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**Review Article**

# Nanobots In Medicine

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## ABSTRACT

Current research into the role of engineered nanomolecules in drug delivery systems (DDSs) for medical purposes has developed numerous fascinating nanocarriers. This paper reviews the various conventionally used and current used carriage system to deliver drugs. Due to numerous drawbacks of conventional DDSs, nanocarriers have gained immense interest. Nanocarriers like polymeric nanopar- ticles, mesoporous nanobots(molecules), nanomaterials, carbon nanotubes, dendrimers, liposomes, metallicnanomolecules, nanomedicine, and engineered nanomaterials are used as carriage systems for targeted delivery at specific sites of affected areas in the body. Nanomedicine has rapidly grown to treat certain diseases like brain cancer, lung cancer, breast cancer, cardiovascular diseases, and many others. These nanomedicines can improve drug bioavailability and drug absorption time, reduce release time, elimi- nate drug aggregation, and enhance drug solubility in the blood. Nanomedicine has introduced a new era for drug carriage by refining the therapeutic directories of the energetic pharmaceutical elements engineered within nanomolecules. In this context, the vital information on engineered nanomolecules was reviewed and conferred towards the role in drug carriage systems to treat many ailments. All these nanocarriers were tested in vitro and in vivo. In the coming years, nanomedicines can improve human health more effectively by adding more advanced techniques into the drug delivery system. In coming years, nanotechnology is likely to have a significant impact in different fields like medicine and electronics. Nanorobotics is emerging as a demanding field dealing with miniscule things at molecular level. Nano robots perform a specific task with precision at nanoscale dimensions. Nano robots are especially used for studies on Alzheimer disease and cancer treatments. These can be seen as the first Nano medicines, with potential application in medicine. Present day treatment includes surgeries which are considered outdated when compared to today's technology.

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## INTRODUCTION

Drug delivery systems (DDSs) have been used in past eras to treat numerous ailments. All medicines rely on pharmacologic active metabolites (drugs) to treat diseases [1]. Some ofthe drugs are designed as the inactive precursor, but they become active when transformed in the body [2]. Their effectiveness depends on the route of administration. In conventional drug delivery systems (CDDSs), drugs were delivered usually via oral, nasal, inhaled, mucosal, and shot methods [3]. The conventionally delivered drugs were absorbed less, distributed randomly, damaged unaffected areas, were excreted early, and took a prolonged time to cure the disease [4]. They were less effective due to many hurdles like their enzymatic degradation or disparity in pH, many mucosal barriers, and off-the-mark effects, and their immediate release enhanced toxicity in blood [5]. Due to all such reasons, the controlled-release drug delivery system was developed. Such evolution in the DDS enhances drug effectiveness in many ways [6]. DDSs have been engineered in recent years to control drug release [7]. Such engineered DDSs used various novel strategies for controlled drug release into the diseased areas. These strategies were erodible material, degradable material, matrix, hydrogel, osmotic pump, and reservoir [8]. they all provided a medium for the medicines to deliver at the desired sites like tissues, cells,or organs. In these approaches, drugs are often available for many diseases [9]. Such strategies were unsuccessful due to lower distribution, less solubility, higher drug aggregation, less target selection, and poor effects for disease treatment [10]. Moreover, drug development is the most expensive, intricate, and time-consuming process [5]. The innovative drug findings involved the identification of new chemical entities (NCEs), [11] having the vital distinguishing characteristics of drug capacity and pharmaceutical chemistry. This methodology, however, was confirmed to be less effective in terms of the overall attainment percentage [12], as 40% of drug development was botched due to its changeable responses and unpredicted noxiousness in humans [13]. From past decades until now, drug development and its delivery are shiftingfrom the micro to the nano level to prolong life expectancy by revolutionizing drug deliverysystems (Figure 1) [14].

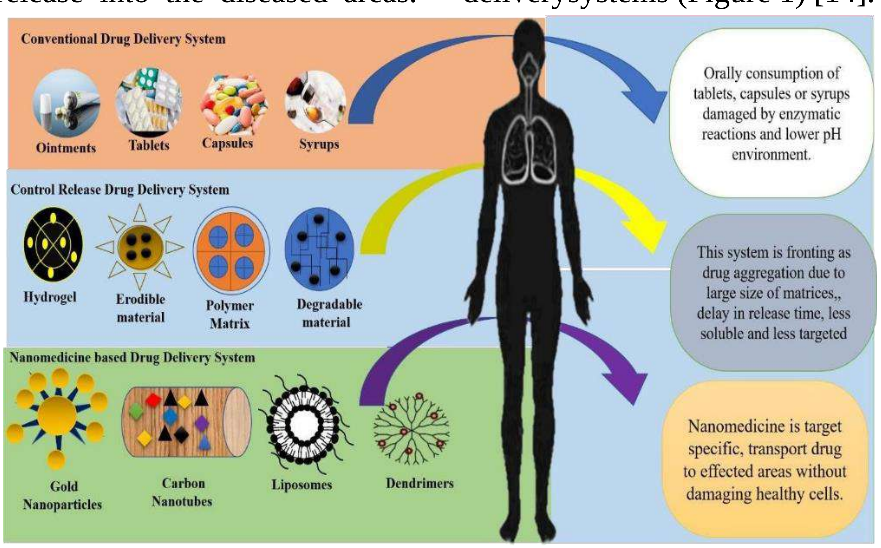


**Figure 1. Illustration of how traditional medications were administered without the use of nanocarri- ers and harm was done to healthy organs or cells. In contrast, modern procedures use nanomedicines to transport medications to specific parts of the body.**

