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"Nano Revolution In Dentistry: Small Particles, Big Impact In Conservative Care And Endodontics"

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Abstract

This review explores the transformative role of nanoparticles in modern dentistry, specifically within conservative dental procedures and endodontics. It delves into the diverse applications of nanomaterials, highlighting their enhanced properties in diagnostics, therapeutic agents, and restorative materials. The article discusses recent advancements in nanoparticle-based techniques, emphasizing their potential for improving treatment outcomes, minimizing invasive procedures, and addressing challenges in dental care. By presenting a comprehensive overview of nano-enabled innovations, this review aims to underscore the significance of these tiny yet powerful elements in reshaping the landscape of conservative dentistry and endodontics.

Introduction

Nanoparticle technology is rapidly advancing within the realm of science and technology. Nanostructured biomaterials play a pivotal role in disease diagnosis, treatment, and prevention, contributing significantly to human health preservation and enhancement. This innovative technology is now emerging as a promising alternative, potentially superior in identifying oral health issues and in the creation of dental materials that are more biocompatible, possess enhanced properties, and exhibit potential in preventing tooth decay.[17,8]
The word “nano,” which is derived from the Greek word (nannos) meaning “dwarf,” is a prefix that literally refers to 1 billionth of a physical size. According to the definition of the National Nanotechnology Initiative, nanotechnology is the direct manipulation of materials at the nanoscale.[17]
The concept of nanotechnology was introduced in 1959 by late Noble Physicist Richard P Faynman. The term “Nanodentistry” was first introduced in 2000 by research scientist Robert Freitas.[8]
The International Organization for Standardization (ISO) has described Nanomaterials(NMs) as a “material with any external nanoscale dimension or having internal nanoscale surface structure”[15]
As per the European Commission’s Recommendation “nanomaterial” is defined as a natural, incidental, or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the range 1–100 nm.[6]

Classification of Nanoparticle:
According to Seigel nanomaterials are categorized as:
- zero-dimensional (nanoclusters and nanoparticles)
- one-dimensional (nanotubes and nanowires)
- two-dimensional (nanoplates and nanolayers)
- three-dimensional (nanospheres and nanorods)

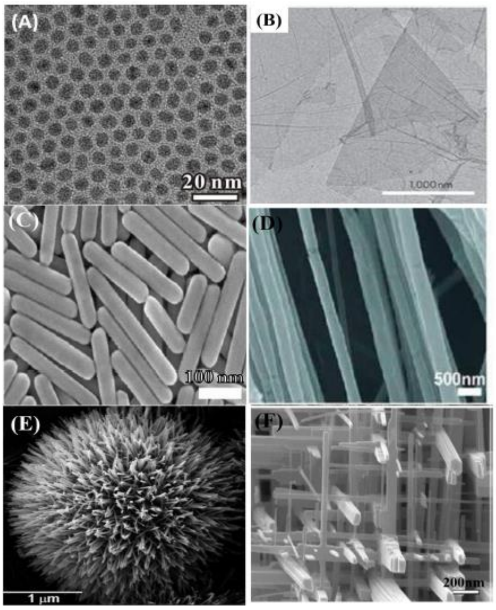


Figure 1: Different Morphologies Of Nanoparticle

Approaches in Nanotechnology:-

- **Bottom-up approach:** Seeks to arrange smaller components into more complex assemblies, the covalent bonds of which are extremely strong.
- **Top- Down approach:** Seeks to produce smaller devices by using larger ones in achieving precision in structure and assembly.
- **Functional approach:** Seeks to develop components of a desired functionality without regard to how they might be assembled.
- **Biomimetic Approach:** Seeks to apply biomolecules for applications in nanotechnology.[9]

