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NANOPARTICLE MEDIATED DRUG DELIVERY SYSTEMS FOR CANCER TREATMENT

Chapter 1: Introduction to Cancer and Targeted Drug Delivery Systems (TDDS)

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Abstract

Cancer is a complex disease characterized by uncontrolled cell growth, invasion, and metastasis. Conventional treatment approaches, including surgery, chemotherapy, radiotherapy, and immunotherapy, often suffer from limitations such as systemic toxicity, poor selectivity, and drug resistance. Targeted Drug Delivery Systems (TDDS) have emerged as an effective strategy to overcome these challenges by delivering therapeutic agents directly to tumor tissues while minimizing damage to healthy cells. This chapter discusses cancer biology, tumor microenvironment, principles of passive and active targeting, various drug delivery carriers, and the applications of TDDS in cancer therapy. Recent advances in nanotechnology and precision medicine are also highlighted, emphasizing the potential of TDDS to improve therapeutic efficacy and patient outcomes.

Keywords: Tumor Microenvironment, Passive Targeting, Active Targeting, Nanotechnology, Drug Delivery Carriers, Precision Medicine, Nanomedicine.





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1. Introduction

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells that can invade surrounding tissues and metastasize to distant organs. It is one of the leading causes of death worldwide and results from genetic mutations, epigenetic changes, and interactions with the tumor microenvironment. Conventional cancer treatments, including surgery, chemotherapy, radiotherapy, and immunotherapy, have improved patient outcomes but are often associated with limitations such as non-specific drug distribution, systemic toxicity, poor bioavailability, and drug resistance. These challenges can reduce treatment effectiveness and negatively impact patient quality of life.

Targeted Drug Delivery Systems (TDDS) have emerged as an innovative approach to overcome these limitations by delivering therapeutic agents directly to tumor tissues while minimizing damage to healthy cells. Advances in nanotechnology and biotechnology have enabled the development of various targeted carriers, such as liposomes, nanoparticles, micelles, dendrimers, and antibody–drug conjugates. This chapter discusses the fundamentals of cancer, the limitations of conventional therapies, and the role of TDDS in improving cancer treatment and advancing precision medicine (1).

1.1 Overview of Cancer

Cancer is a group of diseases characterized by the uncontrolled growth, division, and spread of abnormal cells within the body. Under normal physiological conditions, cell growth and death are tightly regulated to maintain tissue homeostasis. However, genetic and epigenetic alterations can disrupt these regulatory mechanisms, leading to the transformation of normal cells into malignant cells. These cancerous cells acquire the ability to proliferate uncontrollably, invade adjacent tissues, and metastasize to distant organs through the remains one of the leading causes of morbidity and mortality worldwide, affecting individuals of all ages and socioeconomic backgrounds. The disease can originate in almost any tissue or organ and is influenced by a combination of genetic, environmental, lifestyle, and infectious factors. Advances in molecular biology have significantly improved the understanding of cancer pathogenesis, enabling the development of targeted and personalized therapeutic strategies (2).

2. Definition and Characteristics of Cancer

2.1 Definition

Cancer is a pathological condition in which abnormal cells divide uncontrollably and possess the capacity to invade surrounding tissues and spread to other parts of the body. The process of





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cancer development, known as carcinogenesis, involves multiple genetic mutations and cellular alterations that progressively transform normal cells into malignant cells.