In 1959, Feynman was the first physicist to introduce the notion of nanotechnology in the lecture entitled “There’s Plenty of oom at the Bottom”. This concept initiated remarkable developments in the arena of nanotechnology [15]. Nanotechnology is the study of extremely tiny things and is basically the hub of all science disciplines including physics, chemistry, biology, engineering, information technology, electronics, and material science [16]. The structures measured with nanotechnology range from 1–100 nm at the nanoscale level [17]. Nanoparticles have different material characteristics because of submicroscopic size and also provide practical implementations in a wide range of fields including engineering, drug delivery, nanomedicine, environmental indemnification, and catalysis, as well as target diseases such as melanoma and cardiovascular diseases (CVD), skin diseases, liver diseases, and many others [18]. Therefore, medicines linked with nanotechnology can enhance efficiency of medicines and their bioavailability [19]. The relation of nanomolecules to biomedicine was demon- strated in late the 1970s, and over 10,000 publications have referred to this association with the term “nanomedicine”. Almost thirty papers on this term were accessible by 2005 [20]. After 10 to 12 years, Web of Science published more than 1000 nanomedicine articles in 2015 and most of the articles relating nanomolecules (NPs) for biomedical usage [21]. Nanocarriers such as dendrimers, liposomes, peptide-based nanomolecules, carbon nano tubes, quantum dots, polymer-based nanomolecules, inorganic vectors, lipid-based nanopar- ticles, hybrid NPs, and metal nanomolecules are the advanced forms of NPs [22]. Nanoparti- cles are nowadays a growing arena for drug delivery, microfluidics, biosensors, microarrays, and tissue micro- engineering for the specialized treatment of diseases [23–25]. Nanoparticles are less effective and can treat cancer by selectively killing all cancerous cells [26]. In 2015, the Food and Drug Administration (FDA) approved the clinical trials of onivyde nanomedicine in the treatment of cancer [27]. The characteristic properties of nanocarriers are physicochemical properties, supporting the drugs by improving solubility, degradation, clearance, targeting, theranostics, and combination therapy [28]. Studies on nanomedicine based on protein used for drug delivery in which various protein subunits combine to deliver medicine on site to a specific tumor have been reported [29]. Many altered kinds and forms of nanocarriers arranged to carry medicine are protein-based podiums, counting several protein coops, nanomolecules, hydrogels, films, microspheres, tiny rods, and minipellets [30]. All proteins, including ferritin–protein coop, the small heat shock protein (sHsp) cage, plant-derived viral capsids, albumin, soy and whey protein, collagen, and gelatin-implemented proteins are characterized for drug carriage [31].

The nanomedicines are escorted in a new-fangled epoch, meant for drug carriage byrefining the therapeutic directories of the energetic pharmacological elements engineered inside nanomolecules [32]. In this epoch, nanomedicine-based targeted-design structurescan deliver multipurpose freight with favorable pharmacokinetics and capitalized so as to enhance drug specificity, usefulness, and safety, as shown in (Figure 2) [33]. The failureof chemotherapeutic approaches has increased the recurrence chances of disease, whichenhances the complexity of lethal diseases [34].

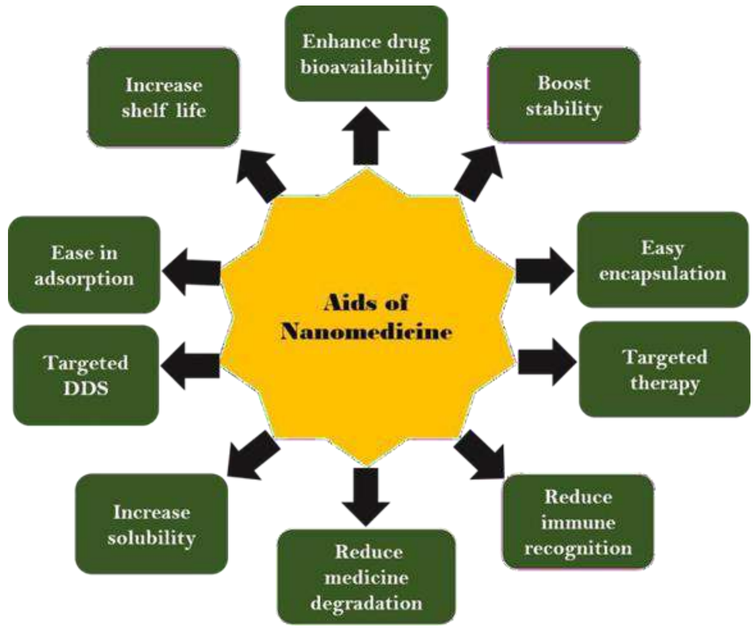


**Figure 2. Aids of using nanomedicine platform for delivering drugs to the tumor complex.**

## HISTORY

Petros and his colleague reported a study about mid-19th century work on nan- otechnology. As they reported, polymers and drugs were conjugated in 1955 [35], the first controlled-release polymer device appeared in 1964, the liposome was discovered by Bangham in 1965, albumin- based NPs were reported in 1972, liposome-based drugs were formulated in 1973, the first micelle was formulated and approved in 1983, the FDA approved the first controlled formulation in 1989, and first polyethylene glycol (PEG) conjugated with protein entered the market in 1990 [36]. Further studies have produced incredibly encouraging results for treating a variety of disorders.

