

Metallic Nanoparticles in Dental Biomaterials: A Review

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Abstract

Nanodentistry is relatively a new concept in dentistry therapy but rapidly developing technique, driving the dental materials industry to substantial growth. Metallic nanoparticles such as iron oxide, gold and silver nanoparticles have been used and modified for dentistry applications due to their intrinsic characteristics as diagnostic and/or therapeutic property for diseases. More recently, there are a number of outstanding applications of the metallic nanoparticles in the fields of dentistry, from periodontics, endodontics, and implantology, to oral cancer therapy. This review highlights the use of metallic nanoparticles in dentistry fields and displays an updated summary of recent advances in the field of nanodentistry.

Keywords: Metallic nanoparticles, nanodentistry, iron, gold, silver, titanium, zinc nanoparticle.

1. Introduction

Nanotechnology was first introduced by Japanese scientist Norio Taniguchi in 1974, is a broad concept that deals with particles at the nanoscale size, normally 1 up to 100 nanometres (more often reaching hundreds nanometres). Many references and research have pointed out that the prefix “Nano” is derived from the Greek word Nanos which is mean dwarf. Nanomaterials (NMs) have been shown to have different properties from those of the same material at a macro scale [1-5].

NMs applications in medical fields have received considerable attention over the latest decade (Figure 1). The reason for that is based on their unique characteristics (Table 1), such as their surface charge, shape and hydrophobicity [6-8]. Medical applications of nanomaterials, specifically dental applications, are a fast-growing field stimulated by advances in modern experiments. NMs have attracted a special attention and have been widely used for dentistry applications such as light polymerization composite resins and bonding systems, bioceramics, endodontic sealers, coating materials for dental implants and mouthwashes [9].

Metallic nanoparticles such as iron oxide, gold and silver nanoparticles have been used and modified for dentistry applications due to their intrinsic characteristics as diagnostic and/or therapeutic agents for diseases. The following outline is provided as an overview of some metallic nanoparticles with some examples of applications.

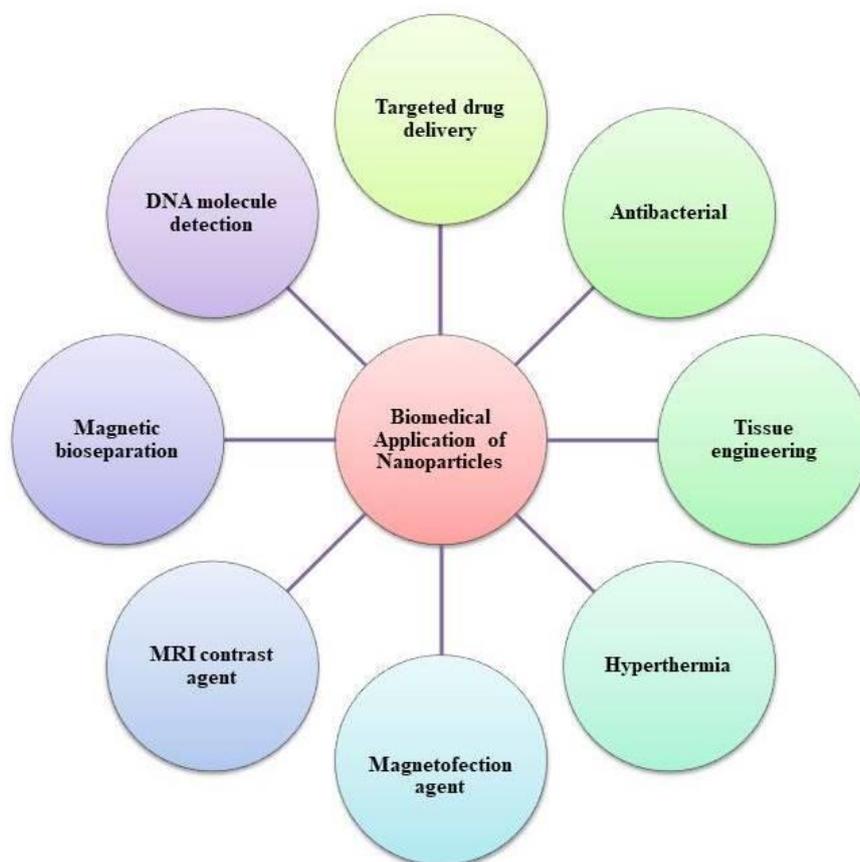


Figure 1. Biomedical applications of nanoparticles

1.1. Iron oxide nanoparticles

Recently, iron oxide nanoparticles (IONPs) have attracted much investigation due to their unique properties such as ultrafine size, magnetic properties, and biocompatibility which are desirable for a wide range of biomedical applications including tissue engineering, targeted drug delivery, gene therapy, stem cell tracking and as magnetic resonance imaging (MRI) contrast agents [10,11]. Ultrafine IONPs are used commercially as T_2 contrast agent for MRI [12].

