



(REVIEW ARTICLE)



Liposome: An advanced pharmaceutical carrier in novel drug delivery system

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Abstract

This comprehensive review delves into the dynamic landscape of liposomal drug delivery systems, illuminating their structural intricacies, mechanisms, and multifaceted applications. Beginning with an exploration of the fundamental principles of liposomes, we navigate through their diverse types, encapsulation techniques, and evolving methodologies. The advantages of liposomal drug delivery, from enhanced bioavailability to targeted interventions and reduced side effects, emerge as pivotal themes. The synthesis of experimental and clinical evidence provides a nuanced understanding of challenges and potential innovations, setting the stage for a detailed exploration of liposomes' applications in various therapeutic domains. As we peer into the future, the review unravels the transformative implications of liposomal drug delivery for personalized medicine, chronic disease management, and advancements in cancer therapeutics. The integration of nanotechnology, the advent of smart liposomes, and regulatory considerations add layers to the narrative, offering a holistic perspective on how liposomal drug delivery systems are shaping the future of pharmacy.

Keywords: Liposomal Drug Delivery System; Nanotechnology Integration; Advancements in Cancer Therapeutics; Liposomes in oncology; Liposomes crossing BBB

1. Introduction

1.1. Background on Drug Delivery Systems

Drug delivery systems (DDS) have undergone a remarkable evolution in response to the constant pursuit of optimizing therapeutic outcomes in pharmacotherapy. In the early stages, drug administration relied on simple formulations. However, advancements in pharmaceutical sciences prompted the development of more sophisticated approaches, laying the groundwork for the emergence of drug delivery systems. These systems aimed to enhance drug efficacy, reduce side effects, and improve patient compliance. The evolution of drug delivery systems reflects a continual effort to overcome challenges associated with conventional drug administration ⁽¹⁾. From the advent of first-generation oral dosage forms to the refinement of controlled-release formulations, each phase of development signifies a quest for precision and efficiency. This historical progression sets the stage for the introduction of advanced systems such as liposomal drug delivery. Understanding the landscape of drug delivery systems is particularly crucial in the field of pharmacy. Pharmacists, as key contributors to patient care, play a pivotal role in ensuring the safe and effective use of medications. A comprehensive knowledge of drug delivery systems empowers pharmacists to contribute to treatment optimization and enhance patient well-being ⁽²⁾.

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1.2. Significance of Innovative Drug Delivery Approaches

Innovative drug delivery approaches represent a pivotal paradigm shift in pharmaceutical sciences, embodying the ongoing commitment to enhancing therapeutic efficacy and patient outcomes. Conventional drug administration often faces challenges such as suboptimal bioavailability, limited targeting, and adverse effects. The emergence of innovative drug delivery strategies seeks to address these challenges by offering precise and controlled mechanisms for drug release ⁽³⁾. One of the key drivers behind the significance of innovative drug delivery approaches is the potential to improve patient compliance. Patient adherence to prescribed medications is a critical factor in treatment success, and innovative delivery systems, such as liposomal drug delivery, aim to simplify dosing regimens and minimize side effects, contributing to better patient adherence ⁽⁴⁾. Additionally, these approaches play a crucial role in personalized medicine, tailoring treatment to individual patient needs. The advent of nanotechnology and advanced materials allows for the customization of drug delivery systems based on patient-specific factors, ushering in a new era of precision medicine ⁽⁵⁾. The deliberate emphasis on liposomal drug delivery systems in this review is rooted in their extraordinary versatility and ability to overcome persistent challenges associated with conventional drug delivery. Liposomes, intricate spherical vesicles composed of lipid bilayers, serve as an exceptional platform for encapsulating an expansive array of therapeutic agents with diverse physicochemical properties ⁽⁶⁾. The unique lipid-based structure of liposomes not only facilitates compatibility with a wide range of pharmaceutical agents but also introduces innovative solutions to traditional formulation hurdles.

