Minireview Article

'Today's Vision Tomorrow's Reality : Nanorobotics in Dentistry'

ABSTRACT –

Nanorobotics is the emerging technology field creating machines or robots whose components are at or close to the scale of a nanometer (10^{-9} meters). A promising area of nanotechnological development is designing and building of *nanorobots*, with devices ranging in size from 0.1–10 micrometers and constructed of nanoscale or molecular components. The concept of nanotechnology involves these robots that are too small, in fact that they can build things with molecules and even change the molecular structure of existing material. Nanorobotics is an interdisciplinary field which involves collaborative efforts between computer scientists, engineers, biologists and other specialists to work towards a common insight. Possibilities for nanorobotics in medicine include early diagnosis and targeted drug-delivery for cancer, surgery, monitoring of diabetes, and other health issues. An increased interest of nanotechnology in dental applications has lead to the inception of a new field called Nanodentistry. Nanodentistry will make it possible to maintain near- perfect oral health through the use of nano-materials, biotechnology and nanorobotics. It might change dentistry, healthcare and human life more profoundly than many development of the past. Nanodentistry includes desensitization of teeth, manipulation of the tissues to re-align and straighten irregular set of teeth, drug delivery, and many more. In this review it is explained that how nanorobots can be used to do preventive, restorative, curative dental procedures.

Key words- Nanodentistry, nano-fillers, nano-materials, nanoparticles, nanorobotics.

INTRODUCTION

Nanotechnology can best be defined as an illustration of activities at the level of atoms and molecules that have solicitation in the real world. A nanometer is a billionth of a meter, or it can be imagined as 1/80,000 of the diameter of a human hair.[1] This size-related challenge is measured, manipulated and assembled on

the scale of 1-100nm. The engineering of such molecular upshots are performed by various robotic devices, which have been entitled as nanorobots.[2] Nanotechnology is associated with the creation of microscopic objects. Some of these objects are too small that they're constructed not with regular materials but with the very atomic building blocks of life. The main focus is creating robots that are so small that they are imperceptible to the naked eye. Operating as a swarm, these tiny robots have the potential to do some miraculous things. The names nanobots, nanoids, nanites, nanomachines, or nanomites have also been used to describe these devices currently under research and development.[3] These microscopic robots will theoretically have the capability to do things which may seem like magic. From building things out of thin air to curing diseases and even solving environmental problems, nanobots can be one of the most important advances mankind has ever created. While this technology may still be quite new, there are already a number of proposed uses for these microscopic little robots.[4]

METHODOLOY FOR SEARCH STRATEGY

A literature search Medline and PubMed databases were searched under the following key terms: "Nanodentistry," "nanorobotics," "nanomedicine," "nanomaterial," "nano," and "nanotechnology." All keywords were restricted in title or abstract without the language limitation. Only highly relevant articles from manual and electronic databases were selected for the present review. The aim of this review is to highlight the current literature regarding the concept of nanorobotics in dentistry.

LITERATURE REVIEW

The word 'nano' is derived from the Greek word for dwarf which combines with a noun to form words such as *nanometer*, *nanotechnology*, and *nanorobot*.[5] A nanorobot is substantially a controllable machine that interact with the body at molecular scales with a high degree of specificity. The field of nanorobotics studies the design, manufacturing, programming and control of the nano-scale robots. Dental nanorobots are programmed to crawl or swim through human tissue with navigational precision, sensing, signaling, information processing, intelligence, swarm behavior at nano scale in real time.[6]

Nobel Prize winning physicist **Richard Feynman**, at an American Physical Society meeting in **1959,** lectured on "There's Plenty of Room at the Bottom," which is often held to have provided inspiration for the field of **nanotechnology**.[7] He described that a process might be developed to manipulate individual

atoms and molecules, using one set of precise tools to build and operate another proportionally smaller set to a needed scale.

The Japanese scientist, **Norio Taniguchi** was the first to use the term **"nano-technology"** in a **1974** conference.[8] He defined nanotechnology as, 'Nano-technology' mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or one molecule."

