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NANOROBOTS- AN EMERGING TECHNOLOGY IN THE FIELD OF NANOSCIENCE

KEY WORDS: Nanomaterials, nanorobots, cancer, chemoprophylaxis.

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ABSTRACT

Nanomaterials as raw materials manufactured robots are called "nanorobots". Due to the advancement of science and technology, nanomaterials have gained potential in the field of medicines and pharmaceuticals. Nanorobots are mainly utilized for the treatment and diagnosis of cancer and are found also effective in other medical purposes like DNA probes, cell imaging materials, and cell-specific delivery vehicles. The present work mainly focuses on the nanorobotic approach for chemoprophylaxis along with the basic details of nanorobots. Future study more on nanorobots may give more new approaches to the prevention and mitigation of various ailments.

INTRODUCTION

The founder of chemotherapy Paul Ehrlich has been inspiring generations of researchers till from one hundred years ago that those drugs only interact with the specific target in the body, by creating "magic bullets" to fight against human diseases. In the field of nanotechnology-enabled drug delivery systems, the attention of this concept has attracted increasingly for the treatment of significant diseases like cancer therapeutics [1].

One of the main cancer treatment options is radiation therapy. About 60% of all cancer patients used radiation therapy at some point during the course of the disease. The traditional radiation therapy treated cancer diseases by damaging their DNA structure but it also kills human normal cells other than cancer cells. Radiation therapy can cause hair loss, depression, nausea, fatigue as well as numerous other symptoms. The main issue with contemporary chemotherapy is not that the medications are ineffective; they are successful in killing tumour cells that are actively developing; rather, it is that the rest of the body cannot tolerate the drug concentrations needed to completely eradicate the cancer cells. The severity of chemotherapy is typically defined by the doses the patient can tolerate rather than the amounts necessary to eradicate all malignant cells because drug concentrations high enough to eradicate tumours can kill the patient before the tumours die [2].

Scientists were concentrating on nanorobots for cancer therapy to prevent this problem (the potential medical applications of nanorobots are vast and ambitious). Chemistry, physics, materials science, and biology are all combined in nanotechnology to create the necessary skills along with these cutting-edge technologies. They are built with precision at nanoscale dimensions between 1 and 100 nm to carry out a specific task or tasks occasionally [3].

Researchers have made significant advancements in the last ten years to create useful nanorobots, they include various systems such as sensors, energy supply, and data transmission. Nanorobots can give surgeons information so that they can handle the medical procedure precisely by mapping the target areas that need to be dissected. A physician who practices nanomedicine might give the patient an injection of a nanorobot that would hunt down cancer cells and eliminate them, curing the illness at its source while sparing healthy cells. A patient undergoing with a nanorobotic treatment would not be aware of the molecular devices operating inside them, other than the rapid improvement in their health [3].

The much efforts from scientists also capable of performing controlled navigation to targeted locations in physiological conditions and environments. In a 2014 review, Wang and co-workers focused mostly on micro- and nanorobots propelled by chemical processes and external fields. They also briefly discussed the developments in in-vitro active drug delivery employing micro- and nanorobots. The rapid and significant advancements of micro-/nanorobots in recent years an active drug delivery based on micro-/nanorobots has forwarded from test tubes to the cellular level and living animal models. For example, Wang and co-workers reported the first example of using chemically propelled microrobots for active drug administration in living mice in 2015. In 2016, it was shown that magnetotactic bacteria functionalized with nanoliposomes can efficiently go to tumor hypoxia zones with the aid of external magnetic fields [1].

The patient's life is entirely in the hands of the operator, surgeon, or doctor during any of the invasive techniques. It is dangerous since one error could lead to disaster. Researchers and scientists are developing a method that is more durable, trustworthy, and biocompatible. They intend to defend the body from the inside rather than treat the outside [3].

Additional characteristics of nanorobots would also

enable us to:

- It has the capacity to store and interpret historical data, spot patterns, and as a result, aid in illness prognosis.
- It can provide external guidance as per programme, targeting specific locations.
- It has the capacity to transport healthy cells or payloads like medications to the desired location.

They are able to travel via natural biological channels, making it possible to customized (and more frequently) manufactured externally[3].