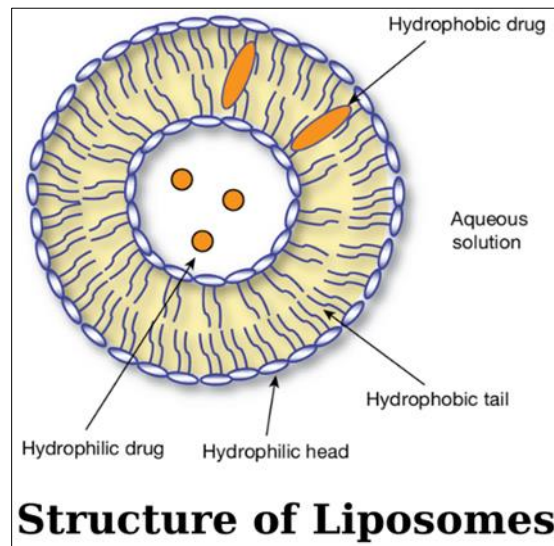


Figure 1 Structure of Liposomes

A primary motivation for highlighting liposomal drug delivery lies in its intrinsic capacity to significantly enhance drug bioavailability ⁽⁷⁾. The encapsulation of drugs within liposomes not only shields them from degradation but also enhances solubility, promoting efficient absorption and distribution within the body. This feature proves especially critical for drugs characterized by low aqueous solubility, a common challenge in conventional formulations. Liposomal encapsulation optimizes the pharmacokinetic profiles of drugs, contributing to heightened therapeutic efficacy. Beyond the enhancement of bioavailability, liposomal drug delivery systems offer a sophisticated means for achieving targeted and controlled drug release ⁽⁸⁾. The surfaces of liposomes can be meticulously engineered to enable specific interactions with target tissues or cells. This targeted approach minimizes systemic exposure, reducing the risk of off-target effects and mitigating adverse reactions. The customization of liposomal surfaces for targeted delivery holds great promise for optimizing the therapeutic index of drugs, ensuring efficacy while minimizing side effects. Furthermore, the inherent biocompatibility of liposomal structures reduces the likelihood of immunogenic responses, a critical advantage in drug delivery applications ⁽⁹⁾. The biocompatible nature of liposomes enhances their safety profile, rendering them an appealing option for various therapeutic interventions. In summary, the multifaceted advantages offered by liposomal drug delivery systems, including enhanced bioavailability, targeted drug delivery, and biocompatibility, underscore their pivotal role in reshaping drug delivery paradigms. This section aims to provide an exhaustive exploration of the rationale behind the intentional focus on liposomal drug delivery systems within the broader context of innovative drug delivery approaches.

2. Fundamentals of Liposomes

2.1. Definition and Structural Anatomy

Liposomes, coined by Bangham et al. in 1965, are microscopic vesicles composed of lipid bilayers, mimicking the structural organization of natural cell membranes. These phospholipid-based structures possess a hydrophilic outer surface and an inner hydrophobic core, creating a bilayered structure that encapsulates an aqueous compartment ⁽¹⁰⁾. The structural anatomy of liposomes can be categorized into various types, primarily distinguished by their size, lamellarity, and method of preparation. The primary components of liposomes are phospholipids, amphiphilic molecules with a hydrophilic head and hydrophobic tail. The arrangement of these phospholipids in bilayers facilitates the formation of liposomal structures, where the hydrophobic tails align inward, shielding themselves from the surrounding aqueous environment, while the hydrophilic heads face outward, interacting with the aqueous surroundings ⁽¹¹⁾. This bilayer configuration is fundamental to the stability and functionality of liposomes. Liposomes come in different sizes, ranging from small unilamellar vesicles (SUVs) with a single lipid bilayer to large multilamellar vesicles (MLVs) containing multiple lipid layers. The size and lamellarity of liposomes influence their drug-loading capacity, stability, and interaction with biological systems ⁽¹²⁾. The structural diversity of liposomes extends to their surface characteristics. Through surface modification techniques, liposomes can be functionalized with various molecules, such as polymers or ligands, to impart specific properties. This functionalization plays a crucial role in targeted drug delivery, enabling liposomes to selectively interact with particular cells or tissues ⁽¹³⁾. Understanding the structural intricacies of liposomes is paramount for harnessing their potential in drug delivery systems. The biocompatible and biodegradable nature of liposomes, combined with their ability to encapsulate a wide range of therapeutic agents, positions them as versatile carriers in pharmaceutical applications ⁽¹⁴⁾.

2.2. Liposomal Types and Their Distinct Characteristics

Liposomes exhibit a spectrum of types, each distinguished by unique characteristics that influence their performance in drug delivery systems. Understanding these types is crucial for tailoring liposomal formulations to specific therapeutic needs.

2.2.1. Small Unilamellar Vesicles (SUVs)

Small unilamellar vesicles are characterized by a single lipid bilayer and a small size, typically less than 100 nanometers. This size imparts certain advantages, such as improved drug loading efficiency and enhanced tissue penetration ⁽¹⁵⁾. SUVs are particularly useful for delivering drugs to target sites with intricate vasculature.

2.2.2. Large Unilamellar Vesicles (LUVs)

Large unilamellar vesicles differ in size, typically ranging from 100 to 1000 nanometers, and possess a single lipid bilayer. Their larger size allows for a higher drug payload, making them suitable for delivering a diverse range of therapeutic agents ⁽¹⁶⁾.

2.2.3. Multilamellar Vesicles (MLVs)

Multilamellar vesicles consist of multiple lipid bilayers separated by aqueous layers. These vesicles vary in size and are commonly larger than 1 micron. The multiple layers enable MLVs to encapsulate a higher volume of drugs, making them advantageous for sustained-release formulations ⁽¹⁷⁾.

2.2.4. Giant Unilamellar Vesicles (GUVs)

Giant unilamellar vesicles, characterized by their larger size, often surpassing 1 micron, provide a unique platform for studying cell membrane properties and interactions ⁽¹⁸⁾. While less common in drug delivery, GUVs contribute significantly to understanding lipid membrane dynamics.

2.2.5. Stealth Liposomes

Stealth liposomes, also known as long-circulating liposomes, are surface-modified to evade recognition by the immune system, leading to prolonged circulation times ⁽¹⁹⁾. Polyethylene glycol (PEG) is commonly employed for stealth

2.2.6. Cationic Liposomes

Cationic liposomes possess a positively charged surface, enabling interactions with negatively charged cell membranes. This characteristic is particularly advantageous for nucleic acid delivery, as cationic liposomes can facilitate cellular

uptake through electrostatic interactions ⁽²⁰⁾. Liposomal types play a pivotal role in tailoring drug delivery systems to specific therapeutic requirements. The choice of liposomal type depends on factors such as drug properties, desired release kinetics, and target tissue characteristics, highlighting the versatility of liposomes in pharmaceutical applications.

