

Review Article on Targeted Drug Delivery System

Mr. Ashish Hiranman Umak and Dr. Jaydeep Babasaheb Pawar

Shantiniketan College of Pharmacy, Dhotre Bk., Ahilyanagar
ashishumak454@gmail.com and jpscop24@gmail.com

Abstract: Drug targeting is a new drug delivery system that aims to deliver the drug to the target site of action or site of absorption without releasing the drug at any other non-target site. The delivery system is designed to retain the intact drug without any modification until reaching and releasing at the target site. The targeted drug delivery systems have several advantages over conventional ones as improvement of pharmaceutical activity, low side effects and reduction of the administered dose. The main purpose of the targeted drug delivery system is to obtain the pharmacological action of the therapeutic agent at diseased organs only without affecting the healthy one especially in the case of cancer treatment with chemotherapeutic agents. Drug targeting can be attained using different carriers that maintain and transport the intact drug to preselected organ or tissue. Different types of carriers can be used for drug targeting such as nanotubes and nanowires, nano shells, quantum dots, Nano-pores, gold nanoparticles, dendrimers, noisome, ufasomes, virosomes, unbosoms, nanobots and transferosomes. There are different mechanisms of drug targeting such as passive targeting, inverse targeting, active targeting, ligand-mediated targeting, physical targeting, dual targeting and double targeting. The drug targeting is a useful delivery system for delivering the therapeutic agent to a specific site without causing toxicity in other organs.

Keywords: Drug targeting, Drug delivery system, Reservoir System

I. INTRODUCTION

Targeted drug delivery represents an advanced and intelligent therapeutic approach capable of transporting a drug precisely to the desired site within the patient's body.¹ Unlike conventional drug delivery systems, where absorption occurs across biological membranes, targeted release systems allow controlled delivery of the drug in its dosage form.¹² This technique ensures sustained and localized release of an optimal therapeutic concentration over an extended period at the diseased tissue, thus maintaining the necessary plasma and tissue levels while minimizing exposure and potential injury to healthy cells¹³.

Developing such systems requires an interdisciplinary approach involving chemists, biologists, and engineers to optimize formulation and performance¹³. The design of a targeted release system must consider factors such as drug characteristics, possible adverse effects, route of administration, target site, and nature of the disease^{12,13}.

Formulations based on this technology are developed by taking into account the specific features of target cells, the presence of molecular transporters or ligands, and the use of various carrier or delivery vehicles⁴. Ideally, an effective targeted drug delivery system should be biochemically inert, non-toxic, non-immunogenic, and remain physically and chemically stable under both in vivo and in vitro conditions^{4,5,6}. It should localize specifically at the target site with uniform capillary distribution, ensuring a predictable and controlled release rate that maintains therapeutic drug concentration without compromising its pharmacological action⁵. Furthermore, minimal drug leakage during transit is desirable^{4,6}.

Compared to conventional drug delivery, targeted systems offer significant pharmaceutical, pharmacokinetic, and pharmacodynamics advantages^{12,13}. Conventional formulations commonly face challenges such as poor solubility, low stability, inadequate absorption, reduced half-life, and large volume of distribution, which limit their efficacy¹³. In contrast, targeted delivery systems enhance drug specificity, improve therapeutic index, and optimize drug utilization, making them more efficient alternatives^{12,13}.



II. NEED FOR TARGETED DRUG DELIVERY

The development of targeted drug delivery systems addresses critical challenges in modern therapeutics by fulfilling essential requirements in drug administration¹. These innovative systems enable the delivery of precise therapeutic quantities to diseased areas while simultaneously protecting healthy tissues from unwanted exposure^{2,3}. The fundamental necessity for such systems arises from multiple therapeutic and pharmaceutical considerations that directly impact treatment efficacy and patient outcomes^{4,5}.

2.1. Therapeutic Efficacy

Targeted drug delivery systems substantially enhance therapeutic efficacy by establishing and maintaining optimal drug concentrations at specific diseased sites^{6,7}. This precise spatial control over drug distribution significantly reduces systemic exposure and the associated adverse effects that commonly accompany conventional drug delivery⁸. The capacity to sustain therapeutic drug levels specifically at target sites while simultaneously minimizing drug concentrations in non-target tissues represents a transformative advancement in disease treatment strategies⁹.

The system's ability to direct drugs to specific organs, cells, or subcellular compartments holds particular clinical significance in managing chronic conditions and complex diseases¹⁰. In cancer therapy, for example, targeted delivery systems can substantially improve the therapeutic index of cytotoxic agents by concentrating their pharmacological effects within tumor tissues while sparing healthy cells¹¹.

2.2. Pharmaceutical Advantages

From a pharmaceutical perspective, targeted delivery systems confer several distinct advantages:

2.2.1. Enhanced Drug Stability—These systems protect therapeutic agents from premature degradation in hostile biological environments, thereby preserving their pharmacological activity until the moment they reach their intended target sites¹². This protection extends the effective lifespan of the drug and prevents loss of therapeutic efficacy.

