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Research Paper

Development of micro/nanobots and their application in pharmaceutical and healthcare industry

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ABSTRACT

Background: Nano robotics is a rapidly emerging, multidisciplinary field combining nanotechnology, pharmaceutics, biomedical engineering and robotics. Nanorobots are programmable Nano scale devices that could change the diagnosis and treatment of human disease.
Objective: To review the development, components, types, medical applications, biocompatibility and toxicity, and future prospects of micro/Nano robots in the pharmaceutical and healthcare sectors.
Methods: Narrative review of the published literature.
Results: Nano robot components include a payload, sensors, power source, controllers, manipulators and a propulsion mechanism. Theoretical designs include the pharmacyte, reciprocate (artificial red blood cell), microbivore (artificial phagocyte), clottocyte (artificial platelet) and chromallocyte (chromosome replacement). Reported or proposed applications include targeted drug delivery, diagnosis and monitoring, Nano dentistry, cancer detection and therapy (including bio hybrid magneto tactic bacteria carrying drug-loaded liposomes), diabetes and glucose sensing, gene therapy, surgery and nerve repair, ultrasound-powered blood detoxification, DNA-based biosensors, coronary artery disease and atherosclerotic plaque removal. Biocompatibility and toxicity are poorly understood: nanorobot-biological interactions depend on material, size, shape and surface coating, and hazard identification is at an early stage. Much of the field remains theoretical because of fabrication and control difficulties.
Conclusion: Nano robotics has wide potential in medicine, with possible advantages including lower costs, faster recovery and minimal invasiveness. Safety, toxicity and manufacturing challenges must be resolved before clinical translation.

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1. INTRODUCTION

The use of customized medication delivery systems is growing because molecular technologies are cutting-edge replacements for cumbersome processes. The physicist Richard Feynman used the term "nanobots" for the first time in his well-known 1959 address, There's Plenty of Room at the Bottom. The Richard Feynman talked about employing nanoparticles and nanobots to cure cardiac problems [1].

Nanorobotics is a new, cutting-edge, multidisciplinary field that calls for the technological expertise of medical, pharmaceutical, biomedical, engineering, as well as other applied and basic scientists. Particularly in their nano-sized constructions, nanorobots differ from macro-world robots. The design and development of nanobots is based on the principles of mechanically synthesised chemistry and molecular nanotechnology. These systems are nano electromechanical components that can reliably and accurately execute pre-programmed tasks using the energy given by a nanomotor or nanomachine that is already built into the system [2].

The scientific field of nanotechnology involves the study of objects at the nanoscale. Materials are designed, produced, synthesised, manipulated, and applied at the nanoscale. [3] Robots at the nanoscale are the subject of nanorobotics. Nanorobots are robots that are a few hundred nanometres in size or less and are made up of different nanoscale-sized components. The field of building robots with parts that are at or near the nanoscale is known as nanorobotics, and it is one that is quickly emerging. In the field of technology known as nanorobotics, tiny robots as small as 0.110 micrometres are designed and manufactured. Other names for nanobots include nanoids, nanites, nano machines, and nano mites [4].

Nanobots is formed from of the words Nano and Bots. Nano is an extremely tiny size. Robots are machines that can be programmed to perform certain tasks, and the unit of measurement for their speed is just the nanosecond, or one billionth of a second (10-9). On nanorobots, several ideas have been created. This technology allows us to develop tools that may be used in a variety of contexts, including the military, the medical industry, and others. In the modern world, robotics is a constantly expanding field. New robots are being designed, researched, and developed for a variety of uses [5].

In the literature, the term "nanorobotics" or "nanobots" is used in several different ways. As a result, there are two main focal areas in the subject of nanorobotics. [6] The very first area refers to the creation, modelling, collaboration and control of nanoscale robots (i.e., nanorobots). Nano systems such as nanorobots, nanomachines, and other nanotechnologies are mainly composed of assemblies of nanoscale elements, where individual diameters range from 1 to 100 nm. These items have overall dimensions in the micrometre range. The difficulty in manufacturing such devices has led to a large portion of the research done in this field remaining purely theoretical at this time. Even if there aren't any artificial nanorobots yet, natural biological nanorobotic systems demonstrate that such systems are still feasible.