### A. Recent Approaches Used in Drug Carriage System for Treatment of Various Diseases

#### 1. Brain Drug Delivery System and Its Types

Under the most pathological circumstances of diseases such as strokes, seizures, mul- tiple sclerosis, AIDS, diabetes, glioma, Alzheimer's disease, and Parkinson's disease, the blood–brain barrier (BBB) is disrupted [103]. An important reason for the breakdownof the blood–brain barrier is the remodeling of the protein complex in intra-endothelial junctions under the pathological conditions [104]. Normally, the blood–brain barrier actsto maintain blood–brain homeostasis by preventing entry of macromolecules and micro-molecules from the blood [105]. If a drug crosses the BBB, it restricts accumulation of the drug in the intracerebral region of brain, and bioavailability is reduced, due to which brain diseases cannot be treated [106]. Therefore, the optimal drug delivery system (DDS) is a cell membrane DDS, virus-based DDS, or exosome-based DDS designed for BBB pene- trability, lesion-targeting ability, and standard safety [107]. For the cure of brain diseases, the nanocarrier-assisted intranasal drug carriage system is widely used [108]. Now, at the advanced level, drugs poorly distributed to the brain can be loaded into a nanocarrier-based system, which would interact well with the endothelial micro vessel cells at the BBB and nasal mucosa to increase drug absorption time and the olfactory nerve fibers to stimulate straight nose-to- brain delivery [109], thus greater drug absorption in brain parenchyma through the secondary nose- to-blood-to-brain pathway [110]. The current strategies used are viral vectors, nanomolecules, exosomes, brain permeability enhancers, delivery through active transporters in the BBB, alteration of administration route, nanomolecules for the brain, and imaging/diagnostics under diseased conditions [111].

**a. Role of Nanocarriers in Alzheimer's Disease**

Alzheimer's disease is one of the fastest growing neurodegenerative diseases in the elderly population. Clinically, it is categorized by abstraction, damage to verbal access, and diminishing in spatial skills and reasoning [112]. Furthermore, engrossment of amyloid β (Aβ) aggregation and anxiety in the brain have significant parts [113]. The treatment of different diseases with nanotechnology-based drug delivery uses nanotechnology-based approaches [114]. In Alzheimer's diseases, polymeric nanomolecules, liposomes, solid lipid nanomolecules, nano-emulsions, micro-emulsions, and liquid-crystals are used for treatment.

**Polymeric Nanoparticles**

I. The drug Tacrine was loaded on polymeric nanomolecules and administered throughan intravenous route. It enhanced the concentration of tacrine inside the brain and also reduced the whole-dose quantity [115].
II. Rivastigmine drug was loaded on polymeric nanomolecules and administered through an intravenous route. It enhanced learning and memory capacities [116].

**Solid Lipid Nanoparticles (SLNPs)**

**SLNPs enhanced drug retention in the brain area, raising absorption across the BBB [117]. Some of the drug's effects are listed below.**

I. Piperine drug is loaded on solid lipid nanomolecules through an intraperitoneal route inside the brain to decrease plaques and masses and to increase AChE enzyme activity [118].
II. Huperzine A improved cognitive functions. No main irritation was detected in rat skin when the drug was loaded on SLNPs in an in vitro study [119].

In recent reports, the coating of SLNPs with polysorbate enhances drug bioavailabil- ity [120,121]. Some of the coated NPs are listed below.

I. The drug clozapine was loaded on a Dynasan 116 [Tripalmitin] lipid matrix coated with surfactant Poloxamer 188, Epikuron 200 to unload the drug safely into the brain microenvironment [122,123].
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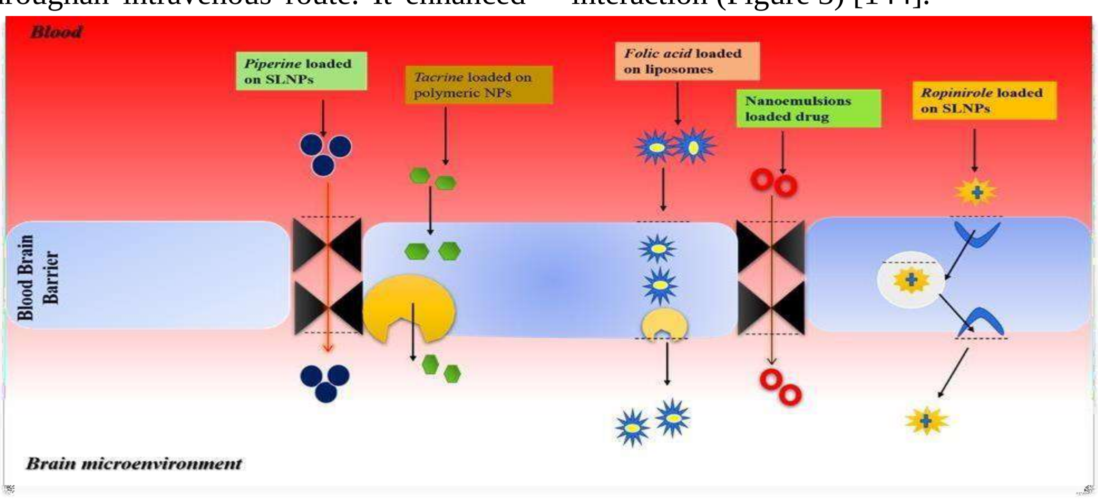


