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Review Article

Nanoparticles (NPs) Based Drug Delivery System: An Inspiring Therapeutic Strategy for Cancer Therapy and Their Future Prospects

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Abstract

Nanoparticles (NPs)-based drug delivery systems (DDs) have emerged as a promising strategy for cancer therapy, offering targeted, controlled, and efficient drug delivery while minimizing systemic toxicity. Their unique physicochemical properties, including high surface area, tunable size, and enhanced permeability, enable precise tumor targeting through passive, active, and stimuli-responsive mechanisms. The various nanocarriers such as liposomes, polymeric NPs, dendrimers, and metallic NPs have been extensively explored for chemotherapy, gene therapy, immunotherapy, and theranostic applications. The ability of NPs to overcome multidrug resistance (MDR), enhance drug bioavailability, and facilitate combination therapies has significantly improved treatment outcomes. Despite the remarkable advancements, challenges such as biocompatibility, large-scale production, and regulatory approval remain critical hurdles. Future research will focus on personalized nanomedicine, smart and multifunctional nanocarriers, gene-editing nanoparticle systems, and green nanotechnology for safer and more effective cancer treatments. The continuous evolution of NPs in cancer therapy holds immense potential to transform oncology, paving the way for patient-specific, minimally invasive, and highly efficient treatment modalities. This review article focuses on nanocarriers such as lipid-based, polymeric, and inorganic nanoparticles as a drug delivery system and their applications in cancer therapy. The current limitations and future perspectives of various nanoparticle-based DDS in cancer therapy are also discussed.

Keywords: *Drug delivery, Nanocarriers, NDDS, Sustained, Targeted*

INTRODUCTION

Targeted drug delivery involves directing therapeutic agents to accumulate at the desired site. Combining therapeutic drugs with nanoparticles and designing suitable targeting routes is a potential strategy to deliver many molecules to specific sites in the body. To achieve high targeting efficacy, the DDS must be retained in the physiological system for a suitable amount of time in order to target specific cells and tissues to release the given medicine while avoiding immune system destruction [1-3].

Nanoparticles are particulate dispersions or minute solid particles that range in size from 10-1000nm. The drug molecules are dissolved, entrapped, encapsulated, or linked to a nanoparticle matrix. Depending on the preparation method NPs, nanospheres, or nanocapsules are obtained. Nanocapsules are systems in which the drugs are confined to a cavity surrounded by a unique polymer membrane [3-4]. At the same time, nanospheres are matrix systems in which the drugs are physically and uniformly dispersed. In recent years, biodegradable polymeric nanoparticles, particularly those coated with a hydrophilic polymer such as polyethylene glycol (PEG) known as long-circulating particles, have been used as potential drug delivery system because of their ability to circulate for a prolonged period, targeting a specific organ, serving as a carrier of DNA in gene therapy, and delivering proteins, peptides, and genes [5-7].

Controlled drug delivery systems can overcome many of the disadvantages that conventional drug delivery systems face. For instance, chemotherapeutic agents used in cancer treatment are traditionally distributed non-specifically, harming both healthy cells and cancer cells, resulting in low effectiveness and high toxicities[8]. Controlled DDSs would be excellent carriers for chemotherapeutic agents, guiding the chemotherapeutic

agents to the tumor site thus increasing the drug concentration in cancer cells and averting toxicity in normal cells [9-10].

The advancement of nanotechnology has made nanoparticles a promising candidate for controlled drug delivery systems. When used as a DDS, NPs can improve the efficacy of the drug by increasing the drug half-life, improving the solubility for some hydrophobic drugs, and releasing the drug in a controlled or sustained fashion. Liposomes were the first discovered nanoparticles of DDS and were used as carriers for drugs and proteins in the 1960s. Since then, more and more materials have been fabricated into nanoparticles and used as DDS [11-12]. This review highlights the types of nanoparticles that can be used for cancer therapy, their therapeutic applications, current delivery strategies for cancer treatment, and the prospects and challenges of NPs in recent basic and clinical research were also discussed. Above all, NPs provide an inspiring therapeutic strategy for cancer treatment.

