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RESEARCH ARTICLE

NANOTECHNOLOGY IN PERIODONTICS: A REVIEW

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ABSTRACT

Nanotechnology as defined by size is naturally broad, including fields of science as diverse as surface science, organicchemistry, molecularbiology, semiconductor physics, energy storage, engineering, microfabrication, and molecular engineering. The associated research and applications are equally diverse, ranging from extensions of conventional device physics to completely new approaches based upon molecular self-assembly, from developing new materials with dimensions on the nanoscale to direct control of matter on the atomic scale. Nanotechnology has been greatly advanced since the past few decades. The role of nanotechnology in field of dentistry has evolved greatly. The use of various nanoparticles and materials in the field of periodontics has brought a new insight in terms of periodontal regeneration, control of biofilms, in treating dentinal hypersensitivity.

Key words: Implants, Nanodentrifices, Nanorobotics, Nanotechnology, Periodontal Regeneration.

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INTRODUCTION

Nano-technology is the production technology to get the extra high accuracy and ultrafine dimensions, i.e. the preciseness and fineness on the order of 1nm m) 10^{-8} to 10^{-9} m in length - Professor Norio Taniguch[1]. Advances in periodontal science and practice over the last decade have radically modified the understanding of periodontal diseases and have opened new, exciting prospects for both non-surgical and surgical therapy of periodontal diseases.[2] Mechanical methods of subgingival debridement accomplished by thorough scaling and root planing, accompanied by oral hygiene procedures, have served as the gold standard of periodontal therapy for decades.[3] A practical, convenient, and pragmatic way to treat periodontal disease has been the dream of every clinician. However, realization of the dream seems to be elusive. The prime concern in any periodontal treatment is a control over the errant microorganisms and resolution of soft tissue inflammation and restoration of lost alveolar support Resolution of soft tissue inflammation appears to be an established accomplishment after scaling, root planning (SRP) and oral hygiene instructions.[4]

Based on the application, use and technology there are 4 approaches of nanotechnology:[5]

1. Top-down approach (Table: 1)
2. Bottom-up approach (Table: 1)
3. Functional approach
4. Biomimetic approach

Application of Nanotechnology in Periodontics:

Nanorobotic Dentifrices: When properly designed, dentifrobots could identify and destroy pathogenic bacteria residing in dental plaque and elsewhere, while sparing the 500 or so species of harmless oralmicroflora and allowing them to flourish in a healthy ecosystem.[6]Dentifrobots would also provide a continuous barrier to halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodor.[7]Subocclusal dwelling nanorobotic dentifrice which can be delivered by mouthwash or toothpaste could patrol all supragingival and subgingival surfaces at least once a day, metabolizing trapped organic matter into harmless and odorless vapors concomitantly performing continuous calculus debridement.[6]The invisibly small dentifrobots with purely mechanical devices[1–10 micron in size], crawling at 1–10 μ/s, would be inexpensive and would safely deactivate themselves if swallowed and would be programmed with strict occlusal avoidance protocol.[8]Dentifrobots also would provide a continuous barrier to halitosis, since bacterial petrification is the central metabolic process involved in oral malodor.[9]

Hypersensitivity Management: Tooth hypersensitivity is one of the most common problems encountered in clinical practice. It is one of the most painful and least successfully treated chronic problems of the teeth. It has been reported that 8-30% of the adult are affected by dentin hypersensitivity. Several treatment methods have been tried to reduce dentinal hypersensitivity, ranging from home-use, over the counter

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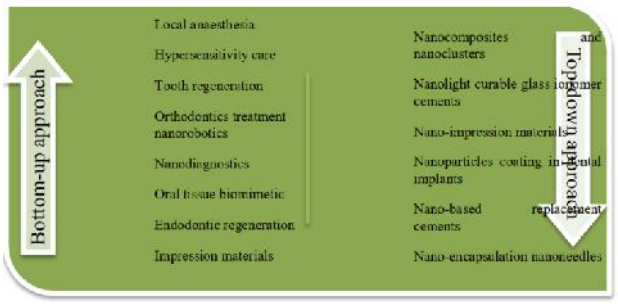


Table 1. Application of top down and bottom-up approach in dentistry

products such as desensitizing mouthwashes, dentifrices, or tray application forms to in-office application products such as varnishes, liners, restorative material, dentinal adhesives, iontophoresis procedures, and more recently, laser. Among the various treatment options, dentifrices have emerged as an important means of treating hypersensitivity.[6] Many of these dentifrices contain potassium nitrate, stannous fluoride, sodium fluoride, sodium mono fluorophosphates, and strontium chloride as an active ingredient and have proven to be effective, leading it to be a frequent choice among both patients and dentists for the treatment of sensitive teeth. The n-HAP-containing toothpaste was effective in reducing dentin hypersensitivity with standard dentifrices tested and could also be advocated in the management of hypersensitivity.[8] Natural hypersensitive teeth have eight times higher surface density of dentinal tubules and diameter with twice as large as non-sensitive teeth. Reconstructive dental nanorobots, using native biological materials, could selectively and precisely occlude specific tubules within minutes, offering patients a quick and permanent cure.[10]

