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NANOSCALE INNOVATIONS IN PERIODONTAL CARE: A COMPREHENSIVE REVIEW OF NANOTECHNOLOGY APPLICATIONS Miniaturizing Dentistry: Exploring Nanotechnology's Impact

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Abstract

Nanotechnology has experienced significant growth in the fields of medicine and dentistry in recent years. Nanotechnology involves studying and creating materials, technologies, and systems with unique physical, biological, and chemical characteristics at a nanoscale. Nanotechnology provides various advancements and enhancements in the prevention, diagnosis, and treatment of oral diseases. This article provides an overview of nanotechnology and its applications in dentistry and periodontology.

Keywords: nanotechnology, nanoparticles, nanoscale, periodontics

Introduction

Greatness is not determined by size; tiny items can often hold great surprises. Nanotechnology encompasses the scientific and engineering aspects related to designing, synthesizing, characterizing, and using materials and technologies at a nanoscale level. ^[1] Norio Taniguchi provided the first definition of "nanotechnology", a researcher at Tokyo Science University, in a scientific paper published in 1974. Based on his explanation, "nanotechnology" primarily involves manipulating materials at the molecular or atomic level through processes such as separation, consolidation, and deformation. The term "nano" was derived from the classical Latin word "nanus" or its ancient Greek equivalent "nanos", which both imply "dwarf". ^[2]

Nanotechnology has revolutionized numerous fields including engineering, chemistry, physics, material science, information technology, biology, and medicinal and dental fields. The significant advancement has been utilized in several healthcare applications such as nanoimaging using biosensors, nanoparticles, and capsules for delivering drugs, immunization, and gene transfer for chemotherapy. ^[3]

The fusion of nanotechnology with the treatment of periodontal disease is one of the breakthroughs in periodontics. Periodontal disease is the most common disease globally, resulting from an inflammatory process affecting the structures surrounding the teeth. The primary obstacle in the treatment of periodontal diseases lies in accessing the inflamed area. In conjunction with current methods, introducing nanotechnology to the treatment process can enhance the treatment protocol, improve precision, and target specific sites more effectively. ^[2]

This review article provides an overview of nanotechnology, its history, manufacturing, classification, its clinical applications in dentistry and periodontics, prevention and treatment of periodontal diseases, and recent advances.

History

The utilization of nanoparticles dates back to the 9th century when they were employed in Mesopotamia to produce glittering pots. Richard P. Feynman, a Nobel laureate, introduced the nanotechnology concept. Norio Taniguchi, a professor, coined the term 'nanotechnology' in 1974. Nanotechnology was first applied after the creation of the scanning tunneling microscope by Nobel laureates Binnig and Rohrer in 1986. R.A. Freitas introduced the term Nanomedicine in 2000. ^[4]

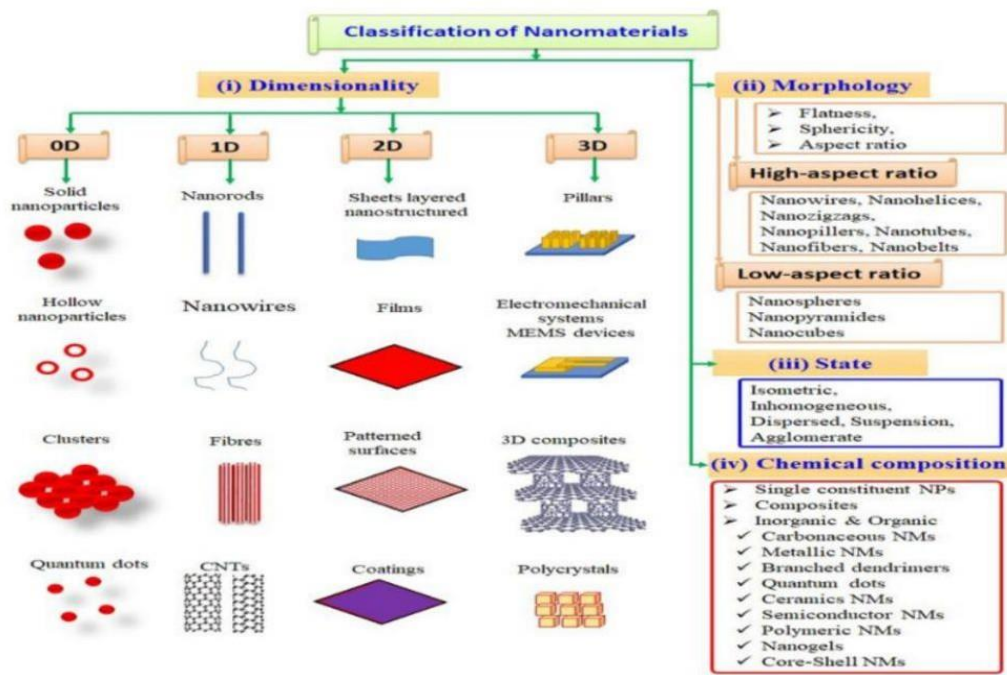
Generations ^[4] Table 1

Table 1: Generations of nanotechnology ^[4]

