their use in Dentistry and Oral Health Care

Abstract

The major goal in dentistry and oral health care is maintaining the health of oral tissues. Thus, to achieve this goal, the advances in nanosciences and nanotechnology have paved the way to approach this goal. The application of these nanotechnologies to dental medicine have given rise to nanodentistry, which is an innovative branch of science. Many studies indicate extensive application of the medical nanosystems in numerous fields of nanodentistry such as prevention, diagnosis, therapeutic, restoration and tissue regeneration. The latter, cover all dentistry specialties such as restorative dentistry, periodontics, endodontic, orthodontics, prosthodontics, oral implantology and regenerative dental Medicine. These dental Medicine nanosystems as nanostructured materials constitute new innovative nanoproducts that make possible the maintenance of oral health care in a very precise, safe and effective way. The objective of this review is to expose briefly, the recent advances in these dental Medicine nanosystems, especially in nanoparticles and nanoparticles-based nanomaterials. In addition, the article sets out to describe the various potential applications of this type of nanostructured materials and the challenges they present in clinical, cosmetic and esthetic dental and oral health care.

Keywords: Dental Medicine Nanosystems; Nanodentistry; Nanoparticles; Nanomaterials; Oral Health Care

Introduction

Nanotechnology is the engineering of functional systems by controlling atoms and molecules to achieve effective, complete control of the structure of matter with new functions. The nanotechnology tools and ideas allow to create a new nanosystem with novel, physico-chemicals, mechanicals, and biological properties. However, the applications of these nanotechnologies has rapidly expanded into all areas of health care science including that of odonatological science [1]. Nanotechnology aided in processing a variety Dental Medicine Nanosystems (DMN) with innovative applications. Nanosystems means the assembly of nanoscale components for the purpose of performing a function. In the literature, nanosystems are described as manufactured nanostructured particles (nanoparticles) and nanostructured materials (nanomaterials) or their combination. The nanomaterials may have intrinsic properties related to their structures and their components or develop new properties related to the simple structuring caused by the incorporation of the nanoparticles. In the recent years, various advances in engineering of nanoparticles and nanomaterials or their combination, have allowed the development of a new innovative DMN. The advances in the applications of these DMN cover all dentistry specialties namely restorative dentistry [2], periodontics [3], endodontic [4], orthodontics [5-6], prosthodontics [7], oral implantology [8-9], regenerative dentistry [10]. They also cover dental fields such as prevention, diagnosis, therapeutic, restoration and tissue regeneration [11]. DMN are numerous, varied and have greatly extended. This field has been the subject of potential in a wide spectrum of dental industry and oral health care. The present review, focuses on the following DMN: nanoparticles [12,13,14], nanoparticles-based nanomaterials [15-17,18], Nanoparticles are divided into, organic nanoparticles [19], inorganic [20] and hybrids [21]. In this regard, they are often used in dentistry and oral health care in free or incorporated form. Dental materials (metals, composites / resin-composites and polymers) are used as restorative systems, adhesives and bonding systems, cement and sealant systems and tissue regenera-
The incorporation of nanoparticles in dental materials proves to be very promising as it makes it possible to obtain new DMN systems. Hence, it will improve the functional and structural properties of dental materials, while optimize clinical, cosmetic and esthetic dental and oral health care performances [22]. On the other hand, recently, the nanosafety of the inorganic nanoparticles for use in diverse biomedical applications including dentistry was investigated. The results of which are encouraging and emphasise the need for more precise and more detailed studies [23].

The aim of this review is to demonstrate and to describe the recent advances in the nanoparticles and their incorporation into dental nanomaterials. In addition, view their potential applications for prevention, therapeutic, restoration, tissues regeneration and diagnosis.