Nanotechnology in dental biofilm: Silver nanotechnology chemistry has proven to be effective against biofilms. Silver disrupts critical functions in a microorganisms.[11]It has high affinity towards negatively charged side groups on biological molecules such as sulfdryl, carboxyl, and phosphate groups distributed throughout microbial cells. Silver attacks multiple sites within the cell to inactivate critical physiological functions such as cell wall synthesis, membrane transport, nucleic acid synthesis (DNA and RNA) and translation, protein folding and function and electron transport.[10]Rapid advances in nanoscale engineering provide opportunities to develop new nanomaterials against virulent biofilms. Nanoparticles can carry and selectively release antimicrobial agents after attachment or within oral biofilms, resulting in their disruption.[6]The mechanism involves “smart release” of agents when triggered by pathogenic microenvironments (e.g., acidic pH or low oxygen levels) for localized and controlled drug delivery to simultaneously kill bacteria and dismantle the biofilm matrix.[8]

Drug Delivery: Chemotherapy in the management of periodontal diseases has a significant albeit adjunctive effect.[12] Systemic antimicrobials are found to be beneficial in the treatment of chronic and aggressive forms of periodontal disease.[13] Among all groups of antibiotics, a combination of amoxicillin and metronidazole was found to be most effective use of systemic antibiotics, however, leads to high propensity for antibiotic resistance, non-compliance to the regimens, possibility of adverse drug reactions, and a very high dosage.[6]Periodontitis can be treated by local drug delivery systems as well.[14]This approach is more favorable as compared to systemic approach because it mainly focuses on improving the therapeutic outcomes by achieving factors like site-specific delivery, low-dose requirement, bypass of first-pass metabolism, reduction in gastrointestinal side effects, and decrease in dosing frequency.[15]Overall, it provides a safe and effective mode of treatment, which enhances patient compliance. Poor oral bioavailability of conventional oral formulations, has paved the way for new therapeutic options, like the use of nanotechnology for drug delivery. A number of polymer-based delivery systems like films, chips, strips, fibers, microparticles, nanofibers, and nanoparticles made from a variety of natural and synthetic material shave been successfully tested to deliver a variety of drugs.

These systems are biocompatible and biodegradable and have strong retention on the target site due to excellent muco-adhesion properties.[6] Triclosan-loaded nanoparticles developed by Pinon-Segundo *et al* (2005)[16],have emerged as a new delivery system for the treatment of periodontal disease. Drugs can be incorporated into nanospheres composed of a biodegradable polymer. The nanoparticles were prepared using poly (D, L-lactide-coglycolide), poly (D L-lactide) and cellulose acetate phthalate. Poly (vinyl alcohol) was used as stabilizer.[17]These triclosan nanoparticles behave as a homogeneous polymer matrix-type delivery system, with the drug (triclosan) molecularly dispersed. A preliminary in vivo study using these nanoparticles has been performed in dogs with only the gingival index (GI) and bleeding on probing (bleeding on probing) being determined. With respect to the gingival index (GI), at days 1 and 8, it was found that a severe inflammation was detected in control and experimental sites. It was concluded that triclosan nanoparticles were able to effect a reduction of the inflammation of the experimental sites.[18] Timed release of drugs may occur from biodegradable nanospheres. This enables timely release of the drug as the nanospheres degrade and specific site drug delivery.[19] For exemplification, restininin which tetracycline is incorporated into microspheres for drug delivery by local means to a periodontal pocket.[20]Another example is Arestin in which tetracycline is incorporated into microspheres for drug delivery by local means to a periodontal pocket.[10]

Oral prophylaxis: Nanorobots incorporated in mouthwash could identify and destroy pathogenic bacteria leaving behind harmless oral flora to flourish in the oral ecosystem.[21] It would also identify food particles, tartar, plaque from the teeth. Being suspended in liquid and able to swim about, they reach surfaces beyond bristles of tooth brush or the fibers of floss.[22] Continuous debridement of supra and sub gingival calculus would be done by nanorobots incorporated in dentifrices.[10]

Nanoparticles: An emerging therapeutic strategy is the use of nanoparticles as drug carriers. The factors that make nanoparticles more advantageous than microparticles, microspheres, and emulsion- based delivery systems are: they are particulate dispersions or solid particles with a size range from 10–1000 nm, the drug is dissolved, entrapped, encapsulated, or attached to a nanoparticle matrix, they are highly dispersible in aqueous medium, offer controlled release rate and enhanced stability.[23]Because of their small size, nanoparticles can access sites unreachable for other devices, like the periodontal pocket regions below the gingival margin.[6]A uniform drug distribution for prolonged time period is obtained, thus decreasing the dosage frequency.[8]