FIRST GENERATION (FROM 2000)	SECOND GENERATION (FROM 2005)	THIRD GENERATION (FROM 2010)	FOURTH GENERATION (FROM 2015/2020)
Passive (steady state nanostructures) Eg: invasive nanostructured coatings; and	Active (evolving function nanostructures) Eg: reactive nanostructure sensors and materials; targeted cancer therapies	Integrated nanosystems Eg: artificial organs that are built from nanoscales; evolutionary biosystems	Heterogenous nanosystems Eg: in nanoscale genetic therapies, molecules can
diagnostics for rapid monitoring that is non-invasive.			assemble themselves.

Classification

Classified according to approach, materials, origin, dimensions of particles, composition, etc. (fig 1) ^[5]



Classification based on composition (fig 2).

Fig 1: Classification of nanoparticles [5]

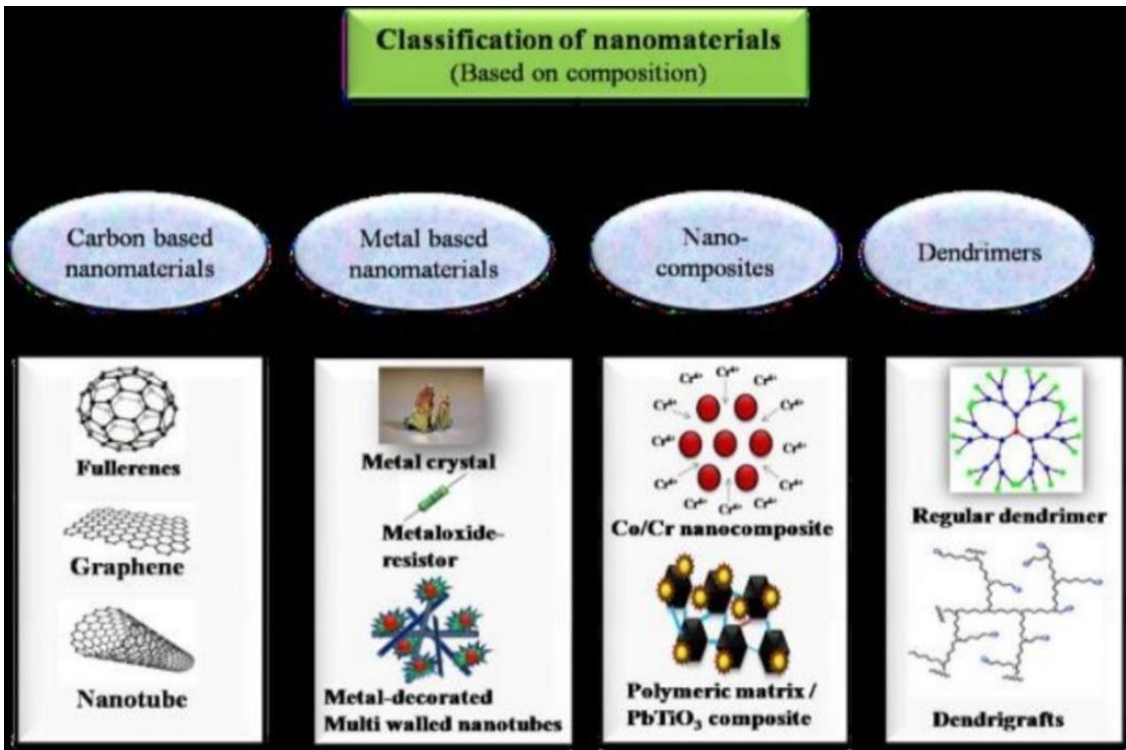


fig 2: Classification of nanoparticles based on composition ^[5]**Manufacturing**

The top-down technique is a method that entails employing destructive procedures to break down large materials into smaller particles, which are then further modified to create nanoparticles. The bottom-up technique involves assembling individual atomic-level substrates by utilizing ionization energy from various sources based on their specific classifications (fig 3). The biomimetic technique involves microorganisms such as fungi, bacteria, or viruses to produce nanoparticles. ^[4]

