Role of Nanotechnology and Nanoparticles in Dentistry: A Review


*King George’s Medical University, Lucknow ** Purvanchal Institute Of Dental Sciences

Abstract: The purpose of this review work was to establish Nanotechnology application in field of Dentistry. There are different nanoparticle as nanobubbles, quantum dots, nanoshells, dendrimers, liposomes, nanorods, fullerences, nanospheres, nanowires, nanobelts, nanorings, and nanocapsules are using in dentistry. Biomedical application of nanotechnology was also diagnostic techniques, drugs, and prostheses and implants. Oral health care could be hauled to unprecedented heights, by the application of various components of nanotechnology, biomaterials, tissue engineering and dental nanorobots for local anaesthesia, hypersensitivity cure. To Diagnosis of Oral Cancer Cantilever array sensors are used in different particle shape and most important in size and different nanoparticles diagnosis test as a multiplexing modality, oral Fluid NanoSensor Test (OFNASET), optical Nanobiosensor and as drug delivery system in the treatment of oral cancer.

Keywords: dentistry, nanotechnology, oral cancer.

INTRODUCTION

Science is undergoing yet another change in helping mankind enter a new era, the era of technology. Prof. Kerie E Drexler, a lecturer and a renowned researcher of nanotechnology, was the first person to use the term “Nanotechnology”. The word “Nano” is derived from the Greek word for “dwarf”. It is the science of dealing skillfully with matters measured in a scale as one millionth of a millimeter or one billionth of a meter, approximately the size of 2 or 3 atoms. Although the word nanotechnology is relatively new, the “natural version” of nanotechnology was already in pole position with preoccupation of life itself thousands of millions of years ago. All natural materials and systems establish their foundation at the nanoscale. Basically, the biological building blocks of life are nano-entities that possess unique properties determined by the size, folding, and patterns at nanoscale. The genetic material deoxyribonucleic acid (DNA) is composed of four nucleotide bases in sizes ranging in the sub-nanometre scale, and the diameter of the double-helix structure of DNA is in the nanometre range. The same is true for proteins and cell membranes which consist of lipids and proteins. Manufacturing “non-natural” nanomaterials is challenging.

The Royal Society and The Royal Academy of Engineering (2004) defined Nanoscience as the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at larger scale. Also defined Nanotechnology is the design, characterisation, production and applications of structures, devices and systems by controlling shape and size at the nanometre scale. The basic idea of this science is to employ individual atoms and molecules to construct functional structures. Just as robots assemble cars from a set of predefined parts, nano-robots will assemble things from atomic...
molecular building blocks. It is a rapidly growing field and its emerging tentacles have led to the origin of a completely new field, popularly known as Nanomedicine.

The first person to contemplate about the possible applications of nanotechnology to medicine was a Physicist, Richard P Feynman. In his a historic lecture in 1959, he quoted a saying, that “this is a development which I think cannot be avoided.” Nanomedicine is a novel branch of science that deals not only with diagnosing and treating diseases but also preserving human health and enhancing longevity using nanoscale structured materials. It has been applied to diverse medical fields such as oncology and cardiovascular medicine, discovery of biomarkers, molecular diagnostics, imaging, implant technology, surgery, drug discovery and drug/gene delivery.

Now-a-days, when people are coming across with applications of nanotechnology to medicine, it seems that Nanodentistry is not a far-fetched dream. Although, the advances of nanotechnology in dentistry have been relatively slow in comparison to its application in medicine. But still we can see that the applicability of Nanotechnology has become a reality in general dental practice procedures and in various specialties. Nowadays, dentists work with nanomaterials in their private practice. Several companies have undertaken to sell products such as nano-hybrid resins, nano-fillers and nano-adhesives. These new materials, upon being handled at a nano scale, increase their mechanical, physical and chemical properties when compared with conventional materials used in clinical practice.