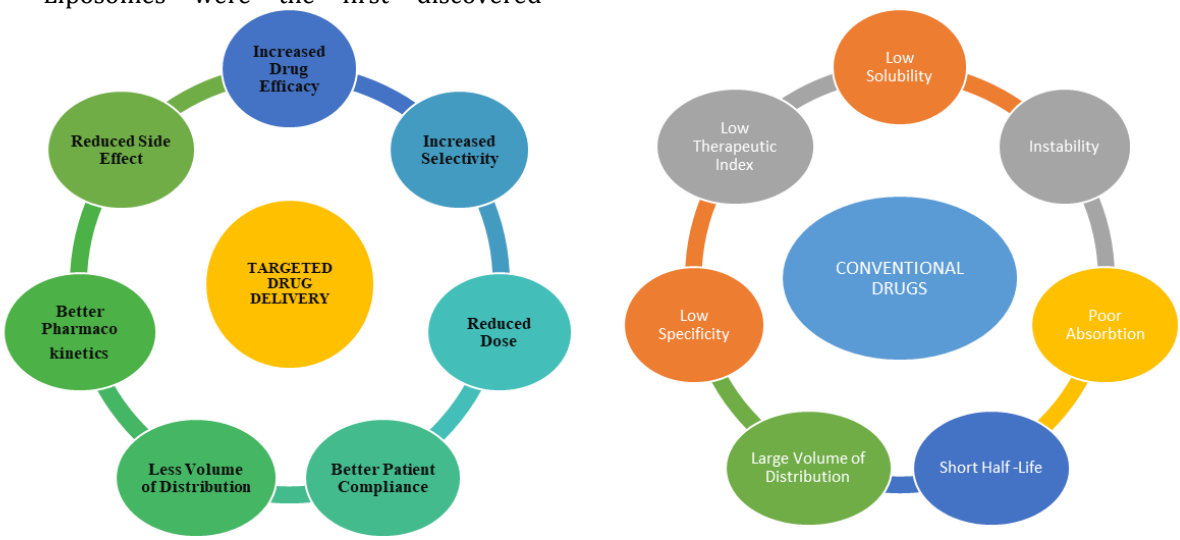

Figure 1: Advantages offered by targeted drug delivery compared with conventional dosage forms

The NPs used in medical treatment usually have specific sizes, shapes, and surface features as these three factors significantly impact the effectiveness of the nano-drug delivery process and, in turn, dictate therapeutic success [13]. NPs with a diameter range of 10 to 100 nm are commonly deemed appropriate for cancer therapy due to their capacity to efficiently transport medications and provide an increased permeability and retention (EPR) effect (Fig. 1). Larger particles over 100 nm are likely to be removed from circulation by phagocytes, while smaller particles (less than 1-2 nm) can readily leak from the normal vasculature to injure normal cells and can be quickly filtered by kidneys (less than 10 nm in diameter). Moreover, the surface characteristics of NPs can influence their bioavailability and half-life. NPs enhance the solubility, stability, and bioavailability (BA) of anticancer drugs, ensuring controlled and sustained drug release at the tumor site [14-15]. The various NP-based formulations, including liposomes, polymeric nanoparticles, dendrimers, and metallic NPs, have been developed to improve chemotherapy, gene therapy, and immunotherapy. Additionally, smart and stimuli-responsive NPs can release drugs in response to tumor-specific conditions such as pH, temperature, or enzymatic activity [16]. NPs are also widely used in photothermal and photodynamic therapies, where they enable selective tumor destruction through heat generation or reactive oxygen species (ROS) production. Furthermore, theranostic NPs combine diagnostic and therapeutic functions, enabling real-time imaging and personalized treatment monitoring. The continuous advancements in nanomedicine are paving the way for more effective, safe, and patient-specific cancer therapies [17-19].

1. MECHANISM OF TARGETED DRUG DELIVERY SYSTEM

A targeted drug delivery system is a system that delivers medication to its intended location while avoiding needless contact with other healthy tissue to minimize adverse effects. Unwanted effects on healthy cells result from non-targeted drug administration, including chemotherapeutic drugs used for cancer treatment [20-21]. Drug effects are more consistent, and dosage is reduced when they are delivered with targeting. The three-step technique for targeted drug release is: (i) Nanocarriers bind to the receptors of targeted cells through multivalent receptor-ligand interactions, (ii) Enter cells through endocytosis (iii), and release drugs during the last stage. Targeted drug delivery can take place in cytosol and cell membranes by interacting with lipid membranes [22-23].

The targeted drug delivery system is designed to enhance therapeutic efficacy while minimizing systemic toxicity by directing drugs specifically to diseased cells, such as cancerous tissues [24-25]. This mechanism relies on two major approaches: passive targeting and active targeting with their detail discussed as below:

1. **Passive Targeting:** This mechanism utilizes the enhanced permeability and retention (EPR) effect, a phenomenon in which nanoparticles (NPs) accumulate in tumor tissues due to leaky vasculature and poor lymphatic drainage. This allows drug-loaded NPs to remain in the tumor microenvironment for an extended period, enhancing treatment effectiveness.

