REVIEW ARTICLE

Design, Development, and Evaluation of Nano Carrier Based Formulations

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Abstract

The design, development, and evaluation of Nano carrier-based formulations represent a pivotal paradigm in modern drug delivery systems. This abstract provides an overview of the advancements, challenges, and potentials in this dynamic field. Nanocarriers, ranging from liposomes and polymeric nanoparticles to metallic and lipid-based systems, offer unparalleled advantages in targeted drug delivery, mitigating off-target effects while augmenting therapeutic efficacy. The strategic engineering of these carriers allows precise control over drug release kinetics, enhancing pharmacokinetics and fostering sustained therapeutic concentrations. However, the development of Nano carrier-based formulations is not without challenges. The intricate synthesis processes, necessitating precise control over particle size, surface properties, and drug loading capacities, demand robust manufacturing protocols. Ensuring biocompatibility, minimizing immunogenicity, and comprehensively assessing long-term safety profiles remain critical concerns for clinical translation and regulatory compliance. Evaluation methodologies, ranging from physicochemical characterization to *in vitro* and *in vivo* assessments, play a pivotal role in delineating the efficacy and safety profiles of these formulations. Cutting-edge techniques such as spectroscopic analyses, advanced imaging modalities, and precise microscopic evaluations enable comprehensive understanding and characterization of Nanocarriers. In conclusion, the design, development, and evaluation of Nano carrier-based formulations stand at the forefront of modern pharmaceutical innovation. Despite challenges, their potential to revolutionize drug delivery systems, enabling precise targeting, controlled release, and enhanced therapeutic outcomes, underscores their significance in shaping the future of medicine. Continued research efforts, technological advancements, and regulatory compliance will further propel the clinical translation and commercialization of these promising formulations.

Key words: Drug delivery, drug release kinetics, Nanocarrier based formulations, safety profiles

INTRODUCTION

Nano carrier-based formulations have emerged as a groundbreaking approach in pharmaceuticals, enabling targeted and efficient delivery of therapeutic agents. These formulations utilize Nanoscale carriers to encapsulate drugs, genes, or imaging agents, offering several advantages over conventional drug delivery systems. The unique properties of Nanocarriers, such as their small size, large surface area to volume ratio, and tunable surface properties, enable precise control over drug release kinetics, biodistribution, and cellular uptake. Nanocarriers come in various forms, including liposomes, polymeric nanoparticles, dendrimers, micelles, and inorganic nanoparticles like quantum dots and gold nanoparticles. Each type offers distinct advantages in terms of drug loading capacity, stability, and compatibility with different therapeutic agents.[1] The use of Nanocarrier-based formulations provides solutions to several challenges encountered in conventional drug delivery. They enhance the solubility of poorly water-soluble drugs, protect drugs from degradation, and enable sustained or triggered release at the target site, reducing systemic side effects.[2] Moreover, these formulations enable targeted delivery to specific cells, tissues, or organs, thereby minimizing off-target effects and enhancing therapeutic efficacy. Functionalization of Nanocarriers with ligands, antibodies, or peptides allows for site-specific targeting by recognizing unique biomarkers present on diseased cells.[3]

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Received: 29-01-2025
Revised: 19-03-2025
Accepted: 27-03-2025

The application of Nanocarrier-based formulations extends beyond therapeutics to include imaging agents for diagnostic purposes. Contrast agents encapsulated within Nanocarriers enhance the resolution and specificity of imaging techniques such as magnetic resonance imaging, computed tomography scans, and fluorescence imaging.[4] However, despite the remarkable potential of Nanocarrier-based formulations, challenges remain in their clinical translation. Issues related to scalability, reproducibility, safety, and regulatory approval need to be addressed for widespread clinical implementation.[5]

Overview of nanotechnology's role in drug delivery systems

Nanotechnology-based drug delivery systems encompass a wide array of nanocarriers such as liposomes, polymeric nanoparticles, dendrimers, micelles, and inorganic nanoparticles. These carriers provide a versatile platform for encapsulating drugs, genes, or imaging agents, thereby protecting them from degradation, enabling controlled release, and facilitating their transport to the desired site of action. The advantages of nanotechnology in drug delivery include:

- Targeted delivery: Nanostructures can be engineered to deliver drugs selectively to specific cells, tissues, or organs by functionalizing their surfaces with targeting ligands. This targeting minimizes systemic side effects and enhances the therapeutic index of drugs.[6]
- Enhanced bioavailability: This capability is crucial for drugs with poor aqueous solubility, enabling their effective delivery and therapeutic action.[7]
- Controlled release: Nanoparticles allow for controlled or sustained drug release kinetics, enabling a more prolonged therapeutic effect and reducing the frequency of dosing.[8]
- Imaging and diagnosis: Nanotechnology facilitates the development of contrast agents and imaging probes that improve the sensitivity and specificity of diagnostic techniques, aiding in early disease detection and monitoring.[9]
- Personalized medicine: The versatility of nanocarriers allows for customization and tailoring of drug formulations based on individual patient needs, contributing to the advancement of personalized medicine.

NANOMATERIALS FOR CARRIER DESIGN IN DRUG DELIVERY

Nanomaterials possess unique properties at the nanoscale, allowing for precise manipulation to create carriers that enhance drug efficacy, stability, and targeting capabilities. Several types of nanomaterials are employed in carrier design, each offering distinct advantages in drug delivery applications.

- Lipid-based nanocarriers: Lipid-based nanocarriers, such as liposomes and solid lipid nanoparticles (SLNs), are composed of lipids or phospholipids. These carriers mimic biological membranes, facilitating the encapsulation of both hydrophilic and hydrophobic drugs. Liposomes, in particular, offer versatility in size and surface modification, allowing for targeted drug delivery and controlled release.
- Polymeric nanoparticles: Polymeric nanoparticles, including polymersomes, dendrimers, and polymeric micelles, are engineered from biocompatible polymers like poly(lactic co glycolic acid) (PLGA) or polyethylene glycol (PEG). These carriers provide tunable properties, controlled drug release, and protection of the payload. Surface modifications enable targeted delivery to specific cells or tissues.[10]
- Inorganic nanoparticles: Inorganic nanoparticles, such as gold nanoparticles, quantum dots, and silica nanoparticles, possess unique physicochemical properties. Their high surface area-to-volume ratio allows for high drug loading capacity, and they can be functionalized for targeted drug delivery and imaging applications. Gold nanoparticles, for instance, exhibit excellent biocompatibility and surface modifications for targeted delivery.[11]
- Carbon-based nanomaterials: Carbon-based nanomaterials such as carbon nanotubes and graphene oxide offer promising platforms for drug delivery due to their high surface area and exceptional mechanical and electrical properties. They can transport various drugs and biomolecules and have the potential for controlled drug release.[12]
- Hybrid nanomaterials: Hybrid nanomaterials combine different types of nanomaterials to leverage their individual advantages. For example, combining lipids with polymers or inorganic nanoparticles can create hybrid carriers with synergistic properties, enhancing drug loading, stability, and targeting.[13]

Various nanomaterials utilized in designing Nanocarriers (lipid-based, polymeric, metallic, etc.)

Various nanomaterials are utilized in designing nanocarriers for drug delivery systems, each offering unique advantages in terms of biocompatibility, stability, drug loading capacity, and controlled release.

Lipid-based nanocarriers

a. Liposomes: Liposomes are spherical vesicles composed of lipid bilayers. They are versatile and capable of encapsulating both hydrophilic and hydrophobic drugs. Liposomes offer biocompatibility, controlled release, and can be surface modified for targeted drug delivery.
b. SLNs and nanostructured lipid carriers (NLCs): SLNs and NLCs are lipid-based nanoparticles that provide

improved drug stability, controlled release, and enhanced drug loading capacity compared to traditional liposomes.