**Dental Prevention and Prophylaxis Applications**

Tooth wear is a dental disease and includes tooth erosion and tooth loss. The comprehension of the main oral problems and the challenges related to DMN in the oral environment and this constitutes the basis for developing innovative and new nanoproduct that can provide an improved oral tissue protection. This could be beneficial especially for improving the effectiveness of preventive therapy for dental pathologies and oral diseases. Currently, established prevention of dental plaque relies heavily on tooth-brushing and the strengthening of tooth enamel by fluoride. Therefore, the development of enhanced dental medicine nanosystems for oral hygiene is of paramount importance in increasing the protection of the teeth and of the oral cavity from detrimental processes [24]. These developments concern nanoparticles and nanoparticle-based materials, in particular, aspects related to preventing the formation of dental plaque, biofilm and primary, secondary infections. However, the organic and inorganic nanoparticles were used in free or incorporated forms, and several strategies are used to design these dental prevention nanostructured materials such as dental medicine nanosystems as show as in Figure 1. On the other hand, the prevention of the biofilm development concerns dental equipment and this is the case in dental unit water lines (DUWL) [25]. It was reported that the problem of the susceptibility of biofilm development and bacterial growth in DUWL, leads to water contamination, which causes health and ecological effects. Overall, recent advances in the design and use of these DMN for dental prevention and prophylaxis are described in Table 1 and 2.

**Figure 1:** Illustration of Dental Medicine Nanosystems design and the strategies of their use for preventive, therapeutic, restoration, tissues regeneration and theirs combination.
Table 1: Use of nanoparticles (NPs) for dental prevention treatments / Prophylactic prevention.

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim (s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymer</td>
<td>Lipid</td>
<td>Free</td>
<td>Incorporated</td>
</tr>
<tr>
<td>Chitosane: BA-NPs</td>
<td>Colloidal Solution (Sodium Fluoride: MA)</td>
<td>- Bioadsorption into dental tissues</td>
<td>Nguyen et al., 2017</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Sustained release of bioactive molecules delivery nanosystem</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Protection against caries development by minimalisation</td>
<td></td>
</tr>
<tr>
<td>Solid Lipid Nanoparticles (SLN)</td>
<td>Transmicroal patch (TP) (Dicyclofenic diethylamine / DDEA): PA</td>
<td>- Incorporation of NPs by inclusion in matrix</td>
<td>Malviya et al., 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- TF loaded with DDEA-SLN applied at the gingival site immediately after dental surgery has the potential to produce therapeutic relief locally which is prolonged 24 h</td>
<td></td>
</tr>
<tr>
<td>Phosphatidylcholin (PC) Cholesterol (CHOL) PC-CH liposomes</td>
<td>Colloidal Solution</td>
<td>- Bioadsorption into dental tissues</td>
<td>Cademartiri et al., 2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Sustained release of bioactive molecules delivery nanosystem</td>
<td></td>
</tr>
</tbody>
</table>


Table 2: Use of nanoparticles (NPs) for dental prevention treatments / Prophylactic prevention.

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim (s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metal</td>
<td>Mineral</td>
<td>Free</td>
<td>Incorporated</td>
</tr>
<tr>
<td>Copper Oxide (CuO-NPs): PA</td>
<td>Colloidal Solution</td>
<td>- Antimicrobial NPs</td>
<td>Amiri et al., 2017</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zirconium (ZrO2-NPs): PA</td>
<td>Bioactive resins</td>
<td>- Incorporation of NPs by inclusion in matrix</td>
<td>Fathima et al., 2017</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silver (Ag-NPs)</td>
<td>Colloidal Solution</td>
<td>- Antimicrobial NPs</td>
<td>Gitigour et al., 2017</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium carbonate (CaCO3): RA-NPs</td>
<td>Toothpaste</td>
<td>- Incorporation of NPs by inclusion in matrix</td>
<td>Dizaj et al., 2015</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


**Dental Therapeutic Applications**

Dental therapeutic treatments can have a triple purpose, preventive therapy, curative therapy and tissues regenerative therapy. The innovative therapeutic nanostructured materials, as nanoparticles or nanomaterials based nanomaterials was recently reviewed [22]. However, their use for dental applications have undergone extensive investigations due to their potential antimicrobial effect. In this regard, the exploitation of their toxic properties to bacteria, fungi and viruses as well as their incorporation into dental materials in order to control oral infections was reported [19-28, 29-30, 31-32, 33]. Accordingly, all these studies, have reviewed the importance of this antimicrobial effect of these nanoparticles whether in free form or incorporated form. Thus, the therapeutic nanostructured materials are a real therapeutic alternative in dentistry. Several strategies are used to design and to formulate this nanostructured materials for the treatment of dental and oral diseases. Regardingly, Figure 1 illustrates the design of the therapeutic dental nanostructured materials. In addition, the recent studies reflect recent advances in DMN for dental therapeutics applications (combination of preventive therapy and curative therapy) are described in Table 3 & 4. On the other hand, concerning tissue regenerative therapy, the understanding of the cell biological processes underlies development and regeneration of oral tissues and leads to novel regenerative approaches and strategies. However, the recent...
advances in regenerative dentistry, by using stem cells, signaling molecules, growth factors molecules, nanomaterials and nanoparticles are reported [10-37-38-39]. Thus, the overall, recent advances in the use of nanoparticles for dental tissues regenerative applications are described in Table 5.