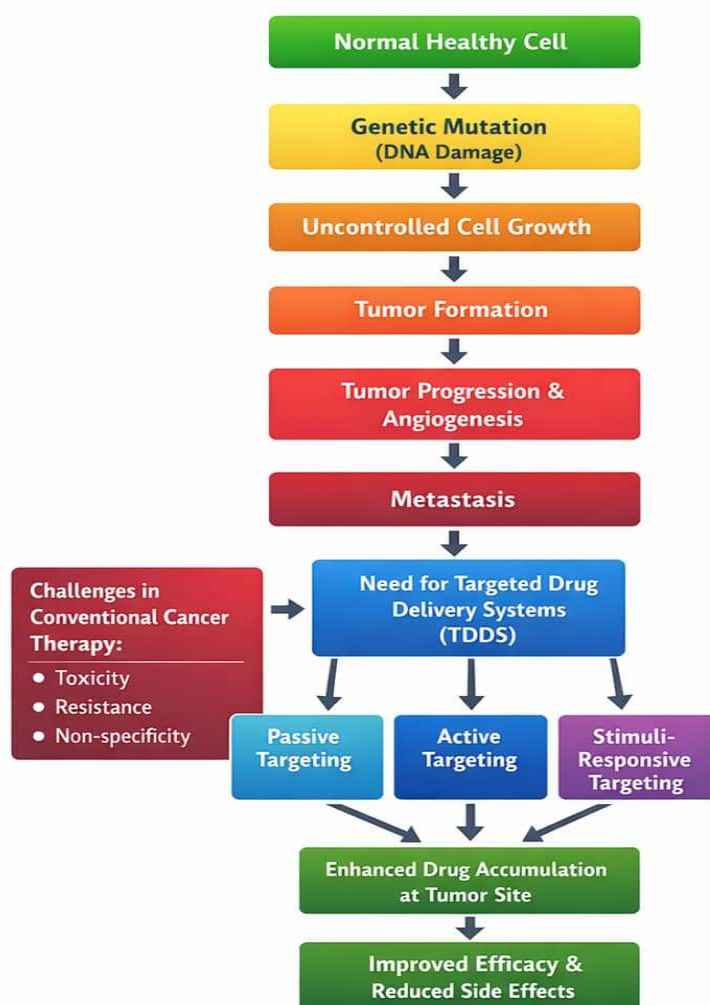


Fig.1 Development of Cancer and Role of Targeted Drug Delivery Systems

2.2 Characteristics of Cancer

Cancer is characterized by uncontrolled cell proliferation, resistance to apoptosis, sustained angiogenesis, invasion and metastasis, genomic instability, immune evasion, and altered cellular metabolism. Cancer cells continuously divide due to disruption of normal growth-control mechanisms and avoid programmed cell death, resulting in abnormal tumor growth. As tumors develop, they stimulate the formation of new blood vessels to obtain oxygen and nutrients. Malignant cells can invade surrounding tissues and spread to distant organs through





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the blood or lymphatic system. Genetic mutations and chromosomal abnormalities contribute to genomic instability and tumor progression. Cancer cells can also evade immune-system recognition and destruction. In addition, they undergo metabolic changes, such as increased glucose utilization, to meet the energy and biosynthetic demands of rapid growth and survival (3).

2.3 Classification of Cancer

Cancer can be classified based on the tissue or cell type from which it originates.

Table 1 Classification of Cancer

Type of Cancer	Origin	Examples
Carcinoma	Epithelial tissues (skin and organ linings)	Breast cancer, Lung cancer, Colorectal cancer
Sarcoma	Connective and supportive tissues	Osteosarcoma, Liposarcoma
Leukemia	Blood-forming tissues and bone marrow	Acute Myeloid Leukemia (AML), Chronic Lymphocytic Leukemia (CLL)
Lymphoma	Lymphatic system	Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma
Myeloma	Plasma cells of bone marrow	Multiple Myeloma
Melanoma	Melanocytes (pigment-producing cells)	Cutaneous Melanoma
Central Nervous System (CNS) Tumors	Brain and spinal cord tissues	Glioblastoma, Astrocytoma

Among these categories, carcinomas are the most prevalent and account for the majority of cancer cases worldwide. The classification of cancer is essential for diagnosis, prognosis, treatment selection, and the development of targeted drug delivery strategies (4).





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3. Cancer Progression and Tumor Microenvironment

Cancer progression is a multistep process through which normal cells undergo genetic and molecular alterations, leading to the formation of malignant tumors capable of invasion and metastasis. This process involves continuous interactions between cancer cells and their surrounding environment, collectively known as the tumor microenvironment (TME). The progression of cancer is influenced by genetic mutations, cellular signalling pathways, immune responses, and various stromal components that support tumor growth and survival.

The tumor microenvironment plays a crucial role in cancer development by providing structural support, nutrients, growth factors, and signalling molecules that promote tumor progression. Understanding the mechanisms of cancer progression and the characteristics of the tumor microenvironment is essential for developing effective targeted therapies and advanced drug delivery systems (5).

3.1 Stages of Cancer Progression

1. Initiation

Initiation is the first stage of carcinogenesis, during which normal cells undergo irreversible genetic mutations caused by carcinogens, radiation, viral infections, or spontaneous DNA damage.

2. Promotion

During promotion, initiated cells undergo selective proliferation due to growth-promoting stimuli. At this stage, abnormal cells begin to multiply but remain localized.

3. Progression

The progression stage involves the accumulation of additional genetic and epigenetic alterations, resulting in increased cellular proliferation, resistance to apoptosis, and tumor formation.