Perio Protect: Perio Protect is a comprehensive method that is customized for individual patients to help manage biofilms, growing in the spaces or pockets between teeth and gum tissue.[24] The overall goal of the Perio Protect Method is to manage oral biofilm by minimally invasive method.[2] This includes a combination of treatments, including a non-invasive chemical debridement used in conjunction with traditional mechanical debridement procedures. The chemical therapy involves a tray delivery of doctor-prescribed solutions to chemically debride biofilm from the periodontal pocket and alter the pocket's microbiological environment to disrupt biofilm growth.[25]

Magnetic Nanoparticles: Among the many types of nanostructures, core-shell magnetic iron oxide nanoparticles are the most commonly used drug carriers in biomedical studies. Chlorhexidine (CHX) a second-generation bis-biguanide antiseptic, acts on the inner cytoplasmic membrane; hence, it is a membrane active type of substance.[26] It prevents plaque accumulation; hence, it is an antiplaque and anti-gingivitis agent and reduces the adherence of *Porphyromonas gingivalis* to epithelial cells.[27] It can be bacteriostatic or bactericidal depending on the dose. It acts against a wide array of bacteria including Gram-positive and Gram-negative bacteria, dermatophytes, and lipolytic viruses and fungi.[28] However, CHX application is limited due to inactivation in body fluid and cytotoxicity toward human cells, especially at high concentrations.[29] To overcome the limitations of CHX, Tokajuc et al (2017)[29], synthesized nanosystems composed of amino silane coated magnetic nanoparticles functionalized with chlorhexidine (MNP@CHX). In the presence of human saliva, MNPs@CHX displayed significantly greater bactericidal and fungicidal activity against planktonic and biofilm-forming microorganisms than free CHX.[29] In addition, CHX attached to MNPs has an increased ability to restrict the growth of mixed-species biofilms compared to free CHX. The observed depolarization of mitochondria in fungal cells treated with MNP@CHX suggests that induction of oxidative stress and oxidation of fungal structures may be a part of the mechanism responsible for pathogen killing. Nanoparticles functionalized by CHX did not affect host cell proliferation or their ability to release the pro-inflammatory cytokine, IL-8. The use of MNPs as a carrier of CHX has great potential for the development of antiseptic nanosystems. Apart from CHX numerous drugs like tetracycline, doxycycline, metronidazole, silver, and Harungana Madagascariensis leaf extracts can also be used as nanoparticle drug delivery systems to treat periodontal diseases.[8]

Nanofibers: Polymeric fibers having diameters in submicron or nanometer range (e.g. 10 × 103 100 × 103 mm) are called nanofibers. They provide numerous remarkable characteristics such as: very large surface area to volume ratio (this ratio can be as large as 103 times that of microfiber), Suppleness in surface functionalities, and superior mechanical performance (e.g., stiffness and tensile strength).[30]Nanofibers can be prepared by drawing, template synthesis, phase separation, self- assembly, and electrospinning.[31]Among this, electrospinning has been accepted as an efficient technique for the fabrication of continuous nanofibers from a variety of polymers.[32] These polymers can either be first dissolved in suitable solvent and then electro spun or can be directly electro spun in molten form. Both hydrophobic and hydrophilic drugs can be incorporated. Polymers can be fabricated to form nanofibrous scaffolds and seeded with various cells.[33]

Due to high surface area, porosity, and resemblance of this 3D structure to natural extracellular matrix, they enable cell adhesion and provide a nano-environment for cellular growth and function. This has led to their wide application in tissue engineering.[8]

Zinc Oxide (ZnO) Nanoparticles: Zinc oxide (ZnO) nanoparticle-coated titanium disks have demonstrated anti-adhesion properties. These ZnO modified surfaces reduce viable bacteria like *S. aureus* and streptococci without cytotoxic effect on osteoblasts and human mesenchymal cells.[33]

The use of metal oxide nanoparticles to coat implants could provide osteoconductive and antimicrobial functionalities to prevent failure.Nevertheless, it may be difficult preventing bacterial adhesion altogether in the complex oral environment. The benefits of ZnO nanoparticles in the presence of saliva and other host-derived components as well as a complex microbiota are yet to be proven clinically.[8]

Silver Nanoparticles (AgNPs)[34]: The use of AgNPs for surface modification has recently emerged as a promising approach. AgNPs exhibited both high anti-adhesion and antibacterial actions against *Streptococcus mutans* when they were coated on the surface of methacrylate resinsin vitro. The AgNPs coatings can induce death of bacteria either through cell membrane nanoparticle interactions or through secondary effects induced by long-term released AgNPs or Ag+ ions, by the production of reactive oxygen species, by alteration of the membrane integrity, and by protein-site-specific interactions that could prevent DNA replication. The concentration of dissolved oxygen has a direct implication on the AgNPs dissolution via the Ag0 oxidation, and a low (or absence of) antimicrobial activity has been reported in anaerobic conditions.[8]

