Nano World Journal

https://doi.org/10.17756/nwj.2023-s1-085

Review Article

Open Access

An Encapsulation on Nano Drug Delivery Systems and their Probable Applications

Likhit Sawant, Jayvardhan Vyas, Parvez Surani, Jatin Dalmia, Aliasgher Tinwala and Samadhan Deshmukh*

Department of Mechanical Engineering, NMIMS, Mukesh Patel School of Technology Management and Engineering, Mumbai, Maharastra, India

***Correspondence to:**
Samadhan Deshmukh
Department of Mechanical Engineering, NMIMS, Mukesh Patel School of Technology Management and Engineering, Mumbai, Maharastra, India.
E-mail: Samadhan.Deshmukh@nmims.edu

Received: November 24, 2022
Accepted: April 23, 2023
Published: April 25, 2023

Citation: Sawant L, Vyas J, Surani P, Dalmia J, Tinwala A, et al. 2023. An Encapsulation on Nano Drug Delivery Systems and their Probable Applications. *NanoWorld J* 9(S1): S444-S449.

Published by United Scientific Group

Abstract

Nanotechnology has developed as one of the most fascinating and sophisticated study topics in this domain. As a drug delivery method, nanoparticles have significant potential. This paper is primarily concerned with the development and application of nanoparticles in health and medication delivery. Nanotechnology advancements have resulted in new and better nanomaterials for biomedical applications. Carbon nanotubes (CNT), Dendrimers, gold nanoparticles, silica, magnetic nanoparticles, lipid, liposomes, etc., nanomaterials have been used in medical applications. For a reliable and efficient drug delivery system (DDS), it is important to comprehend how nanomaterials interact with biological systems, how to target cell-surface receptors, and how to release drugs through active passive, cell-fragging, and intracellular methods. There are several diseases that can be cured with the help of nano drug delivery system (NDDS) in this paper the use of nanoparticles is thoroughly reviewed in curing some deadly diseases like Covid-19, tumor, cancer, leukemia, HIV and Parkinson's disease.

Keywords

Nanoparticles, Nano drug delivery system, Carbon nanotubes, Coronavirus disease

Introduction

Nanotechnology is progressively spreading over all important domains of science and technology, including electronics, aviation, defense, medicine, and dental. This covers the creation, synthesis, evaluation, and use of materials and technology at the nanoscale scale [1]. The name "Nano" comes from the Greek word "Nanos," which meaning "tiny" and is used as a prefix for a billionth part (10^{-9}). According to the American Society for Testing and Materials, nanoparticles are defined as particles with two or more dimensions and a size range of one to one hundred nanometers (ASTM international 2006) [2]. Because of their enormous reactive and exposed surface area and the quantum effects brought on by their specific electronic structures, these nanoparticles exhibit different and improved physical and chemical characteristics in compared to their bulk counterparts. These particles find extensive usage in photochemistry, electronics, biology, and chemistry [3]. Drug delivery methods based on nanoparticles have shown to be an excellent way to reach cancerous tumors where chemotherapy is less effective. Enhanced permeability and retention (EPR) refer to a nanoparticle's ability to assemble and interact with tumor cells [4]. Antiplatelet agents are generally viewed as critical components for treatment of cardiovascular diseases because platelets play such an important part in their development. As a result, the engagement of nanoparticles with the circulatory system has become a critical component of cardiovascular disease prevention and control. Nanoparticles were found to be the safest and least hazardous of all DDS and hyper thermic drugs

for cancer treatment [5]. This paper will cover the types of nanoparticles, mechanism, and the application of NDDS.

Nanoparticles

The DDS when done at the nano level requires different types of nanoparticles which would help in curing the various diseases in this section the various types of nanoparticles are discussed which are majorly used in NDDS.