**Figure 3. Diagram showing the mechanism of targeted drug delivery across BBB in brain microenvi- ronment. Piperine loaded on SLNPs is injected intraperitonially, across BBB efferently to stop plaque**

**formation. Polymeric nanomolecules are used for Tacrine delivery inside the brain, folic acid are loaded on the liposomes crossing blood–brain barrier to treat Alzheimer's disease, while nanoemul- sions and SLNP are loaded with drugs used to deliver medicines inside the targeted brain area to cure Parkinson's disease.**

### C. Advantages and Disadvantages of Nanomedicines

When employed for brain illnesses, nanomedicines have both benefits and drawbacks.

### D. Nanocarriers Role in Major Cancers

#### a. Brain Cancer

Brain malignancy is the most critical disease in the sense of treatment [150]. Malig- nancies of the brain are most difficult to treat due to limits imposed by the blood–brain barrier [151]. The brain microvascular endothelium is present in the BBB and creates barri- ers that distinguish blood from the neural tissues of the brain [152]. The BBB prevents the entry of harmful toxins, xenobiotic and other metabolites from entering the brain [153]. The majority of brain cancers include glioma and glioblastoma. Both of these are among the most lethal forms of brain cancer [154]. The annual occurrence is 5.26 per 100,000 people or 17,000 new diagnoses each year. The most common treatment is radiation surgery and chemotherapy, usually implemented with with temozolomide (TMZ) [155]. Nanoparticles have a high potential to treat brain cancer because of their small size in nm, tissue-specific targeting properties, and ease in crossing the BBB [156].

#### b. Breast Cancer

Cancer causes major deaths all over the world. Tumors spread due to the proliferation of cells [171], which invade through the lymphatic system to various parts of the bodyif they becomes malignant [172]. According to WHO, the ratio of deaths globally due to cancer is assessed to be 13%, attributing 8.2 million deaths every year [173]. Breast cancer is the most recorded type of melanoma present in only females, and its severity leads to mortality more often than lung cancer [174]. In 2012, estimated female breast cancer cases were 1.7 million, with 25% of deaths all over the world [175]. In a recent study, a report published in the name of Global Cancer Statistics 2020: GLOBOCAN estimates the incidence and mortality worldwide for 36 cancers in 185 countries and provides an update on cancer internationally [176]. A reported estimate is 19.3 million new cancer cases (18.1 million excluding non-melanoma skin cancer) and almost 10 million cancer deaths(9.9 million without non-melanoma skin cancer) occurring in 2020 worldwide. Female breast cancer has exceeded lung cancer as the most frequently diagnosed cancer, with an estimated 2.3 million new cases (11.7%), followed by lung (11.4%), prostate (7.3%), colorectal (10%), and stomach (5.6%) cancers [177]. For the effective treatment of breastcancer, surgery, chemotherapy, radiation therapy, hormonal therapy, and targeted therapy are performed [178]. However, nowadays, nanotechnology has gained interest for breast cancer treatment. Various organic and inorganic nanocarriers are used to deliver drugs to the specific target site [179]. Nanocarriers enhance the hydrophobicity of the anticancer drugs and promote specific target drug delivery [180]. Organic nanocarriers include polymeric nanocarriers, liposome nanocarriers, and solid lipid nanocarriers, while inorganic nanocarriers include magnetic nanocarriers, quantum dots, and carbon nanotubes (CNTs); both categories show great results towards treatment of heart diseases [181]. The mechanism of drug delivery in breast cancer is shown in Figure 4.

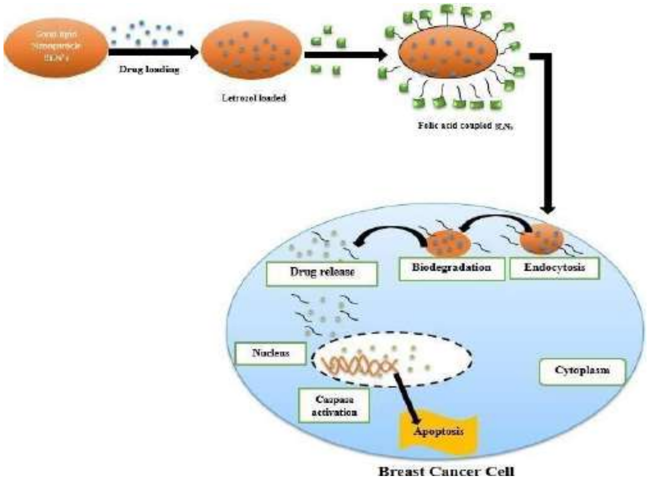


**Figure 4. Schematic representation of mechanism of drug letrozol loaded on solid lipid nanomolecules (SLNs) and folic acid coupled to SLNs. The whole carrier was delivered inside the animal rat model to treat effects on breast cancer cell lines. Inside cytoplasm, biodegradation occurred, as well as drug release and caspases' activation inside nucleus, causing apoptosis.**

### c. Lung Cancer

Lungs are basically responsible for inhalation [194]. The lung is composed airways (conveying the air inside and outside of the lungs) and alveoli (gas exchange zones) [195]. In fact, airways are comparatively tough barriers for particles to enter through, while the barrier along the alveolar wall and the capillaries is relatively fragile in the gas exchange component [196]. The huge exterior area of the alveoli and deep air blood exchange cause the alveoli to be less healthy when affected by environmental injuries. Such injuries may be the reason for some pulmonary illnesses, including lung malignancy [197]. Several nanomolecules are now being established for respiratory applications that aim at eliminating the restrictions of orthodox drugs [198]. Nanoparticles aid the cure of many lung diseases, such as asthma, tuberculosis, emphysema, cystic fibrosis, and cancer [199].