NANOROBOTICS THEORY

Nanotechnology, a technology which deals objects of nanometer size and the particles are called as nanoparticles. Since these nanorobots are minuscule in size, thus it would probably be imperative for them to work altogether and perform both microscopic and macroscopic tasks. An onboard nano-computer that executes pre-programmed instructions in response to local sensor stimuli is used to control its functions.[9] It is based on the idea of creating functional structures by controlling atoms and molecules on a one-by-one basis. In other words nanotechnology is related as "the science of the small."

Mechanism of Action-

The working of a nanorobot is based on nanoparticles that ranges in dimension as same as that of cellular and molecular components.[10] They are controlled by on-board computers capable of performing around 1000 or more computations per second. A Communication and navigation network is installed in the body, that provides a high positional accuracy to all passing nanorobots and keep track of the various devices in the body. Nanorobots are able to distinguish unhealthy cells and destroy them wherever they are located.[11] Nanomedicine can overcome many important medical problems with these nanodevices and nanomaterials.

NANOSTRUCTURES USED IN DENTISTRY

NANOPARTICLES

Nanoparticles (diameters of between 0.1nm and 100nm) of the various compositions represent the most widespread use of nanoscale units in dentistry. Composites containing nanoparticles allow the production of smooth surface after polishing and confer much superior esthetic features to the material. Composite resins containing such particles are easy to shape and have a high degree of strength and resistance to

abrasion. Nanohyhybrid composites are currently the most ubiquito example of such technology.[12] Significantly smoother surfaces were achieved using composites with nanofiller compared to other composites.

NANORODS

Fluoridated hydroxyapatite (FHA) in nanorod morphology and hexagonal cross section were synthesised via hydrothermal process using Apricot Tree Gum (ATG) as a surfactant. The nano sized hydroxyapatite particles can easily integrate into the dental tubules. Similar composition with teeth and bone, biocompatible, adsorbed to the enamel of the teeth, protect the teeth by making a film of artificial enamel around the tooth.[13]

NANOSPHERES

Nanospheres can be used in a similar fashion like the nanorods in formulating in restorative technology.

NANOTUBES

Carbon nanotubes (CNTs) are used as biomedical material because of their unique properties as they can effect nucleation of hydroxyapatite (HA). However, there are only a few reports on the use of CNTs as dental materials. It has been observed that CNTs selectively adhered to the surfaces of dentin and cementum, possibly by adhering to their exposed collagen fibers. Titanium oxide nanotubes have also shown to accelerate kinetics of HA formation in-vitro, so as to serve as coatings, which can accelerate bone growth the surface of the implants. More recently, modified single walled carbon nanotubes has been shown to improve the flexural strength of Resin-based composites.[14]

NANOFIBERS

Nanofibrillar silicate crystals and polymeric nanofibers or bioceramic nanoparticle-incorporated nanofibers have been explored for their potential use in dentistry. Their nanostructure and flexibility have highly contributed in improved dental regeneration. These nanofibers have also demonstrated an improvement the physical properties of the composites when added in correct proportion and with uniform distribution.[15]

NANOFILLERS

Nanofillers are integrated into vinylpolysiloxanes, producing a unique siloxane impression material that has a better flow, improved hydrophilic properties, and enhanced precision detail.[13]

NANOSHELLS

They can prove to be beneficial in the treatment of patients suffering from oral cancer. The nanoshell can be stimulated with infrared light in which the nanoshell absorbs the energy of the light and consequently generates heat. Through this mechanism, nanoshells have a potential photothermal therapeutic ability to destroy bacteria and tumor cells. This method minimizes the risk of trauma to the adjacent tissues. By manipulating the thickness of the layer making up the nanoshells, scientists can design these beads to absorb near-infrared light creating an intense heat that is lethal to cancer cells.[12]

NANOSURGICAL DEVICES

A microstructured silicon surgical knife with a diamond-layered tip has been developed. Diamond that has been chemically rigid, and silicon is non-magnetic and biocompatible. Their advantages are **-** sharper incision and lower penetration pressure.[15] Nanosized suture needles and nano-tweezers are also available under the development which aims in making cell-surgery possible in the near future.

