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Targeted Drug Delivery Systems for Cancer Management: Advancements, Challenges, and Future Directions

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Abstract

Background: Cancer malignancy management remained a critical challenge despite therapeutic advancements attributed to systemic toxicity, non-specificity &drug targeting issues, reduced drug bioavailability and drug resistance problems associated with available chemotherapeutic approaches. Current limitations underline prime requirement for development of highly efficacious patient oriented drug delivery systems.

Objective: Current review is focused to discuss cancer-specific targeted drug delivery systems (TDDS), its types and formulation modifications brought about to shape cancer therapeutics with ultimate benefited therapeutic outcomes and precise controlled-release with minimal possible side effects.

Methods:

Current review discussed the development, possible mode/mechanism of action, and effectiveness of various TDDS, including nanoparticles, liposomes, dendrimers, antibody-drug conjugates, ligand-based biomimetic and, stimuli-responsive drug delivery systems thereby improving targeted drug release phenomenon and ultimate benefited clinical outcomes however certain limitations including tumor heterogeneity, immune system clearance, scalability and manufacturing cost, together with limited penetration to solid tumors and unpredictable Bio distribution ultimately acquire innovative drug delivery platforms for global. Current review is also focused on recent advancements in TDDS over the past decade together with evaluation of its limitations and ascertaining potential future directions for renovating cancer management.

Results: Management of cancer malignancies has been remarkably reformed via TDDS, allowing the potential delivery of anticancer medicaments to the targeted site and preventing systemic side effects. Liposome's, polymeric nanoparticles, dendrimers, Exosomes, stimuli-responsive systems and antibody-drug conjugates presenting significant advancements together with promising clinical outcomes. Currently precision nano-medicine, CRISPR-based carriers, AI integration, and microenvironment-responsive systems are under consideration for efficacious management of cancer malignancies.

Conclusion: TDDS provide a breakthrough approach for cancer management by augmenting treatment efficacy and meanwhile reducing drug induced toxicity. Continued research and interdisciplinary collaboration is required to address intervening hurdles and completely analyzing the potential of TDDS in clinical oncology.

Keywords:

Targeted drug delivery systems, Cancer therapy, Nanoparticles, Liposomes, Antibody-drug conjugates (ADCs), Stimuli-responsive systems, Ligand-targeted nanoparticles, Exosomes, Tumor targeting.

I. Introduction

Cancer malignancy is a leading disorder instituting global health concerns, accounting for considerable mortality rates (19 million cancer malignancy by 2020), putting a therapeutics strain on overall healthcare systems. Higher mortality rates presented its clinical management a challenging issue in the upcoming years (1). Cancers disease is recognized by uncontrolled

growth of abnormal tumor cells with its consequent invasion/penetration to and destruction of normal healthy tissues. Cancer progression may result in uncontrolled disease progression provoking continued increment in global cancer burden leading to the development of highly safe, effective and patient-oriented medications (2).

I. Current Treatment Modalities

Traditional cancer therapies including surgery, radiation therapy, and chemotherapy exhibit particular indications, strengths, along with associated limitations. Surgery is an effective tool for localized tumors and often used in early-stage cancers however is un-suitable for metastatic or hematological malignancies (3). Radiation therapy involves high-energy particles or waves to kill cancer cells however; it also poses the risk of damage to adjacent normal healthy tissues (4).

Chemotherapy remained a mainstay in the management of numerous cancer malignancies, particularly associated with advanced/metastatic cancers. It necessitates the systemic delivery of cytotoxic chemotherapeutic agents disrupting cellular replication especially in rapidly dividing cells (5). Chemotherapeutic medicaments are classified into four major types i.e. alkylating agents, antimetabolites, topoisomerase inhibitors, and mitotic inhibitors. Despite its widespread usage and benefits in extending the survival and ultimate reduction of tumor burden, chemotherapy is linked with cellular toxicity and numerous adverse effects based on non-specific mechanism of action (6).

II. Limitations of Chemotherapy

One major disadvantage of chemotherapy is its inability to distinguish between malignant and normal proliferating cells with resultant undesirable effects on bone marrow, gastrointestinal tract, hair follicles, and other healthy tissues, leading to immunosuppression, nausea, mucositis, alopecia, and exhaustion (7). The intensity of current adverse effects might have a detrimental effect on patient’s quality of life acquiring need for individualized dose adjustment or termination of therapy with ultimate compromise on overall treatment outcome (8).