2.2.2. Improved Bioavailability—Targeted delivery systems enhance drug bioavailability and therapeutic effectiveness by providing protection against hostile physiological environments and facilitating efficient transport across biological barriers that would otherwise impede drug absorption and distribution¹³. This enhanced bioavailability ensures that a greater proportion of the administered dose reaches the target site in an active form.

2.2.3. Controlled Release Properties—The capacity to regulate drug release kinetics enables consistent maintenance of therapeutic drug levels over extended periods, thereby reducing the required dosing frequency and substantially improving patient compliance with treatment regimens¹⁴.

2.3. Clinical Advantages

In clinical practice, targeted drug delivery systems demonstrate significant advantages that directly benefit patient care:

2.3.1. Reduced Side Effects—These systems minimize exposure to healthy tissues by restricting drug distribution exclusively to specific diseased sites, thereby substantially reducing adverse effects commonly associated with conventional systemic drug administration¹⁵. The localized nature of drug delivery protects non-target tissues from unnecessary exposure to therapeutic agents.

2.3.2. Higher Patient Compliance—The reduced dosing frequency and decreased incidence of adverse effects associated with targeted delivery systems collectively contribute to improved patient adherence to therapeutic regimens⁶. Patients are more likely to maintain consistent treatment when experiencing fewer side effects and requiring fewer doses.

2.3.3. Cost-Effectiveness—Although targeted delivery systems require higher initial investment compared to conventional formulations, they demonstrate superior long-term economic benefits by reducing drug waste, decreasing the frequency of drug administration, and minimizing the considerable costs associated with managing treatment-related side effects⁷.



III. PRINCIPLE OF TARGETED DRUG DELIVERY SYSTEM

The principle of a targeted drug delivery system (TDDS) is fundamentally based on the concept of delivering a therapeutic agent exclusively to the specific anatomical or cellular site where it is required, while simultaneously minimizing exposure and potential harm to healthy tissues¹⁶. The primary objective of this approach is to achieve maximum therapeutic benefit while substantially reducing or eliminating undesirable side effects commonly associated with conventional drug administration¹⁷. In traditional drug delivery systems, therapeutic agents distribute indiscriminately throughout the body following administration, resulting in suboptimal drug concentrations at the intended target site and unwanted pharmacological effects in non-target tissues¹⁸. Targeted drug delivery effectively circumvents these limitations by precisely directing the drug to the desired anatomical location in a controlled and efficient manner¹⁹.

The foundational principle of TDDS operates through three interdependent major components that work synergistically:

3.1. Carrier System

The carrier system functions as the vehicle that transports and delivers the drug to its intended destination²⁰. Common carrier systems include liposomes, nanoparticles, dendrimers, and microspheres, each offering distinct advantages for specific therapeutic applications. These sophisticated carrier systems serve multiple functions: they protect the encapsulated drug from premature degradation in hostile biological environments, facilitate controlled and sustained release of the therapeutic agent, and enhance the overall bioavailability of the drug at the target site²¹.

3.2. Targeting Moiety (Ligand)

Targeting moieties consist of specialized molecules such as antibodies, peptides, or carbohydrate structures that are strategically attached to the carrier system¹⁶. These ligands possess the critical capability to recognize and bind specifically to particular receptors or epitopes displayed on the surface of target cells, such as tumor cells or pathologically infected cells. This specific recognition and binding mechanism ensures that the drug-laden carrier system is directed exclusively to cells expressing the target receptor, thereby achieving cellular selectivity and minimizing non-specific drug delivery to healthy tissues¹⁷.

3.3. Drug Molecule

The drug molecule represents the active pharmaceutical ingredient that exerts the desired therapeutic action once it successfully reaches and enters the target site¹⁸. The pharmacological efficacy of the drug is preserved through protection by the carrier system during transit and is released at the target site to perform its intended therapeutic function.

In essence, the principle of targeted drug delivery functions as an intelligent "smart delivery system" that ensures optimal drug delivery through precise spatial and temporal control—guaranteeing that the right drug reaches the right place at the right time in the right amount¹⁹. This sophisticated approach substantially improves therapeutic efficacy, enhances safety profiles, and markedly increases patient comfort and quality of life compared to conventional drug delivery systems²⁰.



