Nano carrier-Based Drug Delivery Systems: Recent Advances in Formulation Strategies, Targeted Delivery and Clinical Translation

Aachal Samadhan Chimkar[1*], Dr. Nikita Maruti Gaikwad[2]
[1]Research Scholar, Department of Pharmaceutics Modern College of Pharmacy Nigdi, Pune, Maharashtra, India.
[1]Associate Professor, Department of Pharmaceutics Modern College of Pharmacy Nigdi, Pune, Maharashtra, India.

Corresponding Author
Aachal Samadhan Chimkar[1*]
[1]Research Scholar, Department of Pharmaceutics Modern College of Pharmacy Nigdi, Pune, Maharashtra, India.
Mail Id - aachalchimkar2001@gmail.com

Abstract:
Conventional drug delivery systems often face significant limitations such as poor solubility, low bioavailability, lack of site-specific targeting, and undesirable side effects. These challenges can reduce therapeutic efficacy and increase toxicity, ultimately affecting patient outcomes. As a result, there is a growing need for advanced drug delivery approaches that can overcome these barriers and provide more precise and efficient treatment. Nano carrier-based drug delivery systems have emerged as a promising solution to address these issues. By utilizing Nano scale materials, these systems enhance drug stability, improve bioavailability, and enable controlled and sustained drug release. More importantly, Nano carriers offer the ability to deliver drugs specifically to targeted tissues or cells, minimizing systemic exposure and reducing adverse effects. This review focuses on recent advances in Nano carrier formulation strategies, including lipid-based, polymeric, and inorganic systems. It also highlights various targeting approaches such as passive targeting through enhanced permeability and retention (EPR) effect and active targeting using ligand-mediated mechanisms. Furthermore, the article discusses the progress in clinical translation, emphasizing the challenges related to large-scale production, regulatory approval, and safety evaluation. In conclusion, Nano carrier-based drug delivery systems represent a transformative approach in modern therapeutics. With continuous advancements in formulation design and targeting strategies, these systems hold great potential to revolutionize disease treatment. Future research should focus on improving scalability, ensuring safety, and accelerating clinical adoption to fully realize the benefits of nanotechnology in healthcare.

Keywords: Nano carriers, Drug delivery, Targeted therapy, Bioavailability, Formulation strategies, Clinical translation

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Introduction:

Limitations of Conventional Drug Delivery-

Conventional drug delivery systems have been widely used for decades, yet they present several critical limitations that affect therapeutic efficiency. A major challenge is the poor aqueous solubility of many drugs, which leads to inadequate dissolution and reduced absorption in the body [1, 2]. This often results in low bioavailability and inconsistent clinical outcomes. Additionally, traditional dosage forms lack specificity, causing drugs to distribute non-selectively across various tissues rather than targeting the intended site of action [3]. To compensate for this inefficiency, higher doses are frequently administered, which increases the likelihood of systemic toxicity and adverse side effects [2, 4]. These drawbacks emphasize the need for more advanced and targeted delivery systems.

Emergence of Nanotechnology in Drug Delivery-

Nanotechnology has emerged as a promising solution to overcome the shortcomings of conventional drug delivery approaches. It

involves the use of materials at the Nano scale range (1–100 nm), where unique physicochemical properties can be utilized to enhance drug performance [2, 5]. Nano scale drug delivery systems, including liposomes, polymeric nanoparticles, and Nano emulsions, have demonstrated significant improvements in drug solubility and stability [1, 3]. Furthermore, these systems can modify pharmacokinetic behavior by improving drug absorption, prolonging circulation time, and enabling controlled release, thereby enhancing overall therapeutic efficacy [5, 6].

Advantages of Nano carrier Systems-

Nano carrier-based systems offer several advantages that make them superior to conventional delivery methods. They improve the solubility of poorly water-soluble drugs and allow for controlled and sustained drug release, ensuring consistent therapeutic levels over time [1, 2]. These systems also enhance drug stability by protecting active compounds from degradation due to environmental or enzymatic factors [3]. Importantly, Nano carriers enable targeted drug delivery either through passive mechanisms such as the enhanced permeability and retention (EPR) effect or through active targeting using specific ligands [6]. This targeted approach helps minimize side effects while improving treatment efficacy.

