

Nanotechnology and its Application in Dentistry

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Abstract

Nanotechnology influences almost every facet of everyday life from security to medicine. The concept of nanotechnology is that when one goes down to the bottom of things, one can discover unlimited possibilities and potential of the basic particle. In nanotechnology, analysis can be made to the level of manipulating atoms, molecules and chemical bonds between them. The growing interest in the dental applications of nanotechnology is leading to the emergence of a new field called nanodentistry. An electronic database search that included PubMed, MedLine, and Cochrane library was conducted. Key words used in the search are nanotechnology dentistry and applications. Language limitation was set as articles reviewed were only those written and published in English language. We did not search the gray literature. Initially, 52 articles were retrieved from the database, and articles considered were those published from 2008 to 2013. Eight articles that met the selection criteria were eventually selected and reviewed.

Keywords: Application, Biotechnology, Dentistry, Nano

Introduction

Definition

Nanotechnology or nanoscience refers to research and development of an applied science at the atomic or molecular level (i.e. molecular engineering, manufacturing).^[1] The word “nano” is said to be derived from the Greek word which stands for “dwarf”.^[2] Nanoscale though small in size has vast potential.^[1] One nanometer is 1 billionth or 10^{-9} of a meter.^[3] The comparative size of a nanometer to a meter is the same as the size of a marble to the size of the earth. The other way of putting it is that a nanometer is the amount a man’s beard grows in the time it takes him to raise a razor to his face.^[4,5]

History

The American Physicist Richard Feynman through his lecture titled “there is plenty room at the bottom” delivered at Caltech in 1959 was touted as the one who provided the inspiration for the field of nanotechnology, but it was the Japanese scientist Norio Taniguchi of the Tokyo University of Science who first

employed the term “nano-technology” in 1974.^[6] However, the term “nanotechnology” as against “nano-technology” was coined by Prof. Kevie E. Drexler in his 1986 book titled Engines of Creation: The Coming Era of Nanotechnology.^[7]

Concept and production of nanostructures

The basic idea of nanotechnology is to employ individual atoms and molecules to construct functional structures.^[8] Nanotechnology can be applied to various medical fields like Pharmacological research, clinical diagnosis, supplementing immune system, cryogenic storage of biological tissues, detection of proteins, probing of DNA structure, tissue engineering, tumor destruction via heating (hyperthermia) separation and purification of biological molecules and cells, magnetic resonance imaging (MRI) contrast enhancement, etc. Nanotechnology influences almost every facet of everyday life from security to medicine. The concept of nanotechnology is that when one goes down to the bottom of things, one can discover unlimited possibilities and potential of the basic particle. In nanotechnology, analysis can be made to the level of manipulating atoms, molecules and chemical bonds between them. The various nanoparticles include nanopores, nanotubes, quantum dots, nanoshells, nanospheres, nanowires, nanocapsules, dendrimers, nanorods, liposomes and so on.^[9,10] More recently, tiny machines called nanoassemblers that could be controlled by computer to perform specialized jobs have been invented. These nanoassemblers could be smaller than a cell nucleus so that they fit into places that are hard to

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reach by hand or with any other technology. It can be used to destroy bacteria in the mouth that cause dental caries or even repair spots on the teeth where decay has set in by the use of computers to direct these tiny workers in their tasks.^[11-13]

Method of Literature Search

To identify publications, we conducted an electronic database search. The search included PubMed, MedLine and Cochrane library. Key words used in the search are nanotechnology, dentistry and applications. Language limitation was set, as articles reviewed were only those written and published in English language. We did not search the gray literature. Initially 52 articles were retrieved from the database, and articles considered were those published from 2008 to 2013.

Study design

The articles included were mainly literature reviews that considered the broad application of nano particles in all aspects of dentistry, and not just a particular specialty. We did not consider case reports, case control studies, clinical trials, editorials or opinion letters.

Eight articles that met the selection criteria were eventually selected and reviewed.

Types of nanotechnologies

Basically, nanotechnologies consist of three mutually overlapping and progressively more powerful molecular technologies:

1. Nanoscale structured materials and devices that can be fabricated for advanced diagnosis and biosensors, targeted drug delivery and smart drugs
2. Molecular medicine via genomics, proteomics, artificial biobotics (microbial robots)
3. Molecular machine systems and medical nanorobots allow instant pathogen diagnosis and extermination and efficient augmentation and improvement of natural physiological function.

Applications of nanotechnology

Nanotechnology has wide industrial and clinical applications in:^[14]

- a. Medicine:
 - -Diagnostics
 - -Drug delivery
 - -Tissue engineering.
- b. Chemistry and environment:
 - -Catalysis
 - -Filtration.
- c. Energy:
 - Reduction of energy consumption
 - Increasing the efficiency of energy production

- The use of more environmentally friendly energy systems
 - Recycling of batteries.
- d. Information and communication:
 - Novel semi-conductor devices
 - Novel optoelectronic devices
 - Displays
 - Quantum computers.
 - e. Heavy industry:
 - Aerospace
 - Refineries
 - Vehicle manufactures
 - Consumer goods
 - Foods.