### Drug Delivery Approach in Heart Diseases

Cardiovascular diseases include myocardial infraction (MI) [213], ischemic impair- ment, coronary artery disease (CAD), heart arrhythmias, pericardial disease, cardiomyopa- thy (heart muscle disease), and congenital heart disease [214,215]. All these illnesses are the basic main cause of mortality and morbidity in the world [216]. Cardiac diseases in humans involve incongruity in the morphogenesis of heart arrangement, functionality, and the healing and periodic shrinkage of cardiac muscles [217,218]. Around 50% of patients suffering from MI die within five years [216]. The insistence for a novel and effective remedy has brought about progress in direct drug carriage to the heart [219]. Modern therapeutic approaches have been developed to stop the incidence of heart failure after myocardial infarction [220]. Liposomes, silica NPs, dendrimers, cerium oxide NPs, micelles, TiO2 NPs, stents with nano-coatings, microbubbles, and polymer–drug conjugates are used for drug delivery. Magnetic nanomolecules like magnetoliposomes (MLs) are made up of the union of liposomes and magnetic nanomolecules. They are used as magnetic-targeted drug delivery [221]. The PEGylation of MLs increases their rate of flow in the blood, and pairing of the MLs with antibodies raises the rate of active target to pretentious positions [222]. Namdari and his co-workers performed experiments in a mice model afflicted with my- ocardial infraction (MI). Liposomes are used with various modifications and in different ways; they are adapted to load drugs on NPs for efficient delivery inside the cell. Cationic liposomes, perfluorocarbon nanomolecules, polyelectrolyte nanomolecules, and polymeric nanomolecules are the modified forms of nanocarriers [223]

### D. Drug Delivery Approach in Skin Diseases

Skin diseases are follicular and cutaneous. These dermatological diseases are treated nowadays with nanotechnology. Nanoparticle delivery for cutaneous disease treatment is preferred, with minor side effects. The conventionally used creams, gels, and ointments are insufficient for delivering drugs due to low penetration in skin tissues. To address this, polymeric, lipid, and surfactant nanocarriers are used. The polymeric micelles enhance drug penetration into the skin tissue to treat skin cancer. As in this reported study, chitosan polymeric NPs, liposomes, and gold nanomolecules can treat atopic dermatitis by improving drug penetration into the dermal and epidermal layers [246]. Gold nanomolecules are extremely small in size and can penetrate easily and effectively with very low toxicity and no skin damage. As such, they are used widely in nanocarrier formulations forskin diseases.

**e. Drug Delivery Approach in Bone Diseases**

Bone diseases includes bone defects due to many pathological factors, such as frac- ture, trauma, osteoporosis, arthritis, infections, and many other diseases. In fact, bone regeneration as a disease treatment is a very complex process, due to which nanomaterials and biological materials are fused to repair bones effectively. The combination of biomate- rial and nanomaterial has reduced bone implantation through the development of bone bioscaffolds [247].

**Mechanism of Drug Delivery**

The drugs encapsulated inside the nanoparticle is delivered through blood to the targeted area in the bones. The management of the sending nanomolecules as shown herenin (Figure 5).

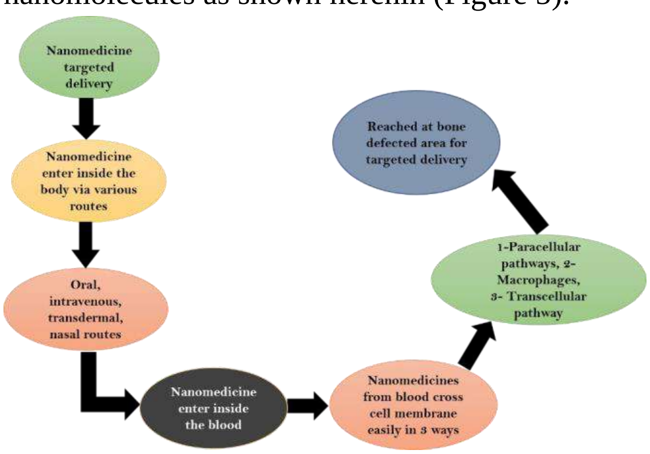


**Figure 5. Mechanism of nanomedicine delivery in bone diseases.**

**f. Drug Delivery Approach in Blood Diseases**

There are various types of blood diseases, like hemopoietic blood disorder, as well as iron deficiency, leukemia, anemia, hemophilia, platelet diseases, and blood cancer. The conventionally used chemotherapeutic system causes damage to the immune system, with high risk of mortality. Bone marrow transplant is also an expensive and intricate process. For example, thalassemia is treated with deferoxamine, a chelating agent to treatexcessive iron in the blood. The siRNA-coated nanocomposite has the inhibitory activity for tumor cells in vivo [248]. The treatment of blood disorders with nanomedicine is stillunder investigation.