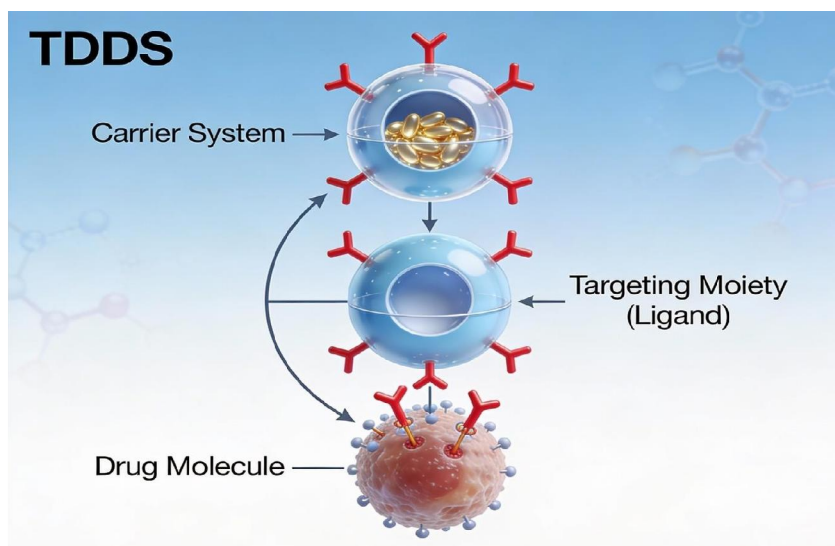


Figure 1: Components of TDD System

IV. TYPES OF TARGETED DRUG DELIVERY

As previously discussed, directing a therapeutic drug to a specific anatomical location not only enhances the therapeutic efficacy of the drug but also substantially reduces the toxicity associated with systemic drug exposure, thereby permitting the use of lower therapeutic doses in clinical practice²². To fulfill these essential therapeutic objectives, two primary approaches are employed extensively and represent the fundamental classification of drug targeting strategies^{23,24,25}.

4.1. Passive Targeting

Passive targeting refers to the spontaneous accumulation of a drug or drug carrier system at a specific diseased site as a consequence of inherent physicochemical or pharmacological characteristics of the disease state itself²². In the context of cancer treatment, for example, the size and surface properties of drug delivery nanoparticles must be precisely controlled to avoid unintended uptake by the reticulo-endothelial system (RES), thereby maximizing the circulation time of the carrier and enhancing overall targeting ability²⁶. This mechanism is sometimes considered a misnomer in that passive targeting essentially represents a straightforward drug delivery system distributed via normal blood circulation, where drug release or pharmacological action is naturally limited to selective disease sites within the body, such as tumor tissue, while sparing other organs such as the liver²⁷. Additional examples of passive targeting include the delivery of antimalarial therapeutic agents for the treatment of intracellular parasitic infections such as leishmania, brucellosis, and candidiasis²².

4.2. Active Targeting

Active targeting represents a more sophisticated approach involving specific ligand-receptor interactions that facilitate intracellular localization of the drug²³. This selective targeting interaction occurs exclusively following initial blood circulation and extravasation of the drug carrier system into the target tissue. Active targeting methodology can be further subdivided into three hierarchical levels of targeting specificity, each representing increasing precision in drug delivery²⁴:

4.2.1. First Order Targeting—This level refers to the restricted anatomical distribution of drug carrier systems exclusively to the capillary bed of a predetermined target site, organ, or tissue²⁵. Examples include compartmental targeting strategies directed toward specific body cavities and spaces such as lymphatic vessels, peritoneal cavity,



pleural cavity, cerebral ventricles, and synovial joints. First order targeting achieves organ-level selectivity without requiring cellular-level specificity.

4.2.2. Second Order Targeting—This level encompasses the selective delivery of therapeutic drugs to specific cell types while avoiding delivery to normal, healthy cells²⁶. A classical example includes the selective delivery of drugs specifically to Kupffer cells (resident macrophages) present in the liver while avoiding hepatocyte populations. Second order targeting achieves cellular-level discrimination based on cell type-specific characteristics.

4.2.3. Third Order Targeting—This most precise level of targeting refers to the delivery of drugs specifically to predetermined intracellular compartments or sites within targeted cells²⁷. This mechanism frequently employs receptor-based ligand-mediated entry strategies, whereby a drug complex enters the cell through receptor-mediated endocytosis. Third order targeting achieves subcellular localization and represents the highest level of targeting specificity, enabling drugs to reach their precise intracellular sites of action.

ACTIVE vs. PASSIVE MECHANISMS

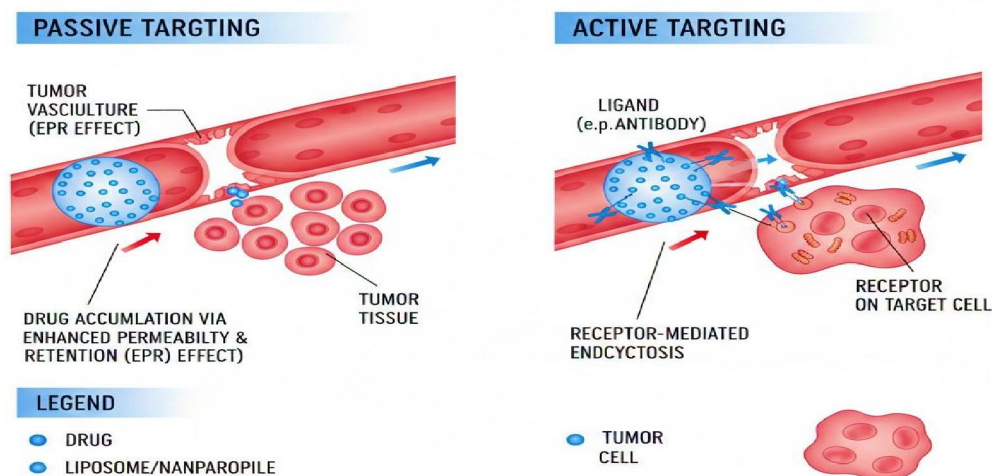


Figure 2: Passive Targeting & Active Targeting in TDDS

V. IDEAL CHARACTERISTICS OF TARGETED DRUG DELIVERY SYSTEMS

A comprehensive targeted drug delivery system must incorporate a multifaceted array of essential characteristics that collectively ensure optimal therapeutic performance, safety, and clinical efficacy²⁸. The following characteristics represent the fundamental requisites for an effective TDDS:

5.1. Physicochemical and Biological Properties

The drug delivery system must possess inherent properties that render it nontoxic to biological tissues, readily biodegradable through natural metabolic pathways, and biocompatible with the physiological environment of the body²⁸. Furthermore, the system must demonstrate exceptional chemical and physical stability under both in vivo conditions within the biological milieu and in vitro conditions during storage and handling. This stability ensures that the therapeutic agent remains protected from premature degradation and maintains its pharmacological efficacy throughout the duration of its residence within the body²⁹.



5.2. Targeted Distribution and Capillary Localization

The system must be precisely engineered to effectively transport the medication to predetermined specific cells, tissues, or organs with high selectivity and efficiency³⁰. The design must ensure consistent and uniform drug distribution throughout the capillary network of the target tissue, thereby achieving optimal local drug concentrations while minimizing systemic exposure. This characteristic is particularly critical for achieving therapeutic selectivity and reducing off-target effects³¹.

5.3. Controlled and Predictable Release Kinetics

It is essential that the release of the drug from the carrier system occurs in a precisely controlled and predictable manner over an appropriate therapeutic duration³². The release profile must be tailored to match the pharmacokinetic requirements of the specific disease state and therapeutic objective, ensuring that drug levels remain within the therapeutic window without fluctuations that could compromise efficacy or safety.

5.4. Sustained Therapeutic Concentration

The system must effectively sustain the drug concentration at the intended target site within the narrow therapeutic range for an extended duration, thereby minimizing the need for frequent dose administration and reducing treatment-related complications²⁹. This sustained maintenance of therapeutic levels ensures continuous pharmacological activity while reducing peaks and troughs in drug exposure.

5.5. Minimal Drug Leakage and Retention

It is essential to ensure minimal drug losses resulting from unintended leakage from the carrier system during transit through circulation and prior to reaching the target site³⁰. Premature drug release in non-target tissues can result in systemic toxicity and reduced therapeutic efficacy at the intended site. The carrier system must therefore provide optimal drug retention and protection until the predetermined release site is reached.

5.6. Biodegradability and Metabolic Elimination

The carrier employed must be biodegradable through natural metabolic processes and should be efficiently eliminated from the body without causing any toxic interactions or accumulation in vital organs³¹. The degradation products must likewise be non-toxic and readily eliminated through normal excretory pathways to ensure long-term safety with repeated dosing.

5.7. Manufacturing Feasibility and Cost-Effectiveness

The preparation process should be straightforward, easily reproducible with consistent batch- to-batch quality, and economically viable for clinical translation and commercial production³². The manufacturing methodology must be scalable to support therapeutic demand while maintaining stringent quality control standards. Additionally, the cost-effectiveness of production must be balanced against therapeutic efficacy to ensure accessibility and affordability for patients requiring long-term treatment.

VI. DIFFERENT TYPES OF CARRIERS APPLIED FOR DRUG TARGETING

Numerous carrier systems have been developed and applied in targeted drug delivery to facilitate precise therapeutic delivery. These diverse carrier platforms each possess unique physicochemical characteristics that enable specific applications in disease treatment and diagnostic imaging³³.