4. Angiogenesis

As tumors grow beyond a certain size, they require a blood supply for oxygen and nutrients. Tumor cells secrete angiogenic factors such as vascular endothelial growth factor (VEGF), stimulating the formation of new blood vessels.





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5. Invasion and Metastasis

Cancer cells acquire the ability to invade surrounding tissues and spread to distant organs through blood vessels or the lymphatic system. Metastasis is responsible for the majority of cancer-related deaths.

3.2 Tumor Microenvironment (TME)

The tumor microenvironment refers to the complex ecosystem surrounding cancer cells. It consists of both cellular and non-cellular components that interact dynamically with tumor cells (6).

Cellular Components

- Cancer cells
- Cancer-associated fibroblasts (CAFs)
- Immune cells (macrophages, T cells, neutrophils)
- Endothelial cells
- Pericytes

Non-Cellular Components

- Extracellular matrix (ECM)
- Growth factors
- Cytokines and chemokines
- Oxygen and nutrient gradients
- Extracellular vesicles

3.3 Role of Tumor Microenvironment in Cancer Progression

The tumor microenvironment (TME) plays a crucial role in the initiation, progression, and spread of cancer. It consists of cancer cells, stromal cells, immune cells, blood vessels, extracellular matrix (ECM), growth factors, and signalling molecules that interact dynamically to support tumor development. The TME promotes tumor growth by providing growth factors and cytokines that stimulate cancer cell proliferation, survival, and progression. These signalling molecules create favorable conditions that enable tumor cells to thrive and evade normal regulatory mechanisms.

A major function of the TME is the promotion of angiogenesis, the process by which new blood vessels are formed. Tumor cells secrete angiogenic factors, such as vascular endothelial growth





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factor (VEGF), which stimulate the development of blood vessels that supply oxygen and nutrients essential for rapid tumor growth. In addition, the TME facilitates metastasis through extracellular matrix remodelling and the release of various enzymes and signalling molecules that enhance cancer cell migration and invasion into surrounding tissues and distant organs.

The tumor microenvironment also contributes to immune evasion by suppressing immune responses and preventing the effective recognition and destruction of cancer cells by the immune system. Through complex interactions with immune cells, tumors can create an immunosuppressive environment that supports their survival. Furthermore, the TME plays a significant role in the development of drug resistance by forming physical and biological barriers that limit drug penetration and reduce therapeutic effectiveness. These barriers often hinder the successful delivery of anticancer agents to tumor tissues, leading to reduced treatment efficacy and disease recurrence. Therefore, understanding the role of the tumor microenvironment is essential for the development of effective targeted therapies and advanced drug delivery systems for cancer treatment (7).

3.4 Significance of Tumor Microenvironment in Targeted Drug Delivery

The unique characteristics of the tumor microenvironment provide opportunities for targeted drug delivery. Features such as abnormal vasculature, acidic pH, hypoxia, and overexpressed receptors can be exploited to enhance selective drug accumulation within tumors. Modern targeted drug delivery systems are designed to interact with these tumor-specific features, thereby improving therapeutic efficacy while minimizing systemic toxicity. Understanding the interactions between cancer cells and the tumor microenvironment is essential for the development of advanced nanocarriers, ligand-mediated targeting systems, and stimuli-responsive drug delivery platforms for cancer therapy (8).

Conventional Cancer Therapies and Their Limitations

Conventional cancer therapy refers to the traditional treatment approaches used to eliminate cancer cells, control tumor growth, and improve patient survival. The major conventional treatment modalities include surgery, chemotherapy, radiotherapy, hormone therapy, and immunotherapy. These therapies have formed the cornerstone of cancer management for many decades and continue to play an important role in clinical practice.

Surgery is one of the oldest and most effective treatment methods for localized cancers. It involves the physical removal of tumors and surrounding affected tissues, providing immediate reduction of tumor burden and aiding in diagnosis and staging.





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Chemotherapy utilizes cytotoxic drugs to destroy rapidly dividing cancer cells. It is commonly used for both localized and metastatic cancers and may be administered alone or in combination with other therapies. Chemotherapeutic agents act by interfering with DNA replication and cell division, leading to cancer cell death.