**g. Future Challenges of Nanomedicines**

In the field of nanomedicine, there are many innovations which show its importance in clinical and other medical aspects. Many scientists have investigated in their research how nanomedicine is involved in treating malignancies and reducing mortality and morbidity rates. However, there are also future challenges that nanomedicines have been facing until now [249]. The implementation of nanomedicine in clinical practice will face many issues with insurance companies, regulatory agencies, and the public health sector. Until now, the FDA has not developed any specific regulation for the products containing nanomaterials. Due to a lack of nanomaterial standardization and other safety issues, US agencies, such as the EPA and NIOSH, are giving less funding to these research endeavors. The opportunities of Nanotechnology include designing Nano sized, bio responsive systems which can diagnose and then deliver drugs to the site of location. Nanotechnology is an area which is changing vision of medical science. Nanotechnology includes characterization, production and application of nanoparticles in science fields [250]. They possess unique electrical, optical and biological properties. Many chemical and physical methods of synthesis have been reported in the literature [2-8]. Due to the ecofriendly nature of synthesis by biological methods, plant extracts, bacteria, algae, fungi and enzymes have also been exploited [8-23]. Biological methods for synthesizing of silver nanoparticles can be considered to be economical and sustainable alternative to the existing chemical or physical methods. Designs of Nano robots include onboard sensors, power supplies, motors, manipulators and molecular computers. Nano robot is an excellent tool for future medicine. We can envision a day when you could inject billions of these Nano robots that would float around in your body. Nano robots could carry and deliver drugs into defected cells. These nano robots will be able to repair tissues, clean blood vessels and airways, transform our physiological capabilities and even potentially counter act the aging process. Nanotechnology as an emerging tool in medicinal applications especially for diabetes, arteriosclerosis, gene therapy, dentistry and cancer showed how actual developments in new manufacturing technologies are enabling innovative works which may help in constructing and employing nano robots most effectively for biomedical problems. Nano robots applied to medicine hold a wealth of promise from eradicating disease to reversing the aging process. Nano robots are also candidates for industrial applications. They will provide personalized treatments with improved efficacy and reduced side effects that are not available today. They will provide combined action drugs marketed with diagnostics, imaging agents acting as drugs, surgery with instant diagnostic feedback. The advent of molecular nanotechnology will again expand enormously the effectiveness, comfort and speed of future medical treatments while at the same time significantly reducing their risk, cost, and invasiveness. This science might sound like a fiction now, but nanorobotics has strong potential to revolutionize healthcare, to treat disease in future. It opens up new ways for vast, abundant research work. Nanotechnology will change health care and human life more profoundly than other developments. Consequently, they will change the shape of the industry, broadening the product development and marketing interactions between Pharma, Biotech, Diagnostic and Healthcare industries. In this review, Nanorobot's mechanism and applications of them in medicine for curing diseases will be discussed.

**A. Composition of Nanorobots**

**1. Biochip**

Synthesis involves the joint use of Nano electronics, photolithography, and new biomaterials. It can be used for manufacturing of Nano robots for common medical applications, such as for surgical instrumentation, diagnosis and drug delivery. Electronics industries currently use biochips for manufacturing. Nano robots with biochips can be integrated in Nano electronics devices, which will allow tele-operation and advanced capabilities for medical instrumentation [8, 11].

**2. Bacteria Based**

This approach uses biological microorganisms, like Escherichia coli bacteria. The model uses a flagellum for propulsion purposes. The use of electromagnetic fields is normally applied to control the motion of this kind of biological integrated device [8-9]

**3. Positional Nano Assembly**

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

**4. Nubots**

Nubot is an abbreviation for "nucleic acid robots. "Nubots are synthetic robotics devices at the nanoscale. Representative Nubots include the several DNA walkers reported by Ned Seaman's group at NYU, Niles Pierce's group at Caltech, John Reif's group at Duke University, Chengde Mao's group at Purdue, and Andrew Turberfield's group at the University of Oxford [8, 9]

**Advantages of Nanotechnology**

1. To cure HIV, Cancer, and other harmful diseases.
2. Nano robots will restore lost tissue at the cellular level.
3. Useful for monitoring, diagnosing and fighting sickness.
4. Able to monitor neuro-electric signals and stimulate bodily systems.

**C. Mechanism of Nanorobots**

The research and development of Nano robots with embedded Nano biosensors and actuators is considered a new possibility to provide new medical devices for doctors. Controls are sought to effectively advance new medical technologies [22, 23]. Development of microelectronics in the 1980s has led to new tools for biomedical instrumentation [24, 25]. Further miniaturization towards integrated medical systems, providing efficient methodologies for pathological prognosis can be designed [26-28]. The use of micro devices in surgery and medical treatments is a reality which has brought many improvements in clinical procedures in recent years [29]. Catheterization has been successfully used as an important methodology for heart and intracranial surgery [30-32]. Now the advent of bimolecular science and new manufacturing techniques is helping us to advance the miniaturization of devices from micro to Nano electronics. Biomedical sensors are being operated by the latest technology which forms the basis for designing bimolecular actuators [33- 35]. A first series of nanotechnology prototypes for molecular machines are being investigated in different ways [18, 36-38], along with some devices for propulsion and sensing are also being studied by some workers [18, 36-39, 41] Nano robot Architecture: The medical Nano robot for biohazard defense should comprise a set of integrated circuit block as an ASIC (application-specific integrated circuit). The architecture has to address functionality for common medical applications [18], providing asynchronous interface for antenna, sensor, and a logic Nano processor, which is able to deliberate actuator and ultrasound communication activation when appropriate. The number of Nano devices to integrate a Nano robot should keep the same hardware sizes with regard to inside body operation applicability [3-6, 35, 47].

