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Chapter 1

Nanotechnology: Bridging Innovation and Clinical Success in Periodontology and Oral Implantology

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Abstract

Nanotechnology has emerged as a transformative field in modern dentistry, offering innovative solutions for the diagnosis, prevention, and treatment of periodontal and peri-implant diseases. The manipulation of materials at the nano scale has enabled the development of advanced biomaterials, drug delivery systems, regenerative scaffolds, and implant surface modifications that significantly enhance clinical outcomes. In periodontology, nanoparticles and nano fibrous scaffolds facilitate targeted antimicrobial therapy, promote periodontal tissue regeneration, and improve wound healing. Nanotechnology-based diagnostic tools also provide opportunities for early detection and monitoring of periodontal diseases through highly sensitive biosensors. In oral implantology, nano-engineered implant surfaces enhance osseointegration by improving cellular adhesion, proliferation, and differentiation, thereby accelerating the healing process and increasing implant stability. Furthermore, nano coatings with antimicrobial and bioactive properties have demonstrated potential in reducing bacterial colonization and preventing peri-implant infections. Despite these promising advancements, challenges related to biocompatibility, long-term safety, cost-effectiveness, and regulatory approval remain to be addressed. Ongoing research and technological innovations continue to expand the scope of nanotechnology in periodontal and implant therapy, paving the way for more predictable, minimally invasive and patient-centered treatment approaches. This chapter highlights the current applications, recent developments and future prospects of nanotechnology in periodontology and oral implantology, emphasizing its potential to revolutionize clinical practice and improve patient outcomes.

Keywords: Nanotechnology, Periodontology, Oral Implantology, Osseointegration, Periodontal Regeneration.

Introduction

Nanotechnology derives its name from the Greek word *"nanos,"* meaning "dwarf," reflecting its focus on materials and structures at an extremely small scale. The National Nanotechnology Initiative (NNI) defines nanotechnology as the science, engineering, and technology conducted at the nanoscale, typically ranging from 1 to 100 nanometers. The concept of nanomedicine was first introduced by Robert A. Freitas Jr. in 1993, who later coined the term "nanodentistry" in 2000 [1].

Over the past few decades, nanoscience has experienced remarkable growth, leading to significant advancements in healthcare and dentistry. The application of nanotechnology in dentistry, particularly in periodontics, has generated considerable interest owing to its potential to revolutionize disease diagnosis, treatment, and prevention. Periodontitis is a multifactorial, polymicrobial inflammatory disease affecting the supporting structures of the teeth and results from a complex interaction between pathogenic microorganisms and a susceptible host [2].

The emergence of nanotechnology has introduced a wide array of nanoscale materials and nanostructured systems that are increasingly being utilized to promote periodontal health and improve therapeutic outcomes. These innovations have opened new avenues in periodontal

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therapy, ranging from targeted drug delivery and regenerative approaches to advanced diagnostic techniques. The application of nanotechnology in periodontal management was notably popularized by Kong et al. [3]. Recent advances in this field continue to provide promising opportunities for enhancing the diagnosis, treatment, prognosis, and prevention of periodontal diseases.

Nanodentistry

Nanodentistry is a specialized field that utilizes nanotechnology, nanomaterials, biotechnology, and nanorobotics for the diagnosis, prevention, and treatment of oral and dental diseases. Over the past few years, significant advancements in nanotechnology have facilitated the development of a wide range of innovative nanomaterials. These materials have demonstrated substantial potential in improving diagnostic accuracy, therapeutic outcomes, and disease prevention strategies. By manipulating structures at the nanoscale, researchers have been able to enhance the properties of conventional dental materials and develop advanced alternatives with superior clinical performance, thereby contributing to the evolution of modern dental care.

Nanotechnology in Periodontics

Periodontal diseases are among the most common oral health conditions worldwide, affecting approximately 20–50% of the global population in both developed and developing countries, thereby representing a significant public health challenge [4]. In recent years, public awareness regarding periodontal health has increased considerably, and a wider range of treatment modalities has become available. Nevertheless, existing therapeutic approaches, ranging from the conventional gold-standard treatment of scaling and root planing to advanced regenerative procedures, possess inherent limitations that often hinder complete disease resolution. These challenges have driven the exploration and integration of emerging technologies into periodontal therapy, with nanotechnology being one of the most promising advancements.

Need for Nanotechnology in Periodontics

- **Tissue Engineering and Regeneration:** Nanotechnology facilitates the fabrication of nanofibrous materials for three-dimensional cell culture and tissue engineering applications. These materials provide a suitable framework for the development of complex tissue architectures that are difficult to achieve using conventional tissue engineering techniques alone.
- **Advanced Drug Delivery Systems:** In therapeutic applications, metallic and polymeric nanoparticles offer significant potential for achieving precise, controlled, and sustained drug release. Through the design of specialized nanostructures, such as hybrid hollow spheres and core-shell systems, targeted delivery of therapeutic agents can be accomplished with improved efficiency and predictability.
- **Enhanced Diagnostic Technologies:** A new generation of biosensors based on the optical properties of colloidal gold nanocrystals and nanoparticles has emerged for use in diagnostics and medical imaging. These nanosensors can also be applied in DNA sandwich assays, thereby facilitating the early detection, diagnosis, and prevention of periodontal diseases.

Applications of Nanotechnology in Periodontics

Nanotechnology has a broad range of applications in periodontics, encompassing various aspects of periodontal care from disease diagnosis to therapeutic and regenerative interventions.