1.2. Gold nanoparticles

Gold nanoparticles (AuNPs) have been investigated and shown to possess intrinsic biocompatibility, low cytotoxicity, and strong oxidation resistance [13]. Due to their surface plasmon resonance, fluorescence, and easy-surface functionalization, AuNPs have been extensively used in diagnostics, photothermal therapy, biomedical imaging, and drug delivery [14].

1.3. Silver nanoparticles

Many of the products used in our daily life contain silver nanoparticles (AgNPs). Health care products, cosmetic, pharmaceutical products, household, antibacterial agents are just an examples of commercial products containing silver nanoparticles. AgNPs are playing an increasingly important role in the field of nanoscience and nanotechnology, especially in nanomedicine. AgNPs possess exceptional physical and chemical properties including optical, electrical, thermal,

and biological properties[15,16].AgNPs have been used in several potential areas of dentistry, such as endodontics, dental prostheses, implantology and restorative dentistry [17].

1.4. Titanium Dioxide nanoparticles

Titanium dioxide (TiO₂) nanoparticles have been explored in recent years as an antimicrobial agent against *Lactobacillus acidophilus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Candida albicans*, etc. They possess high stability, low toxicity and white colour, as well as they offer fordable price. All these features make TiO₂ nanoparticles suitable for use in dental materials [18].

1.5. Zinc oxide nanoparticles

Zinc oxide (ZnO) has been reported to be one of the essential trace elements for the human system. It has been well acknowledged that the biological functions can be affected by the morphology, exposure time, particle size, concentration, and biocompatibility of the ZnO particles [19]. ZnO nanoparticles are widely used in many oral hygiene products including toothpaste and mouth rinses due to its action against pathogenic microorganisms in addition to low production costs and non-toxic properties to human in low concentrations [20].

Table 1.Physical properties of some nanoparticles [8].

Properties	Nanoparticles					
	TiO ₂	TiO ₂	MnO ₂	Au	Au	CdTe (CdSe) core (shell) type II QDs
Size/nm	10, 25 and 60	80, 155	30	2, 40	10–250	10 (naked); 18.8 (coated)
Surface chemistry	Hydrophobic or hydrophilic surface	N/A	N/A	N/A	N/A	Oligomeric phosphine
Administration route and exposure time	Dorsal skin exposure, 60 days	Intranasal instillation, 2, 10, 20 and 30 days	Whole body inhalation, 12 days	i.p. and i.v. injection, 1, 4 and 24 hours	i.v. injection, 24 hours	Intradermal injection, 05 min
Animal Model	Hairless mouse	Mouse	Rat	Mouse	Rat	Mouse and pig
Detection method	TEM and atomic absorption spectrometry	Inductively coupled plasma mass spectrometry (ICP-MS)	Graphite furnace atomic absorption spectroscopy	Autometallo-graphy	ICP-MS	Near-infrared (NIR) excitation
Main observations	Accumulation in spleen, lung, kidney and brain	Accumulation in brain through olfactory bulb	Accumulation in CNS via olfactory bulb	Macrophage uptake in liver, less in spleen, small intestine, lymph nodes	NPs of 10 nm entered testis and brain	Accumulation in sentinel lymph node

1.6. Hybrid nanoparticles

Hybrid nanoparticles (HNPs) made of two or more types of material. The hybridization of noble metals (Gold, Silver or Platinum) with metal-oxide nanoparticles, such as iron oxide nanoparticles, displays the superior features, as compared to the single individual nanoparticles [21,22]. Hoskins and here group have published many of the articles using gold hybrid nanoparticles applied for pancreatic cancer fighting [23-27].

