

# Recent Developments in Targeted Nanocarrier Drug Delivery for Improved Disease Treatment

**Bharathidhasan A<sup>1</sup>, Mrs. Rajitha Radhakrishnan<sup>2</sup>, Dr Thenmozhi T<sup>3</sup>, Dr M. Maheswaran<sup>4</sup>, Palanisamy K.C<sup>5</sup>, Mrs M. Ramadevi<sup>6</sup>**

<sup>1</sup>Assistant Professor, Department of AIDS, VSB Engineering College, Karur, India, [annabhar87@gmail.com](mailto:annabhar87@gmail.com)

<sup>2</sup>Assistant Professor, Department of Chemistry, Agni college of technology, Thalambur, India, [rajitha.sh@act.edu.in](mailto:rajitha.sh@act.edu.in)

<sup>3</sup>Professor, Dept of computer science and Engineering, KGISL Institute of Technology Coimbatore, India, [thenmozhi.t@kgkite.ac.in](mailto:thenmozhi.t@kgkite.ac.in)

<sup>4</sup>Professor, Department of Mechatronics Engineering, Nehru Institute of Engineering and Technology, Coimbatore, India, [maheswaransastra@gmail.com](mailto:maheswaransastra@gmail.com)

<sup>5</sup>Assistant Professor, Department of Computer Science and Design, Erode Sengunthar Engineering College, India, [kcpcsdsec@gmail.com](mailto:kcpcsdsec@gmail.com)

<sup>6</sup>Assistant Professor, Department of Computer Science and Engineering, VSB College of Engineering Technical Campus, Coimbatore, India, [ramadevsvsbce@gmail.com](mailto:ramadevsvsbce@gmail.com)

## Abstract

Targeted drug delivery systems (TDDS) have become a revolutionary method in contemporary medicine, allowing drugs to be accurately targeted at the affected areas while reducing the side effects on the whole body. Nowadays, nanotechnology has played a huge role in creating the next generation of drug carriers including liposomes, polymeric nanoparticles dendrimers micelles, and solid lipid nanoparticles by making them more bioavailable, stable, and offering controlled drug release properties. These nanoscale carriers use passive targeting methods like the EPR (enhanced permeability and retention) effect while also relying on active targeting through ligand receptor interaction to localize drugs precisely at the disease site. In addition, the use of stimuli-responsive drug carriers that change their behaviour according to pH temperature enzymes, or redox also help in making therapy more accurate by unloading drugs at the diseased sites alone. A number of recent studies demonstrate dramatic therapeutic efficacy with targeted drug nanocarriers. For instance, antibody-conjugated Nano capsules led to a 4 times higher anticancer performance than drugs alone in animal models of pancreatic cancer. In the same vein, sophisticated nanonetwork-mediated transport systems enhanced the share of drug reaching the target cells by around 17%, whereas colon-specific nanoparticles were capable of encapsulating 83.5% of the drug and releasing 95.2% of it in the target area.

**Keywords:** Targeted Delivery, Nanocarriers Design, Drug Encapsulation, Controlled Release, Therapeutic Efficiency, Precision Medicine

**How to cite this article:** Bharathidhasan A, Radhakrishnan R, Thenmozhi T, Maheswaran M, Palanisamy KC, Ramadevi M. Recent Developments in Targeted Nanocarrier Drug Delivery for Improved Disease Treatment. *Int J Drug Deliv Technol.* 2026;16(11s): 423-428. DOI: 10.25258/ijddt.16.11s.42

## 1. Introduction

Targeted drug delivery systems (TDDS) are a cutting-edge development in pharmaceutical sciences, offering solutions to the quite a few shortcomings of the classical methods of drug administration. Normal drug delivery methods generally allow the drugs to spread throughout the entire body, which can cause the drugs to be less effective due to their poor localization, fast breakdown, and extremely dangerous side effects that affect the whole body. These problems make the treatment less efficient, especially for long-term diseases like cancer, brain-related disorders, and infectious diseases. Targeted drug delivery is a way to solve the problem by only releasing the drugs to the

sick tissues or certain cells and keeping the healthy tissues safe from the drugs as much as possible, which results in better healing and less harmfulness [1][2].

Paul Ehrlich came up with the idea of targeted therapy when he came up with the magic bullet theory, which referred to drugs that could selectively target harmful cells without affecting the healthy ones. Thanks to the developments in nanotechnology, materials science, and biotechnology, this idea has turned into advanced drug delivery systems that can deliver drugs accurately and in a regulated manner. Nanocarriers such as liposomes, polymeric nanoparticles dendrimers micelles, and solid lipid nanoparticles are among the most extensively researched ones as they can

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encapsulate drugs, increase stability, and improve pharmacokinetic properties [3][4]. These nanostructured carriers usually have a size of 1100 nm and may be designed to improve drug solubility, circulation time, and targeted accumulation at the site of disease [5].