Its applications in periodontics include the following [5]:

1. Diagnosis
2. Treatment of dentin hypersensitivity
3. Control of oral biofilm formation
4. Nanorobotic dentifrices (Dentifrobots)
5. Subgingival irrigation
6. Drug delivery
7. Nanotechnology in Tissue engineering
8. Guided tissue Regeneration
9. Bone Regeneration
10. Bone Replacement materials
11. Guided Bone Regeneration
12. Sinus Augmentation
13. Gene delivery

Diagnosis

The assessment of electrolyte concentrations in gingival crevicular fluid (GCF), particularly sodium, potassium, and calcium ions, reflects the physiological and pathological status of periodontal tissues. Therefore, quantifying these ions may serve as a valuable diagnostic indicator for identifying active periodontal disease.

In 2018, Totu et al. developed an innovative device capable of detecting inorganic ions directly within periodontal pockets through the use of membranes incorporating magnetic nanoparticles and ionophores embedded in various polymeric matrices. The device comprises a series of sodium-selective membranes containing magnetic nano-inclusions, with p-tert-butyl Calix [4] arene serving as the ionophore and polyvinyl chloride functioning as the polymeric matrix. Due to their miniature size, these sensors can directly measure ion concentrations in gingival crevicular fluid within the periodontal pocket, thereby eliminating the challenges associated with collecting adequate fluid samples for laboratory analysis. The sodium-selective ion-sensitive field-effect transistor (ISFET) was evaluated ex vivo in five individuals exhibiting healthy periodontal tissues as well as varying degrees of gingival inflammation, moderate periodontitis, and severe periodontitis, diagnosed on the basis of clinical attachment loss (CAL) and probing depth (PD). The device successfully detected variations in inorganic ion concentrations among the different clinical conditions, demonstrating its potential as a diagnostic tool for the early detection, monitoring, and prevention of periodontal diseases [6].

Dentinal hypersensitivity

Dentinal hypersensitivity is one of the most common complaints reported by patients with periodontal disease, primarily resulting from exposure of the root surface following gingival recession. Nanohydroxyapatite (nano-HAP) crystals have emerged as a promising therapeutic option for the management of this condition. Several in vivo studies evaluating nano-HAP-containing products have demonstrated that hydroxyapatite-based toothpastes are effective in reducing dentinal hypersensitivity. The proposed mechanisms underlying their desensitizing effect include:

- **Enhanced occlusion of dentinal tubules**: Nanosized hydroxyapatite particles penetrate and occlude dentinal tubules more effectively than conventional microsized hydroxyapatite, thereby reducing dentinal fluid movement.
- **Prevention of nerve stimulation**: The sealing of dentinal tubules limits the transmission of external stimuli to pulpal nerve endings, thereby decreasing pain perception.
- **Remineralization and surface protection**: Nano-HAP exhibits strong affinity for dentin apatite and tooth surfaces, facilitating the formation of a new apatite layer that promotes enamel remineralization and provides additional protection to the tooth surface.

Several commercially available nanoparticle-containing dentifrices have been developed for the management of dentinal hypersensitivity, including Nano XIM Care Paste, Nano-P (FGM, Joinville, Brazil), and Aclaim Toothpaste (Group Pharmaceuticals Ltd.) [7].

Wang et al. (2016) evaluated a nano-hydroxyapatite formulation (Desensibilize Nano-P; containing 10% hydroxyapatite, potassium nitrate, and sodium fluoride [900 ppm fluoride]) and reported that its effectiveness in reducing dentinal hypersensitivity was comparable to that of other established desensitizing therapies [8].

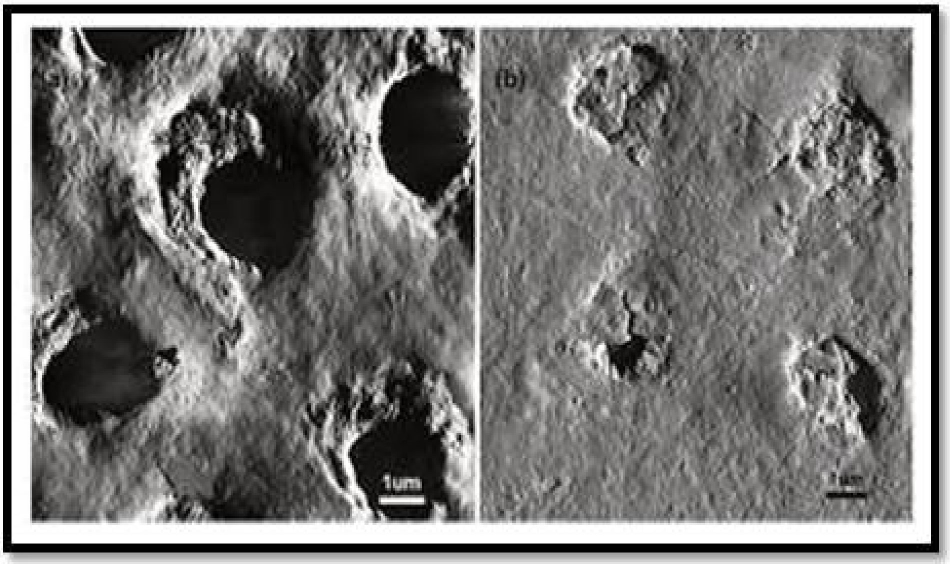

Figure 1: Nanomaterials occluding dentinal tubules

Nanotechnology to control oral biofilm formation

The oral cavity harbors complex polymicrobial communities that predominantly exist as biofilms on teeth, dental prostheses, and mucosal surfaces. These microbial biofilms, composed of bacteria and yeasts, are implicated in the development of various oral diseases, including dental caries, periodontal diseases, candidiasis, as well as endodontic, orthodontic, and peri-implant infections. Nanotherapeutic approaches offer promising strategies for preventing and controlling oral biofilms through the use of nanoparticles possessing antimicrobial, anti-adhesive, and targeted drug delivery properties.

