Review Article

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The Advent and Advances in Nanorobotics: A Comprehensive Review

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ABSTRACT

Background: Nanotechnology has a myriad of applications in dental materials, diagnosis and therapeutics. Nanorobots are controllable microscopic devices measured in nanometres. Their application in medicine holds a wealth of promise from eradicating diseases to reversing the ageing process and are also candidates for industrial applications. Nanotechnology has the potential to revolutionize dentistry to diagnose and treat diseases. It will change human life, dentistry and healthcare more profoundly than many developments of the past. Nanorobots greatly improve the synthesis of new materials with advanced properties, information, production technology, medical applications and transportation. This comprehensive review article highlights the importance of nanorobots, not only in dentistry but also in the up-gradation of human life.

Keywords: Nanorobotics, nanotechnology, nanorobots.

INTRODUCTION

The word Nano has been derived from the Greek word meaning dwarf.[1] The term Nanotechnology was coined by Prof. Kerie E. Drexler.[2] It is the science of manipulating matter measured in a billionth of a meter or nanometer.

Richard Zsigmondy studied about nanomaterials in the early 20th century. Richard Feynman, gave a lecture in 1959 called There's Plenty of Room at the Bottom, where he stated that the principles of physics allow the manipulation of things atom by atom.[3] In 1974, Norio Taniguchi from the Tokyo Science University stated that, Nanotechnology consists of the process of separation, consolidation and deformation of materials by one atom or one molecule.[4]

Nanorobots

They constitute smart structures capable of actuation, signalling, sensing, intelligence, information processing, manipulation and swarm behaviour at the nanoscale. It is the engineering at the atomic or molecular scale by constructing devices with unprecedented capabilities. Bionanorobots can utilize properties of biological materials, their designs and functionalities.[5]

A nanometer scale ranges from 1-100nm or it is a molecular scale that is composed of nano-scale components that algorithmically responds to input forces and information.[6]

The nanorobots cannot be seen with the naked eye and need techniques like Scanning Electron Microscopy (SEM) and Atomic Force Microscopy (AFM), to visualize them.

Atomic Force Microscopy or Scanning Force Microscopy (SFM)

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The AFM has a resolution in fractions of a nanometer. The AFM contains a silicon or silicon nitride cantilever with a sharp probe at its end to scan the specimen surface. In the early 1980s, the scanning tunneling microscope (STM), was developed by Heinrich Rohrer and Gerd Binnig at IBM Research, Zurich.[7]

Scanning Electron Microscopy

It produces images of a sample by scanning its surface with a focused beam of electrons. The electrons interact with atoms in the sample, producing signals that have information about the composition and surface topography of the sample.[8]

Components of Nanorobots[9]

1) 100 nm manipulating arms
2) 2.10 nm sorting rotors for molecular purification
3) Super hard and smooth surfaces made of atomically flawless diamond

Making of Nanorobots

Using DNA origami, pioneered in 2006 by scientist Paul Rothemund, scientists were able to manipulate DNA material into specific shapes and program the 3-D DNA structures to fuse to other cells and operate within other DNA material.[10]

Working of a Nanorobot

To identify a cell with three specific surface proteins, Dr. Stojanovic constructed three different components for molecular robots. Each part consisted of a piece of double-stranded DNA attached to an antibody specific to only one of the surface proteins.[11] On cells where all three components were attached, a robot which was the functional component. initiated a chain reaction. The role of each component was to swap a strand of DNA with another, until the last antibody obtained a strand of DNA that was fluorescently labeled.[12]

Manufacturing Approaches

1) Biochip

Nanorobots were manufactured using nanoelectronics and photolithography for surgical instrumentation, diagnosis, drug delivery and tele-operation for medical instrumentation.[13]

2) Nubot or Nucleic Acid Robot

It is an organic molecular machine at the nanoscale.

Biological circuit gates that are based on DNA materials have been engineered as molecular machines for the purpose of in-vitro drug delivery for targeted health problems.