Together with systemic toxicity, chemotherapy's efficiency is typically hampered by lower drug absorption, limited tumor site accumulation, with ultimate development of multidrug resistance (MDR) (9). Drug resistance mechanisms in cancer cells include increased drug efflux through ATP-binding cassette (ABC) transporters, drug inactivation, changed drug targets, and improved DNA repair capacity. These resistance pathways can drastically limit the efficacy of chemotherapeutic agents, resulting in treatment failure and potential cancer recurrence (10).

Furthermore, the tumor microenvironment (TME), which includes immune cells, fibroblasts, extracellular matrix, and aberrant vasculature, serves as a physical and biochemical barrier to drug penetration and distribution within the tumor mass (11). Further Tumor heterogeneity, both within and among patients, hampers treatment planning and response predictions, necessitating more personalized approaches to cancer therapy (12).

III. Requisite of TDDS

In light of current challenging disputes, TDDS have gained popularity as a novel approach for improving the specificity and efficacy of anticancer therapies. The fundamental goal of targeted drug delivery is to accurately deliver therapeutic medicaments to cancer cells or the tumor microenvironment while limiting their exposure to normal tissues (13). Current tactics not only reduced systemic toxicity but also enhanced medicament concentration at the target region, with resultant improved therapeutic efficacy (4, 14).

TDDS takes an advantage of numerous physiological and molecular properties of tumors, including leaky vasculature, acidic pH, overexpressed receptors, and specific enzymes. Based on these characteristics, targeted drug delivery may be mainly divided into two major classes including active and passive targeting. Active targeting employs ligands, antibodies, peptides, or aptamers that bind specifically to overexpressed cancer cell receptors whereas passive targeting mainly on enhanced permeability and retention (EPR) effects observed in solid tumors (13, 15).

Nanotechnology made fundamental contributions to the development of novel drug carriers including liposomes, dendrimers, micelles, and polymeric nanoparticles that might encapsulate and transport anticancer medications in a sustained way. Furthermore, advancement of biomaterials, surface engineering, and bio responsive systems also provided provision for the development of stimuli-responsive drug delivery systems that release the embedded pharmaceutical moiety in response to specific triggers such as pH, temperature, redox conditions, or enzymes of the tumor environment (4, 14).
Certain TDDS also proved effective during clinical analysis as for example, liposomal doxorubicin (Doxil®) and antibody-drug conjugates such as trastuzumab emtansine (Kadcyla®) have shown enhanced therapeutic & safety profiles upon targeted delivery to particular tumors (13, 15, 16). Ongoing research is looking into novel targeting ligands, multifunctional nano-carriers, and combination techniques that might integrate diagnostic & theranostic approaches, providing bright future for customized and precision oncology.

II. Principles of Targeted Drug Delivery System

TDDS is a transforming technique in cancer therapy that aims to improve the therapeutic profile of anticancer medicines via increase in drug accumulation (Cmax) at the tumor site meanwhile reducing its systemic side effects and cytotoxic activity. Current technique utilizes distinctive biological characteristics of tumor cells and their surroundings to deliver therapeutic medicaments precisely to the targeted area (17). TDDS are essentially divided into three basic categories including passive targeting, active targeting, and stimuli-responsive (triggered) systems.

I. Active targeting

Active targeting is correlated with active binding of a particular ligand to an overexpressed receptor/ antigens allocated over cancer cells surface. Augmented drug release at specified site is enhanced due to by the uptake of therapeutic moiety by cancer cells due to ligand

receptor conjugation with ultimate controlled, specified and efficient drug release at cellular level. This approach up regulates therapeutic outcomes while minimizing adverse effects on healthy tissues (17).

Following are certain factors involved in active targeting of cancer treatment.

Ligand-receptor specificity

Selection of targeting ligands is essential based on its specific matching with particular receptors; uniquely or over-expressed in tumor cells. High specificity helps in targeted drug delivery, associate to augmented uptake by cancer cells and reduced toxicity to normal tissues (18).

Receptor-mediated endocytosis efficiency

Success of active targeting greatly depends upon endocytic uptake of drug molecules in cancer cells or in other words depends on ligands triggered receptor-mediated endocytosis. A drug component penetrates the cell and acquires therapeutic levels at tumor site (19).

Optimization of ligand density

The density of targeting ligands greatly influences its binding affinity and cellular uptake. Optimal density of the ligands can result in effective binding without immune clearance or carrier aggregation, allowing for improved delivery efficiency (20).