2.3. Techniques for Liposomal Encapsulation

Achieving effective liposomal encapsulation involves employing various techniques, each with its own set of advantages and considerations. These methods are instrumental in ensuring the successful incorporation of therapeutic agents into liposomes, enhancing their stability and functionality.

2.3.1. Thin-Film Hydration

One of the classic methods for liposomal preparation is thin-film hydration. Lipids are dissolved in an organic solvent to create a thin lipid film on the container's walls. Hydration with an aqueous solution then leads to the formation of multilamellar vesicles (MLVs) that can be further downsized through sonication or extrusion ⁽²¹⁾. This technique is versatile and suitable for a wide range of liposomal formulations.

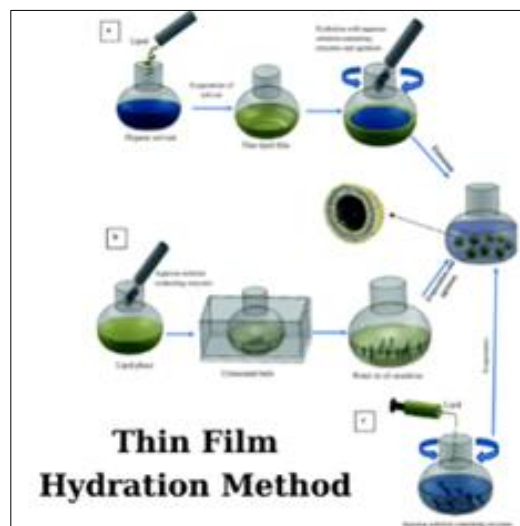


Figure 2 Diagrammatic representation of Thin film Hydration Method

2.3.2. Reverse Phase Evaporation

Reverse phase evaporation involves the use of an organic phase containing lipids, which is then emulsified with an aqueous phase. Subsequent evaporation of the organic phase results in the formation of liposomes ⁽²²⁾. This method is particularly advantageous for encapsulating hydrophobic drugs and achieving high encapsulation efficiencies.

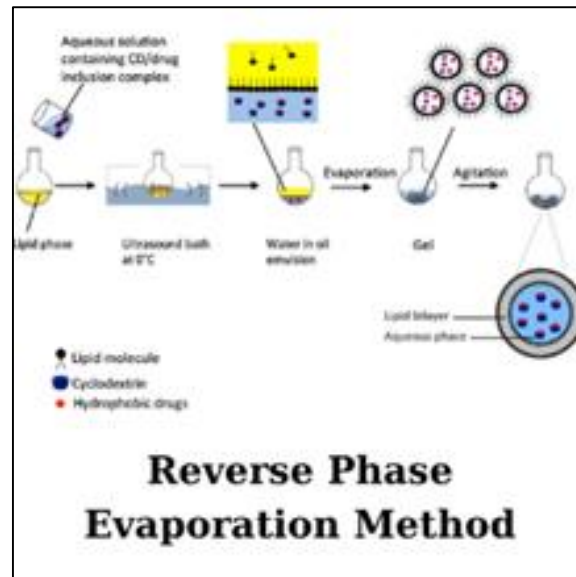


Figure 3 Diagrammatic representation of Reverse Phase Evaporation Method

2.3.3. Ethanol Injection

In the ethanol injection method, lipids are dissolved in ethanol and injected into an aqueous phase under vigorous stirring. Rapid lipid precipitation occurs, leading to the formation of liposomes⁽²³⁾. This technique is suitable for preparing small unilamellar vesicles (SUVs) and is advantageous for encapsulating temperature-sensitive drugs.

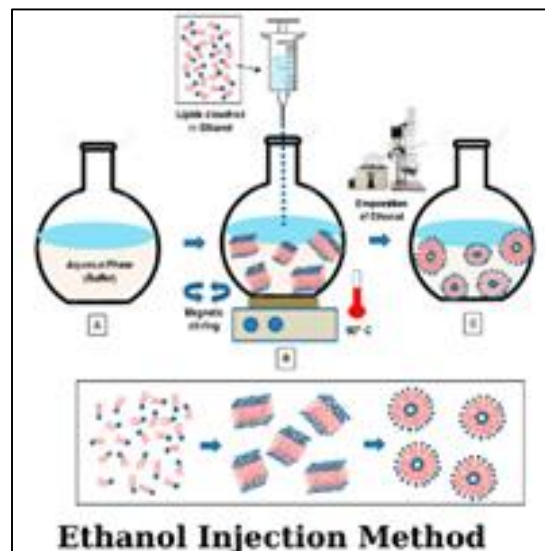


Figure 4 Diagrammatic representation of Ethanol Injection Method

2.3.4. Detergent Removal

Detergent removal involves the use of detergents to solubilize lipids and the subsequent removal of detergents to induce liposome formation⁽²⁴⁾. This technique is especially useful for preparing liposomes encapsulating hydrophobic drugs or peptides.