**METHODS OF NANOTECHNOLOGY**

There are three steps to achieve products of nanotechnology:

1. Scientists must be able to manipulate individual atoms
2. To develop nanoscopic machines, called assemblers, which can be programmed to manipulate atoms and molecules at will.
3. In order to create enough assemblers to build consumer goods, some nanomachines called replicators, will be programmed to build more assemblers.

Assemblers and replicators work together, automatically construct products.

The following approaches are used in nanotechnology:

1. Bottom-up approach: To arrange smaller components into more complex assemblies. This method is used for producing nanoscale structures.
2. Top-down approach: To create smaller devices using larger ones to direct their assembly. These methods are mostly extensions of methods already employed in small scale assembly at the micron scale. By further miniaturization the nanodimensions is entered.
3. Functional approach: To develop components of a desired functionality without regard to how they might be assembled.

Current research is not exclusively focused on achieving assemblers. Instead, research is directed towards the production of a wide array of different nanoscale structures.

**NANOPARTICLES**

Various nanoparticles are nanopores, nanotubes, quantum dots, nanoshells, dendrimers, liposomes, nanorods, fullerenes, nanospheres, nanowires, nanobelts, nanorings, and nanocapsules.

Liposomes are nanoparticles comprising lipid bilayer surrounding an aqueous interior. They have similarity with biological membranes and have been used for improving the efficacy and safety of different drugs. Recently, Stealth liposomes have been developed, that have ability to evade the interception by the immune systems, and therefore have longer half-life. Polymers like polysaccharide chitosan nanoparticles have also been used as drug delivery systems. Polymer-drug conjugation reduces immunogenicity and promotes tumor targeting through the enhanced permeability and retention effect and at the cellular level following endocytic capture allows lysomotropic
Ceramic nanoparticles such as silica, titania, and alumina are used as drug vehicles and can be used in cancer therapy. Gold shell nanoparticles are spherical nanoparticles made of dielectric core covered by a thin metallic shell of gold. These particles have highly favourable optical and chemical properties for biomedical imaging and therapeutic applications. Fullerenes are carbon nanoparticles with a polygonal structure made up of 60 carbon atoms. They have got numerous points of attachment whose surfaces can be functionalized for tissue binding. Nanotubes are most extensively used types of nanoparticles because of their high electrical conductivity and excellent strength. Structurally, it is a sheet of graphite which is rolled to form a seamless cylinder. They have got application in delivery of nanomolecules.

Quantum dots are made of semiconductor materials with fluorescent properties. For applications they need to be covered with other materials allowing dispersion and preventing leaking of the toxic heavy metals.

**BIOMEDICAL APPLICATION OF NANOTECHNOLOGY**

Three applications of nanotechnology are particularly suited to biomedicine: diagnostic techniques, drugs, and prostheses and implants.

**Diagnostics:** Now-a-days sensors are available that can identify bacteriological infections. The principle is precise current measurement on a robust substrate by the way of ion channels which serve as entranceways into cells. High throughput screening (HTS) is massive, fast, repetitive manufacturing or analyzing. If you want to do it fast, you need a small device. If you need to repeat a process step many times, you have to use laminar flows of liquids and plugs. This leads to lab on-a-chip concepts. In a lab-on-a-chip, minuscule amounts of liquids or gases are mixed in small channels, where they react and the reaction product is analyzed on the spot. Nanotechnology is being applied to biomarker-based proteomics and genomics technologies. Nanoparticles can be used for qualitative or quantitative in vivo or ex vivo diagnosis by concentrating, amplifying, and protecting a biomarker from degradation, in order to provide more sensitive analysis. By using magnetic nanoparticle probes, the amplification is comparable to polymerase chain reaction. This enables very early diagnosis before severe cellular damage. Nanoparticles are currently being tested for molecular imaging to achieve a more precise diagnosis with high quality images.