Stimuli-responsive targeted release

Majority of active targeting systems are formulated to respond to tumor-specific stimuli including pH or enzyme levels to selectively release drugs components at particular tumor environment. This mechanism minimizes systemic side effects along with focusing the therapeutic activity at specific tumor site (21).

This mechanistic technique is revolutionizing oncological treatment outcomes thereby enhancing the therapeutic accuracy and effectiveness and reducing cytotoxic harm to normal cells.

By fine-tuning factors including ligand specificity, receptor-mediated internalization, ligand density, and stimuli-responsive drug release, active targeting exhibits tremendous capability towards advancement of cancer therapeutics with resultant improved clinical outcome (22).

II. Passive Targeting

Passive targeting hitches the specific architectural and pathophysiological properties of solid tumors, particularly increased permeability and retention (EPR) effect. Tumors generally present leaky vasculature associated with aberrant angiogenesis and poor lymphatic drainage, allowing macromolecules and nanoparticles to reside in the tumor tissue (23). Current modified system allows nano-carrier systems, including liposomes, dendrimers, micelles, and polymeric nanoparticles, to preferentially concentrate in tumor locations following systemic administration.

However, the effectiveness of the EPR effect may vary significantly depending on tumor type, size, location, and vascularization. Certain tumors, particularly those exhibiting poor vasculature and high interstitial pressure where EPR effect is insufficient passive targeting may result in poor therapeutic efficiency (24). Furthermore, passive targeting lacks specificity to discriminate between cancerous and highly vascularized tissues (25).

III. Stimulus-responsive (triggered) drug delivery system

Stimuli-responsive systems, often described as smart drug delivery systems, are intended to release therapeutic medicaments in response to particular stimuli (internal or external). These technologies control medicament release w.r.t location and time there by improving both drug selectivity and efficacy (26). Internal stimuli that may trigger drug release include pH (acidic tumor environment), redox potential (elevated glutathione levels in cancer cells), enzymes (e.g., matrix metalloproteinases), and hypoxia (reduced oxygen levels) etc. (27) whereas temperature, magnetic fields, ultrasound, and light (particularly near-infrared light for deep tissue penetration) may act as most prevalent external stimulus (28).

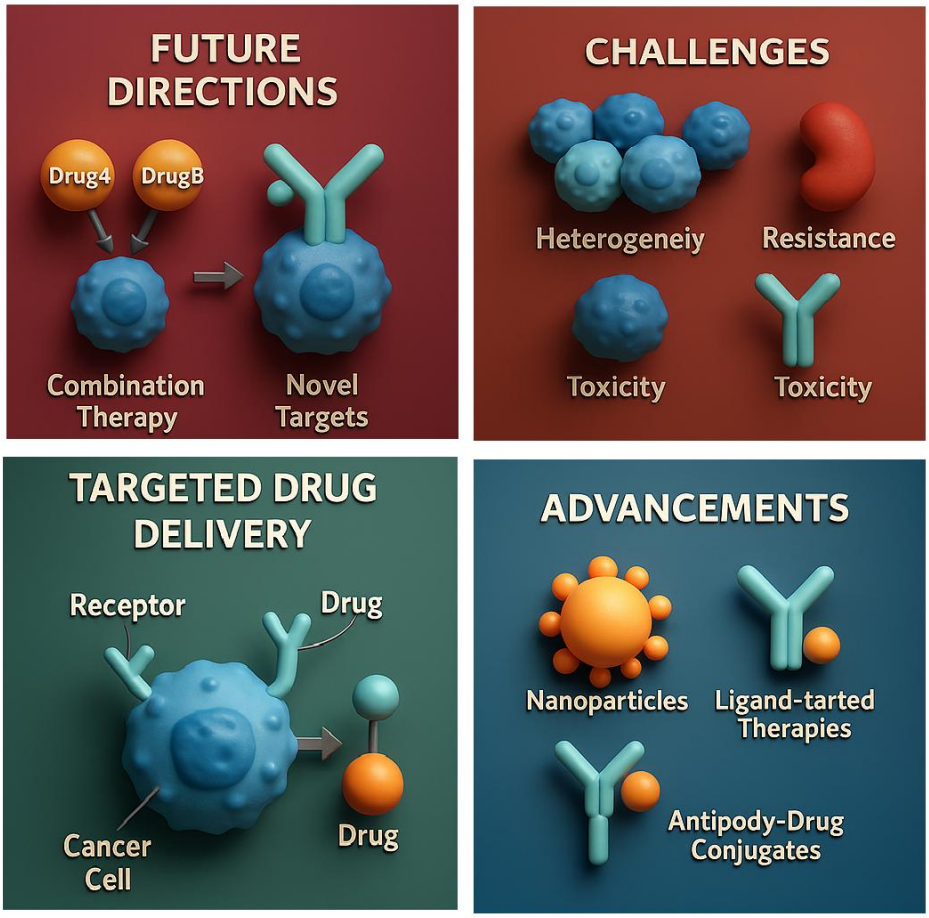

Figure 1Diagramatic representation of the fundamental advancement and possible challenges associated with TDDs.