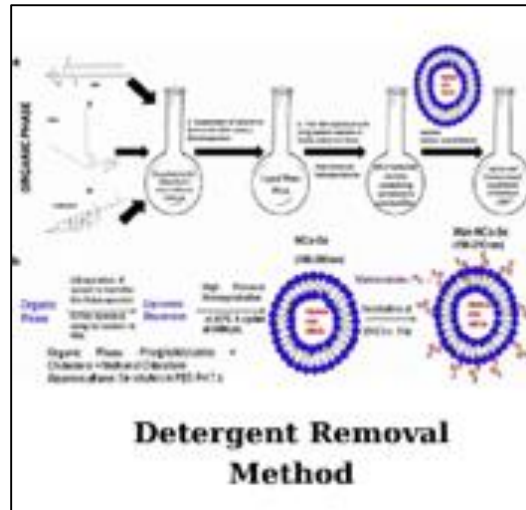


Figure 5 Diagrammatic representation of Detergent Removal Method

2.3.5. Super Critical Fluid

The supercritical fluid method utilizes supercritical carbon dioxide as a solvent for lipids, creating liposomes upon the expansion of the fluid ⁽²⁵⁾. This method offers advantages in terms of scalability and solvent removal, making it suitable for large-scale production.

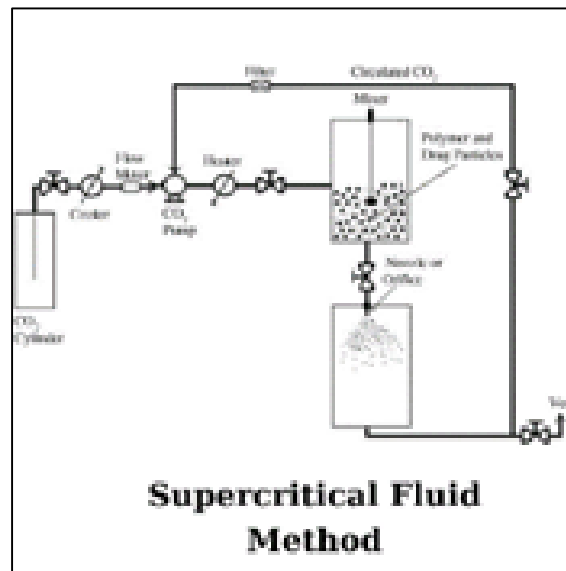


Figure 6 Diagrammatic representation of Supercritical Fluid Method

2.3.6. Extrusion

Extrusion involves forcing liposome dispersions through small pores to achieve size reduction and uniformity ⁽²⁶⁾. This technique is crucial for obtaining liposomes with a defined size and distribution, contributing to their stability and suitability for specific drug delivery applications.

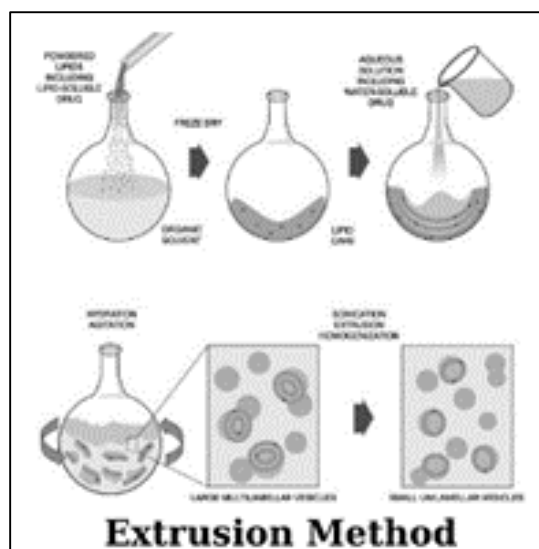


Figure 7 Diagrammatic representation of Extrusion Method

2.3.7. Remote Loading

Remote loading techniques involve creating a pH or ion gradient to facilitate the active loading of drugs into pre-formed liposomes (27). This method is particularly useful for encapsulating weakly acidic or basic drugs and improving encapsulation efficiency. Understanding these encapsulation techniques is pivotal for tailoring liposomal formulations to specific drug delivery needs. Each method offers unique advantages, and the choice depends on the physicochemical properties of the therapeutic agent and the desired characteristics of the liposomal carrier.

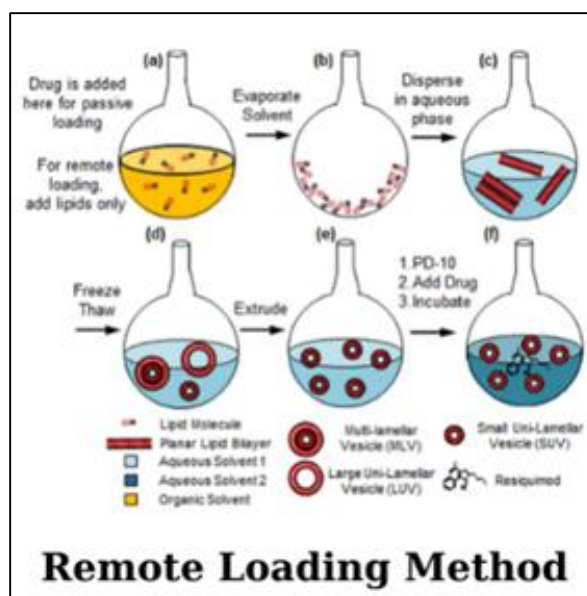


Figure 8 Diagrammatic representation of Remote Method

3. Advantages of Liposomal Drug Delivery

3.1. Enhanced Bioavailability: Mechanisms and Implications

The augmented bioavailability achieved through liposomal drug delivery is pivotal for optimizing therapeutic outcomes. Liposomes play a protective role by shielding drugs from enzymatic degradation and premature metabolism in the bloodstream, ensuring a higher fraction reaches the target site intact. Addressing challenges in drug solubility and stability, liposomes provide a hydrophilic environment within their aqueous core, effectively solubilizing hydrophobic drugs (28). Additionally, liposomes contribute to the stability of encapsulated drugs, preventing chemical degradation