2. **Active Targeting:** In this strategy, nanoparticles are functionalized with specific ligands, such as antibodies, peptides, aptamers, or folic acid, which bind to overexpressed receptors on cancer cells. This receptor-mediated endocytosis facilitates precise drug internalization into cancer cells, improving drug concentration at the target site and reducing off-target effects.
3. **Stimuli-Responsive Targeting:** Advanced drug delivery systems are designed to release drugs in response to specific tumor micro-environmental triggers, such as pH, temperature, redox potential, or enzyme activity. For example, pH-sensitive nanoparticles release their payload in the acidic tumor environment, ensuring site-specific drug activation.
4. **Nanocarrier-Based Delivery:** Various nanocarriers, such as liposomes, polymeric nanoparticles, dendrimers, and metallic nanoparticles, are employed to protect drugs from degradation, enhance bioavailability, and ensure controlled and sustained drug release [26-27].

By integrating these mechanisms, targeted drug delivery systems significantly improve therapeutic precision, reduce drug resistance, and enhance patient outcomes in diseases like cancer.

2. CLASSIFICATION OF NANOCARRIERS UTILIZED IN THE TREATMENT OF CANCER

The main objective of designing nanocarriers is to regulate the surface area, surface properties, and particle size for drug delivery systems so that the NPs containing an appropriate amount of drugs can show the desired pharmacological activity by releasing active ingredients to specific sites of action [28-29]. A few potential advantages of nanocarriers are the ability to overcome several ingrained obstacles *in vivo*, the improvement of a drug's pharmacodynamic and pharmacokinetic properties without altering its molecular structure, and the targeted and non-targeted drug delivery in the nucleus, cytosol, etc. [30].

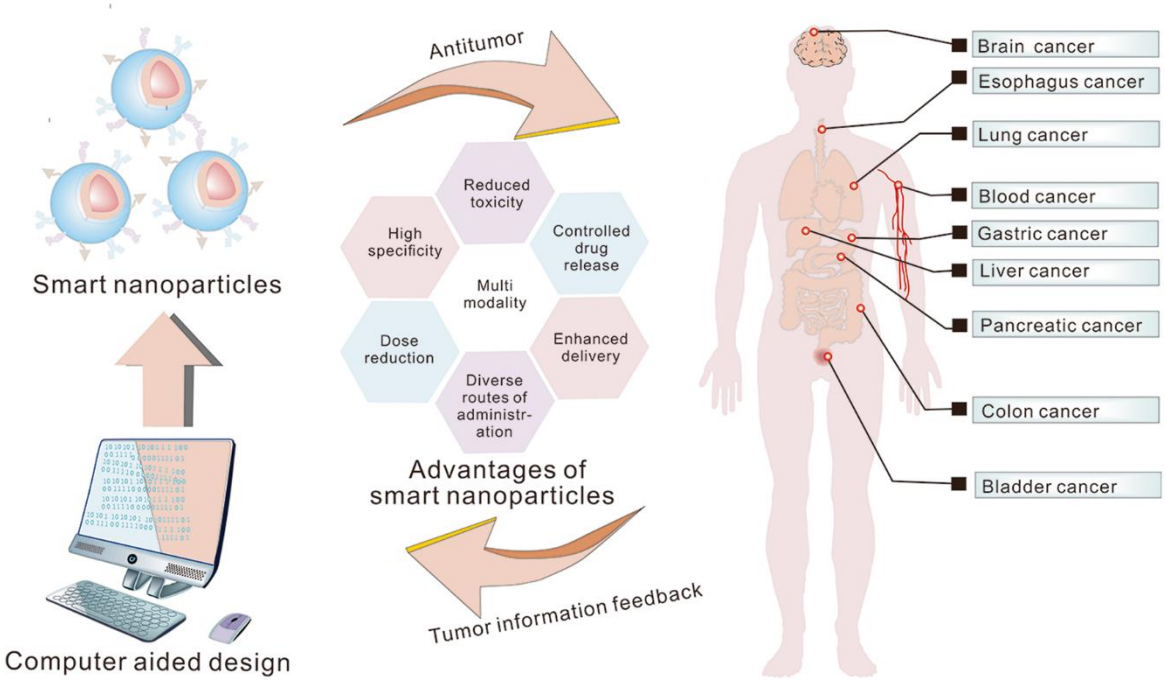

Figure 2: NPs used in the treatment of several types of cancer

1) Lipid-Based Nanoparticles

Lipid-based nanoparticles are made up of an internal water chamber surrounded by at least one lipid bilayer. The liposomes having lipid bilayers can combine with other bilayers, promoting the release of their contents, and making them useful applications for drug delivery (Fig. 2). Lipid-based NPs are regarded as one of the important drug delivery systems because of their many benefits including simple formulation, self-assembly, biocompatibility, high bioavailability and improved physiochemical characteristics to regulate their biological uses. Liposomes, SLNs, NLCs, and lipid polymer hybrid NPs are the four most prevalent forms of lipid-based nanoparticles used in drug delivery [31-32].

a) Liposomes

Liposomes consist of a spherical shape comprising an amphipathic phospholipid bilayer and an inner aqueous core. Their core-shell nanostructure allows them to encapsulate both hydrophobic and hydrophilic molecules effectively (Fig. 3). The lipophilic bilayers of the shell typically encapsulate hydrophobic drugs, while hydrophilic drugs generally are entrapped in the aqueous phase of the core [33]. Liposomes can transport large molecules like various nucleic acids, proteins, and imaging agents, making them a versatile method for delivering drugs [34-35].