III. Types of Targeted Drug Delivery Systems

Advancement in nanotechnology and molecular biology may result in provision of diverse TDDS spectrum, each designed to improve drug specificity, reduce systemic side effects, and ultimately improve clinical outcomes. These systems use a variety of carriers and targeting mechanisms to deliver anticancer drugs to particular sites or in response to particular stimuli (29).

I. Nanoparticles

Nanoparticles are leading advancement in TDDS based on their small size (usually 1-100 nm) and high surface-area-to-volume ratio providing capability of functioning as targeting ligands (30).

II. Liposomes

Liposomes are spherical vesicles made up of phospholipid bilayer that may hold both hydrophilic and hydrophobic medicines. Biocompatible attributes of liposomes avoid the occurrence of immune system, and have been used successfully employed in cancer therapy (Doxil®-Pegylated liposomal doxorubicin) (31).

III. Dendrimers

Dendrimers are branched, tree-like polymers providing precise molecular architecture and multivalency. Their surface can be modified using ligands or PEG chains to enhance drug circulation time (Tmax) and selective targeting (31).

IV. Polymeric nanoparticles

Polymeric nanoparticles commonly manufactured from biodegradable polymers including PLGA (Poly lactic-co-glycolic acid), allow sustained drug release pattern and prevent therapeutic medicaments from degradation. These systems are designed to respond to environmental factors with successful provision of active targeting (32).

V. Monoclonal antibodies and antibody-drug conjugates (ADCs)

Monoclonal antibodies (mAbs) may recognize those antigens that are overexpressed in tumor cells, including HER2, EFGR, and CD20. Upon Conjuagation with medicines, these antibodies may inhibit receptor activity, recruit immunological responses, and deliver lethal side effects (33).

VI. Antibody-Drug Conjugates (ADCs)

Antibody-Drug Conjugates (ADCs) combine the specificity of mAbs and the potency of cytotoxic drugs. After attaching to the target antigen, ADCs internalize and release the medication intracellularly. Trastuzumab emtansine (T-DM1) is used to treat HER2-positive breast cancer, and brentuximab vedotin is successfully employed for management of Hodgkin lymphoma (34).

VII. Ligand targeted Systems

Ligand targeted systems use the attachment of small molecules or peptides that recognize and bind to specific receptors overexpressed in cancer cells, providing allowance for active targeting (35). Folic acid, based on its high affinity towards folate receptor, is commonly used for treatment of ovarian, lung, and breast cancer malignancies (36). Transferrin, a natural iron-transporting glycoprotein, binds to transferrin receptor, which is frequently activated in rapidly proliferating tumor cells (37). Aptamers are synthetic oligonucleotides

that fold into 3D structures, have excellent binding affinity and specificity to their targets, acting similarly to antibodies however with comparatively lower immunogenicity (38).

VIII. Stimulus-responsive Systems

Stimulus-responsive (smart) drug delivery systems are designed to release active product ingredients in response to specific triggering signal in the tumor microenvironment, including both intrinsic (internal) or extrinsic stimuli (39). pH responsive systems involve the utilization of acidic microenvironment of tumor tissues and endosomal compartments to instigate drug release (39). Temperature-sensitive systems are one another type of system that initiates medicament release when subjected to comparatively higher temperature of tumor cells i.e. external hyperthermia (40). Enzyme-sensitive systems react in response to tumor-specific enzymes such matrix metalloproteinases (41). Similarly redox sensitive systems become activated from breakdown of high glutathione concentrations leading to selective intracellular drug release (42).

IX. Exosomes & Biomimetic Systems

Exosomes are tiny cellular vesicles playing natural role in intercellular communication. Based on their endogenous origin, exosomes exhibit low immunogenicity potential along with higher biocompatibility, making them a promising candidates for TDDS. They can be designed to transport therapeutic medicaments via surface-modification to acquire targeted drug delivery (43). Likewise biomimetic systems including cellular membrane-coated nanoparticles (e.g., red blood cell, platelet, or cancer cell membranes), mimicking the biological behavior of native cells, allowing immune response evasion, prolonged drug circulation, and homotypic targeting of tumor cells (44).