and thereby enhancing their shelf life. Sustained release and prolonged circulation achieved through liposomal drug delivery significantly impact bioavailability. Liposomes, designed to control the release kinetics of drugs, lead to a more gradual and controlled delivery, minimizing fluctuations in plasma drug concentrations. An advantage associated with liposomal drug delivery is the evasion of first-pass metabolism. The encapsulation of drugs within liposomes enables them to bypass first-pass metabolism in the liver, allowing a larger fraction of the drug to reach systemic circulation ⁽²⁹⁾. Enhanced cellular uptake, facilitated by the surface properties of liposomes, is crucial for targeted drug delivery. Surface modifications can be made to interact specifically with target cells, improving the delivery of drugs to specific tissues and enhancing bioavailability. Finally, liposomes can take advantage of endocytic pathways for cellular internalization, further enhancing their bioavailability. This mechanism is particularly relevant for drugs requiring intracellular delivery ⁽³⁰⁾. In summary, the mechanisms contributing to enhanced bioavailability in liposomal drug delivery, including protection from degradation, improved solubility and stability, sustained release, avoidance of first-pass metabolism, enhanced cellular uptake, and utilization of endocytic pathways, collectively underscore the significance of liposomes in optimizing the pharmacokinetic profile of therapeutic agents.

3.2. Targeted Drug Delivery: Exploiting Liposome Surface Modifications

Targeted drug delivery is a hallmark advantage of liposomal drug delivery, driven by sophisticated surface modifications that enable specific interactions with target cells. This approach significantly enhances the therapeutic efficacy while minimizing off-target effects. Liposomes offer a versatile platform for surface modification, allowing the attachment of ligands that can selectively recognize and bind to receptors overexpressed on the surface of target cells. The conjugation of targeting ligands, such as antibodies, peptides, or aptamers, facilitates the specific recognition of cancer cells or diseased tissues ⁽³¹⁾. The attachment of ligands to liposome surfaces enhances the homing of liposomes to target sites, allowing for precise drug delivery. This targeted approach not only improves the therapeutic index by concentrating drugs at the site of action but also reduces systemic toxicity by sparing healthy tissues. One notable example is the utilization of folate-targeted liposomes for cancer therapy. Folate receptors are often upregulated in cancer cells, and liposomes functionalized with folate ligands demonstrate improved cellular uptake and enhanced therapeutic outcomes in folate receptor-positive tumors ⁽³²⁾. In addition to ligand-based targeting, liposomes can exploit other surface modifications, such as PEGylation. Polyethylene glycol (PEG) coating imparts stealth properties to liposomes, extending their circulation time in the bloodstream and enabling passive targeting through the enhanced permeability and retention (EPR) effect. This effect leverages the leaky vasculature and impaired lymphatic drainage characteristic of tumors, enhancing liposomal accumulation in cancerous tissues. Furthermore, the application of stimuli-responsive liposomes adds an additional layer of sophistication to targeted drug delivery. These liposomes can respond to specific stimuli, such as changes in pH or temperature, to release their cargo selectively at the target site, further optimizing therapeutic outcomes ⁽³³⁾. In conclusion, targeted drug delivery through liposomal surface modifications represents a paradigm shift in drug delivery strategies. By exploiting the versatility of liposome surface engineering, researchers can tailor drug delivery systems with precision, offering a powerful tool for enhancing therapeutic efficacy while minimizing side effects.

3.3. Reduction of Side Effects: Evidence from Experimental and Clinical Studies

Liposomal drug delivery stands out for its potential to significantly reduce side effects associated with conventional drug formulations. Experimental and clinical studies have provided compelling evidence for the enhanced safety profile of liposomal formulations. One of the notable ways liposomes reduce side effects is by improving the therapeutic index of drugs. The encapsulation of drugs within liposomes enhances their delivery to target tissues while minimizing exposure to healthy organs, leading to a more favorable therapeutic window ⁽³⁴⁾. This has been particularly evident in cancer therapy, where liposomal formulations contribute to the selective targeting of tumors. Liposomal drug delivery minimizes systemic toxicity by allowing for targeted drug release at specific sites. The surface modifications of liposomes, such as PEGylation, provide stealth properties, preventing rapid recognition by the immune system and facilitating prolonged circulation ⁽³⁵⁾. As a result, the systemic exposure of healthy tissues to the drug is reduced, translating into fewer adverse effects. The controlled release kinetics afforded by liposomal drug delivery contribute to reduced side effects. The sustained release of drugs from liposomes results in a more gradual and controlled delivery, avoiding sharp peaks in drug concentrations that can lead to toxic effects ⁽³⁶⁾. Organ-specific toxicity is a common concern with many drugs. Liposomal formulations have demonstrated success in decreasing organ toxicity by directing drug delivery to specific tissues. For example, liposomes functionalized with ligands that target specific cell types allow for the preferential accumulation of drugs in the intended organs, minimizing damage to non-targeted tissues ⁽³⁷⁾. Clinical studies have provided robust evidence supporting the reduction of side effects with liposomal drug formulations. For instance, liposomal doxorubicin has been extensively studied in cancer patients, demonstrating not only improved efficacy but also a favorable safety profile with reduced cardiotoxicity compared to conventional doxorubicin formulations ⁽³⁸⁾. In summary, liposomal drug delivery holds substantial promise in reducing side effects associated with conventional drug formulations. The evidence from both experimental studies and clinical trials

underscores the potential of liposomes to improve the safety profile of therapeutic agents, paving the way for more effective and well-tolerated treatments.