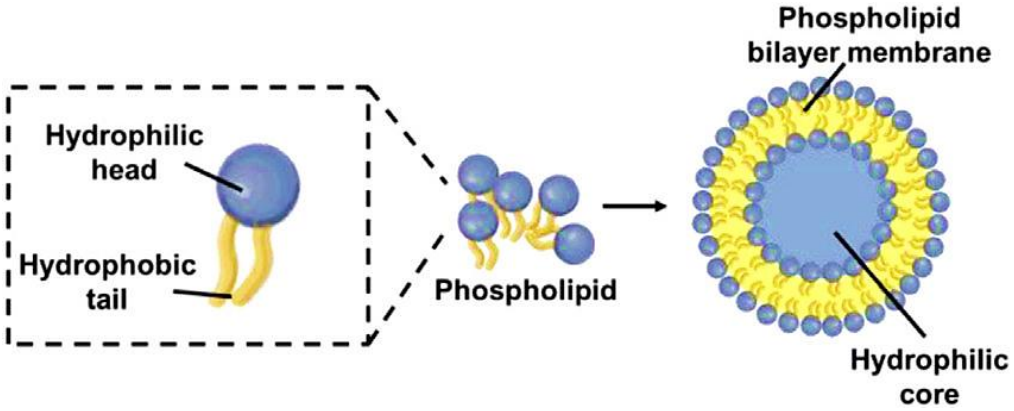

Figure 3: Schematic representation of liposome and their structure with composition [36]

Liposomes are recognized as a versatile system for delivering drugs, offering benefits such as quick absorption, enhanced drug availability in the body, decreased toxicity, and protection against oxidation and hydrolysis. However their limited bio stability, the potential for drug release, and short half-lives make them unsuitable for clinical use [37]. Many strategies have been developed to address these issues, such as targeted liposomes with surface-attached ligands and "stealth" liposomes encased in biocompatible polymers like PEG to prevent immune response triggering [38].

b) SOLID LIPID NANOPARTICLES (SLNPs)

The size of solid lipid nanoparticles (SLNs) ranges from 50-1000 nm and are prepared by melting solid lipids in water and adding an emulsifier to create a stable solution. Heat-sensitive drugs, have poor physicochemical compatibility, and low pharmacokinetic profile can be transported using solid lipid nanoparticles (SLNs). SLNPs consist of fully crystallized lipid components with a highly ordered crystalline structure containing drugs and emulsifiers [39-40]. SLNs provide many advantages, such as improved NPs stability, efficient drug protection, controlled release, and customizable properties through lipid component adjustments [41]. SLNs also offer multiple technological advantages, which include protecting drugs from chemicals, increased physical stability, easy scalability of production, simplified sterilization processes, and the capability to co-deliver two active agents. The significant results have been obtained when solid lipid nanoparticles were utilized as drug delivery systems for chemotherapeutic drugs, especially in the therapy of colorectal cancer and malignant melanoma [42-44]. These nano-systems not only exhibit antitumor effects but also can prevent human umbilical vein endothelial cells from adhering to cancer cell lines originating from human colon-rectum, breast, prostate cancers, and melanoma [45-46].

c) Nanostructured Lipid Carrier (NLC)

Nanostructured Lipid Carriers (NLCs) are produced from a blend of liquid and solid lipids, however at body temperature, the particles are solid. When combined, lipids may produce a variety of shaped solid matrices, including lipid drug conjugate NPs (LDC) and nanostructured lipid carriers (NLC), which are designed to increase drug loading capacity [47-48]. The NLC represents a promising method for delivering drugs, offering better drug retention and increased drug loading capability. If the lipid matrix is made up of similar molecules, these structural characteristics can lead to drug expulsion during storage, which can result in an inadequate loading capacity [49]. However, it can also allow for higher drug loading capacities and improved drug release kinetics when compared to SLNs [50].