Scope and Objective of the Review-

Scope of the Review:

This review summarizes the recent progress in nanocarrier-based drug delivery systems, with particular emphasis on formulation strategies, targeted delivery approaches, and their clinical translation. It discusses how different Nano carrier systems are designed and optimized to improve drug loading, stability, and release characteristics [1, 2].

The review also highlights various targeting mechanisms, including both passive and active approaches that enable site-specific drug delivery and enhance therapeutic efficiency [3]. Furthermore, it examines the current status of clinical translation, addressing key challenges such as safety, scalability, and regulatory considerations [2, 7]. Overall, the review aims to provide a clear understanding of how Nano carrier systems are transforming modern drug delivery.

Objectives of the Review:

To summarize recent advances in Nano carrier formulation strategies [1, 2]

To discuss various targeted drug delivery approaches [3]

To evaluate the role of Nano carriers in improving therapeutic outcomes [2, 5]

To analyze the progress and challenges in clinical translation of Nano carrier systems [6, 7]

To highlight future prospects of Nano carrier-based drug delivery [2]

Nano carrier Drug Delivery Systems: Basic Concepts:

Definition of Nano carriers-

Nano carriers are submicron-sized delivery systems designed to transport therapeutic agents in a controlled and targeted manner. Typically, these carriers fall within the Nano scale range of approximately 1–100 nm, a size that enables unique physicochemical and biological interactions not seen in conventional systems [1, 2]. At this scale, Nano carriers can efficiently navigate biological barriers, improving drug absorption and distribution.

Nanoparticles, one of the most commonly used Nano carriers, are defined as solid colloidal particles in which the drug can either be dissolved, entrapped, encapsulated, or attached to the particle matrix [2]. The concept of drug encapsulation is central to Nano carrier systems, where the active pharmaceutical ingredient is enclosed within or associated with the carrier structure. This approach helps protect the drug from degradation, enhances its stability, and allows for controlled or sustained release over time [3].

Structural Components of Nano carriers-

Nano carriers are typically composed of three main structural elements: the core, the shell, and surface ligands, each playing a specific role in drug delivery. The core forms the inner part of the Nano carrier and serves as the primary reservoir for the drug. It may consist of hydrophobic or hydrophilic materials depending on the nature of the drug being loaded. The core is crucial in determining drug loading capacity and release characteristics [1].

Surrounding the core is the shell, which acts as a protective barrier. The shell stabilizes the Nano carrier, prevents premature drug leakage, and shields the drug from external degradation factors such as enzymes or pH variations. In many systems, the shell also helps in prolonging circulation time by reducing recognition and clearance by the immune system [4].

The outermost layer may include surface ligands, which are functional molecules attached to the Nano carrier surface. These ligands can be

antibodies, peptides, or other targeting moieties that enable the Nano carrier to recognize and bind to specific cells or tissues. This feature is particularly important for active targeting, improving therapeutic precision while minimizing off-target effects [3, 6].

Mechanisms of Drug Loading-

Drug loading into Nano carriers can be achieved through different mechanisms, depending on the type of carrier and the physicochemical properties of the drug. Encapsulation is one of the most widely used methods, where the drug is physically enclosed within the core or matrix of the Nano carrier. This method provides protection from degradation and allows for controlled drug release [2].

Adsorption involves the attachment of drug molecules onto the surface of the Nano carrier through weak interactions such as electrostatic forces, van der Waals forces, or hydrogen bonding. This method is relatively simple but may result in faster drug release compared to encapsulation [4]. Covalent conjugation is a more stable approach in which the drug is chemically bonded to the Nano carrier through covalent linkages. This method ensures strong attachment and controlled release, often triggered by specific biological conditions such as pH or enzymatic activity [6].

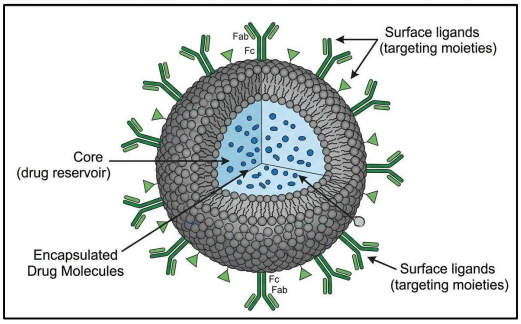

Figure 1. Structure of Nano carrier Drug Delivery System

Classification of Nano carriers:

Nano carriers can be broadly categorized based on the nature of the materials used in their construction. Each class offers distinct structural features and functional advantages that make them suitable for specific therapeutic applications.