HISTORY

- In 1867, James Clerk Maxwell introduced a groundbreaking idea in nanotechnology, envisioning submicroscopic machinery capable capable of manipulating individual atoms and molecules, which he termed Maxwell's demons, now known as 'Nanorobots'[25]
- The term "nanotechnology" was coined by Prof. Kevie E. Drexler in his 1986 book titled Engines of Creation: The Emergence of Nanotechnology.[28]
- Richard P. Feynman, a Nobel Prize laureate, initially presented the concept of nanotechnology in 1959 during his lecture titled "There's Abundant Space at the Bottom," outlining the philosophical underpinnings of this field.[1]
- Norio Taniguchi in 1974 elucidated, "Nanotechnology mainly consists of the processing of separation, consolidation, and deformation of material by one atom or one molecule.[28]
- R.A. Freitas Jr. coined the term ''nanodentistry'' in the year 2000. He developed visions using nanorobots for orthodontics, dentition regeneration, nanomaterials, and robots in dentifrices–dentifrobots.[34]
- Richard Zsigmondy In the early 20th century brought about the concept of nanomaterials. The first observations and size measurements of nano-particles was made during the first decade of the 20th century. They are mostly associated with Richard Adolf Zsigmondy who made a detailed study of gold sols and other nanomaterials with sizes down to 10 nm and less.[33]

NANOPARTICLE TECHNOLOGY IN CONSERVATIVE DENTISTRY

The advent of nanoparticle in dentistry has paved way for its use as powerful tool in treating microcavities, hypersentivity, as restorative material and much more.

Nanoparticle Based Detection Of Microcavities And Treatment

Smaller initial stages of decay known as "microcavities," incipient carious lesions, or white spot lesions can potentially be reversed through remineralization. This process utilizes calcium and phosphorus present in saliva, often aided by fluoride found in drinking water or toothpaste

A specialized nanoparticle technology has been developed to specifically target active carious lesions. These nanoparticles are crafted from food-grade corn starch and are tagged with a harmless fluorescent dye. This tagging enables the illumination of caries,

making them easily visible under a standard dental curing lamp. This innovation allows dentists to distinguish between active and inactive carious lesions. Envisaged as a mouth rinse or for localized application, the product contains nanoparticles in water at a low concentration

The biodegradable nanoparticles derived from food-grade starch are both biocompatible and enzymatically broken down in saliva after use, ensuring their safety and compatibility with the human body.

Zhang et al. (2021) stated the preparation of a stable phosphorylated chitosan-ACP nanocomplexes with the ability to remineralize the enamel sub-surface lesion via mimicking the biomineralization procedure by phosphorylated chitosan and amorphous calcium phosphate (Pchi–ACP). Remineralizing effect of chi–ACP on enamel lesions was similar to that of fluoride.[37]

Dentin Hypersenstivity

Tian and his co-authors (2014) speculated that due to the superior dispersion of nanomaterials, it can easily enter dentinal tubules of 2–3 µm. [36]

Biogenic carbonate hydroxyapatite (CHA) nanocrystals produce re-mineralization of the altered enamel surfaces and closure of dentinal tubules, thus providing a prospective use in desensitizing dentifrices.[3]

Chiang and his co-authors (2014) concluded that calcium carbonates ($CaCO_3$) containing MSN mixed with 30% calcium triphosphate (H_3PO_4) effectively occluded dentin tubules.[37]

Nanocomposites

Addition of nanobioglass has shown to facilitate fluoride release from dental composite. For the anti cariogenic property various nano particles such as chlorhexidine and quarternary ammonium compounds have shown to be effective.[39]

Silsesquioxane-Based Composites - Studies have been reported by Soh et al (2007) that incorporation of silsesquioxane have decreased the shrinkage.[38]

Nanotechnology In Dental Adhesives

Incorporating nanoparticles into dentin bonding agents has demonstrated an enhancement in tubular penetration, consequently elevating the mechanical properties of the dental restoration. Nano silver particles, Nano amorphous calcium phosphate, and Nano quaternary ammonium dimethacrylate (nQADM) are among the extensively researched materials in this domain. Recently, colloidal platinum nanoparticles have exhibited the ability to improve resin bond strength. Additionally, spherical zirconia nanoparticles are utilized in bonding systems to stabilize the hybrid layer.