d) Lipid Polymer Hybrid Nanoparticles

Lipid polymer hybrid nanoparticles (LPHNPs) are core-shell nanostructures that are composed of at least two types of materials to achieve multifunction or to address the limitations of single-component nanomaterials, combining the advantages of the two individual components [51-52]. The hybrid structural design offers the advantages of simultaneous loading of hydrophilic and hydrophobic drugs in the same nanoparticle. Moreover, the surface functionality can be tuned with various ligands such as peptides and monoclonal antibodies. It consists of a lipid core enveloped by polymeric layer, Hybrid lipid-polymeric NPs offer excellent stability, prolonged release, and strong biocompatibility due to the combination of lipid and polymer characteristics [53]. In most cases drugs are cytotoxic so targeted delivery is the only strategy to fight against cancer (Fig. 4). The scope of LPHNPs application has extended beyond a single DDs for anticancer therapy and confirmed that it is a better delivery route and has a good cellular delivery efficacy for cancer treatment in which multiple therapeutic agents (both hydrophilic and hydrophobic) can be administered simultaneously [54-55].

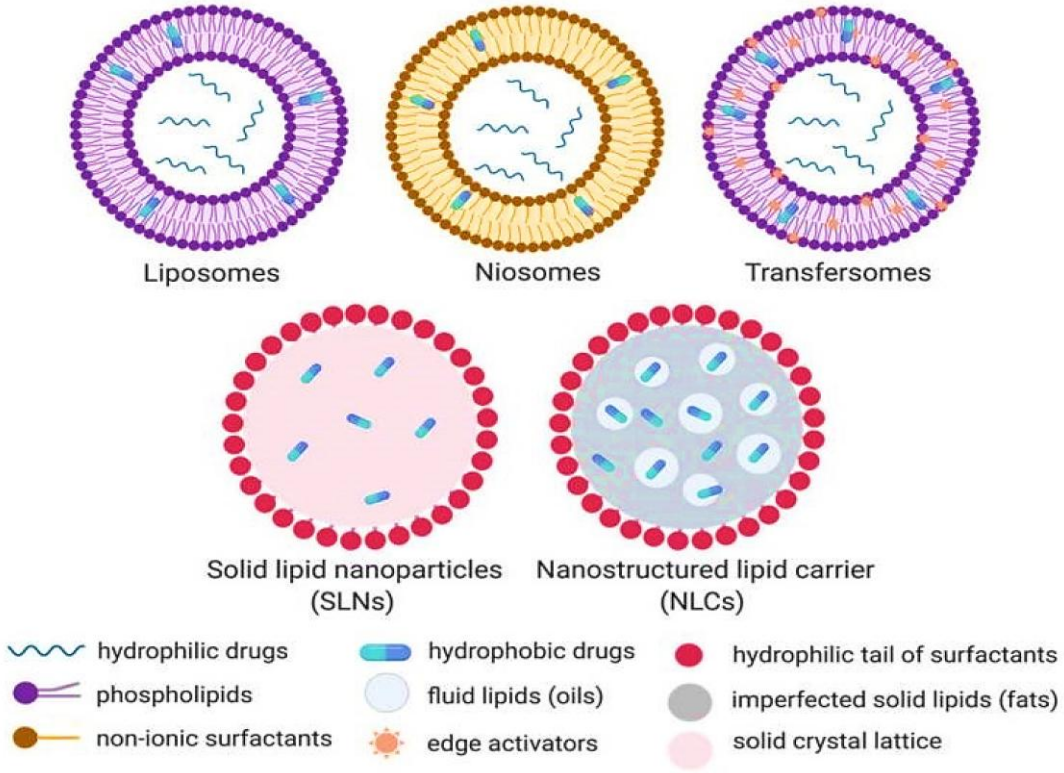

Figure 4: Schematic representation of lipid-based nanoparticles and their types [56]

2) Polymeric Nanoparticles

Polymeric NPs are colloidal solid particles with a size range of (10-1000 nm) made from natural and synthetic polymers, have received the majority of attention due to their stability and ease of surface modification. The polymer characteristics and surface chemistry can be adjusted to create custom DDS that control drug release and target specific diseases [57-58]. The different types of polymeric NPs are nanocapsules, which consist of cavities surrounded by polymer membranes, and nanospheres that are solid matrix systems.

3) Inorganic Nanoparticles

Inorganic nanoparticles have particular properties like SPR (surface plasmon resonance) that organic nanoparticles do not possess. The DDS has various advantages, including excellent biocompatibility, high stability, and surface functionalization [59]. Animal cell experiments have shown that the metal cores of NPs exhibit minimum cytotoxicity and remain stable during intake and targeting of organs, with minimal interactions with the surroundings. However, significant efforts are required to increase the solubility and decrease the toxicity of these materials, particularly when heavy metals are involved in the preparation system [60-61].