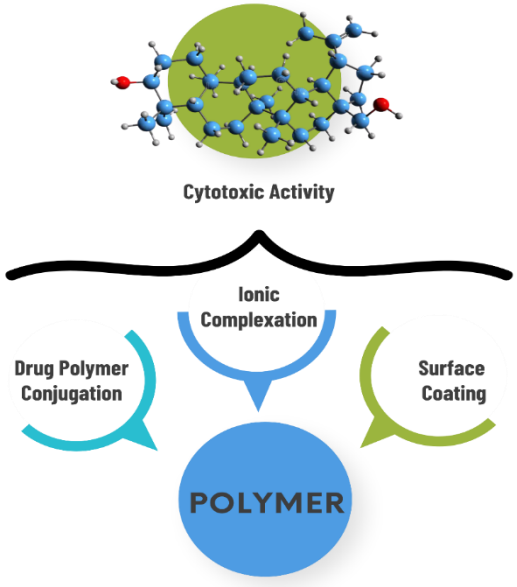

Figure 2 Figure representing the potential involvement of polymers i.e. polymer-drug conjugates, ionic-complexes and surface coated materials for the targeted treatment of tumor cells with application as potential cytotoxic molecules.

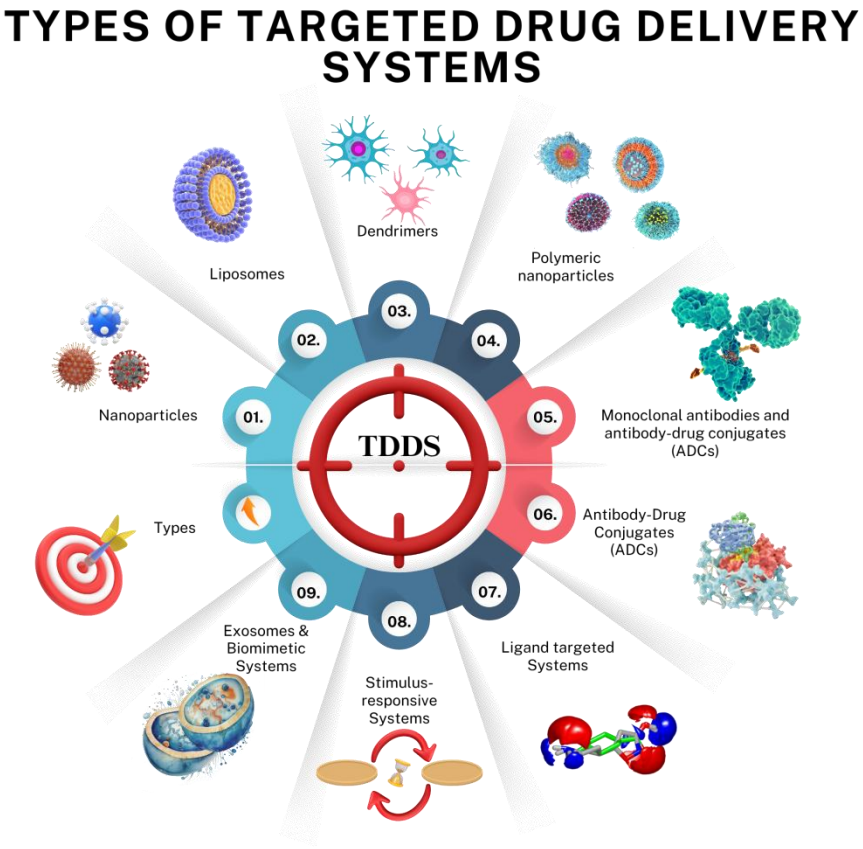

Figure 3 Major types of targeted drug delivery systems, including nanoparticles, Liposomes, Dendrimers, polymeric nanoparticles, monoclonal antibodies, ligand-conjugated systems, stimuli-responsive platforms, and exosomes based biomimetic systems.

4. Advantages and Challenges of TDDS

TDDS have revolutionized the landscape of cancer therapy via provision of more sophisticated therapeutic approach in comparison to conventional treatment methods. However, despite their promising outcome, current systems also came with certain specified challenges that need to be addressed to ensure clinical efficacy and extensive adaptation (45).