A novel concept introduced recently involves nanogels—particles ranging from 10 to 100 nanometers—that swell upon interaction with monomers. This characteristic facilitates the the deep penetration of adhesives into dentin, ultimately augmenting the bond strength.[5,12]

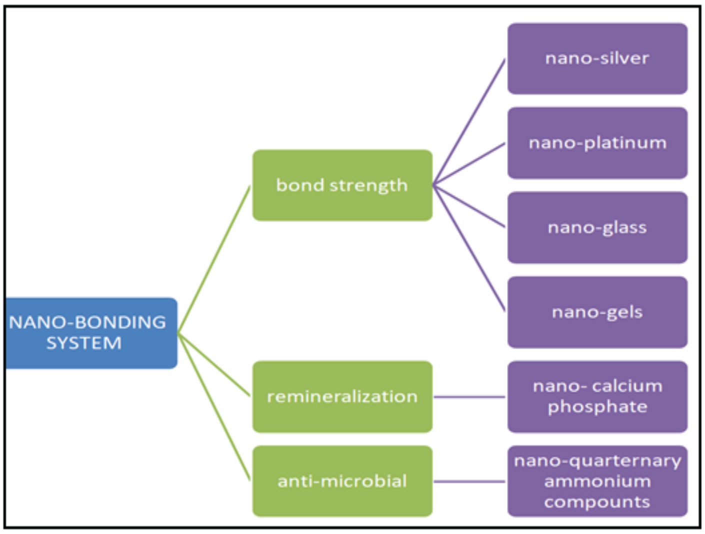


Figure 2. Nanobonding System

Nano-Varnish And Sealants
Bioceramic nanofibers made of hydroxyapatite and fluorapatite possess a nanostructure that enhances solubility, facilitating the effective release of fluoride ions. When integrated into sealant systems, these fibers contribute to preventing caries. Additionally, they offer increased wear resistance and decreased shrinkage.
A nano-filled light-curing varnish has been developed to safeguard Glass Ionomer Cement (GIC) during its initial maturation phase. This varnish prevents water absorption and dehydration of GIC, thereby enhancing its mechanical properties. For instance, EQUIA ('Easy- Quick-Unique-Intelligent-Aesthetic') is one such product utilizing this technology.

Nano Coating Of Restorations
Nano-filled, light-cured preparations are used as a protective coating for composite and acrylic indirect composites like the Optiglaze Glossy Protective Coating Agent (GC Corporation, Japan). These provide an aesthetic glossy surface and can be used in to polish difficult areas such as posterior fissures or interproximal areas of indirect composite restorations.

Nano Polishing System
Micron-sized silica particles are a typical component of conventional polishing pastes. The smaller the abrasive particle size the smoother the polished surface. Chemical-mechanical planarization process is one such approach, used in the semiconductor industry which uses various nanometersized particles to polish surfaces of semi-conductor wafers to a sub-nanometer level. This was adopted to polish dental surfaces by R.M. Gaikwad and I. Sokolov (2008), where they have used silver nano particles and demonstrated that it is easier to remove bacteria from areas polished with silica nanoparticles. And it can be used for dental polishing.[24]

Nano Ceramics
With the integration of nanotechnology and ceramics a new CAD/CAM block of monolithic esthetic material was developed as Lava Ultimate (3M ESPE). The main advantage of this is said to be the easier clinical finishing and polishing with the strength, surface gloss and finish retention similar to ceramic materials which has been the main limitation of composite blocks. A few in vitro studies showed its resistance to toothbrush abrasion and retention of the initial glossy surface finish similar to glass ceramics. However, clinical evaluation is yet to be obtained regarding its marginal integrity and survival.
A nano optimized mouldable ceramics are developed recently and marketed by the name XircOn Ultra, which is approved by FDA. It is a hybrid nano-ceramic that can be bend and flexed in the mouth. It is made by a combination of nano-ceramics and polymers. It is said to be one of the closest material to human teeth. [24]

Nano-optimised Mouldable Ceramics include:
- Nanofillers - Enhances polishing ability and reduces wear.
- Nanopigments - Adjust the shade of the restoration to the surrounding teeth (chameleon effect).
- Nanomodifiers - Increases the stability of the material and prevent sticking to instruments.[29]

Nanoencapsulation
SWRI [South West Research Institute] has developed targeted release systems that encompass nanocapsules including novel vaccines, antibiotics and drug delivery with reduced side effects. Future specialized nanoparticles could be engineered to target oral tissues, including cells derived from the periodontium.[29]

Nanoneedles
Suture needles incorporating nano-sized stainless steel crystals have been developed. Nanotweezers are also under development which will make cell-surgery possible in the near future.[29]
Trade name: Sandvik Bioline, RK 91TM needles [AB Sandvik, Sweden].