The second field focuses on manipulating or putting together nanoscale parts using tools or robots that are larger in scale (i.e., nanomanipulators). The creation of synthetic nanorobots themselves depends heavily on nanomanipulation and nano assembly. The physical and chemical properties at this size are not fully known, and nanoscale manipulation is still in its infancy [7].

The absence of efficient methods in the field of nanotechnology has prevented the development of the nanoscale structures necessary for various applications from a design perspective. Although physicists embrace the idea of making devices atom by atom, chemists do not favour the bottom-up manufacturing method because of the high reactivity of most atomic species. Other difficulties faced by researchers include creating nanorobots with diameters below the nanometer range and controlling many nanorobots (known as swarms). Controlling matter at the molecular scale to change the behaviour

of nanorobots is another challenge related to their construction (dynamics and properties). Overall, research into the production, automation, and power of nanorobots is difficult and cutting-edge [8].

1.1 Components of Nanorobots

Nanorobots are made up of several different parts, including a source of electrical power, a fuel buffer tank, detectors, controllers, manipulators, onboard computers, compressors, pressure tanks, and structural support. The components of a nanorobot include:

(1) **Payload:** A little quantity of medication or a substance is stored in this empty space. The medicine might be released by the nanorobots as they go through the circulation and reach the infection or injury location.
(2) **Micro Camera:** The nanorobot can be manually guided through the body by the operator [9].
(3) **Electrodes**: The electrode on the nanobot can convert the electrolytes in the blood into a battery. These exposed electrodes might also be able to destroy cancer cells by generating an electric current that will heat them to death.
(4) **Lasers:** Hazardous materials such as cancer cells, blood clots, and arterial plaque can be burned by these lasers [10].
(5) **Ultrasonic Signal Generators:** When kidney stones are the target of nanorobots being utilised to target and remove them, these generators are used.
(6) **Swimming Tail:** ~~the~~The nanorobot needs a mechanism to go through the body because it travels against the blood flow.

The nanorobot will feature manipulator arms or a mechanical leg as well as motors for locomotion. Positional assembly and self-assembly are the two basic techniques used in the construction of nanorobots. In self-assembly, picking the molecules and manually assembling them is done with the help of a microscopic set or the arm of a small robot. In positional assembly, researchers group billions of molecules and allow them to form naturally according to their inherent affinities into the desired configuration. The programme called Nanorobot Control Design was created to simulate nanorobots in a fluid environment where Brownian motion is dominant. [11], [12], [13] Chemical sensors on the nanorobots can identify the target compounds. For decentralised action, the nanorobots are equipped with swarm intelligence. The nanorobots' artificial intelligence was developed using algorithms that are based on computational intelligence. The cooperative behaviour of social organisms like ants, bees, and termites that operate decentralised from a central controller serves as the basis for the swarm intelligence technique. The three most common computational intelligence methodologies are particle swarm optimization (PSO), artificial bee colony (ABC), and ant colony optimization (ACO).