Table 3: Use of nanoparticles (NPs) for dental therapeutic treatments / Prevention therapy and Curative therapy

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim(s) and Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymer(s)</td>
<td>Co-polymer(s)</td>
<td>Free</td>
</tr>
</tbody>
</table>
| Chitosan | (C-NPs): EA | | Gel | \- Incorporation of NPs by inclusion in matrix \\
| | | | \- Sustained and release of bioactive molecules delivery nanosystem \\
| | | | \- Bioadhesion into dental tissues \\
| | | | \- C-NPs more cytocompatible \\
| | | | \- A-NPs more stable in saliva environment |
| Chitosan: BA | (A-NPs): BA | | Film | \- Incorporation of NPs by inclusion in matrix \\
| | | | \- Sustained and release of bioactive molecules delivery nanosystem \\
| | | | \- Bioadhesion into dental tissues \\
| | | | \- Antimicrobial effect \\
| | | | \- Antibiofilm effect \\
| | | | \- Potential ability to kill bacteria in short and long term exposure |
| Poly(lactic-co-glycolic acid) (PLGA-NPs) | | Colloidal solution | | \- Sustained and release of bioactive molecules delivery nanosystem \\
| | | | \- Penetration inside dental tubules of demineralized dentin-substrates and resin-dentin interface \\
| | | | \- Antimicrobial effect \\
| | | | \- CHX:PLGA-NPs show low cytotoxicity, slow degradation and gradual CHX release profiles, delivered efficiently inside dental tubules structure, even after bonding resin infiltration and were attached retained on collagen-fibers \\
| | | | \- Bioadhesion effect |
| Poly(DMAEMA)-b-pDMAEMA (PDMAEMA-co-BA) | Micellar solution | | | \- Sustained and release of bioactive molecules delivery nanosystem \\
| | | | \- Bioadhesion effect \\
| | | | \- Cationic and acidic pI-response NPs \\
| | | | \- Antibacterial effect \\
| | | | \- Enhanced topical pH-responsive drug release \\
| | | | \- High affinity for dental and biofilm surfaces \\
| | | | \- High binding capacity to hydroxyapatite and dental pellicle emulating surfaces \\
| | | | \- High antibiofilm efficacy in vivo |


Table 4: Use of nanoparticles (NPs) for dental therapeutic treatments / Prevention therapy and Curative therapy

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim(s) and Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metal</td>
<td>Mineral</td>
<td>Free</td>
</tr>
</tbody>
</table>
| Mesoporous silica | (SiO₂-NPs) | | Colloidal solution | \- Anti-inflammatory effect \\
| | (SiO₂-NPs) | | \- Sustained and release of bioactive molecules delivery nanosystem \\
| | (SiO₂-NPs) | | \- In vitro BE-NPs exhibits notable anti-inflammatory effects in gingival epithelial cells through effective release and cellular internalization approaches |
| Silver (Ag-NPs). | PA | | Disorbicolic cellulose film | \- Sustained and release of bioactive molecules delivery nanosystem \\
| | | | \- Antimicrobial NPs \\
| | | | \- Excellent antibacterial activity |
| Zinc oxide | (ZnO-NPs): PA | | Colloidal solution With Chlorhexidine (CHX): PA | \- Antimicrobial NPs \\
| | | | \- Synergistically antibacterial and anti-biofilm effects |
| Silicon dioxide | (SiO₂-NPs) | | Nanofilm (Poly(ethylene terephthalate-glycol and Silsesquioxane)) | \- Incorporation of NPs by inclusion in matrix \\
| | | | \- Bioadhesion effect \\
| | | | \- Antibacterial property related to the superhydrophilicity of the film |
| Magnesium | (M-NPs) | | Colloidal solution | \- Anti-hypersensitivity effect \\
| | | | \- Polyethylene-glycol (PEG): coating and functionalisation of NPs surface \\
| | | | \- Superparamagnetic PEG-M-NPs navigated inside the dental tubules via an external magnetic field \\
| | | | \- Potential for reducing the permeability of dental tubules by occluding the open tubular area and they could deliver other therapeutic agents inside the tubules |