I. Benefited outcomes of TDDS

i. **Increased therapeutic efficacy:** Based on targeted delivery of therapeutic components directly to the tumor site, TDDS maximizes medicament concentration (Cmax) at the target site and meanwhile decreases its off-target distribution with resultant increased anticancer activity and need for administration of low therapeutic dose (46).

ii. **Reduced systemic toxicity:** Due to lack of target site selectivity, conventional chemotherapy produces severe adverse effects including cytotoxicity to normal healthy cells. Targeted systems limit the delivery of cytotoxic medications to healthy

tissues thus reducing the risk of weight loss, immunosuppression, hair loss, and gastrointestinal side effects etc. (47).

iii. **Controlled and sustained release:** Many TDDS, particularly nanoparticles-based and stimuli-responsive systems, have the capability to release medications in a predefined regulated or sustained manner that eliminates the need of frequent dosing and meanwhile maintaining optimum therapeutic concentrations over particular time duration (48).

iv. **Overcoming multidrug resistance (MDR)**: Certain targeted systems can assist in overcoming MDR in cancer cells via bypassing efflux pumps or interfering with resistance pathways. For example, dendrimer-encapsulated medicines and exosome-based systems may avoid drug efflux and enzymatic degradation (49).

v. **Personalized Therapy**: Successful utilization of biomarkers and ligand-receptor based targeting enabled professionals for providing case-specific therapeutic regimens on molecular level. ADCs and aptamer-based systems are prime examples of current scenario (50).

II. Challenges

i. **Tumor Heterogeneity:** Intra- and inter-tumoral heterogeneity may also act as an intervening factor instigating challenges in the development of TDDS at universal level. expression of numerous receptor and vascular permeability may affect the efficacy of ligand-mediated and EPR-based techniques (51).

ii. **Immune System Clearance:** Despite surface modification, still certain nanoparticles might easily be cleared by the mononuclear phagocyte system (MPS) ultimately reducing the circulation time and accumulation at target site (52).

iii. **Manufacturing & Scalability**: The manufacture of complex systems such as dendrimers, exosomes, and ADCs presents considerable problems in terms of repeatability, stability, and cost. Based on their intricate architecture, nano-medicines face regulatory challenges during FDA approval (14, 53, 54).

iv. **Limited penetration in solid tumors:** Though several TDDS present great targeting capabilities upon *in-vitro* analysis in animal models, however poor tissue penetration and occurrence of excessive interstitial pressure in solid tumors may obstruct drug distribution (55).

v. **Unpredictable Bio distribution.**

Some drug delivery systems may accumulate in different organs such as the liver, spleen, or kidneys due to non-specific uptake or size limits, resulting in unintentional toxicity or and ultimate lower therapeutic index (56).

Table 1. Table indicating the potential benefits and limitation associated with ligand-mediated drug delivery systems.

Advantages vs. Challenges of Targeted Drug Delivery Systems		
Challenges		**Advantages**
Unpredictable Bio distribution	→	Personalized Therapy
Limited Tumor Penetration	→	Overcome Drug Resistance
Manufacturing Issues	→	Controlled Release
Immune Clearance	→	Reduced Toxicity
Tumor Heterogeneity	→	Enhanced Efficacy

III. Clinical Applications and Case Studies of TDDS

TDDS led advancement from the bench to the bedside, providing increased therapeutic efficacy and fewer side effects in cancer treatment. Several formulations have achieved regulatory approval, while others are still in phase of clinical trials (57). This section contains important clinical applications and case studies that demonstrate the effectiveness of various TDDS in oncology.

i. Liposomal formulations

One of the most well-known examples of targeted nanocarriers is liposomal doxorubicin (Doxil®/Caelyx®), that has been licensed by the FDA for the treatment of ovarian cancer, multiple myeloma, and Kaposi's sarcoma. Doxorubicin encapsulation in PEGylated liposomes allowed prolonged circulation time and passive targeting to tumor tissue via the increased permeability and retention (EPR) effect, resulting in comparatively lower cardiac toxicity in comparison to free form (58).

ii. Antibody/Drug Conjugates

Antibody-drug conjugates are a clinically proven type of TDDs that combines the specificity of monoclonal antibodies along with the potential targeting of cytotoxic medicines to cancer cells. For example, trastuzumab emtansine (T-DM1, also known as Kadcyla®) is approved for HER2-positive breast cancer. Trastuzumab, a monoclonal antibody that targets HER2 receptors, delivers the strong cytotoxin DM1 directly to cancer cells thus limiting its systemic exposure (59). Another example is brentuximab vedotin (Adcetris®), an anti-CD30 ADC employed for the treatment of Hodgkin lymphoma and systemic anaplastic large cell lymphoma. These ADCs have proven impressive performance in patients with relapsed or refractory illness, demonstrating their utility in targeted cancer therapy (58).