Nano-hydroxyapatite-Modified Surfaces

• Surfaces modified by hydroxyapatite nanorod arrays exhibited antibacterial activity against *S. aureus* and *Escherichia coli* (significantly superior to titanium surfaces) and induced no cytotoxic effect toward human bone marrow stromal cells.[8]

Bone replacement materials: Hydroxyapatite nanoparticles used to treat bone defects ensures homogeneity.

E.g., Ostim® (Osartis GmbH, Germany) HA, VITOSS® (Orthovita, Inc., USA) HA + TCP, NanOss™ (Angstrom Medica, USA) HA

Other Coatings with Anti-adhesion and Antibacterial Properties: Hexametaphosphate associated with chlorhexidine also displayed antibacterial effects when coating pure grade II titanium. The antimicrobial efficacy of the coated surfaces appears to be associated with long-term release of chlorhexidine, which was capable of inhibiting the growth of *Streptococcus gordonii*, an early colonizer.[6]Graphene oxide (GO) has shown to have anti-adhesion and antibacterial properties. The mechanism in which GO induces antimicrobial effects is not yet fully understood, although the size of the GO sheet appears to play an important role.[8]

Nanotechnology and dental implants: One of the challenges in implantology is to achieve and maintain the osseointegration

as well as the epithelial junction of the gingiva with implants. An intimate junction of the gingival tissue with the neck of dental implants may prevent bacterial colorizations leading to peri-implantitis while direct bone bonding may ensure a biomechanical anchoring of the artificial dental root.[35]Nanotechnology could be utilized to create surfaces with controlled topography and chemistry that would assist understanding biological interactions and developing novel implant surfaces with predictable tissue-integrative properties.
Advances in the fabrication of nanoparticles for coating the implant surface and the nano-patterning of dental implants is leading to better osseointegration and improved physiologic functions ofimplants.[36] The improvement of the bone-forming activity at the bone-implant interface is committed to nanoscale features that have the ability to induce the differentiation of stem cells along the osteogenic pathway that contributes to the mimicry of a cellular environment that favors the process of rapid bone accrual. It also affects the chemical reactivity of the endosseous implant surface and alters its ionic and biomolecular interactions with the surface that leads to enhanced osseointegration.[37] Nanophase HA – the main component present in the hard tissues of the body – represents a promising class of maxillofacial implant formulations with improved Osseo integrative properties.[38]Coating titanium dental implant surface with nanocrystalline HA powders will improve overall dental implant performance. Osteointegration of dental implants is better achieved because adhesion and proliferation of osteoblasts are significantly greater on nanophase HA.[39]Also, apart from nanostructured HA, both nanophase alumina and titania demonstrate the same improved osseo-integrative properties with dental implants. These new coating technologies for applying nanoparticles of HA and related calcium phosphates (CaP) onto the surface of implants have been shown to provide titanium implants with an osteoconductive surface.[40]

Stem cells are extremely sensitive to their nano-environment, and topography is important for tissue-specific differentiation. It is known that the macrophage is the dominant cell in the foreign body response. Once it attaches to an implanted material, single macrophage cells fuse to form multinucleated giant cells. This response is accompanied by the recruitment of fibroblasts and thus fibrous tissue formation at the implant-bone interface. The adherence of giant cells to the implant surface is also associated with the release of enzymes and other bio reactive intermediates that can degrade and cause a loss of implant osseointegration. Nanofeatures of dental implant surfaces are therefore critical in the achievement of osseointegration beyond what is possible with conventional titanium implants. A great variety of techniques using chemical and physical processes are used to create nanofeatures on dental implant surfaces. Chemical processes involve anodic oxidation or titanium etching with a solution of strong acids, *e.g.*, sulfuric acid (H_2SO_4) − hydrogen peroxide (H_2O_2), at a constant temperature and for a specific duration. Physical modifications involve plasma spraying to coat the implants with nanoparticles or blasting with microscopic particles to create a porous layer on the implant surface.[38]

Nanoscale alteration of titanium implant surfaces can alter cellular and tissue responses that may promote osseointegration. Three nanostructured implant coatings have been developed:

• ***Nanostructured Diamond:*** It has ultrahigh rigidity, improved toughness, low friction, and good adhesion to titanium alloys.
• ***Nanostructured Hydroxyapatite Coatings*****:** This is used to achieve the desired mechanical characteristics and enhanced surface reactivity and has been found to increase osteoblast adhesion, proliferation, and mineralization.
• ***Nanostructured Metallo-Ceramic Coatings:*** These offer continuous variation from a nano crystalline metallic bond at the interface to the hard- ceramic bond on the surface. Besides surface contact area and surface topography, bone bonding, and stability play a major role in implant success and osseointegration. Bone growth and implant success could also be accelerated by the use of nanotechnology. Osteoblast configuration on a more complex implant surface is produced by the addition of nanoscale deposits of hydroxyapatite and calcium phosphate particles. Material engineering, and hence implant dentistry, has advanced extensively on the basis of researches conducted on the effects and subsequent optimization of micro-topography and surface chemistry. These new implants constructed on the basis of this technology are more acceptable as they enhance the integration of nano-coatings resembling biological materials to the periodontal tissues. In addition, implant surfaces coated with titanium oxide nanotubes and laced with silver nanoparticles serve the purpose of fighting infection, thus increases the shelf life of the implants.

Nanotechnology in the Management of Peri-implantitis: Peri-implantitis affected parts become covered by an infected smear layer of instrumentation debris after routine implant preparation, which seems to compromise fibrin clot adhesion to such altered surfaces. In addition, continuous flap mobility and early clot retraction could draw the clot-blended graft complex away from the implant surface with subsequent creation of a micro-gap graft, epithelialization, and eventual implant surface recontamination. For that reason, treating a peri-implantitis affected implant surface should include complete removal of the infected biofilm and the smear-like layer, resulting in complete exposure of the roughened titanium implant surface. This should be followed by maximizing clot-blended graft adhesion to the implant surface through application of a graft material with a particle size smaller than that of the implant surface pores. Such mechanical integration is considered to reduce the possibility of the implant bone micro-gap, a factor that could ensure complete protection of the underlying defect-filled regenerative materials or blood clot. Particle size seemed to be an important factor that optimizes adhesion of particles to the exposed implant surface. Such improved adhesion is likely to retard the apical migration of the epithelial attachment, a factor that could enhance re-osseointegration. Further peri-implantitis affected surface conditioning with citric acid improves nanoparticle-sized hydroxyapatite-blended clot adhesion to titanium implant surface.

Growth factors such as platelet-derived growth factor Nano-biomaterials and their role in periodontal rehabilitation (PDGF) have significantly enhanced periodontal therapy outcomes with a high degree of variability, mostly due to the lack of continual supply for a required period of time. One method to overcome this barrier is gene therapy. Platelet-derived growth factor, PDGF-B gene delivery in fibroblasts using nanosized calcium phosphate particles (NCaPP) as vectors, has found to significantly enhance fibroblast proliferation.[41]

Nanophase materials: These are promising materials for various bio-applications as human tissues themselves are composed of nanometer components.

- Nanophase hydroxyapatite Osteoblastic adhesion and growth are vastly increased on nanophase hydroxy apatite (HA) than on traditional HA. In addition, nanophase alumina and titania also show similar features. Hydroxyapatite nanoparticles used to treat bone defects are:
- *Ostim HA (Osartis GmbH, Germany)*
- *Vitosso (Orthovita, Inc) HA + TCP (tricalcium phosphate)*
- *NanOSSTM HA (Angstrom Medica).*[42]

Prosthetic Implants: Nanotechnology would aid in the development of surfaces with definite topography and chemical composition leading to predictable tissue-integration. Tissue differentiation into definite lineage will accurately determine the nature of peri-implant tissues. In addition, antibiotics or growth factors may be incorporated as CaP coating is placed on Ti implants.[43]

Eg: Nanotite™ Nano-Coated Implant.

Advantage of nanodentistry:[44]

- **Prevention:** by using nanosized particles in dentifrices and mouthwashes
- **Disease diagnosis:** by using nanosized quantum dots based on immunofluorescence, that enable the labelling of specific bacteria and thus eases their identification and removal.
- **Restorative dentistry:** by using nanofillers that reduce the polymerization shrinkage and thermal expansion, and enhance the polishing ability, hardness, and wear resistance of composites
- **Regenerative dentistry:** concerning bone grafting, guided tissue regeneration, tissue engineering, nerve regeneration
- **Rehabilitative dentistry:** dental implants that use implant surface nanotextured with titanium.
- Nano-anesthesia by using nanorobots
- Treatment of oral cancer with nano shells and nanoparticle-coated, radioactive sources placed close to or within the tumor.[44]

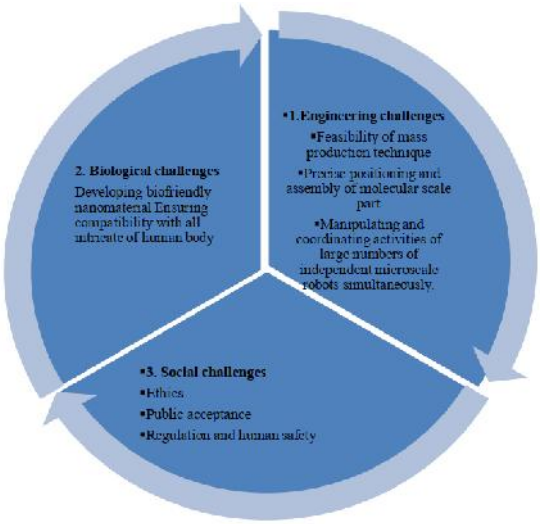
Disadvantages: Nanotoxicology, is defined as the evaluation of the safety of engineered nanostructures and nanodevices.[45] The workers occupied in nanotechnology activities may be the first persons involved.