- **Nanoparticulate Metals**: Metallic nanoparticles such as silver, copper, gold, titanium, and zinc have gained considerable attention because of their broad-spectrum antimicrobial activities and unique physicochemical properties. Among these, silver and copper nanoparticles have been incorporated into or coated onto various biomaterials, including polymethyl methacrylate (PMMA) and hydrogel-based systems, to enhance their antimicrobial performance.
- **Nanoparticulate Metal Oxides**: Research involving copper oxide (CuO) nanoparticles incorporated into polymeric matrices suggests that the release of metal ions plays a crucial role in maximizing antibacterial activity against biofilm-associated microorganisms. Similarly, polyethylene glycol-capped zinc oxide (ZnO) nanoparticles have demonstrated enhanced antimicrobial efficacy against oral biofilms.
- **Quaternary Ammonium Nanoparticles**: Yudovin-Farber et al. (2008) developed quaternary ammonium poly(ethylene imine) (QA-PEI) nanoparticles as antimicrobial agents for incorporation into restorative composite resins. These nanoparticles provide long-lasting antibacterial effects and may help reduce bacterial colonization around restorative materials [9].

- **Chitosan Nanoparticles**: Chitosan-based nano- and microparticles have been extensively investigated as carriers for localized drug delivery. In addition to their delivery capabilities, surface modification with chitosan nanoparticles may inhibit bacterial recolonization and reduce biofilm formation in vivo.
- **Silica and Silicon Nanoparticles**: Mesoporous silica nanoparticle-encapsulated chlorhexidine (Nano-CHX) has demonstrated potent antibacterial activity against oral biofilms, suggesting its potential as an effective antimicrobial delivery system for oral healthcare applications.
- **Hydroxyapatite and Other Calcium Phosphate-Based Systems**: Nanoscale hydroxyapatite particles have been shown to interfere with biofilm formation while simultaneously promoting remineralization of dental hard tissues. A notable example is the casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) nanocomplex, commercially available as Recaldent^{TM}, in which ACP is stabilized by casein phosphopeptide to enhance mineral delivery and enamel remineralization.

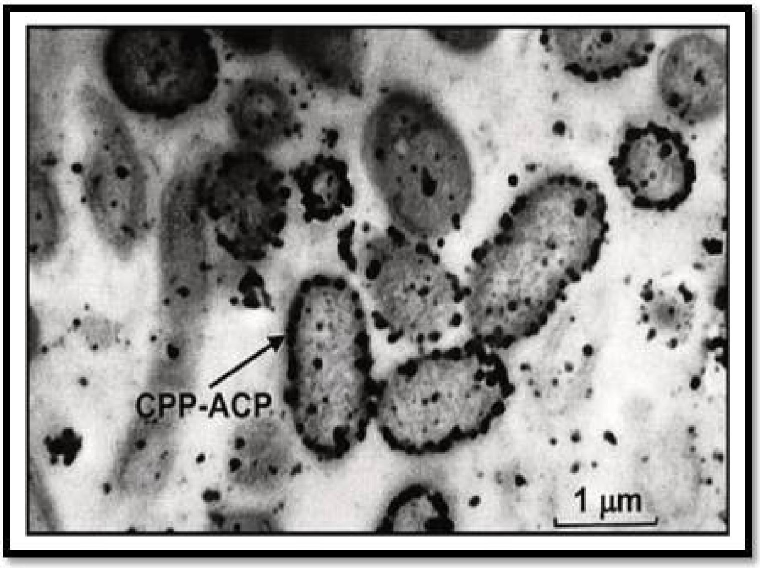

Figure 2: Electron micrograph of supragingival plaque showing CPP-ACP as electron-dense particles associated with the bacterial surface and intercellular matrix

- **Nanocomposites**: The application of a thin nanocomposite coating on tooth surfaces has been shown to significantly inhibit biofilm formation, thereby contributing to improved oral hygiene and reduced microbial colonization.
- **Nanochlorhexidine**: Nanochlorhexidine exhibits potent antibacterial activity against commonly occurring oral bacterial biofilms. Owing to its enhanced antimicrobial properties, it has considerable potential for development as an innovative therapeutic agent for oral and periodontal care [10].
- **Nanotech Floss**: Nanotechnology has also been incorporated into dental floss, resulting in an ultra-thin, smooth, and non-shredding product with superior tensile strength. The unique nanostructure of this dental tape enables the incorporation of flavoring agents as well as the controlled delivery of therapeutic medications during flossing [11].

Nanotechnology in dentifrices

A futuristic application of nanotechnology in oral healthcare involves the use of subocclusally dwelling nanorobotic dentifrices, known as dentifrobots, which could be delivered through mouthwashes or toothpastes using non-viral delivery systems. These nanorobots are envisioned to patrol both supragingival and subgingival surfaces on a daily basis, removing trapped organic debris, converting it into harmless and odorless by-products, and continuously eliminating calculus deposits to maintain optimal oral health.

VE Santos Jr. et al. (2014) evaluated the efficacy of Nano Silver Fluoride (NSF), a novel anticaries agent, when applied annually for the prevention and arrest of dental caries in children. Their study highlighted the potential of nanotechnology-based formulations in caries management. Several toothpaste formulations currently incorporate nanosized particles to enhance their therapeutic properties. The most commonly used nanoparticle-based ingredients include hydroxyapatite, silver, and titanium dioxide. These nanomaterials contribute to remineralization, antimicrobial activity, and improved oral hygiene outcomes. Examples of commercially available nanoparticle-containing dentifrices include Apagard M Plus (nano-hydroxyapatite), Trucare, and Nano Clean Plus (nano-silver), all of which utilize nanotechnology to improve oral health benefits [12].