2. Nanotechnology in dentistry

Dental nanomaterials are specially fabricated materials, designed for use in diagnosing treating and preventing dental and oral diseases, in addition to preserving and improving oral and dental hygiene (Figure 2)[28,29].NMs further used for prostheses and for teeth implantation, oral drugs delivery and curing some oral cancer(Table 2)[30]. The present paper attempts to shed some light on the applications and uses of metallic nanomaterials in various dental fields including periodontist, prosthodontics and oral surgery etc.

2.1.Applications of nanomaterials in periodontists

Periodontal or gum disease is perhaps the most common disease of mankind [31].It is a serious gum infection that damages the soft tissue that affecting mostly adults [32]. It is commonly a progressively destructive change leading to formation of periodontal pockets or spaces between the tooth and gums, which provides an ideal environment for microbial growth and proliferation [33]. Traditional treatment program involves mechanical displacement of dental plaque via scaling and root planning (SRP) accompanied by systemic use of antibiotics via oral administration.

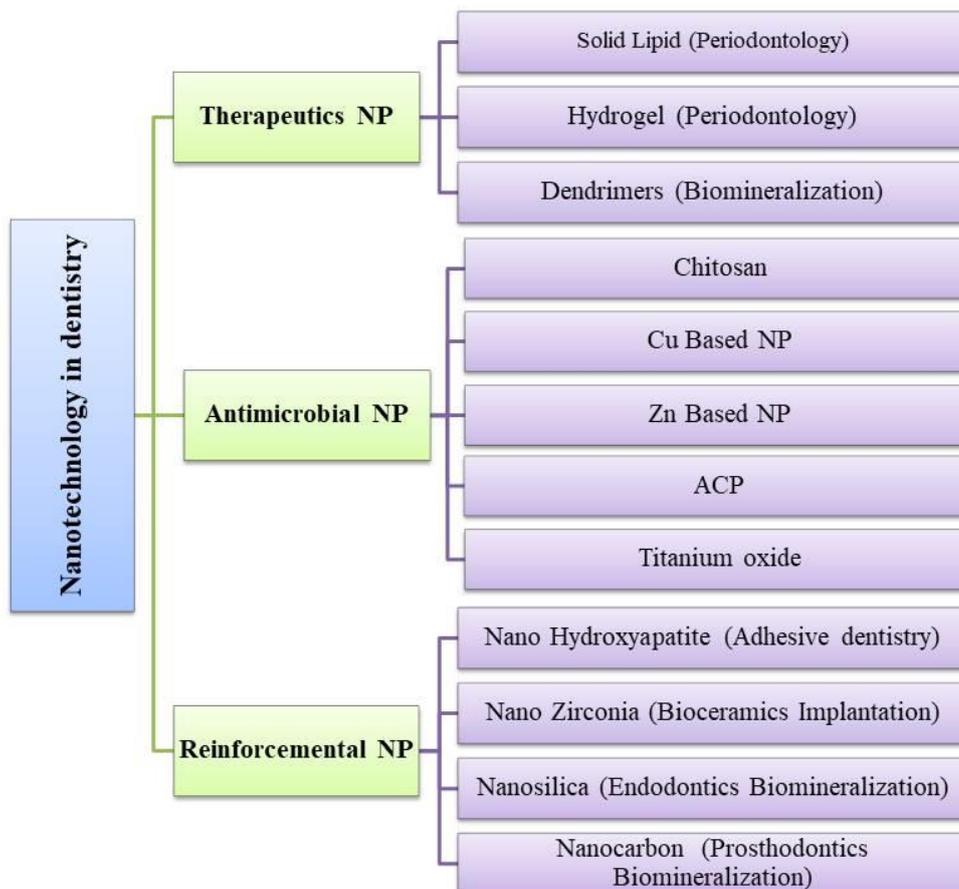


Figure 2 – Nanotechnology applications in dentistry.

