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RESEARCH ARTICLE

NANODENTISTRY-A FUTURISTIC INNOVATION

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ABSTRACT

Nanotechnology refers to the research and development of an applied science at the atomic or molecular level (i.e. molecular engineering, manufacturing). Although the nanoscale is small in size, its potential is vast. Almost every area of human activity will be affected by future nanotechnologies. Nanotechnology is based on the concept of creating functional structures by controlling atoms and molecules on a one-by-one basis. With developments in materials science and biotechnology, nanotechnology is especially anticipated to provide advances in dentistry and innovations in oral health-related diagnostic and therapeutic methods.

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INTRODUCTION

The term nanotechnology was first introduced by Richard Feynman in 1959. The word "nano", which is derived from the Greek word (nannos) meaning "dwarf," is a prefix that literally refers to 1 billionth of a physical size. One nanometer (nm) is a unit of length that equals 1 billionth of a meter. (Saravana and Vijayalakshmi, 2006) The size of atoms is nearly 0.1 nm. Considering that the size of a nanostructure is 1 to 100 nm, it is clearly seen that the nanotechnology works at the level of atoms and molecules. (Erkoc *et al*., 2007) The potential impact of nanotechnology stems directly from the spatial and temporal scales being considered: Materials and devices engineered at the nanometer scale imply controlled manipulation of individual constituent molecules and atoms in how they are arranged to form the bulk macroscopic substrate.

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This, in turn, means that nanoengineered substrates can be designed to exhibit very specific and controlled bulk chemical and physical properties as a result of the control over their molecular synthesis and assembly. The objectives of nanotechnology are to enable the analysis of structures at the nanoscale, to manufacture nanoscale structures, to understand the physical properties of structures at the nanoscale dimension, to develop devices with nano-precision, and to create a link between nanoscopic and macroscopic universes by inventing adequate methods. (Park, 2007)

Synthetic Approaches

Synthetic methods can be classified into two approaches: "top down" and "bottom up" approaches. "Top down" techniques begin with a macroscopic material or group of materials and incorporate smaller-scale details into them. "Bottom up" approaches begin by designing and synthesizing custom-made molecules that have the ability to self-organize or self-assemble into higher order mesoscale and macroscale structures. The challenge is to synthesize molecules that spontaneously self-assemble upon the change of a specific chemical or physical trigger, such as change in the concentration of a specific solute, change in pH or the application of an electric field. The physical mechanisms that push these molecules to self-assemble into organized structures are due to thermodynamics and competing molecular interactions including hydrophilic/hydrophobic forces, hydrogen bonding, and van der Waals interactions that aim to minimize energy states for various molecular configurations. The trick is to design systems that self-assemble into macroscopic higher order structures that display desirable physical and/or chemical properties not displayed by the constituent molecules themselves. (Silva, 2004)

Application of Nanotechnology in dentistry

Freitas described how nanorobots might use specific motility mechanisms to swim or crawl through human tissues with navigational recession; cytopentration (for example, pass-through plasma membranes such as the odontoblastic process without disrupting the cell, while maintaining clinical biocompatibility) and use any of a legion of techniques to monitor, alter or interrupt nerve impulse traffic in nervecells.

These nanorobotics functions may be controlled by annanocomputer that executes pre-programmed instructions in response to total local robots via acoustic signals. (Freitas *et al*., 2000) Nanodentistry's development will deliver nearly perfect oral health by the use of nanomaterials and biotechnologies, including tissue engineering and nanorobotics.

Diagnostic dentistry

Dental caries and periodontal disease are the most common diseases affecting the human race. Methods to prevent and encounter them have been devised, discussed, and implemented since ancient times. However, there is a constant need for improved tools and techniques. Nanotechnology, with its ever-increasing scope, provides dental research new opportunities for progress. Biofilms are considered the root cause of most dental and periodontal diseases. Specific pathogenic microorganisms have been associated with the development of dental caries and plaque-induced periodontal infections. Technology using nanosized quantum dots based on immune fluorescence enables the labelling of specific bacteria, which eases their identification and removal. This technique provides excellent single cell resolution for both in vivo and in vitro labeling of periodontal pathogens (Chalmers *et al*., 2007). Apart from dental caries and periodontal disorders, the oral cavity is often affected by autoimmune disorders and carcinomatous lesions. Highly sensitive diagnostic techniques involving better revelations of auto antibodies, salivary biomarkers and dysplastic cells are required for apt diagnosis and early treatment. The Oral Fluid Nano Sensor Test (OFNASET, The Wong Lab, University of California, Los Angeles) is a highly sensitive, specific, portable, and automated nano electromechanical system, which enables point-of-care detection of salivary proteomic biomarkers and nucleic acids specific for oral cancer, including 4 mRNA biomarkers (SAT, ODZ, IL-8, and IL-1β) and 2 proteomic biomarkers (thioredoxin and IL-8). (Gau *et al*., 2007)

