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

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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 odontological 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 all 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 [15-16-17-18]. 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 nano-safety 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 shown 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 their combination.
Table 1: Use of nanoparticles (NPs) for dental prevention treatments / Prophylactic prevention.

| Type and Composition | Form                  | Aim(s) and Strategy                                                                 |
|----------------------|-----------------------|--------------------------------------------------------------------------------------|
| Chitosane; BA-NPs    | Colloidal Solution    | - Incorporation of NPs by inclusion in matrix                                       |
|                      |                       | - Bioadhesion into dental tissues                                                   |
|                      |                       | - Antibacterial effect                                                               |
|                      |                       | - Mineralisation effect                                                              |
|                      |                       | - Sustained and release of bioactive molecules delivery nanosystem                  |
|                      |                       | - Caries prevention by demineralisation inhibition                                    |
|                      | Transmucosal patch    | - Incorporation of NPs by inclusion in matrix                                       |
|                      | (TP; (Diclofenac diethylamine / DDEA): PA) | - TP loaded with DDEA-SLN applied at the gingival site immediately after dental surgery has the potential to produce therapeutic relief locally which is prolonged 24th |
|                      | Colloidal Solution    | - Sustained and release of bioactive molecules delivery nanosystem                  |
|                      |                       | - Low and continuous release of fluoride at pH                                       |
|                      |                       | - Protection against caries development by mineralisation                            |
|                      |                       | - Remineralisation agents                                                            |
| Organic nanoparticles |                       | - Anti-adhesion agents                                                              |

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

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

| Type and Composition | Form                  | Aim(s) and Strategy                                                                 |
|----------------------|-----------------------|--------------------------------------------------------------------------------------|
| Copper Oxide (CuO-NPs): PA | Colloidal Solution   | - Antimicrobial NPs                                                                 |
|                      |                       | - Preventing dental caries or dental infections                                      |
| Zirconium (ZrO2-NPs): PA | Bioactive resins      | - Incorporation of NPs by inclusion in matrix                                       |
|                      |                       | - Antimicrobial NPs                                                                 |
|                      |                       | - Antibacterial effect                                                               |
|                      |                       | - Anticaries                                                                         |
| Silver (Ag-NPs)      | Colloidal Solution    | - Antimicrobial NPs                                                                 |
|                      |                       | - Antibacterial effect                                                               |
|                      |                       | - Antibiofilm in dental unit water lines                                             |
|                      |                       | - Prevention of water contamination                                                  |
| Calcium carbonate (CaCO3): RA-NPs | Toothpaste | - Incorporation of NPs by inclusion in matrix                                       |
|                      |                       | - Reduced or prevent tooth erosion                                                   |
|                      |                       | - Remineralize initial enamel lesions                                               |

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

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 nanoparticles 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 [19-26]. 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
Table 3: Use of nanoparticles (NPs) for dental therapeutic treatments / Prevention therapy and Curative therapy

| Type and Composition | Form | Aim (s) and Strategy | Reference(s) |
|----------------------|------|----------------------|--------------|
| Mesoporous silica (SiO₂-NPs) | Colloidal solution | - Anti-inflammatory effect | Li et al., 2017 [33] |
| Mesoporous silica (SiO₂-NPs) | Colloidal solution | - Sustained and release of bioactive molecules delivery nanosystem | |
| Mesoporous silica (SiO₂-NPs) | Colloidal solution | - In vitro BE-NPs exhibits notable anti-inflammatory effects in gingival epithelial cells through effective release and cellular internalization approaches | |
| Silver (Ag-NPs) | Micellar solution (Farnesol) | - Sustained and release of bioactive molecules delivery nanosystem | Zhou et al., 2016 [59] |
| Zinc oxide (ZnO-NPs) | Colloidal solution | - Antimicrobial NPs | Afra et al., 2017 [55] |
| Zinc oxide (ZnO-NPs) | Colloidal solution | - Synergistically antibacterial and anti-biofilm effects | |
| Silicon dioxide (SiO₂-NPs) | Nanofilm (Poly(ethylene terephthalate)-glycol and Silica@oxane) | - Incorporation of NPs by inclusion in matrix | Lin et al., 2016 [56] |
| Magnesium (M-NPs) | Colloidal solution | - Anti-hyperosensitivity effect | Dabbagh et al., 2014 [57] |

