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Original Research Article

A Research on Future Scenario in the Field Of Role of Nanorobotics a Device for Diagnosis and Treatment

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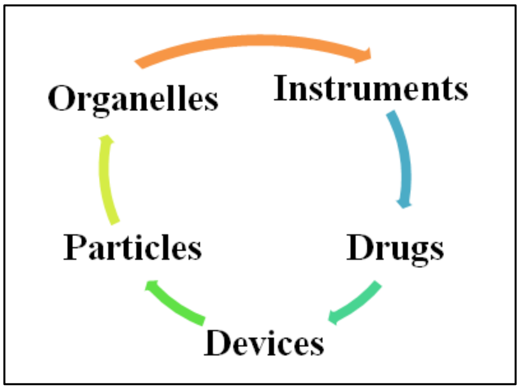
Abstract: Nanorobots are the nano devices that are used for protecting or treatment against pathogens in humans. The use of nanorobots technology has become familiar and increasingly common, especially with pharmaceutical technology. We conducted this research paper by observing the different types of reviews, as well as conducting and evaluating literature review papers. This research is provided detailed overview of the types, properties and application of nanorobot in the diagnosis, prevention and treatment of various diseases. Nanorobots technology is rapidly emerging in the medical field, and this subfield has been termed nanomedicine. Nanorobotics are developing wide potential applications across all fields of medicine, and expanding the number of therapeutic options available, while also improving the efficacy of existing treatments. The most recent applications of these devices include targeted drug delivery to the brain, glucose monitoring in patients with diabetes, bone reconstruction, cancer treatment, blood clot removal, nerve regeneration and protein peptide based drug delivery systems.

Keywords: Nanorobots, Nanotechnology, Application, Composition, Types of nanorobots.

INTRODUCTION

Nanorobots: Nanorobots are the nano devices that are used for protecting or treatment against pathogens in humans. Nanorobotics may be defined as the highly articulated and sophisticated technique that essentially has the enormous ability and integrity to manipulate the specific objects at the molecular as well as cellular levels. Hence, the critical and precise application of Nanorobotics in the so called life services is invariably known as nanobiotechnology. Another school of thought relates the nascent field of Nanorobotics to the particular indulgence of the crucial usage and the elaborated investigative study of such entities as:



Which predominantly either measure or function very much within a size parameter of 1-

100nm*. So as to render these dimensions certain concrete relevance, the red blood cell (RBC) size is almost 5 mcm (5μm, nm); whereas, a micronized aspirin, molecule is found to be less than 1 nm.

Its, however, pertinent to state at this point in time that the present scenario in the domain of the biological applications are at a very early stage of scientific evolution which essentially comprise such areas as;

- Drug Delivery,
- Bioanalysis,
- Therapeutics,
- Biosensors,
- Medical Devices (Tissue Engineering).

Nevertheless, nanobiotechnology does essentially include the following two most predominant areas of research activity particularly in the so called private sector, namely:

- Drug discovery,
- Diagnostics

Important Examples- These essentially comprise:
Scanning Probe Microscope: - It is an important tool which is being used largely in the common usage of the 'cellular study' (functioning on a nanometer scale only).
Nanoparticles: - There are able to provide newer modes of labeling technology in the cell or molecule analysis, duly based upon changing colour with changing particle size.
Contrast Agent X-Ray Imaging: - It is being used as an application possibly empowered with;

- Better image resolution,
- Tissue targeting,
- Retention profile in blood stream.

Nanoparticles :- Do prove to be as better carriers for various drug molecules in very small quantum possibly increasing significantly the following criteria;

- Drug penetration across membranes (In Vivo),
- Altering drug solubility profile, and
- Changing pharmacokinetics perceptively.

Liposomes: - It may also function as the 'Nanoparticles'.

According to nanorobotic theory, "nanorobots are microscopic in size, it would probably be necessary for very large numbers of them to work together to perform microscopic and macroscopic tasks". Advances in the areas of robotics, nano structuring, medicine, bioinformatics, and computers can lead to the development of nanorobot drug delivery system. Some of the examples of Nanorobots are respirocytenanorobots, microbivoresnanorobots, surgical nanorobots and cellular repair Nanorobots. Nanorobots will be used for maintaining and protecting the human body against pathogens. They will have a diameter of about 0.5 to 3 microns and will be constructed out of parts with dimensions in the range of 1 to 100 nanometres. The main element used Nanorobots is carbon because of its inertness and strength in the form of diamond and fullerene. Nanorobots have exterior passive diamond coating especially to avoid attack by the host immune system. They are invisible to our naked eye, which makes them hard to manipulate and work with. Techniques like Scanning Electron Microscopy (SEM) and Atomic Force Microscopy (AFM) are being employed to establish a visual and haptic interface to enable us to sense the molecular structure of these nano scaled devices. Virtual Reality (VR) techniques are currently being explored in nano-science and bio-technology research as a way to enhance the operator's perception by approaching more or less a state of 'full immersion' or 'telepresence'. Fabrication and controls of the nanorobots are the main challenges in the development of nanorobots or nano machine components. Such devices will operate in microenvironments whose physical properties differ from those encountered by conventional parts.