Table 5: Use of nanoparticles for dental tissues regenerative / Tissues regenerative therapy

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Incorporated</th>
<th>Aim(s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inorganic nanoparticles</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gold (Au-NPs)</td>
<td>Calcium phosphate cement (CPC)</td>
<td>- Incorporation of Au-NPs improved cells behavior on CPC, including better cell adhesion and proliferation, and enhanced osteogenic differentiation. - Au-NPs-CPC enhanced the osteogenic functions of cells (hDPSCs) and as bioactive additives thus enhance bone regeneration.</td>
<td>Xia et al., 2017</td>
<td></td>
</tr>
<tr>
<td>Calcium silicate (Ca3SiO5-NPs) (Gentamicin and FGF-2)</td>
<td>Cellodial Solution</td>
<td>- Sustained and release of bioactive molecules delivery nanosystem. - Endodontic materials for biocompatible and osteogenic dental pulp tissue regenerative. - Used as drug carriers to maintain sustained release gentamicin and FGF-2. - The Ca3SiO5-NPs stimulate more odontogenic-related protein than calcium silicate matrix because of the FGF-2 release.</td>
<td>Huang et al., 2017</td>
<td></td>
</tr>
<tr>
<td><strong>Dental Restoration Applications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Dental Restoration Applications

The nanoparticles are promising for incorporation in dental materials-related restorative materials systems, adhesives-bonding systems, cements and sealants systems and prosthesis bases systems. Therefore, these nanoparticles have potential to significantly improve the biological, mechanical, optical, thermal and the physico-chemical properties of dental medicine nanosystems (nanostructured materials). Thus, the production of nanostructured and functionalized dental materials with more efficient biological properties must take into consideration the non-sacrifice of the other properties of these dental materials. Concerning restorative nanomaterials, in the dental implantology, infection is the most common factor that leads to dental implant failure. Antibacterial implant surfaces based on nano-scale modifications appear as an attractive strategy for control of peri-implantitis. The summary of the application of nanoparticles as dental implant coating nanomaterials that control and improve the implant success rate, with focus on enhanced osseointegration and antimicrobial effect was overviewed [34]. The investigation of the addition of an antibacterial agent to dental implants may provide the opportunity to decrease the percentage of implant. However, the use of nanoparticles to coat implants could provide osteoconductive and antimicrobial functionalities to prevent failure. But, the current research in dental adhesives and bonding nanomaterials, aims at increasing the durability of resin–dentin bonds. Thus, the fundamental processes responsible for the aging mechanisms involved in the degradation of resin-bonded interfaces and the potential approaches to prevent and counteract this degradation by creating stable resin–dentin bonds that are able to resist the collagenolytic hydrolysis are also reviewed [35]. In the case of dental cements and sealants nanomaterials, glass ionomer cement (GICs) are usually used as restorative materials have still lots of challenges due to their secondary caries and low mechanical properties. Therefore, many efforts have been proposed to modify the antibacterial and the mechanical features of GICs in order to prevent the secondary caries. Particularly, to achieve this goal, the nanoparticles were incorporated into GICs and their effectiveness has been proven [36]. Finally, in the case of dental prosthesis nanomaterials, the incorporation of nanoparticles was used in order to have a high biocompatibility with the oral tissues, excellent esthetics, superior mechanical properties. Clinical failures of complete or partial dental prosthesis are most likely in the form of fracture either due to fatigue or impact forces of mastication. Several strategies are used to improve and to ameliorate the structure and the functions of these dental restoration materials as well as all the problems related to their contact with the various dental tissues and especially the interfaces. Thus, Figure 1 illustrates the design of the restorative dental nanostructured materials. In addition, the latest studies and in DMN for dental restoration applications (combination of restoration, prevention and therapy) are described in Table 6 (A, B, C, D, E, F) and 7.
Table 6 (A): Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim (s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Titanium microparticle</td>
<td>- Antimicrobial NPs; - Coating the microparticles with Ag-NPs (Ti-Sn-Ag-NPs) or with an Ag-NPs-coated biopolymer (Ti-BP-Ag-NPs) with bactericidal effect; - Ti-BP-Ag-NPs exhibit excellent antimicrobial properties</td>
<td>Venciogolo et al., 2017 [53]</td>
</tr>
<tr>
<td><strong>Palladium (Pd-NPs) Silver (AgNPs): PA</strong></td>
<td>Hydroxyapatite (Ca(PO₄)₂(OH)₆-NPs)</td>
<td>implants</td>
<td>- Incorporation of NPs by Surface coating and immobilization; - Antimicrobial NPs; - Improvement of osteointegration of dental implant; - Using DOX immobilized inside bone with ultra-thin structure deposition of Pd-NPs, AgNPs, HA-NPs</td>
</tr>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Titanium implants</td>
<td>- Antimicrobial NPs; - Fabricate porous titanium implants with interconnected pores and biofunctionalized by embedding (Ag-NPs) in an oxide surface layer grown; - Porous implants released silver ions more than solid implants with strong antimicrobial activity and no signs of cytotoxicity</td>
<td>Van Hengel et al., 2017 [59]</td>
</tr>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Titanium implants</td>
<td>- Antimicrobial NPs; - Presence of Ag-NPs on the titanium surface provides an antibacterial activity; - Osteoconductive Ag-NPs induce a chemical bond with bone to attain good biological fixation for implants; - No changes in mechanical properties</td>
<td>Foliewik et al., 2017 [50]</td>
</tr>
<tr>
<td><strong>Zinc oxide (ZnO-NPs): PA</strong></td>
<td>Dental stone</td>
<td>- Incorporation of NPs by inclusion in matrix; - Additives of ZnO-NPs affect the dental tissue strength and compressive strength; - Surface roughness is lower when ZnO-NPs were added</td>
<td>Dr. Cerretto et al., 2017 [81]</td>
</tr>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Titanium implants</td>
<td>- Antimicrobial NPs; - Antibacterial activity of mixtures of ZnO-NPs and HA-NPs coated titanium surface discs</td>
<td>Abdalnour et al., 2015 [82]</td>
</tr>
</tbody>
</table>