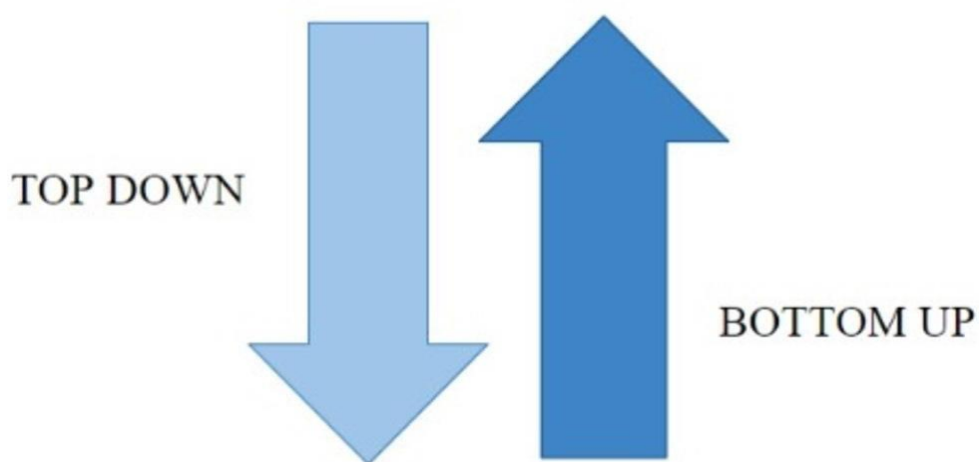


Fig 3: Manufacture of nanoparticles

Nanomedicine

Nanotechnology advancements in medicine have led to the emergence of a new discipline known as nanomedicine. Robert A. Freitas Jr. characterized nanomedicine as the manipulation and treatment of biological systems within the human body at the molecular scale using nano-devices and nanostructures. Nanomedicine encompasses various applications such as delivery of the drugs using nanospheres, tissue scaffolds, and nanorobots for diagnostic and therapeutic uses. Drug molecules carried by the circulatory system might lead to unwanted side effects in non-targeted areas of the body. Nanorobots can identify and eliminate sick cells, regardless of location, making them beneficial for targeted drug administration in cancer treatment during chemotherapy. ^[6]

Metal nanoparticles

Typically, smaller nanoparticles are more efficient at eradicating microorganisms. Various transitional metal oxide and metal nanoparticles have demonstrated antibacterial properties against a broad spectrum of Gram-negative and Gram-positive bacteria, including drug-resistant diseases. NPs can be utilized in nanotechnology to prevent bacterial growth and in biomedicine to treat various diseases (fig 4). There is significant interest in exploring the potential antibacterial properties of several nanoparticles and their derivatives. Antimicrobial properties were found in various metal nanoparticles such as zinc oxide (ZnO), silver oxide (Ag₂O), silver (Ag), gold (Au),

magnesium oxide (MgO), titanium dioxide (TiO₂), copper oxide (CuO), silicon (Si), and calcium oxide (CaO).^[16]

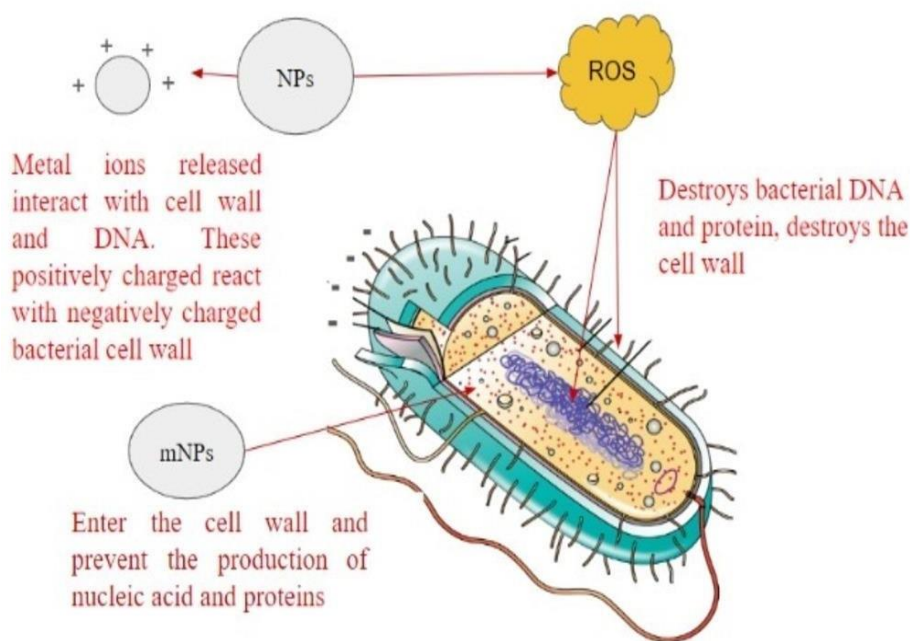


Fig 4: Mechanism of action of metal nanoparticles

Applications in dentistry

Nanodentistry aims to preserve excellent oral health by the application of nanomaterials, nanorobotics, and biotechnology. Nanotechnology has significantly transformed the field of dentistry and oral healthcare. It has revolutionized numerous dental treatments by offering advanced choices to improve dental cleanliness, appearance, and durability.^[7,8]