Ideal Characteristics of Nanorobots

- They are between 0.5 and 3 microns in size, with 1-100 nm parts; otherwise, they can obstruct capillary flow.
- Nanorobots have a passive, diamond exterior that preventing them from being attacked by the immune system.
- It is capable of contacting the physician by encoding information to acoustic waves with carrier wave frequencies ranging from 1 to 100 MHz.
- It can make additional copies of itself to replace damaged or worn-out pieces which is called as Self-replication [3].

Working Principle Of Nanorobots

The challenging subject of nanorobotics, which deals with minute objects at the molecular level, is growing. It provides materials for controlled drug delivery by instructing carriers to go to a particular location. Inside the body, nanorobots and nanoscale-structured materials provide major advancements in diagnosis and treatment of diseases at lower concentrations. A wide range of capabilities should be made possible by the rapid progress in nanoscale devices engineering. The various parts of the nanorobot design could include molecular computers, sensors, motors, manipulators and power supplies. A medical nanorobot's main component will probably be carbon, most likely in the form of diamond or diamondoid/fullerene nanocomposites. Numerous other light elements, including silicon, fluorine, oxygen, nitrogen, hydrogen, and sulphur, will serve specific functions in nanoscale gears and other parts[2].

The Working Principle Of Nanorobots Are Given Below Step By Step:

A. **Introduction of Nanorobots into the Body:** A feasible robot must be tiny and agile, In order to navigate through the human circulatory system, a very intricate network of veins and arteries.
B. **Movement of Device around the Body:** Initially, the device is navigated to the surgical site using normal blood flow. There should be a various propulsion such as propeller, cilia, electromagnetic pump, jet pump membrane propulsion to reach the site of action.
C. **Direction of the Device:** The sensors present in nanobots are able to recognise the defective tissues. The location of the undesired tissue is navigated using the long-range sensors while short-range sensors are used to locate the tumor.
D. **Control of the Device:** Two basic types of sensors are employed. One sensor is employed for actual operation and another one is used for final navigation. It will direct the nanorobot toward the tissues that need to be removed and keeping it away from the tissues that are not to be removed. A camera, spectroscopic method, and UHF (Ultra High Frequency) sonar are used to evaluate the device.
E. **Means of Treatment:** There are various ways to carry out the procedure. The substances can be broken to exert its action, and it gets expelled afterward.
F. **Removal of Nanorobots After Treatment:** After completing their mission inside the human body, the nanorobots that were implanted to carry out specific functions must be removed.
G. When nanorobots are purposefully removed from the body after being introduced semi-permanently into the bloodstream for maintenance, the issue is exactly the reverse. Utilizing chemical sensors is an additional technique for this.
H. **Powering of Nanorobots:** There are two ways to obtained the power needed to operate the nanorobot: either by getting it from a source inside the body or by getting it from the bloodstream. Alternatively, it might be acquired from an external source [3].

Preparation Of Nanorobots

Chemistry, physics, materials science, and biology are all combined in nanotechnology to create the necessary skills to develop these novel technologies. Nanorobots will have a diameter of between 0.5 and 3 microns and be constructed from components that are 1 to 100 nanometers in size.

The Two Basic Strategies For Construction At The Nanoscale Scale Are:

i. In positional assembly: Investigators employ some tools like the arm of a miniature robot or a microscopic set to pick up molecules one by one and manually assemble them.
ii. Self-assembly: It is is much less painstaking, because it takes advantage of the natural capabilities of certain molecules to seek out one another.

In this investigator have to do is to add billions of them to a beaker and allow their natural affinities join them automatically in order to get the necessary configurations. . Making complex nanorobotic systems requires Manufacturing methods that can construct a molecular structure through computer models of diamond mechanosynthesis (DMS).In the 3D workspace the target has surface chemicals enable the nanorobots to find and identify it.Manufacturing better sensors and actuators with nanoscale dimensions makes them determine the source of release of the chemical[2].

Software called the Nanorobot Control Design (NCD) simulator was developed for use with nanorobots in environments with fluids dominated by viscous forces over inertial forces ones and by Brownian motion. The three methods are following:

In A First Method: The scientists conducted a random search for the target using the tiny Brownian movements of the nanorobots.
In A Second Method: The nanorobots monitor for chemical concentrations that are noticeably higher than the background level. A nanorobot that has detected the signal determines the gradient in concentration before moving toward greater concentrations until it reaches the goal.