Legend: NPs: Nanoparticles; MA: Memineralising agents; PA: Pharmacological agents; ADA: Anti-demineralising agents; BA: Bioadhesive agents; RA: Remineralising agents; AAA: Anti-adhesion agents.
Table 5: Use of nanoparticles for dental tissues regenerative therapy

| Metal | Mineral | Form | Incorporated | Aim(s) and Strategy | Reference(s) |
|-------|---------|------|--------------|---------------------|--------------|
| Gold (Au-NPs) | Calcium silicate (Ca$_3$SiO$_4$-NPs) | Colloidal solution | Calcium phosphate cement (CPC) | Incorporation of Au-NPs improved cells behavior on CPC, including better cell adhesion and proliferation, and enhanced osteogenic differentiation | Xia et al., 2017 |
| | | | | Au-NPs-CPC enhanced the osteogenic functions of cells (hDPSCs) and as bioactive additives thus enhance bone regeneration | |
| | | | | - Endodontic materials for biocompatible and osteogenic dental pulp tissue regenerative | Huang et al., 2017 |
| | | | | - Used as drug carriers to maintain sustained release gentamicin and FGF-2 | |
| | | | | - The Ca$_3$SiO$_4$-NPs stimulate more osteogenically-related protein than calcium silicate matrix because of the FGF-2 release | |
| | | | | - Antimicrobial NPs | Heo et al., 2016 |
| | | | | - The Au-NPs were osteogenic agents due to their potential effects on the stimulation of osteoblast differentiation. | |
| | | | | - The Au-NPs were immobilized on the titanium implants surface | |
| | | | | - The Au-NPs enhances the osteogenic differentiation in vivo | |
| | | | | - The Au-NPs have significant influence on the osseous interface formation in vivo | |
| | | | | - Au-NPs can be useful as osseo-integration inducing dental implants for formation of an osseous interface and maintenance of nascent bone formation. | |
| | | | | - BGs-NPs were non-toxic at a concentration of 20 mg/ml | Ajina et al., 2015 |
| | | | | - Increased proliferation cell with smaller BGS-NPs | |
| | | | | - Use in dental and bone treatments as fillers or bone-tissue bond forming materials | |

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

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 functionnalized 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

| Metal and Composition | Type and Composition | Form | Aim (s) and Strategy | Reference(s) |
|-----------------------|----------------------|------|----------------------|--------------|
| Silica (SiO₂-NPs) PA | Hydroxyapatite (Ca₃(PO₄)₂(OH)₂-NPs) | Dental stone | - Incorporation of NPs by inclusion in matrix; - Addition of SiO₂-NPs to affect the dimenlal tensile strength and compressive strength; - Surface roughness lower when SiO₂-NPs were added | De Cesaros et al., 2013 [51] |

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

| Type and Composition | Form | Aim (s) and Strategy | Reference(s) |
|----------------------|------|----------------------|--------------|
| Fluoro-Silica (F-SiO₂-NPs) PA | Resin composite | - Photo-crosslinked polyurethane polymer (PU); - Superhydrophobic coating for preventing microleakage in a dental composite restoration; - Superhydrophobic coatings with low PU:F-SiO₂ ratio (1:3) possessed excellent structure, high contact angle, low sliding angle, good transparency, the prominent cell viability and biocompatibility for clinical application; - Superhydrophobic coatings effectively prevented water permeation in resin composite restoration | Cao et al., 2017 [5] |
| Silica (SiO₂-NPs) PA | Resin composite | - Incorporation of NPs by inclusion in matrix; - Antimicrobial NPs; - Composite resin reinforced with SiO₂-NPs exhibits HA nanowires provide both efficient restorative and high antimicrobial activity | Ai et al., 2017 [21] |
| Silver (Ag-NPs) PA | Graphite oxide sheets | Aluminum Ceramics (Al₂O₃) | - Incorporation of NPs by inclusion in matrix; - High antibacterial activity at very low concentration; - Use as additive for endodontic fillings | Genzerakids et al., 2016 [84] |
| Zirconium (ZrO₂-NPs) | Nanozirconium (ZrO₂-NPs) Nanoparticles | - Incorporation of NPs by inclusion in matrix; - High optical properties; - Achievement of high transparency of polycrystalline alumina ceramics | Trimeurt et al., 2015 [65] |
| Gold (Au-NPs) PA | Gold nanostructures | Silver nanowires | - Incorporation of NPs by inclusion in matrix; - Significant Ag ion release in the presence of Au; - Resin composite modified with mixture of Au-NPs and Ag-NPs have lower light transmission and have opaque appearance; - Higher microhardness | Sokolowski et al., 2014 [66] |
| Glass fibers | Glass fibers | - Antimicrobial NPs; - Nanosystem for cost dental fillings for endodontic therapy; - Glass fibers filaments covered the surface with Ag-NPs who formed film; - Potential mechanical and antibacterial properties | Neumayr-Raissen et al., 2014 [67] |
Table 6 (C): Use of nanoparticles (NPs) in dental nanomaterials for restoration treatments.