Table 6 (B): Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim (s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Fluoro-Silica (F-SiO₂,NPs)</td>
<td>Resin composite</td>
<td>- Photo-crosslinked polyethylene polymer (PU); - Superhydrophobic coatings for preventing microweakness in a dental composite restoration; - Superhydrophobic coatings with low PU-F-SiO₂ ratios (1:3) possessed excellent structure and high contact angle, low sliding angle, good transparency, the prominent cell viability and biocompatibility for clinical application; - Superhydrophobic coatings effectively prevent water penetration in resin composite restoration</td>
</tr>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Graphite oxide sheets</td>
<td>Resin composite</td>
<td>- Incorporation of NPs by inclusion in matrix; - Antimicrobial NPs; - Composite resins reinforced with Ag-NPs induce HA nanoparticles provide both efficient reinforcement and high antimicrobial activity</td>
</tr>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Zirconia (ZrO₂-NPs)</td>
<td>Alumina Ceramics (Al₂O₃)</td>
<td>- Incorporation of NPs by inclusion in matrix; - High antimicrobial activity at very low concentration; - Use as additive for endodontic fillings</td>
</tr>
<tr>
<td><strong>Silver (AgNPs): PA</strong></td>
<td>Sodium (Na⁺-NPs)</td>
<td>Glass fiber filaments covered on the surface with Ag-NPs that formed thin films</td>
<td>- Antimicrobial NPs; - Nanosystem for root filling for endodontic therapy; - Glass fiber filaments covered on the surface with Ag-NPs that formed thin films; - Potent mechanical and antibacterial properties</td>
</tr>
</tbody>
</table>

Table 6 (C) Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments.