In the third approach: Another chemical is released by nanorobots at the target, which other devices use as an additional guiding signal. Therefore the nanorobot utilize this information to identify whether there are sufficient numbers of nanorobots at the target, in order to terminate any additional attractant signal a nanorobot may be releasing. Once a sufficient number of nanorobots have reacted, it is discovered that the nanorobots stop attracting others once. The amount is considered enough when there are several nanorobots covering the target area [2].

The Three Main Requirement For The Prepation Of Nanorobot Are Following:

(i) Externally coated energy harvester electrodes and a cylindrical capacitor,
(ii) A Carbon-nanotube based glucose detector and
(iii) A NEM actuator.

Energy harvester and Metal-Insulator-Metal (M-I-M) cylindrical nano-capacitor

A nanorobot can be autonomous if a nanorobot does not rely on external power sources. Creating an energy source is the first stage in visualizing an autonomous nanorobot. The three most popular types of glucose energy (liberated electrons) harvesting are ; Enzyme, microbial and abiotic based.However, certain inorganic materials, like platinum, graphene, etc., are used as electrodes due to their biocompatibility and proven application scenarios.Through the bio-detector, a Metal-Insulator-Metal (M-I-M) capacitor is linked to the actuator. The charge flow changes depending on the activity of the bio-detector, acting as a switch to regulate the amount of current flowing from the capacitor to the NEM actuator. The simulated structure is strictly kept within a 100 nm dimension to qualify the structure as a nanorobot and allow the nanorobot to immobilise itself on the cell surface and function as a parasite.[4]

Bio-Detector

The programmability in nanomaterials can be seen when a combination of electrical manipulation, bio-detection, and NEM actuation is combined. The second component of our proof-of-concept demonstrates the bio-detection process of cancer cells and gives an electrical output to make logical decision.The active navigation of the nanorobots employing chemical pheromones for binding to and detecting tumour tissues is another aspect of the in-vivo identification of tumour cells.Nanorobots that have been immobilised by glucose or its derivatives help them navigate through blood. The next step would be to use the stored charges for logical decision-making, assuming that the nanorobots can swim independently in blood, get attracted, harvest and store energy from the blood glucose.The bio-detection mechanism sits in the black-box between decision-making and energy that has been captured. A shift in the charge flow between the electrodes should result from the chemical identification of cancer cells.[4]

Actuator

A motion is created by an actuator, a device, by converting energy and signals entering to the system. Up to this point, the concept has been developed to the point where the nanorobots are autonomous bio-detector in terms of power and navigation, capable of bio-detector, and computationally capable of handling a small change in information.Nano-Elecro-Mechanical (NEM) actuator can be produce by the conductance change in the immobilized CNT (carbon-nanotubes) bio-detector. This setup is comparable to a programmable material that changes colour or has fluorescent markings.In this respect, it is anticipated that the working voltage supplied by the energy harvester will decrease from 200 mV to 70 mV. This signal is anticipated to result in a mechanical break that is enough to transcend the stress gradient of the actuator's ceiling structure. The immune system is able to detect the attached nanorobot and the cancer cell when the mechanical break exposes a detectable medication [4].

Subcomponents Included In A Nanorobots Preparation Are Following:

Payload: This is a void section that carries a small dose of drugs or medication. It can move through the blood and release the medication to an injured or infected area.

Micro Camera: The nanorobot may attach a tiny camera, and it can be observed when directing through the body manually.

Electrodes: By using the electrolytes in the blood, the electrode attached on the nanorobot may create a battery. These protruding electrodes can destroy the malignant cells by producing an electric current and scorching the cancer cells up to death.

Lasers: These lasers can burn the harmful material such as cancer cells, blood clots, or arterial plaque.

Ultrasonic Signal Generators: These generators are utilized when the nanorobots are used to target and damage kidney stones.

Swimming Tail: Nanorobots are propelled into the body. In order to move, the motor and either manipulator arms or mechanical legs are used. They developed software to simulate nanorobots in a fluid environment where Brownian motion predominates. The target molecules can be found by the nanorobots' chemical sensors.[3]

Techniques such as Scanning Atomic Force Microscopy (AFM) and Electron Microscopy (SEM) are being engaged to acknowledge the molecular structure of the nanoscaled device.[3]

The Following Tasks Must Be Resolved:

- Calculation of the magnetic field's inhomogeneous force on various carriers.
- The conditions (such as the magnitude of the magnetic field gradient, the degree of magnetization of the carrier, the size distribution, etc.) must be defined in order to obtain quantitative estimates of the parameters and determine whether it is possible to keep device containing medicinal preparations against the vessel wall.
- Analysis of magnetic carrier movement in a body fluid (blood) under the influence of an uneven magnetic field to determine the possibility of their delivery to the walls of blood vessels.[5]

The simple theory of nanorobot platform design can help to close the gap between current research on cancer treatment using bio-nano-sensing in conjunction with cutting-edge nano transistor technology.[4]

Nanorobots as chemoprophylaxis and its ongoing treatment strategies

Nanorobots can be apply in various field such as Dentistry, Cancer, Diabetes, Kidney Disease, Gout, Tissue Reconstruction and Delicate Surgeries etc.

