Review article

The Biomedical Applications of Nanorobots - A mini Review

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ABSTRACT
Nanotechnology is the most advanced research technique used in different fields of science like agriculture, food, therapeutics, energy and so on. Nanorobots are small scale materials having wide variety of uses in the field of diagnosis and therapeutics. Nanorobots or nanobots are self-propelled nanomotors and nanodevices which are biodegradable. These are made from bio- nano components that have the ability to carry the drug cargo to the target site and deliver these loaded drugs to the diseased cells. We can programme these nanobots for the transport of molecular payloads and can execute many site- specific functions, in vivo health monitoring etc. Diabetes is the most common health condition where the glucose or sugar levels are high in the body. On the other hand, cancer is also a life- threatening disease where the cell undergoes uncontrolled proliferation. Cancer stem cells must be killed to control the cancer because they can migrate through metastasis to other sites of the body and spread the malignant tumor. These tumors have rapid vascularization and if the blood supply can be restricted in these blood vessels, the tumor cells can be killed. Application of nano robotics in monitoring the blood glucose, killing the cancer cells, its advantages and challenges are reviewed in this paper.

KEYWORDS: Diabetes type 2; Nanobiosensors; Nanobots; Medical bionanotechnology; Nanorobot components

Introduction

Nano technology is a branch of science that uses particles like atoms, molecules at the size of nanoscale in the field of medicine, agriculture, food, energy, textile, antibacterial activity, therapeutic imaging, targeted drug delivery, biosensors, and so on.[1-15] A field of nanotechnology called nanomedicine is the former application in medicine in drug preparation, delivery of drugs, therapeutics, diagnostics etc. Nano robots are defined as those that are useful in medical applications like in vivo monitoring of blood parameters, diagnosis, blocking the blood supply to the tumor cells thereby causing them to shrink and die etc., in the form of small miniature particles. Nano robotics is the recent technology used in various clinical applications, such as, treating complicated diseases like diabetes, aneurysm.[15-16] Components of nanobots include sensors, actuators and processing of information. Diabetes has affected the world at an alarming rate and it has been classified as a major cause of morbidity and mortality from a mild disorder in the aged people which was considered earlier.[17-18] Type 2 diabetes has affected approximately 90 percent of diabetic patients in the USA, and the remainder diabetic people have type 1 diabetes.19Diabetes is a condition where the blood glucose or sugar levels are high in the blood stream and the patients do not get glucose delivered to the cells. Use of nanotechnology in treating diabetes is rendered by monitoring glucose levels using nanoscale materials.[20] Cancer is another deathly disease where the conventional therapies of radiation and chemotherapy has brought down several side effects.[21-22] The targeted drug delivery using the nanobots can help to save the benign cells from killing and can improve the recovery rate of the cancer patients.

Concept of Nano Robots

Nanotechnology along with robotics is called as nano robotics andnano robots or nanobots are the devices manufactured in nano scale and conventional therapies of radiation and chemotherapy has brought down several side effects.[21-22] The targeted drug delivery using the nanobots can help to save the benign cells from killing and can improve the recovery rate of the cancer patients.

Concept of Nano Robots

Nanotechnology along with robotics is called as nano robotics andnano robots or nanobots are the devices manufactured in nano scale and are used in wide applications like dentistry, energy, food and are becoming significant in the clinical field in diagnosis and therapeutics.[23-24] A nano robot consists of various components like sensors, actuators, nano controllers, which are applied in drug delivery and detectionof disease biomarkers as shown in Figure 1. The major characteristics of nano robots includes the controlled size (0.5to2-micron), prevention from immune system rejection and self-replication.[25] Nano robots contain microchips that send signals when embedded into the human body after detecting the changes in metabolic activity or disease.

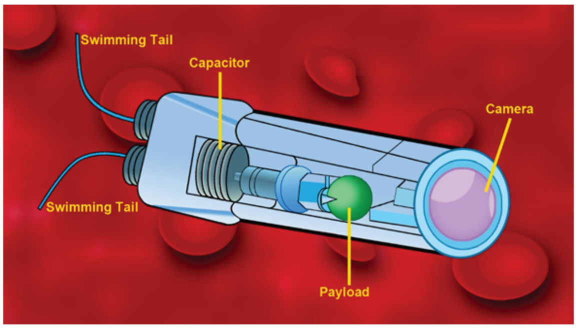

Figure 1. The structure and different parts of a typical nanorobot

Nanobots can be defined as the modified machine version of small microbes such as, a bacteria or virus. Nanobots can be engineered using biological or synthetic material, but they are adapted in such a way that they can perform atomic level preprogrammed tasks. They are designed as autonomous and are usually powered by a small battery or cell or sometimes solar cells. The emerging technology of nanobots in medicine opens up better opportunities of exploiting nanomedicine against diseases like diabetes and cancer. Ultrasonic powered nanobots were designed to remove bacteria and toxins from blood and engineers have recently designed an ultrasound-powered robot of the size of a cell which can swim through the bloodstream and remove the harmful bacteria as well as various harmful toxins on its way.