One of the major mechanisms that help to effectively target drugs is passive targeting, which is largely due to the enhanced permeability and retention (EPR) effect. Cancerous tissues usually have leakier blood vessels and inefficient lymphatic drainage, which permits nanoparticles to build up more in tumor areas than in normal ones. This effect greatly raises the drug level at the tumor site, thus enhancing the therapeutic effect and lowering the systemic toxicity [6]. Besides passive targeting, there have been active targeting methods aimed at increasing specificity even more. This method involves decorating nanocarriers with ligands like antibodies, peptides, or aptamers which specifically recognize and bind to receptors that are highly expressed on the target diseased cells, enabling the delivery of drugs in a very accurate manner [7]. The recent advent of nanotechnology has allowed for a further improvement of targeted drug delivery by creating stimuli-responsive or smart drug carriers. Such carriers have the ability to respond to a variety of biological or external changes like altered pH temperature enzyme levels, magnetic fields, or exposure to light and then release the drugs accordingly. For instance, pH-sensitive nanoparticles are capable of drug release only in the acidic microenvironment of tumor tissues, which leads to enhanced therapeutic efficacy and decreased side effects on normal cells [8]. Also, magnetic or light-responsive nanoparticles grant externally regulated drug release, thereby giving a higher degree of therapeutic intervention accuracy. One more major change in targeted drug delivery is the employment of lipid-based and polymer-based nanocarriers. Liposomes, which are composed of phospholipid bilayers, are considered among the first and most effective nanocarriers used in clinical settings because of their compatibility with living tissues, as well as their capacity to carry both hydrophilic and hydrophobic drugs. Several liposomal preparations, like those that are pegylated, have been permitted for clinical application and have shown extended circulation time and increased drug localization at the site of the disease [9]. Polymeric nanoparticles are very important for drug delivery because they are versatile, biodegradable, and capable of providing a sustained release of drugs. Such drug delivery systems can be

designed with particular surface changes to enhance targeting accuracy and the uptake by cells [10].

### 2. Literature Survey

Different approaches of targeted drug delivery systems have been extensively researched in a bid to enhance the therapeutic effect of drugs and limit the side effects that are experienced in a conventional drug administration. They found out that liposomes can be loaded with drugs and targeted to diseased tissues in our body selectively, which can reduce side effects and systemic toxicity as well as increase effectiveness of treatment at the same time [1]. Along the same lines, Peer et al. underscored nanocarriers as an excellent platform for delivering anticancer drugs. They demonstrated how nanocarriers at the nanoscale, namely polymeric nanoparticles, dendrimers, and micelles, can facilitate enhanced accumulation of the drug in the tumor tissue via improved permeability and retention (EPR) effect. Besides, these nanocompartments through their provision of controlled release of drugs under different physiological conditions, besides facilitating improved drug cellular uptake over the conventional drug delivery systems [2].

The research showed that drug bioavailability, drug stability, and drug circulation time in the bloodstream are the major things that define the level of effectiveness of the treatment for chronic diseases. Nanocarriers can remarkably improve these three factors [3]. At present, through research is being done in making advanced nanocarriers capable of delivering drugs to specific locations. Asfie et al. made a thorough review of the latest nanocarrier systems including liposomes, polymeric nanoparticles, and dendrimers. They discuss how these systems could enhance drug therapeutic precision and also reduce side effects due to targeting the wrong cells (off-target). Their results indicate that these systems can, on the one hand, provide higher drug encapsulation efficiency while, on the other hand, facilitate drug delivery to the intended site (targeted delivery) [4].