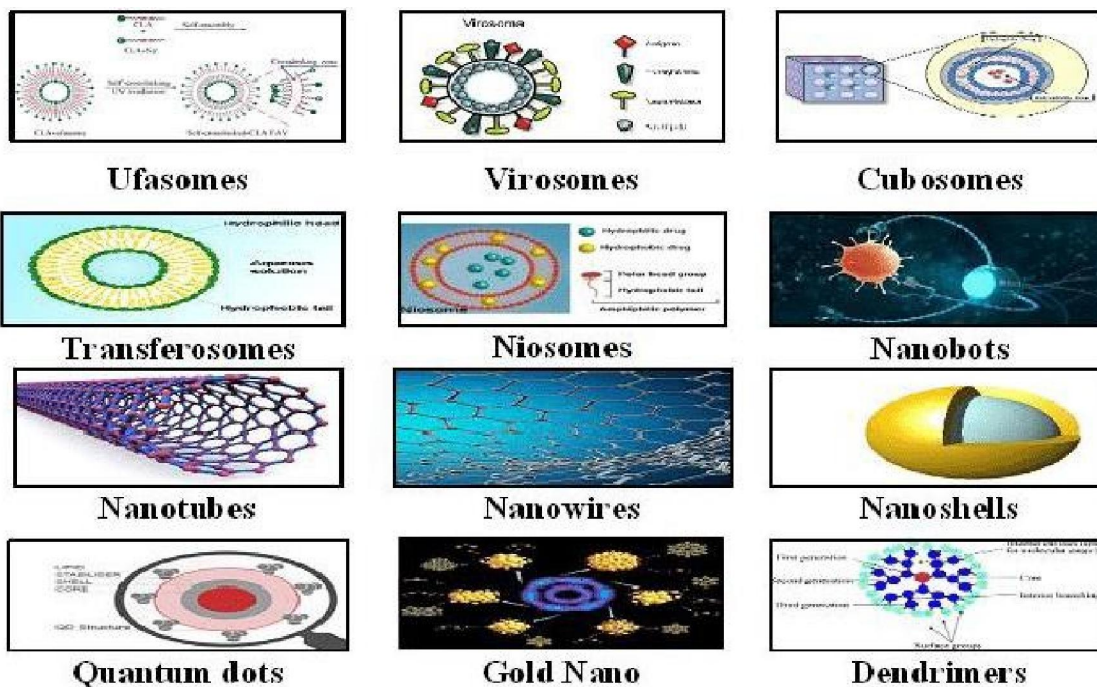


Figure 3: Different Types of Carriers Applied For Drug Targeting 55

6.1. Carbon Nanotubes

Carbon nanotubes represent a sophisticated drug delivery system consisting of hollow cylindrical structures composed of carbon atoms that can be readily filled and hermetically sealed with the desired therapeutic agent³⁴. These nanoscale tubes are predominantly employed for targeted drug delivery to cancer cells, where their cylindrical geometry provides optimal space for drug loading. Liu and colleagues successfully demonstrated the efficacy of carbon nanotubes for targeting tumors in murine models, while McDevitt and colleagues achieved effective tumor targeting through antibody-functionalized and radiolabeled carbon nanotubes³⁵.

6.2. Nanowires

Nanowires are ultrathin wire-like nanostructures with extremely small diameters, typically composed of metallic or organic compound materials. The defining characteristic of nanowires is their exceptionally large surface area relative to their volume, enabling selective binding with specific biological molecules upon introduction into the body³⁶. Nanowires demonstrate particular utility in the detection and treatment of neurodegenerative disorders, including seizure disorders and Parkinson's disease. Additionally, nanowire systems can be employed for the detection and precise anatomical localization of tumor tissue. Hong and colleagues exemplified this application by utilizing fluorescent zinc oxide nanowires for molecularly targeted imaging of malignant cancer cells³⁷.

6.3. Nanoshells

Nanoshells represent an innovative nanoparticulate strategy consisting of a hollow dielectric silica core surrounded by a contiguous gold shell³⁸. These hybrid nanostructures possess dual functionality, enabling their application in both diagnostic imaging and therapeutic drug delivery purposes. The outer gold surface of nanoshells can be conveniently functionalized with antibodies or targeting ligands, permitting selective conjugation to specific anatomical sites, particularly cancer cells. Loo and colleagues investigated the capacity of nanoshells to simultaneously perform diagnostic imaging and therapeutic treatment of malignant tumors³⁹.



6.4. Quantum Dots

Quantum dots are nanocrystalline semiconductor particles possessing distinctive and tunable optical properties that confer the capacity for sensitive fluorescent imaging of tumor tissue⁴⁰. This unique optical characteristic renders quantum dots particularly valuable as a carrier system for targeted cancer drug delivery. Pardo and colleagues successfully integrated quantum dots with carbon nanotubes for synergistic cancer targeting and drug delivery applications.

6.5. Nanopores

Nanopores are nanostructures containing extremely minute apertures that selectively allow the passage of individual DNA molecules in single-stranded configuration, thereby enabling extraordinarily precise and efficient DNA sequencing⁴¹. This technology possesses significant potential applications in genetic engineering and broader biotechnological applications. Schneider and colleagues demonstrated the feasibility of DNA translocation through nanopores fabricated in graphene membranes.

6.6. Gold Nanoparticles

Gold nanoparticles have been extensively utilized by researchers to develop ultrasensitive detection systems for nucleic acids and for identifying protein biomarkers associated with various cancer types⁴². The exceptional optical and chemical properties of gold nanoparticles enable their application in clinical diagnostics with remarkable sensitivity. Peng and colleagues successfully employed gold nanoparticles in the diagnostic detection of lung cancer.

6.7. Dendrimers

Dendrimers are synthetic nanoparticulate structures characterized by a precisely defined diameter and highly organized architecture⁴³. These molecules consist of a controlled central core surrounded by multiple concentric layers of polymeric branches, creating a unique three-dimensional structure. The dendrimeric architecture features numerous surface sites available for chemical attachment of therapeutic drugs. Dendrimers have demonstrated significant utility in gene transfection and medical imaging applications. Abd-El-Aziz and Agatemor provided comprehensive review of the expanding biomedical applications of dendrimers⁴⁴.