Deal Feature of Nanobots

- The size of Nanobot should be in between 0.5 – 3microns with the large parts 1 to 100 nm.
- The capillary flow stopped by larger size nanobots from above range.
- Nanobots will be stopping it by attacking from the immune system which has passive, diamond external.
- These nanorobots will be in communicating with doctor about acoustic signal by transporter of radio emission frequencies of 1 to 100 MHz, with coding messages.
- Self- Replication process done, when nanobots probably generate its numerous copies to restore worn out units. This method referred to as Self-replication process.

Advantages of Nanobots

- Nanorobots achieved remote areas in human body which is difficult to surgeon for operate.
- Nanobots technique is non-invasive and higher accuracy.
- Nanobots technology used with enhance bioavailability.

- It is used in targeted treatment like solely malignant cell treated.
- Not much post treatment care is necessary because its inconsiderably invasive technique, so less post treatment care is needed.
- Nanorobots are small in size and higher limit of the dimensions of nanobots is 3 micron in order that it will simply flow within the body while not obstruction the capillary flow.
- The nanobots technology is cost effective technique by producing batch processing, it reduces cost than initial cost of development is more.
- Drug molecules are not active in areas wherever therapy not required and decreased in unwanted adverse effects.
- Drug particles are transported by nanorobots and released when required; the advantages of the large interstitial zone can be achieved during mass transfer.
- Computer controlled process with nobs to set amount, frequency and release time.
- For the manufacturing of nanobots large amount of resources is available.
- Disease is speedy eliminate by treating with nanorobots.
- Nanobots are Long durability.
- Using of nanobots quicker and a lot of precious diagnosis.
- Nanorobots are automated and easy to dispose.
- They continue to be operational for years, decades or centuries
- The possibilities of any after effects or recurrences are utterly eliminated.
- Damage tissue of patient should be repaired in a very few hours instead of weeks or months, and if programmed correctly, the entire damaged organ can be healed in some days.
- After the damage tissue is absolutely healed, nanorobots should separate out through programming.
- The operated single units need minimal amount of energy.

Disadvantages of Nanobots

- The preliminary design of nanobots price is extremely high.
- The design of the nanobots is more complex one.
- Nanobots are tough to Interface, Customize and Design, Complicate.
- If nanorobots self-replicate, a dangerous version of the nanorobots may be created.
- These nanorobots if used by terrorists may also be make use of as bio weapons and should become harm to the society.
- Nanorobots will have negative effects if functioning of it should not be correct.
- Privacy is the alternative ability danger involved with nanorobots. As nanorobots deals with the designing of compact and minute gadgets, there are probabilities for greater.
- Electrical nanorobots are at risk of electric interference from outside sources like radio frequency or electric powered fields, and stray fields from other in vivo electrical gadgets.

Composition of Nanorobots

A] Biochip

The Synthesis involves the joint use of the photolithography, nano electronics & the new biomaterials. For the manufacturing of the nano robots for the common medical applications such as for drug delivery, surgical instrumentation & diagnosis, it can be used. The electronics industries currently use the biochips for manufacturing. The nano robots with the biochips can be integrated in the nano electronics devices which will allow the tele-operation & the advanced capabilities for the medical instrumentation.

B] Bacteria Based

These approaches use the biological microorganisms like the Escherichia coli bacteria. The model uses the flagellum for the propulsion purposes. To control the motion of this kind of the biological integrated device the use of the electromagnetic fields is normally applied.

C] Positional Nano Assembly

The Robert Freitas & Ralph Merkle in 2000 are developing the practical research agenda which is specifically aimed at the developing positional-controlled the diamond mechanic synthesis & the diamonded Nano factory that would be capable of the building diamonded medical nano robots.

D] Nubots

The nubot is an abbreviation for the "nucleic acid robots. " The nubots are the synthetic robotics devices at the nanoscale. The representative nubots include the several DNA walkers reported by the Ned Seaman's group at the NYU, Niles Pierce's group at the Caltech, John Reif's group at the Duke University, Chengde Mao's group at the Purdue & the Andrew Turberfield's group at the University of Oxford.

Types of Nanorobots

Some researchers classify nanorobots in drug delivery and therapeutics according to the their applications, which are described below,

Pharmacyte: It is a medical nanorobot having a size of 1-2 µm able to carrying up 1 µm 3 a given drug in the tanks. They are controlled using mechanical systems for sorting pumps. They are provided with a molecular markers or chemotactic sensors that guarantee full targeting accuracy. Glucose and oxygen extracted from the local environments such as blood, intestinal fluid and cytosol are the on board power supply. After the nanorobot completing tasks they can be removed or recovered by centrifuge nanapheresis.