Polymeric nanoparticles

a. Polymeric micelles: These are self-assembled structures formed by amphiphilic block copolymers. Polymeric micelles enhance the solubility of poorly water-soluble drugs and can be tailored for controlled drug release.
b. Polymeric nanoparticles (e.g., PLGA, PEG): Polymeric nanoparticles, such as those made from PLGA or PEG, offer biocompatibility and controlled drug release. They are widely used for encapsulating various drugs and biomolecules.[14]

Inorganic nanoparticles

a. Gold nanoparticles: Gold nanoparticles exhibit excellent biocompatibility and unique optical properties. They can be functionalized for targeted drug delivery and imaging applications.
b. Iron oxide nanoparticles: These nanoparticles possess magnetic properties, making them valuable for magnetic targeting and imaging in drug delivery applications.
c. Silica nanoparticles: Silica nanoparticles offer high stability and versatile surface modification capabilities for drug delivery and imaging.
d. Nanofiber: Nanofibers can be greatly useful in the treatment of diabetic wound healing, where curcumin, the known antibacterial and anti-inflammatory element, plays an important role.[15]
e. Nanosponge: Nanosponges can penetrate through skin. They can bind poorly soluble drugs within the matrix and improve the drug bioavailability. The nanosponges can release drugs in a controlled and expected manner at the target site. Topical nanosponges can be more patient compliant with benefits by lesser doses and side effects.[16]

Carbon-based nanomaterials

a. Carbon nanotubes: Carbon nanotubes have a high surface area and unique mechanical properties, enabling them to carry drugs and biomolecules for targeted delivery.
b. Graphene and graphene oxide: Graphene-based materials have exceptional mechanical strength and can be functionalized for drug delivery, imaging, and biosensing applications.[17]

Properties influencing carrier selection and fabrication methods for Nanocarrier-based formulations

Selecting appropriate carriers for nano-based formulations involves considering several crucial properties that impact drug delivery efficacy. These properties guide the choice of materials and fabrication methods to ensure optimal performance in terms of drug loading, stability, targeting, and release kinetics.

Biocompatibility and safety

Carriers must exhibit high biocompatibility to avoid adverse reactions on administration. Compatibility with biological systems ensures minimal toxicity and immunogenicity, promoting safe drug delivery. Materials such as lipids, biodegradable polymers (e.g., PLGA), and certain inorganic nanoparticles possess favorable biocompatibility profiles.[18]

Drug loading capacity

The carrier's ability to efficiently encapsulate and release the drug payload influences its effectiveness. High drug loading capacity ensures maximum therapeutic benefit. Porous structures, high surface area materials like mesoporous silica nanoparticles, and specific functional groups enhance drug loading efficiency.

Controlled release characteristics

Tailoring carriers for controlled or sustained drug release is vital. The release profile should match therapeutic requirements, providing prolonged action and reducing dosing frequency. Factors influencing release kinetics include carrier composition, surface modifications, and fabrication methods.

Targeting and specificity

Surface functionalization with ligands or antibodies enables targeted delivery to specific cells or tissues, minimizing off-target effects. The carrier's surface should allow for easy modification to facilitate specific recognition and binding to target sites, improving therapeutic efficacy.

Stability and shelf life

Carriers should maintain stability during storage and in physiological environments to ensure drug integrity. Materials and fabrication methods that prevent degradation or premature drug release, such as proper encapsulation techniques and stabilizing agents, contribute to enhanced stability.

Fabrication methods play a pivotal role in determining the properties and performance of nano-based carriers

Emulsification and solvent evaporation

Commonly used for lipid-based carriers such as liposomes and SLNs. This method allows control over carrier size, drug encapsulation, and release kinetics.

Nanoprecipitation

Polymer-based carriers used in the formation of nanoparticles through controlled precipitation of polymers. It offers versatility in size, drug loading, and surface modification.[19]

Layer-by-layer assembly

Involves sequential deposition of alternating layers of polymers or materials to create nanoscale multilayered structures. This method allows precise control over carrier properties and drug release.

Template synthesis

Utilization of inorganic nanoparticles like silica or metal as a carrier in Template synthesis. Templates guide the synthesis of nanoparticles with specific sizes and structures, influencing drug loading and release properties.[20]

Self-assembly techniques

Including molecular self-assembly or micelle formation, enabling the creation of carriers with controlled properties through the spontaneous arrangement of molecules.[21]

FORMULATION DEVELOPMENT STRATEGIES FOR NANOCARRIER-BASED FORMULATIONS

Formulation development strategies for Nanocarrier-based formulations encompass a systematic approach to optimize drug encapsulation, stability, targeting, and controlled release. These strategies are pivotal in designing effective drug delivery systems.

