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Nanotechnology in Periodontics: A New Horizon

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Abstract

Nanotechnology or nanoscience as it is referred as the development and research in the field of applied science and whose aim is the control of matter on an atomic or molecular level.

Nanotechnology is a developing trend and scaling new heights in the recent years and like other fields of medicine is also set to transform dentistry in a huge way. Dentistry is facing a major revolution in the era of of nanoscience having already been targeted with the development of novel namomaterials, nanoparticles and nanodevices along with its applications which are of human interest. Nanodentistry can help in the maintenaince of oral health by employing the use of nanodevices which will allow precise control on various techniques in oral health care like oral analgesia, dentine replacement therapy, permanent hypersensitivity cure, periodontal cure ,complete orthodontic realignment along with many other treatment alternatives. In the field of Periodontology Nanotechnology and its application have improved the diagnosis, treatment, prognosis and prevention of the periodontal diseases. It utilizes nanomaterials, nanobiotechnology along with nanorobots for the treatment and maintenance of periodontal health.

The purpose of this paper is to review the phenomenon of nonotechnology as applied to periodontics along with other fields of Dental Health.

Keywords: Nanodentistry, Nanomaterials, Nanoregenerators

Introduction

The word "Nano" as one of the most attractive prefixes in the contemporary material science is simpler than it seems. Namely, the progress of humanity is underlain by a continual increase in sensitivity of human interactions with their physical surroundings[1]. The emergence of nanotechnology for medical applications i.e nanomedicine, which is defined as the science and technology of diagnosing, treating, and preventing diseases and traumatic injury, relieving pain, and preserving and improving human health, using nanoscale-structured materials. . Similarly, the development of "nanodentistry" will allow the maintenance of near-perfect oral health through the use of nanomaterials, biotechnology including tissue engineering, and nanorobotics.

The first mention of some of the distinguishing concepts in nanotechnology was by James Clerk Maxwell in 1867.The first observation and size measurements of Nano-particles were made during the first decade of the 20th century. They are mostly associated with Richard Zsigmondy who made a detailed study of gold sols and other nanomaterials with size down to 10nm and less. The vision of nanotechnology was introduced in 1959 by late Noble Physicist Richard P Feynman in a dinner talk. He quoted, "there is plenty of rooms at bottom" and proposed employing machine tools to make smaller machine tools which are to be used in turn to make still smaller machine tools and so on all the way down to atomic level[2].

The term, "Nano dentistry", was first introduced in 2000 by research scientist Robert Freitas. It was proposed that Nano technological developments will enable dental consumers to achieve optimal oral health through the utilization of nanomaterials, tissue engineering and dental nanorobotics. Although the routine use of dental robots may be years ahead for the identification and destruction of pathogenic bacteria in the periodontal sulcus ,nanotechnology in the area of dental materials is now an emerging trend.[3]

Types of Nanotechnology

There are two types of techniques in nanotechnology4

A) Top-Down: From top (larger) to bottom (smaller)

Here structures are minimized to a nanometric scale. It is the most frequent application of nanotechnology. Materials that are made by this approach include nanocomposites, nanosolution, impression materials, nanoencapsulation, nanoneedles, and bone replacement materials.

B) Bottom-Up: From bottom (smaller) to top (larger).

These begin with a nanometric structure (molecule) and create a mechanism larger than the original structure. Materials which are used for dentine hypersensitivity, local anaesthesia, tooth repair, tooth repositioning, nanodentrifices and diagnosis of oral cancer are under this type of approach.

Broadly it consists of 3 mutually overlapping & progressively more powerful molecular technologies,

i. Nanoscale- structured materials & devices that can be fabricated, advanced diagnostics & biosensors, targeted drug delivery & smart drugs.
ii. Molecular medicine via genomics, proteomics & artificial biobotics (microbial robots)
iii. Molecular machine systems & medical nanorobots allowing instant pathogen diagnosis & extermination, & efficient augmentation & improvement of natural physiological function

Nanomaterials

Nanomaterials are those materials with components less than 100nm in at least one dimension and include clusters of atoms, grains less than 100nm in size, fibers that are less than 100nm in diameter, films less than 100nm in thickness and nanoholes, and nano composites that are a combination of these.