**Nanodrugs:** With the use of nanotechnology, targeting drug molecules to the site of action is becoming a reality resulting in a personalized medicine, which reduces the effect of the drug on other sites while maximizing the therapeutic effect. Carbon buckyballs and nanotubes are useful as drug delivery vehicles because their nanometer size enables them to move easily inside the body crossing different barriers. Liposome and polymer based nanoparticles are the most widely used as drug delivery systems, as they are biodegradable and do not accumulate in the body. Various anticancer drugs, such as paclitaxel, 5-fluorouracil, and doxorubicin have been successfully formulated using polymers and liposomes as drug delivery systems. Biodegradable nanoparticle based vaccines for oral vaccination are under development and may allow targeting of antigens to specific dendritic cell receptors.

Cosmetics based on quantum dots are already sold in large quantities. Nanophase Technologies Corp. produces nanocrystalline materials such as zinc oxide for use in sunscreens and other products. These particles are between 3 and 200 nm and are protective, non-toxic and cause minimal damage to DNA in sunlight.

**Prostheses and Implants:** Nanotechnology also has applications in tissue engineering for bones, teeth and other tissues. John Jansen, the professor of Dentistry in Netherland, believes that techniques based on biological nanostructures are feasible for tissue engineering. Researchers put a biological material in a mold—a straitjacket, as it were—which forces it to assume the shape of a body part, such as a hipbone. Biomimetic nanostructures start with a predefined nanochemical or physical structure. A nanochemical structure may be an array of large
reactive molecules attached to a surface, while a nanophysical structure may be a small crystal. Researchers hope that by using these nanostructures as seed molecules or crystals, a material will keep growing by itself.22

**NANOTECHNOLOGY IN DENTISTRY**

Nanodentistry is a very promising field, in virtue of which oral health care could be hauled to unprecedented heights, by the application of various components of nanotechnology, nanomaterials, tissue engineering and dental nanorobots. Following are the applications of nanotechnology in dentistry:

1. Local anaesthesia:

In the age of nanodentistry, a colloidal suspension consisting of myriad of active analgesic micron-size dental robots will be infused on patient’s gingiva. Thereafter, these wandering nanorobots reach the pulp via the gingival sulcus, lamina propria, and dentinal tubules. After reaching pulp, dentist may command the analgesic dental robots to switch off all sensitivity in tooth requiring treatment. When treatment of a particular tooth would be done, all sensations would be restored swiftly, since nanorobots will abjure the control of nerve signals after receiving commands from dentist and will exit from same path used for entry.22

2. Hypersensitivity cure:

Any alteration in the hydrodynamic pressure transmitted to the pulp is most likely to be a cause of dentin hypersensitivity. This hypothesis rests upon the fact that dentinal tubules and tubules with diameter twice as large than nonsensitive teeth are 8 times more numerous on surface than nonsensitive teeth. In coming future, this complain of patients will be alleviated by dental nanorobots, which would selectively occlude tubules, utilizing native biological materials.22

**HOW DENTAL NANOROBOTS REACH PULP:**

After reaching the dentin, the nanorobots enter dentinal tubular holes that are 1 to 4 µm in diameter and march toward the pulp, guided by myriad of chemical gradients, temperature differentials and even position of navigation, all aforementioned factors are controlled by nanocomputer which is operated by the dentist. There are many pathways to travel from dentin to pulp. Tubular density may present noteworthy challenges to navigation, owing to different tubular branching patterns. Nanorobots can complete the journey to the pulp chamber in roughly 100 seconds at a speed of 100 micrometer/sec, since the distance is supposed to be 10mm. 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 insinuates that such voyage be reasonable by cell-sized nanorobots of similar mobility to reach to pulp.27-30

4. Diagnosis of Oral Cancer:

- Cantilever array sensors: Based on ultrasensitive mass detection technology:26
  - Picogram (10-12) – bacterium
  - Femtogram (10-15) – virus
  - Attogram (10-18) – DNA

Nanoelectromechanical systems (NEMS):

