INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

Review On Nanoparticle : Nano Vehicles For Anticancer Drugs

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ARTICLE INFO

Received: 24 Sep 2024
Accepted: 28 Sep 2024
Published: 13 Oct 2024

Keywords:
Nanoparticles, Nano vehicles, Anticancer drugs, Drug delivery, Targeted therapy, Chemotherapy, Biocompatibility, Tumor targeting, Controlled release, Nanotechnology, Liposomes, Dendrimers, Polymerics Nanoparticles, Enhance permeability and retention effect, Ligand receptor interactions, Nanomedicine

DOI:
10.5281/zenodo.13926263

ABSTRACT

The Development of nanoparticles based drug delivery systems has emerged as a promising stratergy in the fight against cancer. These nano vehicles offer several advantages over traditional chemotherapy, including targeted drug delivery reduces side effect and improved therapeautic efficacy. These various explores the various type of nano particle used for anticancer drug delivery such as liposomes, dendrimers, polymeric nano particle Their mechanism of action including enhanced permeability and retention effect, Active targetting via ligand receptor interactions and stimuli responsive release. We also discuss the current state of clinical trials and regulatory challenges faced in the commercialization or nanoparticles based therapies. Comprehensivers analysis of recent advancements and ongoing research. This review highlights the potentials of nanoparticles to revolutionize cancer treatment and underscores the need for further studies to optimize their design and application. Nanoparticles have emerged as a promising platform for the delivery of anticancer drugs, offering targeted therapy with enhanced efficacy and reduced side effects. This review explores the various types of nanoparticles utilized as nano vehicles, including liposomes, dendrimers, polymeric nanoparticles, and metallic nanoparticles. We examine their physicochemical properties, drug loading capabilities, and mechanisms of drug release. Key advancements in nanotechnology that facilitate tumor- specific targeting through passive and active mechanisms are discussed. The review also addresses the current challenges in nanoparticle drug delivery, such as stability, biocompatibility, and the potential for clinical translation. Case studies of successful nanoparticle-based anticancer therapies are highlighted to underscore their therapeutic potential. Future perspectives on the integration of personalized medicine and nanotechnology for cancer treatment are also provided.

INTRODUCTION

Nanoparticles have emerged as a revolutionary approach in the delivery of anticancer drugs. Leveraging their small size and unique properties, nanoparticles can enhance the efficacy and reduce

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

the side effects of conventional chemotherapy. This review explores the use of nanoparticles as nano vehicles for anticancer drugs, focusing on their design, mechanisms of action, and clinical applications. Cancer remains one of the leading causes of morbidity and mortality worldwide, posing significant challenges for conventional therapeutic approaches. Traditional chemotherapy, while effective, often results in severe systemic toxicity and adverse side effects due to the non-specific distribution of anticancer drugs. This necessitates the development of novel drug delivery systems that can selectively target tumor cells while sparing healthy tissues. Nanoparticles (NPs) have gained significant attention as potential vehicles for the delivery of anticancer drugs. The unique properties of nanoparticles, including their small size, large surface area, and tunable surface chemistry, enable them to improve the pharmacokinetics and biodistribution of therapeutic agents. Nanoparticles can be engineered to encapsulate drugs, protect them from degradation, and release them in a controlled manner at the tumor site. Furthermore, the surface of nanoparticles can be modified with targeting ligands that recognize specific markers on cancer cells, thereby enhancing the specificity and efficacy of the treatment. This review aims to provide a comprehensive overview of the current state of nanoparticle-based drug delivery systems for cancer therapy. We will explore the various types of nanoparticles used in this context, including liposomes, dendrimers, polymeric nanoparticles, and metallic nanoparticles. Each type of nanoparticle offers distinct advantages and limitations, which will be discussed in detail. The mechanisms by which nanoparticles can achieve targeted drug delivery will be examined, with a focus on passive targeting through the enhanced permeability and retention (EPR) effect, and active targeting using ligands that bind to receptors overexpressed on cancer cells. We will also highlight recent advancements in nanoparticle engineering that have led to improved targeting capabilities and therapeutic outcomes. Despite the promising potential of nanoparticles in cancer therapy, several challenges remain. Issues related to the stability, biocompatibility, and scalability of nanoparticle formulations must be addressed to facilitate their clinical translation. Additionally, the potential immunogenicity and toxicity of nanoparticles require careful consideration. Through case studies of successful nanoparticle-based anticancer therapies, we will illustrate the practical applications and benefits of these systems. Finally, we will discuss future perspectives on the integration of nanotechnology with personalized medicine, aiming to tailor cancer treatments to the unique genetic and molecular profiles of individual patients.