1.2 Created the Following Varieties of Nanorobots

Pharmacyte: The Pharmacyte is a 1- to 2-m-long nanorobot. According to the requirements of the task, a nanorobotics system's onboard tanks can store payload that can either be released into adjacent extracellular fluid or injected directly into the cytosol using a transmembrane injector mechanism [14].
Respirocyte's: Respirocyte's are blood-borne, spherical red blood cells with a diameter of 1 m that are developed as nanorobots. The exterior shell is made of a diamondoid 1000 atomic pressure vessel with reversible molecule-selective pumps. Throughout the body, respiratory cells transport carbon dioxide and oxygen molecules. The respirocyte is composed of 18 billion atoms that are precisely arranged in diamondoid pressure tanks, each of which has the capacity to contain up to 3 billion molecules of oxygen and carbon dioxide. [15] The respirocyte would deliver 236 times more oxygen to the body's tissues than do regular red blood cells. [15], [16] The body's respirocytes can be programmed to expel dangerous substances like carbon monoxide.
Microbivores: Microbivores, also known as nanorobotic phagocytes, are nanorobots that function like synthetic white blood cells. The microbivore is a ruby and diamond spheroid device with 610 billion well positioned structural atoms that is 3.4 mm in diameter along its major axis and 2.0 mm in diameter along its minor axis. It also contains 610 billion carefully positioned structural atoms. It catches and breaks down the germs into tiny molecules in the blood stream. Microbivores' main function is to absorb and

digest the pathogens in the blood stream by means of the phagocytosis mechanism. These four constituent elements make up the microbivore**:**

- An array of reversible binding sites.
- An array of telescoping grapples.
- A morcellation chamber.
- Digestion chamber.

During the process cycle, the target bacteria use a species-specific reversible binding site to adhere to the microbivore surface. When the reversible binding site comes into close contact with the surface because of a collision between the bacterium and the microbivore, it can recognise and weakly link to the bacteria. One cycle of phagocytosis in a microbivore might take up to 30 seconds to complete.

Clottocytes: When platelets harm the endothelial cells of blood vessels, a process known as haemostasis occurs These platelets become triggered when exposed collagen from broken blood vessels encounters them. The entire time it takes for blood to naturally clot ranges from 2 to 5 minutes. The ability of nanotechnology to shorten clotting times and stop blood loss has been demonstrated. In certain individuals, blood clots have been found to form randomly. The illness is managed with medications like corticosteroids. Reliable communication mechanisms would be required to govern the coordinated mesh release from surrounding clottocytes, as well as to regulate multidevice-activation radius within the local clottocyte population. The onboard sensors of the clottocyte instantly detect the change in partial pressure as clottocyte-rich blood enters the injured blood vessel, frequently signalling that it is bled out of the body. When the first clottocyte is 75 m from the air-serum contact, oxygen molecules from the air diffuse into the serum at a temperature comparable to that of the human body. The dissemination of this finding to surrounding clottocytes was accomplished using quick sonic pulses [17].

Chromallocyte: By completely replacing entire chromosomes in individual cells, the Chromallocyte would reverse the consequences of hereditary illness and other cumulative gene damage, delaying the onset of old age [8].

1.3 Biocompatibility and Toxicity of Nanorobots

The complexity of the interactions between the materials used to make nanorobots and biological matter, which varies, may cause the surface features of the nanorobots to change depending on the environment in which they are utilised, has left researchers with a partial understanding of the mechanisms governing interactions between nanorobots and living systems. As a result, the associated potential risks and hazards have not been thoroughly identified. Experimental studies have demonstrated that the same material's particles can behave completely differently for a variety of reasons, such as variations in surface coating. In addition, there are a great number of other factors to consider while dealing with nanorobots, such as the material, size, form, surface coating, sensing and actuation mechanisms employed, and the working environment in which the nanorobot is functioning. However, significant efforts have been made to identify primary entrance channels such as the lung, stomach, and maybe the skin as well as probable targets such as the lung, liver, heart, and brain. Hazard identification of the usage of nanorobots in the human body is still in its early stages [18].

1.4 Medical Application of Nanorobots

1.4.1 Nanobots in Medicine and Targeted Drug Delivery

Drug delivery can be done with nanobots. Drugs typically travel throughout the body before reaching the area that is afflicted by the disease. Nanotechnology allows us to precisely target a drug, enhancing its efficacy and reducing the chance of adverse side effects. [19] Drug delivery nanobots depend on systemic circulation in addition to the force and navigation required for targeted distribution and tissue penetration. To assure exact delivery of therapeutic payloads to targeted disease areas, drug delivery vehicles are sought for to have some special characteristic involving pushing force, controlled navigation, and tissue penetration. The motor-like nanobots might be able to swiftly transport and deliver therapeutic payloads to disease sites, boosting therapeutic efficiency and minimising systemic side effects of extremely risky drugs [20].