Gold nanoparticles

The use of metallic nanoparticles in the biomedical sector, particularly gold nanoparticles, has aroused attention due to their multiple benefits. Various shapes of gold nanoparticles such as spherical, rod like, cage like, etc. can be easily synthesized with sizes ranging from 1 nm up to 100 nm (Figure 1). Gold nanoparticles are often created via the colloidal synthesis process for use in biological applications. With the use of this technique, nanostructures' dimensions, forms, and optical properties may be precisely controlled. It is made up of a stabilizer, a reductant, and a metal precursor. Gold nanostructures with spherical shapes are employed in a number of medication delivery methods. These nanoparticles, which have a relatively high single dispersion, are produced when aqueous chloroauric acid is reduced with sodium citrate. By adjusting the amounts of sodium citrate and chloroauric acid, the size of the nanoparticles may be controlled. In this procedure, citrate acts as a stabilizing and reducing agent. Conjugates of gold nanoparticles with drug molecules increase the drug efficiency and play a vital role to cure endocellular diseases [6, 7].

Liposomal nanoparticles

Liposomes are relatively new nanoparticles used in DDS. The biocompatibility and biodegradability of liposomes allow for several uses in the food, cosmetics, and nanomedicine industries. Additionally, liposome nanoparticles offer cutting-edge technology to deliver active molecules to the precise region of action. Nano liposomes' stability relies on their size and polydispersity, which are important determinants in their formation. Anthracyclines, for example, infiltrate the DNA and kill the cell bodies. Introduction of nano liposomes results in reduction by almost 50% in acute and chronic diseases by reducing the delivery of drugs only to specific tissues and not affecting unintended tissues. Nano liposomes are also widely used for gene delivery of DNA, RNA, siRNA, etc. Use of nano liposomes increases the efficiency of DDS significantly thus increasing its importance in the field of NDDS [8].

Silica nanoparticles

Silica nanoparticles have gained popularity in recent times as they provide better thermal, physical, mechanical, and thermal properties. Silica obtained from natural resources contains impurities, so it cannot be used to produce silica nanoparticles. The Sol-gel process, reverse micro emulsion, and flame synthesis are just a few of the methods utilized to create silica nanoparticles. Due to their capacity to form homogeneous filler dispersion, which regulates the overall composition of the composite material, silica nanoparticles are one of the most important fillers used in advanced composite materials. This is obtained with the help of surface modification by using silane coupling agents [1].

Carbon nanotubes

The CNTs are part of the fullerene family which are allotropes of carbon and comprise of cylindrical structure. CNTs can have a thickness of up to one layer of carbon atoms. Depending on how many layers of carbon atoms are present, CNTs are divided into single- and multi-walled types. CNTs carry electricity in a manner similar to how human body neuron's function. So, CNTs can be used in neuro regeneration. CNTs can be easily combined with drug molecules in solvent form and are biocompatible with neural systems. These properties make them an excellent candidate for drug delivery. CNTs are used to treat many neurodegenerative diseases. CNTs also provide mechanical support for neural tissues and help in nerve growth by stimulating regeneration of neurons [9].

Magnetic nanoparticles

A medication or therapeutic radionuclide is linked to a magnetic particle, then delivered into the body and focused in the target location using a magnetic field in magnetic nanoparticles for magnetic targeting. Through the use of drug-conjugated magnetic nanoparticles, procedures requiring enzyme reactions, or adjustments to physiological factors like pH, osmolality, or temperature, drug release can be magnetically induced. The following benefits of magnetic nanoparticles, whether they are organic or inorganic: They might be heated in a magnetic field to cause medication release or tissue hyperthermia/ablation. They could be seen (Magnetic Resonance Imaging uses superparamagnetic nanoparticles to do this); driven or locked in place using a magnetic field. It is possible to use magnetic nanoparticles to treat musculoskeletal issues, chronic renal illness, and anemia. The fundamental drawback of magnetic drug delivery is the weakening of the magnetic gradient with distance from the target, which restricts the strength of the external field that can be utilized to establish a magnetic gradient and control nanoparticles retention period or drug desorption [10].

Dendrimers

Dendrimers are conjugated with metal ions, then reduced to produce zero valent DENs. During the earliest stages of synthesis, metal ions are complexed with the dendrimer's inner tertiary amine groups. After this reaction, the solution is rapidly swirled while a reducing agent, generally excess BH_4^-, is added. Dendrimers can act as size-selective "Nano filters," offering substrate selectivity to metal catalysts that are intrinsically non-selective. Catalytically active DENs can be regenerated by adding functional groups to the dendrimer's perimeter [11].