Lipid-Based Nano carriers-

Lipid-based Nano carriers are among the most extensively studied systems due to their biocompatibility and similarity to biological membranes.

Liposomes are spherical vesicles composed of one or more phospholipid bilayers surrounding an aqueous core. This bilayer structure allows the incorporation of both hydrophilic drugs (within the aqueous core) and hydrophobic drugs (within the lipid bilayer), making those highly versatile [8]. Their structural resemblance to cell membranes enhances cellular uptake and reduces toxicity.

Solid Lipid Nanoparticles (SLNs) consist of a solid lipid matrix that remains stable at both room and body temperatures. Drugs are embedded within this matrix, allowing for sustained and controlled drug release. SLNs also provide improved drug stability and protection from degradation [9].

Nanostructured Lipid Carriers (NLCs) are a modified form of SLNs, combining solid and liquid lipids to create a less ordered matrix. This structure enhances drug loading capacity and prevents drug expulsion during storage, thereby improving stability and therapeutic performance [10].

Applications: Lipid-based Nano carriers are widely used in anticancer therapy for targeted drug delivery and reduced toxicity. They have also gained significant importance in vaccine delivery, particularly in modern mRNA vaccines, due to their ability to protect and efficiently deliver nucleic acids [11].

Polymeric Nano carriers-

Polymeric Nano carriers offer flexibility in design and can be engineered for controlled drug release and targeted delivery.

Polymeric Nanoparticles are made from biodegradable polymers such as PLGA or chitosan. These systems can encapsulate drugs within their matrix or adsorb them onto the surface, allowing for sustained drug release and improved stability [12].

Polymeric Micelles are formed by the self-assembly of amphiphilic block copolymers in aqueous environments. They consist of a hydrophobic core, which solubilizes poorly water-soluble drugs, and a hydrophilic shell that enhances circulation time and stability in biological fluids [13].

Polymersomes are vesicle-like structures similar to liposomes but composed of polymer bilayers. They provide enhanced mechanical stability and allow for the encapsulation of both hydrophilic and hydrophobic drugs [14].

Applications: These systems are widely used in targeted drug delivery, particularly in cancer therapy, where they can be engineered to respond to specific biological stimuli such as pH or enzymes [13].

Inorganic Nano carriers-

Inorganic Nano carriers are known for their unique physical and chemical properties, making them useful in both therapeutic and diagnostic applications.

Gold Nanoparticles exhibit excellent optical and electronic properties, which make them suitable for imaging, bio sensing, and cancer therapy, including photo thermal treatment [15].

Magnetic Nanoparticles**,** typically composed of iron oxide, can be guided to specific sites in the body using external magnetic fields. This property allows for magnetic targeting and is also useful in imaging techniques such as MRI [16].

Mesoporous Silica Nanoparticles (MSNs) are characterized by their highly porous structure, offering a large surface area and high drug loading capacity. Their tunable pore size allows controlled drug release and surface modification for targeted delivery [17].

Biological Nano carriers-

Biological Nano carriers are derived from natural sources and offer excellent biocompatibility and low immunogenicity.

Exosomes are Nano sized vesicles naturally secreted by cells. They play a role in intercellular communication and can be harnessed as drug delivery vehicles due to their inherent ability to transfer biomolecules between cells [18].

Biomimetic Nanoparticles are engineered by coating synthetic nanoparticles with natural cell membranes, such as red blood cells or cancer cells. This coating helps evade immune detection and enhances targeting efficiency [19].

Table 1: Classification and Characteristics of Nano carriers

Nano carrier	**Material**	**Size Range (nm)**	**Application**
Liposomes	Phospholipids	50 – 200	Drug delivery, vaccines
Solid Lipid Nanoparticles	Solid lipids	50 – 1000	Sustained drug release
Nanostructured Lipid Carriers	Solid + liquid lipids	50 – 500	Enhanced stability, drug delivery
Polymeric Nanoparticles	Biodegradable polymers	10 – 1000	Controlled drug delivery
Polymeric Micelles	Block copolymers	10 – 100	Solubility enhancement
Polymersomes	Polymer bilayers	50 – 500	Drug encapsulation
Gold Nanoparticles	Gold	1–100	Imaging, cancer therapy
Magnetic Nanoparticles	Iron oxide	10 – 100	Magnetic targeting, imaging
Mesoporous Silica Nanoparticles	Silica	50 – 300	High drug loading
Exosomes	Biological vesicles	30 – 150	Drug delivery, diagnostics
Biomimetic Nanoparticles	Cell membrane-coated	50 – 200	Targeted delivery