Pit & fissure sealants

The nanofissure sealant results in excellent wear resistance and a reduced shrinkage, easy to place, hydrophilic material and feasible sealing ability. Due to high fluoride release, it may also lead to remineralization. (Shweta Dwivedi *et al*., 2013)

Tooth Repair

Nanodental techniques for major tooth repair may develop through several stages of technological development, first utilizing genetic engineering, tissue engineering and tissue regeneration and later synthesizing whole new teeth invitro and installing them. Ultimately, the nanorobotic manufacture of a biologically autologous whole replacement tooth including both mineral and cellular components should become feasible. (Kaira and Singh, 2012)

Tooth Renaturalization

Dentalrenaturalization procedures may become a popular addition to the normal dental practice, providing perfect techniques for esthetic dentistry. This trend may start with patients who desire to have their old dental fillings excavated and their teeth reformed with native biological materials. But demand will grow for full coronal re-naturalizations in which all fillings, crowns, and other necessary modifications to the visible dentition are removed, with the affected teeth reformed so as to be indistinguishable from the natural originals. (Saravana and Vijayalakshmi, 2006)

Dentin Hypersensitivity

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 natural biological materials, could selectively and exactly occlude specific dentinal tubules within minutes, offering patients quick and permanent treatment. On reaching the dentin, the nanorobots enter dentinal tubules that are 1 to 4 µ min diameter and proceed toward the pulp, guided by a combination of chemical gradients, temperature differentials and even position of navigation, all under the sway of the nano computer as directed by the dentist. (Whitesides and Love, 2001)

Nanocomposite resins

Non-agglomerated discrete nano particles that are distributed in resins or coatings to produce nano composites have been successfully manufactured by Nano products Corporation. The nano filler used is the Alumino silicate powder with a mean particle size of 80 ran 1:4 M ratio of alumina to silica and a refractive index of 1.508. (Saravana and Vijayalakshmi, 2006) These nano composites have superior flexural strength, hardness, modulus of elasticity, decreased polymerization shrinkage and better handling properties. (Freitas, 2005) A recent study by Xu *et al*. has evaluated the incorporation of nanosized $CaPO_4$ particles into resin based-composites, which showed improvement in stress bearing capacity as well as ion release that could prevent dental caries. (Xu *et al*., 2007)

Nano solution

Nanosolutionshave the ability to produce unique and dispersible nanoparticles, which can be added to different solvents, paints & polymers in which they are dispersed homogenously. Nano technology in bonding agents ensures homogeneity and that the adhesive is perfectly mixed. (Kim *et al*., 2005)

Nanomeric

These are monodisperse non agglomerated and non-aggregated silica nanoparticles. They reduce the interstitial spacing and increase the filler loading.

Nanoclusters

These are zirconia-silica particles (2 to 20 nm) and zirconylsalt (from 75 nm) which are spheroidal agglomerated particles. They have Enamel, Dentin and body shades because of radiopacity and there is high gloss retention with silica nanomer. Adper single bond 2 adhesives incorporates 10% by weight of 5 nm diameter spherical silica particles that prevents agglomeration. As discrete particles, their extremely small size keep them in colloidal suspension. (Saravana and Vijayalakshmi, 2006)

Nanoparticulate based disinfection in endodontics

The efficacy of nanoparticles to disinfect root canals has gained popularity recently. The nanoparticles evaluated on endodontics include Chitosan, zinc oxide and silver. The efficacy of chitosan and zinc oxide nanoparticles against Enterococcus fecalis has been attributed to their ability to distroy the cell wall. In addition, these nanoparticles can also disintegrate the biofilms within the root canal system. Silver nanoparticles are being evaluated for use as root canal disinfecting agents. It has been shown that 0.02% silver nanoparticle gel is able to kill and disrupt Enterococcus faecalis biofilm. (Sivaramakrishnan and Neelakantan, 2014)