Siegel has classified nanomaterials as zero dimensional, one dimensional, two dimensional and three dimensional nanostructures. Various nanostructures include[5]:

1. Nanoparticles
2. Nanopores
3. Nanotubes
4. Nanorods
5. Nanospheres
6. Nanofibres
7. Nanoshells
8. Dendrimers & dendritic copolymers.

Inorganic nanoparticles either currently in use or under development include

- Semiconductor nanoparticles
- Metal nanoparticles
- Metal oxide nanoparticles
- Silica nanoparticles
- Polyoxometalates
- Gold nanocrystals

One important feature of nanostructured materials is the development of self-assembly. Here, without human intervention an autonomous organization of components into patterns or structures occurs. Through the correct setting of conditions the whole process can be manipulated and facilitated. Self-assembly is common to many dynamic multi-component systems, right from smart materials and self healing structures to netted sensors and computer networks[5].

Self-assembly has been classified into- static and dynamic processes based on the dissipation of energy by the system. In static self-assembly, formation of ordered structure requires energy but it is stable once it is formed. When choosing a material for self-assembly the materials should have a critical number of charged groups, below which assembling procedure does not work. To form a well defined stable multi-layer, the appropriate opposite charged density is required for the matched materials.

Application of Nanotechnology In Periodontics

Nanorobotic Dentifrice (Dentifrobots)-

Subocclusal dwelling nanorobotic dentrifice delivered by a mouthwash or a toothpaste could patrol all supragingival and subgingival surfaces, metabolizing trapped organic matter into odorless and harmless vapors thus performing continuous calculus debridement. These invisibly small (1-10micron) dentifrobots, perhaps measuring 10^3- 10^5 nanodevices per oral cavity and crawling at speed of 1-10 microns/sec, might have the mobility of tooth amoebas .If needed these mechanical devices would safely deactivate themselves incase of swallowing and would be programmed with strict occlusal avoidance protocols. 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 ecosystem.

Since bacterial putrefaction is the central metabolic process involved in oral malodor dentifrobots could also provide a continuous barrier to halitosis. With this kind of daily dental care available from an early age, conventional tooth decay and gum diseases could be controlled and prevented in a much better way.

Nanosolutions

These include production of unique and dispersible nanoparticles that can be added to various solvents, paints, and polymers in which they are dispersed homogenously.

Nanotechnology in bonding agents ensures homogeneity and so the operator can thus be assured that the adhesive is perfectly mixed every time[6].

Nanofibers

Nanofibers that are less than 100 nm in diameter, including nanorods, nanoplatelets, nanotubes, nanofibrils and quantum wires are other major nanomaterials which are widely being explored for various applications, of which management of the periodontal diseases could be the prime target.

The three dimensional synthetic biodegradable scaffold designed using nanofibers serve as an excellent framework for cell adhesion, proliferation, and differentiation. Therefore, nanofibers, irrespective of their method of synthesis, have been used as scaffold for musculoskeletal tissue engineering (including bone, cartilage, ligament, and skeletal muscle), skin tissue engineering, vascular tissue engineering, neural tissue engineering, and carriers for the controlled delivery of drugs, proteins, and DNA.

Natural Polymeric Materials As Nanofiber[7].