### E. Medical Applications of Nanorobots

Nano robots are expected to enable new treatments for patients suffering from different diseases, and will result in a remarkable advance in the history of medicine. Nanoparticles, liposomes and dendrimers are some nanomaterials being investigated for use in Nano medicine. Nanotechnology has provided the possibility of delivering drugs to specific cells using nanoparticles. Recent developments in the field of bimolecular computing have demonstrated the feasibility of processing logic tasks by biocomputers. Studies targeted at building biosensors and Nano-kinetic devices required to enable medical nanorobotics operation and locomotion, have also been progressing [38]. In recent years, the potential of nanotechnology has indeed motivated many governments to devote significant resources to this new field. The U.S. National Science Foundation has launched a program in "Scientific Visualization" in part to harness supercomputers in picturing the Nano world [3, 53]. In order to build electronics at nanoscales, firms are collaborating to produce new Nano products. Such companies include IBM, PARC, Hewlett Packard, Bell Laboratories, and Intel Corp. The use of Nano robots may advance biomedical intervention with minimally invasive surgeries and help patients who need constant body functions monitoring, or improve treatments efficiency through early diagnosis of possible serious diseases. For example, the Nano robots may be utilized to attach on transmigrating inflammatory cells or white blood cells, thus reaching inflamed tissues faster to assist in their healing process Nano robots will be applied in chemotherapy to combat cancer through precise chemical dosage administration, and a similar approach could be taken to enable Nano robots to deliver anti-HIV drugs [18-20, 54, 65]. Nano robots could be used to process specific chemical reactions in the human body as ancillary devices for injured organs. Monitoring diabetes and controlling glucose levels for patients will be a possible application of Nano robots. Nano robots might be used to see and break kidney stones. Another important possible feature of medical Nano robots will be the capability to locate atherosclerotic lesions in stenos blood vessels, particularly in the coronary circulation, and treat them either mechanically, chemically or pharmacologically. Cardiovascular problems are generally correlated with the obesity, human sedentary lifestyle, or hereditary characteristics [31, 43, and 61]

### F. Simulation

The use of micro devices in surgery and medical treatments is a reality which brought many improvements for clinical procedures in the last few years. For example, the catheterization has been used as an important methodology for many cardiology procedures in the same way as the development of micro technology [63] has lead on the 80's to new tools for surgery, now nanotechnology will equally permit further advances providing better diagnosis, and new devices for medicine through the manufacturing of nanoelectronics [8-12]. Nano robots may be considered as the most suitable tool for specialists to solve several problems in medicine in the coming few year here including cardiology interventions and medical analyses. In our study, the Nano robot includes external sensors to inform it of collisions and to identify when it has encountered a chemical signal or abrupt changes of temperature for targeted areas. As a practical approach for medicine, thermal and chemical parameters from the patient's body are used for the Nano robot activation. It is well known that there is significant temperature heterogeneity over inflamed plaque surfaces. They are typically hotter. The temperature difference at the site of the lesion from the core temperature can reach up to ~2ºC. Hence, in order to simulate various levels of inflammation, it was used for different wall temperatures in the atherosclerotic plaque region and the temperature distribution in the stenosed coronary artery was calculated. Significant temperature gradients were found in the recirculation zone, following the stenosis [52-55]. The Trans cardiac concentration gradient of some soluble adhesion molecules has been recently found to be correlative with the progression of coronary atherosclerosis. Therefore, their concentration in the blood vessel is also monitored, using a uniform distribution release from the plaque. In a similar manner, the concentrations of some specific proinflammatory cytokines is monitored, whose elevated concentrations are known as an evidence of formation of atherosclerotic lesions. The Nano robots swim in a near-wall region searching for the atherosclerotic lesion. The atherosclerotic lesion was reduced due to Nano robot's activation. The parameters generated from the CFD simulation, namely velocities, temperature, signaling values, pro-inflammatory cytokines and soluble adhesion molecules concentrations, are transferred to the NCD [3, 5-7, 36] simulator to be included into the Nano robots operating environment [45- 47]. As the Nano robot should perform a pre-defined task in a specific target area, the trigger must be activated when the Nano robot is as close as possible to the target. The Nano robot motion takes the advantage of the blood flow velocity profile in such areas, which shows significantly lower velocities. Thus, the rapid activation could result in lower demand of energy. Optimization of control algorithms and activating triggers is the key for rapid behavior response in minimal energy cost. The optimal trigger values are defined running the Nano robots control programs. Therefore, the investigated stenos artery models provide important information useful to Nano robot manufacturing design in terms of sensors and actuators. The Nano robot's activation goal is to decrease the artery occlusion.