3) Bacteria Based

This approach used biological microorganisms, like bacterium Escherichia coli and Salmonella typhimurium. The model made use of a flagellum for propulsion and electromagnetic fields for motion.[14]

4) Positional Nanoassembly

Nanofactory Collaboration, founded by Robert Freitas and Ralph Merkle in 2000, developed a positionally-controlled diamond mechanosynthesis and a diamondoid nanofactory that would be capable of building diamondoid medical nanorobots.

5) Biohybrids

This system combined biological and synthetic structural elements for biomedical or robotic applications. It made use of a biodegradable material attached to magnetic particles for easy guidance around the body.

6) Surface-bound Systems

These primitive nanomachines underwent machine-like motions when confined to the surface of a macroscopic material. The surface anchored motors were used to move and position nanoscale materials on a surface.

7) Virus Based

Retroviruses undergo reverse transcription to deliver genetic packaging in a vector. This retroviral gene therapy has the ability to re-engineer cellular DNA by making use of viral vectors.

8) 3D Printing

Nanoscale 3D printing built a three-dimensional structure through additive manufacturing at the nanoscale. 3D printing used a laser etching machine, which etched into each plate, the details needed for each segment of the nanorobot. The plate was transferred to the 3D printer and the etched regions were filled with the required nano liquid resin, which was hardened by a focused laser beam. This process was repeated until the nanorobot was built from the bottom up. Intricate structures with interlocked and moving parts could be manufactured due to the high resolution of the process.

Applications of Nanorobots

1) Dentition Re-naturalization

Reconstructive dental nanorobots maintain the natural tooth and improve its esthetic aspect and durability by replacing the upper layers of the enamel or by excavating old amalgam restorations and preparing cavities with artificial biocompatible materials, like sapphire and diamond, with a hardness of 20-100 times larger than the natural enamel and a larger resistance to fracture.[15,16]

2) Dentin Hypersensitivity Cure

Nanorobots were capable of selectively and precisely occluding tubules, by using local and native materials, offering a quick and permanent cure for patients.[17]

3) Covalently-bonded Diamondized Enamel

Tooth appearance and durability can be enhanced by replacing the upper layers of enamel with covalently- bonded artificial materials like diamond or sapphire. Their hardness and failure strength are 20-100 times that of natural enamel or contemporary ceramic veneers. Sapphire is susceptible to acid corrosion, is brittle and prone to fracture resistance.

4) Nanorobotic Dentifrice (Dentifrobots)

A subocclusal nanorobotic toothpaste or mouthwash could metabolize trapped organic matter into harmless and odorless vapors. Continuous calculus debridement was done using invisibly small (1-10 microns) dentifrobots, 1000-100000 per oral cavity, crawling at 1-10 microns/second.[18]

Dentifrobots played an important role in preventing cavities and periodontal diseases by identifying and destroying pathogenic bacteria in the subocclusal area while allowing the harmless bacterial flora from the mouth to develop in a healthy ecosystem. The dentifrobots were programmed to avoid all occlusal surfaces and deactivate if chewed.[15,16,19] As putrefaction was the central metabolic process involved in the odour of the oral cavity, dentifrobots ensured a continuous barrier against halitosis.[2]

5) Nanocomputers

Nanocomputers would be used to activate, control and deactivate nanomechanical devices.

Nanorobotic devices could be programmed to allow dentists to perform precise interventions at the cellular and molecular level.

6) Controlled Oral Anesthesia

A colloidal suspension containing millions of active, anesthetic, micron-sized dental nanorobots was applied to the patient's gum. Nanorobots in contact with the surface of the crown or mucosa reached the pulp via the gingival sulcus, lamina propria or dentinal tubules in approximately 100 seconds. Once in the pulp, they shut down all sensations by interrupting the traffic of the nervous impulse, under the control of the dentist through the nanocomputer aboard the nanorobots. At the end of the oral procedures, the dentist was able to command the nanorobots to redo the nervous traffic of the tooth in question and to exit the tooth the same way they entered.[2,16,18] This provided comfort for the patient by reducing the anxieties and needle phobias, a larger base of selection and a quick complete reversible action and disappearance of side effects and complications of anesthesia.[2,19]

