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RESEARCH ARTICLE

NANOTECHNOLOGY: RIPPLE EFFECT OF ATOMS

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ABSTRACT

Greatness does not come from size. Surprises come in small packages. Nanoscale though small in size has vast potential. One nanometer is 1 billionth or 10^{-9}meter .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 basic idea of nanotechnology is to employ individual atoms and molecules to construct functional structures. Nanotechnology influences almost every facet of everyday life. 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.

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INTRODUCTION

Nanotechnology or Nanoscience refers to research and development of an applied science at the atomic or molecular level .The word "nano" is said to be derived from the Greek word which stands for "dwarf".[1] The field of *Nanotechnology*, is revolutionizing diverse areas of research product, development, manufacturing and commerce.[2] The basic concept of nanotechnology is that when one goes down to rock bottom of things, one can discover unlimited possibilities and potentials of the basic particle.At the nanoscale size, materials exhibit very different properties in terms of strength, conductivity, color and toxicity from materials of the same composition at a larger scale.[2] *Nanodentistry* is often defined as the science and technology of diagnosing, treating and preventing oral and dental diseases, relieving pain, preserving and improving dental health using nanostructured material. A variety of new dental products are available, ranging from implants to oral hygiene products that rely on nanoscale properties.[2]

BACKGROUND: The concept of nanotechnology was put forward by the American Physicist and Nobel Laureate Dr. *Richard Phillips Feynman*(fig.1), who presented a paper called '*There's Plenty of Room at the Bottom'* in December 29, 1959 at the annual meeting of the American Physical Society meeting at California Institute of Technology.In his historic lecture hetalked about the storage of information on a very small scale, writing and reading in atoms, about miniaturization of the computer, building tiny machines, tiny factories, and electronic circuits with atoms. This laid the foundations of allthe basic concepts of Nanotechnology but the first use of the word "nanotechnology" has been attributed to *Taniguchi* in a paper published in 1974 "*On the Basic Concept of Nanotechnology*.[3] The potential application of nanotechnology in medicine was put forward by *Albert R. Hibbs,* who gave the idea of putting the mechanical surgeons directly inside the blood vessel and it goes into the heart and looks around to find out the faulty valve and it takes a little knife and slices it out.

Some other small machines are often permanently incorporated within the body to help some inadequately functioning organ.[3] Once one considers the potential applications of nanotechnology to medicine, nanodentistry was not a distant dream.*R.A. Freitas Jr* (fig.2)., in the year 2000, coined the term ‘‘nanodentistry’’. He gave ideas of using nanorobots for orthodontics, dentition regeneration, nanomaterials, and robots in dentifrices–dentifrobots. Most of his ideas were and still remain science fiction, but now these ideas are gradually being realized into practice. Today many applications of nanotechnology are known and are used in the field of dentistry.[4]

Fig. 1. Richard Phillips Feynman

Fig. 2 – R.A. Freitas Jr

APPROACHES TO NANOTECNOLOGY

Numerous approaches have been utilized successfully in nanotechnology and as the technology develops, further approaches may emerge.[5]

Bottom-up approaches: To arrange smaller components into more complex assemblies.

Nanodentistry as bottom-up approach

- Inducing anesthesia
- Major Tooth Repair
- Hypersensitivity Cure
- Dental Durability and Cosmetics
- Nanorobotic Dentifrice (dentifrobots)
- Local drug delivery
- Nanodiagnostics
- Therapeutic aid in oral diseases.

Top-down approaches: To create smaller devices by using larger ones to direct their assembly.

Nanodentistry as top down approach

- Nano Light-Curing.
- Glass Ionomer Restorative.
- Nano Impression Materials.
- Nano-Composite Denture Teeth.
- Nanosolutions.
- Nanoencapsulation.
- Plasma Laser application.
- Prosthetic Implants.
- Nanoneedles.
- Bone replacement materials.[6]

NANOROBOTS

A nanorobot can be defined as an artificially fabricated object able to freely diffuse in the human body and interact with specific cell at the molecular level by himself. (Fig.3) is a schematic representation of a nanorobot that can be activated by the cell itself when it is needed (Levy et al. 2000).[7, 8]