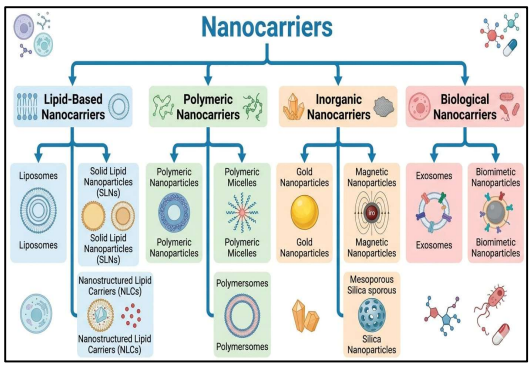

Figure 2. Classification of Nano carriers

Recent Advances in Nano carrier Formulation Strategies:

Continuous progress in nanotechnology has led to the development of advanced formulation strategies that improve the efficiency, specificity, and safety of drug delivery systems. These innovations focus on modifying Nano carriers to enhance their interaction with biological systems and achieve controlled, targeted therapeutic effects.

Surface Engineering-

Surface engineering plays a crucial role in determining how Nano carriers behave in the biological environment. By modifying the outer surface, it is possible to improve stability, prolong circulation time, and enhance targeting efficiency.

PEGylation involves the attachment of polyethylene glycol (PEG) chains to the surface of Nano carriers. This hydrophilic coating creates a steric barrier that reduces protein adsorption and recognition by the immune system, thereby extending circulation time in the bloodstream [20].

Ligand conjugation refers to the attachment of specific molecules such as peptides, vitamins, or small ligands onto the Nano carrier surface. These ligands bind selectively to receptors overexpressed on target cells, enabling active targeting and improved cellular uptake [21].

Antibody modification is a more precise targeting approach, where monoclonal antibodies are conjugated to Nano carriers. These antibodies recognize and bind to specific antigens present on diseased cells, particularly cancer cells, enhancing therapeutic specificity [22].

Purpose:

These surface modifications collectively help in increasing circulation time, minimizing rapid clearance by the reticuloendothelial system (RES), and improving accumulation at the target site, thereby enhancing therapeutic outcomes.

Stimuli-Responsive Nano carriers-

Stimuli-responsive Nano carriers are designed to release drugs in response to specific internal or external triggers, ensuring controlled and site-specific drug delivery.

PH-responsive systems exploit the acidic microenvironment of tumors or inflamed tissues. These Nano carriers remain stable at physiological pH but release the drug when exposed to lower pH conditions, improving drug accumulation in tumor tissues [23].

Temperature-responsive systems release drugs in response to changes in temperature. For example, mild hyperthermia at the tumor site can trigger drug release from thermo sensitive Nano carriers, enhancing treatment efficacy [3].

Enzyme-responsive Nano carriers are designed to respond to specific enzymes that are overexpressed in certain diseases. These enzymes trigger the breakdown of the Nano carrier structure, leading to controlled drug release at the desired site [24].

Smart Nanocarriers-

Smart Nano carriers represent a new generation of delivery systems that combine multiple functionalities within a single platform.

These multifunctional nanoparticles are engineered to perform several tasks simultaneously, such as targeting, drug delivery, and controlled release. They can respond to environmental stimuli while also carrying targeting ligands, making them highly efficient [21]. A key advancement in this area is the development of theranostic systems, which integrate therapeutic and diagnostic functions into one Nano carrier. This allows simultaneous drug delivery and real-time monitoring of treatment response.

Example:

A typical theranostic Nano carrier may deliver an anticancer drug while also containing imaging agents (such as fluorescent or magnetic components) that help track the distribution and effectiveness of the treatment within the body [3, 22].