DIAGNOSIS AND TESTING

Medical nanorobots can perform a vast array of diagnostic, testing and monitoring functions, both in tissues and in the bloodstream. These devices could continuously record and report all vital signs including temperature, pressure, chemical composition, and immune system activity, from all different parts of the body. Such nanorobots are swallowed by the patient for diagnostic purpose reach the surface of stomach lining and begin their search for signs of any infection. Contributions arising from nanotechnology in dentistry have been made mostly in three fields: atomic force microscopy (AFM), imaging contrast enhancers, and biochips.[16]

NANOROBOTS IN GENE THERAPY

Gene therapy is the alteration of faulty genes in the body to treat disease. Usually DNA that is does not contain any faulty gene is inserted into the body's cells by various methods. The most common method of insertion is by viral vectors. All viruses attach to body cells and insert their genetic information into the cell, so by attaching the DNA with the 'normal' gene to the virus, the faulty gene can be replaced. Nanotechnology provides an alternative to viral vectors for the method of insertion. Nanorobots can readily treat genetic diseases by estimating the molecular structures of the DNA and proteins found in the cell. Floating inside the nucleus of a human cell, an assembler-built repair vessel performs some genetic maintenance.[17] With trillions of these machines swarming through a patient's bloodstream, "internal medicine" would take on new magnitude and ailments such as cancer, viral infections or arteriosclerosis which are attacked at the molecular level could be cured.

NANOTECHNOLOGY FOR PREVENTING DENTAL CARIES

The use of a toothpaste containing nanosized calcium carbonate enabled remineralization of early enamel lesions. Furthermore, bacteriostatic effects of silver, zinc oxide, and gold nanoparticles on Streptococcus mutans has been reported.[16] As compared to the other nanoparticles, silver nanoparticles had an antimicrobial effect in lower concentrations and with lower toxicity.

DENTAL IMPLANTS

Nanotechnologies are increasingly used for surface modifications of dental implants. The determining factors for successful osseointegration are surface contact area and surface topography. Bone growth and increased predictability can be effectively expedited with implants by using nanotechnology. The addition of nanoscale deposits of hydroxyapatite and calcium phosphate creates a more complex implant surface for osteoblast formation. TiO_2 nanoparticles are mostly used in medical and in the field of dentistry. These new implants are more acceptable, because they enhance the integration of nano coatings resembling biological materials to the tissues. Bioactive CaP nanocrystals deposited on titanium implants are resorbable and stimulate bone apposition and healing.[18]

APPLICATION IN PERIODONTOLOGY

Nanotechnology is emerging as an interdisciplinary field that is undergoing rapid development and has brought about enormous changes in dentistry. It has various applications in Periodontology, including therapy for dentin hypersensitivity, dentition renaturalization, continuous oral health maintenance using mechanical dentifrobots and also in other preventive, restorative and curative procedures.[19]

Oral hygiene and halitosis

Recently, nanorobotic dentifrices (dentifrobots) delivered by mouthwash or toothpaste could patrol all supragingival and subgingival surfaces atleast once a day and can destroy pathogenic bacteria residing in plaque while allowing harmless oral microflora to flourish in healthy ecosystem. It metabolizes trapped organic matter into harmless and odourless vapours and performing continuous calculus debridement. These invisibly small dentifrobots (1-10 micron), crawlings at 1-10 microns/seconds would safely deactivate themselves if swallowed. Further being suspended in liquid and able to swim about, devices would be able to reach surfaces beyond reach of toothbrush bristles or fibers of floss.[19]

Bone replacement materials

Bone is a natural structure that is composed of organic compound (mainly collagen) and reinforced with inorganic ones. Nanotechnology aims to emulate this natural structure for orthopedic and dental application and more particularly for the development of nanobone. It incorporates nano-crystalline particles of hydroxyapatite (HA) that are similar in size, chemistry, and morphology to HA particles occurring in human bone. Nanocrystals shows a loose microstructure with nanopores situated between the crystals. The surface of these pores are modified such that they absorb protein due to addition of silica molecules. Bone defects can be treated by using these hydroxyapatite nanoparticles. These can be used in maxillofacial injuries requiring bone graft, cleft patient and osseous defects in periodontal surgeries.[20]