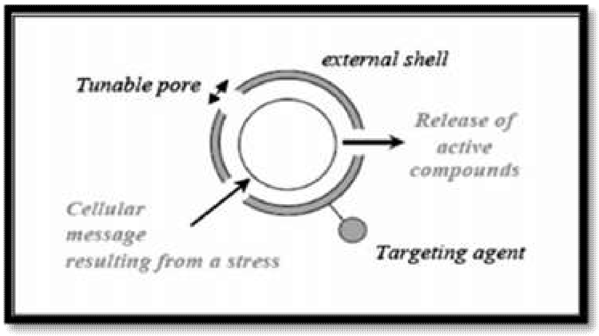

Fig. 3

Dental nanorobots are spider like diamondoid structures, disposed into nanotubes, as the supersleek surfaces should reduce to a merest chance of activating the defense mechanism of the host (fig 4).[8]

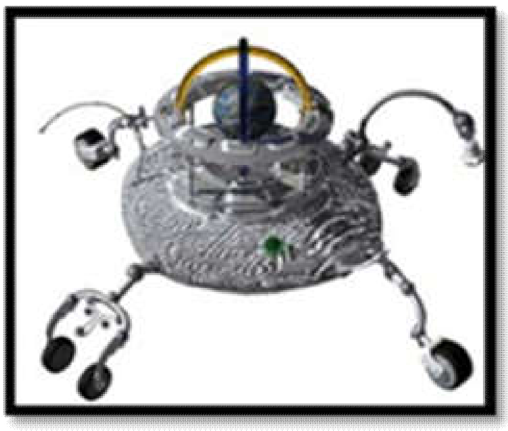

Fig. 4. Dental nanorobot

Mechanism of action: Once it enters inside the human body, nanorobots reaches the target sites as it was preprogramed in the nanocomputer on board, by utilizing the internal sources (the energy liberated by the radioactive fragments attached to the nanorobot body), but also the external sources (such as the host's body heat or the electrolytes and the metabolism of the glucose in the blood flow) of energy. When the target of the nanorobot is achieved inside the human body, they are retrieved by granting their exit via the usual human excretory channels. They may also be cleared away by active scavenger systems called nano-terminators.[8, 9] In dentistry nanorobots are used for inducing local anesthesia, treatment of dentin hypersensitivity, cavity preparation and restoration, maintenance of oral hygiene and orthodontic treatment etc.

APPLICATIONS IN CLINICAL DENTISTRY

NANODIAGNOSIS: Nanorobotic devices can be used in the early detection of diseases like cancer and for the detection of biomarkers and pathogens.[10]Cancer nanotechnology could open up new opportunities for personalized cancer diagnosis and treatment approaches by means of multifunctional nanoparticles in four main area: detection of cancer disease-specific biomarkers, imaging of tumors and their metastases, the functional delivery of therapeutic agents to target cells, and realtime monitoring of treatment in progression.[11] Saliva may be used as a non-invasive diagnostic tool for analyzing the biochemical indices of proteomic and genomic markers.[10]Applications of nanodiagnosis include sensor systems likenanoelectro mechanical systems (NEMSs), oral fluid nano-sensor test (OFNASET), and optical nanobiosensors.[10]

Nano Electromechanical Systems (NEMS): Nanotechnology based NEMS biosensors that exhibit ingenious sensitivity and specificity for detection of abnormal cells at molecular level are being developed. They convert (bio) chemical to electrical signal.[12]

Fig. 5. Oral fluid nanosensor tests

OFNASET: Oral fluid nanosensor tests (OFNASET) (Fig. 5) are micro-electromechanical systems consisting of sensor array chips used for the detection of electrochemical sensors of cancer such as salivary protein and RNA biomarkers. It is used for multiplex detection of salivary biomarkers for oral cancer. And, it can also be used for diagnosis of breast, pancreatic, and lung cancers; Type II diabetes; Alzheimer's disease; and Sjögren's syndrome.[10, 12]

Optical nanobiosensors: Optical nanobiosensors use the principles of optics for the transduction of biochemical interactions into suitable output signals. It is a unique fiberoptics-based tool which allows the minimally invasive analysis of intracellular components (Cytochrome C)(Fig. 6).[10, 12]