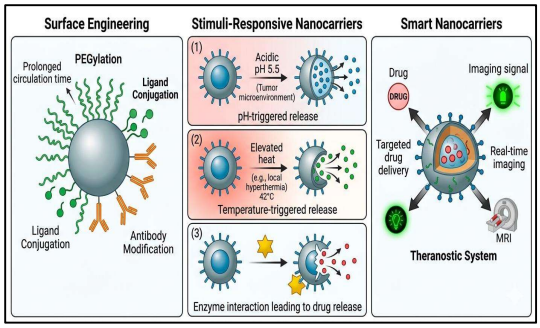

Figure 3. Recent Advances in Nano carrier Formulation Strategies

Targeted Drug Delivery Strategies:

Targeted drug delivery has become a key focus in modern therapeutics, particularly in the design of Nano carrier systems. By directing drugs specifically to diseased tissues or cells, these strategies enhance therapeutic efficacy while minimizing systemic side effects.

Passive Targeting-

Passive targeting relies on the natural physiological characteristics of diseased tissues, especially tumors. One of the most important mechanisms involved is the enhanced permeability and retention (EPR) effect. Tumor tissues often have leaky blood vessels with large fenestrations and poor lymphatic drainage. These features allow Nano sized drug carriers to preferentially accumulate in tumor sites [25].

As a result, Nano carriers circulating in the bloodstream can passively localize in tumor tissues without the need for specific targeting ligands. This phenomenon leads to increased drug concentration at the tumor site, improving therapeutic outcomes while reducing exposure to healthy tissues [26].

Active Targeting-

Active targeting involves the functionalization of Nano carriers with specific ligands that can recognize and bind to receptors overexpressed on target cells. This ligand–receptor interaction enhances cellular uptake and improves drug delivery precision. One common approach is folate receptor targeting, where folic acid is used as a ligand to bind to folate receptors that are highly expressed on many cancer cells [27].

Transferrin targeting utilizes transferrin proteins that bind to transferrin receptors, which are often up regulated in rapidly dividing cells due to their increased iron requirements [28].

Antibody targeting is a highly specific method where monoclonal antibodies are conjugated to Nano carriers. These antibodies recognize specific antigens on cancer cells, enabling selective delivery of therapeutic agents [29].

Intracellular Targeting-

Beyond reaching the target tissue, effective drug delivery often requires transport to specific intracellular organelles. Nuclear targeting is important for drugs that interact with DNA, such as anticancer agents. Nanocarriers can be engineered with nuclear localization signals to facilitate transport across the nuclear membrane [30].

Mitochondrial targeting focuses on delivering drugs to mitochondria, which play a critical role in apoptosis and cellular metabolism. This approach is particularly useful in cancer therapy, where inducing mitochondrial dysfunction can trigger cell death [31].

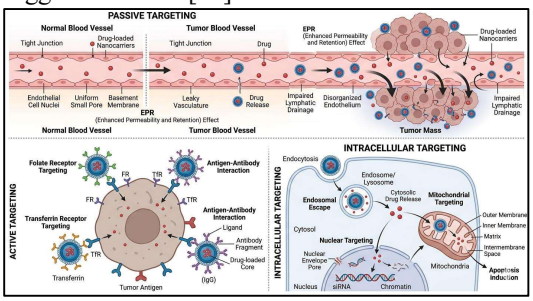

Figure 4. Mechanism of Targeted Nano carrier Drug Delivery

Therapeutic Applications of Nano carrier-Based Drug Delivery Systems:

Nano carrier systems have significantly expanded the scope of modern therapeutics by enabling precise, efficient, and controlled delivery of drugs across a wide range of diseases. Their versatility allows them to address complex biological barriers and improve treatment outcomes in various clinical conditions.

Cancer Therapy-

Cancer treatment has been one of the most extensively explored areas for Nano carrier applications.

Targeted chemotherapy using Nano carriers helps deliver anticancer drugs directly to tumor tissues, reducing damage to healthy cells. By utilizing passive targeting (EPR effect) and active targeting (ligand-mediated), Nano carriers enhance drug accumulation at the tumor site, improving efficacy and minimizing systemic toxicity [32].

Gene therapy involves the delivery of genetic material such as DNA, siRNA, or mRNA using Nano carriers. These systems protect nucleic acids from degradation and facilitate their entry into target cells, enabling gene silencing or expression for therapeutic benefit [33].

Immunotherapy has also benefited from nanotechnology, where Nano carriers are used to

deliver immune-modulating agents, vaccines, or checkpoint inhibitors. This approach enhances immune system activation against cancer cells and improves treatment response [34].