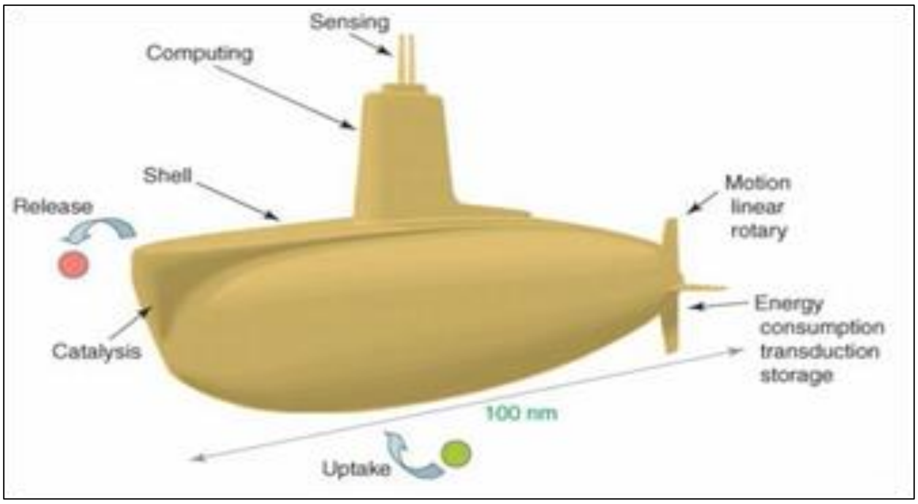


Figure 1: Fictitious Pharmacyte

Diagnosis and Imaging: They have microchips that are overlaid with human molecules. The chip is projected to send an electrical signal when the molecules detect a disease. Gives an example of special sensor nanobots that can be introduced into the blood under the skin where they verify blood contents and notify of any possible diseases. They can also be used to monitor the sugar level in the blood. Advantages are the low price to produce and easily to manipulate **[**1**].**

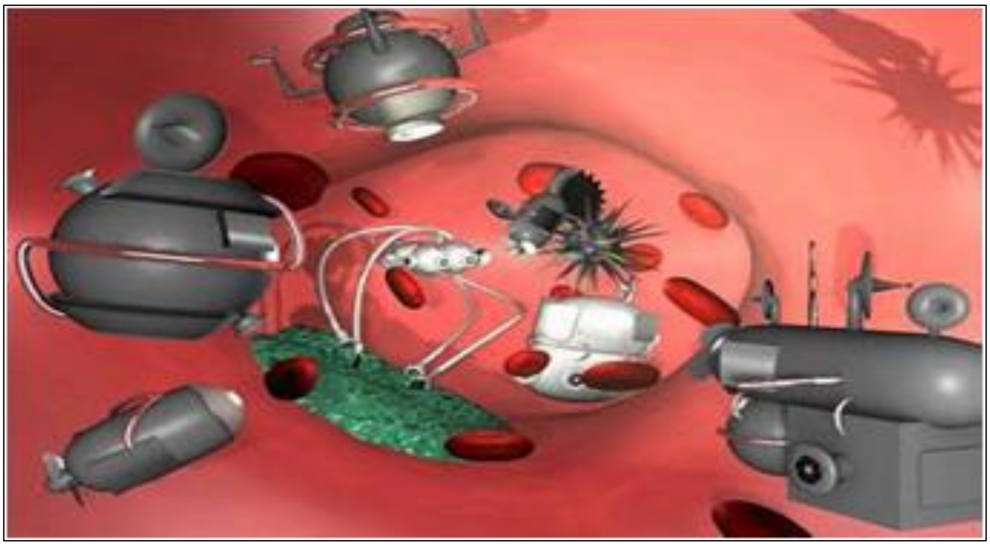


Figure 2: Nanorobots in blood vessel for Diagnosis and Imaging

Respirocyte: It is an Artificial Oxygen Carrier nanorobot which is about an artificial red blood cell. The power is obtained by endogenous serum glucose. This artificial cell is able to give 236 times more oxygen to the tissues per unit volume than RBCs (Red blood cells) and to administer acidity [2].