7) Orthodontics

Orthodontic nanorobots were able to manipulate the paradental tissues, including gums, paradental ligament, cementum and alveolar bone, allowing a quick and painless straightening, rotating or vertical positioning as well as rapid tissue repair within minutes or hours.[15,16]

A stainless-steel wire that used nanotechnology, combined ultra-high strength with good deformability, corrosion resistance and surface finish was also invented.[18]

8) Nanoencapsulation

Targeted release systems that encompassed nanocapsules were used in vaccines and antibiotics.[20]

9) Nanotissue Engineering

The replacement of the whole tooth, including the mineral and cellular components, was called complete dentition replacement. This therapy was possible through genetic engineering, nanotechnology and tissue engineering. Chan et al. recreated dental enamel, with the help of nanorods consisting of a highly organized microarchitectural structure.[18]

10) Nanodiagnostics

Nanodiagnostic devices would be used for early disease identification at the molecular and cellular levels. Nanomedicine could increase the reliability and efficacy of in-vitro diagnostics, through the use of nanodevices that could collect and analyze human fluids or tissue samples at the subcellular level. Nanodevices could be inserted into the body to identify and quantify the early presence of a disease, toxic molecules and tumor cells.[2,21]

11) Diagnosis and Treatment of Oral Cancer

Saliva was used as a non-invasive and inexpensively obtained diagnostic medium that contained genomic and proteomic markers for molecular disease identification.

Nanoshells contain an outer metallic layer that selectively destroy cancer cells, while keeping normal cells intact. Nanoparticle-coated, radioactive sources were placed close to or within the tumor to destroy it. Nanovectors could be used for drug delivery across the blood–brain barrier in the treatment of Alzheimer's and Parkinson's diseases.[22,23]

12) Nanosolutions

These homogenous nanoparticles could be used as bonding agents or sterilizing solutions in the form of emulsified oil nanodroplets that bombard pathogens.[17]

13) Nanoimpression Materials

Nanofillers integrated in vinylpolysiloxanes, produced an addition siloxane impression material that had fewer voids, better flow, improved hydrophilic properties, better model pouring and enhanced detail precision.[20,24]

14) Bone Replacement Materials

Nanotechnology aimed to emulate bone natural structure for orthopedic and dental applications for the development of nanobone. Nanocrystals have a loose microstructure, with nanopores situated in-between the crystals. Bone defects could be treated by using hydroxyapatite nanoparticles.[20]

15) Nanoneedles

Nanosized stainless-steel crystals incorporated into suture needles had been invented and developed. Cell surgery would be possible in the near future with nanotweezers.[18]

16) Nanocomposites

Nanocomposites used building blocks in the nanometer range to design and create new materials with unprecedented flexibility and improvement in their physical properties.

These nanocomposites had high surface to volume and aspect ratio. They displayed a better balance of esthetics and strength, but nanoparticle clumping or agglomeration weakened their structure. This problem could be overcome by coating the particles during the manufacturing process. This resulted in a smoother, creamier consistency and improved flow characteristics. These properties contributed to the dentin-like cutability and polishability of the material, once the material was cured to its hardened state.[20,25]

17) Dental Implants

The reconstructive nanobots used nanorobotic manufacturing as well as tissue and gentic engineering procedures for the growth of a new tooth in-vitro, followed by its integration in the dental alveoli. The nanotherapy of complete replacement of the dentition with biological teeth, including both mineral and cellular compounds could be done in one session.[2,15,16,26]

The addition of nanoscale deposits of calcium phosphate and hydroxyapatite, created a complex implant surface for osteoblast formation. These new implants enhanced the integration of nanocoatings resembling biological materials to the tissues.[18,27,28]

18) Carbon Nanotubes

Carbon nanotubes (CNTs) were made by rolling up a sheet of graphene into a cylinder. Both CNTs and GNRs (graphene nanoribbons) could be derived from a graphene sheet.

CNTs were classified into single-walled (SWNT), double-walled (DWNT), and multiwalled CNTs (MWNT). The structure of SWNT was a one-atom-thick layer of graphene rolled into a seamless cylinder. MWNT consisted of two or more layers of rolled-up concentric layers of graphene. DWNT consisted of two concentrically rolled up graphene sheets.