Nanomaterials for Tissue Regeneration

Nanobiomaterial-based tissue scaffolds are used for pulpal cell culture. Scaffolds based on nanofibers of biodegradable type I collagen or fibronectin are used for regeneration. Other nanobiomaterials that can be used for cell culture include natural silk and an injectable self-assembling collagen-I scaffold, which

when loaded with exfoliated teeth stem cells resulted in the formation of pulp-like tissue and functional odontoblasts. Nanohydroxyapatite-based bone graft materials are also being used to treat large bone defects.[20]

Oral anesthesia induction

Nanorobotic oral anesthetics are composed of a colloidal solution of activated nanosized local anesthetic molecules. When applied to the gingival or the oral mucosa and signaled, the anesthetic travels via the epithelial and connective tissues of the gingiva to reach the pulp, thus providing selective anesthesia, which is under the control of on-board nanocomputer as directed by the dentists. These nano-active solutions are directed to the target site by chemical and temperature gradients. Upon reaching the pulp and establishing control over the nerve-impulse traffic, these nanorobots may be commanded to shut all neurosensory sensations to a particular tooth or multiple teeth as desired by the dentist.[21] Nanorobot analgesic offer greater patient comfort, reduced anxiety, no-needle, greater selectivity and control ability of the analgesic effect, fast and completely reversible action and avoidance of most of side effects and complications.

Dental hypersensitivity

Dentin hypersensitivity is a common condition of transient tooth pain associated with variety of exogenous stimuli. Clinical cause of dentin hypersensitivity is exposed dentinal tubules as a result of gingival recession, cracked teeth, erosion, abrasion, abfraction or tooth fracture. Normally hypersensitive teeth have eight times higher surfaces density of dentinal tubules and the diameter is twice as large than non-sensitive teeth. Reconstructive dental nanorobots are able to selectively and precisely block dentinal tubules within minutes, offering a quick and permanent cure. These nanorobots travel toward the dental pulp via the dentinal tubules, all under the control of the onboard nanocomputers as directed by the dentists. There are many pathways to travel nanorobots from dentin to pulp. Because of different tubular branching pattern, tubular density may present significant challenge to navigation. Assuming a total path of length of about 10mm from the tooth surface to the pulp and a modest travel speed of about 100µm/second. As the nanorobots pass through the journey of enamel, dentin reaches to pulp, once they

are installed in the pulp, having established control over nerve impulse traffic, dental nanorobots may be commanded by the dentist to shut down the sensitivity in the selected tooth that requires treatment.[22]

Periodontal drug delivery system

Mordern drug delivery systems are designed to provide a targeted controlled slow drug release system. Nanotechnology advances are the cornerstone of a paradigm shift in targeting and safely delivering agents thereby improving controlled release, improving patient safety delivering agents and compliance, and reducing side effects. Utilizing nanoparticles to deliver therapeutic molecules has been explored for periodontal regeneration. Local targeted delivery has been enhanced by use of nano-sensors, nano-switches, and other nano-delivery systems. The most common molecular type is the small drug that can be antibacterial in periodontal diseases. Poly (D,L-lactide-co-glycolide) PLGA nanoparticles were developed to encapsulate minocycline for periodontal infections. The nanoparticles of size 85–424 nm have an entrapping efficiency of up to 29.9%.[23] The release was shown to be sustained for several weeks, which resulted in a considerable antibacterial effect compared to the minocycline-free nanoparticles. Triclosan nano particles were able to reduce gingival inflammation. Arestin is one such example where tetracycline incorporated into microspheres and has shown promising results when locally delivered into periodontal pockets. Examples of nanoscale delivery vehicles are now under investigation include polymeric particles, dendrimers, nanoshells, liposomes, magnetic nanoparticles, gold nanoparticles etc.