Most robots possess a solar cell or a battery pack to run itself, but these are too big to be incorporated in a nanobot. Nuclear technology may open an avenue where a thin film can beembedded with a radioactive material, and the nanobots can fuel themselves, eventually, with the particles released by decaying of the radioactive atoms. In nanobot the primary material may be silicon, as it can be used for delicate electronics and to make successful scaled down robot. The properties of silicon are-it is tiny (few 100 nm), strong, can conduct electricity, flexible, biodegradable, cost effective, and can be manipulated in many ways. The different classes of nanobots used in medicine are as follows:[26]

(i) Clottocytes- These are also called artificial mechanical platelets which can finish the hemostasis in nearly 1 sec. The design is like a spherical nanorobot which is powered by serum-oxyglucose, with and approximate diameter 2 μm. It is entrapped in a biodegradable fiber mesh which is efficiently folded on-board. After release, the soluble film coating above the fibre mesh would solubilize when in blood plasma contact to yield a sticky mesh.

(ii) Respirocytes- These are the artificial mechanical red blood cells which are blood-borne spherical nanorobots with a diameter of 1 μm. They can carry both oxygen and carbon dioxide molecules all over the body. These respirocyte nanobots are made up of 18 billion atoms each which are precisely organized inside the diamondoid pressure tanks. These tanks can store up to 3 billion carbon dioxide and oxygen molecules. These nanobots can deliver 236 times more amount of oxygen to the tissues in our body compared to the natural red blood cells.

(iii) Vasculoids- Vasculoids behave like an artificial nanomedical vascular system and are capable of all the blood functions that includes the circulation of all macromolecules, such as, the hormones, respiratory gases, cytokines, waste products, glucose, and cellular components. The engineering of this nanodevice is highly complex and it has 500 trillion independent cooperating nanorobots.[27]

(iv) Pharmacytes- These are the medical nanorobots with size of 1-2 μm that have the capacity to carry a drug load of 1μm3 inside the tanks and can be controlled by mechanically shorting pumps. As per the necessities, the drug load can be delivered in the cytosol or extracellular fluid with the help of a transmembrane injector system. These nanobots are provided with specific molecular markers or some chemotactic sensors which ensures 100% accuracy of targeting. The power supply of these nanobots is provided with the glucose and oxygen that is taken from the microenvironment, like, intestinal fluid, blood, and cytosol. Once the drug is delivered, these nanobots can be removed by from the system by conventional excretory pathways or centrifuge nephrosis.[28]

(v) Chromallocytes- Chromallocytes are the nanorobots with the shape of a lozenge that can work as an efficient gene delivery system. They can enter specific cells inside the patient's body and can fix the damaged gene by repairing it and then without causing any harm withdraws from the body. Chromosome replacement therapy (CRT) is dependent on this type of nanobots.[27]

(vi) Dentifrobots-Dentifrobots are the dental nanorobots incorporated in mouthwash or dentifrice-containing nanorobots. They have a typical spider format and after getting delivered by the toothpaste or mouthwash they patrol through the subgingival and supragingival surfaces. These nanobots can break down the trapped organic matter and convert them into odourless and harmless vapours. Dentifrobots can perform debridement of calculus and can be applied for preventive/ restorative and curative dentistry.

(vii) Microbivores-Microbivores are the artificial mechanical WBC or nanorobotic phagocytes which are oblate spheroid device prepared from diamond and sapphire. The diameter of microbivores is 3.4 μm along its major axis and is 2.0 μm diameter along the minor axis. It contains 610 billion precisely arranged structural atoms and these nanobots can absorb and digest the microbial pathogens present in the bloodstream through phagocytosis. These engineered nanorobots show 80 times higher efficiency compared to the marcophages.[28]

Applications of Nano Robots in Disease Management

For the detection or measurement of toxic chemicals in the environment, nanorobots may be used in health care. Robots at micro or nanoscale have been designed for the elimination or treatment of medical problems including the blood clots, scare tissue, arteriosclerosis, tumors, kidney stones and different types of infections.[29-31] The complex nanomechanical systems facilitates the biomedical instrumentation, tele-operation, targeted drug delivery or monitoring the metabolic disorders such as diabetes.[32] Nanorobots have also received a large number of patents.[33] Integration of the medical nanorobot architecture into the living system might be of theranostic significance. Magnetic resonance imaging(MRI)-guided nanorobots or nanomotors operating in the living organism may be applied for early disease diagnosis which is of critical importance in cancer. These controllable nanomedicines are able to algorithmically respond to input forces and information.[34-35] In an earlier study a novel intravitreal delivery microvehicles were designed and named slippery micropropellers which can reach the retina after active propulsion inside the vitreous humor. These are made from helical magnetic micropropellers which contain a liquid coating of layer that minimizes the adhesion to the polymeric network that surrounds it. The diameter of these propellers are in sub micrometer scale which enables them to penetrate the biopolymeric network and propel inside the vitreous body of the porcine to travel inside the eye at a distance of a centimeter or more. Clinical optical coherence tomography study has confirmed the propeller movement and the arrival of the micro propellers to the retina. Thus, this has contributed a significant ophthalmological drug delivery system.[36]