Fig. 1. Physicochemical properties of engineered nanomaterials leading to nanotoxicology[46]

Researchers, technicians, cleaners, workers involved in production, transport or storage, emergency responders to disasters of nanomaterials and possibly medical staff involved in the filed may be exposed to these potential xenobiotic. Epidemiologic studies on workers handling nanomaterials found a depression of antioxidant enzymes and increased expression of cardiovascular markers.[46,47] Figure. 1illustrates a range of possible physicochemical properties of engineered nanomaterials leading to nanotoxicology.

The size of the nanoparticles selects the place of their vital impact in the body; in humans, large inhalable materials with particle size above 2.5 μ will mostly deposit on nose and throat, but nanoparticles locate in deeply into the respiratory tract, and can pass through the lungs into the bloodstream and reach potentially susceptible sites such as the liver, spleen, kidney, brain and heart. There were also found unwanted influences because of the dissolution of nanoparticles in body fluids such as in the environment of the stomach, blood and airways.[44] Nanoparticles can interact with complex networks of immune cells located within and beneath epithelial surfaces and these NPs can act as allergens during the neonatal period, triggering the immune system to induce allergic inflammation in later life stages. Detrimental cardiovascular consequences due to NPs exposure have been reported in epidemiological studies. Wang and their group reported that nano-cerium-element doped titanium dioxide induces apoptosis of Bel 7402 human hepatoma cells in the presence of visible light. Nanoparticles like zinc oxide and sunscreen titanium dioxide can cause oxidative damage to DNA in vitro and in cultured human fibroblasts. Inhaled ultrafine particles (UFPs) can increase access to the blood stream and can then be dispersed to other organs in the body; this has been shown for synthetically produced nanoparticles such as C60 fullerenes which accumulate in the liver. Even big particles outside the 'nano' range can enter the stratum corneum of human skin and get to the epidermis and occasionally the dermis and may be taken up into the lymphatic system. There is a strong possibility that nanoparticles can be assimilated into the body through the lungs, skin and gastrointestinal tract. Additionally, studies have been conducted in investigating the dissolution of nanoparticles in artificial body fluids such as fluids representing the environment of the stomach, blood and airways and found adverse influences.[48]

CHALLENGES FACED BY NANODENTISTRY:



Nano-Hazards

Since nanotechnology is a very recent discovery and is only just being put in to use, there are issues that need to be addressed. As long-term effects of nanotechnology are unknown, therefore, potential hazards caused by the nanotechnology might not show for many years. Various factors govern the number of free Nanoparticles in nature such as their physio-chemical properties, quantity, and time of exposure. Nanomaterials released in the environment can be further modified by temperature, pH, different biological conditions, and presence of other pollutants. It has been reported that nanomaterials can enter the human body through several ports. Accidental or involuntary contact during production or use is most likely to occur via the lungs and skin, from which a rapid translocation is possible to other vital organs through the bloodstream. Carbon black Nanoparticles have been implicated in interfering with cell signaling. It could also have unwanted effects on the DNA of cells, which could potentially cause genetic defects if this were to happen it would take a lot of time and research to put right. There is a need for developing systemic solutions, monitoring, and recording of the potential hazard as well as finding timely responses in order to achieve safety for human health and the environment.[18]

Problems for Research in Nanotechnology in India: The production and application of Nanorobots in India might find the following problems: poor and slow strategic decisions, inappropriate funding, lack of involvement of private agencies, inadequate trained manpower and problem of retaining them.[49] Humankind has been exposed to airborne nanosized particles throughout their evolutionary stages, but only with the industrial revolution such exposures have increased dramatically because of anthropogenic sources (internal combustion engines and many other sources of thermodegradation).[50] The expanding field of nanotechnology increases the number of sources for human exposures to nanoparticles by different routes: inhalation (respiratory tract), ingestion (gastrointestinal tract), dermal (skin) and injection (blood circulation).[38] Regarding the dermal route invasion by nanoparticles there are involved sunscreen lotions, skin care lotions, paints and coatings, sealants, air fresheners (spray). The lungs can be invaded by nanomaterials from inhaling paints and coatings, skin care sprays, sunscreen sprays, food additives and colorings. The gastrointestinal tract can be a host for nanoparticles from food supplements, health supplements, food packaging.[46]

FUTURE SCOPE

Research has to be done in the field of nanoparticles for its application in various aspects, which were previously thought to be impossible in medicine and therapeutics, in drug delivery and gene therapy, in the development of nano-tweezers for cell surgery, in detection and modification of molecular signaling and for patient-specific treatment.