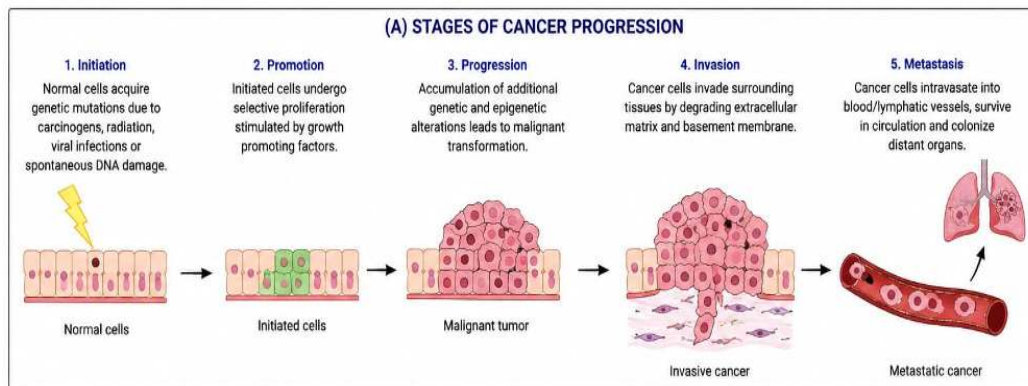


Fig. 2. Stages of cancer progression

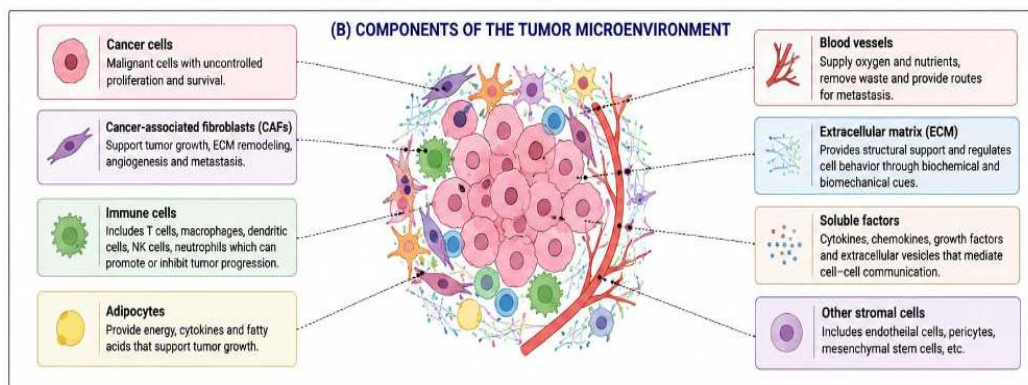


Fig. 3. Components of the tumor microenvironment

Radiotherapy employs high-energy ionizing radiation to damage the DNA of cancer cells, thereby inhibiting their growth and proliferation. It is widely used for local tumor control and can be applied before or after surgery to improve treatment outcomes.

Hormone therapy is used for hormone-dependent cancers such as breast and prostate cancer. This approach suppresses hormone production or blocks hormone receptors, thereby reducing tumor growth and progression.

Immunotherapy enhances the body's immune system to recognize and destroy cancer cells. Various immunotherapeutic approaches, including immune checkpoint inhibitors, monoclonal





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antibodies, and cancer vaccines, have shown significant success in treating several types of cancer.

Collectively, these conventional treatment strategies have contributed substantially to cancer management and remain essential components of modern oncology. However, their effectiveness is often influenced by tumor type, stage of disease, and patient-specific factors (9, 10).

5. Limitations of Conventional Cancer Therapies

Although conventional cancer therapies have significantly improved patient survival and disease management, several limitations continue to affect their overall effectiveness. One of the major challenges is the lack of specificity, as many therapeutic agents cannot selectively target cancer cells and often damage healthy tissues. This non-specific action results in various adverse effects and reduced patient quality of life. Systemic toxicity is another important concern, particularly with chemotherapy and radiotherapy. These treatments frequently affect rapidly dividing normal cells, leading to side effects such as nausea, vomiting, hair loss, fatigue, immunosuppression, and organ toxicity. Additionally, prolonged treatment may result in the development of drug resistance, where cancer cells become less responsive to therapy, reducing treatment effectiveness.

Poor drug accumulation at the tumor site further limits therapeutic outcomes, as only a small portion of the administered drug reaches the target tissue. Tumor heterogeneity, characterized by differences among cancer cells within the same tumor, also contributes to variable treatment responses and therapeutic failure. Furthermore, conventional therapies often show limited effectiveness against metastatic cancers and may not completely eliminate residual cancer cells, increasing the risk of recurrence. The high cost of treatment, long treatment durations, and the need for continuous medical care also impose a significant economic burden on patients and healthcare systems. These limitations have driven the development of Targeted Drug Delivery Systems (TDDS), which aim to improve treatment specificity, enhance therapeutic efficacy, and reduce systemic toxicity (10, 11).