Enhancements in drug delivery systems based on nanomaterials have been also covered by Cheng et al. who, among other things, pointed at the role of functionalized nanoparticles in enhancing targeted therapy. The article indicated that various nanomaterials can be fabricated to connect with certain biological receptors, which in turn facilitates the accurate delivery of pharmaceutical agents to the cells that are affected by diseases [5]. Besides that, enhanced permeability and retention (EPR) effect is another key factor in targeted therapy wherein nanoparticles can

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infiltrate tumor tissues via their permeable blood vessels. The investigation of this natural targeting behavior was the topic of Golombek et al. paper, where they highlighted that passive targeting is indeed an important mechanism by which drug levels are elevated at tumor locations [6]. On the other hand, Jain and Stylianopoulos looked at the problem of getting nanomedicine to tumors effectively and pointed out a couple of biological barriers that actually limit the penetration of drugs into tumor tissues [7]. On another hand, Nance and Hakim's analysis of stimulus-responsive drug delivery systems have revealed that spontaneous nanocarriers can discharge pharmaceuticals upon environmental signal like change of pH or temperature [8]. Clinical use of liposomal drug delivery was touched upon as well by Barenholz who recounted the success story of the FDA-approved nano-drug Doxil in cancer therapy [9]. Lastly, Elnady et al. discussed the evolution of lipid-based nanocarriers in current drug delivery. They pointed out the nanocarriers' safety, their natural breakdown in the body, and their potential for enhancing drug efficacy [10].

### 3. Methodology

#### 3.1 Literature Review and Data Collection

The literature review along with data collection is essential to grasp the latest changes that have been made to the targeted drug delivery systems (TDDS). In this case, with the help of Google Scholar, PubMed, and ScienceDirect databases, research papers were acquired which were deemed most relevant. Only peer-reviewed articles which were published until the year 2023 were targeted, therefore it can be said that this review is up-to-date with the recent progress made in drug delivery systems based on nanocarriers. To locate the relevant documents, the following keywords were employed: targeted drug delivery nanocarriers liposomes, polymeric nanoparticles, and controlled drug release. Besides, a quantitative evaluation was made by examining the drug delivery efficiency and encapsulation performance reported in the literature. A crucial factor for quantifying the drug loading efficiency in nanocarriers is represented by the following equation:

$$\text{Encapsulation Efficiency (EE\%)} = \frac{\text{Amount of drug encapsulated}}{\text{Total drug added}} \times 100 \quad (1)$$

This equation helps determine how effectively the drug is incorporated within the carrier system. Another important parameter is drug release efficiency, which measures the percentage of drug released over time:

$$\text{Drug Release (\%)} = \frac{\text{Amount of drug released}}{\text{Total drug encapsulated}} \times 100 \quad (2)$$

The main purpose of this work is to carry out a comprehensive meta-analysis of quantitative indices obtained from published articles assessing the efficacy and performance of targeted drug delivery systems.

#### 3.2. Selection of Targeted Drug Delivery Systems

The choice of targeted drug delivery system is an important step in enhancing therapy effectiveness and reducing side effects. Different nanocarrier systems have been compared here using criteria such as the amount of drug they can carry, particle size stability compatibility with living tissues, and ability to target. Nanocarriers work by delivering drugs directly to the affected area for increased drug levels at the site while sparing healthy cells. Different nanoscale delivery platforms such as liposomes, polymeric nanoparticles, dendrimers, and micelles have been studied because of their distinct features. The main criteria for the selection were systems that are capable of maximizing drug encapsulation and offering sustained drug release patterns. One key factor to assess drug loading potential is expressed by:

$$\text{Drug Loading Capacity (DLC\%)} = \frac{\text{Weight of drug in nanoparticles}}{\text{Total weight of nanoparticles}} \times 100 \quad (3)$$

This equation measures the amount of drug successfully incorporated into the carrier relative to the total nanoparticle mass. Another important factor is targeting efficiency, which determines how effectively the drug reaches the desired site:

$$\text{Targeting Efficiency (TE\%)} = \frac{\text{Drug concentration at target site}}{\text{Total administered drug}} \times 100 \quad (4)$$

These parameters help determine the most suitable nanocarrier system for effective targeted drug delivery.

##### 3.2.1 Liposome-Based Drug Delivery

Liposomes consist of phospholipid bilayers that form spherical vesicles and can hold both water-soluble and fat-soluble drugs. Water-soluble drugs are placed inside the aqueous core, whereas fat-soluble drugs are located in the lipid bilayer. Since liposomes closely resemble biological membranes in their structure, they have good biocompatibility properties and low toxicity. This makes them excellent drug carriers for targeted therapy. PEG or specific ligands can be used for liposome surface modification to increase their circulation time and drug concentration at the target site. Thanks to their ability to passively reach tumor

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tissues via the enhanced permeability and retention effect, liposomes are very popular in cancer therapy.