Fullerene Material As Nanomaterial
The use of fullerene materials centres around nano-biosensing, introduced to the medical field in 1962 by Clark and Lyons.
The development of the nano-toothbrush consist of nanosilver or nanogold materials placed between the bristles where bacteria can become implanted.
Nano-calcium fluoride included in specific mouthwash solutions inhibits dental carries and dentine permeability. Nanoparticles with calcium carbonate in toothpaste promote the remineralization of teeth and microhardness of the enamel layer. Nano-hydroxyapatite crystals have been used in toothpaste manufacturing to enhance dental health outcomes since they act as preventive materials against enamel wear.[7]

Nanorobots
Nanorobots, also referred to as nanites or nanomachines, are theoretical microscopic devices ranging from 1 to 100 nanometers. These devices have the potential to construct precise atomic structures, resembling crystals, following detailed blueprints. Comprised of carbon-based molecules, they function as miniature machines.[23]
The energy required to power nanorobots can be obtained through metabolizing local glucose and oxygen, along with externally supplied acoustic energy. Communication with these devices can be achieved using broadcast-type acoustic signaling. Nanorobots have the capability to induce oral analgesia, desensitize teeth, manipulate tissues for realigning and straightening irregular dental configurations, and enhance the durability of teeth. Their applications extend to preventive, restorative, and curative dental procedures.[26]

Nanorobotic Dentifrices
Nanaorobots incorporated into dentifrices and mouthwashes remove organic residues at a rate of 10 micron per second preventing accumulation of calculus.[16] They can selectively identify and destroy pathogenic species. These invisibly small robotic inexpensive mechanical devices can get deactivated if swallowed by the patient.[17]

Nanoterminators
Application of nanorobots may become uncontrollable to some extent. If these pass through the blood stream and arrive at one of the vital centers, they may confound these systems and a catastrophic happen. Nanoterminators (killers of nanorobots) and also self-destruction of self-destruction of nanorobots are new proposed mechanisms have been developed to destroy these nanorobots and overcome this problem. Nanorobots are new proposed mechanisms that have been developed to destroy these nanorobots and overcome this problem.[11]

NANOPARTICLES IN ENDODONTICS
Biofilms are highly organized, surface-adherent structures of microcolonies. The main component of biofilms is an exopolymeric matrix consisting of polysaccharides, proteins, enzymes, and bacterial metabolites.

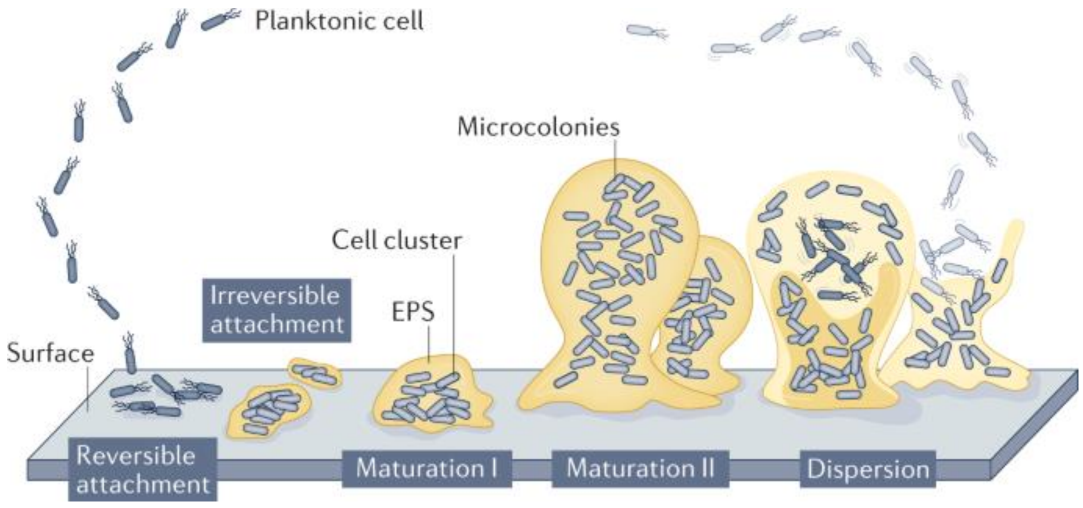


FIGURE 3. CYCLE OF BIOFILM FORMATION

Antimicrobial Nanoparticles For Root Canal Disinfection

- **Chitosan**

Chitosan (poly [1, 4–b–D-glucopyranose]) is a deacetylated derivative of chitin.