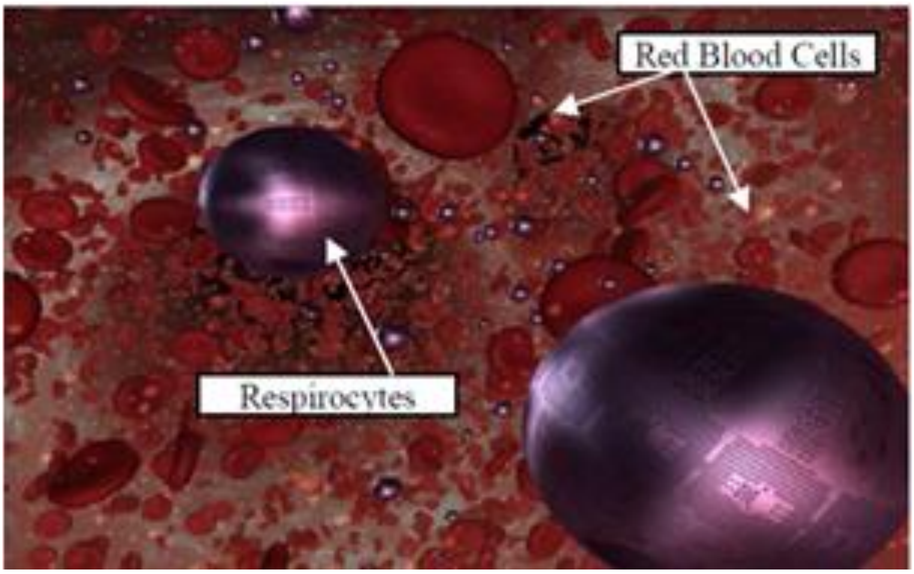


Figure 3: Respirocytes

Microbivores: It is an oblate spheroidal device for nanomedical applications with 3.4 µm in diameter along its major axis and 2.0 µm in diameter along its minor axis. The nanobot can continually consume up to 200 pW. This power is used for digest trapped microbes. . Another distinctive feature is related to the ability to phagocyte approximately 80 times more efficiently than macrophages agents, in terms of volume/sec digested per unit volume of phagocytic agent.

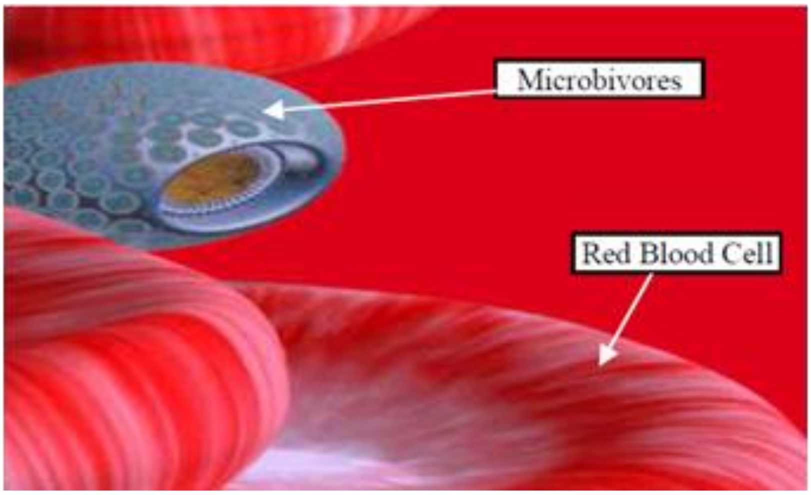


Figure 4: Microbivores

Clottocytes: This is a type of nanorobot, with a unique biological capability: "instant" hemostasis using clottocytes, or artificial mechanical platelets. It is known that platelets are roughly spheroidal nucleus-free blood cells measuring approximately 2 µm in diameter. Platelets join at a place of bleeding. There they are activated, becoming tacky and lumping together to form a tampon that aid stamp the blood vessel and stop the bleeding. They also delivery substances that help promote coagulating.

Chromallocyte: The Chromallocyte would replace entire chromosomes in individual cells thus reversing the effects of genetic disease and other accumulated damage to our genes, preventing aging. Inside a cell, repair machine will first size up the situation by examining the cell's contents and activity, and then take action by working along molecule-by-molecule and structure-by structure; repair machines will be able to repair the whole cell [3].