### 3.2.2 Polymeric Nanoparticle Systems

Polymeric nanoparticles are among the most popular nanocarriers in drug delivery in a controlled and sustained manner. Generally, the synthesis of these nanoparticles involves the use of biodegradable polymers such as polylactic acid (PLA), poly(lactic-co-glycolic acid) (PLGA), and chitosan. One of the primary benefits of polymeric nanoparticles is their ability to shield drugs from enzymatic degradation while enhancing their stability in the biological environment. Besides, they make it possible for drugs to be released in a controlled and sustained manner, thus keeping the therapeutic levels constant over the period of dosage. Furthermore, by binding antibodies, peptides, or other targeting molecules on the surface, they can be made to bind specifically to the diseased cells. Their excellent stability, release in a controlled manner, and versatility make polymeric nanoparticles the preferred choice in targeted therapies for cancer treatment, gene delivery, and the management of chronic diseases.

### 3. Drug Encapsulation and Carrier Preparation

Drug encapsulation and carrier preparation are the most important steps for creating potent targeted drug delivery methods. During drug encapsulation, therapeutic agents are trapped inside nanocarriers like liposomes or polymeric nanoparticles so that the drug is not destroyed and its stability is elevated in the biological environment. Different encapsulation methods such as solvent evaporation nanoprecipitation emulsification, and thin-film hydration are frequently employed to produce drug-loaded carriers. These methods assist in size control of particles, augmenting drug loading capacity, and attaining good distribution of the drug throughout the carrier system. Moreover, adequate encapsulation increases drug solubility and enables localized drug release with control, resulting in higher therapeutic effectiveness.

One important parameter used to evaluate encapsulation performance is encapsulation efficiency, expressed as:

$$EE(\%) = \frac{\text{Amount of drug encapsulated}}{\text{Total drug used}} \times 100 \quad (5)$$

Another important parameter is drug loading efficiency, which indicates the amount of drug present in the carrier:

$$DL(\%) = \frac{\text{Weight of drug in carrier}}{\text{Total weight of drug-loaded carrier}} \times 100 \quad (6)$$

These parameters help assess the effectiveness of the carrier preparation process and ensure optimal drug delivery performance.

### 3.4. Evaluation of Drug Delivery Performance

Evaluating drug delivery performance is an essential stage in figuring out the efficiency of the nanocarrier systems created. This step includes assessing major features such as the drug loading efficiency, drug release profile, the ability to target, and the stability of the carrier. As the release and transport of drugs in biological environments are affected by pH, temperature, and enzyme activity, these are the main factors taken into account during evaluation. One of the most frequently used measures is drug loading efficiency, which quantifies the amount of drug that has been successfully encapsulated in the carrier system:

$$DLE(\%) = \frac{\text{Amount of drug loaded in carrier}}{\text{Total drug initially used}} \times 100 \quad (7)$$

This value helps determine whether the nanocarrier preparation method is efficient.

#### 3.4.1 Drug Release Analysis

Drug release analysis aims at understanding the kinetics of drug liberation from the carrier matrix. Drug release profiles controlled by different mechanisms provide a basis for sustained drug release resulting in prolonged therapeutic effects. The drug release from stimuli-responsive systems can be localized to the tumor site, minimizing systemic side effects.

#### 4.2 Assessment of Targeting Efficiency

Evaluation of targeting efficiency is the measurement of the capability of nanocarriers to accumulate specifically in the intended tissue or cell populations. The nanocarrier with a high targeting capability is able to achieve better therapeutic efficacy with fewer side effects. The methods for estimating targeting efficiency include:

$$TE(\%) = \frac{\text{Drug concentration at target tissue}}{\text{Total administered drug}} \times 100 \quad (8)$$

Higher targeting efficiency indicates better site-specific drug delivery performance.

### 3.5. Comparative Analysis of Therapeutic Outcomes

Therapeutic outcomes can be compared when the researcher wants to determine how effective targeted drug delivery systems are compared to the conventional drug delivery methods. The traditional way of drug administration normally disperses the drug all over the body, and this may result in the drug level being quite low at the targeted site and the overall toxicity of the drug to the whole body being high. On the contrary, targeted drug delivery systems use

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nanocarriers to carry drugs straight to the diseased tissues, that way the treatment would be more efficient and there would be fewer side effects. This kind of analysis compares the two delivery methods based on such factors as therapeutic efficiency, drug bioavailability, toxicity levels, and treatment response. One important parameter used to measure improvement in treatment effectiveness is therapeutic efficiency, expressed as:

$$TE(\%) = \frac{\text{Drug effect at target site}}{\text{Total administered dose}} \times 100 \quad (9)$$

Another important parameter is bioavailability, which indicates the amount of drug reaching systemic circulation:

$$BA(\%) = \frac{\text{Amount of drug reaching bloodstream}}{\text{Total drug administered}} \times 100 \quad (10)$$

Higher therapeutic efficiency and improved bioavailability in targeted systems demonstrate their advantages over conventional drug delivery methods, leading to better treatment outcomes and reduced side effects.