Neurological Disorders-

Treating neurological diseases remains challenging due to the presence of the blood–brain barrier (BBB), which restricts the entry of most drugs into the brain. Nanocarriers are designed to cross the blood–brain barrier through mechanisms such as receptor-mediated transport or surface modification. This enables effective delivery of therapeutic agents to the central nervous system [35].

For example, in Alzheimer's disease, Nano carriers have been explored for delivering drugs that target amyloid-beta plaques or tau proteins. These systems improve drug penetration into the brain and may enhance treatment outcomes in neurodegenerative conditions [36].

Infectious Diseases-

Nano carrier systems offer promising strategies for managing infectious diseases by improving drug delivery and enhancing immune responses.

In antimicrobial drug delivery, Nano carriers increase the solubility and stability of antibiotics, enhance their penetration into infected tissues, and help overcome issues such as drug resistance by maintaining effective drug concentrations [37].

In vaccine delivery, Nano carriers act as adjuvants and carriers, protecting antigens and ensuring efficient delivery to immune cells. This leads to improved immune responses and has been particularly important in the development of modern vaccines [38].

Other Diseases-

Beyond cancer and infections, Nano carriers are increasingly being explored for other chronic and complex diseases.

In cardiovascular diseases, Nano carriers can deliver drugs directly to damaged blood vessels or atherosclerotic plaques, improving therapeutic precision and reducing systemic exposure [39].

In diabetes, Nano carrier systems are being investigated for controlled insulin delivery and improved glucose regulation. These systems aim to provide sustained release and reduce the frequency of administration, enhancing patient compliance [40].

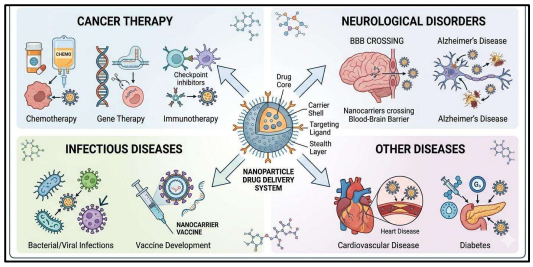

Figure 5. Therapeutic Applications of Nano carrier Drug Delivery Systems

Characterization Techniques of Nano carriers:

Characterization of Nano carriers is essential to ensure their quality, stability, and performance in drug delivery. Various analytical techniques are employed to evaluate their physical and functional properties.

Particle Size and Distribution-

Particle size plays a crucial role in determining the biological behavior of Nano carriers, including cellular uptake, bio distribution, and drug release.

Dynamic Light Scattering (DLS) is one of the most commonly used techniques to measure particle size and size distribution. It works by analyzing the scattering of light caused by the Brownian motion of particles in suspension. The data obtained helps determine the average particle size and the polydispersity index (PDI), which indicates the uniformity of particle size distribution. A lower PDI value suggests a more homogeneous system [41].

Surface Charge-

The surface charge of Nano carriers influences their stability and interaction with biological membranes.

Zeta potential is used to measure the surface charge of particles. It indicates the degree of electrostatic repulsion between particles in a dispersion. High positive or negative zeta potential values generally suggest good stability, as particles repel each other and resist aggregation. Additionally, surface charge affects cellular uptake and circulation behavior in the body [42].

Morphology-

Understanding the shape and surface characteristics of Nano carriers is important for predicting their behavior in biological systems.

Transmission Electron Microscopy (TEM) provides high-resolution images that reveal the internal structure and size of nanoparticles. It allows visualization of the core and overall morphology at the Nano scale [43].

Scanning Electron Microscopy (SEM) is used to study surface morphology and texture. It provides

detailed three-dimensional-like images of the particle surface, helping assess shape and aggregation [44].

Drug Loading and Encapsulation Efficiency-

Drug loading and encapsulation efficiency are critical parameters that determine how much drug is successfully incorporated into the Nano carrier. Encapsulation efficiency indicates the percentage of drug that is entrapped within the carrier relative to the total amount used during formulation.

$$\text{Encapsulation Efficiency (\%)} = \frac{\text{Amount of Drug Encapsulated}}{\text{Total Drug Added}} \times 100$$

A higher encapsulation efficiency reflects better formulation performance and improved drug delivery potential [45].