Nanomedicine

Advances in biomaterials and biotechnology have resulted in the formation of a new field called nanomedicine,^[15] which was first put forward in 1993 by Robert A. Freitas Jr. Nanomedicine is the science of preventing, diagnosing and treating disease using nanosized particles.^[14,16,17]

Nanomedicine includes various applications ranging from drug release with nanospheres to tissue scaffolds based on nanotechnologic design that realize tissue formation, and even nanorobots for diagnostics and therapeutic purposes.^[18] Drug molecules transported through the body by the circulatory system may cause undesirable adverse effects in untargeted regions. Nanorobots on the others hand can recognize unhealthy cells and can find and destroy them wherever they are located.

Drug delivery to the exact target is of particular importance in cancer in order to destroy all of the cancer cells and at the same time avoid harming healthy cells.^[19] Nanomedicine can overcome many important medical problems with basic nanodevices and nanomaterials, some of which can be manufactured today. Nanomedicine provides improvements in available techniques in addition to developing fully new techniques.^[18,20]

Nanotechnology in dentistry

Because of the growing interest in the future of dental application of nanotechnology, a new field called nanodentistry is emerging. The development of nanodentistry will allow nearly perfect oral health by the use of nanomaterials and biotechnologies including tissue engineering and nanorobots.^[15]

The new treatment opportunities in dentistry include local anesthesia, dentition renaturalization, permanent cure of hypersensitivity, complete orthodontic realignment during a single office visit, covalently bonded diamondized enamel and continuous oral health maintenance with the help of

mechanical dentifrobots (nanorobotic dentifrice) that destroy caries-causing bacteria and even repair blemishes on the teeth where decay has set in.^[21]

Application of nanotechnology in diagnosis and treatment

Nanodiagnosics

Nanodiagnostic devices can be used for early disease identification at the cellular and molecular levels. Nanomedicine could increase the efficiency and reliability of *in vitro* diagnostics, through the use of selective nanodevices to collect human fluids or tissues samples and to make multiple analyses at the subcellular level. Nanodevices can be inserted into the body to identify the early presence of a disease or to identify and quantify toxic molecules and tumor cells.^[15,22]

Diagnosis and treatment of oral cancer

Exosome is a membrane bound secretory vesicle containing a proteomic and genomic marker whose level is elevated in malignancy. This marker has been studied by using atomic force microscopy which employs nanoparticles. The nanoelectromechanical system, oral fluid nanosensor test, and optical nanobiosensor can also be used for diagnosing oral cancer. Nanoshells which are miniscale beads are specific tools in cancer therapeutics. Nanoshells have outer metallic layers that selectively destroy cancer cells while leaving normal cells intact. Undergoing trial are nanoparticle-coated, radioactive sources placed close to or within the tumor to destroy it.^[23]

Tissue engineering and dentistry

Potential applications of tissue engineering and stem cell research in dentistry include the treatment of orofacial fractures, bone augmentation, cartilage regeneration of the temporomandibular joint, pulp repair, periodontal ligament regeneration and implant osseointegration. Tissue engineering enables the placement of implants that eliminate a prolonged recovery period, that are biologically and physiologically more stable than previously used implants, and that can safely support early loading.^[24,25]

Bone grafts with better characteristics can be developed with the use of nanocrystalline hydroxyapatite. It was shown that nanocrystalline hydroxyapatite stimulated the cell proliferation required for periodontal tissue regeneration.^[26]

Bio-nano surface technology and dental implants

Osteoblast proliferation has been induced through the creation of nano-size particles on the implant surface.^[25,27] Roughening the implant surface at the nanoscale level is important for the cellular response that occur in the tissue.^[28,29] Many studies have shown that nanotopography of the implant surface considerably affects osteogenic cells and that the nanoscale surface morphology enhances osteoblast adhesion. The nanoscale surface morphology augments area and thus provides an increased implant surface area that can react with the biologic environment.^[30,31]

Bone replacement materials

Nanotechnology aims to emulate the natural structure present on bone, which is composed of organic compounds (mainly collagen) and reinforced with inorganic ones. Nanocrystals show a loose microstructure, with nanopores situated between the crystals. The surfaces of the pores are modified such that they adsorbed protein, due to the addition of silica molecules. Bone defects can be treated using the hydroxyapatite nanoparticles.^[32]