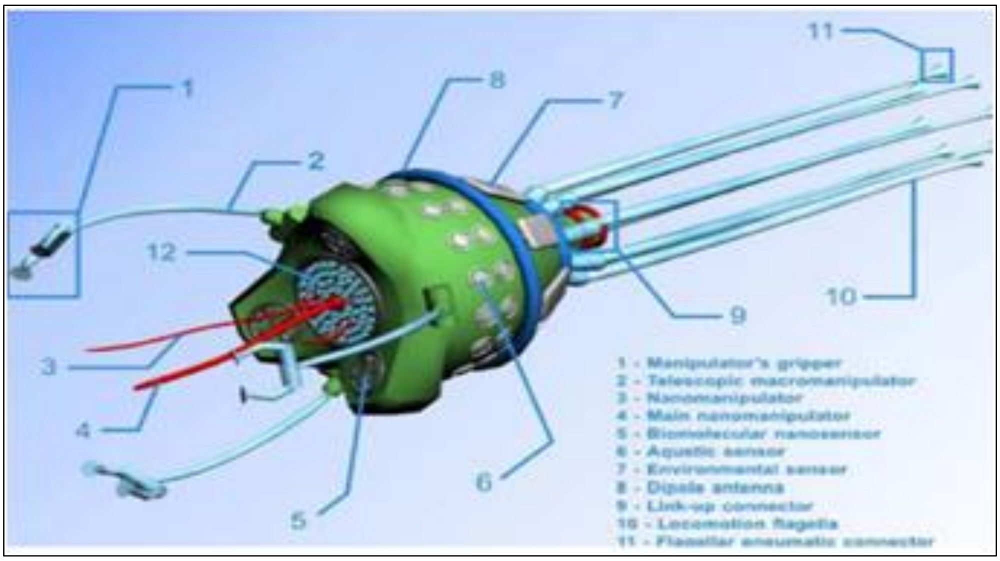


Figure 5: Diamondoid Cell-Repair Nanorobot

Advantages of Nanorobots

- Use of nanorobot drug delivery systems with increased bioavailability.
- Targeted therapy such as only malignant cells treated.
- Reach remote areas in human anatomy not operatable at the surgeon's operating table.
- As drug molecules are carried by nanorobots and released where needed the advantages of large interfacial area during mass transfer can be realized.
- Non-invasive technique.
- Computer controlled operation with nobs to fine tune the amount, frequency, time of release.
- Better accuracy.
- Drug inactive in areas where therapy not needed minimizing undesired side effects [4].
- Small size- The upper limit of the size of nanorobot is 3 micron so that it can easily flow in the body without blocking the capillary flow.
- Cost effective (if mass produced) - Manufacturing by batch processing reduces the cost even if the initial cost of development is high.
- Less post treatment care - As it is minimally invasive technique, therefore less post treatment care is required **[**5].

Structure and Design of Nanorobots: The components of nanorobots are made of carbon because it is inert and possess good strength and in the form of diamonded or fullerene. The other components are hydrogen, oxygen, nitrogen, sulphur, silicon and fluorine, etc. which are used on nanoscale. The components of nanorobots are as follows; Medicine cavity: It is a hollow section inside the nanorobot used to hold small doses of medicine in those robots which are capable of releasing medication directly to the site of injury or infection. Probes, knives and chisels: These are used to remove plaque and blockages these probes, knives and chisels are used. These parts help Nanorobot to grab and break down the material. Also they might need a device to crush clots into very small pieces. If a partial clot breaks free and enters the bloodstream, it may cause more problems further down the circulatory system. Microwave emitters and ultrasonic signal generators: These are used for destroying cells like cancerous cells without rupturing it. By using fine-tuned microwaves or ultrasonic signals, a nanorobot could break the chemical bonds in the cancerous cell, killing it without breaking the cell wall. Alternatively, the robot could emit microwaves or ultrasonic signals in order to heat the cancerous cell enough to destroy it. Electrodes: With the help of electrodes nanorobots generate electric current, heating the cells until it dies. Lasers: Lasers are used to burn the harmful materials like cancerous cells, blood clots and plaques i.e. these lasers vaporize tissues. With the help of powerful laser vaporizing cancerous cells is the challenging work, but this laser does not harm to surrounding tissues. Power supply for nanorobots: The major requirement for the nanorobot is, of course, power. The nanorobots require power to allow it to perform all of its required operations. There are two possible ways. The first is to obtain the power from a source within the body, either by having a self-contained power supply, or by getting power from the bloodstream. The second possibility is to have power supplied from a source external to the body. Medical application of nanorobots: Nanorobots are expected to enable new treatments for patients suffering from different diseases and will result in a remarkable advance in the history of medicine. The use of nanorobots may advance biomedical intervention with minimally invasive surgeries and help patients who need constant body functions monitoring, or ever improve treatments efficiency through early diagnosis of possible serious diseases. For example, the nanorobots may be utilized to attach on transmigrating inflammatory cells or white blood cells, thus reaching inflamed tissues faster to assist in their healing process. Some of the applications of nanorobots are as follows;

Application of Nano Robots in Dentistry

Nanorobotic Dentifrices (Dentifrobots): These when delivered either by mouthwash or tooth paste, can cover all sub gingival surfaces, thereby metabolizing trapped organic matter into harmless and odourless vapours. Properly configured dentifrobots can identify and destroy pathogenic bacteria that exist in the plaque and elsewhere. These invisibly small dentifrobots are purely mechanical devices that safely deactivate themselves when swallowed [6].