(a) Quantum Dot: The quantum dots are semiconductor nanocrystals ranging from 2 to 10 nm, comprising inorganic core shell nanocrystals with unique electronic, optical and structural properties and aqueous organic coated shell. The core nanocrystals of QDs determine the colour emitted, while the external aqueous layer can be used for attachment of biomolecules like peptides, protein, or DNA. It has a unique photophysical properties that allow for visualization of tumors while the drug is being delivered at the targeted site [62-63].

(b) Gold Nanoparticles: In gold NPs (AuNPs) drugs can be conjugated to surfaces via ionic or covalent bonding and they can deliver them and control their release through biological stimuli or light activation. Gold NPs are viewed as having significant promise in targeted drug delivery diagnosis due to their large specific surface area, surface plasmon resonance, stable properties, surface chemistry, and ability to be multi-functionalized [64-65].

(c) Iron Oxide Nanoparticles: Iron oxide NPs exhibit core dimensions ranging from 10 to 100 nm. Their distinctive characteristics, including small size, elevated surface-to-volume ratio, and magnetic properties, make them suitable for targeted drug delivery systems. To enhance their biocompatibility and stability in physiological environments, the surfaces of these magnetic NPs are typically coated with materials like polysaccharides or smaller carbohydrates, providing the final product with a robust core [66]. A key use of these nanoparticles is as contrast agents in MRI scans, which facilitate precise tumor localization, staging, and assessment of treatment responses.

Nanocarriers have revolutionized cancer therapy by enabling precise drug delivery, improving BA, and reducing systemic toxicity. These nanocarriers are broadly classified into lipid-based, polymeric, inorganic,

and hybrid systems. Lipid-based nanocarriers, such as liposomes and solid lipid nanoparticles (SLNs), provide biocompatibility and controlled drug release, making them widely used for chemotherapy. Polymeric NPs, including dendrimers and micelles, offer high drug-loading capacity, enhanced stability, and stimuli-responsive properties, enabling targeted therapy. Inorganic nanocarriers, such as gold NPs, quantum dots, and iron oxide NPs, are employed for theranostics, combining imaging and therapy. Hybrid nanocarriers integrate organic and inorganic materials to enhance multi-functionality, allowing for combination therapies like chemo-photothermal or immunotherapy [65-67].

3. THERAPEUTIC APPLICATION OF NPs FOR CANCER THERAPY

Traditional therapies have several drawbacks regarding their effectiveness and adverse effects due to uneven distribution and toxic effects. Thus, careful dosage is necessary to eradicate cancer cells with minimal toxicity effectively. For the drug to reach its target, it must navigate several barriers as the process of drug metabolism is highly complicated [68]. Under physiological conditions, the drug needs to pass through the tumor microenvironment (TME), reticulo endothelial system (RES), and blood-brain barrier (BBB), and undergo kidney filtration. The RES, or macrophage system, comprises blood monocytes, macrophages, and additional immune cells. The mononuclear phagocyte system (MPS) in the liver, spleen, or lungs interacts with the drugs and activates macrophages or leukocytes that quickly eliminate the drug [69-70].

Nanoparticles (NPs) have revolutionized cancer therapy by enabling targeted, controlled, and efficient drug delivery while minimizing systemic toxicity. Their versatility allows for various therapeutic applications, enhancing treatment efficacy and overcoming challenges associated with conventional chemotherapy [71].

1. **Targeted Drug Delivery**: NPs can be functionalized with ligands (such as antibodies, peptides, or aptamers) that recognize and bind to specific cancer cell receptors, ensuring precise drug delivery while sparing healthy tissues. This targeted approach enhances therapeutic efficacy and reduces adverse effects.
2. **Chemotherapy Enhancement**: NPs improve the solubility, stability, and BA of chemotherapeutic agents, allowing for controlled and sustained drug release. Nano-formulations such as liposomes and polymeric NPs encapsulating drugs like doxorubicin and paclitaxel have demonstrated increased tumor accumulation and reduced systemic toxicity.
3. **Gene and RNA-Based Therapy**: NPs serve as effective carriers for gene-editing tools (e.g., CRISPR/Cas9), small interfering RNA (siRNA), and messenger RNA (mRNA) to target cancer-related genes. This approach offers precise genetic intervention, reducing tumor growth and resistance to chemotherapy [72-73].
4. **Photothermal and Photodynamic Therapy (PTT/PDT)**: Metallic and hybrid NPs, such as gold and silica-based nanomaterials, can absorb near-infrared (NIR) light, generating localized heat to destroy tumor cells (PTT) or activating photosensitizers for reactive oxygen species (ROS) production to induce cell death (PDT).
5. **Immunotherapy and Vaccine Delivery**: NPs play a crucial role in cancer immunotherapy by delivering immune-modulating agents, enhancing antigen presentation, and stimulating the body's immune response. Lipid-based NPs have been explored for cancer vaccine formulations, boosting anti-tumor immunity.
6. **Overcoming Multidrug Resistance (MDR)**: NP-based drug delivery systems help bypass drug efflux mechanisms in resistant cancer cells, ensuring sustained intracellular drug accumulation. Surface-modified NPs can inhibit drug transporters, enhancing the efficacy of chemotherapeutic agents.
7. **Combination Therapy Platform:** Multifunctional NPs enable the co-delivery of multiple therapeutic agents, such as chemotherapy combined with immunotherapy or photothermal therapy, leading to synergistic effects and improved treatment outcomes [74-75].
8. **Tumor Imaging and Theranostics**: NPs incorporating contrast agents (such as quantum dots, iron oxide, or gold NPs) provide real-time tumor imaging for early diagnosis and therapy monitoring. Theranostic NPs combine diagnostic and therapeutic functionalities, allowing personalized treatment strategies.