Photodynamic Therapy

Antimicrobial photodynamic therapy (PDT) is a treatment modality for removal of infectious pathogens. It uses a photosensitizer and light of a specific wavelength, eg, toluidine blue at 600-nm wavelength. Effective oral biofilm destruction with methylene blue dye (photosensitizer) encapsulated within poly (D,L-lactide-co-glycolide) PLGA nanoparticles (≈150 nm to 200 nm in diameter). A newly developed photosensitizer, indocyanine green (ICG), with loaded nanospheres when activated with 805-nm wavelength using a diode laser, has a PDT-like effect and may serve as a potential photodynamic periodontal therapy.[22]

ADVANTAGES

Nanodevices cannot be seen by the naked eye yet possess powerful capabilities. Nanorobotics is developing faster day by day in medical field because of its effectiveness, comfort and at the same time significantly reducing the risk and invasiveness. With advent of molecular nanotechnology many severe ill patients can be cured and renewed back to their lives. They have the potential to bring significant benefits, such as improved health, better use of natural resources, and reduced environmental pollution. Nanorobotics will diagnose a disease, prevent or treat it at early signs.[24]

DISADVANTAGES

Despite its varied applications and several benefits, nanotechnology cannot be termed as flawless. It is very expensive and its developing cost is very high. The design of the nanorobot is a very complicated and requires a lot of resources. Due to their reduced size, the increased surface area of nanoparticles results in an unforeseen interactions amongst these particles pressing uncertainty as to how these particles will react under different conditions and whether they will be able to cross cell membranes and enter cells. The augmented chemical reactivity of nanoparticles brings about the production of reactive oxygen species (ROS), which may cause oxidative stress, inflammation, and damage to DNA, proteins and membranes, ultimately leading to toxicity.[25] Nanorobots can cause a brutal risk in the field of terrorism. The terrorism and anti-groups can make use of nanorobots as a new form of torturing the communities as nanotechnology also has the capability of destructing the human body at the molecular level.[26] Privacy is the other potential risk involved with Nanorobots.

HOW SAFE ARE THESE NANOROBOTS

Nanotechnology has achieved a tremendous progress in the past several decades. The nonpyrogenic nanorobots used in *invivo* are bulk, carbon powder and macrocrystall sapphire. Purogenic nanorobots are alumina, silica and trace elements like copper and zinc.[27,28] If inherent nanodevice surface pyrogenecity cannot be avoided, the pyrogenic pathway is controlled by invivo medical nanorobots. Nanorobots may release inhibitors, antagonists or down regulators for the pyrogenic pathway in a targeted fashion to selectively absorb the endogenous pyrogens, chemically modify them back into the body in a harmless inactivated form.

CONCLUSION-

The multidisciplinary field of nanotechnology is bringing the science of almost incomprehensibly small device closer and closer to reality. The effect of this development will at some point be so fast that they will probably affect virtually all fields of science and technology. It is anticipated that most of the applications of nanorobots would be in medical field as it can interact with materials on molecular and atomic level. They could rebuild tissue molecules in order to repair a wound, or rebuild the walls of veins and arteries to stop bleeding and save lives.[29] They could make their way through the bloodstream to the heart and perform heart surgery molecule by molecule without many of the risks and discomfort associated with traditional open-heart operations. Nano-enabled technologies thus provides an alternative and superior approach to assess onset or progression of diseases, to identify targets for treatment interventions as well as the ability to design more biocompatible, microbe resistant dental materials, and implant.[30] Nanodentistry has strong potential to revolutionize dentistry to diagnose and treat diseases. Treatment options will become more numerous and exciting. All this demand, even more so than today, the best technical abilities, professional skills that is the hallmark of the contemporary dentists.