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6. Introduction to Targeted Drug Delivery Systems (TDDS)

Targeted Drug Delivery Systems (TDDS) have emerged as an innovative approach to overcome the limitations of conventional cancer therapies, such as non-specific drug distribution, systemic toxicity, poor bioavailability, and drug resistance. TDDS are designed to deliver therapeutic agents directly to the target site, thereby enhancing treatment efficacy while minimizing adverse effects on healthy tissues.

The concept of targeted drug delivery originated from Paul Ehrlich's "magic bullet" theory, which envisioned selective treatment of diseased cells without harming normal cells. In cancer therapy, TDDS exploits unique tumor characteristics, including abnormal vasculature, enhanced permeability, altered pH, and overexpressed receptors, to achieve site-specific drug delivery.

Table 2 Major Limitations of Conventional Cancer Therapies

Limitation	Impact on Treatment
Non-specific targeting	Damage to healthy tissues
Systemic toxicity	Severe adverse effects
Drug resistance	Reduced therapeutic efficacy
Poor tumor accumulation	Low drug concentration at target site
Tumor heterogeneity	Variable treatment response
Recurrence and metastasis	Disease progression
High treatment cost	Increased economic burden





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Various carrier systems such as liposomes, polymeric nanoparticles, dendrimers, micelles, solid lipid nanoparticles, nanogels, and antibody–drug conjugates have been developed for targeted delivery. These systems can improve drug stability, prolong circulation time, enhance cellular uptake, and provide controlled drug release.

Based on their mechanism of action, TDDS can be classified into passive targeting, active targeting, and stimuli-responsive targeting. Overall, TDDS represents a major advancement in cancer therapeutics and plays a vital role in the development of precision medicine by improving therapeutic outcomes and reducing systemic toxicity (12, 13).

6.1 Principles of Cancer Targeting

The effectiveness of anticancer therapy largely depends on the ability of therapeutic agents to reach tumor tissues in sufficient concentrations while minimizing exposure to healthy organs. Conventional drug delivery approaches often result in widespread distribution of drugs throughout the body, leading to systemic toxicity and reduced therapeutic efficiency. To overcome these limitations, cancer-targeting strategies have been developed to selectively direct drugs to tumor sites. These strategies exploit the unique physiological, biochemical, and molecular characteristics of tumors to improve drug accumulation, enhance therapeutic efficacy, and reduce adverse effects.

Cancer targeting forms the fundamental basis of Targeted Drug Delivery Systems (TDDS). The objective is to achieve site-specific delivery of therapeutic agents, thereby maximizing drug concentration within the tumor while minimizing damage to normal tissues. Depending on the mechanism of targeting, cancer-targeting strategies are broadly classified into passive targeting and active targeting (14).

6.1.1 Passive Targeting

Passive targeting is based on the natural physiological characteristics of tumor tissues, particularly the Enhanced Permeability and Retention (EPR) effect. Solid tumors exhibit rapid and abnormal angiogenesis, resulting in blood vessels that are irregular, poorly organized, and highly permeable. These leaky blood vessels contain large fenestrations ranging from 100 to 800 nm, allowing Nano sized drug carriers to preferentially extravagate into tumor tissues. In addition to enhanced vascular permeability, tumors often possess impaired lymphatic drainage systems. As a result, nanoparticles and macromolecular drug carriers that enter the tumor microenvironment are retained for extended periods. This phenomenon is known as the





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Enhanced Permeability and Retention (EPR) effect and serves as the basis for passive tumor targeting.

Passive targeting does not require specific interactions between the drug carrier and cancer cells. Instead, it relies on the physicochemical properties of the carrier, including particle size, surface charge, shape, hydrophobicity, and circulation time. Nanocarriers such as liposomes, polymeric nanoparticles, micelles, dendrimers, and solid lipid nanoparticles are commonly designed to exploit the EPR effect. The success of passive targeting depends on several factors. Particle size plays a crucial role, as particles that are too small may be rapidly eliminated through renal filtration, whereas larger particles may be removed by the mononuclear phagocyte system. Surface modification with hydrophilic polymers such as polyethylene glycol (PEG) can prolong circulation time and enhance tumor accumulation.

Passive targeting offers several advantages, including simplicity of design, improved drug bioavailability, prolonged circulation, and enhanced tumor localization. However, its effectiveness may vary among different tumor types because the EPR effect is highly heterogeneous. Variations in vascular permeability, blood flow, and tumor microenvironment characteristics can significantly influence drug accumulation. Consequently, passive targeting alone may not always provide sufficient specificity for effective cancer therapy (15,16).