Methods employed in optimizing carrier drug interactions for Nanocarrier-based formulations

Optimizing carrier drug interactions is crucial for enhancing the efficiency and efficacy of Nanocarrier-based formulations in drug delivery systems. Several methods and approaches are employed to fine-tune these interactions, ensuring optimal drug loading, controlled release, and stability within the carriers.

Surface modifications and functionalization

Altering the surface properties of carriers through chemical or physical modifications plays a significant role in enhancing carrier-drug interactions. Surface functionalization with ligands, polymers, or targeting moieties facilitates improved drug encapsulation, stability, and specific interactions with the drug molecule.[22]

pH and ionic strength adjustments

Modulating the pH or ionic strength of the formulation environment can influence carrier drug interactions. Changes in pH can alter the surface charge of carriers, affecting drug loading and release. Ionic strength adjustments impact electrostatic interactions between the carrier and drug molecule, influencing encapsulation efficiency.

Hydrophobic/hydrophilic balance

Manipulating the hydrophobic/hydrophilic nature of carriers or drugs can optimize interactions. Amphiphilic carriers can accommodate both hydrophobic and hydrophilic drugs by adjusting the carrier's composition to achieve better compatibility and loading.

Coating and encapsulation techniques

Various encapsulation methods, such as emulsification, nanoprecipitation, or solvent evaporation, influence carrier drug interactions. These techniques allow precise control over drug encapsulation by adjusting parameters such as temperature, shear forces, and mixing conditions.

Molecular dynamics simulations and computational modeling

Molecular modeling techniques aid in understanding and predicting carrier drug interactions at the molecular level. Computational simulations provide insights into the binding affinities, orientation, and stability of drug molecules within carriers, guiding optimization strategies.

Characterization techniques

Utilizing various characterization methods like surface analysis (e.g., scanning electron microscopy [SEM], atomic force microscopy [AFM]), spectroscopic techniques (e.g., Fourier transform infrared spectroscopy [FTIR], nuclear magnetic resonance), and thermal analysis (e.g., Differential scanning calorimetry [DSC], thermogravimetric analysis [TGA]) provides detailed insights into carrier drug interactions. These techniques help assess changes in structure, morphology, and physicochemical properties on drug loading.[23]

Binding affinity studies

Conducting binding affinity assays or studies, such as isothermal titration calorimetry or fluorescence spectroscopy, helps quantify and understand the strength and nature of interactions between the drug and carrier molecules.

Techniques for maximizing drug loading capacity and controlling release kinetics for Nanocarrier-based formulations

Maximizing drug loading capacity and controlling release kinetics are critical aspects of designing effective Nanocarrier-based formulations. Several techniques and strategies are employed to optimize drug loading efficiency and achieve controlled release profiles.

Maximizing drug loading capacity

a. Carrier engineering: Tailoring the carrier's composition, size, and surface properties can significantly impact drug

loading capacity. For instance, increasing the surface area or porosity of carriers like nanoparticles enhances their drug-loading capacity.[24]

b. Drug carrier compatibility: Understanding the physicochemical properties of the drug and carrier is crucial. Matching the hydrophobic/hydrophilic nature of the drug with the carrier matrix improves drug encapsulation efficiency.[25]
c. Solvent selection and evaporation methods: Optimizing the choice of solvents and evaporation methods during carrier preparation influences drug solubility and loading. Techniques like solvent evaporation and cosolvent evaporation enhance drug encapsulation by controlling precipitation kinetics.[26]
d. pH and temperature modifications: Adjusting pH or temperature during carrier drug interaction processes can improve loading capacity by altering drug solubility or carrier conformation.
e. Complexation and encapsulation techniques: Employing complexation methods or utilizing carrier-aided encapsulation techniques, such as nanoprecipitation, emulsification, or spray drying, enhances drug encapsulation within the carriers.[12]