4. Challenges and Limitations in Liposomal Drug Delivery

4.1. Stability Challenges: Strategies for Overcoming Instabilities

Liposomal drug delivery, while offering numerous advantages, encounters challenges related to stability, which can impact the efficacy of therapeutic agents. Several strategies have been developed to address these instabilities and enhance the robustness of liposomal formulations.

4.1.1. Liposome Leakage and Drug Leakage

Liposome leakage, leading to premature drug release, is a common challenge. To tackle this, researchers have employed various liposome stabilization techniques. The use of cholesterol in liposomal formulations has been demonstrated to enhance membrane rigidity, reducing drug leakage and increasing liposomal stability⁽³⁹⁾.

4.1.2. Oxidative Degradation

Oxidative degradation of lipids within liposomes is another stability concern, particularly relevant for long-circulating formulations. The incorporation of antioxidants, such as alpha-tocopherol, into liposomal membranes has proven effective in mitigating oxidative stress and preserving the stability of liposomes during circulation⁽⁴⁰⁾.

4.1.3. Aggregation and Fusion

Aggregation and fusion of liposomes can compromise their stability and alter drug release profiles. The addition of steric stabilizers, such as polyethylene glycol (PEG), on the liposome surface inhibits aggregation by creating a repulsive force between liposomes, preventing undesired fusion events⁽⁴¹⁾.

4.1.4. In Vivo Challenges

Stability challenges extend into in vivo environments, where interactions with plasma proteins and the mononuclear phagocyte system (MPS) can impact liposomal integrity. Surface modifications, such as PEGylation, help to shield liposomes from recognition by the immune system, extending their circulation time and improving stability⁽⁴²⁾.

4.1.5. Temperature Sensitivity

Temperature sensitivity is a critical stability concern, particularly for thermosensitive liposomal formulations. Incorporating phase transition lipids, like dipalmitoylphosphatidylcholine (DPPC), can enhance stability by providing structural support at physiological temperatures⁽⁴³⁾.

4.1.6. Encapsulation Techniques

Instabilities during the encapsulation process can impact the efficiency of drug loading. Innovative techniques, such as supercritical fluid technology, offer advantages in terms of reducing exposure to organic solvents and maintaining the stability of liposomal formulations during drug loading⁽⁴⁴⁾. In summary, stability challenges pose significant hurdles in liposomal drug delivery, but ongoing research has led to the development of various strategies to overcome these issues. From membrane stabilization to addressing in vivo challenges, these approaches contribute to the continued improvement of the stability and reliability of liposomal drug delivery systems.

4.2. Manufacturing Hurdles: Current Practices and Future Innovations

Liposomal drug delivery, despite its advantages, encounters challenges in the manufacturing process that influence the scalability, reproducibility, and cost-effectiveness of liposomal formulations. Addressing these challenges is crucial for the widespread adoption of liposomal drug delivery in clinical settings. Scaling up the production of liposomal formulations from laboratory to commercial scale poses significant challenges. Current manufacturing practices often involve complex processes, such as thin-film hydration or extrusion methods, which may not be easily scalable⁽⁴⁵⁾. Future innovations in scalable manufacturing technologies are essential to meet the growing demand for liposomal therapeutics. Achieving consistent liposomal formulations is a key concern due to batch-to-batch variability. Variations in lipid composition, size distribution, and drug encapsulation efficiency can occur during the manufacturing process, impacting the reproducibility of liposomal drug delivery systems⁽⁴⁶⁾. Robust quality control measures and innovative manufacturing techniques are needed to minimize variability. The cost-effectiveness of liposomal drug production

remains a challenge. Traditional manufacturing methods often involve multiple purification steps, leading to increased production costs. Future innovations should focus on streamlining manufacturing processes to reduce costs while maintaining the quality and efficacy of liposomal formulations. Ensuring sterility is critical in pharmaceutical manufacturing. However, many traditional sterilization methods, such as autoclaving, may compromise liposomal stability and drug encapsulation efficiency ⁽⁴⁷⁾. Developing novel, liposome-friendly sterilization techniques is imperative to maintain product integrity. Meeting regulatory standards for liposomal drug products is a significant hurdle. Stringent regulations require extensive documentation of the manufacturing process and quality control measures. Continuous collaboration between researchers, manufacturers, and regulatory bodies is crucial to streamline compliance without compromising innovation. Traditional batch manufacturing may not be optimal for achieving continuous, efficient production of liposomal drugs. Continuous manufacturing approaches, such as microfluidics, offer potential advantages in terms of process control, reduced variability, and faster production rates ⁽⁴⁸⁾. Implementing and optimizing continuous manufacturing in liposomal drug production is an area of ongoing research.

In conclusion, addressing manufacturing hurdles is essential for the successful translation of liposomal drug delivery from the laboratory to clinical applications. Overcoming scale-up challenges, ensuring batch consistency, enhancing cost-effectiveness, developing liposome-friendly sterilization methods, achieving regulatory compliance, and exploring continuous manufacturing approaches are crucial steps in advancing the manufacturing capabilities of liposomal drug delivery systems.

4.3. Immunogenicity Concerns: Unraveling the Complexities

Immunogenicity is a significant concern in liposomal drug delivery, impacting both the safety and efficacy of therapeutic agents. The complex interplay between liposomes and the immune system introduces challenges that necessitate a nuanced understanding for the successful implementation of liposomal formulations. The inherent immunogenicity of liposomes can trigger immune recognition and clearance by the reticuloendothelial system (RES), particularly in the liver and spleen ⁽⁴⁹⁾. Opsonization, the process by which liposomes are tagged for removal by immune cells, can lead to decreased circulation time and compromised drug delivery to the intended target sites. The activation of the complement system is a double-edged sword in liposomal drug delivery. On one hand, complement activation can lead to accelerated blood clearance, limiting the therapeutic window. On the other hand, controlled complement activation may enhance the targeting of liposomes to specific tissues ⁽⁵⁰⁾. Surface modifications, such as PEGylation, are commonly employed to mitigate immunogenic responses. However, anti-PEG antibodies can still develop over time, potentially neutralizing the benefits of PEGylation and impacting the pharmacokinetics of liposomes. Understanding the dynamics of immune responses to surface modifications is crucial for predicting long-term effects. Pre-existing immunity in patients can also influence the response to liposomal formulations. Individuals with prior exposure to liposomes may develop anti-liposome antibodies, potentially compromising the effectiveness of subsequent liposomal treatments ⁽⁵¹⁾. Tailoring liposomal formulations to minimize immunogenicity in diverse patient populations is a pressing challenge. Regulatory agencies have stringent guidelines for assessing immunogenicity in drug development. These guidelines necessitate comprehensive evaluations, including the detection of anti-drug antibodies and potential clinical implications. Compliance with regulatory standards is paramount to ensuring the safety and efficacy of liposomal drug delivery systems. Addressing immunogenicity concerns requires the development of strategies to mitigate immune responses. This may involve the use of novel liposomal formulations, alternative surface modifications, or co-administration of immunomodulators to modulate immune reactions ⁽⁵²⁾.

In conclusion, unraveling the complexities of immunogenicity in liposomal drug delivery is essential for advancing the field. Recognizing the impact of immune recognition, complement activation, responses to surface modifications, pre-existing immunity, and adhering to regulatory guidelines are critical steps in optimizing the safety and efficacy of liposomal formulations.

5. Applications in Pharmacy

5.1. Cancer Therapy: Liposomes in Oncology

Liposomes have evolved into essential tools in cancer therapy, presenting unique advantages in addressing challenges associated with traditional chemotherapy. One of the hallmark features of liposomes in cancer therapy is their prowess in targeted drug delivery. Surface modifications, such as ligand conjugation, enable specific recognition and binding to cancer cells, allowing for precision in drug delivery to tumor sites while minimizing collateral damage to healthy tissues ⁽⁵³⁾. Liposomes contribute to improved pharmacokinetics of anti-cancer drugs. Their ability to evade the mononuclear phagocyte system (MPS) and prolonged circulation time enhance drug bioavailability, ensuring a sustained release and heightened therapeutic efficacy. Liposomes play a pivotal role in overcoming drug resistance, a common challenge in

cancer treatment. By encapsulating various therapeutic agents, including conventional chemotherapeutics and targeted drugs, liposomes offer a multifaceted approach to addressing resistance mechanisms⁽⁵⁴⁾. The encapsulation of anti-cancer drugs within liposomes facilitates targeted drug release at tumor sites, minimizing exposure to healthy tissues and consequently reducing side effects associated with systemic chemotherapy. Beyond drug delivery, liposomes are employed for imaging and diagnosis in cancer therapy. Loaded with contrast agents or imaging probes, liposomes enable non-invasive monitoring of tumor response to treatment and assist in early cancer detection. The adaptability of liposomal formulations lends itself well to personalized medicine approaches. Tailoring liposomes based on individual patient characteristics and the molecular profile of their cancer enables more precise and effective treatment strategies⁽⁵⁵⁾.

In conclusion, the applications of liposomes in cancer therapy encompass targeted drug delivery, improved pharmacokinetics, overcoming drug resistance, minimizing side effects, imaging, and personalized medicine. These aspects collectively position liposomes as pivotal contributors to the advancement of oncology.