Mechanism of Passive Targeting

1. Systemic administration of drug-loaded nanocarriers.
2. Circulation through the bloodstream.
3. Extravasation through leaky tumor vasculature.
4. Retention within tumor tissue due to poor lymphatic drainage.
5. Gradual drug release at the tumor site.

Advantages of Passive Targeting

- Exploits natural tumor physiology.
- Enhances drug accumulation at tumor sites.
- Reduces systemic toxicity.
- Improves pharmacokinetic properties.
- Suitable for various Nanocarrier systems.

Limitations of Passive Targeting

- Dependence on the EPR effect.





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- Variable effectiveness among tumor types.
- Limited cellular specificity.
- Restricted penetration into deep tumor regions.

6.1.2 Active Targeting

Active targeting represents a more sophisticated approach in which drug carriers are engineered to specifically recognize and bind molecular markers expressed on cancer cells or tumor-associated tissues. This strategy involves the surface modification of drug carriers with targeting ligands that selectively interact with receptors overexpressed on tumor cells. Unlike passive targeting, active targeting relies on molecular recognition mechanisms. After accumulating in the tumor region, ligand-functionalized carriers bind specifically to target receptors, resulting in enhanced cellular uptake through receptor-mediated endocytosis. This process significantly increases intracellular drug concentration and improves therapeutic efficacy. Various ligands have been employed for active targeting, including monoclonal antibodies, antibody fragments, peptides, aptamers, carbohydrates, vitamins, and small molecules. The choice of ligand depends on the expression profile of receptors on the target cancer cells.

Several receptors commonly exploited for active targeting include:

- Folate receptors
- Transferrin receptors
- Epidermal Growth Factor Receptors (EGFR)
- Human Epidermal Growth Factor Receptor 2 (HER2)
- Integrin receptors
- CD44 receptors

For example, Folate-conjugated nanoparticles selectively target cancer cells overexpressing Folate receptors, while antibody-functionalized nanocarriers can specifically bind HER2-positive breast cancer cells. Active targeting enhances drug localization, promotes receptor-mediated internalization, and improves treatment specificity. Furthermore, it enables selective delivery of chemotherapeutic agents, genes, proteins, and imaging agents. This approach is particularly useful in precision medicine and personalized cancer therapy (17).

Mechanism of Active Targeting

1. Drug-loaded carrier is functionalized with a targeting ligand.
2. Systemic administration and circulation.





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3. Accumulation at tumor tissue.
4. Specific binding to overexpressed receptors.
5. Receptor-mediated endocytosis.
6. Intracellular drug release and therapeutic action.

Advantages of Active Targeting

- High specificity toward cancer cells.
- Enhanced cellular uptake.
- Improved therapeutic efficacy.
- Reduced systemic toxicity.
- Suitable for personalized medicine.

Limitations of Active Targeting

- Complex formulation design.
- High production costs.
- Receptor heterogeneity.
- Potential immunogenicity.
- Biological barriers affecting delivery.

Both passive and active targeting strategies play critical roles in modern cancer therapeutics. While passive targeting utilizes the physiological characteristics of tumors to enhance drug accumulation, active targeting employs molecular recognition mechanisms to improve cellular specificity. The combination of these approaches has significantly advanced targeted drug delivery systems and continues to drive the development of next-generation cancer treatments.

Table 3 Comparison of Passive and Active Targeting

Feature	Passive Targeting	Active Targeting
Basis	EPR effect	Ligand–receptor interaction
Specificity	Moderate	High
Cellular Uptake	Limited	Enhanced
Complexity	Simple	Complex
Cost	Lower	Higher





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Examples	Liposomes, polymeric nanoparticles	Antibody-conjugated nanoparticles, folate-targeted systems
Major Limitation	Tumor heterogeneity	Receptor heterogeneity

7. Drug Delivery Carriers for Cancer Therapy

The success of targeted drug delivery systems largely depends on the selection of appropriate drug carriers capable of transporting therapeutic agents safely and efficiently to tumor tissues. Drug delivery carriers serve as vehicles that encapsulate, protect, and transport anticancer drugs to specific sites within the body. These carriers improve drug solubility, stability, bioavailability, pharmacokinetic behavior, and therapeutic efficacy while minimizing systemic toxicity. Advances in nanotechnology and biomaterials have led to the development of a wide range of carrier systems designed to overcome biological barriers and enhance tumor-specific drug delivery.