1.4.2 Diagnosis and Testing

Medical nanobots are equipped to perform a wide range of examination, testing, and monitoring procedures in tissues and the blood. These devices have the capability of continuously recording and reporting all vital signs, including temperature, pressure, chemical composition, and immune system activity from all parts of the body. [3] When swallowed by a patient for diagnostic purposes, nanobots travel toward the surface of the stomach lining and begin scanning for disease signs.

1.4.3 In Dentistry

As a result of nanotechnology, a new field called Nano dentistry is developing. By producing mouth analgesia, desensitising the tooth, and producing oral analgesia, nanorobots can move the tissue to realign and straighten crooked teeth and increase the durability of teeth. Additionally, it is revealed how preventive, restorative, and curative treatments are carried out by nanorobots. Nanorobots aid in dental desensitisation, oral anaesthetic, tooth straightening, increased tooth durability, significant tooth repairs, and enhanced tooth aesthetics, among other dental procedures. Nanorobots can cover all subgingival surfaces when delivered through toothpaste or mouthwash, metabolising trapped organic pollutants into tasteless vapours that are safe to breathe. With the proper setup, dental robots can find and get rid of harmful germs both in the plaque and elsewhere. The mechanical elements that make up these invisibly little dentifrobots securely turn off when eaten. While allowing the beneficial oral flora to thrive in a balanced ecosystem, a mouthwash containing intelligent nanorobots could recognise and eliminate harmful germs. The teeth are being worked on by several invisible nanorobots in synchrony. To heal severely damaged teeth, nano dental approaches use tissue engineering, tissue regeneration, and genetic engineering. Dental straightening, rotation, and vertical repositioning can be accomplished quickly and painlessly with orthodontic nanorobots by directly manipulating the alveolar bone, cementum, gingiva, and periodontal ligament. This can take anywhere from 3 minutes to hours [21].

1.5 Nanorobots in Cancer Detection and Treatment

The accurate detection and treatment of cancer can be aided by nanobots. Nanobots are very site specific, in contrast to conventional drugs, meaning that they are programmed to exclusively detect and treat diseased cells, leaving healthy cells unaffected and resulting in a small amount of side effects. Early-stage tumour cells can be located inside a patient's body using nanorobots with integrated chemical biosensors. [22], [5] To measure the strength of E-cadherin signals, integrated nano sensors can be used. These indicate the discovery of tumour cells inside the body of the patient at an early stage of development. For patients to give a successful course of treatment, it is essential to create efficient TDD (Targeted drug delivery) to lessen the side effects of chemotherapy [23].

1.6 Delivery of Therapeutic and Imaging Agents for Cancer Therapy

In comparison to passive diffusion approaches, medical nanorobotics has the ability to administer medications with greater accuracy and speed. Since the released drug can be externally activated, the nanorobotic platform can distribute a significant amount of the therapeutic agent in a targeted region of the tumour during tumour therapy.

1.7 Biohybrid Nanorobots Cancer Therapy

In comparison to passive diffusion approaches, medical nanorobotics has the ability to administer medications with greater accuracy and speed. Since the released drug can be externally activated, the nanorobotic platform can distribute a significant amount of the therapeutic agent in a targeted region of the tumour during tumour therapy. Biohybrid nanorobots can be employed for precise payload distribution inside of living creatures. It has been discovered that magnetotactic bacteria, which naturally produce magnetic iron oxide nanoparticles, are associated with in-vitro liposomes containing therapeutic payloads. [24] In a study utilising an external magnetic field, the drug-loaded liposomes were delivered in vivo to a mouse cancer site using these modified bacteria.