Mechanism of action

Chitosan demonstrates contact-mediated killing by leveraging the electrostatic attraction between its positively charged properties and the negatively charged membranes of bacterial cells. This interaction leads to a modification in cell wall permeability, ultimately causing cell rupture and the release of intracellular components, including proteins.

Concerning fungi, there is a hypothesis suggesting that chitosan can penetrate the cell, reaching the nucleus where it binds with DNA. This binding is believed to hinder RNA and protein synthesis, potentially contributing to the inhibition of fungal growth.

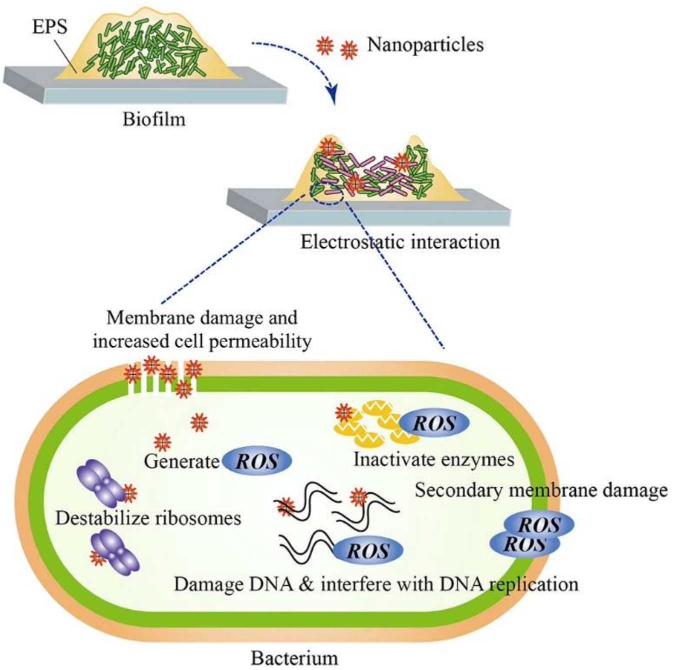


FIGURE 4. Mechanism Of Action Of Chitosan

- **Silver Nanoparticles**

Silver in metallic state appears inert. In presence of dampness it appears in ionized form. Problems with use of silver NPs are the blackening of dentin and toxic effect on mammalian cells.

Mechanism of Action

Silver exhibits antibacterial effects by targeting multiple sites within bacterial cells. Initially, the particles interact successively with the sulfhydryl groups found in proteins and DNA, leading to modifications in hydrogen bonding and unwinding of the DNA structure. Subsequently, they disrupt cell-wall synthesis. Silver nanoparticles (Ag-NPs) disrupt the structure of microbial cell membranes, enhancing their permeability, which results in the leakage of cellular contents

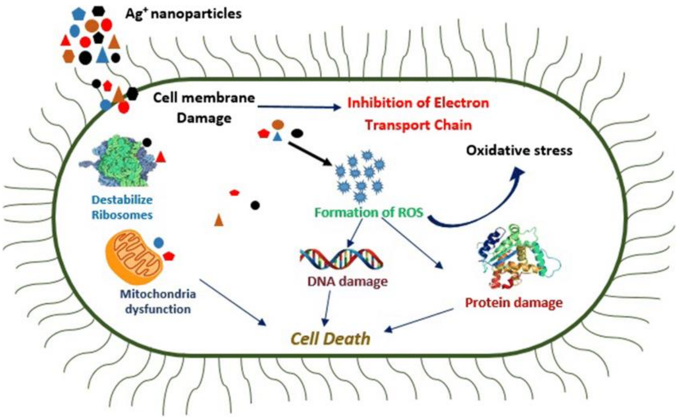


FIGURE 5. Antibacterial Mechanism Of Silver Nanoparticle

- **Bioactive glass nanoparticles**

In 1971, a novel material possessing antibacterial characteristics and the capability to adhere to bone structure was developed. This material, named Bioglass, comprised 45% SiO2, 24% Na2O, 24.5% CaO, and 6% P2O5. The antimicrobial property of bioactive glass was demonstrated by its ability to:

[i] release ions upon contact with an aqueous medium,
[ii] elevate the surrounding pH,
[iii] raise osmotic pressure around bacterial cells, leading to the inhibition of bacterial growth,
[iv] precipitate calcium and phosphate ions within the bacterial cell membrane, thereby disrupting its functions.

- **Functionalized Antimicrobial Nanoparticles**

Functionalization could alter the surface composition, charge, and structure of the material wherein the original bulk material properties are left intact. In a functionalized nanoparticle, the inorganic or polymeric materials usually form the core substrate.[40]

- **Zinc Oxide Nanoparticles**

Zinc oxide nanoparticles display potent antibacterial efficacy by creating a high pH environment that annihilates microbial cells. They enhance the permeability of the cell wall, leading to the release of cytoplasmic contents and subsequent cell destruction. Within the microbial cell, zinc oxide nanoparticles break down into zinc ions, disrupting the cell's auxiliary processes and causing additional harm. The antibacterial impact of these nanoparticles is concentration-dependent, with higher concentrations yielding the maximum antibacterial effect.

- **Magnesium-containing nanoparticles**

Nanoparticles containing magnesium can either be magnesium-oxide nanoparticles or those containing magnesium halogens like chlorine, bromine, and fluorine. These nanoparticles enter bacterial cells, disrupting the cell's membrane potential. This penetration facilitates DNA binding and lipid peroxidation by the nanoparticles, resulting in further damage to the bacterial cell. When present in an aqueous form, these nanoparticles were observed to exhibit bactericidal properties due to the formation of superoxide anions on the surface of the bacterial cell.[18]

- **Poly (Lactic-Co-Glycolic) Acid**

Synergism effect of light and methylene blue-loaded NP in the reduction of bacterial counts in both planktonic phase and root canal has been found. It has been concluded that the use of poly (lactic-co-glycolic) acid NPs encapsulated with photoactive drugs might be a promising adjunct in antimicrobial endodontic treatment.[2]

- **Endodontic instruments**

Nickel–titanium (NiTi, Nitinol) is a family of nearly equiatomic nickel–titanium, shape memory (SMA) and superelastic alloys. The potential application of NiTi for endodontic files was first introduced by Harmeet Walia in 1987.[10]

Adi Ram Adini et al. (2011) examined the effects of cobalt coatings with impregnated WS2 nanoparticles on file fatigue and failure and found significant improvement in fatigue resistance and time of breakage of the coated files possibly because of reduction of friction between files and surrounding tissues.[35]

Nanoparticle co-coated endodontic files experience less friction, phase transformation and mechanical deterioration as compared to their uncoated counterparts. This suggests that the coated EFs might be less susceptible to breakage under work related strain, as occurs during treatment.[30]

Nanoparticle Technology In Intracanal Medicaments

- **Calcium Hydroxide Nanoparticles**

Nano-calcium hydroxide resulted in less reduction of dentine microhardness compared to conventional calcium hydroxide dressing. Conventional calcium hydroxide resulted in a greater decrease in fracture resistance compared to the application of their nanosized counterparts. Cytotoxicity was found to be greater for nano-calcium hydroxide compared to conventional calcium hydroxide, but this finding was not statistically significant.

- **Combination of Antimicrobial Nanoparticles and Calcium Hydroxide**

When AgNPs were added to calcium hydroxide, the antimicrobial activity of this combination was more effective than calcium hydroxide, with or without chlorhexidine, and AgNPs alone. It has also been reported that the combination of calcium hydroxide and ZnONPs exhibited higher antimicrobial efficacy compared to ZnONPs alone. Another study found that the antimicrobial properties of this pairing was further enhanced by the addition of chlorhexidine.