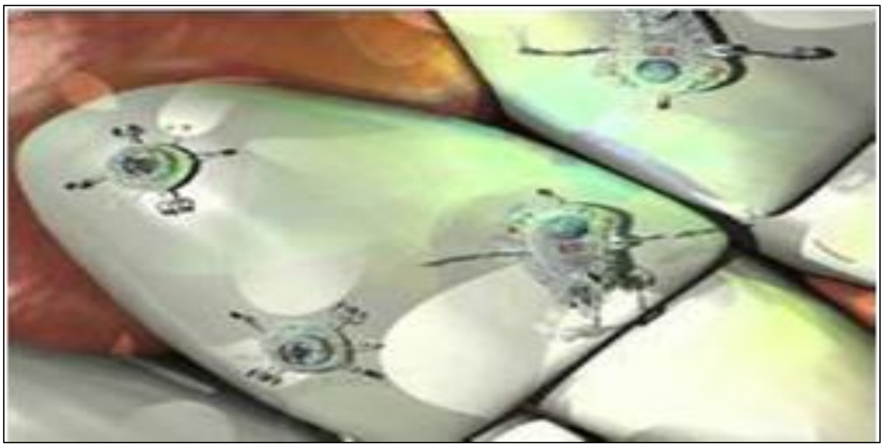


Figure 6: Dentifrobots

Nanoanesthesia: Oral anaesthesia is the most common procedures in dental practice, for that dental professionals will instil a colloidal suspension containing millions of active analgesic micron-sized dental nanorobot 'particles' on the patient's gingiva. After contacting the surface of the crown or mucosa, the ambulating nanorobots reach the dentin by migrating into the gingival sulcus and passing painlessly through the lamina propria or the 1 to 3-micron thick layer of loose tissue at the cement identinal junction. On reaching dentin, the nanorobots enter dentinal tubules holes that are 1 to 4 microns in diameter and proceed toward the pulp, guided by a combination of chemical gradients, temperature differentials, and even positional navigation, all under the control of the onboard nano computer as directed by the dentist. Tubules diameter increases as it nears the pulp, which may facilitate nanorobot movement. Once installed in the pulp and having established control over nerve impulse traffic, the analgesic dental nanorobots may be commanded by the dentist to shut down all sensitivity in any particular tooth that requires treatment. Then on the hand-held controller display, the selected tooth immediately becomes numb. After the oral procedures are completed, the dentist orders the nanorobots to restore all sensation, to relinquish control of nerve traffic and to engross, followed by aspiration. Nanorobotic analgesics offer greater patient comfort and reduced anxiety, no needles, greater selectivity, and controllability of the analgesic effect, fast and completely reversible switchable action and avoidance of most side effects and complications. Some other applications in the dentistry are tooth repair; Tooth repositioning, Dentin hypersensitivity etc. [7].

Application of Nano Robots in Cancer Treatment

The patient will have more chances for treating from cancer if it diagnosed earlier. Nanorobots with chemical biosensor (nanosensor) are used for detecting the tumours cells in early stage of cancer development. This nanosensor will sense the presence of malignant cells in the body. The therapeutic index of most anticancer drugs is narrow, causing toxicity to normal stem cells, hematological adverse effects, gastrointestinal among other. The Conventional chemotherapeutic agents work by destroying rapidly dividing cells, which is the main property of neoplastic cells. Most of the anti-cancer drugs like Doxorubicin are used in several types of cancer, such as HD (Hodgkin's disease), in which treatment is administered in combination with other antineoplastic agents in order to reduce their toxicity. Considering the properties of nanorobots to navigate as blood borne devices, they can help on such extremely important aspects of cancer therapy [8]. Nanorobots with embedded chemical biosensors can be used to perform detection of tumour cells in early stages of development inside the patient's body. Integrated nano sensors can be utilized for such a task in order to find intensity of Ecadherin signals. Therefore a hardware architecture based on nano bioelectronics is described for the application of nanorobots for cancer therapy. The scientists have genetically modified salmonella bacteria that are drawn to tumors by chemicals secreted by cancers cells. The bacteria carry microscopic robots, about 3 micrometers in size that automatically release capsules filled with drugs when the bacteria reach the tumor. By delivering drugs directly to the tumor, the nanorobot, which the team named bacteriobot, attacks the tumor while leaving healthy cells alone, sparing the patient from the side effects of chemotherapy [9, 10].

