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IMPORTANCE & APPLICATIONS OF NANOTECHNOLOGY

Nanotechnology - A Boon to Prosthodontics

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Introduction

Nano means dwarf and nanometer is 10^{-9} or billionth of meter. Nano-technology is manipulation of atom of nano size [1-4] which was advocated by Nobel Laurete Richard Feynman in 1959 [5,6]. Eric Drexler in mid1980 highlighted the importance of nanotechnology [7].

Nanodentistry is defined as the science that deals with the maintenance of oral health through the application of nanomaterials, tissue engineering and nanorobotics. Prosthodontics is a branch of dentistry related to replacement of missing tooth and facial defects with artificial prosthesis [8-11]. Also nanocomposites, alloys and resins have been used in prosthetic dentistry due to their improved mechanical properties. Basic concepts one nanometer (nm) is one billionth, or 109, of a meter. The bond and distance between the atoms are from 0.12 to 0.15 nm, and the diameter of the DNA is around 2 nm [12].

There are many nanoparticles like nanotubes, nanopores, nanodots, nanowires, nanobelts, nanorods, nanospheres and nano capsules were used in dentistry [13]. Nanomaterials constituents are less than 100 nm, with significant clinical performance, different optical, magnetic and chemical property. Also they assemble themselves into different pattern without other particle participation [14].

Classification of nano-materials

The general classification of nano-materials based on the nature [15-20].

1. Organic nano-materials

1. Polymer based nano-materials: They are non-toxic and have nanosphere or nano-capsule shapes, which can be easily activated.
2. Lipid-based nano-materials: These nano-materials are size between 10 to 1000 nm and used in bio-medical application. They have solid core made of lipophilic molecules and the surfactants on the outer aspect.

2. Inorganic nano-materials

1. Metal: They are derived from precursors of metal.
2. Metal oxide nano-materials. Metal oxide nano-materials are synthesized because of higher reactivity and effectiveness like Cerium Oxide (CeO_2), Zinc Oxide (ZnO), Aluminium Oxide (Al_2O_3), Titanium Oxide (TiO_2), Magnetite (Fe_3O_4), Iron Oxide (Fe_2O_3), and Silicon Dioxide (SiO_2).

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3. Ceramic nano-materials: These are inorganic nonmetallic materials obtained by heating and cooling process and they have a wide application in prosthodontic dentistry.

4. Semiconductor nano-materials. Their properties are in between metals and non-metals. They are widely used in electronic devices.

3. Carbon based nano-materials: They are carbon nanotubes, nanofibers and nanocarbon blocks.

Classification of nanoparticles [21,22]

1. Basis of origin: A. Natural B. Artificial.

2. Basis of dimension: Zero dimensional or nano size, one-dimensional or nanorods, and two-dimensional or thin films.

3. Basis of structural configuration: Carbon based nanoparticles, metal nanoparticles, dentrimers and composite resin.

Synthesis of nanomaterials

The two methods used for synthesis are Top down and bottom up method.

1. **Top-down synthesis:** The nano size materials brought by milling, sputtering, laser ablation and thermal decomposition. They have a wide application in medical and dental field.

2. **Bottom up method:** Nanomaterials are produced by addition method by chemical vapor deposition, sol-gel, spinning, pyrolysis, and biosynthesis.

Availability of nanomaterials

Nanomaterials are available in powder, fiber, tube, membrane and block form. Nanoparticles have been used from beginning and the most developed form [23].

Nanofibers: Silicate nanofibers have been used for reinforcement of composite resin. They improve the mechanical and physical properties of composite resin.

Dendrimers: They are macrosize particles manufactured by the series of specific polymers surrounding the core to improve the efficiency of the material [24].

Nanopores: Titanium nanopores are 30 nm in size which facilitae osseointegration of dental implants [25].

Nanoshells: They are beads coated with gold by layering method, which absorb infra-red light which is lethal to cancer cells [26].

Nanotubes: Titanium oxide nano tube is the most commonly used material, which facilitate the formation of bone thereby increasing the osseointegration potential.

Nanorods: Their size is similar to enamel rod [27].

Nanoparticles: These are the commonly used materials in prosthodontic dentistry with 0.1 -100 nm.

1. **Zno nanoparticles:** These nanoparticles release Zinc ion which affect the membrane of a cell. The advantages are photocatalytic activity, high stability, bactericidal effects on both Gram positive and Gram negative bacteria and bacterial pores in high temperature and pressure [28-33].