Natural polymers have the advantage of being very similar, and often identical, to macromolecular substances present in the human body. Therefore, the biological environment favours the recognization and interaction with natural polymers . Some of the natural polymers used as biomaterials are collagen, hyaluronic acid, gelatin, chitosan, elastin, silk, and wheat protein.

synthetic polymers represent the largest class of biomaterials and include PLA poly(ethylene tereothalate), (PET) for blood vessel tissue engineering; PLC in neural and cartilage tissue engineering; and several copolymeric compounds such as PLLA-CL as a biomimetic ECM for smooth muscle and endothelial cells

Applications of Nanofiber[8,9,10,11]

Nanofibers for bone tissue engineering

The design of scaffold for bone tissue engineering is based on the physical properties of bone tissue such as mechanical strength, pore size, porosity, hardness, and the overall 3D architecture. For bone tissue engineering, scaffold with a pore size in the range of 100-350 μm and porosity greater than 90% are preferred for better cell/tissue growth and hence enhanced bone regeneration.

Nanofibers for cartilage tissue engineering

Articular cartilage tissue has a limited capacity for repair due to the reduced availability of chondrocytes and complete absence of progenitor cells in the vicinity of the wound to mediate the repair process. Therefore tissue engineering has a potential approach to regenerate cartilage tissue that holds promising results. One of the methods of engineering cartilage tissue is through the use of 3D scaffolds combined with chondrocytes or progenitor cells .[12]

Nanofibers for ligament tissue engineering

Ligament ruptures result in abnormal joint kinematics and often irreversible damage of the surrounding tissue leading to tissue degenerative diseases, which do not heal naturally and cannot be completely repaired by conventional clinical methods. Recently, tissue engineering methods involving nanofibers have been successfully employed to meet this challenge (Lin et al 1999). In particular, aligned nanofibers enhanced cell response and hence were explored as scaffolds for ligament tissue engineering.

Nanofibers for skin tissue engineering and graft material

Engineered skin tissue is an excellent alternative, not only to close the wound but also to stimulate the regeneration of the dermis. Along with collagen, several other natural and synthetic polymers have been explored for skin tissue engineering (Matthews et al 2002); however the use of these biomaterials as nanofibers has been very limited. Min et al 2004 developed nonwoven silk fibroin nanofibers by electrospinning for skin tissue engineering. Due to their high porosity and high surface area to volume ratio, fibroin nanofibers coated with type 1 collagen were found to promote keratinocyte/fibroblast adhesion and spreading. Therefore the silk fibroin nanofibers show potential to be developed as a scaffold for skin tissue engineering.

A graft with nano-structured PLGA-Poly(lactic-co-glycolic acid) on the exterior surface (promoting smooth muscle cell function) and conventional PLGA on the interior surface (promoting endothelial cell function) could be utilized to enhance integration into juxtraposed vascular tissue and thus increase implant efficacy.

Application of alumina nanofibers in tissue engineering

Osteointegration is a major requirement for bone and dental implants. It has been demonstrated that a decrease in surface feature size can enhance osteointegration (Webstar 2001).

Alumina,titania, HA, and their composites are the most well studied materials for both dental and orthopedic applications. Due to similarity between physical geometry of HA and alumina nanofiber, Price et al hypothesized that alumina nanofibers may enhance osteointegration (Price et al 2003). They studied the influence of alumina nanofibers on the behavior of osteoblast cells. Their results demonstrated that the alumina nanofibers enhanced cell adhesion and synthesis of osteoblastic phenotypic markers such as alkaline phosphatase and calcium (Webstar et al 2005).

The above studies elucidate that carbon and aluminum nanofibers can be promising materials for orthopedic/ dental tissue engineering applications.

Nano Impression[8]

Impression materials are available with nanotechnology application. Nanofillers are integrated in the vinylpolysiloxanes, producing a unique addition siloxane impression material. The main advantage of this material is that it has better flow, improved hydrophilic properties and hence fewer voids at margin along with better model pouring and enhanced detail precision. Trade name- Nanotech Ellite H-D+.