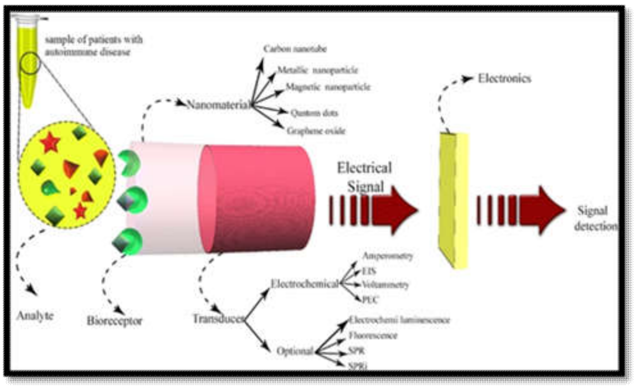

Fig. 6. Optical nanobiosensors

NANOPREVENTION

NANOSILVER FLUORIDES: For many years fluoride preparations have been known to prevent dental caries and several high strength topical preparations are available for this purpose.[13] Due to its unique characteristics, such as high specific surface area and a high fraction of surface atoms silver nanoparticles (AgNPs) have attracted the attention.[14] The effectiveness of NSF in the arrest of caries can be attributed to the synergism of it's components, chitosan, AgNPs, and fluoride formulation. Silver is used in the form of nitrates to cause antimicrobial effects, but when AgNPs are used, the surface area available for exposure to the microbe is greatly increased. According to Sondi I, AgNPs are capable of anchoring and penetrating the bacterial cell wall and causes structural changes in the cell membrane such as cell membrane permeability and cell death. "Pits" are formed on the surface of the celland nanoparticles are deposited. Danilcauk and Kim suggest that the creation of free radicals by AgNPs may be considered another process which leads to the cell death.[14]
Silver Diamine Fluoride or SDF's main advantage in preventing dentine caries is due to its efficacy. It is noninvasive, and hence, there is a very low risk of transmitting disease. One of the disadvantages of using SDF is that it stains the lesions black. The SDF solution also has a metallic taste on the oral mucosa and forms reversible white lesions when SDF comes into contact with the tissues. On the other hand NSF does not stain the teeth black and also children have not complained about the metallic taste and also no lesions were found on oral tissues.[14]

ii) NANOHYDROXYAPATITE TOOTHPASTE: Nano-hydroxyapatite (n-HAp) is one of the most biocompatible and bioactive materials, and has gained wide acceptance in dentistry in recent years.Nano-sized particles have similarity to the apatite crystals of tooth enamel in morphology and crystal structure.[15] Nanohydroxyapatite toothpastes deliver a nanocrystalline form of hydroxyapatite particles at a size 20–50 nm which is conducive for natural repair.[10] A study conducted by K. Najibfard et al. concluded that nHAP dentifrice caused remineralization comparable to fluoride dentifrices, and inhibited caries development, thus suggesting that an nHAP dentifrice can be used as an effective alternative to fluoride toothpaste.[16]The caries remineralizing action of nHAP employed in a dentifrice formulation can be explained by the potential of hydroxyapatite nano-crystals to precipitate on the lesion surface, believed to be facilitated by its strong surface bioactivity coupled with its chemical and physical similarity with natural enamel.[10] nHAP-containing dentifrices can be recommended for children or those who are concerned about dental fluorosis. Since the remineralizing efficacy of topical fluorides is strictly dependent on the availability of calcium and phosphate ions, nHAP dentifrices can be used in xerostomic patients with diminished amounts of saliva.[16]

NANOTREATMENT

NANOADHESIVES: Recently, 3M ESPE introduced a new product, a nanofilled resin-modified glass ionomer cement which utilizes a Ketac-nano primer for the optimum bonding to enamel and dentin. Ketac-nano primer is a one-component water-based acidic primer having a pH 3. The use of Ketac-nano primer does not require the preconditioning step; in spite of that the use of either 37% phosphoric acid or Ethylenediaminetetraacetic acid (EDTA) solution prior to the application of the Ketac-nano primer to dentin significantly improved the bond strength.[17]