Application of Nanorobots in Cancer Treatment: For the purpose of identifying tumour cells in the early stages of cancer growth, nanorobots with chemical biosensors (nanosensor) are employed. The presence of cancerous cells in the body will be detected by this nanosensor. Given that nanorobots may move through blood as bloodborne devices, they can aid in such crucial areas of cancer therapy. The reserchers have genetically modified salmonella bacteria that are lured to tumors by chemicals released by cancer cells. When the bacteria reach the tumour, tiny robots around 3 micrometres in size that release capsules containing medications autonomously. The nanorobot, which the researchers termed bacteriobot, kills the tumour while leaving healthy cells alone by delivering medications there directly, protecting the patient from the side effects of chemotherapy.

Applications of DNA Nanorobot in Treatment of Cancer: A targeted drug delivery system using a DNA nanorobot can be utilised to enhance medical procedures. There are various chemotherapy medications made specifically to kill rapidly dividing cells. Fast-diversifying cells, not only include cancer cells, however it also include stomach lining, hair follicles, blood cells, etc. Chemotherapy medications frequently cause a number of adverse effects, including nausea and vomiting, hair loss, low blood cell counts, etc. as they assault all of these rapidly dividing cells. It can be overcome by the help of DNA Nanorobot.[3]

Its ongoing treatment strategies: Nanorobots' continuous treatment plans aim to provide non-surgical solutions for all of these issues. Using nanorobots for medical therapy offers more precise medical care than traditional surgical techniques. Chemotherapy can be replaced in the treatment of cancer by using nanorobots to kill cancer cells. Medical nanorobots may be used in the field of eye surgery in the future. The use of nanorobots in surgical procedures and medical treatments will make them safe for all patients and provide a useful tool for locating the origin of dreadful diseases. [3]

Future Aspect Of Nanorobots

1. Application Nanorobots In Diagnosis:

Dental nanorobots might use specific motility mechanisms to penetrate human tissue with navigational precision, acquire energy, and sense and manipulate their surroundings in real-time. From an in vivo perspective, nanodevices might be inserted into the body to identify the early presence of a disease, or to identify and quantify toxic molecules, and tumor cells. The nanoelectromechanical system, oral fluid nanosensor test, and optical nano biosensor which also comes under nanorobots can also be used for diagnosing oral cancer [6].

2. Nanorobotic Dentifrices:

Nanorobotic dentifrices, when delivered either by mouthwash or toothpaste, can cover all subgingival surfaces, thereby metabolizing trapped organic matter into harmless and odorless vapors. 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 [7].

3. Function Of Nanorobots For Biomedical Application:

Nanorobots have been used to transport micro and even smaller objects in closed or open fluidic environments by direct pushing and non-contact methods. For biomedical applications such as drug delivery further surface bio-functionalization with specific chemicals, such as drug molecules, is required. Qiu et al. successfully functionalized artificial bacterial flagella (ABFs) with three types of lipid-based nanoscale drug carriers (dipalmitoyl phosphatidylcholine (DPPC)-based liposomes [8], DOTAP/DOPE liposomes [9], and lipoplexes [10] these functionalized ABFs (f-ABFs) were able to perform wireless single-cell targeting under low-strength magnetic fields.

4. Nano Swimmers:

Nano swimmers are self-propelled devices in which the directional self-propulsion or swimming is driven by biological, enzyme, magnetic, or chemical propulsion mechanisms [11]. Recently, spirulina cell-based helical microswimmers with magnetite coatings were used for targeted delivery against gastrointestinal diseases [12].