CNT combined with biopolymers could aid in the restoration of bone defects. Sodium Hyaluronate-SWCNT was used for bone regenerative procedures, in normal and adverse metabolic states. MWCNT particles promoted hydroxyapatite crystallization on their surfaces, acting as a core for initial hydroxyapatite crystallization.[29]

19) Nanomedicine

Nanomedicine included targeted drug delivery and early diagnosis for cancer biomedical instrumentation, pharmacokinetics, surgery, health care and monitoring of diabetes.[30] Non-replicating nanorobots could be injected into the patient to perform treatment on a cellular level. Nanoscale machines integrated into a desktop-scale machine that would build macroscopic products using carefully controlled nanofactories.[31]

20) Diagnosis and Treatment of Diabetes

The simulated nanorobot prototype model contained embedded Complementary Metal Oxide Semiconductor (CMOS) nanobioelectronics.[32] The nanorobot detected glucose levels in the blood stream and was not attacked by the white blood cells due to its biocompatibility. The chemical sensor onboard the nanorobot could determine glucose levels and the need for a patient to inject insulin or any prescribed medication.

The nanorobots try to keep the glucose levels at approximately 130 mg/dl as a target for the Blood Glucose Levels, at a typical glucose concentration.

In the medical nanorobot architecture, the measured data could be transferred to the mobile phone carried by the patient. If the glucose reached critical levels, the nanorobot could send an alarm through the mobile phone.[33]

21) Surgery

Surgical nanorobots could be introduced through the vascular system into various vessels and cavities in the human body. They may be programmed or guided by a human surgeon and could act as a semiautonomous on-site surgeon inside the body.[34]

These devices could search for pathology and diagnose and correct lesions by nanomanipulation, coordinated by an on-board computer that is controlled by the surgeon via coded ultrasound signals.[35]

22) Gene Therapy

Medical nanorobots can treat genetic diseases by chromosomal replacement therapy.

The molecular structures of DNA and proteins are compared to information stored in the database of a larger nanocomputer positioned outside the nucleus and connected to the cell-repair ship by a communications link. The proteins are reattached to the DNA chain, which re-coils into its original form. Cancer, viral infections and arteriosclerosis would be attacked at the molecular level and eradicated.[36]

23) Hematology

This ranged from developing artificial methods of transporting oxygen in the body after major trauma, to improving clotting capabilities in the event of a dangerous hemorrhage.

Respirocytes are hypothetical nanorobots engineered to function as artificial red blood cells. In emergencies where a patient stopped breathing and blood circulation had ceased, respirocytes could be injected into the blood stream for the purpose of transporting respiratory gases until the patient was stabilized. Respirocytes were capable of supplying 200 times more respiratory gas molecules than natural red blood cells of equal volume.

Clottocytes accumulate at the bleeding site, in order to form a barrier, which would trap blood cells when the nanobot arrives at the site of the injury. The clotting ability of one injection of clottocytes would be around 10,000 times more effective than an equal volume of natural platelets.[37]

24) Biohazard Defense

Nanobots with protein-based biosensors transmit real-time information in areas where laboratory analysis is unavailable and public infrastructure is limited. This was applicable for biomedical monitoring of areas affected by an epidemic or pandemic disease as well as in remote or war-torn countries during humanitarian missions.

Increased concentration of the enzyme would trigger the nanorobot prognostic protocol which could send electromagnetic signals to a mobile phone. The information would be retransmitted via the telecommunication system, providing information on the exact location of the person infected, increasing the speed of contamination quarantine.[37,38]

25) Endodontic Sealers

Endodontic sealers caused a hydration reaction when introduced into root canals, where nanocomposite structure of hydroxyapatite and calcium silicate was formed. The addition of nanoparticles also facilitated delivery of material from capillary needles and its adaption to irregular dentin surfaces. It set hard in a few hours and had good sealing ability and dimensional stability. Its alkaline pH of 12.8, gave antimicrobial properties.[39,40]

Silicon-based sealer containing gutta-percha powder and silver nanoparticles of less than 30 µm were available as capsules that could be mixed and injected as a cold flowable filling system. It had dimensional stability, good biocompatibility,[41] good sealing ability and was resistant to bacterial penetration.[42]

26) Photodynamic Therapy

Antimicrobial photodynamic therapy used a photosensitizer and light of a specific wavelength, as a treatment modality for removal of infectious pathogens.[43]

27) Brain Disorders

Magnetic nanoparticles open the blood-brain barrier and carry out molecular delivery directly to the brain.