Nanoparticles of solid lipid

It is discussed how to employ solid lipid nanoparticles as a carrier system for both corrective dynamic therapy and water-soluble medication. They have developed into a versatile liposome substitute as a medication carrier. They are polymer-based and intended to decrease lethality while enhancing sedate delivery. The features that make them appealing

include their small size, large surface area, high medication stacking, and stage communication at the interface. Pharmaceutical execution has the opportunity to be improved. Solid lipid nanoparticles are one of the unique potential colloidal transporter systems as polymers, which are better alternatives for parenteral nutrition that are identical from oil in water emulsions [12].

Nano Drug Delivery Mechanism

Nanoparticles have different properties or shape and size which help in curing several diseases, so these nanoparticles are injected into the person. The resistance, systematic toxicity and non-specificity of the therapeutic agents are the biggest barriers in DDSs. As a result, the key characteristics of a nano based DDS are the drug's ability to target cells selectively and specifically. Nano carriers can target cells particles work by different mechanisms which have been discussed in this section.

Passive targeting

A mechanism known as EPR effect may cause changes in the bio-distribution of DDS, often referred to as passive targeting. Passive targeting will greatly increase the quantity of drug delivered to disease sites such as sites of inflammation and infection and also sites of tumors [13, 14]. Due to the distinctive EPR effect, the concentration of drug supervised by drug loaded or conjugated polymeric nano carriers reaches up to 10-100-fold higher within the tumor unlike free drug [15].

Passive targeting is the convection or passive diffusion of nano carriers into the tumor interstitium and cells through leaky tumor capillary fenestrations. This is the most frequent approach for big molecules to pass through large pores since convention must be followed when net filtration is zero. Without using cellular energy, diffusion is a way to move molecules along a concentration gradient across the cell membrane. Oxygen and other low-molecular-weight molecules are mostly transported by diffusion. Despite this, interstitial hypertension makes convection across the tumor interstitium inefficient, leaving diffusion as the primary drug delivery method [16].

Effect of EPR causes selective accumulation of nano carriers and drugs. If nano carriers can avoid immune surveillance and circulate for a long time, the effect of EPR will be maximized. Nonetheless, there are constraints to passively reaching the tumor. One being the degree of tumor vascularization and angiogenesis determines passive targeting. Hence, nano carrier extravasation varies by tumor type and anatomical location. Another hindrance is that most solid tumors have high interstitial fluid pressure, which prevents successful absorption and uniform delivery of drugs in tumor tissues and nano carriers [17].

Active targeting

Active or ligand-mediated targeting is the technique of combining DDSs with ligands targeted against cell surface antigens or receptors to increase their site-specific actions. The market now offers a variety of immunotoxins, immunoconjugates, and radio immuno pharmaceuticals. One benefit of this approach is the possibility for additive or synergistic interactions between a cytotoxic medication connected to the DDS and a signaling antibody utilized as a targeting moiety [14]. Targeted ligands are linked to the nano carrier's surface in active targeting to bind to the determined receptors present at the target spot. The ligand is selected to bind to a receptor that is overexpressed by cancer cells or cancer vasculature but is not expressed by healthy cells. In addition, all targeted cells should express targeted receptors in a consistent manner. The binding affinity of the ligand has an impact on tumor penetration due to the binding site barrier. Due to the complicated flow conditions of the bloodstream, high affinity binding is preferable for locations where cells are easily accessible, such as tumor vasculature [16].

Since the circulatory system at tumor sites does not often serve as a barrier, ligands are anticipated to constantly have direct access to a specific molecule deposited on the tumor tissues around them, enabling active targeting. To highlight the wide range of molecules options, a variety of targeting molecules were selected. These findings show that the active targeting nano carriers are more effective than non-targeted nano carriers at binding, entering and killing tumor cells. An active targeting method improves a medication's anticancer efficacy by increasing cellular uptake and intracellular retention of DDS. Because actively targeted nano carriers can give intracellular medication accessibility, the active targeting method is a good approach for treating multidrug resistance, an issue where the passive targeted nano carriers are unsuccessful [17].

Targeting molecules are conjugated to the surface of nano carriers in active targeting. As this has an influence on anti-cancer, nanoparticles in the procedure have the ability to transmit their contents to target cells in close proximity, bind to the cell membrane and act as an extracellular sustained release drug repository, or they can be internalized by the cells [18, 19].

Application of NDDS for Various Diseases

NDDSs have ability of increasing the water solubility and stability of drugs which reduces enzyme degradation, cycle time, and uptake rate of the cells and tissues that are to be targeted, thus it increases effectiveness and improve the safety of drugs. The treatment of various types of severe diseases and dysfunctions of the body which could be either cured or can cut down the effect of any chronic or incurable disease are covered in this section.

Treatment of Covid-19

Primarily preventative measures, such as nonspecific supportive care, social distance, and quarantine, may presently be used due to a lack of authorized vaccinations and specialized treatments. To combat the present Covid-19 mutation and any future mutations of the CoV family, researchers throughout the globe are focusing their efforts on developing a successful vaccination and specialized therapy. Researchers will be able to design specialized medicines and vaccines by greater understanding the coronavirus genome as well as the mechanisms of viral replication and pathogenesis. While nanomedicine has been hailed as one of contemporary science's most significant

and promising disciplines, this review also covers numerous traditional treatment methods and clinical-stage medication candidates discovered since SARS-CoV first appeared. In addition to the entrance stage, nanomedicine as a viable antiviral strategy might target the many processes in CoV's lifecycle. S protein initiates virus entrance via endosomes or membrane fusion as the first stage in its lifecycle (entry protein). As a result, nanoparticles are typically engineered to limit corona viral entrance by blocking S protein. Researchers produced PEGylated gold nano rods loaded with peptide pregnancy-induced hypertension (PIH), which possesses HR1 inhibitory action (IC50 = 1.171 M), using docking-based virtual screening. Three domains of the S2 subunit are HR1, HR2, and fusion peptides. *In vitro* and *in vivo*, PIH-gold nano rods induce tenfold greater HR1 inhibition and, as a result, tenfold lower HR1/HR2 complex (6-HB)-mediated membrane fusion of MERS-CoV, as well as possible biostability and biocompatibility. A peptide inhibitor was recently discovered to be linked to the surface of nanoparticles, and molecular dynamics simulations demonstrated its anti-SARS-CoV-2 activity. The receptor-binding domain of SARS-CoV-2 exhibits structural matching with the peptide inhibitor, which was derived from ACE2. Another nanostructure, functionalized quantum dots, interfered with S protein and prevented CoV entry (229E). Quantum dots penetrate cells readily and inhibit viral multiplication [20-23].

Treatment of leukemia

Leukemia is a blood cancer which is caused due to massive increase in white blood cells so Acharya et al. for this they synthesized nano particulate systems which were either single or dual drugs. The average sizes of those particles ranged between 200 - 300 nm whose zeta potential was negative. Their studies showed that antileukemic effect which was observed on K562 cells by all the drugs and were capable to show during initial period i.e., 2 days of incubation; this was done promoting apoptosis regulating activities by doing caspase activation and cell cycle arrest by doing mitochondrial damage. By inhibition of Bcr-Abl multiple biochemical reactions were observed which were helpful in antileukemic effect [24].

Treatment of lung cancer

Ibrahima et al. explained the usage of turmeric in the treatment of lung cancer by using nanoparticles to describe the techniques and procedures. Turmeric had received a lot of interest because of its potential anti-cancer effects, although it has a lot of problems with water solubility and absorption. Turmeric is a natural polyphenolic hydrophobic molecule with anti-inflammatory and cost-effective properties which has been utilized to treat a variety of illnesses. Turmeric contains several compounds which are engaged in a multi-step process that has been linked to an upsurge in carcinogenesis. Turmeric can inhibit cancer suppressing genes, cyclooxygenases, and lipoxygenases, in other ways. Anti-carcinogenic and anti-inflammatory properties were discovered. Turmeric also inhibits the production of TNF-α, an inflammatory cytokine that controls the growth of most cancers in cells. Turmeric is encapsulated in krill using a redesigned thin drug lipid film called lipid-based liposomes. Extrusion or sonification is both used in the hydration process. In liposomal formulations, this technique has resulted in good physicochemical and oxidative stability. Such low-cost liposomal nano-nutraceutical formulations might be utilized to easily solubilize, stabilize, and monitor the distribution of biologically active and hydrophobic substances for the treatment of cancer and other provoking diseases [25].

Treatment of tumor spheroids

According to Niora et al., a versatile approach for *in vitro* investigation of nanoparticle penetration and effectiveness in tumours is the use of three-dimensional (3D) tumour spheroids in combination with light-sheet fluorescence microscopy in a head-to-head comparison of a range of commonly used lipid-based nanoparticles. Cancer cell-based 3D structures are called multicellular tumour spheroids. These are produced utilizing a variety of *in vitro* techniques and are composed of monolayer tumour cells. To easily test the functioning of any fluorescent nanoparticles in 3D tumour spheroids, light sheet microscopy and extensive picture analysis may be used. The only constraint on nanoparticle testing is the built-in process of light sheet microscope optics, which includes lasers and detectors. As a result, they propose a robust approach for measuring the penetration performance of nanoparticles *in vitro*, a metric that could be critical to the therapeutic effects of the corresponding DDS [26].

Treatment of human immunodeficiency virus (HIV)

Garrido et al. examined nanoparticles for HIV therapy, especially gold nanoparticles, as gold nanoparticles have been utilized in gene and cancer imaging and medicinal delivery. Gold nanoparticles are ideal for clinical application due to their tiny size, which allows them to enter tissues and cells more easily due to their inert nature which means they produce less host reaction. Their multivalence enables the conjugation of several molecules on the nanoparticle surface at the same time, as well as the delivery of these payloads at the same time. Gold nanoparticles can also transport chemicals to the brain by crossing the blood-brain-barrier (BBB). Transporter mediated transcytosis; transcellular lipophilic diffusion, receptor-mediated endocytosis, para cellular hydrophilic diffusion, and absorptive mediated endocytosis are all methods that can transport gold nanoparticles over the BBB. Furthermore, cell viability experiments revealed that these gold nanoparticles do not induce short-term cell damage and may be attached to an antiviral molecule while retaining antiviral efficacy. When the size of nanoparticles is increased, brain concentration and spleen accumulation are both enhanced. As a result, particle size has been shown to be a factor in brain penetration, with particles smaller than 10 nm expected to enter the central nervous system more efficiently, and it has been concluded that inorganic gold crystals with diameters of 2 to 10 nm serve as a base scaffold for combining molecules with a variety of properties on their surface [7].

Treatment of Parkinson's disease

Parkinson's disease is a chronic condition which is cause due to imbalance of blood sugar in body as the pancreas gland either stops or produce very small amount of insulin which

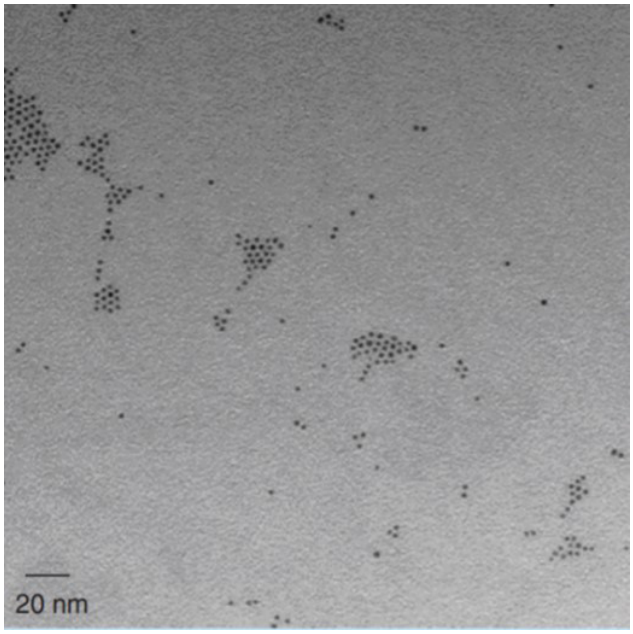

Figure 1: TEM image of gold-p-mercaptobenzoic acid nanoparticles [7].

helps to maintain blood sugar level whose cure is currently does not exist currently, but it can go into remission i.e., after some medication body does not show any symptoms so Kaushik et al. have studied that because of nanoparticle's site-directed target delivery and capacity to cross through the BBB into the central nervous system, they have emerged as a promising treatment for neurodegenerative illnesses including Diabetes. Cumbersome compounds such as medicines and genes have been shown to be transported across the BBB using nanoparticles surface functionalized with peptidomimetic antibodies. Biocompatible gold nanoparticles have been shown to cause strong synuclein aggregation at concentrations as low as 20 nm. Graphene and superparamagnetic iron oxide nanoparticles were among the nanoparticles studied. Cerium oxides NPs, in fact, have exhibited neuroprotective efficacy strong antioxidant and anti-apoptotic properties. Biological networking visualizations and biochemical, mathematical models have subsequently been used to describe connections (including the activation or inhibition of biological molecular activities and routes between objects) and show the pharmacokinetic process in a particular system. The biological interactions are typically created via a research study for the specified entities under various circumstances and characteristics. Furthermore, synthetic biology encompasses a new age of technological methods which has been used to develop synthetic bio-models for illness cures. Biomedical theragnostic and cancer therapy, for example, has been described as rational techniques for encoding the biological processes of biological systems. In order to better understand how genes are regulated, how proteins are made for cascade effects, and other biological interactions throughout the development of Parkinson's disease, synthetic models may be utilized. Based on the information currently known about the genes/proteins implicated in the genesis of Parkinson's disease, our work established a comprehensive biochemical route for Parkinson's disease containing -synuclein. Known biocompatible nanoparticles for inhibiting synuclein were also compared to traditional medication molecules in

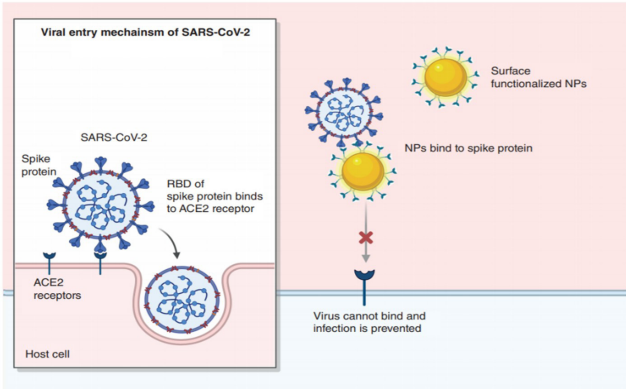

Figure 2: Nanoparticle-based treatment for coronaviruses by preventing viral entrance. The abbreviations NP, SARS-CoV-2, and RBD stand for nanoparticle, receptor-binding domain, and severe acute respiratory syndrome, respectively [23].

terms of their *in silico* biophysical and biochemical interactions [27].

Conclusions

The interest in the field of NDDS has gained importance over the years due to the rise in the wide range of potential applications. This paper highlighted different kinds and properties of nanoparticles used in drug delivery; the main focus was on particles like. Further the different kinds of mechanisms where discussed, these mechanisms also play a vital role in curing various diseases as every disease attack and harm body differently also it attaches to the body in a different manner depending upon their structure thus there are different mechanisms to attack on them. Covid-19 virus parent cell is mutating rapidly and hence there is a great chance that vaccines might not be so much effective, but nanoparticles might help as NDDS is also tested and found effective in many severe diseases like cancer, HIV, leukemia, Parkinson's disease, Tumor which were also mentioned. The NDDS is important field to study not only because it has so many applications but also in future it can be used in several more ways such as:

- In space industry to inject nanoparticles in astronauts so to regulate their oxygen flow in blood.
- In the defense sector where army personals can carry nanoparticles which can help them to bear the pain of any injury.
- Nanoparticles can also be used for air and water purification.

Acknowledgements

None.

Conflict of Interest

The authors declare no conflict of interests that are relevant to the content of this article.

Credit Author Statement

Likhit Sawant: Conceptualization, Methodology,

Investigation, Formal analysis, Writing - review and editing; Jayvardhan Vyas: Investigation, Formal analysis, Writing - original draft preparation, Writing - review and editing; Parvez Surani: Writing - original draft preparation, Resources; Jatin Dalmia: Writing - original draft preparation; Aliasgher Tinwala: Resources; Samadhan Deshmukh: Resources, Supervision. All the authors read and approved the manuscript.

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