iii. Ligand-Specific Nanoparticles

Clinical trials are being carried out to assess ligand-targeted nanoparticles that bind to particular receptors overexpressed in cancer cells. For example, BIND-014, a docetaxel-loaded polymeric nanoparticle that targets prostate-specific membrane antigen (PSMA), has shown promising outcomes in Phase II clinical trials conducted for metastatic castration-resistant prostate cancer and non-small cell lung cancer (60). BIND-014 showed improved

drug accumulation in tumors with limited side effects in comparison to standard chemotherapy (61).

iv. Multi-Responsive Systems in Clinical Evaluation

Although several stimuli-responsive drug delivery devices are still in the preclinical stages of development, few get entered into the clinical trials. For example, ThermoDox®, a heat-sensitive liposomal doxorubicin formulation, is intended for use in conjunction with localized hyperthermia. Upon heating from hyper-thermic tumor microenvironment, the liposomes deliver their embedded medication directly at the tumor site. ThermoDox® has been successfully amaysed in clinical studies for liver cancer and recurrent breast cancer (62).

v. Exosomes and Biomimic Carriers

Exosome-based drug delivery technologies are gaining popularity due to their natural ability to target tumor areas while evading immune clearance (63). Early-phase research are looking into using modified exosomes loaded with short RNAs or chemotherapeutics for targeted delivery in glioblastoma and pancreatic cancer. These devices opened up interest for potential precision therapy of cancer cells in near future (64).

Table 2. An overview of targeted drug delivery systems currently in clinical trials: Exosomes, liposomes, and antibody-drug conjugates are certain examples of new nano-carrier platforms effectively targeted to treat different tumor malignancies including breast, ovarian, pancreatic, and lymphomas.

Drug Delivery System	Targeted Tumor
Exosome-based Paclitaxel	Pancreatic, Breast Cancer
Folate-Targeted Liposomes	Ovarian, Lung Cancer (Folate receptor)
ThermoDox® (Heat-Sensitive Liposomes)	Liver, Breast Cancer (with hyperthermia)
BIND-014 (PLGA NP)	Prostate, Lung Cancer
Adcetris® (Brentuximab Vedotin)	CD30+ Lymphomas
Kadcyla® (T-DM1)	HER2+ Breast Cancer
Doxil® (Liposomal Doxorubicin)	Kaposi's Sarcoma, Ovarian, Myeloma