The nanoparticles react to a radio-frequeny field by dissipating heat, creating a mechanical stress on the barrier. This allowed a localized and temporary opening of the barrier for diffusion of therapeutics into the brain.[44]

Advantages of Nanorobots[45]

- Nanorobot drug delivery systems have increased bioavailability.
- Targeted therapy.
- Fewer mistakes on account of computer control and automation.
- Reach remote areas in the human body, not operatable at the surgeon's operating table.
- drug molecules are carried by nanobots and released where required.
- Non-invasive technique.
- Computer controlled operation with nobs to fine tune the frequency, amount, time of release.
- Better accuracy.
- Drug inactive in areas where therapy is not needed minimizing undesired side effects.

Disadvantages of Nanorobots[45]

- The cost is very high.
- The design of the nanorobot is very complicated.
- Electrical systems can create stray fields.
- Electrical interference can cause electrical disturbances in nanorobots.
- Hard to interface, customize and design.
- Complex structure.
- Risk in the field of terrorism.
- Loss of privacy.

Challenges faced by Nanodentistry[9]

1) Engineering Challenges

- Precise positioning and the assembly of molecular scale part.

- Manipulating and coordinating activities of large number of independent microscale robots simultaneously.

2) Biological Challenges

- Smaller particles are more bioactive and toxic.
- They can easily cross the skin, lungs and the blood-brain barrier.
- There are biochemical reactions like the creation of free radicals that damage cells once they enter the body.

3) Social Challenges

Highest at risk are the workers, working for the manufacturers producing products that contain nanoparticles.

Environmental Impact

The durability of nanoscale materials, their persistence in excretion of absorbed products and some materials having a potential to bond with and reconfigure DNA, pose a threat to wildlife.

Nanohazards

The number of free nanoparticles in nature, depend on their physical and chemical properties, quantity and time of exposure and they can be modified by temperature, pH, different biological conditions and presence of pollutants. Nanomaterials can alter the environment, proving to be harmful to human health.

Nanoparticles are rapidly translocated from the lungs and skin, to some vital organs via the bloodstream. It could have unwanted effects on the DNA of cells, which could cause genetic defects. Nonbiodegradable nanoparticles may get deposited in various organs and lead to an unwanted reaction within biological tissues.[46]

Lung Damage

Nanoparticles caused lung damage by triggering an autophagic cell death. An autophagy inhibitor, counteracted nanoparticle-induced lung damage and prevented cell death.[47]

CONCLUSION

Nanorobots and nanomedicine provide personalized treatments with improved efficacy and reduced side effects that are not available today.

They provide combined action–drugs marketed with diagnostics, imaging agents acting as drugs and surgery with instant diagnostic feedback. The advent of molecular technology would expand the effectiveness, speed and comfort of future medical treatments by decreasing their risk, cost and invasiveness.

Nanorobots have more bioavailability, targeted therapy, reduce surgeon mistakes, reach remote areas in the human anatomy, large interfacial area for mass transfer, are non-invasive, computer control of delivery, better accuracy, less side effects and have a greater speed of drug action.

Future healthcare will make use of highly sensitive diagnostics for an enhanced personal risk assessment. Nanomedicine holds the promise to lead to better therapy, earlier diagnosis and improved follow up care, making the health care system, more effective and affordable. Nanomedicine needs to improve the understanding of pathophysiologic basis of a disease, bring more sophisticated diagnostic opportunities and yield more effective therapies and preventive properties.

Molecular technology is destined to become the core technology underlying all of the 21st century medicine and dentistry.

CONFLICTS OF INTEREST

The authors declare they have no potential conflict of interests regarding this article.

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