2. **Au nanoparticles:** Liquid chemical method is used to produce gold nanoparticles by Chloroauric acid ($HAuCl_4$) reduction [34]. They are utilized in immunochemical studies and detection of protein interactions and detection of cancer cells and different kinds of bacteria by Gold nanorods [35,36]. The advantges are nontoxic, not inducing any ROS related process, high ability functionalization,polyvalent effects ease of detection and photothermal activity [37-40].

3. **Silver nanoparticle**: Silver nanoparticles are obtained by reducing the Silver ions at 800 degree to 1000 degree [41]. The antibacterial property is because of alteration of hydrogen bond ,unwinding of DNA and disturbance of synthesis of cell wall [42]. Silver ions are reactive and alter the structure of bacterial cell wall and nuclear membrane leads to cell death [43]. {111} faces particles are highly dense and reactive. Antiviral, antifungal and antimicrobial action of silver nanoparticle is due to the release of bioactive silver ions which will react with the membranes of bacteria and fungai [44]. Silver nanoparticles are smaller and insoluble and exhibit high antibacterial activity [45-48]. They pierce the cell wall of the bacteria and alter the membrane leads to cell death [49].

4. **TiO_2 nanoparticles:** The production of reactive oxygen species leads to increase the membrane fluidity thereby disintegrate the cell wall. The advantages are suitable photocatalytic properties, high stability, effective antifungal for fluconazole resistant strains [50-54].

5. **Si nanoparticles**: These nanoparticles affect the cell functions like adhesion,spreading etc.The advantages are non-toxicity, stability [53,55,56].

6. **CuO nanoparticles:** Copper oxide nanoparticles are produced by reduction of copper sulphate by microwave irradiation [57]. They are usually 1 to 10 nm with antifungal and antibacterial effect [58-59]. They can be applied to biosensors and electrochemical sensors [60]. They also serve as antifungal or antibacterial agents [61]. The advantages are effective against Gram positive and Gram negative bacteria, high stability, antifungal activity [31,62,63].

7. **MgO and CaO nanoparticles**: These nanoparticles damage the cell membrane which causes oozing of the intracellular content leads to bacterial death.The advantages are harmful effect on Gram positive and Gram negative bacteria, high stability, low cost and availability [56,63-66].

Organic nanoparticles: Chitosan nanoparticles: Chitosan poly, (1,4) ß_d glucopyranosamine), a derivative of chitin, the second most abundant natural biopolymer, obtained from crustaceans and shrimps. The structure of chitin is similar to cellulose, due to its chelation property it destroy the enzyme activity of bacterial cell.

Poly (lactic) coglycolic acid: They are commonly used as nanoparticles encapsulted photoactive drugs, which had antimicrobial activity [67].

Nonorganic nanoparticles

Bioactive glass nanoparticles: They consists of SiO_2, Na_2O, and P_2O_5 in various concentrations. The size varies from 20 to 60 nm. They have high pH, osmotic effects and Ca/P precipitation.

Mesoporous calcium silicate: The size of the nanoparticles around 100 nm used for apical filling of root canal of tooth [68]. They are injectable, apatite mineralization, osteostimulation, drug delivery and antibacterial efficiencies. Tetracycline loaded calcium deficient hydroxyapatite are osseoconductive material used in dental implants [69].

Synthesis of nanoparticles: They are synthesized either biologically or chemically.

Biological synthesis: They are synthesized from extracts of fungus and plants or proteins and polysaccharides [70-76]. The material selection depends on size, property, solubility, stability and biocompatibility [77].

Applications of nanotechnology [78]

a. **Medicine**: Diagnostics, drug delivery and tissue engineering.

b. **Chemistry and environment**: Catalysis and filtration.

c. **Energy**: Decreases energy utilization and rises the energy production and recycling of batteries.

d. **Information and communication:** Novel semi-conductor devices, novel optoelectronic devices, displays and quantum computers.

e. **Heavy industry:** Aerospace, refineries, vehicle manufactures consumer goods and foods.

Application of nanotechnology in prosthodontic dentistry

Dental materials

The most commonly used material in dentistry is nano-fillers reinforced composite resin size from 20-600 nm. Also evidence of sustained release of calcium fluoride nanoparticles reinforced conventional or resin of modified glass ionomer [79]. The impact of nano calcium phosphate nanoparticles on host responses at both cellular and tissue lead to fabrication of nanostructures, which increases the osseo-conductivity and the durability [80]. Also nano-tubes have larger dimension, more pores with high modulus has more structural reliability [81].

Removable prosthodontics

Reinforcement of carbon nanotubes decreases the polymerization shrinkage and facilitate the mechanical properties. They have honeycomb shape carbon atoms with 10 -100 nm size multilayer incorporated in PMMA, which will help enhance its properties [82-84]. Carbon Nanotubes (CNT) are strong, resilient and very light weight and available in single walled which possess the basic cylindrical structure and multiwalled with 2 or more coaxial cylinders. Carbon nanotubes reinforced light cure denture resin showed more impact strength and flexural strength [85] and CNT-PMMA which was drug free having antimicrobial adhesive properties to prevent microbe-induced complication [86]. However, drawbacks of CNT incorporated PMMA is blackening of the prosthesis.

PMMA resin materials

Nanocomposite denture fabricated using stereolithographic method and the denture teeth are resistant to stain [87,88]. The addition of zirconium oxide (nano-ZrO_2) NPs increase the tensile bond strength and reduces the translucency of Polymethyl methacrylate (PMMA) denture base material. The improvement in tensile strength is directly proportional to the concentration of nano-ZrO_2. The Polymethylmethacrylate (PMMA)/ Titanium dioxide NPs (TiO_2) nano-composites incorporation have antibacterial effect specially for candida [85]. Carbon nanotube reinforced light cure resin showed better impact and flexural strength [89]. CNT-PMMA which was drug free having antimicrobial adhesive properties to prevent microbe-induced complication. The major drawback of CNT and silver nanoparticles incorporated PMMA is blackening of the prosthesis [90,91].

Fixed prosthodontics

Nanofiller reinforced composite resin has [92,93] highest mechanical strength, low polymerization shrinkage, reliability, durability, low thermal expansion coefficient, low water sorption, excellent marginal integrity and handling properties [94,95]. Also the nanogold reinforced composite resin has improved antibacterial and adhesive properties.

Nanofillers reinforced vinylpolysiloxanes [96] has better flow, accuracy and hydrophilic property. Nanofillers reinforced ceramics are moldable and polishable with improved esthetics and handling characteristics [97].

Dental implants

Nanoparticle coated dental implants has more surface area which facilitates osseointegration. Hydroxyapatite and calcium phosphate nanoparticles coated implants improve the osseintegration like biologic material [98,99] and reduce the metallic release [100]. The nanotitanium implants facilitate healing and finest osseointegration [100] and [101] also provide implant surfaces with better biological properties for the adsorption of protein, adhesion and differentiation of cells and tissue integration [102]. At macroscopic level, the screw designs, the thread shape and the pitch distance give stability to implant [103] Dental implant should be designed to maximize favourable stresses and minimize undesirable stress along the bone implant junction.

Modifying surface properties of dental implants have shown to have better bone to implant contact thereby improving their clinical performance. Nano features can be created on dental implants by either chemical or physical processes. Chemical processes such as anodization, acid etching, chemical grafting and ionic implantation, whereas physical processes such as plasma spray and grid blasting can be applied for surface modification.

a. **Anodization**: It is a prevailing method to create nanostructures with diameters less than 100nm on titanium implants [104]. Voltage and galvanic current are used for this procedure.

b. **Acid etching**: Use of strong acids are effective in producing nanopits on titanium surface. Ex.sulphuric acid (H_2SO_4) and hydrogen peroxide.Nano patterns created on titanium screw shaped implants have shown to have better osteointegration.

c. **Plasma spray**: The process starts by using vacuum to remove all the contaminants, Gold, Silver Titanium can be coated using this technique. Thin CP coating on dental implants have encourage bone tissue formation over a period compared to uncoated. The CP coating dissolves and releases Ca^{2++} and HPO_4^{2-} which in turn increases the saturation of blood in peri-implant region and enhances cell adhesion, differentiation into osteoblast and synthesis of mineralized collagen. Also facilitate osseointegration. Advantages of plasma spray are seen during healing which is decreased considerably and bone remodeling period.

d. **Grid blasting**: A porous layer is created on the surface of dental implants by collision of microscopic particles in this process. Aluminia is the most prevalent material used for blasting [105]. Nanotextured titanium surface [106] prepared using a chemical etching technique showed more pre-osteoblast cells attachment. Scattering of Ag over the Titanium produces clusters have antibacterial activity [106,107]. Single step technique for producing and depositing silver NPs on a substrate is ablation of Ag foils was conducted in open air via laser and an inert gas jet for directing the NPs to the substrate which had antibacterial activity against Lactobacillus Salivarius [108]. The Ag conjugated chitosan has more effect on A. Flavus [109] and Porphyromonas gingivalis and Streptococcus mutans [110] and distinct group of bacteria [111].

Laser ablation

It's a better method to improve the surface topography and osseointegration of dental implants. Dipcoating and modified laser ablation also another method of modifying the surface of dental implants. The modified laser coated implants showed more bond strength at the bone and implant junction [106].

Dental ceramic in prosthodontics

Ceramic dentures have high strength, suitable color, and low thermal and electrical conductivity [112]. Also more stability, wear resistance, high hardness, good biocompatibility, no allergies but prone for porcelain crack [113]. ZrO2 had more abrasion resistance, corrosion resistance and biocompatibility, whose elasticity, flexural strength, and hardness are higher than Titanium alloys.

CAD/CAM milled Zirconia had more strength and bending resistance of zirconia are significantly higher than alumina ceramic, but they still lack toughness and high sintering temperature [114]. The nanostructures ceramics had more translucency, superplasticity, good toughness ductility and improved mechanical properties [115,116]. At room temperature, nano-TiO_2 ceramic exhibits very high toughness when compressed to 1/4 of the original length without any breakage [117]. Nano ZrO_2 also showed more fracture toughness, hence suitable for dental restorations [118-120].

Nanoimpression materials

Nanofillers reinforced vinylsiloxane materials had improved hydrophilicity, hence less chance for voids especially at the finish line area [121,97]. Also these silicone impression materials has high tear resistance, resistance to distortion and better hydrophilic properties. Production of infinitely small details which reducing the distortion [122].

The material is available in light fast, light regular set, medium and heavy viscosities. Eg. NanoTech Elite H-D+, Imprint II Penta H.

Nanocomposites

They import smooth surface, high esthetic features and more strength [123,97]. Rationale for incorporating nanoparticles in composite is to improve the esthetic property of the material and reduction in polymerization shrinkage, improved mechanical properties, wear resistance and biocompatibility.

Restorative dentistry

Use of Polyhedral Oligomeric Silsesquioxane (POSS) in composite

Polyhedral Oligomericsil Sesquioxanes (POSS) is an organic–inorganic hybrid nano composite, whose molecule size is 1.5nm and isotropic in nature [124]. Sellinger et al., was first to mention the use of POSS in dental restorative material [125]. Fong et al mentioned that the reinforcement of POSSMA with nanocomposites improve the mechanical properties of the resin [126]. Xiaorong Wu et al., in his study found that nanocomposites reinforced with 2 wt % POSS showed an increased flexural strength by 15%, compressive strength by 12%, compressive modulus by 4%, hardness by 15% and a decrease in volumetric shrinkage of 56% [127].

Silver containing nanomaterials exhibit gray discoloration of all dental restorative materials.Hence low concentration of silver for any kind of reinforcement [128].

Glass ionomer cement

Glass Ionomer Cement (GIC) invented by Wilson unique property like adhesion,anticariogenicity,thermal compatibility and biocompatibility.

Nevertheless, their use as a restorative material in stress bearing areas is limited due to its poor mechanical strength [125]. Incorporation of nanosized fillers will not only increase its mechanical properties but also increase the release of fluoride and bioacitivity [126]. Nano light polymerizing glass ionomer using Fluoraluminosilicate (FAS), has excellent polishability, improved esthetics and wear resistance [127].

Local anesthesia

Nanorobots containing oral anaesthetic suspension penetrate the various layers of mucosa and reach the pulp.They reduced the anxiety,sensitivity,fast and completely reversible [128,129].

Other applications

Drug delivery polymer nanofiber materials have been studied as drug delivery systems, scaffolds for tissue engineering and filters.

Nanocarbon fiber containing implants had more osteoblast adhesion to orthopedic/dental implant due to its high surface roughness [130].

Nanoparticles containing drugs can be administered in any kinds of routes which includes oral and inhalation method [131]. Nanoparticles modified the properties of drug by changing the size, shape which increases the bio-availability and reduce the frequency of drug administration [132-134].

ZnQ Quantam dots technology comprises anticancer drugs in the core surrounded by biocompatible polymer which is used in anticancer drug therapy there by the drugs reach the cancer cells [135].

