

The lack of standardized methods for evaluation the efficacy and safety of nanocarriers

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Abstract

Nanocarriers have emerged as promising platforms for drug delivery, offering targeted therapy and enhanced efficacy while minimizing adverse effects. Physicochemical characterisation, in vitro and in vivo research, and other metrics and assays are used to assess the safety and efficacy of nanocarriers. However, the translation of these technologies from bench to bedside is hindered by the lack of standardized methods for evaluating their efficacy and safety. Variations in reported results restrict interpretation and validation in nanocarrier research and development due to the absence of uniform evaluation techniques. This paper reviews the current landscape of nanocarrier evaluation methodologies, highlights the challenges posed by the absence of standardization, and proposes detailed strategies to address this crucial issue. Standardized evaluation protocols are essential to ensure reproducibility, comparability, and regulatory approval, thus accelerating the clinical translation of nanocarrier-based therapies.

Keywords: “nanocarriers, drug delivery, efficacy, safety, standardization, evaluation methods”.

Introduction

Nanocarriers, including liposomes, polymeric nanoparticles, dendrimers, and micelles, have garnered significant attention in the field of drug delivery due to their ability to encapsulate and deliver therapeutic agents with enhanced precision and efficacy [1]. By overcoming biological barriers, such as poor solubility, limited bioavailability, and off-target effects, nanocarriers offer substantial advantages in the treatment of various diseases. Nanocarriers, a class of nanoparticles designed for drug delivery, have emerged as a significant innovation in the field of pharmacy and pharmacology [2]. These nanoscale vehicles can enhance the efficacy and safety of therapeutic agents by improving their solubility, stability, and bioavailability, while also enabling targeted delivery to specific tissues or cells. Nanocarriers represent a promising advancement in pharmacy and pharmacology, offering innovative solutions to longstanding challenges in drug delivery [3]. By improving the delivery and efficacy of therapeutic agents, nanocarriers hold the potential to revolutionize treatment paradigms across a wide range of diseases. However, the successful clinical translation of nanocarrier-based therapies requires rigorous evaluation of their efficacy and safety, which is currently hindered by the lack of standardized methods [4]. This study aimed to evaluate the lack of standardized methods for evaluation the efficacy and safety of nanocarriers.

Types of Nanocarriers

Liposomes: These are spherical vesicles composed of lipid bilayers, capable of encapsulating both hydrophilic and hydrophobic drugs. Liposomes can merge with cellular membranes, facilitating the direct delivery of their contents into cells. An example is the liposomal formulation of doxorubicin (Doxil), which is used to treat various cancers with reduced cardiotoxicity compared to conventional doxorubicin [1].

Polymeric Nanoparticles: Made from biodegradable polymers such as polylactic acid (PLA) or polylactic-co-glycolic acid (PLGA), these nanoparticles offer controlled and sustained drug release. They are particularly useful in delivering vaccines and anticancer drugs, improving the pharmacokinetic profile of the drugs they carry [5].

Solid Lipid Nanoparticles (SLNs): These nanoparticles consist of a solid lipid core stabilized by surfactants, combining the advantages of liposomes and polymeric nanoparticles. SLNs are employed in improving the oral bioavailability of poorly water-soluble drugs and in topical formulations [2].

Dendrimers: These are highly branched, star-shaped polymers with numerous surface functional groups, which can be modified to carry drugs. Dendrimers provide precise control over drug release and targeting due to their uniform size and surface functionality [6].

Nanocrystals: These are pure drug particles in the nanometer range, stabilized by surfactants. Nanocrystals enhance the dissolution rate and bioavailability of poorly soluble drugs, making them suitable for oral and parenteral administration [7].

Overview of Nanocarriers in Drug Delivery

This section provides an overview of different types of nanocarriers commonly employed in drug delivery, including liposomes, polymeric nanoparticles, dendrimers, and micelles. It discusses their structural characteristics, mechanisms of drug encapsulation and release, targeting strategies, and applications in various disease treatments. Understanding the diversity of nanocarrier platforms is essential for comprehending the challenges associated with their evaluation [2].