### G. Nanorobotics in Dentistry

The growing interest in the future of dental applications of nanotechnology is leading to the emergence of a new field called Nano dentistry. Nano robots induce oral analgesia, desensitize tooth; manipulate the tissue to re-align and straighten irregular set of teeth and to improve durability of teeth. Further Nano robots can be used to do preventive, restorative and curative procedures [23-27]. Nano dental techniques involve many tissue engineering procedures for major tooth repair. Mainly nanorobotics manufacture and installation of a biologically autologous whole replacement tooth that includes both mineral and cellular components leading to complete dentition replacement therapy

#### a. Tooth Durability and Appearance

Nano dentistry has given material that is nanostructured composite material, sapphire which increases tooth durability and appearance. Upper enamel layers are replaced by covalently bonded artificial material such as sapphire. This material has 100 to 200 times the hardness and failure strength than ceramic. Like enamel, sapphire is a somewhat susceptible to acid corrosion. Sapphire has best standard whitening sealant, cosmetic alternative. New restorative Nano material to increase tooth durability is Nanocomposites [32, 47, 64-66]. This is manufactured by Nano agglomerated discrete nanoparticles that are homogeneously distributed in resins or coatings to produce nanocomposites. The Nano filler include an alum inosilicate powder having a mean particle size of about 80 nm and a 1:4 ratio of alumina to silica. The Nano filler has a refractive index of 1.503, it has superior hardness, modulus of elasticity, translucency, esthetic appeal, excellent color density, high polish and 50% reduction in filling shrinkage. They are superior to conventional composites and blend with a natural tooth structure much better.

#### b. Nano Impression

Impression material is available with nanotechnology application. Nano filler are integrated in the vinylpolysiloxanes, producing a unique addition siloxane impression material. The main advantage of material is it has better flow, improved hydrophilic properties hence fewer voids at margin and better model pouring, enhanced detail precision.

G. Nano Robots for Brain Aneurysm For brain aneurysm prognosis, Nano robots need to track the vessel endothelial injury before a subarachnoid hemorrhage occurs. These changes on chemical concentration are used to guide the Nano robots to identify brain aneurysm in the early stages of development.

**H. Nanorobots in Cancer Detection and Treatment**

Cancer can be successfully treated with current stages of medical technologies and therapy tools. However, a decisive factor to determine the chances for a patient with cancer to survives: how earlier it was diagnosed; what means, if possible, a cancer should be detected at least before the metastasis has begun. 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 [35, 38, 43-47]. Considering the properties of Nano robots to navigate as blood borne devices, they can help on such extremely important aspects of cancer therapy. Nano robots with embedded chemical biosensors can be used to perform detection of tumors 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 E-cadherin [62-64] signals. Therefore, a hardware architecture based on Nano bioelectronics is described for the application of Nano robots for cancer therapy. Analyses and conclusions for the proposed model are obtained through real time 3D simulation [22-27].

I. Nanorobots in Gene Therapy Medical Nano robots can readily treat genetic diseases by comparing the molecular structures of both DNA and proteins found in the cell to known or desired reference structures [18-20, 64]. Any irregularities can then be corrected, or desired modifications can be edited in place. In some cases, chromosomal replacement therapy is more efficient than repair. Floating inside the nucleus of a human cell, an assembler-built repair vessel performs some genetic maintenance. Stretching a supercoil of DNA between its lower pair of robot arms, the Nano machine gently pulls the unwound strand through an opening for further analysis. Upper arms, meanwhile, detach regulatory proteins from the chain and place them in an intake port. The molecular structures of both DNA and proteins are compared to information stored in the database of a larger nano computer positioned outside the nucleus and connected to the cell repair ship by a communications link. Irregularities found in either structure are corrected and the proteins reattached to the DNA chain [56-58], which re-coils into its original form. With a diameter of only 50 nanometers, the repair vessel would be smaller than most bacteria and viruses, yet capable of therapies and cures well beyond the reach of present-day physicians. With trillions of these machines coursing through a patient's blood stream, "internal medicine" would take on new significance. Disease would be attacked at the molecular level, and such maladies as cancer, viral infections and arteriosclerosis could be wiped out.

## CONCLUSIONS

Nanotechnology-based nanomedicine is a diverse field for disease treatment. Nowa- days, in every sort of disease, nanotechnology is emerging as the best therapeutic to cure disease. At California University, researchers are developing methods to deliver cardiac stem cells to the heart. They attached nanovesicles that directly target injured tissue to increase the amount of stem cells there. Thus, the involvement of stem cells with nanotech- nology will develop many solutions for the disease-based queries in the medical arena. However, nanomedicine and nano drugs deal with many doubts. Irregularities and toxicity and safety valuations will be the topic of development in the future. Nanotechnology willbe in high demand. Nowadays, drug-targeted delivery through nanomolecules is catch- ing the attention of pharmaceutical researchers all over the world. Nanomedicine will overcome all the side effects of traditional medicines. This nanoscale technology will be incorporated in the medical system to diagnose, transport therapeutic drugs, and detect cancer growth, according to the National Cancer Institute. Experts are trying to treat SARS- CoV-2 with nanomedicine, as nanomolecules with 10–200 nm size can detect, for site- specific transfer, SARS-CoV-2, exterminate it, and improve the immune system of the body. Nanotechnology could help to combat COVID-19 by stopping viral contamination. Highly accurate nano-based sensors will be made in the future that will quickly recognize the virus and act by spraying to protect frontline doctors and the public. Furthermore, many antiviral disinfectants are being developed through nanobiotechnology to stop virus dissemination. In the future, nanotechnology will evolve to develop drugs with high activity, less toxicity, and sustained release to target tissue. Therefore, personalized medicine and nanomedicine both will be potential therapies to treat COVID-19 successfully, as well as to treat upcoming diseases in future.

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