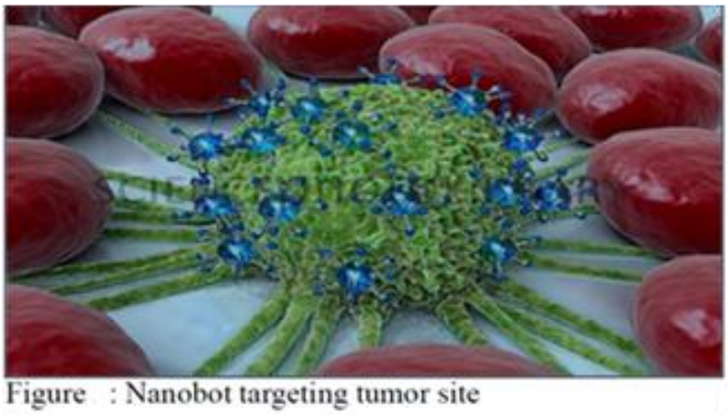


Figure 7: Nanorobots Targeting Tumor Site

Nanorobots in the diagnosis and treatment of diabetes: Nanorobots are considered a new possibility for the health sector to improve medical instrumentation, diagnosis, and treatment of diabetes. Patients with diabetes must take small blood samples many times a day to control glucose levels. Such procedures are uncomfortable and extremely inconvenient. To avoid this kind of problem the level of sugar in the body can be observed via constant glucose monitoring using medical nanorobotics. The simulated nanorobot prototype model has embedded Complementary Metal Oxide semi-conductor (CMOS) nanobioelectronics. It features a size of ~2 micronmeter, which permits it to operate freely inside the body. The nanorobot uses embedded chemosensor that involves the modulation of hSGLT3 protein glucosensor activity. Through its onboard chemical sensor, the nanorobot can thus effectively determine if the patient needs to inject insulin or take any further action, such as any medication clinically prescribed. They flow with the RBCs through the bloodstream detecting the glucose levels. At a typical glucose concentration, the nanorobots try to keep the glucose levels ranging around 130 mg / dl as a target for the Blood Glucose Levels (BGLs). In the medical nanorobot architecture, the significant measured data can be then transferred automatically through the RF signals to the mobile phone carried by the patient. At any time, if the glucose achieves critical levels, the nanorobot emits an alarm through the mobile phone.

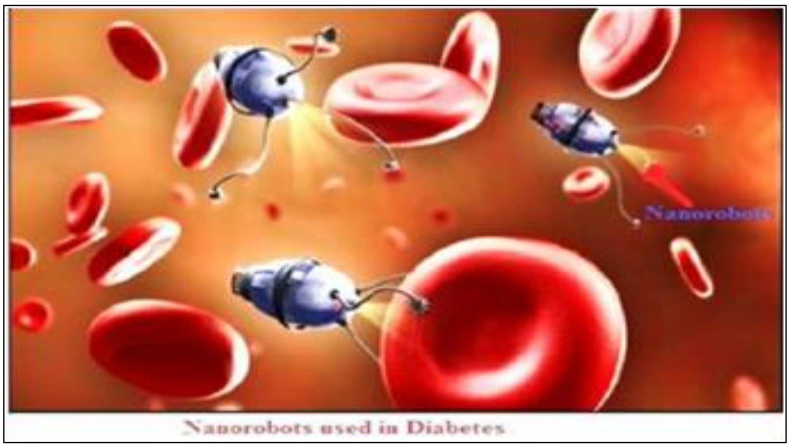


Figure 8: Nanorobots use in diabetes

An artificial oxygen carrier nanorobot: “Respirocyte” is the artificial mechanical red cell, an imaginary nanorobot which floats along in the blood stream. It is essentially a small pressure tank that can be pumped full of oxygen (O2) and carbon dioxide (CO2) molecules. Later on, these gases can be released from the small tank in a controlled manner. These atoms are mostly carbon atoms arranged as diamond in a porous lattice structure inside the spherical shell. Outside of each device there are gas concentration sensors. When the nanorobot passes through the lung capillaries, O2 partial pressure is high and CO2 partial pressure is low, so the onboard computer tells the sorting rotors to load the tanks with oxygen and to dump the CO2. When CO2 partial pressure is relatively high and O2 partial pressure relatively low the onboard computer commands the sorting rotors to release O2 and to absorb CO2. Respirocytes simulate the action of the natural hemoglobin-filled red blood cells, but they can deliver 236 times more oxygen per unit volume than a natural red cell. As artificial phagocyte (Microbivore): Microbivore is an artificial mechanical phagocyte of microscopic size whose primary function is to destroy microbiological pathogens found in the human bloodstream, using the “digest and discharge” protocol. The chief function of microbivore is to wipe out microbiological pathogens found in the human bloodstream, using the “digest and discharge” procedure. Microbivores upon given intravenously (I.V) would achieve complete clearance of the most severe septicemic infections in hours or less, far better than the weeks or months needed for antibiotic-assisted natural phagocytic defenses.

Heart-Attack Prevention: Nanorobots can also be used to prevent heart-attacks. Heart-attacks are caused by fat deposits blocking the blood vessels. Nanorobots can be made for removing these fat deposits. The nanorobots remove the yellow fat deposits on the inner side of blood vessels. This will allow for both improving the flexibility of the walls of the arteries and improving the blood flow through them [11]. From this hypothesis, such technology will help for delivery of drugs like lipid lowering substances such as lovastatin, simvastatin etc. These drug molecules will enter with nanorobots and give delivery at the site of action [12, 13].