Cancer Therapy: Nanocarriers can improve the therapeutic index of anticancer drugs by enhancing their accumulation in tumor tissues while minimizing systemic toxicity. The enhanced permeability and retention (EPR) effect allows nanocarriers to preferentially accumulate in tumor tissues due to their leaky vasculature.

Targeted Drug Delivery: By attaching ligands such as antibodies or peptides to the surface of nanocarriers, drugs can be directed to specific cells or receptors. This targeted approach is beneficial in treating diseases with specific molecular markers, such as certain types of cancer and infectious diseases [4].

Controlled and Sustained Release: Nanocarriers can be engineered to release their payload over a prolonged period, reducing the frequency of dosing and improving patient compliance. This is particularly useful for chronic conditions such as diabetes, where long-acting insulin formulations are in development [8].

Crossing Biological Barriers: Nanocarriers can facilitate the transport of drugs across challenging biological barriers, such as the blood-brain barrier (BBB). This has significant implications for the treatment of central nervous system (CNS) disorders, including Alzheimer's disease and brain tumors [9].

Vaccines: Nanocarriers are being explored for their potential in vaccine delivery, enhancing the immune response and providing longer-lasting immunity. Lipid-based nanoparticles have been utilized in mRNA vaccines, such as those developed for COVID-19 by Pfizer-BioNTech and Moderna [9].

Current Evaluation Methods for Nanocarriers

Evaluation of nanocarrier efficacy and safety involves a myriad of parameters and assays, ranging from physicochemical characterization to in vitro and in vivo studies. This section provides a detailed examination of current evaluation methods, including:

Physicochemical characterization: Techniques for assessing nanocarrier size, morphology, surface charge, drug loading capacity, and encapsulation efficiency. Physicochemical characterization of nanocarriers is a critical aspect in the development and application of nanotechnology in fields like drug delivery, diagnostics, and materials science [10]. It involves analyzing the physical and chemical properties of nanocarriers to ensure they meet the desired specifications for their intended use. Below are key components and methods involved in this characterization process:

Key Components of Physicochemical Characterization

Particle Size and Size Distribution

Dynamic Light Scattering (DLS): Measures the size distribution by analyzing the scattering of light by the particles in suspension.

Transmission Electron Microscopy (TEM): Provides detailed images to determine the shape and size at the nanoscale.

Scanning Electron Microscopy (SEM): Offers high-resolution images of the surface morphology and size.

Surface Charge (Zeta Potential)

Zeta Potential Analysis: Evaluates the surface charge of the nanocarriers, which influences their stability in suspension and interaction with biological membranes [11].

Shape and Morphology

Electron Microscopy (TEM, SEM): Visualizes the shape and surface structure.

Atomic Force Microscopy (AFM): Provides topographical mapping and detailed surface characteristics.

Chemical Composition and Structure

Fourier Transform Infrared Spectroscopy (FTIR): Identifies the chemical bonds and functional groups present in the nanocarriers [12].

X-ray Diffraction (XRD): Determines the crystalline structure of the materials.

Nuclear Magnetic Resonance (NMR) Spectroscopy: Provides information about the molecular structure and dynamics.

Surface Area and Porosity

Brunauer-Emmett-Teller (BET) Analysis: Measures the surface area and porosity, which are important for applications like drug loading and release.

Thermal Properties

Differential Scanning Calorimetry (DSC): Analyzes thermal transitions such as melting and crystallization.

Thermogravimetric Analysis (TGA): Assesses the thermal stability and composition by measuring weight changes upon heating [12].

Drug Loading and Release

Encapsulation Efficiency: Determines the amount of drug encapsulated within the nanocarriers.

Release Kinetics Studies: Evaluate how the drug is released over time under various conditions.

Stability Studies

Colloidal Stability: Monitors changes in size, shape, and surface charge over time to ensure long-term stability.

Chemical Stability: Assesses degradation or chemical changes under different environmental conditions.

Methods for Characterization

Spectroscopic Techniques

UV-Vis Spectroscopy: Measures the absorbance and concentration of nanocarriers.