Subgingival irrigation

Ozone has been utilized as an adjunctive agent to mechanical subgingival debridement for periodontal irrigation because of its antimicrobial properties. However, the clinical application of ozonized water is limited by its short half-life of approximately 20 minutes, as it rapidly decomposes back into oxygen. Consequently, it must be used within 5–10 minutes of preparation to ensure optimal efficacy.

To address this limitation, Chiba et al. developed ozone nano-bubble water (NBW3) using advanced nanobubble generation technology. NBW3 contains an ozone concentration of 1.5 mg/L, which corresponds to the oxidation titer determined by electron spin resonance analysis.

Nanobubbles are extremely small gas nuclei measuring less than 100 nm in diameter. They are generated through the collapse of microbubbles ($\leq 50\ \mu$m in diameter) within an electrolyte under conditions of ultra-high temperature and pressure. This unique structure enables NBW3 to retain ozone in the form of stable gas nuclei, thereby prolonging its antimicrobial activity.

When protected from ultraviolet radiation, NBW3 can maintain its antimicrobial effectiveness for more than six months. Hayakumo et al. (2013) evaluated the clinical use of NBW3 as an adjunct to mechanical subgingival debridement in the management of periodontitis. Their findings suggested that subgingival irrigation with ozone nano-bubble water may serve as a valuable supplementary approach in periodontal therapy [13].

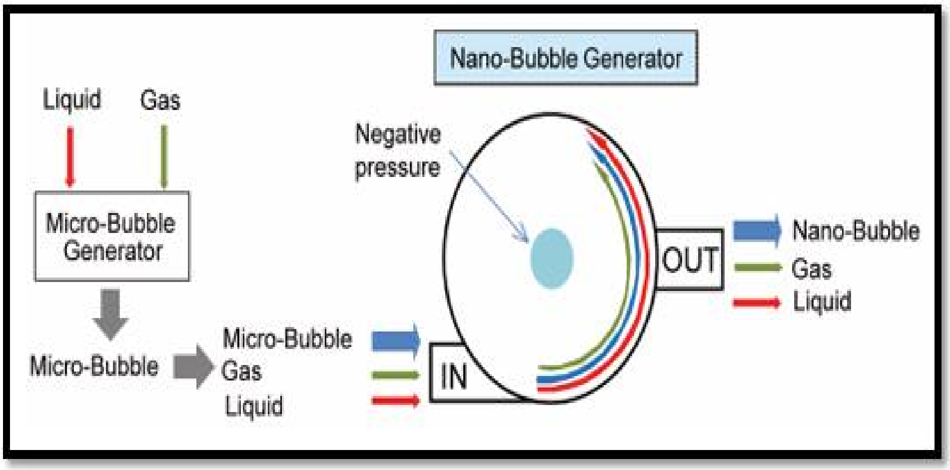

Figure 3: Nano-Bubble Generator

Nanotechnology in periodontal drug delivery

A variety of local drug delivery systems, including films, fibers, gels, and strips, have been developed for the management of periodontal diseases. However, their clinical effectiveness has often been limited due to the challenges associated with accessing and maintaining therapeutic concentrations within periodontal pockets.

To overcome these limitations, numerous researchers have explored the application of nanomaterials as local drug delivery vehicles for periodontal therapy. Among these developments, Pinon-Segundo et al. designed and characterized triclosan-loaded nanoparticles, proposing them as a novel and effective drug delivery system for the treatment of periodontal diseases.

One commercially available nanotechnology-based product is Nano-Bio Fusion (NBF) gingival gel, which is used as an adjunct to scaling and root planing. NBF gingival gel is a patented bioadhesive antioxidant formulation containing naturally derived antioxidants such as propolis, vitamin C, and vitamin E. The technology behind this formulation enables ultrafine antioxidant particles to penetrate the moist oral environment and enter target cells, thereby promoting tissue rejuvenation, protection, and optimization of gingival and oral soft tissues. Following application, the gel forms a nano-bioactive protective layer that enhances the absorption of active ingredients, leading to improved clinical outcomes and visible therapeutic benefits [14].

Several studies have reported the use of a broad spectrum of nanoparticles, nanocarriers, and nanostructured scaffolds for periodontal drug delivery. These systems include nanoscale polymersomes, calcium-deficient hydroxyapatite (CDHA)-based apatitic nanocarriers, poly (D,L-lactide-co-glycolide acid) (PLGA) nanoparticles, chitosan nanoparticles, nano-doxycycline (nano-DOX), composite nanofibers composed of PLGA and gum tragacanth (GT), silver (Ag) and gold (Au) nanoparticles, mesoporous silica (SiO_2) nanoparticles, and PLGA nanospheres.

Among the therapeutic agents delivered through these nanocarrier systems, tetracycline and doxycycline have been the most frequently investigated antibiotics. In addition, other antimicrobial agents, including minocycline, metronidazole, azithromycin, clarithromycin, and glutaraldehyde, have also been successfully incorporated into nanoparticle-based delivery platforms for periodontal applications [15].