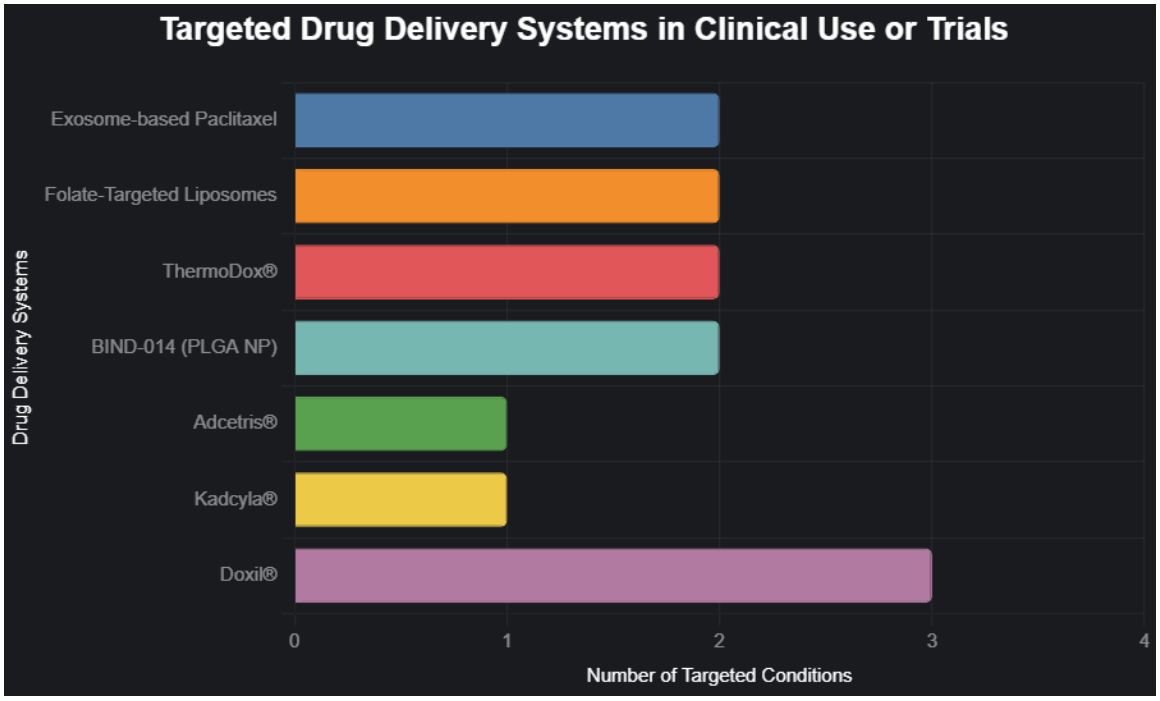

Figure 4 Numerous TDDS under clinical trials including exosomes, liposomes, and antibody-drug conjugates and nano-carrier platforms effectively targeted to treat different tumor malignancies including breast, ovarian, pancreatic, and lymphomas.

5. Future Directions for TDDA

The theme of TDDs is quickly expanding, exploring various novel techniques being actively searched in ongoing research. Future efforts aim to improve drug specificity, its delivery efficiency, and also overcome the aforementioned limitations (65).

i. **Precision nanomedicine:** As omics technologies (genomics, proteomics, and metabolomics) progresses, personalised medicine delivery systems based on specific patient profiles are emerging. These platforms could adjust the therapeutic delivery methods based on effective utilization of tumor biomarkers, thereby enhancing treatment outcomes (66).

ii. **Smart and Multifunctional Nanocarriers:** Multifunctional carriers can perform various functions—such as targeting, imaging, and therapy (theranostics) and are also gaining popularity. These systems may frequently employ diagnostic agents or biosensors that may provide real-time information on drug release and therapeutic efficacy (67).

iii. **CRISPR and Gene Editing-based Delivery**: The use of tailored nanocarriers to carry CRISPR-Cas9 components shows promising outcomes in revamping cancer-causing genomic abnormalities. Current technique seeks to eradicate oncogenes at their own source rather than simply blocking their protein products (68).

iv. **Tumor Microenvironment (TME) Targeted Systems**: The complexity of the TME, including hypoxia, acidic pH, and immunosuppressive cells, presents both a challenge issues as well as an opportunity for targeted drug delivery. Systems designed to

modulate or exploit these micro-environmental conditions are under exploration for improving therapeutic responses (69).

v. **Integration with artificial intelligence (AI):** AI and machine learning algorithms are being utilized to predict drug response, optimize nanoparticles based formulation, and identify the best case cohorts. Such data-driven approaches could greatly speed up the clinical translation of targeted medicaments (70).

6. Conclusion

TDDS represent a significant advancement in the field of cancer therapy, offering improved efficacy, reduced toxicity, and enhanced patient outcomes in comparison to conventional treatments. Advanced implementation of nanotechnology, bio-molecular engineering, and disease-specific targeting strategies, has provided allowance for precise delivery of therapeutic medicament to tumor sites and meanwhile extraordinary protection to healthy tissues. Clinical applications such as liposomal formulations, antibody-drug conjugates, and ligand-targeted nanoparticles have already demonstrated considerable success, while emerging approaches like stimuli-responsive platforms and biomimetic carriers hold promising outcomes in near future. Despite existing challenges related to scalability, targeting specificity, and regulatory approval, continued interdisciplinary research and innovation are paving the way for the next generation of personalized cancer therapies.

Declaration

Data Source: The information presented in this review article was compiled through a comprehensive literature search using various electronic databases, including PubMed, Science Direct, Scopus, Web of Science, and Google Scholar. Peer-reviewed journal papers, systematic reviews, meta-analyses, and clinical trial reports published between 2010 and 2025 were the primary sources used to ensure the inclusion of the most relevant and up-to-date findings. Keywords utilized in the search included "targeted drug delivery", "cancer therapy", "nanoparticles", "monoclonal antibodies", "ligand-targeted systems", "stimuli-responsive delivery", and "biomimetic drug carriers". Additional information was acquired from trustworthy sources, including the National Cancer Institute (NCI), World Health Organization (WHO), and ClinicalTrials.gov. Articles were chosen for their scientific quality, relevance to the issue, and effect on the field, with a premium given to studies involving the experimental validation or clinical use of targeted drug delivery systems in cancer.

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