REFERENCES

1. Ignatyev MB. Necessary and sufficient conditions of nanorobot synthesis. Dokl. Math. 2010;82(1):671–75.
2. Sierra DP, Weir NA, Jones JF. A review of research in the field of nanorobotics. U.S. Department of Energy – Office of Scientific and Technical Information Oak Ridge, TN. SAND 2005;6808:1–50.
3. Drexler Eric. K. Nanosystems: Molecular Machinery, Manufacturing and Computation: John Wiley & Sons. 1992.
4. Yarin AL. Nanofibers, nanofluidics, nanoparticles and nanobots for drug and protein delivery systems. Scientia Pharmaceutica 2010;78(3):542.
5. Gupta I, Gokhale ST, Gupta R, Shweta. Nanorobotics in periodontics. J Dent Sci Res 2013;4(2):6-9.
6. Abhilasha M. Nanorobots. Int J Pharma Bio Sci 2010;1(1):1-10.
7. Couvreur P, Vauthier C. Nanotechnology: Intelligent design to treat complex disease. Pharm Res 2006;23(7):1417-42.
8. Kinosita K. Jr., Yasuda R, Noji H, Adachi K. A rotary molecular motor that can work at near 100% efficiency. Philos Trans: Biol. Sci. 2000;355(1396):473-89.
9. Howard J. Molecular motors: structural adaptations to cellular functions. Nature 1997;389:561-7. PMID: 9335494 DOI: 10.1038/39247
10. Vale RD. Switches, latches, and amplifiers: common themes of G proteins and molecular motors. J. Cell Biol. 1996;135:291-302. PMID: 8896589
11. Sujatha V, Suresh M. Nanorobotics a futuristic approach. J Dent Sci 2010;1(1):86-90.
12. Requicha AAG. Nanorobots NEMS and Nanoassembly. Proc. IEEE 2003;91(11):1922-1933.
13. B. Ji and H. Gao, Mechanical properties of nanostructure of biological materials. J Mech Phys Solids 2004;52:1963–1990.
14. Akasaka T, Nakata K, Uo M, Watari F. Modification of the dentin surface by using carbon nanotubes. Biomed Mater Eng. 2009;19(2-3):179-85. PMID: 19581712
15. Subbiah T, Bhat GS, Tock RW, Parameswaran S, Ramkumar SS. Electrospinning of nanofibers. J Appl Polym Sci. 2005;96:557–569.
16. Mathur B. Nanorobotics-Headway towards dentistry. Int J Res Sci Tech 2011;1(3):1-9.
17. Pedram A, Pishkenari HN. Smart Micro/Nano-robotic Systems for Gene Delivery. Curr Gene Ther 2017;17(2):73-79.
18. Kubo K, Tsukimura N, Tsukimura N. Cellular behavior on TiO_2 nanonodular structures in a micro-to-nanoscale hierarchy model. Biomaterials 2009;30:5319–5329. PMID: 19589591
19. Shetty NJ, Swati P, David K. Nanorobots: Future in dentistry. Saudi Dent J. 2013;25(2):49-52.

20. Dalai et.al. Nanorobot: a revolutionary tool in dentistry for next generation. J. Contemp. Dent. 2014;4:2:106-112.
21. Gupta AK, Singh G, Mehta A, Ommid M. Nanomedicine: Is really the future of anaesthesia. Br J Anaesth. 2011;107(23).
22. Jalaluddin Md, Krishnam R. Nanorobots. Ann Essences Dent. 2012;4:4:63-65.
23. Chaturvedi TP, Srivastava R, Srivastava AK, Gupta V, Verma PK. Doxycycline poly e-caprolactone nanofibers in patients with chronic periodontitis - a clinical evaluation. J Clin Diagn Res. 2013;7(10):2339-42. PMID: 24298524
24. Saadeh Y, Vyas D. Nanorobotic Applications in Medicine: Current Proposals and Designs. Am J Robot Surg. 2014;1(1):4-11. doi: 10.1166/ajrs.2014.1010. PMID: 26361635.
25. Vaughn JR. Over the horizon: Potential impact of emerging trends in information and communication technology on disability policy and practice. National Council on Disability, Washington DC. 2006:1–55.
26. Bharath N, Gayathri GV, Mehta DS. Nanorobotics in dentistry- The present status and future perspective. J Dent Prac Res 2011;1(2):41-7.
27. Chandra Mouli PE, Manoj SK, Parthiban S. Nanotechnology in dentistry- A review. Int J Biol Med Res 2012;3(2):1550-53.
28. de Ávila BEF, et al. Hybrid biomembrane–functionalized nanorobots for concurrent removal of pathogenic bacteria and toxins. Sci Robot. 2018;3(18):eaat0485. PMID: 33141704.
29. Rybachuk AV, Chekman IS, Nebesna TY. Nanotechnology and nanoparticles in dentistry. J Pharmcol Pharm 2009;1:18-20.
30. Harini G, Kaarthikeyan G. Advanced drug delivery systems in treating periodontal diseases-A review. IOSR J Dent Med Sci. 2014;13(1):27-32.