An ideal drug delivery carrier should possess several characteristics, including biocompatibility, biodegradability, high drug-loading capacity, controlled drug release, prolonged circulation time, and the ability to selectively target cancer cells. Various carrier systems have been investigated and successfully applied in cancer therapy, including liposomes, polymeric nanoparticles, dendrimers, micelles, solid lipid nanoparticles, nanogels, and antibody-drug conjugates (18).

7.1 Liposomes

Liposomes are spherical vesicular structures composed of one or more phospholipid bilayers surrounding an aqueous core. Due to their unique architecture, liposomes can encapsulate both hydrophilic and hydrophobic drugs. Hydrophilic drugs are entrapped within the aqueous core, whereas hydrophobic drugs are incorporated into the lipid bilayer.

Liposomes are among the most extensively studied and clinically successful nanocarriers for cancer therapy. They enhance drug stability, prolong systemic circulation, and reduce toxicity by protecting therapeutic agents from premature degradation. Surface modification with polyethylene glycol (PEG) can further improve circulation time by reducing recognition by the reticuloendothelial system. In addition, liposomes can be functionalized with targeting ligands such as antibodies, peptides, and aptamers to achieve active targeting. Several liposomal





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formulations have received regulatory approval for cancer treatment. For example, liposomal doxorubicin has demonstrated reduced cardiotoxicity compared with conventional doxorubicin therapy (19).

7.2 Polymeric Nanoparticles

Polymeric nanoparticles are solid colloidal systems ranging from 10 to 1000 nm in size and are prepared using natural or synthetic polymers. These carriers can be designed as Nano spheres, in which drugs are uniformly dispersed throughout the polymer matrix, or Nanocapsules, where drugs are enclosed within a polymeric shell. Polymeric nanoparticles offer excellent control over drug release profiles and can be engineered for passive or active targeting. Biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA), polylactic acid (PLA), and chitosan are commonly used in their fabrication. These systems protect drugs from enzymatic degradation, improve bioavailability, and allow sustained drug release. Their surface can also be modified with targeting ligands to enhance selective uptake by cancer cells (20).

7.3 Dendrimers

Dendrimers are highly branched, tree-like macromolecules consisting of a central core, repetitive branching units, and numerous surface functional groups. Their well-defined architecture and monodisperse nature make them attractive carriers for drug delivery applications. The multiple surface groups available on dendrimers allow the attachment of drugs, targeting ligands, imaging agents, and diagnostic molecules. Furthermore, dendrimers possess internal cavities capable of encapsulating therapeutic compounds. Due to their nanoscale size and multifunctionality, dendrimers have shown considerable promise in targeted cancer therapy, gene delivery, and theranostic applications (21).

7.4 Polymeric Micelles

Polymeric micelles are self-assembled nanostructures formed from amphiphilic block copolymers in aqueous environments. They consist of a hydrophobic core surrounded by a hydrophilic shell. The hydrophobic core serves as a reservoir for poorly water-soluble anticancer drugs, while the hydrophilic shell stabilizes the structure and prolongs circulation time. Polymeric micelles have attracted considerable interest for improving the solubility and bioavailability of hydrophobic chemotherapeutic agents. These carriers can passively accumulate in tumors via the EPR effect and may also be modified with targeting ligands for active targeting (22).





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7.5 Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles are nanoscale carriers composed of physiologically compatible lipids that remain solid at body temperature. These carriers combine the advantages of liposomes and polymeric nanoparticles while minimizing some of their limitations. SLNs provide controlled drug release, improved drug stability, and protection against chemical degradation. Their lipid composition contributes to excellent biocompatibility and reduced toxicity (23).

7.6 Nanogels

Nanogels are nanosized hydrogel particles composed of crosslinked hydrophilic polymers capable of absorbing large amounts of water. Their highly hydrated structure provides a favorable environment for the encapsulation of proteins, nucleic acids, and chemotherapeutic agents. Nanogels exhibit excellent biocompatibility and can be engineered to respond to environmental stimuli such as pH, temperature, enzymes, and redox conditions. These properties make them highly suitable for controlled and site-specific drug delivery (23).

7.7 Antibody-Drug Conjugates (ADCs)

Antibody-drug conjugates represent an advanced targeted delivery platform that combines the specificity of monoclonal antibodies with the potency of cytotoxic drugs. ADCs consist of three components: a monoclonal antibody, a linker molecule, and a cytotoxic payload. The antibody selectively binds to specific antigens expressed on cancer cells. Following receptor-mediated internalization, the cytotoxic drug is released intracellularly, leading to targeted cancer cell destruction while minimizing damage to healthy tissues. Several ADCs have demonstrated remarkable clinical success and have become important components of precision oncology (24).