Pulp regeneration

Nanotechnology has potential in the region of dental pulp regeneration. The development of tissues to replace diseased or damaged dental pulp can provide a revolutionary alternative to pulp removal. The α-melanocyte-stimulating hormone (α-MSH) is known to possess anti-inflammatory properties. Recently, it has been suggested that nanofilms containing α-MSH could help revitalize damaged teeth. (Fioretti *et al*., 2010) Further research is needed to evaluate these proposed therapeutic and regenerative approaches.

Dentifrobots

Subocclusalnanorobotic delivered by mouthwash or toothpaste could monitor all supragingival and subgingival surfaces at least once daily, metabolizing trapped organic matter into harmless and odorlessvapors and performing continuous calculus debridement. These invisibly small dentifrobots which crawl at 1- 10 microns/sec are inexpensive, purely mechanical devices that would safely de-activate themselves if swallowed and would be programmed with strict occlusal avoidance protocol. Properly configured dentifrobots could identify and destroy pathogenic bacteria residing in the plaque and elsewhere, while allowing the ~500 species of harmless oral microflora to flourish in a healthy environment. Dentifrobots also would provide a continuous barrier to halitosis, since bacterial putrefication is the central metabolic process involved in oral malodour. (Saravana and Vijayalakshmi, 2006; Freitas, 2000)

Guided tissue regeneration

The concept of guided tissue regeneration (GTR) is being researched to replace earlier functional graded membranes with novel 3-layered membranes. The former system included bilayered GTR membranes with a porous surface on one side (for cellular in growth), and a smooth surface on the opposite side (for cellular occlusion). A novel system has come up with a 3-layered GTR membrane composed of an innermost layer made of 8% nanocarbonated hydroxyapatite/collagen/ polylactic-coglycolic acid (nCHAC/PLGA) porousmembrane, a middle layer of 4% nCHAC/ PLGA, and an outer layer of PLGA nonporousmembrane. These 3 layers combine to form a highly flexible, biocompatible, osteoconductive and biodegradable composite membrane. When osteoblastic cells were cultured on this membrane, they showed a more positive response compared to a pure PLGA membrane. (Liao *et al*., 2007)

Tissue engineering

Recent events have generated research on new approaches to tissue engineering and local gene delivery systems in periodontal tissue regeneration. A gene-activated matrix (GAM) provides a platform to combine these 2 techniques. GAM provides a structural template for therapeutic gene expression and fills the defects for cell proliferation and adhesion, as well as the synthesis of extracellular matrix. A recent developmentin this aspect is a GAM composed of chitosan/collagen scaffold acting as a 3-d carrier, incorporated with chitosan/plasmid nanoparticles that encode platelet-derived growth factor. This matrix demonstrated a sustained and steady release of condensed plasmid DNA over 6 weeks, which resulted in a high in vitro proliferation of cultured periodontal ligamentfibroblasts, thus demonstrating potential for periodontal tissue engineering. (Peng *et al*., 2009)

Lab-on-a-chip methods

Lab-on-a-chip (LOC) is a device which integrates several laboratory functions on a single chip. LOCs deal with the handling of extremely small fluid volumes down to less than picoliters. Assays are performed on chemically sensitized beads populated into etched silicon wafers with embedded fluid handling and optical detection capabilities. Complex assays can be performed with small sample volumes, short analysis times, and markedly reduced reagent costs. LOC methodologies have been used to assess the levels of interleukin-1beta (IL-1beta), C-reactive protein (CRP), and matrix metalloproteinase-8 (MMP-8) in whole saliva, which are potential use of these biomarkers for diagnosing and categorizing the severity and extent of periodontitis. (Herr and Anson, 2007; Christodoulides *et al*., 2007)