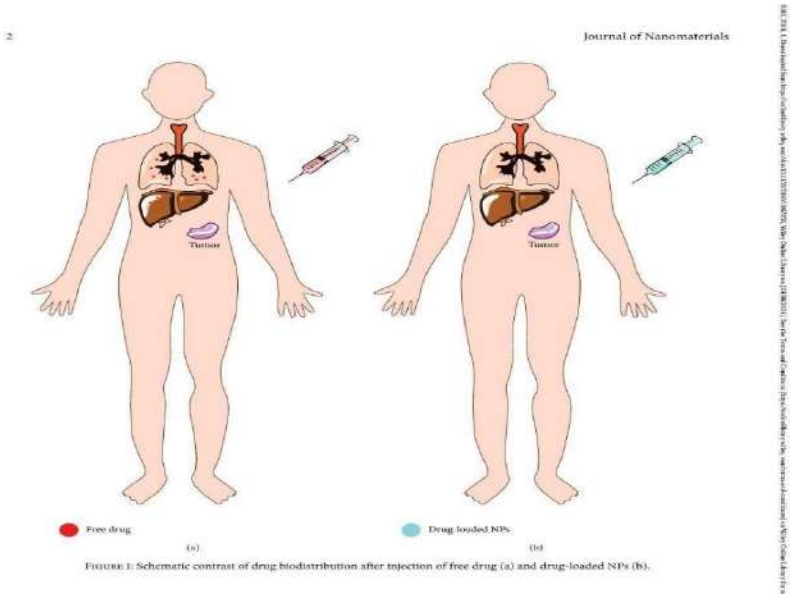

FIGURE 1: Schematic contrast of drug biodistribution after injection of free drug (a) and drug-loaded NPs (b).

CANCER CELL TARGETED DRUG DELIVERY

Mechanisms of Targeted Cancer Cell Drug Delivery. Cancer cells are otherwise normal cells with unique mutations in genes regulating growth, which cause them to divide uncontrollably and give them the ability to metastasize. Cancer cells successfully compete with normal cells for oxygen, glucose, and amino acids for division and growth, but a tumor can only grow to about 2 mm^3 without forming blood vessels (angiogenesis). There are more than one hundred types of cancer, more than 85% of which are solid. Current treatment includes surgery, radiotherapy, chemotherapy, hormone therapy, and immunotherapy. However, the inability of drugs to specifically target cancer cells hinders most treatment. It is often quicker

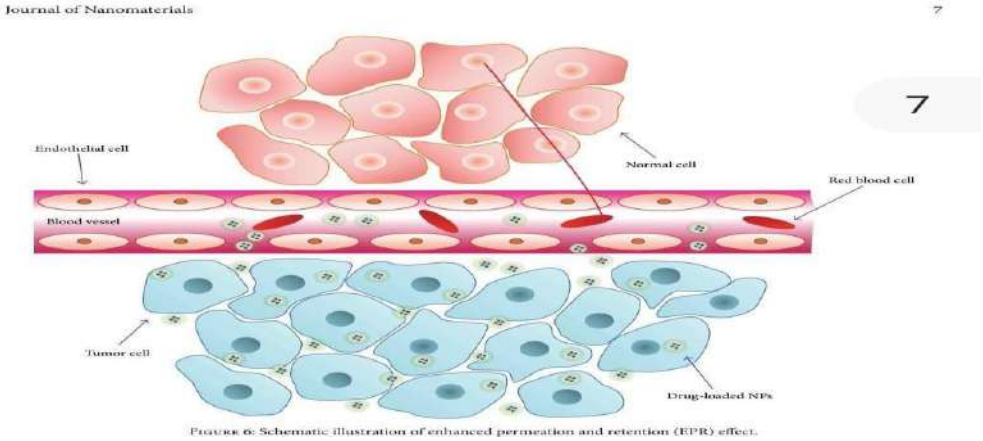

FIGURE 6: Schematic illustration of enhanced permeation and retention (EPR) effect.