| Metal          | Type and Composition | Form                  | Aim(s) and Strategy                                                                 | Reference(s) |
|----------------|----------------------|-----------------------|-------------------------------------------------------------------------------------|---------------|
| Copper (Cu-NPs)| PA                   | Orthodontic adhesive  | - Incorporation of NPs by inclusion in matrix
- Antimicrobial NPs
- NPs did not show mechanical properties.
- At higher concentrations they produce more mechanical resistance.
- Prevent the degradation of adhesive-dentin interfaces. | [93]          |
| Zirconia (ZrO₂-NPs) | Titanium dioxide (TiO₂-NPs) | Adhesive resin-composite | - 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 vitro. | [94]          |
| Sepiolite (Mg₃Si₄O₁₀(OH)₂-NPs) | | Medacrylate dentin bonding | - Mg₃Si₄O₁₀(OH)₂-NPs can be considered as novel fillers to improve the mechanical properties of dentin bonding agents.
- Incorporation of the Mg₃Si₄O₁₀(OH)₂-NPs improved the bond strength to dentin with the highest values obtained at 1 νL. | [95]          |
| Zinc oxide (ZnO-NPs) | PA                   | Adhesive resin-composite | - 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. | [96]          |
| Silver (Ag-NPs) | Calcium phosphate (Ca₃(PO₄)₂-NPs) | Adhesive resin-composite | - Antimicrobial NPs
- Quaternary ammonium hydroxides (QAH). Ag-NPs antibacterial effect.
- Ca₃(PO₄)₂-NPs released calcium phosphate ions and remineralized tooth lesions and neutralized acids.
- Combining Ag-NPs Ca₃(PO₄)₂-NPs QAH, a new class of composites and adhesives with antibacterial and remineralization double benefits. | [97]          |

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

| Metal          | Type and Composition | Form                  | Aim(s) and Strategy                                                                 | Reference(s) |
|----------------|----------------------|-----------------------|-------------------------------------------------------------------------------------|---------------|
| Zinc oxide (ZrO-NPs) | PA                   | Glass monomer cements (GMCs) | - Incorporation of NPs by inclusion in matrix
- Antimicrobial NPs
- Inhibition of ZrO-NPs at concentration 1% and 2% did not promote their antimicrobial activity against S. mutans.
- Most important advantages of the GMCs are associated with their ability to release long-term antimicrobial agents. | [98]          |
| Hydroxyapatite (Ca₃(PO₄)₂(OH)₂-NPs) | Fluorapatite (Ca₃(PO₄)₂(F-NPs) | Glass monomer cements (GMCs) | - Incorporation of NPs by inclusion in matrix
- Bioactive HA-NPs and F-NPs improved mechanical properties of GMCs. | [99]          |
| Ferritite (Mg₂SiO₄-NPs) | | Glass monomer cements (GMCs) | - Highest compressive strength, flexural strength, and diametral tensile strength.
- Addition of 1 νL Mg₂SiO₄-NPs to the ceramic component of GMC is desired for dental restorations applications. | [100]         |
| Hydroxyapatite (Ca₃(PO₄)₂(OH)₂-NPs) | Calcite (CaCO₃-NPs) | Tricalcium Dicalcium Silicate Cement (TDS) | - The analyze of hydration reactions and bioceramic properties
- Hydrochemical properties were improved.
- Good properties, including sealing ability, biocompatibility, and the capacity to induce tissue regeneration. | [101]         |
| Titanium dioxide (TiO₂-NPs) | Hydroxyapatite (Ca₃(PO₄)₂(OH)₂-NPs) | Tricalcium Dicalcium Silicate cement (TDS) | - Incorporation of TiO₂-NPs with weight ratio of 1% increased the setting time, compressive strength and pull out bond strength of modified cement. | [102]         |
| Bioactive glass (BG-NPs) | | Glass monomer cements (GMCs) | - BG-NPs incorporated GMC enhanced mechanical properties and biomineralization properties without cytotoxicity. | [103]         |