Figure 4: Nano-Bio Fusion gel for application in periodontal pockets

Nanomaterials for periodontal tissue engineering

Contemporary approaches to periodontal tissue engineering primarily focus on the use of synthetic scaffolds as carriers for cell delivery and tissue regeneration. These scaffolds provide a supportive framework that facilitates cell attachment, proliferation, migration, and differentiation, ultimately promoting the formation of functional tissues along with the secretion of extracellular matrix components essential for regenerative processes.

Nanoengineered scaffolds offer unique mechanical and biological properties that are difficult to achieve using conventional fabrication techniques. In addition, a variety of bioactive molecules and proteins can be incorporated into these scaffolds at the nanoscale level, enabling enhanced therapeutic effects and precise regulation of cellular responses.

Electrospun nanofibers composed of poly(lactic-co-glycolic acid) (PLGA) or gelatin have been successfully utilized for culturing human periodontal ligament (PDL) cells, demonstrating excellent support for cell adhesion, proliferation, and osteogenic differentiation.16 Furthermore, the incorporation of silica or hydroxyapatite (HA) nanoparticles onto the surface of these nanofibers has been shown to improve protein adsorption, thereby enhancing the attachment of PDL fibroblasts. Studies have also reported that scaffolds containing nanosized HA exhibit significantly greater protein adsorption, cell adhesion, and in vivo bone formation compared with scaffolds containing conventional HA. Additionally, when PDL stem cells were cultured on nanoengineered surfaces, improved cell viability and enhanced differentiation were observed [17].

A novel Gene Activated Membrane (GAM) incorporating chitosan/plasmid nanoparticles encoding platelet-derived growth factor (PDGF) was developed using a porous chitosan-collagen composite scaffold. This innovative design demonstrated potential for enhancing periodontal defect regeneration and advancing periodontal tissue engineering strategies. Wu et al. (2014) developed a biodegradable scaffold composed of type I collagen, poly (ε-caprolactone) (PCL), and nanoscale hydroxyapatite (nHA) (COL/PCL/nHA). Owing to the excellent biocompatibility and osteoinductive properties imparted by nHA, this scaffold showed considerable promise as a regenerative biomaterial for periodontal tissue engineering applications [18].

Guided Tissue Regeneration

A three-layered graded nanocomposite membrane has been developed as a promising biomaterial for guided tissue regeneration (GTR) based on the concept of functional graded materials (FGM). The membrane consists of an 8% nano-carbonated hydroxyapatite/collagen/poly (lactic-co-glycolic acid) (nCHAC/PLGA) porous layer on one surface, a non-porous pure PLGA layer on the opposite surface, and an intermediate layer containing 4% nCHAC/PLGA.

The incorporation of nano-carbonated hydroxyapatite significantly enhances the biocompatibility and osteoconductive properties of this biodegradable composite membrane. Owing to its compositional similarity and nanoscale crystal structure that closely resemble natural bone tissue, the membrane provides a favorable environment for cellular attachment, tissue regeneration, and new bone formation, making it a promising candidate for guided tissue regeneration applications [19].

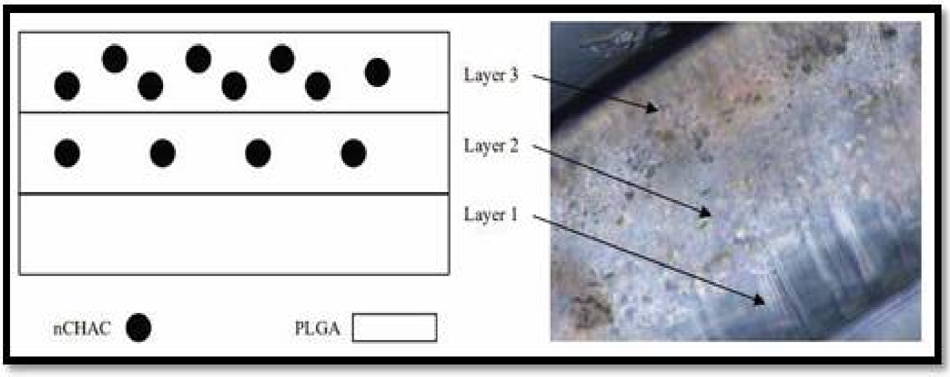

Figure 5: Schematic representation of three-layered membrane

Bone Regeneration

Bone regeneration is a therapeutic approach aimed at restoring alveolar bone that has been lost as a consequence of advanced periodontal disease. The procedure focuses on reconstructing the lost osseous structures and re-establishing the supporting architecture around the affected tooth. However, conventional regenerative techniques are often limited by factors such as the restricted availability of graft materials, unpredictable resorption rates, high treatment failure rates, and persistent postoperative discomfort. These challenges have stimulated extensive research into the development of more effective regenerative strategies. Among the most promising advancements are three-dimensional (3D) scaffold matrices and nanoengineered biomaterials designed to enhance new bone formation. Scaffolds have been successfully applied in various tissue engineering applications, including periodontal regeneration and alveolar bone reconstruction, owing to their ability to provide structural support and promote cellular growth.

Several nanomaterials have been investigated as bone graft substitutes for regenerative procedures, including citric acid-based nano-hydroxyapatite (CA-NHA) composite grafts, nanocrystalline hydroxyapatite, titanium-reinforced nano-hydroxyapatite grafts, nanosized calcium sulfate crystals, nanoceramic composite materials, and chitosan nanofiber membranes [20].

Dayashankar et al. (2017) evaluated the effectiveness of a citric acid-based nano-hydroxyapatite (CA-NHA) composite graft for the treatment of intrabony defects in patients with chronic periodontitis. Their findings demonstrated that the CA-NHA group exhibited significantly greater improvements in both clinical and radiographic parameters compared with the conventional NHA group, suggesting that CA-NHA is a promising regenerative material for periodontal therapy [21].