MECHANISMS OF ACTION

Passive Targeting :-

Nanocarrier Systems Drugs delivered intravenously tend to evenly disperse throughout the body. However, tumor cells tend to take up particles of a certain size to a greater degree than healthy cells due to a combination of leaky tumor blood vessels and faulty particle screening. This is known as the enhanced permeation and retention (EPR) effect and is the mechanism behind passive targeting. The EPR effect is influenced by NP properties including particle size, shape, and surface charge, and it in turn influences circulation time, penetration speed, and intracellular internalization. For example, phagocytic cells faciltate larger particle uptake, while

nonphagocytic cells favor their size is smaller than 100 nm. The nanoparticle surface properties could play a central role in blood circulation and subsequent cellular internalization. NPs with a negative surface charge will circulate longer in the blood, but positively charged NPs are more readily taken up by cancer cells (which have negative surface charge). In order to clarify the influence of shape on the cellular uptake of PEGylated NPs, Li et al. performed large-scale molecular simulations to study different NP geometries with identical surface area, ligand-receptor interaction strength, and PEG grafting density. They found that spheres exhibited the fastest internalization rate, followed by cubes, while rods and disks were the slowest. Delivery platforms include liposomes, polymeric micelles, targeted polymer drug conjugates, and dendrites. They all consist of macromolecule collections in which drugs are dissolved, entrapped, or conjugated to the surface. Several liposomal drug delivery systems have Active Targeting: Active targeting uses ligands bound to the NP surface to improve their uptake selectivity. These ligands can react with target cells and will often protect NPs from enzyme destruction. Ligands with a high binding affinity to the target cell will strongly increase delivery efficiency. The most basic form of active targeting involves functionalizing a NP with a ligand that binds to a molecule overexpressed on cancer cells. The issue with this, of course, is that healthy cells still express the same molecule, and as healthy cells greatly outnumber cancer cells most of the NPs miss their target. This issue can be mitigated by using multiple ligands or by using ligands of different types. Approaches to identify potential receptors in and on cancer cells include in vivo phage screening and aptamer screening . Using in vivo phage screening, F3 was dis- covered to bind well with nucleon, which is present at tumor cell surfaces and in tumor endothelial cells. The cytoplasmic proteins annexin-1 , plectin-1, and p32 protein were also found through in vivo phage screen- ing. By studying the expression of the known cell surface receptors in tumor vessels, other molecular markers can be detected. For example, dvß3, dvß5 integrins, and ED-B were discovered in angiogenic vessels using this principle. Gene expression analysis has also been used to discover overexpression of collagen in tumor endothelial cells. A detailed review on various markers and their discovery methods was given by Ruoslahti et al. Many antibodies have been approved for use in clinical treatment by the FDA, such as rituximab, ipilimumab, and trastuzumab . Antibodies are among the most studied ligands because of their high specificity and availability. An antibody conjugated dendrimer was found to bind exclusively to human prostate adenocarcinoma (LNCaP) cells that express PSmA. Although antibodies have many merits, they are difficult to conjugate to NPs, result in a short circulation time, and are expensive. Peptides are a promising alternative, as they are smaller, simpler, more stable, and easier to produce. Among peptides, RGD is often used due to its strong binding with avß3 integrin receptors. Nucleic acid base aptamers combine the advantages of both antibodies and peptides, but they degrade quickly. Other small molecules can also be used as ligands, such as folic acid for folate receptors. Such molecules are small, stable, and easy to produce. Unfortunately, ligand detection for relevant substrates is challenging. Even with proper binding ligands and receptors, binding incompatibility can limit therapeutic efficiency. Multiple ligands with different charges can increase overall the binding affinity, but the limited binding ability and capacity of receptors will govern the quantity and quality of the binding. For instance, overly strong binding can actually reduce tumor penetration, hinder selectivity, and lead to an overdose of carriers. Active targeting alters the natural distribution patterns of a carrier,

directing it to a specific organ, cell, or organelle. In contrast, passive targeting relies on the natural distribution of the drug and the EPR effect. Both of these processes depend on blood circulation and the location of initial drug delivery. However, no actively targeted NPs are commercially available currently.