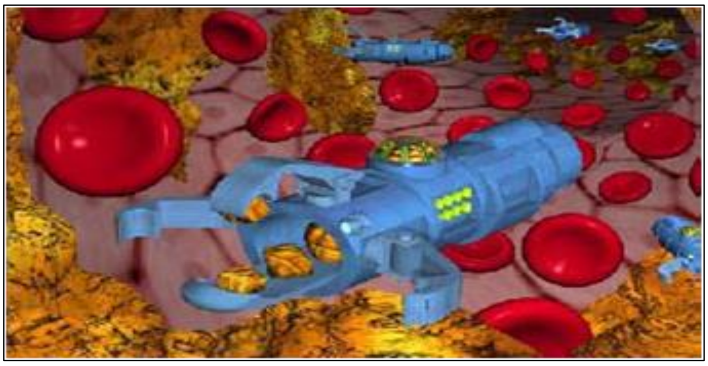


Figure 9: Nanorobots Removing Fat Deposit

Cleaning Wounds: Nanorobots could help remove debris from wounds, decreasing the likelihood of infection. They would be particularly useful in cases of puncture wounds, where it might be difficult to treat using more conventional methods [14].

Nanorobots in Kidney Disease: Nanorobots are used to break the kidney stones with the help of ultrasonic shocks. Kidney stones are painful and a large stone does not pass out in urine. Sometimes doctor break this stones by ultrasonic frequency but, these are not effective in always. Nanorobots break up these kidney stones by using small laser and these smaller pieces are passing out in urine outside the body [15].

RESULT AND DISCUSSION

We focused in this article on the medical application of nanorobots to diagnose and treat specific diseases such as cancer, heart disease, diabetes, arthritis, and more. This research is provided detailed overview of the types, properties and application of nanorobot in the diagnosis, prevention and treatment of various diseases. Now a day’s health care industry focusing on the development of nanotechnology for the diagnosis and treatment of various diseases. Development of nanorobots is an interesting and hopeful area of nanotechnology which is produce on nanoscale. Many drugs exhibit is the problem of less bioavailability of drug and require the administration of higher amount for treatment of various diseases. To overcome such problem, nanorobots are the novel solutions that deliver the drug to the target thus small dose are sufficient to achieve the desired therapeutic effect. Nanorobots are tiny device which is measure on the nanometer scale. Nanorobots also known as nanite, nanobots, or nanomites. Nanorobots are used in the diagnosing, treatment and prevention of the diseases, relieving pain and improving the human health. Advances in technology have increased our ability to manipulate the world around us on an ever-increasing scale. Nanorobots technology is rapidly emerging in the medical field, and this subfield has been termed nanomedicine. The use of nanorobots technology has become familiar and increasingly common, especially with pharmaceutical technology. An exciting and promising area of nanotechnological development is the fabrication of nanorobots, which are devices with components fabricated at the nanoscale. This field of study is littered with potential applications, many of which are currently being researched and developed. These devices are also useful tools for drug delivery in our medical system, which is a very important aspect of medicine. Nanorobots can perform tasks such as actuation, sensing, signaling, information processing and intelligence at the nanoscale. The most recent applications of these devices include targeted drug delivery to the brain, glucose monitoring in patients with diabetes, bone reconstruction, cancer treatment, blood clot removal, nerve regeneration and protein peptide-based drug delivery systems. Therefore, they are playing an important role in the field of biomedical sciences especially in cancer treatment, brain aneurysm treatment, kidney stone removal and other therapies that help in saving lives of patients. We this research focuses on nanorobots in biomedical applications, recently developing techniques for drug delivery.

CONCLUSION

Nanorobotics are developing wide potential applications across all fields of medicine, and expanding the number of therapeutic options available, while also improving the efficacy of existing treatments. It is certainly possible within a generation of time that the use of nanorobotic technology will become ubiquitous in medicine. Considering the serious side effects of existing treatments such as radiation and chemotherapy, nanorobots from the field of nanomedicine could be an innovative, helpful and promising machine technology for patients in the treatment and diagnosis of life-threatening diseases. In the future, the main emphasis in medicine will shift from medical science to medical engineering, where nanorobotic technology will be the new technology revolution. Nanorobots applied to medicine have promise from eradicating disease to reversing the aging process (wrinkles, bone loss and age-related conditions are all treatable at the cellular level); Nanorobots are also candidates for industrial applications. They will provide personalized treatments with better efficacy and fewer side effects that are not available today. They will provide combined action- drugs marketed with diagnostics, imaging agents acting as drugs, surgery with immediate diagnostic feedback. This science may seem like a fantasy now, but nanorobotics has strong potential to revolutionize healthcare in the future for disease treatment. This opens up new avenues for vast, abundant research work. Future health care will use sensitive new diagnoses for better individual risk assessment. The greatest impact can be expected if the major diseases that place the greatest burden on the aging population are: heart disease, cancer, musculoskeletal conditions, neurodegenerative and psychiatric diseases, diabetes and viral infections.

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Authors' Contribution

The first authors developed the proposal, undertook the literature search and review, and then collect and analyse the data under supervision of my respective advisers. The second author gives constructive comments and guidance and work with the main author with respect to the research objective.

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