5. Dentin Hypersensitivity:

Dentin hypersensitivity is a pathological fact caused by changes in pressure transmitted hydrodynamically to the pulp. This is based on the fact that hypersensitive teeth have eight times the higher surface density of dentinal tubules and tubules with diameters twice as large as non-sensitive teeth.Reconstructive dental nanorobots selectively and precisely occlude specific dentinal tubules within minutes, using native biologic materials, offering patients a quick and permanent cure from hypersensitivity [13].

6. Treatment Of Oral Cancer:

Nanomaterials for brachytherapy like "BrachySil" (Sivida, Boston & Perth, Australia) deliver 32P, are in the clinical trial. Drug delivery system that can cross the blood-brain barrier is the vision of the future with this technology. Parkinson's disease, Alzheimer's disease, and brain tumors will be managed more efficiently. Nanovectors for gene therapy is in a developing stage to correct disease at the molecular aspect [14].

Nanoparticles play a key role in developing new methods for detecting cancer [Fig. 1]. Detection of cancer in an early stage is a critical step in improving cancer treatment. Various nanoparticles used are cantilevers, nanopores, nanotubes, and quantum dots [15].

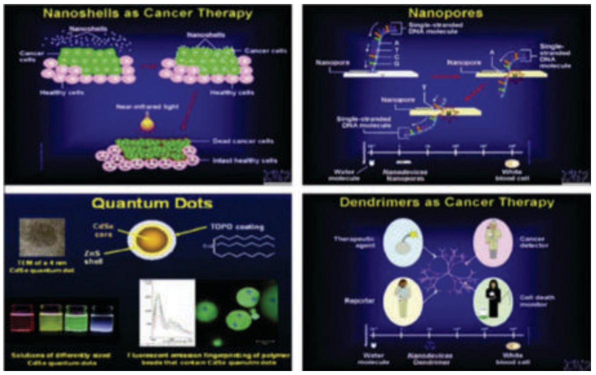

Fig. 1 Detection and treatment of oral cancer.

7. Nano Impression:

Impression material is available and it will be used widely in the future with nanotechnology applications. Nanofiller is integrated in the vinyl polysiloxanes, producing a unique addition to siloxane impression material. Impression materials are available with nanotechnology applications and development is going on for future prospects. The main advantage of this material is that it has better flow, improved hydrophilic properties hence fewer voids at the margin, better model pouring & enhanced detail precision [15]

8. Future Aspect In Genetic Code:

Another interesting nanodevice is nanopore. Improved methods of reading genetic code will help researchers in detecting errors in genes that may contribute to cancer. Nanopores contain a tiny hole that allows DNA to pass through one stand at a time making DNA sequencing more efficient. [15].

Other Clinical Applications Of Nanorobotics:

1. Medical Application of Nanorobots: The use of nanorobots may advance biomedical intervention with minimally invasive surgeries and help patients who need constant body functions monitoring, and improve treatment efficiency through early diagnosis of possible serious diseases.

a. Hemophilia: Nanorobots must be able to remove the blockage without losing small pieces in the bloodstream, could travel elsewhere in the body,and cause more problem . The robot must be so small enough so that it doesn't block the flow of blood itself assist in their healing process. One particular kind of nanorobot is the clottocyte or artificial platelet clottocyte; clotting could be up to 1,000 times faster than the body's natural clotting mechanism. Clottocyte used to treat patients with serious open wounds [16].

2. Application of Nanorobots in Dentistry:

a. Nanorobotic Dentifrices (Dentifrobots): These invisibly small dentifrobots are purely mechanical devices that safely deactivate themselves when swallowed. Nanorobotic Dentifrices delivered either by mouthwash or toothpaste, can cover all subgingival surfaces, thereby metabolizing trapped organic matter into harmless and odorless vapors. Properly configured dentifrobots can identify and destroy pathogenic bacteria that exist in the plaque.

b. Maintenance of Oral Hygiene: A mouthwash full of smart nanorobots could identify and destroy pathogenic bacteria while allowing the harmless flora of the mouth to flourish in a healthy ecosystem. Sub occlusally swelling nanorobots are delivered by dentifricepatrol. They prevent tooth decay and provide a continuous barrier to halitosis.

c. Tooth Repair: Nanorobots provide complete dentition replacement therapy, including both mineral and cellular components.It also involves in genetic engineering, tissue engineering, and tissue regeneration procedures for major tooth repair.

d. Dentin Hypersensitivity: Dentin hypersensitivity is a pathological phenomenon caused by pressure transmitted hydrodynamically to the pulp. Reconstructive dental nanorobots precisely offering patients, a quick and permanent cure from hypersensitivity [17].

e. Esthetic Dentistry: In esthetic dentistry, nanorobots are used for dentition renaturalization. And also excavate old amalgam restorations and remanufacture teeth with biological materials, in distinguishable from original teeth.