Nanodiagnosics: Nanodiagnostic devices are capable of identifying diseases at both molecular and cellular levels in the early stages. Nanodevices could be implanted in the body to detect tumor cells, and diseases in their early stages, or to detect and measure toxic substances, and similar entities.^[9]

Oral cancer diagnosis and treatment: Saliva is a cost-effective and non-invasive diagnostic tool that contains genomic and proteomic markers for the identification of molecular diseases. Exosomes which are membrane-bound vesicles show increased levels during malignancy, it is analysed through atomic force microscopy by using nanoparticles. Optical nano biosensors, oral fluid nanosensor tests, and nanoelectromechanical systems are also applicable for the diagnosis of oral cancer. ^[9]

Dentifrobots: Delivered by toothpaste or mouthwash, nanorobotic dentifrices cover all subgingival areas and the trapped organic debris is metabolized into odorless, safe vapors. Dentifrobots, when configured properly, can detect and further eliminate harmful bacteria found in plaque and other areas. These dentifrobots are mechanical devices that upon ingestion disable themselves safely. ^[9]

Nanocomposites: Nanoparticle technology has been integrated into composite resins to enhance restorative materials. Nanotechnology has facilitated the creation of nano-sized filler particles incorporated individually or as nanoclusters into composite resins. Composite materials containing nanofillers resulted in smoother surfaces that showed superior esthetics than composites without nanofillers. Nanocomposites have smaller diameters and larger filler content, which explains this phenomenon. ^[6]

Orthodontics: An orthodontic robot ensures painless vertical repositioning, tooth realignment, and rotation, while also facilitating quick tissue healing. Currently, there is ongoing research on a novel stainless-steel wire that incorporates nanotechnology. This wire offers a unique combination of

exceptional tensile strength, favorable capacity to withstand deformation, resistance to corrosion, and a high-quality surface finish. ^[10]

Dentinal hypersensitivity: Hypersensitivity occurs when changes in pressure are transmitted hydrodynamically via the pulp. Hypersensitive teeth exhibit dentinal tubules that have a diameter twice as large and a surface density eight times more than those found in non-sensitive teeth. Nanorobots with specific features can block tubules quickly and permanently utilizing local materials, providing patients with a precise treatment option. ^[9]

Oral fluid nanosensor test (OFNASET): The OFNASET (fig 5) is a portable, automatic, user-friendly integrated device that allows for quick and simultaneous detection of numerous salivary proteins and nucleic acids. The salivary biomarker detector is suitable for disease screening in dental offices. ^[5]



Applications in periodontics

Local drug delivery: Local drug delivery systems efficiently carry active compounds to specific target sites, tissues, or cells, allowing for prolonged presence and excellent contact with the periodontium. The main goal is to suppress the pro-inflammatory aspect of the immune response or enhance the regulatory immune response. The long-term effectiveness relies on maintaining the presence of anti-inflammatory agents at the target site, which is accomplished by nanotechnology. Moreover, it additionally reduces the frequency of administration of drug hence enhancing the patient's quality of life and compliance with therapy. Drugs may be administered as polymeric nanocarriers made of silver, silica, chitosan, gold, polylactic-co-glycolic acid (PLGA), gelatin, and other polymers. ^[11]

Lasers: Exposing a surface covered with nano-titanium particles to laser irradiation has been demonstrated to enhance the formation of collagen. Applying this technique makes it possible to perform gingival depigmentation and other periodontal treatments. Sadony and Abozaid demonstrated that the combination of a diode laser and nanoparticles can cleanse the surface of dentin. ^[4]

Plaque Biofilm management: Biofilms include a diverse range of bacteria, leading to heightened antibiotic resistance and pathogenicity. Nanoscale materials such as zinc oxide, copper oxide, titanium dioxide, chitosan, carbon nanotubes, quaternary ammonium compounds, and gold disrupt the bacterial cell membrane by producing reactive oxygen species which shows antibacterial activity. ^[4]