NANOCOMPOSITE: The term nanocomposite is used for composite materials which are composed of nanomaterials integrated with ceramic, metal of polymer matrix. The emergence of nanocomposites has enabled the use of a single restorative material, universally, in various areas of the oral cavity, as these composite materials possess favorable esthetic and excellentmechanical properties, such as high initial polish and polish retention, and improved handling characteristics.[18, 19] Nanofillers used in nanocomposites are very different from traditional fillers and to reduce the filler particle size below 100 nm, synthetic chemical processes were used to produce building blocks on a molecular scale. There are mainly 2 kinds of nanofiller particles – nanomeric particles (NM) and nanoclusters (NC). The nanomeric particles are monodisperse non-aggregated and non-agglomerated silica nanoparticles.[20, 21] There are 2 types of nanocluster fillers. The first type consists of zirconia-silica particles synthesized from a colloidal solution of a zirconyl salt and silica.The second type of nanocluster filler, are synthesized from 75 nm primary particles of silica and has a broad secondary particle size distribution with a 0.6 µm average.[21]

NANO GLASS IONOMER CEMENT: Glass ionomer cements (GICs) have a wide range of applications in dentistry. Glass ionomer cement has revolutionized the restorative approaches, mainly in minimally invasive dentistry.[15]The incorporation of nanoparticles (the average particle size of glass ionomer particles were around 10-20µm) into the glass powder of glass ionomers results in wider particle size distribution, which resulted in higher mechanical values. These nanoparticles can occupy the empty spaces between the Glass ionomer particles and act as reinforcing material in the composition of the glass ionomer cements.[22, 23] The nanofiller components of nano ionomers also enhance some physical properties of the hardened restorative materials. Its bonding mechanism are often attributed to micro-mechanical interlocking provided by the surface roughness, presumably combined with chemical interaction through its acrylic/itaconic acid copolymers. Nano light-curing glass ionomer (Fig. 7) restorative material blends nanotechnology originally developed for Filtek™ Supreme Universal Restorative with fluoraluminosilicate (FAS) technology. Their most important advantages include: superb polish, excellent esthetics, and improved wear resistance. The clinical indications include: - primary teeth restorations; - transitional restorations; - small Class I restorations; - sandwich restorations; - class III and V restorations; - core build-ups.[23]

Fig. 7. Nano light-curing glass ionomer

NANODRUG DELIVERY: Nano-scale drug-delivery systems take advantage of the fact that nano-scaled materials (10−9 to 10−7 m) can exhibit different physical properties, electrical, mechanical and optical, that differ from those observed in the macroscopic and atomic realms. Through rational design, nano-scale drug-delivery systems can be manufactured to combine desirable designs, both biological and synthetic, for various applications like implantable, inhalable, injectable, oral, topical and transdermal drug delivery.[24, 25] There are several nanobiomaterial structures developed for drug delivery. Spherical nanoparticles are the simplest to create, other shapes and constructions like nanocapsules, nanotubes, nanogels and dendrimersoffer advantages for certain applications.[24]

NANOIMPLANTS: Implants are commonly used in dentistry for restoring teeth.Nanosurface modifications have been implemented to improve the efficacy of endosseous titanium implants at commercial and experimental levels. Although limited, in vitro studies provide information on their biological capability. Titanium surfaces with enhanced microscale and nanoscale morphological features exhibited better osteoblastic behavior, such as increased cell attachment, proliferation, alkaline phosphatase activity, and upregulated gene expression of bone-related proteins, when compared to surfaces with microfeatures alone. Studies also revealed the new potential of nanofeatured titanium surfaces as a smart material for inducing cell-specific affinity, eg, selective attractiveness for osteogenic cells but not for fibroblasts.[26]

LOCAL ANESTHESIA: Nanogels are composed of nanostructured crosslinked polymeric networks of high biocompatibility and biodegradability behaviors. Tan et al., while reviewing the application of nanogel systems in the administration of LAs, have concluded that nanogels exhibit excellent thermodynamic stability, high solubilization capacity, low viscosity, ability to withstand sterilization techniques, and high blood circulation time, which are considered as the properties of fundamental importance for the development of novel drug delivery systems. According to Lee et al., injections made with nanogels are found to be less painful when compared to cosolvent-based formulations, which is a property of particular relevance in clinical pediatric dentistry.[27, 3]