Stimuli-Responsive Release:

Nanoparticles can be engineered to release their payload in response to internal (e.g., pH, enzymes) or external (e.g., light, magnetic fields) stimuli, ensuring that the drug is released at the tumor site.

Types of Nanoparticles

1. **Liposomes:**

Spherical vesicles with a phospholipid bilayer, widely used for drug encapsulation.

2. **Polymeric Nanoparticles:**

Made from biodegradable polymers like PLGA, offering controlled release of drugs.

3. **Metal Nanoparticles:**

Gold and silver nanoparticles used for their unique optical properties and ease of functionalization.

4. **Dendrimers:**

Branched, tree-like structures that offer high drug-loading capacity.

5. **Carbon Nanotubes:**

Cylindrical nanostructures used for their high surface area and ability to penetrate cells.

Advantages of Nanoparticles in Cancer Therapy

1. Enhanced Permeability and Retention (EPR) Effect: Tumors often have leaky vasculature and poor lymphatic drainage, which allows nanoparticles to accumulate more in tumor tissue compared to normal tissues.
2. Targeted Drug Delivery: Nanoparticles can be functionalized with ligands, antibodies, or peptides to specifically target cancer cells, minimizing damage to healthy cells.
3. Controlled Release: Nanoparticles can be designed to release their payload in response to specific stimuli such as pH, temperature, or enzymes present in the tumor microenvironment.
4. Improved Solubility and Stability : Many anticancer drugs have poor solubility and stability. Encapsulation in nanoparticles can enhance their solubility and protect them from degradation.

Current Advancements and Clinical Applications

1. Clinical Trials: Numerous nanoparticle-based formulations are in various stages of clinical trials. For instance, Abraxane (albumin-bound paclitaxel) has been approved for the treatment of breast cancer, non-small cell lung cancer, and pancreatic cancer.
2. Combination Therapies: Nanoparticles are being explored for co-delivery of multiple drugs, synergizing their therapeutic effects and reducing the likelihood of drug resistance.
3. Personalized Medicine: Advancements in genomics and proteomics are enabling the development of personalized nanoparticle therapies tailored to the molecular profile of an individual's tumor.

Challenges and Future Directions

1. Toxicity and Biocompatibility: Ensuring that nanoparticles are non-toxic and biocompatible remains a critical challenge.
2. Manufacturing and Scalability: Producing nanoparticles in a consistent and scalable manner is essential for clinical translation.
3. Regulatory Hurdles: Comprehensive regulatory guidelines are needed to address the unique aspects of nanoparticle-based therapeutics
4. Overcoming Biological Barriers: Enhancing the ability of nanoparticles to penetrate deep into tumor tissues and avoid rapid clearance by the immune system is an ongoing area of research.

CONCLUSION:

Nanoparticles represent a promising and versatile platform for the delivery of anticancer drugs. Their ability to enhance drug solubility, stability, and targeting while minimizing side effects makes them a valuable tool in the fight against cancer. Continued research and clinical development are essential to fully realize their potential and bring more nanoparticle-based therapies to patients. Nanoparticles have emerged as a revolutionary platform for the delivery of anticancer drugs, offering significant advantages over conventional therapies. Their unique properties, such as small size, large surface area, and the ability to be engineered for targeted delivery, make them ideal candidates for enhancing the efficacy and reducing the side effects of anticancer treatments. Nanoparticles represent a transformative advancement in anticancer drug delivery, with the potential to significantly improve treatment outcomes and quality of life for cancer patients. Continued interdisciplinary research and collaboration will be crucial in overcoming current limitations and realizing the full potential of nanoparticle- based therapies in oncology

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HOW TO CITE: Pagar Namrata , Nikam Harshada, Review On Nanoparticle : Nano Vehicles For Anticancer Drugs, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 10, 717-723. https://doi.org/10.5281/zenodo.13926263