Among the various bioactive agents incorporated into nanomaterials, Bone Morphogenetic Protein-2 (BMP-2) is one of the most extensively utilized molecules for promoting alveolar bone regeneration due to its potent osteoinductive properties [22].

Bone Replacement Material

NanoBone is a patented and innovative bone graft substitute designed for regenerative applications. It consists of nanocrystalline hydroxyapatite (HA) particles embedded within an amorphous silica gel (ASG) matrix. This unique composition facilitates the retention of nanosized HA particles at the graft site while simultaneously stimulating the bone healing process through the biological effects of silicon.

Following implantation, the amorphous silica gel matrix is gradually replaced by newly formed organic tissue components, including collagen-rich extracellular matrix, mesenchymal stem cells, and various growth factors involved in bone regeneration. Owing to their osteoconductive properties and ability to support new bone formation, hydroxyapatite nanoparticles have shown considerable potential for the management of osseous defects associated with periodontal diseases.

Figure 6: NanoBone Granules

Guided Bone Regeneration

Barrier membranes are a critical component of guided bone regeneration (GBR) procedures, as they help stabilize and protect the blood clot while preventing the migration of soft tissue cells into the bone defect site. This selective barrier function creates a favorable environment for bone regeneration and healing.

For successful outcomes in GBR, barrier membranes must possess several essential characteristics, including biocompatibility, bioactivity (osteoconductivity), controlled biodegradability, effective tissue integration, space creation and maintenance capabilities, ease of clinical handling, and minimal risk of postoperative complications.

Given that biocompatibility and adequate mechanical strength are fundamental requirements for regenerative biomaterials, significant efforts have been directed toward improving the performance of collagen-based membranes used in GBR. Recent advances in electrospinning technology have enabled the fabrication of nanofibrous scaffolds that offer enhanced surface area, superior mechanical properties, and biomimetic characteristics compared with conventional polymer microfibers. These nanofibrous structures more closely resemble the natural extracellular matrix, thereby supporting cellular attachment and tissue regeneration. However, electrospun collagen scaffolds often exhibit reduced mechanical stability when exposed to hydrated conditions. To overcome this limitation, collagen fibers are frequently cross-linked with natural polymers such as chitosan using agents like glutaraldehyde. The incorporation of chitosan into collagen-based membranes provides several advantages, including enhanced bone formation, improved osteoinductive potential, greater mechanical strength, increased osteogenic activity, and better handling characteristics during clinical procedures [23].

Sinus Augmentation

A wide variety of grafting materials have been employed to fill the space created during sinus lift procedures. Both synthetic and naturally derived alloplastic biomaterials have been utilized as bone graft substitutes, including materials such as bioglass, hydroxyapatite, and calcium sulfate (CS).

To address the limitation of the rapid resorption associated with conventional calcium sulfate, nanocrystalline calcium sulfate (nCS) was developed. The nCS granules, measuring approximately 400–800 μm in size, are composed of densely packed nanocrystalline particles ranging from 200–900 nm. For convenient clinical application, these granules are supplied pre-mixed with medical-grade calcium sulfate hemihydrate powder. Upon the addition of saline, the material forms a moldable paste that can be easily placed into osseous defects.

Unlike conventional CS, nCS degrades gradually over a period of 3–4 months, thereby providing a prolonged stimulus for bone regeneration. Mazor et al. (2015) evaluated the effectiveness of nanocrystalline calcium sulfate as a grafting material in bilateral sinus augmentation procedures. Their study demonstrated that nCS could be successfully used either alone or in combination with platelet-rich fibrin (PRF) during sinus augmentation performed using both osteotome and lateral window techniques. Based on their findings, the authors suggested that nCS represents a promising and clinically viable graft material for sinus elevation procedures [24].

Gene delivery

Gene therapy is founded on the principle that diseases can be treated by introducing genetic material into specific target cells to replace, modify, or supplement defective genes responsible for disease progression.

For successful gene transfer, the delivered genetic material must overcome various biological barriers that can influence the distribution and degradation of macromolecules within the body. Therefore, encapsulating genes within suitable delivery carriers is essential to protect them from degradation and ensure their safe transport to the intended target site.

Although both viral and non-viral vectors have been developed for gene delivery applications, non-viral systems have gained considerable attention owing to their lower immunogenicity, improved safety profile, and greater flexibility in modifying their physicochemical properties. Nano-sized calcium phosphate particles (NCaPP) have been investigated as carriers for the delivery of the Platelet-Derived Growth Factor-B (PDGF-B) gene to fibroblasts. Studies have demonstrated that NCaPP exhibit excellent biocompatibility and effectively facilitate the transfection of PDGF plasmids into fibroblasts under in vitro conditions, highlighting their potential as promising gene delivery vectors [25].

Nanotechnology in Implantology

Dental implants are widely utilized in contemporary dental practice for the replacement of missing teeth. A major challenge in implantology is achieving and maintaining long-term osseointegration while ensuring a stable epithelial attachment between the gingival tissues and the implant surface.

Numerous investigations have focused on improving implant osseointegration through various surface modification strategies. Despite these advances, precise regulation of implant surface characteristics at the protein and cellular levels, particularly within the nanometer scale, continues to be a significant challenge for both researchers and implant manufacturers. Nanotechnology offers promising solutions by enabling the fabrication of implant surfaces with precisely controlled topographical and chemical properties. Such surfaces can facilitate a better understanding of biological interactions at the tissue–implant interface and contribute to the development of advanced implants with predictable tissue-integrative capabilities. Furthermore, several processing techniques adapted from the electronics industry can be employed to engineer implant surfaces with highly controlled nanoscale features, thereby enhancing their biological performance and clinical success.