REFERENCES

1. Selvakumar J, Radhika B, Shamini S, Mahendra J, Preethi R, Shyma, MN, Poorani R.. Emerging Nanotechnologies in Dentistry: A Review. *World J Pharma Res* 2019 8(13): 599-620.
2. Arpita R, Swetha JL, Babu MR, Sudhir R. Recent trends in non-surgical periodontal care for the general dentist-a review. *Bangladesh J Dent Res Educ* 2014:4(2): 78-82.
3. Adams D, Hinrichs J, Claffey N. Non-surgical pocket therapy: mechanical, pharmacotherapeutics, and dental occlusion. *J Am Dent Asso* 1998; 129: 34-S-9-S.
4. Kumar AJ, Anumala N, Avula H. Novel and often bizarre strategies in the treatment of periodontal disease. *J Indian Soc Periodontol*, 2012; 16: 4.
5. Kapoor SM. 2017. Nanodentistry. The IDA Times Mumbai 8.
6. Arjunkumar R. 2018. Nanomaterials for the management of periodontal diseases. Dental Applications of Nanotechnology. Springer, p. 203-15.
7. Freitas Jr RA. Nanodentistry. *J Am Dent Asso* 2000;131: 1559-65.
8. Chaughule RS.. Dental Applications of Nanotechnology. Springer. 2018
9. Jan SM, Mir RA, Behal R, Shafi M, Kirmani M, Bhat MA.Role of nanotechnology in dentistry. Sch *J App Med Sci* 2014; 2(2D): 785-9.
10. Hemalatha R, Sivachandran A, Kalaivani R. Nanotechnology - A Novel Strategy in Periodontal Regeneration. *Int J of Med Biosci* 2014; 3: 26-8.
11. Morones-Ramirez, J. R. J. A. Winkler, C. S. Spina, J. J. CollinsSilver enhances antibiotic activity against Gram-negative bacteria. Sci Transl Med 2013; 5(190): 1-11.
12. Addy M and Renton-Harper P. Local and systemic chemotherapy in the management of periodontal disease: an opinion and review of the concept. *J oral rehab* 1996; 23(4): 219-31.
13. Pejčić A, Kesić L, Obradović R, Mirković D.. Antibiotics in the Management of Periodontal Disease. *Acta facultatis medicae Naissensis* 2010; 27.
14. Jayakaran TG, Arjunkumar R. Nanocomposite hydrogels as local drug delivery in periodontics. *J Pharmac Sci and Res* 2013; 5(12): 277-278.
15. Joshi D, Garg T, Goyal AK, Rath G. 2016. Advanced drug delivery approaches against periodontitis. *Drug delivery* 23: 363-77.
16. Pinon-Segundo E, Ganem-Quintanar A, Alonso-Pérez V, Quintanar-Guerrero D. Preparation and characterization of triclosan nanoparticles for periodontal treatment. Int J Pharmaceut 2005;294: 217-32
17. Sinha V, Bansal K, Kaushik R, Kumria R and Trehan A. Poly-ϵ-caprolactone microspheres and nanospheres: an overview. *Int J Pharmaceut 2004;* 278: 1-23.
18. Kong LX, Peng Z, Li SD, Bartold PM. Nanotechnology and its role in the management of periodontal diseases. Perio 2000 2006; 40(1): 184-96.
19. Kamaly N, Yameen B, Wu J and Farokhzad OC. Degradable controlled-release polymers and polymeric nanoparticles: mechanisms of controlling drug release. Chemical reviews 2016; 116: 2602-63.
20. Manjunath RG, Rana A. Nanotechnology in periodontal management. J Adv Oral Res 2015; 6(1): 31-8.
21. Patil M, Mehta DS, Guvva S. Future impact of nanotechnology on medicine and dentistry. J Indian Soc Periodontol 2008; 12(2): 34-40.
22. Balan B, Narayanan S. Nano robotics-its time for change. Int J Oral Care Res. 2014; 2: 41-6.
23. Mohanraj V, Chen Y. Nanoparticles-a review. Tropical J Pharmaceut Res 2006; 5: 561-73.