- **Porous Calcium Silicate and Bioactive Glass Nanoparticles**

Porous calcium silicate nanospheres were able to infiltrate dentinal tubules and enhance mineralization, setting up a promising foundation for the development of novel intracanal dressings. With the addition of AgNPs, mesoporous calcium silicate nanoparticles showed sustained release of Ag ions and inhibited *E. faecalis* colonization. Combination of AgNPs and nano-zinc with mesoporous calcium silicate nanoparticles exhibited good antibiofilm efficacy, minimal cytotoxicity, sustained ion release, dentinal tubule infiltration and negligible changes to the mechanical properties of dentine.

Root Canal Sealers And Obturating Materials

- **Quaternary Ammonium Compounds**

QPEI nanoparticles exhibit broad antimicrobial effects and stimulate programmed cell death. Their integration into sealers like AH PlusTM and Pulp Canal SealerTM influences bone cell growth via signaling pathways, varying with concentration, cell type, and sealer type. Yet, concerns about polymerization, solvent absorption, mechanical changes, and cytotoxicity warrant consideration.

- **Chitosan Nanoparticles**

A combination of chitosan nanoparticles and ZnONPs improved the antibiofilm efficacy of a calcium hydroxide-based sealer, Apexit PlusTM, however only the sealer modified with ZnONPs was effective against the endodontic isolate strain of *E. faecalis.*

- **Nanoparticle Incorporated Obturating Material**

Dong Keun et al (2015) came up with a newly developed a nanodiamond-gutta percha composite (NDGP) embedded with nanodiamond - amoxicillin (ND-AMC) conjugates.

Studies have shown nanodiamonds to be biocompatible agent for drug delivery, imaging with effective antimicrobial activity.[21]

Embedding amoxicillin-linked NDs into GP may facilitate the eradication of residual bacteria within the root canal system after completion of obturation.[21]

Dianat and Ataie (2011) have also introduced nanosilver guttapercha, the standard gutta-percha that is coated with nanosilver particles. The nanosilver gutta-percha demonstrated antibacterial effect against *Enterococcus (E.) faecalis, Staphylococcus (S.) aurous, Candida (C.) albicans* and *Escherichia (E.) coli.* [31]

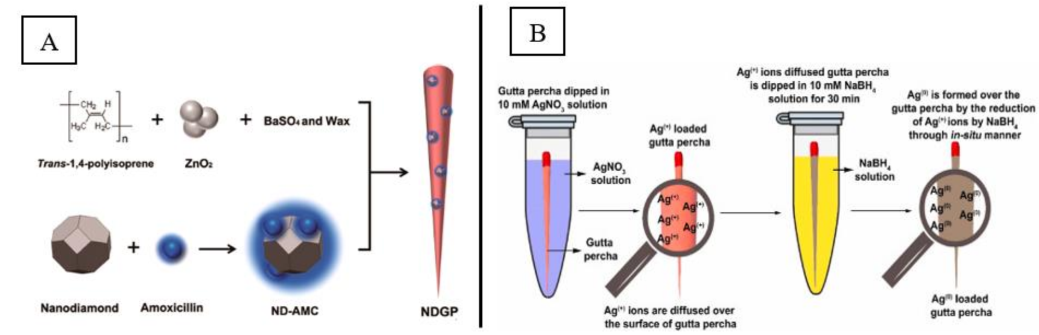


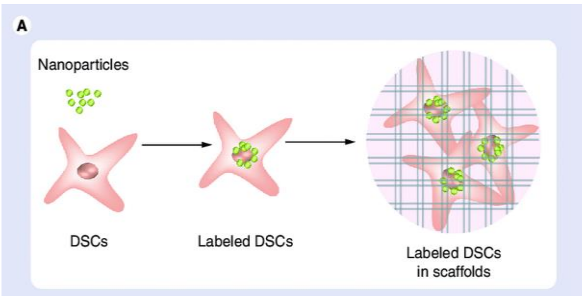
FIGURE 6. A) Synthesis Of NDGP B)Nanosilver GP