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

| Type and Composition | Form | Aim(s) and Strategy | Reference(s) |
|----------------------|------|---------------------|--------------|
| Tensile ... (TiO₂-NPs) | Acrylic resin denture (PMMA) | - Antimicrobial NPs | Ton et al., 2017 |
| ... (TiO₂-NPs) | Acrylic resin denture (PMMA) | - Incorporation of TiO₂-NPs in PMMA polymer matrix was proved to have antibacterial effects while modified viscosity characteristics and expected lower mechanical parameters | [60] |
| ... (TiO₂-NPs) | Acrylic resin denture (PMMA) | - Success of non-leachable PMMA composite was successfully used with stereolithographic technique for complete denture manufacturing | Rashid et al., 2017 |
| Inorganic nanoparticles | Calcium phosphate (CaP-NP): MA | Acrylic resin denture (PMMA) | - Increase the fracture toughness, the elastic modulus and the Glass Transition Temperature of PMMA resins used in fixed provisional restorations | Toupour et al., 2018 |
| Neem (ZnO-NPs) | Poly (methyl methacrylate) resin | Acrylic resin denture (PMMA) | - Inhibition of colonies of main microorganisms associated with dental prostheses | De Carne et al., 2016 |
| Silver (Ag-NPs): PA | | | - No change of the mechanical properties | [59] |

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

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

| Type and Composition | Form | Aim(s) and Strategy | Reference(s) |
|----------------------|------|---------------------|--------------|
| Copper (Cu-NP): PA | Collodial solution | - Antimicrobial NPs | Shihong et al., 2017 |
| Zinc (Zn-NP): PA | | - Antimicrobial effect | [57] |
| Silver (Ag-NPs): PA | Resin-composite | - Antimicrobial NPs | Yamada et al., 2017 |
| Silver (Ag-NPs): PA | Orthodontic resins | - Antimicrobial NPs | Lee et al., 2017 |
| Silver (Ag-NPs): PA | Collodial solution | - Antimicrobial NPs | Kamischo et al., 2015 |
| Silver (Ag-NPs): PA | Epoxy resin | - Antimicrobial NPs | Argüeta-Torregrosa et al., 2014 |
| Zinc oxide (ZnO-NPs): PA | flowable resin composite | - Antimicrobial NPs | Hagen et al., 2013 |

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

| Type and Composition | Metal | Polymer | Mineral | Free | Form Incorporated | Aim(s) and Strategy | Reference(s) |
|----------------------|-------|---------|---------|------|-------------------|---------------------|--------------|
| Organic nanoparticles | Quaternary PolyEthylenglycol (QPEG) NPs, PA-NPs | Resin composite | - Incorporation of NPs by inclusion in matrix<br> - Antimicrobial NPs<br> - Antibacterial effect by direct contact<br> - Preventing bacterial recontamination during restoring teeth | [92] |
| Hybrid nanoparticles | Polysaccharide-acrylic (PSA), Zinc oxide (ZnO), Silica (SiO2), Dimethylglycine (DMH), Hypochlorite for sodium (NaClO); (PSA-ZnO-SiO2-DMH-Cl-NPs): PA | Titanium implants | - Antimicrobial NPs<br> - PSA-ZnO-SiO2-DMH Cl-NPs were immobilized on the surface of titanium plates<br> - Modified surface exhibited excellent antibacterial activity<br> - No obvious cytotoxicity<br> - Novel surface system provides a promising self antibacterial biofilm for metallic implants without using antibiotics | [94] |
| Zinc oxide (ZnO-NPs): PA, Chitosan (C-NPs): BA | Orthodontic resin composite | - Incorporation of NPs by inclusion in matrix<br> - Antimicrobial NPs<br> - Biodegradation effect<br> - 10% of NPs mixture (ZnO NPs and C NPs) has induced an antibacterial activity in resin composite | [92] |

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

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**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.

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