6.8. Liposomes

Liposomes are microscopic vesicular structures composed of a bilayer membrane derived from natural phospholipid molecules⁴⁵. These spherical compartments possess the remarkable capacity to encapsulate both hydrophilic (water-soluble) and lipophilic (lipid-soluble) therapeutic agents. The percentage of drug successfully entrapped within liposomes is determined by the inherent physical and chemical properties of the specific therapeutic agent and the composition of the lipid mixture. Huwyler & colleagues conducted extensive investigations into tumor-targeting strategies utilizing liposomal formulations of antineoplastic drugs⁴⁶.

6.9. Niosomes

Niosomes are non-ionic surfactant-derived vesicular structures possessing the capacity to encapsulate both hydrophilic and lipophilic therapeutic agents in a manner similar to liposomes⁴⁷. However, niosomes demonstrate superior colloidal & chemical stability compared to liposomes.

Niosomes have demonstrated exceptional efficacy for targeted delivery of antineoplastic, anti-inflammatory, antibacterial, antifungal, and antiviral therapeutic agents. Liu and colleagues designed and evaluated a novel niosomal delivery system formulated with daunorubicin (DNR) for selective targeting against acute myeloid leukemia (AML)⁴⁸. Ahmed and colleagues prepared piroxicam-loaded niosomes designed to specifically localize the analgesic and anti-inflammatory therapeutic effects at the site of pain.



6.10. Ufasomes

Ufasomes are vesicular dispersions composed of unsaturated fatty acid bilayers, prepared through the combination of fatty acids and ionic surfactants in the presence of cholesterol as a stabilizing agent. These lipid-based carriers represent an exceptionally suitable delivery system for drugs intended for topical dermatological application⁴⁹. The stratum corneum constitutes the primary physiological barrier limiting percutaneous drug penetration. This penetration barrier can be effectively overcome through the application of ufasomal delivery systems. Kaur and colleagues investigated and demonstrated enhanced antifungal activity of oxiconazole- loaded ufasomes against the fungal pathogen *Candida albicans*⁵⁰.

6.11. Pharmacosomes

Pharmacosomes are complex nanostructures composed of neutral molecules possessing both positive and negative electrostatic charges, combined with both hydrophilic and lipophilic chemical character in an optimized ratio of polyphenolic compounds with phospholipid molecules⁵¹. The therapeutic drug is conjugated to the lipid complex through electrostatic interactions or hydrogen bonding mechanisms. The nomenclature "pharmacosome" derives from the Greek terms "Pharmakon" (meaning drug) and "soma" (meaning carrier). Semalty and colleagues successfully developed and comprehensively evaluated pharmacosomal formulations of aceclofenac⁵².

6.12. Virosomes

Virosomes are sophisticated drug delivery systems described as unilamellar vesicular structures prepared from phospholipid bilayers⁵³. The surface architecture of virosomes is functionalized with virus-derived glycoproteins, which are strategically attached to facilitate selective recognition and targeted delivery. Lucarini and colleagues designed an innovative delivery platform utilizing erythro-magneto-hyaluronic acid-conjugated virosomes for the treatment of cerebral tumors.

6.13. Cubosomes

Cubosomes are nanostructured drug delivery systems prepared from specific lipid molecules and characterized by a liquid crystalline cubic architecture suitable for parenteral injection⁵⁴. Azhari and colleagues employed Tween 80 as a stabilizing agent for phytantriol-based cubosomes, demonstrating their utility for the delivery of macromolecular therapeutic agents to the brain.

VII. CONCLUSION

The development of targeted drug delivery systems represents a paradigm shift in pharmaceutical therapeutics, offering unprecedented opportunities to overcome the limitations of conventional drug administration. By enabling precise delivery of therapeutic agents to specific diseased tissues while minimizing systemic exposure, these systems have demonstrated remarkable potential in enhancing treatment efficacy and reducing adverse effects across various medical conditions, particularly in oncology, cardiovascular diseases, and chronic inflammatory disorders.

Despite significant advances in ligand-based targeting, stimulus-responsive carriers, and nanoparticle platforms, several challenges remain that must be addressed before targeted delivery can achieve its full clinical potential. Issues related to scale-up manufacturing, long-term biocompatibility, immunogenicity, and the complexity of biological barriers continue to pose obstacles to widespread clinical translation. Additionally, the heterogeneity of disease states and individual patient variability necessitate more personalized approaches to targeting strategy selection.

Looking forward, the integration of emerging technologies such as artificial intelligence for rational design, advanced biomaterials with enhanced targeting capabilities, and combination approaches that leverage multiple targeting mechanisms hold promise for next-generation delivery systems. The continued collaboration between chemists, biologists, clinicians, and regulatory experts will be essential in navigating the path from bench to bedside. As our understanding of disease biology deepens and technological capabilities expand, targeted drug delivery systems are



poised to become a cornerstone of precision medicine, ultimately transforming patient outcomes and redefining the therapeutic landscape.