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim (s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper (Cu-NPs): PA</td>
<td>Exothermic adhesive</td>
<td>Incorporation of NPs by inclusion in matrix; Antimicrobial NPs; NPs did not affect mechanical properties; At higher concentrations they produce more mechanical resistance; Prevent the degradation of adhesive-dentin interfaces.</td>
<td>Gotzner et al., 2017</td>
</tr>
<tr>
<td>Zirconia (ZrO₂-NPs); Titanium dioxide (TiO₂-NPs)</td>
<td>Orthodontic adhesive</td>
<td>Incorporation of NPs by inclusion in matrix; Antimicrobial NPs; Antibacterial activity; Adding ZrO₂-NPs and TiO₂-NPs to orthodontic adhesive increased compressive strength, tensile strength, and shear bond strength in vivo.</td>
<td>Feldheim et al., 2017</td>
</tr>
<tr>
<td>Magnesium oxide (MgO-NPs); Calcium oxide (CaO-NPs): PA</td>
<td>Mediate dentin bonding</td>
<td>Mg₃(SO₄)₂(OH)₆·NPs can be considered as novel fillers to improve the mechanical properties of dentin bonding agents; Incorporation of the Mg₃(SO₄)₂(OH)₆·NPs improved the bond strength to dentin with the highest values obtained at 1% NPs.</td>
<td>Fallahzadeh et al., 2017</td>
</tr>
<tr>
<td>Titanium dioxide (TiO₂-NPs)</td>
<td>Adhesive resin-composite</td>
<td>Antimicrobial NPs; Photocatalytic NPs; Incorporate carboxylic acid functionalized TiO₂-NPs into adhesive resin; Reactive oxygen species generated by functionalized TiO₂-NPs through visible-light irradiation enhanced shear-bond strength to human teeth with low porosity.</td>
<td>Sun et al., 2017</td>
</tr>
<tr>
<td>Zinc oxide (ZnO-NPs): PA</td>
<td>Adhesive resin-composite</td>
<td>Incorporation of NPs by inclusion in matrix; Antimicrobial NPs; Use of single bond of adhesive with 10% of ZnO-NPs; Increases of anti-microbial properties without affecting bond strength.</td>
<td>Saffarpour et al., 2016</td>
</tr>
<tr>
<td>Silver (Ag-NPs): PA</td>
<td>Adhesive resin-composite</td>
<td>Antimicrobial NPs; Quaternary ammonium methacrylates matrix (QAM); Ag-NPs antimicrobial effect; Ca₃(PO₄)₂·H₂O released calcium phosphate ions and remineralized tooth lesions and neutralized acids; Combines Ag-NPs Ca₃(PO₄)₂·H₂O·QAML, new class of composites and adhesives with antibacterial and remineralization double benefits.</td>
<td>Cheng et al., 2015</td>
</tr>
</tbody>
</table>


Table 6 (D) Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments.

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim (s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc oxide (ZnO-NPs): PA</td>
<td>Glass-ionomer cement (GICs)</td>
<td>Incorporation of NPs by inclusion in matrix; Antimicrobial NPs; Inclusion of ZnO-NPs at concentrations 1% and 2% did not promote their antimicrobial activity against S. mutans; Most important advantages of the GICs are associated with their ability to release long-term antimicrobial agents.</td>
<td>Garcia et al., 2017</td>
</tr>
<tr>
<td>Hydroxyapatite (Ca₅(PO₄)₂·OH)·NPs; Fluorapatite (Ca₅(PO₄)₂·F-NPs)</td>
<td>Glass-ionomer cement (GICs)</td>
<td>Incorporation of NPs by inclusion in matrix; bioactivity HA-NPs and F-NPs improved mechanical properties of GICs; Highest compressive strength, flexural strength, and diametral tensile strength. Addition of 1 wt% Mg₃(SO₄)₂·H₂O·NPs to the ceramic component of GIC is desired for dental restorations applications.</td>
<td>Burackshard et al., 2016; Szydłowski et al., 2014</td>
</tr>
<tr>
<td>Ferrous (Fe₂O₃·NPs)</td>
<td>Glass-ionomer cement (GICs)</td>
<td>Incorporation of NPs by inclusion in matrix; bioactivity HA-NPs and F-NPs improved mechanical properties of GICs; Highest compressive strength, flexural strength, and diametral tensile strength. Addition of 1 wt% Mg₃(SO₄)₂·H₂O·NPs to the ceramic component of GIC is desired for dental restorations applications.</td>
<td>Burackshard et al., 2016; Szydłowski et al., 2014</td>
</tr>
<tr>
<td>Hydroxyapatite (Ca₅(PO₄)₂·OH)·NPs; Calcium (CaCO₂·NPs)</td>
<td>Trescolithium-Dicalcium Phosphate Cements (TDC)</td>
<td>- The analysis of hydration reactions and physicochemical properties; Physicochemical properties were improved; Good properties including setting ability, biocompatibility, and the capacity to induce tissue regeneration.</td>
<td>Moreno-Vargas et al., 2017</td>
</tr>
<tr>
<td>Titanium dioxide (TiO₂-NPs)</td>
<td>Hydroxyapatite (Ca₅(PO₄)₂·OH)·NPs; Calcium (CaCO₂·NPs)</td>
<td>Trescolithium-Dicalcium Phosphate Cements (TDC)</td>
<td>Incorporation of TiO₂-NPs with weight ratio of 1% increased the setting time, compressive strength and pull-out bond strength of modified cement.</td>
</tr>
<tr>
<td>Titanium dioxide (TiO₂-NPs)</td>
<td>Bioactive glass (BG-NPs)</td>
<td>Glass-ionomer cement (GICs)</td>
<td>- BG-NPs incorporated GIC enhanced mechanical properties and biomineralisation properties without cytotoxicity.</td>
</tr>
</tbody>
</table>