3.In Cancer Detection and Treatment: Cancer can be successfully treated with current stages of medical technologies and therapy tools. Another important aspect to achieve a successful treatment for patients, is the development of efficient targeted drug delivery to decrease the side effects from chemotherapy. Considering the properties of nanorobots to navigate as bloodborne devices, they can help on such extremely important aspects of cancer therapy. Nanorobots with embedded chemical biosensors can be used to perform detection of tumor cells in early stages of development inside the patient's body. Therefore, a hardware architecture based on nanobioelectronics is described for the application of nanorobots for cancer therapy [18].

4. In Surgery: Surgical nanorobots could be introduced into the body through the vascular system or at the ends of catheters into various vessels and other cavities in the human body. A surgical nanorobot, guided by a human surgeon, could act as a semiautonomous on-site surgeon inside the human body.

5. Cryostasis: The extraordinary medical prospects proposal made long ago: that the dying patient could be frozen, then stored at the temperature of liquid nitrogen for decades or even centuries untill the necessary medical technology to restore health is developed, Called cryonics. We cannot prove today that medical technology will (or will not) be able to reverse freezing injury 100 years from now seems likely that we should be able to reverse freezing injury - especially when that injury is minimized by the rapid introduction through the vascular system of cryoprotectants and other chemicals to cushion the tissues against further injury [19].

Limitations Of Nanorobots

1. The cost of utilizing nanotechnology may be quite high and continue to rise, which may result in a significant financial burden for us. It is also fairly difficult to manufacture, which may be one of the reasons why products made with nanotechnology have a higher price tag.
2. If the nanorobots are misused with the assistance of utilizing terrorists, it is possible that they will also be utilized as a bioweapon, which may end up posing harm to society.
3. The power supply is the most difficult challenge to overcome. More work needs to be done in the way of research so that robots can eventually overcome the immunological reaction of the body.
4. Because the presence of nanobacteria in our bodies can have catastrophic consequences, we can conclude that nanobots are foreign to our bodies. The fact that there are so many foreign particles in the body poses a huge challenge for biodegradability. Our immune system may be put to the test if we rely too much on nanotechnology, and a potentially hazardous variant of the bots may be generated if the nanobots are able to multiply themselves.
5. Choosing the appropriate materials to construct nanorobot devices is one of the major challenges. Although the qualities of certain materials, such as cobalt and certain rare earth metals, are desirable, the human body cannot tolerate them because they are hazardous.
6. There is a requirement for financial support. It takes a significant amount of investment to get these things in order; money from the government can only get us so far, and we really need the kinds of investments that huge firms can do to bring us over the finish line of the regulatory process.
7. We also need to work closely with the medical doctors, as they are the ones who will be employing this technology to treat patients. This means that we need to collaborate closely with them. It is not uncommon for them to have unrealistic expectations regarding what it is that we may be able to deliver, and it is also possible for us to have unrealistic expectations regarding what it is that they are actually doing. As a result, it can be difficult to bring together the medicine, the science, and the technology.
8. At the nanoscale, the viscosity of blood makes it nearly impossible for drug-carrying nanorobots to navigate their way through blood vessels. Because the Brownian motion of the molecules causes collisions between molecules, the behaviour of the nanorobot subsequently becomes unpredictable and cannot be controlled. This instability has been one of the most significant constraints on the research, as well as a significant challenge that researchers are attempting to surmount. The other significant obstacle is the development of suitable feedback sensors, which will enable autonomous control on a more granular scale [20,21]

CONCLUSION

The main goal of writing this literature was to provide an idea of technological development of nanotechnology in medicine by introducing a nanorobot, an emerging method of drug delivery. Nanorobots can develop cancer treatment, health facility and human life better than several conventional therapy of past. It is more efficient method of delivering the drug and new way for the repairing of damaged tissue. The main focus is to reduce the side effect of chemotherapy on the patient by forming a localized drug delivery. Nano robots have many advantage in drug delivery like better bioavailability, targeted therapy, non-invasive technique, more accuracy and precision, less side effect etc. In the future, nanotechnology could allow object to harvest energy from the environment.

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