REFERENCES

- [1]. Langer R. Drug delivery and targeting. *Nature*. 1998;392(6679 Suppl):5-10.
- [2]. Torchilin VP. Targeted pharmaceutical nanocarriers for cancer therapy and imaging. *AAPS J*. 2007;9(2):E128-E147.
- [3]. Jain KK. Advances in the field of nano- and microtechnology for drug delivery. *Clin Pharmacol Ther*. 2005;77(6):595-598.
- [4]. Allen TM, Cullis PR. Liposomal drug delivery systems: From concept to clinical applications. *Adv Drug Deliv Rev*. 2013;65(1):36-48.
- [5]. Allen TM, Cullis PR. Drug delivery systems: Entering the mainstream. *Science*. 2004;303(5665):1818-1822.
- [6]. Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. *Adv Drug Deliv Rev*. 2002;54(5):631-651.
- [7]. Varshney SK, Immunological aspects of targeted drug delivery systems. *J Drug Target*. 2012;20(3):195-209.
- [8]. Mohanraj VJ, Chen Y. Nanoparticles—A review. *Trop J Pharm Res*. 2006;5(1):561-573.
- [9]. Feng SS, Chien S. Chemotherapeutic engineering: application and further development of chemical engineering principles for novel drug delivery systems. *J Control Release*. 2003;83(1):1-11.
- [10]. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanoparticles for drug delivery: Towards improved efficacy and reduced toxicity. *Nat Rev Drug Discov*. 2007;6(9):771-786.
- [11]. Gradishar WJ. Albumin-bound paclitaxel: a next-generation taxane. *Expert Opin Pharmacother*. 2006;7(8):1041-1053.
- [12]. Müller RH, Keck CM. Challenges and solutions for the delivery of biotech drugs—a review of drug nanocrystal technology and lipid nanoparticles. *J Biotechnol*. 2004;113(1-3):151-170.
- [13]. Soppimath KS, Aminabhavi TM, Kulkarni AR, Rudzinski WE. Biodegradable polymeric nanoparticles as drug delivery devices. *J Control Release*. 2001;70(1-2):1-20.
- [14]. Couvreur P, Barratt G, Fattal E, Legrand P, Vauthier C. Nanocapsule technology: A review. *Crit Rev Ther Drug Carrier Syst*. 2002;19(2):99-134.
- [15]. Kabanov AV, Gendelman HE. Nanomedicine in the diagnosis and therapy of neurodegenerative disorders. *Prog Polym Sci*. 2007;32(8-9):1054-1082.
- [16]. Brannon-Peppas L, Blanchette JO. Nanoparticle and targeted systems for cancer therapy. *Adv Drug Deliv Rev*. 2012;64(3):206-212.
- [17]. Cho K, Wang X, Nie S, Chen ZG, Shin DM. Therapeutic nanoparticles for drug delivery in cancer. *Clin Cancer Res*. 2008;14(5):1310-1316.
- [18]. Sinha R, Kim GJ, Nie S, Shin DM. Nanotechnology in cancer therapeutics: bioconjugated nanoparticles for drug delivery. *Mol Cancer Ther*. 2006;5(8):1909-1917.
- [19]. Duncan R, Izzo L. Dendrimer biocompatibility and toxicity. *Adv Drug Deliv Rev*. 2005;57(15):2215-2237.
- [20]. Rawat M, Singh D, Saraf S, Saraf S. Nanocarriers: promising vehicle for bioactive drugs. *Biol Pharm Bull*. 2006;29(9):1790-1798.
- [21]. Misra R, Acharya S, Sahoo SK. Cancer nanotechnology: application of nanotechnology in cancer therapy. *Drug Discov Today*. 2010;15(19-20):842-850.
- [22]. Maeda H, Wu J, Sawa T, Matsumura Y, Hori K. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review. *J Control Release*. 2000;65(1-2):271-284.
- [23]. Byrne JD, Betancur PA, Brannon-Peppas L. Active targeting schemes for nanoparticle systems in cancer therapeutics. *Adv Drug Deliv Rev*. 2008;60(15):1615-1626.
- [24]. Goldberg M, Langer R, Jia X. Nanoparticle-mediated drug delivery: passing the guard. *Curr Opin Chem Biol*. 2007;11(4):378-385.