Nanoscale surface modifications

Alteration of implant surface roughness has been demonstrated to improve bone-to-implant contact (BIC) and thereby enhance the overall clinical success of dental implants. Several surface modification techniques, including grit blasting, anodization, acid etching, chemical grafting, and ion implantation, are routinely employed to create favorable surface characteristics on metallic implants. In many cases, these methods are used in combination; for example, acid etching may be performed following grit blasting to remove residual contaminants left by the blasting process and to further optimize the implant surface for biological integration [26].

Carbon Nanomaterials for Implant Dentistry

Carbon nanotubes (CNTs) have attracted considerable attention in implant dentistry due to their potential use as surface coatings on titanium implants. Previous studies have demonstrated that osteoblasts produced higher levels of alkaline phosphatase (ALP) and calcium when cultured on non-functionalized multiwalled carbon nanotubes (MWCNTs) grown on anodized nanotubular titanium surfaces compared with anodized titanium surfaces without MWCNTs and conventional non-anodized commercial titanium implant surfaces.

In another study, titanium plates were chemically aminated and subsequently coated with collagen, followed by the application of carboxylated MWCNTs onto the collagen layer. Mouse osteoblasts cultured on these nanotube-coated surfaces exhibited significantly enhanced cell adhesion and proliferation, indicating improved biocompatibility and osteogenic potential.

In addition to promoting cellular responses, carbon nanotubes (CNTs) and carbon nanofibres (CNFs) have been investigated for their ability to enhance the mechanical properties of dental implants, particularly fracture toughness. Chen et al. incorporated MWCNTs into hydroxyapatite (HA) coatings using laser surface alloying techniques, thereby improving the structural and functional characteristics of implant coatings.

Titanium Nanotube Coatings on Dental Implants

The creation of nanostructured implant surfaces has emerged as an effective approach for improving osseointegration. Several surface modification techniques, including grit blasting, anodization, acid etching, chemical grafting, and ion implantation, are commonly employed to alter titanium (Ti) implant surfaces. These modifications enhance bone-to-implant contact (BIC) and contribute to improved clinical outcomes.

Among these methods, anodization is a relatively recent technique used to generate oxide nanotube (NT) coatings on metallic surfaces such as titanium. By carefully regulating anodization parameters, including voltage and duration, the nanoscale characteristics of the coating can be precisely controlled. Titanium NT coatings have been shown to promote the formation of nanostructured hydroxyapatite in simulated body fluids (SBF), enhance extracellular matrix (ECM) secretion and mineralization, and improve various osteoblastic functions. Furthermore, these coatings can stimulate the differentiation of mesenchymal stem cells (MSCs) toward the osteogenic lineage even in the absence of additional osteogenic supplements (OS).

Lee et al. developed dental implants coated with TiO_2 nanotube arrays incorporated with recombinant human bone morphogenetic protein-2 (rhBMP-2). Their findings demonstrated that implants possessing TiO_2 nanotube array surfaces loaded with rhBMP-2 achieved superior bone-to-implant contact and promoted enhanced bone remodeling when compared with conventional implant surfaces [27].

Management of Peri-implant mucositis and Periimplantitis

Infections related to dental implants are primarily characterized by microbial colonization, biofilm accumulation on implant surfaces, and subsequent infection of the surrounding peri-implant tissues.

Nanotubes (NTs) incorporated onto titanium (Ti) implant surfaces not only create a favorable nanotopographical environment that enhances bone formation and osseointegration but also function as effective reservoirs and delivery systems for therapeutic agents. A variety of bioactive substances, including antimicrobial agents, osteogenic stimulators, and anti-inflammatory compounds, have been integrated into NTs to improve implant performance and clinical outcomes.

To further enhance their therapeutic potential, elements such as silver, strontium, and zinc have been incorporated into NTs, providing prolonged antibacterial activity while simultaneously promoting osteogenesis and bone regeneration [28]. In addition, biologically active molecules such as antibiotics and growth factors can be incorporated into implant surfaces to support tissue healing and prevent infection. An example of such an approach is the Nanotite^{TM} Nano-Coated Implant.

Recently, three major types of nanostructured implant coatings have been developed:

- **Nanostructured diamond coatings:** These coatings exhibit exceptional hardness, superior toughness compared with conventional microcrystalline diamond, reduced friction, and excellent adhesion to titanium alloys.
- **Nanostructured hydroxyapatite coatings:** Nanostructural modifications of hydroxyapatite coatings improve mechanical properties and surface reactivity. These coatings have been shown to enhance osteoblast attachment, proliferation, and mineralization, thereby supporting improved osseointegration.
- **Nanostructured metalloceramic coatings:** These coatings provide a gradual transition from a nanocrystalline metallic interface to a hard ceramic outer surface, thereby combining the beneficial properties of both materials [29].