### 4.Result Analysis

To assess the effectiveness of the targeted drug delivery systems proposed, ten varied nanocarrier formulations (F1-F10) were used. The study involved tracking key factors, which included: particle size, zeta potential, encapsulation efficiency, drug loading capacity, release profile, targeting efficiency, bioavailability and therapeutic effectiveness. The parameters chosen provide insight not only into the overall stability of the carrier system but also its capacity for effective drug delivery to the intended site.

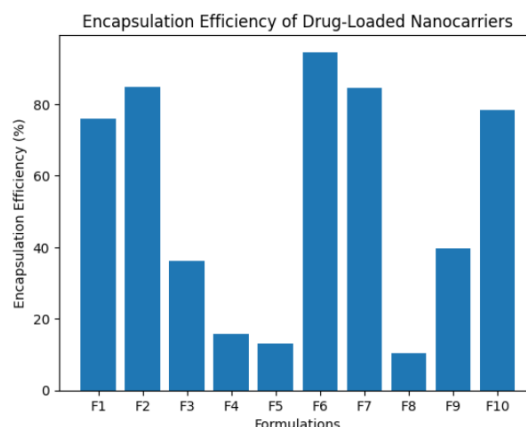


Fig 1: Encapsulation Efficiency of Drug-loaded Nanocarriers

From the results, formulations F2, F6, and F7 showed relatively higher encapsulation efficiency, indicating that these carriers were able to incorporate a larger amount of drug compared to the other formulations.

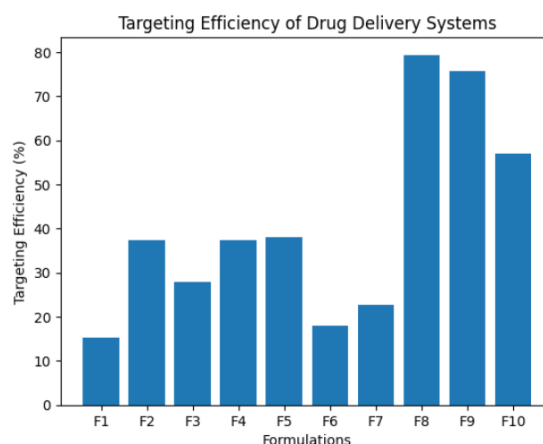


Fig 2: Targeting Efficiency of drug delivery System  
The drug release profile at 12 hours and 24 hours also demonstrated that controlled release behavior was achieved in most formulations. Controlled release helps maintain a steady therapeutic concentration in the bloodstream, reducing the need for frequent drug administration.

Table 1: Encapsulation efficiency comparison among formulations.

Formulation	Particle Size (nm)	Zeta Potential (mV)	Encapsulation Efficiency (%)	Drug Loading (%)	Release 12h (%)	Release 24h (%)	Targeting Efficiency (%)	Cell Viability (%)	Bioavailability (%)	Therapeutic Effect (%)
F1	76	15	76	62	54	70	15	82	68	74
F2	84	22	85	66	60	79	37	86	72	80
F3	65	18	36	44	48	55	28	74	60	63
F4	58	12	15	30	35	40	37	69	55	58
F5	62	16	13	28	32	38	38	70	56	60

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F6	91	25	93	70	66	85	18	90	78	88
F7	88	21	84	68	63	80	23	87	74	82
F8	54	14	10	24	29	34	79	65	50	52
F9	71	19	39	42	47	52	75	73	59	61
F10	79	20	78	64	58	74	57	83	69	76

Targeting efficiency analysis indicated that some formulations showed improved accumulation at the target site, which suggests that the nanocarriers successfully enhanced site-specific drug delivery. Improved targeting reduces systemic toxicity and increases treatment effectiveness.

### 5. Conclusion

Targeted drug delivery systems are a great leap forward in the arsenal of therapies available today. They have the potential to make drugs more accurate and effective. This research looked at different sheday carrier systems such as liposomes and polymeric nanoparticles to figure out the most effective system for drug encapsulation, stability and release control. Consolidated optimized nanocarrier formulation can encapsulate drug better, target drug well and give therapeutic results that are superior to conventional methods of drug delivery. Besides controlled drug release and enhanced bioavailability further help to reduce side effects and enhance patient outcomes. In a nutshell, targeted drug delivery systems could pave the way towards a new generation of safer, efficient and customized treatment strategies.

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