In-Vitro Drug Release Studies-

In-vitro drug release studies are conducted to evaluate how the drug is released from the Nano carrier over time.

The dialysis method is widely used, where the Nano carrier formulation is placed inside a dialysis membrane and immersed in a release medium. The drug diffuses through the membrane into the surrounding medium, and samples are collected at regular intervals to measure release [46]. Release kinetics are then analyzed to understand the pattern of drug release, such as zero-order, first-order, or diffusion-controlled release. This helps predict in-vivo performance and optimize the formulation for sustained or controlled drug delivery.

Clinical Translation of Nano carrier Systems:

The transition of Nano carrier-based drug delivery systems from laboratory research to clinical application represents a critical step in modern therapeutics. While significant progress has been made, challenges related to safety, regulatory approval, and large-scale manufacturing continue to influence their successful translation.

Approved Nano medicines-

Several Nano carrier-based formulations have successfully reached the market, demonstrating their clinical potential.

One of the most notable examples is liposomal doxorubicin, a formulation in which the anticancer drug doxorubicin is encapsulated within liposomes. This design reduces cardio toxicity and improves drug accumulation in tumor tissues through enhanced circulation and passive targeting [47].

Another important example is liposomal amphotericin B, used in the treatment of fungal infections. Encapsulation of amphotericin B in liposomes significantly reduces its nephrotoxicity while maintaining antifungal efficacy, making it safer for clinical use [48]. These approved Nano medicines highlight the advantages of Nano carriers in improving therapeutic index and patient outcomes.

Nano carriers in Clinical Trials-

A large number of Nano carrier-based systems are currently under clinical investigation for various diseases, particularly cancer, infectious diseases, and neurological disorders.

Ongoing Nano medicine trials focus on developing advanced formulations such as polymeric nanoparticles, lipid nanoparticles, and targeted Nano carriers. These studies aim to enhance drug delivery efficiency, reduce side effects, and improve patient compliance. Many trials are also exploring combination therapies, where Nano carriers deliver multiple agents simultaneously for synergistic effects [49].

Despite promising results, challenges such as variability in biological response, scalability issues, and long-term safety remain areas of active research.

Regulatory Considerations-

The clinical translation of Nano carriers requires strict regulatory evaluation to ensure safety, efficacy, and quality.

Regulatory agencies such as the Food and Drug Administration (FDA) have established guidelines for the development and approval of Nano medicines. These guidelines emphasize detailed characterization of Nano carriers, including their size, surface properties, stability, and drug release behavior [50]. Safety evaluation is a critical component, involving comprehensive studies on toxicity, immunogenicity, bio distribution, and long-term effects. Due to the unique properties of nanomaterial, conventional evaluation methods may not always be sufficient, requiring specialized assessment approaches [7].

Overall, regulatory frameworks are evolving to address the complexities associated with Nano carrier systems and to facilitate their safe integration into clinical practice.

Table 2: Clinically Approved Nano carrier Drugs

Drug	Nano carrier	Indication	Approval Year
Doxorubicin	Liposome	Breast canc	1995

(Doxil®)		er, ovarian cancer	
Amphotericin B (AmBisome®)	Liposome	Fungal infections	1997
Paclitaxel (Abraxane®)	Albumin nanoparticle	Breast cancer	2005
Daunorubicin (DaunoXome®)	Liposome	Kaposi's sarcoma	1996

Challenges and Limitations:

Despite the promising potential of Nano carrier-based drug delivery systems, several challenges continue to limit their widespread clinical application. Toxicity issues remain a major concern. Due to their small size and high surface reactivity, Nano carriers may interact unpredictably with biological systems, leading to cytotoxicity, immunogenic reactions, or long-term accumulation in organs such as the liver and spleen. The lack of comprehensive long-term toxicity data further complicates their safe use [51].

Stability problems can affect the performance of Nano carriers during storage and in biological environments. Issues such as aggregation, premature drug leakage, and degradation may reduce therapeutic efficacy. Maintaining physical and chemical stability over time is essential for successful formulation development [52].

Manufacturing challenges also pose significant barriers. Scaling up Nano carrier production from laboratory to industrial level while maintaining consistency, reproducibility, and quality is complex and costly. Variations in particle size, drug loading, and surface characteristics can impact the final product's performance [53]. Regulatory hurdles further complicate clinical translation. Due to the unique properties of nanomaterials, existing regulatory frameworks may not fully address their evaluation. Detailed characterization, safety assessment, and quality control are required, often leading to longer approval timelines and increased development costs [54].