1.8 Nanorobots in the Diagnosis and Treatment of Diabetes

To maintain a healthy human metabolism, glucose must be delivered through the bloodstream, and determining the proper level of glucose in the blood is crucial to the detection and management of diabetes. [25] The function of this protein as a sensor to detect glucose makes it the most intriguing component. The nanorobot has no interference in sensing blood glucose levels, regardless of whether it is invisible or apparent for immunological reactions. [26] The patient's mobile phone can then automatically receive the important measured data thanks to the medical nanorobot architecture's use of RF signals. If the glucose ever reaches dangerous levels, the nanorobot immediately sends an alarm to the phone and effective response can be taken.

1.9 Nanobots in Gene Therapy

Medical nanobots can quickly cure inherited disorders by comparing the molecular structures of DNA and proteins found in the cell to desired reference structures. suspicious can be changed or remedied there. A human cell's nucleus contains a repair vessel created by assemblers for genetic maintenance. It compares the information stored in its larger nano computer, which is outside the nucleus and connected to the cell-repair ship by a communications link. Although this larger nano computer is smaller than most bacteria and viruses, it would still be able to administer treatments and offer cures. Viral infections, cancer, and diseases like arteriosclerosis could all be wiped out since disease would be fought at the molecular level. Since disease will be addressed at the molecular level, cancer, viral infections, and arteriosclerosis may all be cured. Most human diseases involve a molecular breakdown at the cellular level, and cellular function is largely regulated by gene expression and the resulting protein synthesis [27].

1.10 Nanorobots in Surgery

The human body's vascular system or the catheter tips can be used to insert surgical nanorobots into various cavities and veins. A human surgeon uses surgical nanorobots that are programmed or commanded to act as an on-site, semi-autonomous surgeon inside the human body. This program-controlled surgical nanorobot detects pathogens, recognises lesions, and treats them with nano-manipulation directed by an on-board computer all while consuming less energy and corresponding with the supervising surgeon via encrypted ultrasonic communications. [28] Such a medical tool might perform a range of activities, such as detecting pathology and then treating lesions with nanomanipulation while communicating with the supervising surgeon via coded ultrasound signals. [29] Neurosurgery is a field that, spinal cord damage and nerve damage are significant issues. Recently, several approaches have been pursued to optimise and improve the results of nerve reconnection, including stimulating axon regeneration with growth factors and enriched scaffolds. [30] A necessary stage in the repair function is re-establishing connection to transected axons [31].

1.11 Cleaning the Blood with Ultrasound Powered Nanobots

Nanorobots propelled by ultrasound that are the size of one cell float through the blood, removing poisons and bacteria as they move. The gold nanowires and hybrid red and platelet blood cells that make up the nanorobots are made of. Together, they complete the work of two distinct cells at once. MRSA germs, an antibiotic-resistant type of Staphylococcus aureus, are bound by platelets, tiny blood cells that facilitates in blood clotting. Red blood cells are used in conjunction with other cells to help absorb and neutralise the toxins generated by the MRSA bacteria [32].

1.12 Cryostasis

In view of the enormous medical opportunities that lay ahead of us, renewed interest has been shown in an old theory that the dying patient may be frozen and held at liquid nitrogen temperature for decades or perhaps centuries until the necessary medical technology to restore health was produced. This service, known as cryonics, is now offered by several businesses. The method is experimental since we can't be certain that it will work until we have developed a medical technology built on a mature

nanotechnology's foundation. The ability of medical science to reverse freezing harm in 100 years from now is something that cannot be proven by current technology. But given the amazing developments we anticipate, it looks possible that we will be able to reverse freezing damage, especially when that damage is contained by the rapid introduction through the vascular system of cryoprotectants and other substances to cushion the tissues against further destruction [33].

1.13 DNA Nanorobots as Biosensors

Technology for nano sensing is also being created. It is also being researched how to detect certain analytes using genetically altered versions of pore-forming proteins, such as Staphylococcus aureus alpha haemolysin. Another illustration is the utilisation of cholera toxins' ability to bind to a bilayer membrane in the presence of gangliosides to identify biological warfare agents. An optical DNA biosensor platform has been developed using etched optical fibre bundles with microsphere probes functionalized with oligonucleotides. The development of brain implants that can detect the onset of a stroke and provide perioperative online monitoring during coronary bypass surgery is also ongoing [34].