The integration of nanotechnology in cancer therapy continues to evolve, with promising advancements in personalized medicine, smart drug delivery, and combination therapies, paving the way for more effective and less toxic cancer treatments. The drug delivery nanoparticles can be used in cancer therapy to achieve controlled drug release and disease-specific localization by tuning the various characteristics and surface chemistry [75-77]. Because of their small size, nanoparticles can extravasate through the endothelium in inflammatory sites, epithelium (e.g., intestinal tract and liver), tumors, or microcapillaries.

4. APPLICATIONS OF NANOPARTICLES (NPs)

NPs have emerged as powerful tools across various scientific and industrial fields due to their unique physicochemical properties, such as high surface area, tunable size, and enhanced reactivity. In medicine, NPs play a crucial role in drug delivery, targeted cancer therapy, gene therapy, and imaging, improving treatment efficacy while minimizing side effects. In diagnostics, quantum dots and magnetic NPs enable precise disease detection and bioimaging [78]. NPs aid in wastewater treatment, pollutant removal, and air purification due to their superior adsorption and catalytic properties.

- **Tumor targeting using the nanoparticulate delivery system:** The reasoning behind utilizing

nanoparticles for targeting tumors relies on two main points: (1) NPs can deliver a concentrated drug dose directly to tumor locations due to the enhanced permeability and retention effect associated with active nanoparticles. (2) By confining drug distribution to target organs, NPs can minimize the exposure of healthy tissues to the drug. An experiment involving mice showed that those treated with doxorubicin encapsulated in poly (isohexylcynoacrylate) nanospheres had a greater concentration of doxorubicin in the liver, spleen, and lungs compared to mice that received free doxorubicin.

- **Nanoparticles for gene delivery:** Polynucleotide vaccines work by delivering genes encoding relevant antigens to host cells where they are expressed. The antigenic protein is produced within the vicinity of professional antigen-presenting cells to initiate an immune response. Such vaccines produce both humoral and cell-mediated immunity because intracellular protein production, as opposed to extracellular deposition, stimulates both aspects of the immune system.
- **Nanoparticle for drug delivery into the brain:** The blood-brain barrier (BBB) is a biological barrier that is challenging for conventional therapeutics to treat central nervous system (CNS) diseases. The BBB is a highly selective and semipermeable endothelial cell line that protects the brain from being invaded by foreign pathogens and unwanted substances in circulation. The blood-brain barrier is comprised of endothelial cells, pericytes, astrocytes, and a basal membrane. Molecules can cross the BBB by diffusion mechanisms as long as the molecules are lipophilic, not ionizable at physiological pH, and have a size below 400 kD. Due to their small size and design, nanoparticles can penetrate through tight junctions in the BBB and protect the drug from enzymatic degradation [76-80].

The food and agriculture sector benefits from NPs for food packaging, antimicrobial coatings, and nano-fertilizers, improving crop yield and shelf life. Additionally, NPs have revolutionized electronics, cosmetics, and textiles by enhancing conductivity, UV protection, and durability. Their widespread applications continue to expand, driving innovation in multiple disciplines [80].

5. CURRENT CHALLENEGS, LIMITATIONS & FUTURE PRESPECTIVES

The NPs is a promising drug delivery system designed to improve the pharmacological and therapeutic properties of conventional drug. The remarkable advancements in nanoparticles (NPs)-based drug delivery systems for cancer therapy, several challenges and limitations hinder their widespread clinical application:

1. **Stability and Scalability**: Many NPs face stability issues, aggregation, and degradation during storage and circulation. Large-scale, cost-effective production with reproducible quality remains a significant hurdle.
2. **Toxicity and Biocompatibility**: While NPs aim for targeted delivery, unintended toxicity and long-term biocompatibility concerns persist, necessitating thorough preclinical and clinical evaluations.
3. **Targeting Efficiency**: Achieving precise tumor targeting remains challenging due to biological barriers like the reticuloendothelial system (RES) clearance, off-target distribution, and heterogeneity of tumors.
4. **Regulatory and Approval Complexities**: The translation of NP-based therapeutics from bench to bedside is slow due to stringent regulatory requirements, lack of standardized evaluation criteria, and extensive safety testing.
5. **Cost and Manufacturing Issues**: The high cost of NP synthesis, purification, and functionalization, along with complex manufacturing techniques, limits their affordability and scalability.
6. **Drug Loading and Release Control**: The some NPs struggle with low drug-loading capacity and uncontrolled release, affecting therapeutic efficiency and dosing precision.
7. **Immunogenicity and Clearance**: NPs can trigger immune responses, leading to rapid clearance from the body, which reduces their circulation time and therapeutic impact [81-82].

These limitations through innovative formulations, advanced nanomaterial engineering, and interdisciplinary collaborations will be crucial for the successful clinical translation of NPs in cancer therapy [83]. The future of NPs-based drug delivery systems in cancer therapy is highly promising, with ongoing advancements aimed at overcoming current challenges and enhancing therapeutic efficacy discussed as below:

[A]. Personalized and Precision Nanomedicine: The future of cancer therapy lies in personalized and precision nanomedicine, where nanoparticles (NPs) are tailored based on an individual's genetic and proteomic profile. The integration of genomics and proteomics will allow the identification of specific biomarkers that can be targeted using engineered NPs, enhancing therapeutic efficiency. Artificial intelligence (AI) and machine learning algorithms will play a crucial role in optimizing NP formulations, predicting patient responses, and improving drug delivery strategies. This approach will help minimize adverse effects, improve drug BA, and maximize treatment success, ultimately transforming cancer therapy into a more patient-specific and effective approach.

[B]. Smart and Stimuli-Responsive NPs: Future advancements in nanotechnology will focus on the development of smart and stimuli-responsive NPs that can react to specific tumor micro-environmental conditions. These NPs will be designed to release drugs in response to factors such as pH changes, enzymatic activity, or temperature variations within the tumor site. This targeted drug release mechanism enhances

therapeutic efficacy while reducing systemic toxicity and off-target effects. By integrating stimuli-responsive polymers, nanocarriers will provide precise spatiotemporal control over drug delivery, improving treatment outcomes and minimizing adverse reactions in cancer patients [84-85].

[C]. Hybrid and Multifunctional Nanocarriers: The development of hybrid and multifunctional nanocarriers will revolutionize cancer therapy by combining the advantages of different nanomaterials. For instance, hybrid NPs incorporating liposomes with polymeric or metallic nanoparticles can offer enhanced drug-loading capacity, controlled release, and increased stability in physiological conditions. These multifunctional platforms can also enable combination therapies, such as chemo-photothermal therapy or immunotherapy, for improved therapeutic effects. Integrating various functional elements into a single nanocarrier, hybrid NPs can simultaneously target tumors, deliver drugs efficiently, and provide real-time imaging capabilities, paving the way for next-generation cancer treatment strategies.

[D]. Overcoming Biological Barriers: One of the critical challenges in NP-based drug delivery is overcoming biological barriers that limit drug accumulation at tumor sites. To address this, researchers are developing stealth NPs with biomimetic coatings such as cell membranes or polyethylene glycol (PEGylation) to evade immune detection and prolong systemic circulation. These engineered NPs can efficiently penetrate solid tumors by utilizing active targeting ligands or size-controlled transport mechanisms. Improving circulation time, reducing rapid clearance by the reticuloendothelial system (RES), and enhancing tumor selectivity, stealth NPs will significantly improve the efficacy of nanoparticle-based cancer therapies, leading to better clinical outcomes [86-87].

CONCLUSION

Nanoparticles (NPs)-based drug delivery systems have emerged as a revolutionary approach in cancer therapy, offering targeted, controlled, and efficient drug delivery with minimized systemic toxicity. These nanoscale carriers enhance drug solubility, prolong circulation time, and improve bioavailability, leading to better therapeutic outcomes. The various nano-platforms, including liposomes, polymeric nanoparticles, dendrimers, and metallic nanoparticles, have shown remarkable potential in overcoming multidrug resistance and enhancing tumor penetration. Despite significant progress, challenges such as large-scale production, stability, and regulatory approvals remain hurdles for clinical translation. Future advancements in nanomedicine, integrating personalized therapy, artificial intelligence, and smart nanocarriers, hold immense promise for optimizing cancer treatment and improving patient outcomes.

List Of Abbreviations

NPs: Nanoparticles; **BA:** Bioavailability; BBB: blood-brain barrier; **CNS:** Central Nervous System; **AI:** Artificial Intelligence; **RES:** Reticuloendothelial System; **DDS:** Drug delivery system.

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