Controlling release kinetics

a. Matrix and coating modifications: Altering the carrier matrix or introducing coatings influences drug release kinetics.
b. pH or temperature responsiveness: Utilizing stimuli-responsive materials that respond to changes in pH, temperature, or external stimuli allows for controlled release triggered by specific environmental cues.
c. Surface functionalization: Incorporating specific ligands or polymers onto the carrier surface facilitates controlled release. These functional groups can modulate interactions between the carrier and the drug, affecting release kinetics.
d. Nanoparticle size and shape: Smaller nanoparticles typically exhibit faster release rates due to higher surface area-to-volume ratios.
e. Use of nanopores or channels: Some carriers incorporate nanopores or channels that regulate drug diffusion and release kinetics by controlling the pathways through which drugs are released.

CHARACTERIZATION TECHNIQUES

Comprehensive characterization methods to assess physicochemical properties of Nanocarriers

Comprehensive characterization of Nanocarriers is essential to understand their physicochemical properties, ensuring their suitability for drug delivery applications. Various techniques are employed to assess different aspects of these carriers.

Particle size and distribution

a. Dynamic light scattering: Measures particle size distribution in solution based on light scattering.
b. Transmission electron microscopy: Provides high-resolution images to visualize particle morphology and size at the nanoscale.
c. SEM: Offers surface imaging and topographical information of the carriers.

Surface charge and zeta potential

a. Zeta potential measurement: Evaluates surface charge, stability, and potential aggregation tendencies of nanoparticles in solution.
b. Electrophoretic light scattering: Measures the mobility of charged particles in an electric field, determining zeta potential.

Surface chemistry and composition

a. FTIR: Identifies functional groups and chemical bonds present on the carrier surface.[27]
b. X-ray photoelectron spectroscopy: Analyzes the elemental composition and chemical state of surface atoms.
c. Energy dispersive X-ray spectroscopy: Determines elemental composition and distribution within the carriers.

Drug loading and encapsulation efficiency

a. High-performance liquid chromatography: Quantifies drug content and release from carriers.
b. Ultraviolet vis spectroscopy: Measures drug concentration based on absorption characteristics.

Morphology and structure

a. AFM: Offers high-resolution surface imaging and measures particle height.[28]
b. Small angle X-ray scattering or small angle neutron scattering: Determines carrier structure, including size, shape, and internal structure.

Thermal properties

a. DSC and TGA: Analyzes thermal transitions, stability, and degradation temperatures of carriers.

Drug release kinetics

a. Dialysis method: Evaluates drug release from carriers by separating released drug from carriers using dialysis membranes.
b. *In vitro* release studies: Monitor drug release over time under controlled conditions to determine release kinetics.

Stability studies

a. Accelerated stability testing: Assesses the stability of carriers under various environmental conditions (e.g.,

temperature, pH) to predict shelf life and degradation patterns.

In vitro biocompatibility

a. Cell viability assays: Evaluate the cytotoxicity and biocompatibility of carriers using cell cultures.

CONCLUSION

Nanocarrier-based formulations have redefined pharmaceutical delivery systems, offering targeted and efficient approaches for therapeutic agents. These formulations leverage nanoscale carriers to encapsulate drugs, genes, or imaging agents, presenting advantages over conventional delivery systems. Their small size, tunable properties, and precise control over release kinetics enable tailored drug delivery, biodistribution, and cellular uptake. With diverse forms such as liposomes, polymeric nanoparticles, and inorganic particles, they cater to various loading capacities and compatibility needs. These carriers provide solutions to conventional delivery challenges, enhancing drug solubility, stability, and enabling targeted, sustained release, reducing systemic side effects. They facilitate targeted delivery to specific cells or organs, minimizing off-target effects and supporting imaging for diagnostic purposes. Despite their promise, challenges in scalability, safety, and regulatory approval persist for widespread clinical use. Overcoming these hurdles will be critical for harnessing the full potential of Nanocarrier-based formulations in transforming drug delivery, advancing personalized medicine, and improving therapeutic outcomes.

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Source of Support: Nil. **Conflicts of Interest:** None declared.