Nanotechnology based NEMS biosensors that exhibit exquisite sensitivity and specificity for analyte detection, down to single molecule level are being developed. They convert (bio) chemical to electrical signal.2,26

Multiplexing Modality: Sensing large numbers of different biomolecules at a time.26

**Oral Fluid NanoSensor Test (OFNASET):** The Oral Fluid NanoSensor Test (OFNASET) technology is used for multiplex detection of salivary biomarkers for early diagnosis of oral cancer. It has been established that the combination of two salivary proteomic biomarkers (thioredoxin and IL-8) and four salivary mRNA biomarkers (SAT, ODZ, IL-8, and IL-1b) can diagnose oral cancer with high specificity and sensitivity.31

**Optical Nanobiosensor:** 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 in apoptosis, or programmed cell death as become possible by the use of nanobiosensor, a sole fiberoptics based tool.32

5. Treatment of Oral Cancer:

Nanomaterials For Brachytherapy: BrachySiITM (Sivida, Australia) delivers 32P, clinical trial.

Drug Delivery Across The Blood-Brain Barrier: More effective treatment of brain tumours, Alzheimer’s, Parkinson’s in development.

Nanovectors For Gene Therapy: Non-viral gene delivery systems.

Photodynamic Therapy: Hydrophobic porphyrins are potentially interesting molecules for the photodynamic therapy (PDT) of solid cancers or ocular vascularization diseases.33

6. Dental durability, Appearance and Dentifrobots:

Tooth durability and appearance may be enhanced by replacing upper enamel layers with pure sapphire and diamond which can be made more fracture resistant as nanostructured composites, probably including entrenched carbon nanotube.26 Toothpaste or mouthwash could be used to deliver nanorobotic dentifrice, which would abide subocclusally, since they would have an inbuilt programme to avert occlusal region. Their function would be alike conventional dentifrices but the approach would be entirely different, as they would be infinitesimal [1-10 micron] mechanical devices, crawling at a speed of 1-10 microns/sec, functioning by metabolising trapped organic matter into harmless and odorless vapors and debriding calculus incessantly. From the safety point of view, if swallowed accidentally, they would deactivate themselves. Dentifrobots would be programmed to identify and destroy pathogenic bacteria residing in the plaque and oral cavity, while sparing around 500 species of harmless oral micro flora. Thus by killing bacteria, dentifrobots would provide a blockade against halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodor.34 With this kind of daily dental care available from an early age, conventional tooth decay and gingival disease will disappear.

7. Orthodontic treatment:

Orthodontic nanorobots could directly influence the periodontal tissues, allowing brisk and painless tooth straightening, rotating and vertical repositioning within minutes to hours. This is in contrast to current molar up righting techniques, which require weeks or even months to complete.26

8. Tooth Repair:

Nanodental techniques for major tooth repair may develop through several stages of technological progress, first taking small steps of genetic engineering, tissue engineering and regeneration, and then marching ahead with a gargantuan leap of development of whole new teeth in-vitro and their installation.35

9. Dentition Renaturalization:

Aesthetic dentistry would enter an entirely novel era with the addition of dentition renaturalization procedures to the conventional dental practice armamentarium. Demand will witness a sudden spurt for full coronal renaturalization procedures, in which all fillings, crowns and other 20th century treatment techniques will be replaced with the affected teeth remanufactured to become alike original teeth.2

10. Nanocomposites:

Nanoproducts Corporation has successfully manufactured nonagglomerated discrete nanoparticles that are homogeneously distributed in resins or coatings to produce nanocomposites. The nanofiller used include an aluminosilicate powder having a mean particle size of 80 ran and a 1:4 M ratio of alumina to silica and a refractive index of 1.508. Advantages are superior hardness, superior flexural strength, modulus of elasticity and transluency, 50% reduction in filling shrinkage, and excellent handling properties.26,36