Nanotechnology has wider application in encapsulation and emulsion formation and sensor development. Also Processing and packing was demonstrated by Garber nano medicine aids in early detection and prevention, enhanced diagnosis and follow up of diseases. Invention of gold nano devices has made gene sequencing less difficult and also used to detect genetic sequences when they are adhered with the short DNA segments. Damaged tissue can be repaired or reproduced using nanotechnology.

Nanomaterials containing bonding agents, mouth rinses reduce the demineralization of tooth, which prevent caries formation [136]. Silver nanoparticles containing restorative materials are effective against Streptococci and lactobacillus [137]. Carbonate hydroxy nanoparticles containing restorative materials are repairing the tooth defect [138]. Nano needles Suture needles incorporating nanosized stainless steel crystals have been developed [139,98].

Nanodigital dental technology reduces the radiation dose and produce high quality images [140]. Gandly Killed 100% of HIV and germs [141] formulated Nano disinfectants and sterilizing solution.

The colloidal silver and gold nanoparticles present in between the bristles of nano tooth brush could lead to a reduction in gingivitis and periodontitis. There is higher affinity of silver towards the negative molecules, which disrupts the cell wall and predisposes to the removal of plaque or biofilm [142].

Nano toothpastes are very effective by preventing the agglomeration of the bacterial molecules in the porosities of hydroxyapatite crystals because of the porosities present in the enamel prisms. The toothpaste helps in closing these porosities and aids in tooth color as well. Recently, titanium oxide is used as a whitening agent in toothpaste [143]. Nanodentrifices are reaches the supra and subgingival areas and metabolize the organic matter and turn them into harmless and odorless. Dentirobots continuously provide barrier to bacteria causing putrifaction odor [144].

Mouthwashes containing silver nanoparticles and triclosan-loaded nanoparticles have exhibited antibacterial and plaque control actions, which are vital for the prevention of periodontal disease [145,146]. Also nanoparticle containing dentrifices prevent plague and tar formation thereby facilitate remineralization and reduce sensitivity [147]. Nanorobots containing dentifrice's occlude the minute opening of the dentinal tubules and instantly reduce the sensitivity [97].

Bone is said to be a natural nanostructure comprises organic material such as collagen. Nanotechnology targets to imitate the development of nanobone, which has wider application in dentistry. Nanocrystals lies between the crystals of nanobone dissplay properties that are consistently far more superior to their individual constituent phases. Nanoparticle modified hydroxyapatite bone cells are used to treat bone defects in periodontal diseases [148].

Hazards of nanomaterials

Magnetic nanoparticles can induce toxic and harmful cellular impacts, which are not common in the bulkier micron-sized counterparts. Moreover, nano-materials can enter into the organisms via ingestion or inhalation and can translocate different organs and tissues, thus exhibiting hazardous impacts. The Ag containing nano-materials release Ag with adverse impacts on aquatic organisms such as algae, bacteria, daphnia, and fish [149-152]. Respiratory systems are the main target for the possible toxicity of nano-materials, which is caused by the addition of the inhaled particles to the portal entries and to the heart.

The nanomaterials binding protein have the leathal effect on enzymatic activities and protein unfolding and fibrillation [153-156]. Moreover, novel nanoparticles elicit a risk of exposure during manufacture or usage. So, complete risk assessments have to be taken into consideration and recycling and recovery of the materials are also much needed. Therefore, further investigation is required to fill the wide knowledge gap in the area of Nano toxicity as this will aid to improve risk assessment [157].

The nanoparticles released in the environment might alter temperature, pH which can alter the soil, water and prove harmful to flora and fauna. Also they will cross the blood brain barrier. It is very difficult to detect the nanoparticles in the environment. Hence, futuristic research is needed to detect the nanoparticles in the environment to find out the remedy for the nanoparticles toxicity and to standardize the safety of the environment from the impact of nanomaterials [158].

The fabrication and delivery of nanoparticles are an expensive procedure which has sub-optimal funding currently. The biocompatibility of nanomaterials is yet to be established. Social issues of public acceptance, ethics, and human safety have to be further contemplated upon. Nanomaterials can be pyrogenic, thus production of a bio friendly material is a biological challenge. Social challenge such as ethics, public acceptance and human regulation is still a matter of concern, which needs to be addressed before nanotechnology can enter the modern dental armamentarium [159].

Conclusion

The use of nanotechnology in prosthodontics is vast. The advent of new nanomaterials would enhance the efficacy of the materials and prosthesis. However, one cannot ignore the adverse effect of nanotechnology, so one should consider it before employment for any dental and medical purposes.

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