Fluorescence Spectroscopy: Analyzes the fluorescent properties, useful for tracking and imaging applications [13].

Microscopy Techniques

TEM and SEM: Provide high-resolution images for detailed morphological analysis.

AFM: Offers 3D surface profiles and mechanical property measurements.

Scattering Techniques

DLS: Evaluates size distribution in a colloidal suspension.

Small-Angle X-ray Scattering (SAXS): Investigates the size, shape, and internal structure.

High-Performance Liquid Chromatography (HPLC): Separates and quantifies components, useful for drug loading studies.

Gel Permeation Chromatography (GPC): Measures molecular weight distribution.

Importance in Nanomedicine

Safety and Efficacy: Ensures nanocarriers are safe and effective for medical applications.

Quality Control: Standardizes the production and quality of nanocarriers.

Regulatory Compliance: Meets the requirements set by regulatory bodies for the approval of nanomedicines.

Physicochemical characterization is fundamental to the successful development and application of nanocarriers, providing insights that guide their design, optimization, and deployment in various technological and medical fields [13].

In vitro assays: Methods for evaluating drug release kinetics, cellular uptake, cytotoxicity, and targeting efficiency using cell culture models.

In vivo studies: Approaches for assessing pharmacokinetics, biodistribution, therapeutic efficacy, and systemic toxicity in animal models.

Immunological and toxicological assessments: Studies to evaluate immunogenicity, hemocompatibility, and organ-specific toxicity of nanocarriers.

Challenges Posed by Lack of Standardization

The absence of standardized evaluation methods poses several challenges to the field of nanocarrier research and development:

Inconsistencies in experimental protocols lead to discrepancies in reported outcomes, hindering the interpretation and validation of results [14].

Lack of comparability between studies impedes the identification of optimal nanocarrier formulations and strategies for specific applications [14].

Regulatory agencies require standardized data to assess the safety and efficacy of nanocarrier-based therapies for clinical trials and commercialization [15].

The variability in evaluation methods complicates efforts to establish structure-activity relationships and mechanistic insights into nanocarrier performance [16].

Proposed Strategies for Standardization

To address the lack of standardized methods for evaluating nanocarrier efficacy and safety, the following strategies are proposed:

Establishment of standardized protocols: Collaborative efforts within the scientific community to develop consensus-based protocols for evaluating nanocarrier performance in vitro and in vivo.

Validation studies: Systematic validation of standardized methods across different laboratories and experimental conditions to ensure reliability and reproducibility [17].

Quality control measures: Implementation of quality control measures for nanocarrier characterization and evaluation to ensure consistency and reliability of data.

Regulatory guidance: Engagement with regulatory agencies to establish guidelines for standardized evaluation of nanocarrier-based therapies, facilitating regulatory approval and clinical translation [18].

Standardization Initiatives in Nanocarrier Research

This section highlights ongoing initiatives and consortiums dedicated to standardizing evaluation methods for nanocarriers. Examples include the International Nanomedicine Characterization Laboratory (INCL), the Nanotechnology Characterization Laboratory (NCL), and the European Nanomedicine Characterization Laboratory (EU-NCL). These initiatives aim to promote collaboration, share best practices, and develop consensus-based protocols for nanocarrier characterization and evaluation [18].

Future Perspectives and Emerging Technologies

Continued advancements in nanotechnology, analytical techniques, and computational modeling offer opportunities to refine and optimize standardized evaluation methods for nanocarriers. This section discusses future directions and emerging technologies that hold promise for enhancing the reproducibility, accuracy, and efficiency of nanocarrier evaluation. Examples include the use of organ-on-a-chip systems, microfluidic platforms, and high-throughput screening assays for rapid and comprehensive assessment of nanocarrier performance.

Conclusion

Standardized evaluation methods are essential for advancing the field of nanocarrier-based drug delivery and realizing their full clinical potential. By addressing the lack of standardization, researchers can enhance the reproducibility, comparability, and reliability of data, thereby accelerating the development and commercialization of nanocarrier-based therapies for improved patient outcomes.

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