Trade name: Filtek O Supreme Universal Restorative Pure Nano O

11. Nanosolution:

Nanosolutions produce unique and dispersible nanoparticles, which can be used in bonding agents.
This ensures homogeneity and ensures that the adhesive is perfectly mixed everytime.26,36


12. Impression materials:

Nanofillers are integrated in vinylpolysiloxanes, producing a unique addition of siloxane impression materials. The material has better flow, improved hydrophilic properties and enhanced detail precision.26,36

Trade name: Nanotech Elite H-D

13. Nanoencapsulation:

Latest development in the field of targeted release systems is credited to SWRI [South West Research Institute] which has developed nanocapsules including novel vaccines, antibiotics and drug delivery with reduced side effects. In this series of development, most recent name is Osaka University in Japan that holds the privilege of developing targeted delivery of genes and drugs to human liver in 2003. In this research project, engineered Hepatitis B virus envelope L particles were allowed to form hollow nanoparticles displaying a peptide that is imperative for liver-specific entry by the virus in humans. Likewise, in future specialized nanoparticles could be engineered to target oral tissues, including cells derived from the periodontium [Yamada et al, 2003]. 26,36

14. Other products of SWRI:

a). Medical appendages for hastened healing:

• Biodegradable nanofibres - will serve as delivery platform for haemostatic
• Role of silk nanofibres in wound dressings is under scanner.

• Nanocrystalline silver particles with antimicrobial properties on wound dressings [ActicoatTM, UK]

b) Protective clothing and filtration masks, utilizing antipathogenic nanoemulsions and nanoparticles

c) Bone targeting nanocarriers: Calcium phosphate based biomaterial has been developed. This bone biomaterial is an easily flowable, moldable paste

Downloaded from www.jrdindia.org

that conforms to and interdigitates with host bone. It supports growth of cartilage and bone cells.26,36

15. Nanoneedles:

Suture needles incorporating nano-sized stainless steel crystals have already been developed.

Trade name: Sandvik Bioline, RK 91TM needles
[AB Sandvik, Sweden]

Nanotweezers are also under development which will make cell surgery possible in near future.26,36

16. Materials used for bone replacement:

Hydroxyapatite nanoparticles used to treat bone defects are: 26,36

VITOSSO (Orthovita, Inc, USA) HA +TCP
NanoOSTM (Angstrom Medica, USA) HA
Ostim® (Osartis GmbH, Germany) HA

POSSIBLE RISKS FROM NANO PARTICLES:

Nanobiotechnology could dramatically improve public health, but there is concern that technical developments could cause unforeseen adverse effects. Humans have been exposed to nanoparticles throughout their evolutionary phases; however this exposure has been increased in the past century because of the industrial revolution. Nanotechnology is also being applied in medical sciences trying to achieve a personalized medicine. Epidemiological studies have shown that urban population with airborne particulate matter (nanoparticle also constitute a part of particulate matter) deriving from combustion sources, such as motor vehicle and industrial emissions, contributes to respiratory and cardiovascular morbidity and mortality. Similarly nanoparticles may also contribute to the toxicological profile of nanoparticles in biological systems. The smaller particles have more surface area per unit mass, and this property makes nanoparticles very reactive in the cellular environment. The respiratory system, blood, central nervous system, gastrointestinal tract and skin have been shown to be targeted by nanoparticles.4,22

CONCLUSION:

Nanodentistry will eventually allay any apprehension of patients towards dentistry, since,
Unlike conventional dental techniques and instruments; it would not mandate the patient to sit in bizarre postions with their mouth wide open, for hours; thus redeeming them from inexplicable mental trauma. Nanotechnology has vast untapped potentials, which if exploited sagely and ethically can revolutionize both medicine and dentistry. Its advent would not only lead to a leviathan technology leap in aforementioned fields, but it would also substantially haul down the cost, hence making dental treatment accessible and affordable to even most impecunious sections of society.

REFERENCES:


