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RECENT ADVANCES IN NANOTECHNOLOGY BASED DRUG DELIVERY SYSTEMS

***Y. Venkateswara Rao, T. Naga Pallavi, G. Varshitha, A. Keerthi, G. Sofiya, K. Gowri Sankar, P. Srinivasa Babu**

Department of Pharmaceutical Analysis, Vignan Pharmacy College (Autonomous), Vadlmudi, Guntur, Andhra Pradesh.

***Corresponding Author: Dr. Y. Venkateswara Rao**

Assistant Professor, Department of Pharmaceutical Analysis, Vignan Pharmacy College (Autonomous), Vadlmudi, Guntur, Andhra Pradesh. **DOI:** https://doi.org/10.5281/zenodo.22267339

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ABSTRACT

However, recent developments in nanotechnology have revolutionized drug delivery systems through overcoming limitations associated with conventional formulations such as low bioavailability, nonspecific delivery, and toxicity. Nanocarriers, which are usually sized between 1 nm and 100 nm, have distinct physicochemical properties like high surface area-to-volume ratio and modifiable surface chemistry, making them suitable for effective loading and targeted delivery of drugs. A wide variety of nanocarriers such as micelles, liposomes, dendrimers, carbon nanotubes, metallic nanoparticles, and quantum dots have been investigated for their capability to increase the bioavailability, stability, and controlled release of pharmacological compounds.Current nanotechnology-based systems use either passive or active targeting methods using the EPR effect or ligand-receptor interactions on the surface of cells to achieve higher drug accumulation at target sites without causing harmful side effects on healthy tissues. Controlled and triggered drug release systems based on stimuli such as pH, temperature, and enzyme action improve the efficacy of treatments. Generally, nanotechnology drug delivery systems are a dynamic area of study that holds promise for transforming drug delivery methods. As technology improves in the future, the drawbacks currently present are likely to be addressed, making the process safer, more efficient, and precise.

KEYWORDS: Nanotechnology, Drug delivery system, Nanocarriers, Targeted drug delivery Controlled release, Nanomedicine.

1. INTRODUCTION

The evolution of nanotechnology has led to the transformation of the discipline of pharmaceutical sciences and medicine in the 21st century. The word "nano" comes from the Greek word "nanos," meaning "dwarf" and denotes the sizes of 1 x 10-9 meters.[1] Nanoscience focuses on the exploration of materials exhibiting special properties between 1 and 100 nm, while nanotechnology is the exploitation of these special properties in developing innovative products.[2] The most significant historical event for the emergence of nanotechnology occurred in 1974 when the term "nanotechnology" was coined by Professor Norio Taniguchi during an international symposium on industrial production in Tokyo. Specifically, he was discussing some issues concerning semiconductor technology and ion beam milling.[3] Since that time, nanotechnology has been evolving in different disciplines in science and even in daily living.[4]

Nanotechnology has proven itself in resolving the limitations associated with existing dosages in pharmaceutical science. Traditional dosages, such as tablets and capsules, face several challenges like low bioavailability, poor tissue distribution, and undesired impact on healthy tissues.[5] Nano-engineering of matter enables the fabrication of novel drug delivery systems that can overcome such drawbacks.[6] Nanotech applications in the field of pharmaceuticals are all related to the molecular level, meaning that the materials exhibit unique physicochemical properties when compared with other counterparts. These properties are attributed to high surface area-to-volume ratios, and quantum effects in this context are common.[7] Due to the potential of designing such materials at this level, several nanocarrier systems have been developed with particular focus on specific therapeutical needs.[8]

Present nanotech studies in this field mainly focus on designing drug delivery systems that can be activated by certain biological factors as well as target specific parts of the body while delivering effective drug dosages for extended periods of time.[10] Nanotech is very important in managing such difficult diseases as cancer, particularly those that cannot be managed by traditional methods.[10] Advancements in drug delivery through the use of nanotechnology have transformed the ways of dealing with therapeutic issues in pharmaceutical science.[11]

2. CLASSIFICATION OF NANOCARRIERS

2.1 Micelles: Micelles are self-assembled spherical nanostructures produced by amphiphiles in an aqueous environment. The size of micelles varies from 10 to 100 nm. Their structure consists of two layers – a hydrophilic shell and a hydrophobic core. Therefore, micelles can solubilize hydrophobic drugs and improve their bioavailability. Micelles belong to the most universal carriers able to transport various therapeutic agents.[12]

2.2 Liposomes: Liposomes are spherical vesicles constructed from phospholipids. The sizes of liposomes range from 30 nm to several microns. Hydrophilic and lipophilic drugs are encapsulated into the interior of liposomes and liposomal membrane. Modification of liposomes through attaching various biological moieties enables their targeted delivery. Liposomes have proven highly effective against malignancies.[13]

2.3 Dendrimers: The dendrimers are branched structures produced according to a core and then branches added to the core structure. Hence, there are a number of functional groups in these molecules which can be manipulated during the process of synthesis. There are two distinctive features about dendrimers: firstly, the presence of internal cavities where drugs can be loaded; secondly, the presence of external functional groups that can be modified and attached to target vectors. There are tremendous possibilities of using dendrimers for drug delivery. The internal cavities will help in loading drugs while the functional groups on the surface can help in binding target vectors. They exhibit precise nature regarding their structure, size, and surface functionality which makes them ideal choices for drug deli. Dendrimers can be easily degraded and have high drug loading capacity.[14]

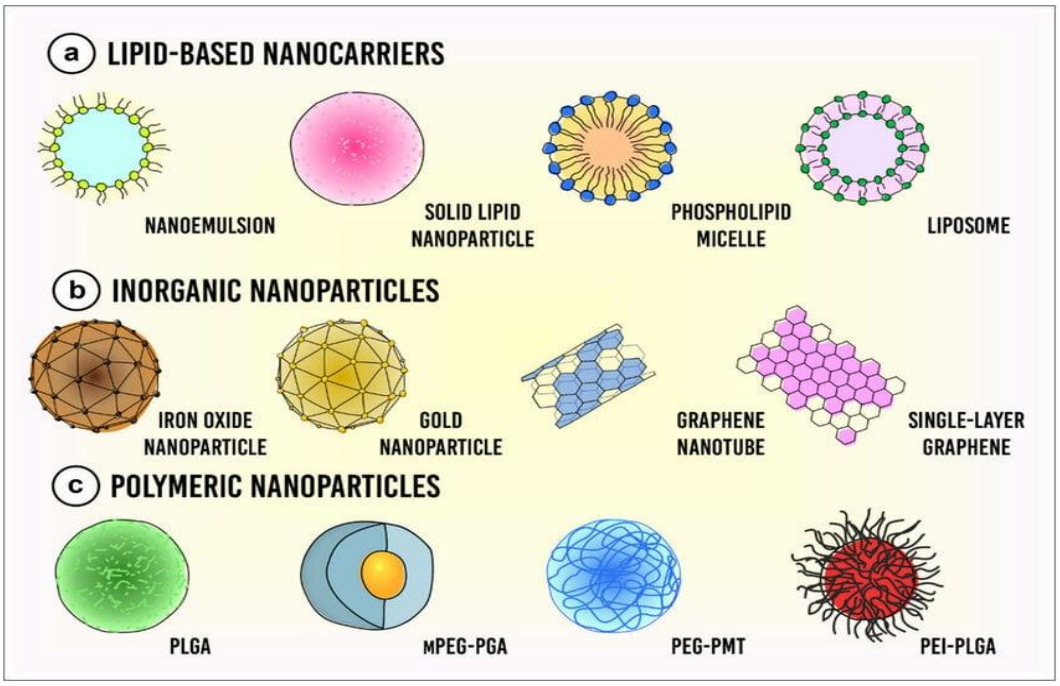

Fig. 1: Types of Nanocarriers.

2.4 Carbon Nanotubes: The carbon nanotubes consist of a tubular structure of graphene sheets, and they are found in either the single walled or multi-walled structures. Their high surface area-to-volume ratio makes them very effective at loading drugs while their hollow structure makes it possible to trap different therapeutic agents inside them. Carbon nanotubes have shown very good efficacy in biomedical applications because of their property of entering into cells through the cell membrane.[15]

2.5 Metallic Nanoparticles: Metallic nanoparticles consist of gold and iron oxide-based metallic nanoparticles. The iron oxide nanoparticle consists of a magnetic core of (4-5 nm) surrounded by hydrophilic polymeric coatings like PEG and Dextran. They are ideal for use in imaging and therapy since they possess magnetic properties. However, the gold nanoparticles are known to show very high biocompatibility and are easily functionalized.[16]

2.6 Quantum Dots: The quantum dot is a kind of nanoparticle, which is a semiconductor in nature and possesses optical properties like fluorescence, with a diameter of 1-100 nm. The quantum dots have good optical properties and can be used for purposes such as imaging and drug delivery because of their specific attribute.[17]

Table 01: Comparative analysis of selected nanocarriers in drug delivery.

Nanocarrier	Size Range	Material	Drug loading capacity	Release mechanism	Targeting ability	Advantages	limitations	Applications
Micelles	10-100nm	Amphiphilic polymers	Hydrophobic core	Diffusion	Passive (EPR) effect	Solubilizes poorly soluble drugs	Low solubility in blood	Cancer therapy
Liposomes	50-500nm	Phospho-lipid bilayer	Hydrophobic + lipophilic	Fusion, diffusion	Passive+ active	Biocompatible, versatile	Leakage, short shelf life	Cancer, vaccines
Dendrimers	1- 10nm	Branched polymers	Surface+ encapsulation	Diffusion, degradation	Active targeting	High loading, precise structure	Cytotoxicity, costly	Drug delivery
Carbon Nanotubes	1- 50nm	carbon	Surface adsorption	Diffusion	Active (functionalized)	High surface area	Toxicity concerns	Drug delivery
Metallic Nanoparticles	1-100nm	Gold, silver metals	Surface conjugation	Stimuli-responsive	Active targeting	Imaging + therapy	Toxicity, accumulation	Cancer, diagnostics
Quantum dots	2- 10nm	Semi-conductor crystals	Surface attachment	Stimuli-responsive	Active targeting	Excellent imaging properties	Toxicity	Bioimaging, diagnostics

3. MECHANISM

3.1 Controlled Release Mechanism: Controlled release mechanism for nanotechnology-based drug delivery system follows different physicochemical processes. Drugs are loaded into the nanocarrier using physicochemical methods, which include physical loading, chemical bonding, or adsorption of drugs.[18] Controlled release mechanisms include release through the matrix, where the drug releases through polymer matrix at a controlled pace, or release through reservoirs, where drug molecules release from a rate-limiting membrane. Stimuli-responsive release involves response to external stimuli such as pH, temperature, or enzyme-induced reactions for drug release.[19]

Table 02: Physicochemical properties required in nano carriers-based drug Drug delivery.

PROPERTY	OPTIMAL RANGE	IMPACT ON DELIVERY	MEASUREMENT METHOD	CLINICAL SIGNIFICANCE
Size	10-200nm	Cellular uptake	DLS	Biodistribution
Zeta potential	-10 to +10mv	stability	Electrophoresis	Circulation time
PDI	<0.3	uniformity	DLS	Batch consistency
Surface area	>100M	Drug loading	BET analysis	Release kinetics
Drug release rate	0.1-1.0k/hr	Therapeutic effect	Dissolution study	Efficacy
Encapsulation efficiency	>70%	Drug retention	UV-Vis/HPLC	Dose optimization
Stability	>6 MONTHS	Prevents aggregation	Stability studies	Shelf life
Hydrophobicity	1-5	Membrane permeability	Partition coefficient	Absorption & distribution

3.2 Active Targeting: Active targeting employs certain methods of molecular targeting to ensure delivery of medicines to desired target sites. This kind of technology involves various molecular targeting methods, such as antibodies and fragments of these antibodies, aptamers, peptides, and small molecules like folate and glycoproteins.[20] The target molecules include overexpressed biomarkers of the causative cells. One example of targeting of a biomarker includes CA-125 biomarker in ovarian cancer cells.[21]

Table 03: Ligand-Mediated Targeting Strategies in Nanomedicine.

Targeting ligand	Target	Disease application	Binding affinity (kd)	Ligand type	Internalization mechanism	Clinical status
Folate	Folate receptor	Cancer	10^{-10}M	Small molecule	Receptor -mediated endocytosis	Phase III
Transferrin	Transferrin receptor	Brain disorder	10^{-9}M	Protein	Clathrin -mediated endocytosis	Phase II
3RGD Peptide		Angiogenesis	10^{-9}M	Peptide	Integrin-mediated uptake	Phase II
Anti -HER2	HER2 Receptor	Breast cancer	10^{-8}M	Monoclonal antibody	Receptor -mediated endocytosis	Approved
Aptamers	PSMA	Prostate cancer	10^{-11}M	Nucleic acid	Receptor-mediated uptake	Phase I
Hyaluronic acid	CD44 Receptor	Cancer	10^{-6}M - 10^{-8}M	Polysaccharide	Receptor -mediated endocytosis	Phase II
Galactose	Asialogyco-protein receptor	Liver diseases	10^{-6}M - 10^{-7}M	Sugar ligand	Receptor -mediated endocytosis	Phase I

3.3 Passive Targeting: This type of drug delivery system utilizes the EPR effect, which is a phenomenon that can be seen in most pathological conditions. The principle behind passive targeting involves making use of the abnormal vascular architecture present in the diseased tissues, failure of lymphatic clearance, altered pH, temperature, and molecular size and shape.[22]

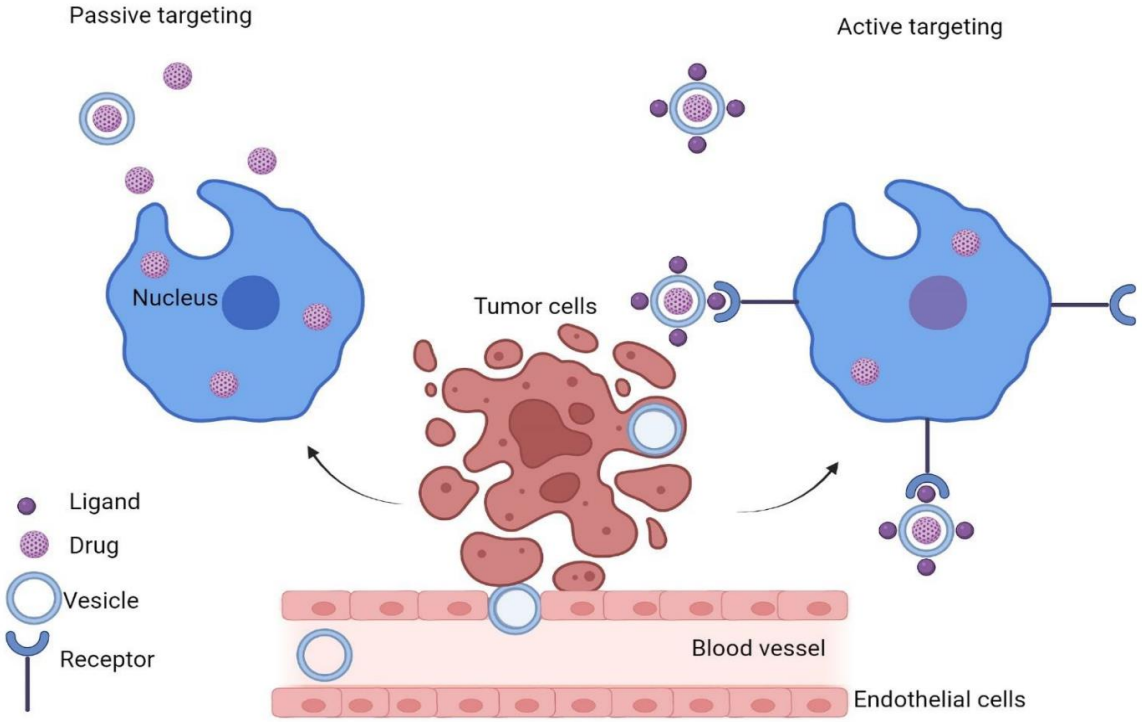

Fig. 2: Mechanism of Nano carrier drug delivery.

4. Applications: Use of nanocarriers in making novel drug delivery systems has introduced changes in drug delivery mechanisms provided in various disease states. These methods improve drug bioavailability, help in targeting the drugs and provide for controlled release.[23]

4.1. Gastrointestinal Disorders: Delivery systems that make use of nanoparticles are a very effective way for treatment of inflammatory bowel disease. Nanoparticle-based delivery systems target the colon and avoid the drugs being distributed systematically. The drugs in the form of nanocarriers withstand the GI environment while being delivered locally to the site of inflammation.[24]

4.2. Bone Regeneration: New methods of bone regeneration have emerged due to nanoengineering technologies. Hydrogel and nanocrystalline hydroxyapatite have improved regenerative capacity of bones. Nano structural assemblies resembling bones

called as rosettes are developed by chemically binding the DNA bases.[25]

4.3. Retinal Disorders: A special design of nanocarrier-based delivery systems is developed to overcome the obstacles encountered when using intravitreal drug delivery method in cases of posterior eye disorders. Liposomes, nanospheres, and nano emulsion are used as carriers to increase permeability and sustained release of drugs. Cyclodextrin nanoparticles suspensions prove to be highly effective for delivering lipophilic compounds to retina.[26]

4.4. Management of Diabetes: Nanotechnology has been used in many different ways to control the condition of diabetes patients. Nanopore devices protect the transplanted beta cells from immune responses without affecting their capacity to generate insulin. Nanospheres can be used to release insulin into the body in a controlled manner. The nanorobots help detect blood glucose and take necessary actions. Moreover, nano polymers make it possible to orally administer insulin by protecting it from enzymes and increasing its absorptivity.[27]

4.5. Tuberculosis: Nanotechnology-based treatments for tuberculosis include preventive and curative methods against TB. Both liposome and lipid nanoparticles have played a significant role in delivering anti-TB drugs. Drug delivery systems improve the sustained release properties of the drugs. Additionally, the drug delivery systems improve stability and pharmacodynamics.

4.6. Dentistry: In dentistry, nanotechnology has advanced the procedure through innovative technology. By utilizing mouthwashes and toothpaste, nanorobotic dentifrices can help maintain the oral cavity's health. In fact, the machines continuously work to remove any calculus or organic matter from the oral cavity. They achieve this through microscopic operations. Some other applications in orthodontics include the utilization of nanorobots which are capable of manipulating the periodontal tissue of teeth for their manipulation without inflicting any pain.[28]

4.7. Cancer Therapy: In the field of medicine, nanotechnology can be employed in the transportation of drugs into the body. It has several uses in the application of cancer therapy. Traditional means of treating cancer have some limitations including drug resistance and toxicity. Nonetheless, nanocarriers have solved this problem by utilizing the following:

4.7.1. Targeted Delivery: They deliver the drugs directly into cancer cells using the process of molecular recognition. This is considered a breakthrough in comparison to traditional chemotherapy methods. The surface of these active transporters is modified to incorporate specific ligands including antibodies, peptides, or even chemical groups, which react with cancer receptors. They enable the carrier to attach selectively to cancer cells instead of healthy cells. As a result, high concentration of the drug is achieved in these cancer cells. In addition to this, it minimizes the side effects on other organs in the body.

4.7.2. Enhanced Penetration: EPR effect of nanoparticles due to their specific properties is another peculiarity of tumor vasculature that contributes to the enhanced accumulation of nanoparticles in the tumor mass. The mechanism of the EPR phenomenon can be explained by the abnormal tumor vasculature that features enlarged gaps between endothelial cells, non-uniform basement membrane, and poor lymphatic drainage. It is possible to select proper parameters of nanocarriers in order to enhance this effect and to ensure deep penetration of nanoparticles in tumor tissue. In some cases, nanocarriers react to specific features of the tumor microenvironment (for example, pH and enzymes produced by tumor cells), therefore ensuring low level of toxicity. Contemporary nanocarriers feature multiple drug release mechanisms that make it possible to deliver drugs in sequential or controlled release mode depending on cancer type and treatment.

5. Advantages and Disadvantages

5.1. Advantages: There are plenty of advantages of using nanoparticles in drug delivery system compared to traditional methods of delivery utilized in medicine. Improved solubility and permeability lead to a high level of drug bioavailability. Targeted drug delivery results in minimizing side effects and toxicity. Flexibility of nanocarriers can be employed for loading multiple medications making it easier to apply combination drug therapy.[30] In addition, the possibility to track the activity of the drug delivery system through imaging opens up opportunities for evaluating the effectiveness of therapy. Sustained release properties of such systems ensure high levels of therapeutic substances for an extended period of time; thereby, reducing the dosing rate and improving compliance.[29]

5.2. Disadvantages: However, there are still several limitations related to drug delivery systems based on nanoparticles:

5.2.1. Manufacturing Issues: The issue related to scaling up the production process is rather challenging due to the necessity of controlling the particle size distribution and regulating their surface properties. Increased expenses associated with manufacturing nanocarriers negatively impact the adoption of the latest innovations on a more extensive scale.[30]

5.2.2. Biological Barriers: Despite the ability of nanocarriers to overcome various biological barriers, some problems remain regarding effective tissue penetration and cellular uptake. In addition, elimination from the bloodstream by the reticuloendothelial system reduces the efficiency of the delivery process.

5.2.3. Regulatory Issues: In view of the peculiarities associated with nanomaterials, some issues arise in connection with the development of regulatory guidelines for ensuring safety and efficacy. Long-term information about the consequences of using nanoparticles is insufficient, particularly the risk of accumulating nanocarriers that cannot be degraded.[31]

6. CONCLUSION

The application of nanotechnology in the delivery systems for medicines is a new era in the world of pharmaceutical sciences. Due to the use of various kinds of nanocarriers which provide different mechanisms to deliver the drugs, many challenges encountered in pharmacology can be resolved successfully. Although there are several difficulties related to the manufacturing process, overcoming the biological barriers and regulation compliance, the fast advancement of the technologies is assisting in tackling these problems. In the upcoming years, the complexity and functionality of the delivery systems are likely to increase.

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