Hypersensitivity Cure[13]

Dentine hypersensitivity is another pathologic phenomenon that may be amenable to nanodental cure. Dentine hypersensitivity may be caused by changes in pressure transmitted hydrodynamically to the pulp. This etiology is suggested by the finding that hypersensitive teeth have 8 times higher surface density of dentinal tubules-and tubules with diameters twice as large than the nanosensitive teeth. There are many therapeutic agents for this common painful condition that provide temporary relief, but reconstructive dental nanorobots could selectively and precisely occlude selected tubules in minutes, using native biological materials, offering patients a quick and permanent cure.

On reaching the dentin, the nanorobots enter the dentinal tubular holes that are 1 to 4 μm in diameter and proceed toward the pulp, guided by a combination of chemical gradients, temperature differentials and even position of navigation, all under the control of the onboard nanocomputer as directed by the dentist. There are many pathways to travel nanorobots from dentin to pulp. Because of different tubular branching patterns, tubular density may present significant challenge to navigation. Assuming a total path of length of about 10 mm from the tooth surface to the pulp and a modest travel speed of about100 μm\second, Nanorobots can reach the pulp chamber via traversing through enamel and dentin in approximately 100 seconds. The presence of natural cells that are constantly in motion around and inside the teeth including human gingival, pulpal fibroblasts, cementoblasts, odontoblasts, and bacteria inside dentinal tubules, lymphocytes within the pulp or lamina propria suggests that such journey be feasible by cell-sized nanorobots of similar mobility. Once installed in the pulp, having established control over nerve impulse traffic, the analgesic dental nanorobots may be commanded by the dentist to shut down all sensitivity in selected tooth that requires treatment. When the dentist presses the icon for the desired tooth on the hand held controlled display monitor, the respective tooth immediately anesthetized. After the oral procedures are completed, the dentist commands the nanorobots via the same acoustic data links to restore all sensation to the tooth via similar path. This analgesic technique is patient friendly as it reduces anxiety, needle phobia, and most importantly is quick and completely reversible.

Biomimetics: Amlogenins, hydroxyapetite, enamel replication and repair[14]

It is well known that many of the mineralized tissues are made up of self assemble nanosized building blocks produced by matrix medicated biomineralization. Understanding of underlying mechanism of biomineralization and its adaptation in materials science to develop functional materials and structure is termed as "Biomimetics".

Perhaps the most tempting venue for speculation on the phase of nanorestoration of tooth structure is that nanotechnology mimicking processes that occur in nature (biomimetics), such as the formation of dental enamel.

A recent in vitro study by Wang and colleagues has further elucidated mechanism of interaction among amelogenin nanospheres, nanoparticles and nanorods at critical points during the HA crystal-growth process. The results offer further evidence for cooperativity in interfacial matching between organic and inorganic nanophases that may resemble processes that occur in actual enamel formation. In other attempt to mimic enamel formation, Uskokovic' and colleagues also recently described such a synergy among protein self-assembly, proteolysis (through a pivotal role of matrix metalloproteases-20 (MMP-20), also known as enamelysin) and crystallization. The emergence of an amelogenin-interactive role in macromolecular self assembly and enamel mineralization for a second protein, enamelin, also has been reported recently by Fan and colleagues.

Regularity of amelogin nanosphere assembly into microribbons was also observed by Du and colleagues, who hypothesized amelogenin's pivotal role in directing and ordering apatite crystal growth.

Hydroxyapatite nanoparticles used to treat bone defects are

- Ostim (Osartis GmbH, Germany)HA(hydroxyapetite)
- VITOSS(Orthovita,Inc.,USA)HA+TCP(Tricalcium phosphate)
- NanoOss(Angstrom Medica,USA)HA

Nano needles[8]

Suture needles incorporating nanosized stainless steel crystals has been developed.

Trade name-Sandvik Bioline, RK91 tm needles (AB Sandvik, Sweden)

Nanotweezers are also under development which will make cell surgery possible in the near future.