1.14 Nanobots in Coronary Artery Disease

Coronary artery disorders (CADs), which account for most of the morbidity and mortality, are the main cause of cardiovascular disease, which is the leading cause of death in the modern world. Although state-of-the-art technologies have increased our understanding of the cardiovascular system, the diagnosis and treatment methods for CADs remain limited. Nanotechnology has demonstrated significant promise for therapeutic application as a new cross-disciplinary strategy. [35] Nanotechnologyhave significantly increased the specificity and sensitivity of biosensors for biomarker detection and molecular imaging methods, including magnetic resonance imaging, fluorescence imaging, nuclear gama scan, and multimodal imaging approaches.

1.15 Heart Attack Prevention

Cardiac attacks can be avoided by using nanobots. Fat accumulations in the blood arteries are what lead to heart attacks. These fat deposits can be removed by nanorobots. On the inside of blood arteries, the nanorobots scrape off the yellow fat deposits. This will enable improved blood flow via the arteries as well as improved artery wall flexibility [36].

1.16 Future Aspects of Nanorobots

The field of medicine may be transformed by nanorobots. Smaller than today's robots, bacteria-sized robots could be used by doctors to cure everything from cancer to heart disease. To cure illnesses and treat other ailments, robots might work individually or in groups. Some people think that semiautonomous nanorobots will soon be implanted within people's bodies, allowing the robots to patrol the body and respond to any problems that arise. These robots would remain inside the patient's body permanently [37], unlike acute treatment. Your blood will likely contain microscopic nanorobots over the next decade to fifteen years that can help prevent illness or even broadcast your thoughts to a wireless cloud. They will operate within you at the molecular level, protecting the biological system and fostering a long, healthy and happy life [38].

2. CONCLUSION

The usage of nanorobotics has a wider scope than any other newly emerging sub-field. because it uses the most advanced molecular technology (Nanotechnology), which has various applications in the field of medicine. In conjunction with human physiology, these robots can be utilised rather widely everywhere. It offers many benefits over traditional care, including lower costs, faster recovery times, and little to no invasion. A significant medical revolution, analogous to the industrial revolution that reshaped the globe in the era of integrative activity, will take place. We might be completely free of disease by the end of the next few decades thanks to a multitude of internal nanobots that are protecting

us. Some of the best examples of nanorobotics potential for future development are cancer diagnosis, data storage, and pipeline monitoring. Hence, nanorobotics is a prime location to explore deeper.

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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

Conflict of Interest Statement

Authors declare that no conflicts of interest.

Informed Consent

All participants were informed about the purpose of the study, and their voluntary consent was obtained prior to data collection.

Ethical Approval

Not Applicable.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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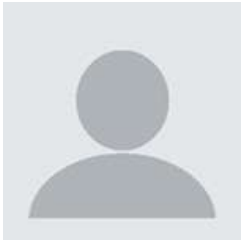
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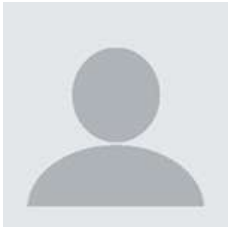
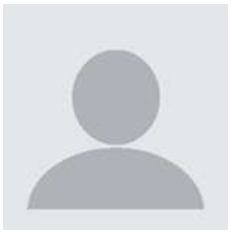
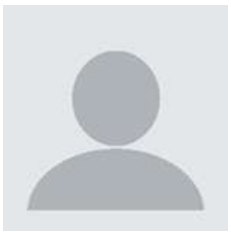
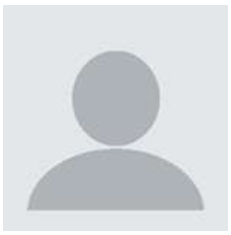
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