Nanoanesthesia

Application of nanotechnology can be used to induce anesthesia. The gingiva of the patients is instilled with a colloidal suspension containing millions of active, analgesic, micron-sized dental robots that respond to input supplied by the dentist. After contacting the surface of crown or mucosa, the ambulating nanorobots reach the pulp via the gingiva sulcus, lamina propria and dentinal tubules, guided by chemical gradient, temperature differentials controlled by the dentist. Once in the pulp, they shut down all sensation by establishing control over nerve-impulse traffic in any tooth that requires treatment. After completion of treatment, they restore sensation thereby providing patient with anxiety-free and needless comfort. Anesthesia is fast acting, and reversible, with no side effects or complications associated with its use.^[15,32]

Nanosolutions

They provide unique and dispersible nanoparticle, which can be used in bonding agents (trade name: Adper, Single Bond Plus, Adhesive Single Bond). A new flowable composite (Dentiflow) has an acceptable shear bond strength for bonding orthodontic brackets and can be used without liquid to reduce the bonding procedure time while maintaining an acceptable bond strength.^[33,34] Ceram-X Mono™; a nanocomposite was reported to have a lesser bond strength compared with traditional orthodontic composite but was within clinically acceptable range for bonding.^[35]

Nanoparticles have also been used as sterilizing solution in the form of nanosized emulsified oil droplets that bombard pathogens.^[32,36]

Impression Materials

Nanofillers are integrated into vinylpolysiloxanes, producing a unique siloxane impression material that has a better flow, improved hydrophilic properties and enhanced precision detail.^[3,32]

Nanoneedles

Suture needles incorporating nano-sized stainless steel crystals have been developed (trade name: Sandrik Bioline, RK91 needles, AB Sandrik Sweden). Nano tweezers are also under development, which will make cell surgery possible in the near future.^[32]

Nanorobotic dentrifices (dentifrobots)

Dentifrobots in the form of mouthwash or toothpaste left on the occlusal surface of teeth can clean organic residues by moving throughout the supragingival and subgingival surfaces, metabolizing trapped organic matter into harmless and odorless vapors and performing continuous calculus debridement. These nanorobots can move as fast as 1-10 μ /s and are safely self-deactivated when they are swallowed.^[32]

Hypersensitivity cure

Hypersensitivity may be caused by changes in the pressure transmitted hydrodynamically to the pulp. The dentinal tubules of a hypersensitive tooth have twice the diameter and eight times the surface density of those in nonsensitive teeth. Dental nanorobots could selectively and precisely occlude selected tubules in minutes using native logical materials, offering patients a quick and permanent cure.^[32]

Orthodontic Treatment

Use of excessive orthodontic force might cause loss of anchorage and root resorption. Katz *et al.*^[37] in their study have reported a reduction in the frictional force produced by orthodontic movement by coating the orthodontic wire with inorganic fullerene-like tungsten disulfide nanoparticles (IF-WS₂) known for their excellent dry lubrication properties. Cao *et al.*^[38] in a study reported that brackets coated with the nitrogen-doped titanium oxide thin film showed high antimicrobial and bacterial adhesive properties against normal oral pathogenic bacteria through visible light, which is effective in prevention of enamel demineralization and gingivitis in orthodontic patients. Considering the effect of surface treatment on bond strength, a high bond strength between stainless steel brackets and artificially aged composite restoration in surfaces of restored teeth treated with diamond bur was reported by some authors.^[39] Concerning nanoindentation of orthodontic archwires, application of decontamination regimen and clinical use had no significant effect on the nickel titanium archwires, but did have a statistically significant effect on the steel archwires. Decontamination of the steel wires significantly increased the observed surface hardness and reduced the surface roughness. Clinical use demonstrated a statistically significant increase in the observed elastic modulus and a decrease in surface roughness.^[40] Orthodontic nanorobots could directly manipulate the periodontal tissues, allowing rapid and painless tooth straightening, rotating and vertical repositioning as well as rapid tissue repair within minutes to hours.^[32,37]

Nanocomposite

The latest advancement in the manufacturing process of dental composite resins is the utilization of nanoparticle technology.^[19,32,41] Nanotechnology has enabled the production of nanodimensional filler particles^[42] which are added either singly or as nanoclusters into composite resins. Nanofillers are different from traditional fillers^[43,44]

in that when the filler for traditional composite is produced, large particles are minimized by pinning and these methods cannot reduce the size of a filler that is smaller than 100 nm.^[42] Nanoparticles allow the production of composites with a smooth surface after the polishing process and confer superior esthetic features to the material. Composite resins with such particles are easy to shape and have a high degree of strength and resistance to abrasion. Therefore, resins containing nanoparticle are used in wider areas than composites with hybrid and microfilled fillers.^[45] It has been observed that no relevant difference in terms of enamel lesions and cracks occurred after debracketing of orthodontic brackets bonded with flowable orthodontic composite compared with traditional orthodontic composite.^[46]