Subgingival irrigation: Subgingival irrigation using antiseptic chemicals such as chlorhexidine (CHX), povidone-iodine, or hydrogen peroxide is commonly done alongside scaling and root planing, despite having limitations. Ozone is receiving attention for its antimicrobial effects on various microorganisms without inducing resistance. However, it has a short half-life of approximately 20 minutes and degrades rapidly into oxygen. Ozone nano-bubble water (NBW3) was created to address this limitation using nano-bubble technology. A nano-bubble is a gas nucleus that is smaller than 100 nm in diameter and is created by collapsing a microbubble (50 μm in diameter or less) in the electrolyte at extremely high pressure and temperature. When a physical stimulus is applied in the electrolyte during the collapse of a micro-bubble, the ions in the aqueous solution gather around the gas nucleus, preventing the gas from dispersing (known as the salting-out phenomenon). The ions' characteristics allow the nano-bubble to remain stable in an aqueous solution for an extended period. NBW3 traps ozone gas as gas nuclei and demonstrates antibacterial properties for over 6 months when shielded from UV light. ^[12]

Dental implants: Metal implants and plates are commonly and effectively utilized in surgery to replace teeth and bone. The failure rate is minimal, around 5%. The main cause of failure is insufficient bone growth surrounding the biomaterial immediately after implantation. The implant surface and tissue contact are crucial. The surface properties and shapes are mostly regulated at the micron level, while tissue reaction is mainly influenced by processes controlled at the nanoscale. One potential approach is surface engineering including nanoscale topography and coatings to enhance the osseointegration of implants intended for lifelong functionality. The novel implants, developed using this technology, improve the interaction of nanocoatings that mimic biological materials with the periodontal tissues.

^[13] Chemical coatings involve the application of nanoparticles made from diamond, hydroxyapatite, graphene, titanium oxide, and metalloceramic materials. The Nono Tite BIOMET 3i implants, which are coated with nanohydroxyapatite, are readily accessible in the market and contain around 50% of this material ^[4]. Osteoblast development on a sophisticated implant surface is facilitated by including nanoscale hydroxyapatite and calcium phosphate deposits. ^[13] Implant surfaces coated with titanium oxide nanotubes and silver nanoparticles are designed to combat infection, hence extending the lifespan of the implants. ^[4]

Self-assembling implants: C.X. Li et al. investigated the effectiveness of nanostructured self-assembling dental implants in patients with type II diabetes. They found that these implants showed reduced marginal bone loss and improved osseointegration compared to traditional dental implants.

Bone replacement materials: Bone is a naturally occurring nanostructure primarily consisting of organic substances, particularly collagen. Nanotechnology aims to replicate this inherent structure to create nanobones, which can be utilized in dental applications. ^[4]

1

1. **Ostim (Oartis GmbH, Germany) - HA:** The hydroxyapatite is a pure, nanocrystalline substance that is entirely produced through synthetic means. The crystals have a needle-like form and possess an average crystallite size of 18nm. It undergoes complete degradation following implantation. It has applications in traumatology, orthopedics, spine surgery, and maxillo-facial surgery. ^[4]
2. **VITOSS (Orthovita, Inc., USA):** It is an enhanced iteration of B-Tricalcium Phosphate (B-TCP). It possesses a very porous structure and shares similarities with the main mineral components found in actual bone. ^[4]
3. **NanOss (Angstrom Media, USA):** It is osteoconductive and gradually transforms into human bone. ^[4]

Bone regeneration: Nanostructured biomaterials excel in promoting bone regeneration because of their distinct chemical and physical characteristics. They accurately replicate the structure and nanoarchitecture of bone, while also enabling the recreation of important features of its metabolic environment on a nanoscale level. Scientists have focused on developing nanostructured polymer/ceramic composites that imitate the function and composition of natural bone. Natural bone consists of both organic (mainly type I collagen) and inorganic (mostly multi-substituted HA) components. Bioceramics with calcium and phosphate have been developed, however, due to their inadequate mechanical characteristics, degradability, and porosity, newer bioceramics are now designed at the nanoscale level. The unique mechanical characteristics of polymers and the osteoconductivity of artificial calcium phosphate ceramic phases are combined in nanostructured composites for bone regeneration. ^[15]

Conclusion: The present era is characterized by the prevalence of nanotechnology due to the growing research and utilization of nanotechnology across several fields. The potential for innovative, patient-focused treatments makes nanosciences in dentistry and periodontics highly promising for the future. The research revolving around nanotechnology in dentistry and periodontics in particular is extensive and promises an exciting and enticing future, which will lead to a much efficient growth and development of periodontics and oral implantology.

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