Nano Anesthesia[7,8]

One of the most common procedures in dentistry is the injection of local anesthetic, which can involve long waits and varying degrees of efficacy, patient discomfort and complications. Well-known alternative, such as transcutaneous electronic nerve stimulation, cell demodulated electronic targeted anesthesia(CDET) and transmucosal, intraosseous or topical techniques, are of limited clinical effectiveness. To induce oral anesthesia in the era of nanodentistry, dental professionals will instill a colloidal suspension containing millions of active analgesic micrometer-sized dental nanorobot “particles” on the patient’s gingiva. After contacting the surface of the crown or mucosa, the ambulating nanorobots reach the dentine by migrating into the gingival sulcus and passing painlessly through the lamina propria or the 1-3 micrometer thick layer of loose tissue at the cementodentinal junction. Once on the dentine, the nanorobots enter dentinal tubule holes that are 1 to 4 micrometer in diameter and proceed towards the pulp, guided by a combination of chemical gradients, temperature differentials and even positional navigation, all under the control of the onboard nanocomputer, as directed by the dentist. There are many pathways to choose from. Dentinal tubule number density is typically 22,000mm^{-2} near the dentinoenamel junction, 37,000mm^{-2} midway between the junction and the pulpal wall , and 48,000mm^{-2}close to the pulp in coronal dentine, with the number density slightly lower in the root (for example, 13,000mm^{-2} near the cementum). Tubule diameter increases nearer the pulp, which may facilitate nanorobot movement, although circumpulpal tubule openings vary in number and size. Tubule branching patterns may present a significant challenge to navigation, because they exhibit an intricate and profuse canalicular anatomizing system that crisscrosses the intertubular dentin, with dentinal branching density most abundant in locations where tubule density is low.

Dentinal tubules are continuous between primary dentin and regular secondary dentin in young and old teeth, but not between primary and irregular secondary dentin. Regular secondary dentin becomes highly sclerosed in older teeth, and many tubule openings on the outer dentine surface can become completely occluded in some circumstances, probably requiring significant detouring by the dental nanorobots. On the other hand, a small number of microcanals, large tubules or giant tubules, with diameter of 10 to 50 micron or even larger may exist in some cases, possibly affording easier transit.

Nano anesthesia offers greater patient comfort and reduces anxiety, and there is avoidance of most side effects and complications.

Drug Delivery[15]

Recently, Pinon- Segundo et al produced and characterized triclosan-loaded nanoparticles by the emulsification- diffusion process, in an attempt to obtain a novel delivery adequate for the treatment of periodontal disease. The nanoparticles were prepared using poly (D,L –lactic- colycolide), poly (D,L-lactic) and cellulose acetate phthalate. Poly (vinyl alcohol) was used as a stabilizer. Batches were prepared with different amounts of triclosan in order to evaluate the influence of the drug on nanoparticle properties. Solid nanoparticles of less than 500nm in diameter were obtained. These triclosan particles behave as a homogenpous polymer matrix-type delivery system, with the drug (triclosan) moleculaly dispersed. Release kinetics indicates that the depletion zone moves to the center of the device as the drug is released. This behavior suggests that the diffusion is the controlling factor of the release. Nanomaterials including hollow sphere, core-shell structure, nanotubes and nanocomposite have been widely explored for controlled drug release. It is conceivable that all of these materials could be developed for periodontal drug delivery devices in the future. Drugs can be incorporated into nanospheres composed of a biodegradable polymer, and this allows for timed release of the drug as the nanospheres degrade. This also allows site-specific drug delivery.

Conclusion

Nanotechnology will change dentistry, healthcare and human life more profoundly than many developments in the past. It has both its pros and cons with both abuse and misuse on its use. However, nanotechnology also comes with its share of significant benefits, like improved health, better use of natural resources, along with reduced environmental pollution. As nanotechnology expands in other fields, clinicians, scientists, and manufacturers will thrive to discover its uses and advances in the field of dentistry. Applications of nanotechnology in dentistry are filled with opportunities and possibilities for the future that can only be limited by our imagination.

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