Unlike in hybrid composite where large particles can be separated from the matrix, only poorly attached nanoclusters are separated during abrasion in nanocomposites, and thus retention is enhanced with well-polished surface.^[45] The fillers in nanocomposites have higher translucence since they are smaller than the wavelength of light, thereby allowing the generation of more esthetic restorations with a vast range of color options.^[44] Nanofiller technology has enabled the production of nanofill composites by bringing together the esthetic features of microfill composites and the mechanical features of hybrid composites.^[44,47]

Nanocomposites artificial teeth

Inorganic fillers in nanodimensions are diffused homogeneously without any accumulation in the matrix in the artificial teeth produced from nanocomposites. Studies have shown that nanocomposite artificial teeth are more durable than acrylic teeth and microfill composite teeth and have a higher resistance to abrasion.^[48-51]

Nanoencapsulation

Targeted release systems that encompass nanocapsules including novel vaccines, antibiotics and drug delivery with reduced side effects have been developed by the South West Research Institute.^[3] An example is an attempt to generate effective and satisfactory drug delivery system for the treatment of periodontal diseases by producing nanocapsules impregnated with triclosan. Application of triclosan into the test area alleviated inflammation.^[52]

Nanotechnology for preventing dental caries

The use of a toothpaste containing nanosized calcium carbonate enabled remineralization of early enamel lesions.^[53]

Digital dental imaging

Advances in digital dental imaging techniques are also expected with nanotechnology. The radiation dose obtained using digital radiography with nanophosphor scintillators is diminished and high quality images obtained.^[54]

Major tooth repair/nanotissue engineering

Replacement of the whole tooth, including the cellular and mineral components, is called complete dentition replacement. This is made possible through a combination of nanotechnology, genetic engineering and tissue engineering.^[23]

Surface Disinfectants

Nanotechnology was deployed to the production of a surface disinfectant called Eco-True which was reported to have 100% destructive effect on HIV and germs. Clinical applications of the disinfectant include sterilization of instruments and incisions for the purpose of preventing post-operative infections.^[55] EnviroSystems of San Jose employed nanotechnology to produce strong but environmentally friendly chemicals.^[56]

Stem cells imaging/tracking

For the evaluation of therapeutic efficacy of transplanted stem cells, it is important to track their survival, migration, fate and regenerative impact *in vivo*. Stem cells can be tracked *in vivo* after transplantation using different labeling techniques. Initial labeling can be with fluorescent dyes or magnetic nanoparticles such as superparamagnetic iron oxide. Visualization of the labeled cells could be done using imaging systems e.g. MRI.^[57,58]

Hazards of Nanoparticles

The nonpyrogenic nanorobots used *in vivo* are bulk Teflon, carbon powder and monocrystal sapphire. Pyrogenic nanorobots are alumina, silica and trace elements like copper and zinc. Nanorobots may release inhibitors, antagonists or down regulators for the pathway in a targeted fashion to selectively absorb the endogenous pyrogens, chemically modify them, then release them back into the body in a harmless inactivated form.^[32]

The extensive application of nanomaterials in a wide range of products for human use possesses a potential risk for toxicity risk to human health and environment. American health association concluded that short-term exposure to elevated particulate matter concentrations in outdoor air significantly contributes to increased acute cardiovascular mortality, particularly in at risk subset of the population.^[1] An *in vitro* cytotoxicity assessment of an orthodontic composite containing titanium dioxide (TiO₂) nanoparticles by Heravi and others revealed that orthodontic adhesive containing TiO₂ nanoparticles indicated comparable or even lower toxicity than its nanoparticle free counterpart. It was concluded that incorporation of 1% by weight of TiO₂ nanoparticles to the composite structure does not result in additional health hazards compared to that occurring with pure adhesive.^[59] In another study,^[60] it was reported that leached components from composite material induced embryotoxicity in mouse blastocyst *in vitro*, while no toxicity was observed when subcutaneously implanted *in vivo*.

Future of Nanotechnology

Nanotechnology is foreseen to change health care in a fundamental way. It forms the basis of novel methods for disease diagnosis and prevention. It will be useful in therapeutic selection tailored to the patients profile and will come in handy in drug delivery and gene therapy.

Conclusion

Nanotechnology is set to revolutionize clinical dental practice. In no distant future, oral health care services will become less stressful for the dental surgeons, more acceptable to patients and the outcome will significantly become more favorable. Rapidly progressing investigations will ensure that developments that seem unbelievable today are possible in the future. Optimal utilization of the advantages and opportunities offered by nanotechnology in clinical dental practice will facilitate improvements in oral health. However, as with all technologies, nanotechnology carries a significant potential for misuse and abuse on a scale and scope never seen before if not properly controlled and directed.

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