Local anesthesia

A colloidal suspension containing millions of active analgesic micron-size dental robots will be infused on the patient's gingiva. After contacting the surface of crown or mucosa, the ambulating nanorobots reach the pulp via the gingival sulcus, lamina propria and dentinaltubules guided by combination of chemical gradients, temperature differentials and even positional navigation all under the control of on boardnano computer as directed by the dentist. Once installed in the pulp, the analgesic dental robots may be commanded by the dentist to shut down all sensitivity in any particular tooth that requires treatment. After oral procedures are completed, the dentist orders the nanorobots to restore all sensation, to relinquish control of nerve traffic and to egress from the tooth by similar pathways used for ingress; following this, they are aspirated. Nanorobotic analgesics offer greater patient comfort and reduced anxiety without the use of needles, greater selectivity and controllability of the analgesic effect, fast and completely reversible action, and avoidance of most side effects and complications. (Freitas, 2000)

Nerve regeneration

Nanoparticles can also be applied to reconstruct damaged nerves, with self-aggregatingrod-like nanofibers called *amphiphiles*. Aggregated amphiphiles may reach up to several micrometers in length and can be utilized in vivo to bridge tissue defects in the spinal cord. (Ellis-Behnke *et al*., 2006) This application holds huge potential in the oral surgical arena, such as the possible reconstruction of a damaged inferior alveolar nerve after extensive oral surgical procedures.

Implants

Nanotechnologies are increasingly used for surface modifications of dental implants as surfaces properties such as chemistry and roughness play a determinant role in achieving and maintaining their long-term stability in bone tissue. Direct bone-to-implant contact is desired for a biomechanical anchoring of implants to bone rather than fibrous tissue encapsulation. (Catledge, 2002) Recently three nano-structured implant coatings are developed: Nano structured diamond: They have improved toughness, ultrahigh hardness over conventional microcrystalline diamond, low friction, and better adhesion to titanium alloys. Nano structured processing applied to hydroxyapatite coatings: This is used to achieve the desired mechanical characteristics and increase surface reactivity and has increased osteoblast adhesion, proliferation, and mineralization. Nano structured metalloceramic coatings: These provide continuous variation from a nanocrystalline metallic bond at the interface to the hard ceramic bond on the surface. (Colon *et al*., 2006)

Nanostructured ceramics, polymers, carbon fibers, metals and composites enhance osteoblast adhesion and calcium/phosphate mineral deposition. Studies have suggested that nanophaseZnO and TiO(2) may reduce S.epidermidis adhesion and increase osteoblast functions necessary to promote the efficacy of orthopedic implants. (Meyer and Bühner, 2006)

Bone grafting

Different alloplastic bone grafts are being developed with nanoscale particles. The most popular ones are nanoHAP (n-HAP) bone grafts, which are available in crystalline, chitosan-associated and titanium-reinforced forms. (Reves *et al*., 2012; Kailasanathan *et al*., 2012) These n-HAP composite bone graft scaffolds are highly biocompatible, have superior mechanical properties, and induce better cellular responses compared to ‘plain’ chitosan scaffolds. (Chesnutt *et al*., 2009; Chesnutt *et al*., 2009) Apart from HAP, the use of calciumsulphate ($CaSO_4$) as a biodegradable and osteoconductive bone substitute has been utilized since 1892. As $CaSO_4$degrades, calcium phosphate forms, which helps in the attachment of osteoblasts and new bone deposition. Nanosized crystals of conventional $CaSO_4$ bone grafts have now developed, with particulate sizes ranging from 200-900 nm, while the conventional $CaSO_4$ bone graft particle size ranges from 30-40 μm.

These nanoparticles are further condensed into pellets of 425-1000 μm. This nanotization of particles results in a graft material which is more resistant to degradation and lasts longer (12-14 weeks) than conventional $CaSO_4$ (4-6 weeks). This rate of degradation matches the rate of bone growth in the intrabony defects, resulting in better treatment outcomes. (Kathuria *et al*., 2012) Antibacterial nanoceramic composite material has recently been developed by impregnating nanocalcium phosphate, walled carbon nanotubes, and zinc oxide (ZnO) nanoparticles into an alginate polymer matrix. Carbon nanotubes provide a strong, flexible, and inert scaffold on which cells could proliferate and deposit new bone, while the ZnO nanoparticles provide the antibacterial properties. This material enhances HAP formation inbone defects. (Beherei *et al*., 2011) The use of nanoparticulate bone grafts show promise in postextraction ridge preservation, intrabony defects regeneration, root perforations, sinus-lift procedures, implant dehiscence, and fenestration corrections.