**Table 6 (E):** Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments.

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim(s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inorganic nanoparticles</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Titanium dioxide (TiO₂-NPs) | Acrylic resin denture | - Antimicrobial NPs  
- Incorporation of TiO₂-NPs in PMMA polymer matrix was proved to have antibacterial effects while modified viscosity characteristics and improved lower mechanical parameters  
- The newly obtained 0.4% nanocomposite was successfully used with  
- Poroelastic technique for complete denture manufacturing | Ton et al., 2017 [80] |
| Silicon dioxide (SiO₂), triethylsilane (TES), TEVS-SiO₂-NPs | Acrylic resin denture | - Incorporation of SiO₂-NPs in PMMA polymer matrix  
- TiO₂-NPs are the best candidate for improving the properties of PMMA composites | Kamalabadi et al., 2017 [81] |
| Silver (Ag-NP); PA | Calcium phosphate (CaP-NP); MA | Dimethacrylate resin | - Incorporation of NPs by inclusion in matrix  
- NPs formation in site by a photopolymerization process  
- Mixed CaP-NPs: Ag-NPs as slow-releasing filters for remineralization and antibacterial activity  
- Optical properties were compromised by the presence of silver  
- Higher fracture strength and elastic modulus  | Nara et al., 2017 [82] |
| Silver (Ag-NP); PA | Calcium phosphate (CaP-NP); MA | Dimethacrylate resin | - Incorporation of NPs by inclusion in matrix  
- Antimicrobial NPs  
- Inhibition of biofilm of main microorganisms associated with dental plaque  
- No change of the mechanical properties | De Castro et al., 2016 [83] |
| Silver (Ag-NP); PA | Poly (methyl methacrylate) resin | Poly (methyl methacrylate) resin | - Incorporation of NPs by inclusion in matrix  
- Antimicrobial NPs  
- Inhibition of biofilm of main microorganisms associated with dental plaque  
- No change of the mechanical properties | De Castro et al., 2016 [83] |

**Legend:** NPs: Nanoparticles; MA: Memineralisant agents; PA: Pharmacological agents; ADA: Anti-demineralisant agents; BA: Bioadhesive agents; RA: Remineralisant agents; AAA: Anti-adhesion agents.

**Table 6 (F):** Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments.

<table>
<thead>
<tr>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim(s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inorganic nanoparticles</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Copper (Cu-NPs); PA | Collodial solution | Collodial solution | - Antimicrobial NPs  
- Antimicrobial effect  
- In situ generated NPs by ultrasonic dental surgical instruments  
- Dispersion during some types of dental surgery | Shubhang et al., 2017 [84] |
| Silver (Ag-NP); PA | Resin-composite | Resin-composite | - Antimicrobial NPs  
- Antimicrobial activity  
- Incorporation of NPs by surface coating of resin-composites  
- Immobilization of NPs on yttria-stabilized zirconia polymer  
- Low cytotoxicity and total silver leaching level | Yamada et al., 2017 [85] |
| Silver (Ag-NP); PA | Orthodontic resin-composite | Orthodontic resin-composite | - Incorporation of NPs by inclusion in matrix  
- Antimicrobial NPs  
- Prevent oral pathogen growth during orthodontic treatment  
- In vitro potential antimicrobial activities | Li et al., 2017 [86] |
| Silver (Ag-NP); PA | Collodial solution | Collodial solution | - Antimicrobial NPs  
- Antimicrobial effect  
- Highly prolonged bactericidal activity against dentofacial plaque  
- Used as dental filling of composite materials | Karmack et al., 2015 [87] |
| Silver (Ag-NP); PA | Epoxy resin | Epoxy resin | - Incorporation of NPs by inclusion in matrix  
- Antimicrobial NPs  
- Antimicrobial activity against dental pathogens | Clamies et al., 2017 [88] |
| Silver (Ag-NP); PA | Collodial solution | Collodial solution | - Antimicrobial NPs  
- Antimicrobial activity against dental pathogens | Argueta-Sanchez et al., 2014 [89] |