Future Perspectives:

The future of Nano carrier-based drug delivery systems is highly promising, with ongoing advancements expected to overcome current limitations and expand their clinical applications. Personalized Nano medicine is an emerging approach that aims to tailor drug delivery systems according to individual patient characteristics, such as genetic profile and disease condition. This strategy has the potential to improve therapeutic outcomes and minimize adverse effects by delivering precise and patient-specific treatments [7]. AI-driven drug delivery design is gaining attention as artificial intelligence and machine learning tools are increasingly used to optimize Nano carrier design. These technologies can predict drug–carrier interactions, optimize formulation parameters, and accelerate the development process, reducing time and cost [55]. Multifunctional Nano carriers represent the next generation of drug delivery systems. These advanced platforms integrate multiple capabilities, such as targeted delivery, controlled release, and diagnostic imaging, within a single system. Such "all-in-one" systems are expected to play a key role in theranostics and precision medicine [56].

Critical Analysis and Research Gaps:

13.1 Critical Analysis-

Although nanocarrier-based drug delivery systems have shown remarkable progress in research settings, their real-world clinical impact is still evolving. Many studies report enhanced targeting efficiency and improved therapeutic outcomes; however, these results are often not consistently replicated in clinical conditions. One important limitation is the variability in patient physiology, which can influence how nanocarriers distribute, accumulate, and interact within the body. The effectiveness of passive targeting, particularly through the EPR effect, is also not uniform across all tumors. Differences in tumor type, vascular structure, and disease stage can significantly affect drug accumulation. Similarly, surface-engineered nanocarriers designed for active targeting may lose efficiency due to interactions with biological fluids, leading to the formation of a protein corona that alters their behavior and reduces targeting specificity.

From a practical standpoint, large-scale manufacturing remains challenging. Maintaining consistency in particle size, drug loading, and stability during scale-up is difficult and can impact product quality. In addition, long-term safety and toxicity data are still limited, especially concerning repeated administration and accumulation in vital organs. Regulatory

pathways are also complex and continuously evolving, which can delay the approval and commercialization of new nanocarrier systems.

13.2 Research Gaps-

Despite ongoing advancements, several gaps remain that need focused research attention:

Limited long-term safety and toxicity studies in humans

Lack of standardized methods for characterization and evaluation

Insufficient clinical evidence to confirm targeting efficiency in diverse populations

Inadequate predictive models bridging preclinical and clinical outcomes

Challenges in large-scale, reproducible manufacturing processes

Poor understanding of nano–bio interactions, especially protein corona formation

Need for more effective strategies to overcome biological barriers such as tumor heterogeneity and the blood–brain barrier

Limited application of emerging technologies like artificial intelligence in formulation optimization

Addressing these gaps will be essential for improving the reliability, safety, and clinical success of nanocarrier-based drug delivery systems.

Conclusion:

Nano carrier-based drug delivery systems have emerged as a transformative approach in modern therapeutics, offering significant advantages over conventional drug delivery methods. By improving drug solubility, stability, and bioavailability, Nano carriers enhance the overall therapeutic performance of a wide range of pharmaceutical agents. Their ability to provide controlled and sustained drug release further contributes to maintaining optimal drug concentrations, reducing dosing frequency, and improving patient compliance. A key strength of Nano carrier systems lies in their capacity for targeted drug delivery. Through both passive mechanisms, such as enhanced permeability and retention, and active strategies involving ligand–receptor interactions, Nano carriers enable precise delivery of drugs to specific tissues or cells. This targeted approach not only increases treatment efficacy but also minimizes systemic toxicity and adverse effects, which is particularly important in diseases such as cancer and neurological disorders. Despite existing challenges related to safety, scalability, and regulatory approval, the clinical translation of Nano carrier systems continues to progress steadily. Several Nano medicines have already demonstrated success in clinical practice, and ongoing research is focused on overcoming current limitations. Looking ahead, advancements in personalized medicine, smart Nano carriers, and integration with emerging technologies are expected to further expand their therapeutic potential. Overall, Nano carrier-based systems are poised to play a crucial role in shaping the future of precision and effective healthcare.

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