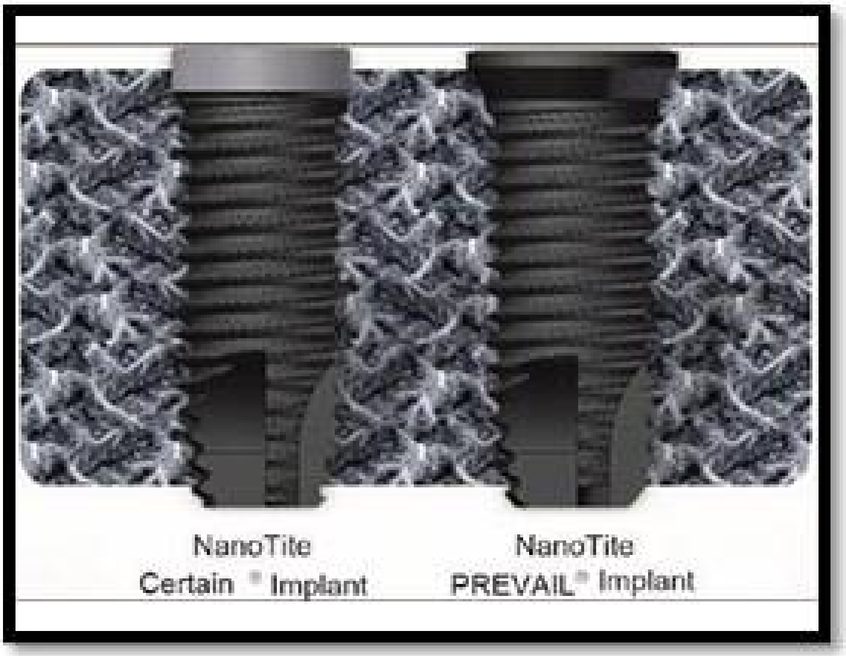

Figure 7: Nanotite Implant

Safety Considerations for The Use of Nanomaterials

Dental practitioners should employ biocompatible nanomaterials sourced from certified and reliable manufacturers while strictly adhering to established clinical guidelines regarding the safe administration of therapeutic ions. Additionally, these materials must be carefully evaluated to ensure their compatibility with the complex biological environment of the oral cavity.

Furthermore, it is essential to thoroughly assess and address the potential health risks and safety concerns associated with the use of nanomaterials in nanomedicine to ensure their safe and effective clinical application.

Toxicology of Nanomaterials

Despite the numerous benefits attributed to nanomaterials, concerns regarding their potential harmful effects on human health have increased considerably. Although research investigating the acute and long-term toxicity of nanoparticles continues to expand, the available evidence remains incomplete. Findings from animal studies indicate that certain nanoparticles may possess the potential to produce adverse biological effects, highlighting the need for further safety evaluations [30].

Carcinogenicity of Nanoparticles

Current evidence regarding the genotoxic and carcinogenic effects of nanoparticles remains limited. It is still uncertain whether exposure to nanoparticles developed for medical applications can contribute to cancer development in humans. Based primarily on carcinogenicity studies conducted in experimental animals, titanium dioxide (TiO_2) nanoparticles and carbon black nanoparticles have been classified by the WHO/International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans. Studies evaluating the carcinogenic potential of multi-walled carbon nanotubes (MWCNTs) have reported limited evidence following intraperitoneal administration in animal models; however, data concerning their carcinogenic effects following pulmonary exposure are currently lacking.

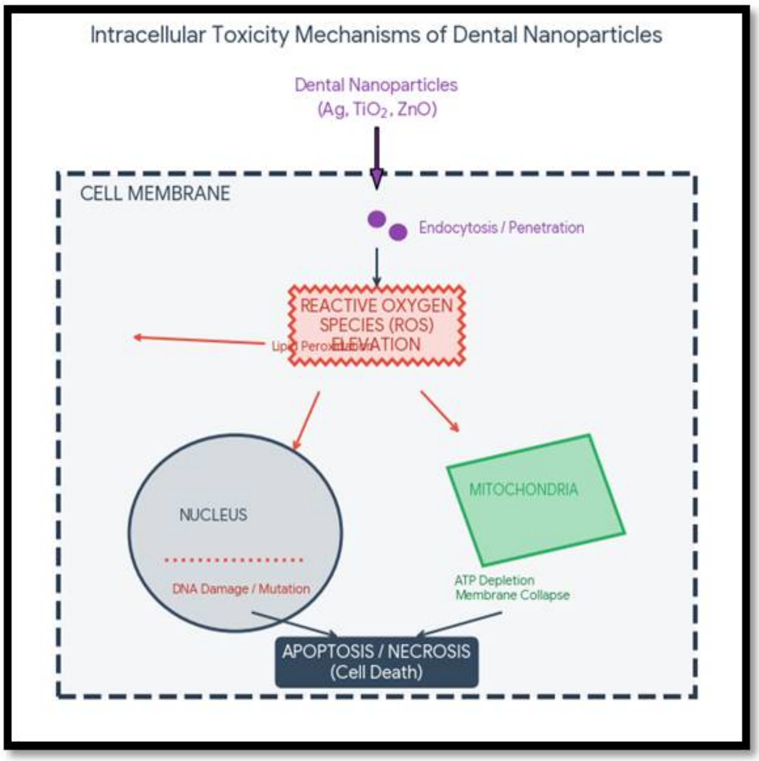

Figure 8: Schematic representation of the toxic effects induced by nanoparticles

Conclusion and Future Directions

Research in the field of nanodentistry is still developing and remains less advanced than many other areas of biological science. Nanomaterials have demonstrated considerable potential in promoting new bone formation within intrabony defects, as well as in applications related to tooth regeneration and dental aesthetics. Furthermore, recent advances in nanotechnology have significantly improved periodontal drug delivery systems by enabling the incorporation of therapeutic agents into specialized carriers that provide targeted, sustained, and controlled release at the desired site of action.

Nanotechnology has the potential to transform the future of dentistry, making periodontal diagnosis, treatment, and therapeutic procedures more precise, efficient, and technologically advanced. Nevertheless, extensive research infrastructure and comprehensive investigations are essential to address the stringent scientific and clinical requirements necessary for the successful development and widespread implementation of nanotechnologies in dental practice.

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