24. Schaudinn C, Gorur A, Keller D, Sedghizadeh PP, Costerton JW. Periodontitis: an archetypical biofilm disease. J Am Dent Asso 2009; 140: 978-86.
25. Mushtaq A. Newer non-surgical modalities in the periodontal therapy. 2017.
26. Bhardwaj A, Bhardwaj A, Misuriya A, Maroli S, Manjula S, Singh AK. Nanotechnology in dentistry: Present and future. J Int Oral Health 2014; 6(1): 121-6.
27. Eley B. Antibacterial agents in the control of supragingival plaque—a review.British Dent J 1999; 186: 286-96.
28. Kolliyavar B, Shettar L, Thakur S. Chlorhexidine: The gold standard mouth wash. J Pharmaceut Biomed Sci. 2016; 6.
29. Tokajuk G, Niemirowicz K, Deptuła P. Use of magnetic nanoparticles as a drug delivery system to improve chlorhexidine antimicrobial activity. Int J Nanomed 2017; 12: 7833
30. Sharma R, Singh H, Joshi M. Recent advances in polymeric electrospun nanofibers for drug delivery. Crit Review Therape Drug Carrier Syst. 2014; 31.
31. Almetwally AA, El-Sakhawy M, Elshakankery M, Kasem M. Technology of nano-fibers: Production techniques and properties-Critical review. J Text Assoc 2017; 78: 5-14.
32. Huang Z-M, Zhang Y-Z, Kotaki M and Ramakrishna S. A review on polymer nanofibers by electrospinning and their applications in nanocomposites. Composites science and technology. 2003; 63: 2223-53.
33. Zhang Q, Li Y, Lin ZYW. Electrospun polymeric micro/nanofibrous scaffolds for long-term drug release and their biomedical applications. Drug Discovery Today. 2017; 22: 1351-66.
34. Abou El-Nour KM, Eftaiha Aa, Al-Warthan A and Ammar RA. Synthesis and applications of silver nanoparticles. Arab J Chem 2010; 3: 135-40.
35. Deepa D, Arunkumar K. Nanobiomaterials and Their Role in Periodontal Rehabilitation. Dental Applications of Nanotechnology. Springer, 2018, p. 23-35.
36. Dizaj SM, Rad AA, Safaei N. The Application of Nanomaterials in Cardiovascular Diseases: A Review on Drugs and Devices. J Pharmacy Pharmaceut Sci 2019; 22: 501-15.
37. Gittens RA, McLachlan T, Olivares-Navarrete R. The effects of combined micron-/submicron-scale surface roughness and nanoscale features on cell proliferation and differentiation. Biomaterials 2011; 32: 3395-403.
38. Ogle OE, Byles N. Nanotechnology in dentistry today. West Indian Med J 2014; 63(4): 344-8.
39. Elias CN, Meirelles L. Improving osseointegration of dental implants. Expert review of medical devices 2010; 7: 241-56.
40. Zhao L, Huo K, Chu PK. Titania Nanotube Coatings on Dental Implants with Enhanced Osteogenic Activity and Anti-Infection Properties. In Nanobiomaterials in Clinical Dentistry 2012; 337-57. Elsevier Inc.
41. Subramani K, Lavenus S, Rozé J, Louarn G, Layrolle P. Impact of nanotechnology on dental implants. Emerging Nanotechnologies in Dentistry. Elsevier, 2018, p. 83-97.
42. Kanaparthy R, Kanaparthy A. The changing face of dentistry: nanotechnology. Int J nanomed. 2011; 6: 2799-804
43. Halkai KR, Mudda JA, Shivanna V, Rathod V, Halkai R. Biosynthesized silver nanoparticles from fungi as antimicrobial agents for endo-perio lesions – A review. Annu Res Rev Biol 2016; 10: 1-7.
44. Gavrilescu CM, Paraschiv C, Horjinec P, Sotropa DM, Barbu RM. The advantages and disadvantages of nanotechnology. Romanian J oral rehab2018; 10(2): 153-9.
45. Oberdörster G, Oberdörster E, Oberdörster J. Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. Environmental health perspectives. 2005; 113(7): 823-39.
46. Viswanath B, Kim S. Influence of nanotoxicity on human health and environment: The alternative strategies. In Reviews of environmental contamination and toxicology. 2016; 61-104. Springer, Cham
47. Jennifer M, Maciej W. Nanoparticle technology as a double-edged sword: cytotoxic, genotoxic and epigenetic effects on living cells. J Biomater Nanobiotech 2013; 4(1): 53-63.
48. Utembe W, Potgieter K, Stefaniak AB, Gulumian M. Dissolution and biodurability: Important parameters needed for risk assessment of nanomaterials. Particle and fibre toxicology 2015; 12: 1-12.
49. Dalai D, Bhaskar D, Agali C, Singh N, Gupta D, Bumb S. Futuristic application of nano-robots in dentistry. Int J Adv Health Sci. 2014; 1: 16-20.
50. Smeets R, Stadlinger B, Schwarz F. Impact of dental implant surface modifications on osseointegration. BioMed Res Int 2016;1-16

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