**Legend:** NPs: Nanoparticles; MA: Memineralisant agents; PA: Pharmacological agents; ADA: Anti-demineralisant agents; BA: Bioadhesive agents; RA: Remineralisant agents; AAA: Anti-adhesion agents.
Table 7: Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments

<table>
<thead>
<tr>
<th>Metal</th>
<th>Type and Composition</th>
<th>Form</th>
<th>Aim(s) and Strategy</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quadrupled PolyEthyleneimine (QPEI-NPs); PA-NPs</td>
<td>Resin-composite</td>
<td>- Incorporation of NPs by inclusion in matrix</td>
<td>Silve et al., 2015 [93]</td>
</tr>
<tr>
<td>Polymeric nanoparticles</td>
<td>Polystyrene-acrylic (PSA); Zn-oxide (ZnO); Silica (SiO2); Dimethyldichlorosilane (DMDS); Hypochlorite de sodium (NaClO); (PSA-ZnO-SiO2-DMDS-Cl-NPs); PA</td>
<td>Titanium implants</td>
<td>- Antimicrobial NPs</td>
<td>Li et al., 2017 [94]</td>
</tr>
<tr>
<td>Hybrid nanoparticles</td>
<td>Zinc oxide (ZnO-NPs); PA</td>
<td>Orthodontic resin composite</td>
<td>- Incorporation of NPs by inclusion in matrix</td>
<td>Nabakoski et al., 2013 [95]</td>
</tr>
</tbody>
</table>


**Dental Diagnosis Applications**

The cancer diagnosis which involves the design, characterization, production, and application of dental nanosystems was reviewed [40]. Recently, an increased amount of efforts have been made to develop less invasive early diagnostic modalities for oral cancer, of which the in vivo high resolution imaging of oral epithelial tissues using novel optical systems and the chemical analysis of saliva show great promise as valuable tools. The metallic nanoparticles as iron nanoparticles (Fe-NPs) single or conjugated with polysaccharides, and gold nanoparticles (Au-NPs) single or conjugated with antibodies or peptides for specific cellular biomarkers were used in dental diagnostic. They have recently been investigated as optical or magnetical contrasting agents in medical imaging techniques for early detection of oral cancer, and for identifying and differentiating infectious pathogens [41].

**Conclusion**

The applications of nanostructured materials (nanoparticles and nanomaterials or their combination) such as dental medicine nanosystems (DMN) generally imply products that may bring prevention, diagnosis and therapy diseases and / or restoration of disorders and / or tissues regenerative of oral cavity benefits. The advances in surface and interface processing and engineering of nanoparticles, nanomaterials and their combination, allowed the design of a new nanostructured materials with innovative properties which can be a real support for the improvement of dental treatments. Currently, there is a wide range of this DMN developments and applications in different fields and specialties of dentistry and made dental procedures fast, reliable, effective, safe and less painful. The development of the DMN have raised substantial interest thanks to their use nowadays either in pre-clinical investigation they have already been approved and are in clinical practice of dentistry and oral health care. Currently, the challenge is to detail the cytotoxicity studies in vitro and especially in vivo, with the aim of taking numerous research outcomes and convert them into strategies for the development of clinical, cosmetic, esthetic dental practice and oral health care marketable nanoproducts. In addition, the development of new functional nanostructured materials and their design in the form of nanosystems, including “nanomachines” or “nanorobots” more effective and more suitable for dental treatment and oral health are in full evolution.

**References**

4. Chung SH, Park YS. Local drug delivery in endodontics: A lit-
29. Höfner SM, Malmsten M (2017) Membrane interactions...


56. Lin X, Hwangbo S, Jeong H, Cho YA, Ahn HW, Hong JK...