Photodynamic Therapy

Biofilm removal by methylene blue dye (photosensitizer) encapsulated within poly(D,L – lactide -co-glycolide) PGLA nanoparticles which are 150-200 nm in diameter are being used for photodynamic therapy.
Utilizing an 805 nm diode laser, nanospheres loaded with the photosensitizer indocyanine green present a promising approach in photodynamic periodontal therapy. [16]
“Quantum dot” nanocrystals are tiny particles measuring only a few nanometers across, about the same size as a protein molecule or a short sequence of DNA. Quantum dots can be used as photo sensitizers and carriers. They can bind to the antibody present on the surface of the target cell and when stimulated by UV light, they can give rise to reactive oxygen species and thus will be lethal to the target cell.[26]

Pulp regeneration

Nano-assemblies Poly-L-Lysine Dendrigraft (DGL), Poly-Glutamic Acid (PGA) and Melanocyte Stimulating Hormone (alpha MSH). PGA-alpha-MSH induces the reduction of inflammation of pulp connective tissue. These promote the initiation of the regeneration of pulp connective tissue, providing adhesion and multiplication of pulp fibroblasts .
Nanofibrous and microporous membranes are very promising to promote dental pulp regeneration as a mimetic extracellular matrix.[20]
The strategy of functionalization of nanofibers by nanoreservoirs of BMP-2 or BMP-7 shows a great efficiency for bone regeneration and increases the differentiation of MSC (mesenchymal stem cell), accelerating the tissue regeneration in vivo.
Electrospun gelatin scaffolds with nano-hydroxyapatite enhance the differentiation of DPSC towards an odontoblast-like phenotype. Nanofibrous poly(l-lactic acid) scaffolds functionalized by BMP-7 and dexamethasone promote dentin regeneration.[20]



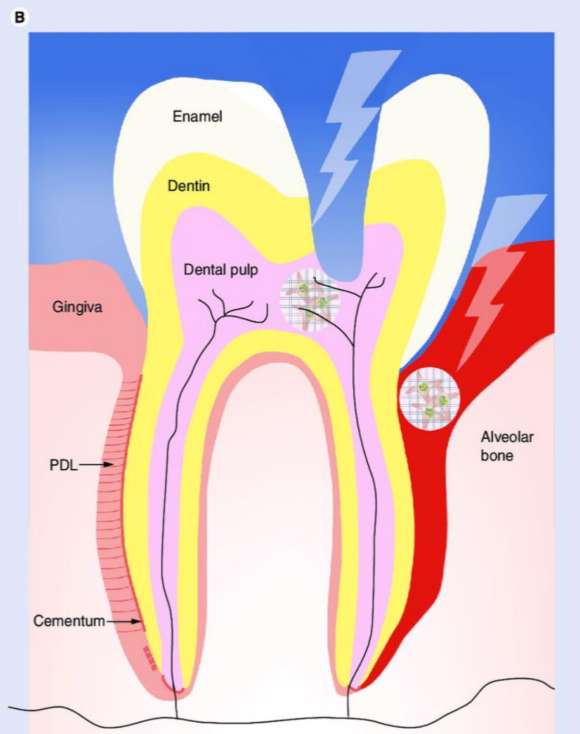


Figure 7. A) Nanoparticle Labelled Stem Cell B)Nanoparticle Based Endodontic Regeneration

CHALLENGES

Nanoparticle technology is growing at very fast rate and improving staus of oral health care remarkably though it still faces a lot of challenges as a novel approach.

1. Engineering challenges
- Feasibility of mass production technique
- Manipulating and coordinating activities of large numbers of independent microscale robots simultaneously
- Precise positioning and assembly of molecular scale part
- Economical nanorobot mass production technique.

2. Biological challenges
- developing biofriendly nanomaterial
- Biocompatibility

3. Social challenges
- Ethics
- Public Acceptance
- Regulation and Human Safety

CONCLUSION

Nanomedicine is the controlled use of nanotechnologies nanoparticles in healthcare, leading to new pathways for the diagnosis and treatment of human diseases. In dentistry, nanoparticles are intentionally embedded into products to improve material properties. Research to improve upon existing nanomaterials is still ongoing, with future directions towards more efficient and cost effective nano-biosensing devices to diagnose in high accuracy.

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