Fig. 8. Nanorobotic local anesthesia

NANONEEDLES: The nanoneedles developed by NanoPass Technologies consist of tiny pyramid-shaped 'micro needles' made out of silicon and with a central bore hole to allow the passage of large molecules. The nanoneedle is designed to penetrate the membrane of a living cell for the targeted drug delivery into the cytoplasm or the nucleus.[18]Nanoneedles can be used to deliver molecules such as nucleic acids, proteins, or other chemicals to the nucleus, or can even be used to carry out cell surgery. Using the nanoneedle approach, we can get drugs to a very specific location within the nucleus; this is the key advantage of this method.[19]Recently, in dentistry suture needles incorporating nano sized stainless steel crystals have also been developed. Trade name: Sandvik Bioline, RK 91 TM needles.[28]

POTENTIAL FUTURE APPLICATIONS

NANOROBOTIC DENTIFRICES: Nanorobotic technology used in toothpaste and mouthwashes in the form of dentifrobots (fig. 33) are useful in monitoring the gingival and tooth surfaces regularly and removal of harmful materials and calculus (Jr Freitas, 2000). [3]The toothpastes (dentrifices) that contain the apatite nanoparticles can be used for both biofilm management and for remineralization of submicrometer-sized enamel lesions. Dentifrobots could also provide a continuous barrier to halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodor.[3] The futuristic proposals of Dentifrobots include Subocclusal -dwelling nanorobotic dentifrice delivered by mouthwash or toothpaste could patrol all supragingival and subgingival surfaces at least once a day, metabolizing trapped organic matter into harmless and odorless vapors and performing continuous calculus debridement (invisibly small (1–10µm) dentifrobots, 103–105 nanodevices/oral cavity and crawling at 1–10µm/s).[3]

MAJOR TOOTH REPAIR/ NANOTISSUE ENGINEERING: The introductionof nanomaterials (NM) and tissue engineering (TE) in dentistry and have revolutionized perspectives and are changing their clinical activities.In recent decades NM and TE have been integrated in dentistry with the introduction of nanotechnologies in the constitution of scaffold matrices (rigid and soft), the use of growth factors and stem cells, and with the introduction of biomodulation techniques for dental hard tissue reconstruction.[29] Over time, various techniques were attempted in regeneration of entire tooth, like the assembly of bioengineered component parts, the pellet engineering, the chimeric tooth engineering, the gene manipulated tooth regeneration. Presently, the two most followed routes for the regeneration of the entire tooth are: scaffold-based tooth regeneration and simulation of the embryonic development of natural teeth. The first method is to implant in vivo a scaffold with stem cells formed in vitro. At the beginning the technique consisted of inserting cells from swine dental germs in a scaffold then implanted into rats and it gave encouraging results (in about 15% of cases), but with training of dental structures smaller than normal teeth. Then, there was remarkable results using autotransplantation in the swine, getting tooth regeneration using dental bud cells alone or combined with bone marrow fluid in gelatin-chondroitin-hyaluronan tri-copolymer scaffold. More recently, with the introduction of nanofibrous scaffolds based on PLLA/MWNTs/HA, PLLA/HA or PCL/gelatin with or without HA obtained by electrospinning were used and the results were found to be better though not decisive. The second method is based on the concept of mimicking the embryological development to create natural teeth in animals using embryonic, neural and bone-marrow-derived stem cells without the use of a scaffold. Perfect formed teeth were obtained and then is successfully implanted.[29, 30]

CONCLUSION

Nanotechnology will definitely bring enormous changes into the field of dentistry, healthcare, and human life more profoundly than many developments of the past.[31, 32]It sounds like science fiction, but to treat an oral disease, we dentists will ask the patients to rinse with a solution containing millions of microscopic machines called "nanoassemblers". These minute workers, receiving signals from a computer controlled by the dentist, will swarm in the areas of patient's mouth and eliminate the disease and bacteria causing the disease.[33] One factor that hasbe taken into consideration when developing nanotechnologies is the cost of the device or therapy being developed. There are numerous complex therapies being developed to treat a wide range of diseases, not only in dentistry but also in biomedicine more broadly, but they are going to never see clinical use as it will be too expensive to synthesize and thus too expensive for purchasers to procure. Cost is an important factor that is often forgotten in the development of new therapies and devices, but is ultimately the hurdle that will decide it’s progressesion.[33, 34] It also posses a lot of risk to the human beings. Its safety and biocompatibility should be evaluated before its application in human and further research in this field is needed before wide application.[31,35]

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