However, the disadvantages of using systemic antibiotic therapy include the insufficient concentration of systemic drugs that reach the intended site of action, increased multidrug-resistant microorganisms, and unsure patient compliance [34]. One of the most effective methods to reducing bacterial adhesion and preventing biofilm formation in dentistry is by deliver AgNPs due to their antibacterial properties [35]. Liao and colleagues have previously reported that titanium plates deposited by Nanosilver nanoparticles surface Ti-AgNP had demonstrated a significant antibacterial and antiadhesive activities in vitro related to *Porphyromonasgingivalis* and *Actinobacillusactinomycetemcomitan*, which are proved to be periodontal and peri-implantitis pathogens [36]. In another research, a biosynthesized AgNPs have been used to evaluate the antibacterial activity against *Porphyromonasgingivalis*, *Bacillus pumilus*, and *Enterococcus faecalis*. The study showed that AgNPs have effective antibacterial activity against *P. gingivalis*, *B. pumilus*, and *E. faecalis*. Hence, show an insight for the use of these nanoparticle AgNPs in the treatment of endodontic, periodontal, and combined lesions [37]. Pradhan and colleagues have reported the ability of nano colloidal of silver and gold that present in between the bristles of the toothbrush to reduce gingival inflammation [38].

Table 2- Current applications of nanotechnology in dentistry with available products in markets [30].

Field	Available Materials	Company	Country
Restorative Dentistry	Ketac™ 3M ESPE	3M ESPE	USA
	Ceram X™	DENTSPLY	USA
	Fuji IX GP	GC	Belgium
	Nano-primer, Premise™	Kerr/Sybron	USA
Regenerative Dentistry and Tissue Engineering	Ostim®	Osartis GmbH	Germany
	VITOSSO™	Orthovita-Inc	USA
	Nano-Bone®	ARTOSS	Germany
Periodontics	Arestin®	Valeant	USA
	Nanogen®	Orthogen	USA
Preventive Dentistry	NanoCare® Gold	Nano-Care	Germany
Orthodontics	Ketac™ N100 Light Curing Nano-Ionomers	3M ESPE	USA
	Filtek Supreme Plus Universal	3M ESPE	USA
Prosthodontics	Nanotech elite H-D plus	Zhermack	Italy
	GC OPTIGLAZE color®	GC	Belgium
Oral Implantology	Nanotite™ Nano-coated implant	BIOMET 3i	USA

2.2.Applications of nanomaterials in orthodontic

One of the most commonly problem in dentistry is formation of white spot lesion during orthodontic treatment. This case gets worse with poor dental care patients. An increased growth of bacteria in the adhesion area, bond between an orthodontic brackets and tooth enamel, has been discussed by a great number of authors in literature [39-42]. The use of nanomaterials in orthodontics offers promising scope in dentistry to boost the influences of fixed orthodontic appliances and enhance the control of therapy.

Ahnand colleagues reported that a composite adhesive containing AgNPs had found to be significantly lower cariogenic streptococci adhesion to experimental composite adhesives (ECAs) than conventional orthodontic composite. They applied AgNPs in various concentrations 0 ppm, 250 ppm, and 500 ppm. They concluded that AgNPs can be used in lower concentrations without affecting the material's mechanical properties [43]. In another study, TiO₂ nanoparticles were mixed with light cure orthodontic composite paste (Transbond XT) in three different ratios 1, 5, and 10%. The researcher found that the TiO₂ NPs at all applied concentrations had a significant effect on creation and extension of inhibition zone [44]. Furthermore, silver nanoparticles have been used in orthodontics to reduce the orthodontic composite clinical failure by increasing the bond strength. For this purpose, silver and hydroxyapatite HA nanoparticles were prepared and added to the primer of Transbond XT at 1%, 5% and 10% silver concentrations. The effect of the addition of silver/HA nanofiller to the orthodontic adhesives was observed. Tests indicate that the incorporation of 5% and 1% of silver nanoparticles have maintains and increases the shear bond strength of the products. However with further increase of the silver ratio up to 10 % the efficiency of the system goes down [45].

Friction is one of the major issues influencing the alignment or retraction of teeth throughout orthodontic treatment. To overcome this issue, many methods have been proposed including Nano-coated arch wires and brackets [46]. Behroozian and colleagues reported that coating of porcelain brackets with ZnO nanoparticles enhances the friction resistance in the sliding technique [47]. In a study by Li and colleagues, a layer of TiO₂-xNy film was formed onto the MBT bracket (0.022") using radiofrequency magnetron sputtering. The results indicated that Nano-TiO₂-xNy film can reduce the friction between archwire and bracket [48].