Bionic mandible

The bionic mandible helps in reconstructing the entire mandible similar to normal mandible in sensation and function. It is not far from achieving, just like the first bionic arm constructed on Sullivan by Todd Kuiken and his team using nano robotic myeoelectric prosthetic limb. (Hamilton, 2006)

Bone substitute

The rosette nanotubes and nanocrystallinehydroapatite hydrogel nanocomposites can be utilised as improved bone. HRN–helical rosette nanotubes are formed by chemically immobilizing two DNA base pairs, creating a novel type of soft nanomaterial that biomimics natural nanostructural component of bone. They are 3.5nm in diameter and are self- assembled. Nanocrystalline hydroxyl apatite of 2% and 10%wt was well dispersed into helical rosette nanotubes. It demonstrated improved mechanical properties, enhanced osteoblast adhesion up to 236% compared to hydroxyapatite, Stimulated hydroxyapatite showed nucleation and mineralization along their main axis in a way similar to hydroxyapatite/collagen assembly pattern in natural bone. (Zhang *et al*., 2008)

Orthodontic Treatment

Orthodontic nanorobots can directly manipulate the periodontal tissues, including gingiva, periodontal ligament, cementum and alveolar bone, allowing swift and painless tooth straightening, rotating and vertical repositioning within minutes to hours. This is in divergence to current molar-uprighting techniques, which require weeks or months to complete. (Freitas, 2000)

Impression materials

Nanofillers are integrated in vinyl poly siloxanes, thus producing unique addition silicone impression materials. This material is claimed to have better properties such as flow, adhesiveness. It also has improved hydrophilic properties hence fewer voids at margin and better model pouring and enhanced detail precision. (Jhaveri and Balaji, 2005)

Nanoencapsulation

SWRI [South West Research Institute] has developed targeted release systems that encompass nanocapsules including novel vaccines, antibiotics and drug delivery with reduced side effects. At present, Osaka University, Japan in 2003 developed a targeted delivery of genes and drugs to human liver. Engineered Hepatitis B virus envelope L particles were allowed to form hollow nanoparticles displaying a peptide that is indispensable for liver-specific entry by the virus in humans. Future specialized nanoparticles could be engineered to target oral tissues, including cells derived from the periodontium.[1] (57% UNIQUE)

Nanoneedles

Scientists have achieved a subtle surgical operation on a particular living cell, by means of a needle that is just a few billionths of a meter wide. Nanoneedles are nanosized stainless steel needles, which will make cell surgery possible in the near future. Nanoneedles are marketedunder the trade name of SandvikBioline, RK 91TM needles (AB Sandvik, Sandviken, Sweden). Nanoneedlescan be used to deliver molecules such as nucleic acids,proteins, or other chemicals to the nucleus, or may even be used to carry out cell surgery. (Dunphy *et al*., 2006) Using the nanoneedle approach, we can get to a very specific location within the nucleus; this is the key advantage of this method.

Nanotweezers

Nanotweezers were developed by Danish research group (Nanohand), which can be used for both imaging and manipulation of nanosized objects to make cell surgery feasible in the near future. In the continuation of research into manipulating carbon nanotubes inside scanning electron microscopes, 21st century nanosmiths have begun crafting a suite of research tools, including nanotweezers, nanobearings, and nano-oscillators. These nanotweezer probes consist of two wires tapered consecutively through a nanopipette and kept electrically isolated. (Whitesides, 2001)

Optical Nanobiosensor

The nanobiosensor is a unique fiberoptics-based tool which allows the minimally invasive analysis of intracellular components such as cytochrome c, which is a very important protein to the process which produces cellular energy and is well-known as the protein involved inapoptosis, or programmed cell death. (Song *et al*., 2004)

Conclusion

The impact of nanotechnology on the field of dentistry is creating major changes with improvement in oral health. Nanotechnology providing advanced restorative materials, new diagnostic and therapeutic techniques, and pharmacologic approaches will improve dental care. However, as with any other technology, it also carries a potential for misuse and abuse. A successful future for nanotechnology will only be achieved through sharing of ideas and research finding, through testing and discussion.

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