8. Applications of TDDS in Cancer Treatment

Targeted Drug Delivery Systems (TDDS) have significantly improved cancer treatment by enabling the selective delivery of therapeutic agents to tumor tissues while minimizing damage to healthy cells. By enhancing drug accumulation at the target site, TDDS improves therapeutic efficacy and reduces systemic toxicity associated with conventional therapies. TDDS has been widely applied in the treatment of various cancers, including breast cancer, lung cancer, colorectal cancer, brain tumors, and hematological malignancies. In breast cancer, targeted nanocarriers and antibody-based systems improve the delivery of drugs such as doxorubicin and trastuzumab to cancer cells. In lung and colorectal cancers, nanoparticle-based formulations enhance drug stability, cellular uptake, and tumor-specific accumulation. For





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brain tumors, specialized nanocarriers capable of crossing the blood–brain barrier facilitate effective drug delivery to tumor tissues.

In haematological cancers such as leukemia and lymphoma, antibody–drug conjugates and ligand-targeted nanoparticles provide selective targeting of malignant cells, improving treatment outcomes while reducing adverse effects. Furthermore, the combination of TDDS with immunotherapy enables the targeted delivery of immune modulators, vaccines, and genetic materials, enhancing antitumor immune responses (25).

9. Recent Advances and Future Perspectives

Recent advances in targeted drug delivery systems (TDDS) have been driven by developments in nanotechnology, biotechnology, biomaterials, and precision medicine. Innovative carrier systems such as multifunctional nanocarriers, antibody–drug conjugates, and stimuli-responsive nanoparticles have significantly improved the selective delivery of anticancer agents. Theranostic nanocarriers, which combine diagnostic and therapeutic functions, enable simultaneous disease detection, treatment, and monitoring.

Stimuli-responsive delivery systems that respond to factors such as pH, temperature, enzymes, light, and magnetic fields have gained considerable attention due to their ability to provide controlled and site-specific drug release. Additionally, gene delivery technologies involving siRNA, mRNA, and CRISPR-based systems offer promising opportunities for cancer treatment at the molecular level. Artificial intelligence (AI) and machine learning are also being increasingly utilized to optimize drug carrier design, predict therapeutic outcomes, and support personalized treatment strategies.

Despite these advancements, challenges such as biological barriers, carrier toxicity, large-scale manufacturing, regulatory requirements, and treatment costs continue to limit widespread clinical application. Future research is expected to focus on precision nanomedicine, biomimetic carriers, personalized therapeutics, and combination therapies. The integration of advanced technologies is anticipated to further enhance the safety, efficacy, and clinical success of targeted cancer therapies (26).

10. Conclusion

Cancer remains one of the most challenging diseases worldwide, and conventional therapeutic approaches often suffer from limitations such as non-specific drug distribution, systemic toxicity, poor bioavailability, and treatment resistance. These challenges have driven the





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development of Targeted Drug Delivery Systems (TDDS), which represent a major advancement in modern cancer therapeutics. By selectively delivering therapeutic agents to tumor tissues, TDDS enhances drug accumulation at the target site while minimizing exposure to healthy organs. Various carrier systems, including liposomes, polymeric nanoparticles, dendrimers, micelles, nanogels, solid lipid nanoparticles, and antibody-drug conjugates, have demonstrated significant potential in improving therapeutic outcomes. Passive and active targeting strategies further contribute to enhanced treatment specificity and reduced adverse effects.

Recent advances in nanotechnology, gene therapy, stimuli-responsive systems, artificial intelligence, and precision medicine have expanded the capabilities of targeted drug delivery and opened new avenues for cancer treatment. Although challenges related to clinical translation, safety, and regulatory approval remain, ongoing research continues to address these limitations.

In conclusion, targeted drug delivery systems have emerged as a transformative approach in oncology, offering improved efficacy, reduced toxicity, and enhanced patient outcomes. As scientific and technological innovations continue to evolve, TDDS is expected to play an increasingly important role in the development of personalized and next-generation cancer therapies, ultimately contributing to more effective and patient-centered cancer management.

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WISELEAF SCIENTIFIC VENTURES

26. Jadhav SP, Ahire SM, Shewale VV, Patil CD, Pagar RY, Sonawane DD, Mahajan SK. Formulation of Tablet of Nifedipine co-crystal for enhancement of solubility and other physical properties. Biotech Res Asia. 2025 Mar 25;22(1):191-200.