2.3. Applications of nanomaterials in prosthodontics

In recent years, many of researches have been achieved in the field of nanomaterials in dentistry applications. Many of these researches have been conducted into the incorporation of nanometals into biomaterials used in Prosthodontics. Incorporation of on iron oxide nanoparticles / calcium phosphate cement scaffolds (IONP-CPC) have been used to investigated human dental pulp stem cells (hDPSCs) seeding on IONP-CPC for bone tissue engineering. The result showed that the osteogenic differentiation of hDPSCs was considerably improved via IONP incorporation into CPC [49].

Poly(methyl methacrylate (PMMA), also known as acrylic, is widely used for dentures and temporary crowns. Different nanoparticles have been incorporated into the polymer matrix to improve the performance of PMMA. In this respect, TiO₂ and Fe₂O₃ nanoparticles been incorporated into PMMA as pigments to match the gingiva colour. Moreover, these materials exhibited low porosity, high molecular weight and reduce *Candida albicans* ability to adhere to acrylic resin materials [50].

Totu and colleagues have incorporated 0.4% TiO₂ nanoparticles into a 3D printed PMMA denture base to improve its mechanical antibacterial properties. The study showed that PMMA supplemented with TiO₂ NPs illustrate significant improvements in polymer characteristics, in addition, to prove to have antibacterial effects, specifically on *Candida* species [51].

2.4. Applications of nanomaterials in oral cancers

Cancer is commonly treated by surgery, chemotherapy and radiotherapy, based on cancer's stage, location and type. However, none of the previous therapies, either alone or in combination are effective in preventing this disease [52]. Nanotherapy has been broadly directed towards cancer therapy. Cancer nanotherapeutics is rapidly progressing field and is being implemented to overcome problems in conventional therapeutic such as low dissolution rate of chemotherapy, poor bioavailability, and low therapeutic indices [53].

Recently, Satapathy and colleagues investigated the anti-angiogenic and anti-metastatic effect of hybrid-nanoparticle (QAuNP) using quinacrine and gold on oral squamous cell carcinoma (OSCC) - cancer stem cells (CSCs). The xenograft experiment showed that proliferation of OSCC-CSCs is strongly inhibited by QAuNP, led to apoptosis *in vitro* and disrupted angiogenesis *in vivo* in addition to tumour regression [54]. In another study by Wang and colleagues investigated the effect of ZnO NPs on CAL 27 human tongue cancer cells *in vitro*. The cytotoxicity results of the ZnO NPs formulation on CAL 27 cell line revealed significant reduction of cell viability after 24 h. The IC₅₀ value of ZnO NPs on CAL 27 was 25 µg/ml [55].

2.5. Applications of nanomaterials in endodontics

Numerous researches have exhibited that pulpal infection and periradicular lesion resulting from polymicrobial infection, with predominantly gram-negative anaerobes. Endodontic treatment failure is usually connected with the presence of residual bacteria in the root canal [17]. Therefore, a combination of mechanical instrumentation and antibacterial irrigation is so important for successful treatment. Application of nanoparticles as antimicrobial agents have been widely investigated in recent times [17,56-59].

Wu and colleagues assessed the effect of silver nanoparticles as an irrigant or medicament against *Enterococcus faecalis* biofilms formed on root dentin. Biofilms were treated with AgNP solution (0.1%) in first stage and gel (0.02% and 0.01%) in second stage. The result indicated that AgNPs in solution form did not cause any significant change to the biofilm structure. However, the gel form containing 0.02 % was much higher resulting in disrupts the structural integrity of the *E. faecalis* biofilm [59]. In this context, Afkhami and colleagues performed a study to estimate the ability of Ca(OH)₂ with or without a silver nanoparticle to remove *Enterococcus faecalis* from root canals. A total of 54 single-rooted extracted human teeth contaminated with *E. faecalis* were used for this study. The samples were treated with Ca(OH)₂, Ca(OH)₂ with chlorhexidine, or Ca(OH)₂ with silver nanoparticles. Authors have observed that the mixture of Ca(OH)₂ and AgNPs was the most effective medicament against *E. faecalis* bacteria after one week [60].

3. Conclusions

Under the limitations of this study, it was concluded that:

- The application of nanotechnology in dentistry offers some exciting opportunities. Some of these applications have already been converted into commercial products.

- Incorporation of metallic nanoparticles in dentistry was proved to be exciting tools in the treatment of oral cancers.
- Utilization of metallic nanoparticles significantly reduced microbial colonization over dental.
- Evidence reveals that the addition of metallic nanoparticles to composite resin improves the mechanical properties.

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