- [25]. Davis ME, Shin DM. Nanoparticle therapeutics: an emerging treatment modality for cancer. *Nat Rev Drug Discov.* 2008;7(9):771-782.
- [26]. Sharma A, Sharma US. Liposomes in drug delivery: progress and limitations. *Int J Pharm.* 1997;154(2):123-140.
- [27]. Owens DE, Peppas NA. Opsonization, biodistribution, and pharmacokinetics of polymeric nanoparticles. *Int J Pharm.* 2006;307(1):93-102.
- [28]. Weissig V, Pettis RJ. Mitochondrial gene therapy: in vivo transfection of mitochondrial DNA. *Mitochondrion.* 2003;2(6):431-441.
- [29]. Tan ML, Choong PF, Dass CR. Recent developments in liposomal and polymer-based nanoparticles for drug delivery system in cancer therapy. *Expert Opin Drug Deliv.* 2010;7(8):907-917.
- [30]. Gu F, Zhang L, Teply BA, Mann N, Wang A, Radovic-Moreno AF, et al. Precise engineering of targeted nanoparticles by using self-assembled biointegrated block copolymers. *Proc Natl Acad Sci USA.* 2008;105(7):2586-2591.
- [31]. Nystrom AM, Fadeel B. Safety assessment of nanomaterials: implications for nanomedicine. *J Control Release.* 2012;161(2):403-408.
- [32]. Shi J, Votruba AR, Farokhzad OC, Langer R. Nanotechnology in drug delivery and tissue engineering: from discovery to applications. *Nano Lett.* 2010;10(9):3223-3230.
- [33]. Wang AZ, Langer R, Farokhzad OC. Nanoparticle delivery of cancer drugs. *Annu Rev Med.* 2012;63:185-198.
- [34]. Liu Z, Tabakman S, Welsher K, Dai H. Carbon nanotubes in biology and medicine: in vitro and in vivo detection, imaging, and drug delivery. *Nano Res.* 2009;2(2):85-120.
- [35]. McDevitt MR, Chattopadhyay D, Kappel BJ, Jaggi JS, Schiffman SR, Antczak C, et al. Tumor targeting with antibody-functionalized, radiolabeled carbon nanotubes. *J Nucl Med.* 2007;48(7):1180-1189.
- [36]. Xia Y, Yang P, Sun Y, Wu Y, Mayers B, Gates B, et al. One-dimensional nanostructures: synthesis, characterization, and applications. *Adv Mater.* 2003;15(5):353-389.
- [37]. Zheng G, Patolsky F, Cui Y, Wang WU, Lieber CM. Multiplexed electrical detection of cancer markers with nanowire sensors. *Nat Biotechnol.* 2005;23(10):1294-1301.
- [38]. O'Neal DP, Hirsch LR, Halas NJ, Payne JD, West JL. Photo-thermal tumor ablation in mice using near infrared-absorbing nanoparticles. *Cancer Lett.* 2004;209(2):171-176.
- [39]. Loo C, Lowery A, Halas N, West J, Drezek R. Immunotargeted nanoshells for integrated cancer imaging and therapy. *Nano Lett.* 2005;5(4):709-711.
- [40]. Gao XH, Cui YY, Levenson RM, Chung LWK, Nie SM. In vivo cancer targeting and imaging with semiconductor quantum dots. *Nat Biotechnol.* 2004;22(8):969-976.
- [41]. Deamer D, Akeson M. Nanopores and nucleic acids: prospects for ultra-rapid sequencing. *Trends Biotechnol.* 2000;18(4):147-151.
- [42]. Taton TA, Mirkin CA, Letsinger RL. Scanometric DNA array detection with nanoparticle probes. *Science.* 2000;289(5485):1757-1760.
- [43]. Svenson S, Tomalia DA. Dendrimers in biomedical applications—reflections on the field. *Adv Drug Deliv Rev.* 2012;64:102-115.
- [44]. Abd-El-Aziz AS, Agatemor C. Applications of dendrimers in nanomedicine and diagnostics. *Polymer.* 2014;55(24):5868-5881.
- [45]. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo SW, Zarghami N, Hanifehpour Y, et al. Liposome: classification, preparation, and applications. *Nanoscale Res Lett.* 2013;8(1):102.
- [46]. Huwyler J, Wu D, Marti W. Liposomal doxorubicin-the first FDA approved nano-drug: lessons to learn. *J Liposome Res.* 2018;28(2):102-113.
- [47]. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. *Int J Pharm.* 1998;172(1-2):33-70.



- [48]. Liu DZ, Liu Z, Wang L, Zhang C, Zhang N, Huang Y, et al. Nanostructured lipid carriers as novel delivery systems for daunorubicin: development, characterization, and in vitro studies. *J Control Release*. 2007;119(3):285-294.
- [49]. Cevc G, Gebauer D. Hydration-driven transport of deformable lipid vesicles through fine pores and the skin barrier. *Biophys J*. 2003;84(2):1010-1024.
- [50]. Kaur M, Jassal G, Agrawal Y. Formulation and evaluation of ufasome-based antifungal delivery system. *J Drug Deliv Sci Technol*. 2015;28:96-103.
- [51]. Semalty A, Semalty M, Rawat M, Singh D. Pharmacosomes: formulation, characterisation and applications. *Expert Opin Drug Deliv*. 2005;2(1):75-87.
- [52]. Semalty A, Semalty M, Singh D, Rawat M. Development and characterization of pharmacosomes of aceclofenac. *Acta Pharm*. 2007;57(3):335-347.
- [53]. Wiethoff CM, Middaugh CR. Barriers to nonviral gene delivery. *J Pharm Sci*. 2003;92(2):203-217.
- [54]. Larsson K. Cubic lipid-water phases: structure and biomembrane aspects. *J Phys Chem*. 1989;93(21):7304-7314.
- [55]. Prabahar, Kousalya & Alanazi, Zahraa & Qushawy, Mona. (2021). Targeted Drug Delivery System: Advantages, Carriers and Strategies. *Indian Journal of Pharmaceutical Education*. 55. 346-353.