Diabetes is a medical condition that uses high levels of insulin and is of two types, type1 and type2. Type1 diabetes is the inability of the pancreas to produce insulin and type2 is inability of cells to take insulin. Nano robots are used to control and monitor the insulin levels regularly. A nano robot called as Complementary Metal Oxide semi-conductor (CMOS) contains a sensor that detects hSGLT3 protein activity which helps in regulating the glucose levels.37 Chitosan nano particles are used as a carrier of insulin which can be consumes orally that allows insulin to absorb into the blood effectively.38 Glucose concentrations are measured by using nano sensors that uses carbon nano tube electrodes.[39] Nano robots help in detection of toxic chemicals and the measurement of concentration in the cellmicroenvironment. The signals are transferred to the cell phones which alerts the patients to take the necessary actions.40 In another study it was shown that nanobots can monitor the level of a molecule hSGLT3. This molecule can regulate the level of glucose in diabetes patients. This glucose monitoring nanorobot utilizes the chemosensor, that can monitor the modulation of hSGLT3 protein gluco-sensor activity. The designed chemical sensors can efficiently determine the requirement for insulin in the patient's body and can inject it.41 In diabetes management, blood glucose self-monitoring and proper time of insulin injection can be monitored using the glucose nanosensors, carbon nanotubes, the layer-by-layer technique, quantum dots, oral insulins, artificial pancreases, microspheres, and nanopumps which is discussed earlier.[42]

Cancer cells are also targeted and killed by using nanobots. Researchers have functionalized the nanobots with DNA aptamer on the outside which can bind to nucleolin. Nuceolin is a protein that is specifically expressed by the tumor-associated endothelial cells. The inner cavity of the nanobot had the blood coagulation protease thrombin bound to it. The nucleolin-targeting aptamer sequenceacts both as a targeting domain as well as a molecular trigger enabling the mechanical opening of this DNA nanorobot. When the nucleolin is bound with the aptamer, the thrombin inside the nanobot is exposed thereby activating the coagulation at site of tumor. The tumor-bearing mouse models were taken for demonstrating this intravascular thrombosis through intravenous injection of the DNA nanorobot which delivered the thrombin specifically to the tumor-associated blood vessels. This caused tumor necrosis eventually inhibiting the growth of tumour. This engineered nanorobot was proven to be safe and immunologically inert.[43] Magnetic nanoparticles (Fe_3O_4) were chemically conjugated with anti-epithelial cell adhesion molecule antibody (anti-EpCAM mAb) and attached to a multiwalled carbon nanotubes (CNT) which was loaded with doxorubicin hydrochloride (DOX), an anticancer drug to design a multi-component magnetic nanobot. The enrichment of Fe_3O_4 NP s with dual catalytic-magnetic functionality enabled the autonomous propulsion of these engineered nanobots. The resultant was that these nanobots showed high velocity propulsion within the complex biological fluids. Cancer cell targeting was shown using human colorectal carcinoma (HCT116) cells. These nanobots released the DOX within the lysosomal compartment inside the cells after the Fe_3O_4 gate opened and there was reduction in tumor spheroid formation with high efficacy compared to free DOX.[44]

Limitations and Hopes in Nanorobot Design

Navigation is a fundamental necessity for cell-specifications and communications of nanorobots. Nanorobots through a fluid phase appears as a major challenge due to the continuous collisions within the body fluids that may result in the deviation of a nanorobot from its specific target.[45] Nanorobots have been designed which are magnetically guided towards the injury site or their movement may be facilitated using the micro-motors powered by the chemical reactions within the body.46 Nanorobots should be able to metabolize the oxygen and glucose in vivootherwise an external power source is utilized for both delivery of therapeutic agent and locomotion that may raise concerns due to possible interference between these two tasks of nanorobots. These external control problems remain as further concerns when multiple nanomachines are used.[47-48] Heat dissipation, in development of a large number of nanorobots, communication of nanorobots which is necessary to perform the complex task progress and receive the messages or other challenges should be addressed. This is an advanced simulation technique, wireless communication and size reduction procedure in order to obtain more efficient and functional nanorobots for long-term benefits.Insulin overdose can be produced due to closed loop systems which can act as antagonist to the clinical side. Insulin overdose can result in hyperglycaemia that can be controlled by addition of glucagon. Exposure of insulin for prolonged period of time also results in changes in cell metabolic processes like cell division.[49-51] Other basic limitations of using nano robots include effective cost, complicated design, regulatory issues, increased power supply, challenges with immune system and so on. In case of cancer drug delivery and killing the cancer cells by constricting the blood vessels may also lead to damages to the normal cells. The specificity of these nanobots action, if not controlled, can lead to detrimental effects.

Conclusion

Nano robotics gives hope for future diagnostic and treatments. It reduces the adverse effects caused in drug therapy for diabetes. These are used to treat many diseases which are not possible from ancient methods. Nano robots are going to transform the medical industry in future. Reducing the challenges of this nano robotics and implementing new and advanced technologies with higher material science knowledge can assist a high standard for the clinical fields and therapeutics.

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