5.2. Infectious Disease Treatment: Targeting Microbial Agents

Liposomes have demonstrated significant potential in the treatment of infectious diseases by providing a versatile platform for targeted delivery of antimicrobial agents. Liposomes offer a tailored approach to antimicrobial drug delivery. Their ability to encapsulate a variety of antimicrobial agents, including antibiotics, antivirals, and antifungals, allows for targeted delivery to specific sites of infection⁽⁵⁶⁾. This targeted delivery minimizes off-target effects and enhances the therapeutic efficacy of the drugs. The rise of drug-resistant microbial strains poses a significant challenge in infectious disease treatment. Liposomal formulations of antimicrobial drugs can enhance drug efficacy and overcome resistance by improving drug solubility, bioavailability, and sustained release at the infection site. The lipid bilayer of liposomes can also facilitate the bypassing of certain resistance mechanisms. Liposomes have the capacity to traverse cell membranes, enabling the intracellular delivery of antimicrobial agents. This is particularly crucial for infections involving intracellular pathogens, such as certain bacteria or viruses⁽⁵⁷⁾. The ability to reach the intracellular space enhances the spectrum of activity of antimicrobial drugs. Biofilm formation by microbial agents poses a challenge in the treatment of infections. Liposomal formulations have shown promise in disrupting biofilms, as liposomes can penetrate these protective structures, delivering antimicrobial agents to the embedded pathogens more effectively. Liposomes have been explored for antiviral applications, including the treatment of viral infections such as HIV. Liposomal formulations of antiviral drugs can enhance drug stability, improve pharmacokinetics, and allow for targeted delivery to viral reservoirs. Liposomes can be engineered not only for drug delivery but also for immunomodulation. In infectious disease treatment, liposomes can be designed to enhance the host immune response, contributing to the clearance of microbial agents⁽⁵⁸⁾.

In summary, liposomes offer a versatile platform for the targeted delivery of antimicrobial agents, addressing challenges such as drug resistance, intracellular infections, biofilm disruption, and antiviral applications. These applications highlight the potential of liposomal formulations in advancing the treatment of infectious diseases.

5.3. Central Nervous System Disorders: Crossing the Blood-Brain Barrier

Liposomes have demonstrated tremendous potential in addressing the challenges of treating Central Nervous System (CNS) disorders, primarily by facilitating the delivery of therapeutic agents across the formidable Blood-Brain Barrier (BBB). The BBB restricts the passage of many drugs into the brain, presenting a significant hurdle in the treatment of CNS disorders. Liposomes, owing to their unique lipid bilayer structure, offer a promising avenue for drug delivery across the BBB⁽⁵⁹⁾. Functionalization of liposomes with specific ligands can further enhance their ability to traverse the BBB efficiently. Liposomal formulations have been employed for the delivery of neuroprotective agents. This is particularly relevant in conditions like neurodegenerative disorders, where protecting neurons from degeneration is crucial. Liposomes can encapsulate neuroprotective compounds, ensuring their targeted delivery to the affected regions of the brain. Neuroinflammation is a common feature of many CNS disorders. Liposomes, when loaded with anti-inflammatory drugs, can be directed to sites of neuroinflammation. This targeted approach minimizes systemic side effects and enhances the therapeutic impact on conditions involving neuroinflammatory responses⁽⁶⁰⁾. In the realm of gene therapy for CNS disorders, liposomes serve as effective carriers for gene delivery. Modified liposomes can encapsulate genetic material and facilitate its safe and targeted delivery to neurons, offering potential in the treatment of genetic-based neurological disorders. Liposomes have been explored for the delivery of antimicrobial agents to the CNS, addressing neurological infections. By encapsulating antibiotics or antiviral drugs, liposomes can enhance drug stability and achieve targeted delivery to combat infections within the brain. Liposomes are not limited to therapeutic applications; they also play a role in neurodiagnostics. Liposomal formulations loaded with imaging agents can be employed for non-invasive imaging of brain structures, aiding in the diagnosis and monitoring of CNS disorders⁽⁶¹⁾.

In summary, liposomes offer a versatile platform for addressing CNS disorders by effectively crossing the BBB. Their applications span from the delivery of neuroprotective agents and anti-inflammatory drugs to gene therapy and imaging agents, demonstrating significant promise in advancing the treatment and diagnosis of various neurological conditions.

6. Recent Advances and Innovations in Liposomal Drug Delivery

6.1. Integration of Nanotechnology: Synergies and Synergistic Approaches

Recent strides in liposomal drug delivery underscore the integration of nanotechnology, fostering synergies that amplify the therapeutic potential of liposomal formulations. Nanotechnology offers precise targeting through the development of liposomal nanocarriers. These nanocarriers, equipped with targeting ligands, enhance specificity by homing in on specific cells or tissues ⁽⁶²⁾. Nanotechnology advancements have led to the creation of environmentally responsive liposomes that release their cargo in response to specific stimuli. These stimuli may include changes in pH, temperature, or the presence of enzymes, ensuring controlled drug release. Fabrication of liposomes at the nanoscale, facilitated by nanotechnology, enhances their stability and bioavailability. Nanoscale liposomes can efficiently penetrate tissues and cells, optimizing drug delivery ⁽⁶³⁾. The integration of liposomes with other nanoscale systems, such as polymeric nanoparticles, results in hybrid drug delivery systems. These hybrids synergize the advantages of both systems, enhancing drug loading capacity and overall efficacy. Nanotechnology enables the development of liposomal co-delivery systems, where different therapeutic agents are encapsulated within the same carrier. This synergistic approach enhances therapeutic outcomes by combining the effects of multiple drugs. Nanoscale surface engineering of liposomes involves the precise modification of their surfaces. This process, made possible by nanotechnology, includes attaching targeting ligands and polymers to optimize pharmacokinetics and enhance in vivo circulation ⁽⁶⁴⁾.

In conclusion, the integration of nanotechnology into liposomal drug delivery systems represents a pivotal advancement, ushering in innovative approaches and synergies. From precision targeting to environmentally responsive liposomes and nanoscale formulations, these developments hold significant promise for advancing the field.

6.2. Smart Liposomes: Responsive and Stimulus-Triggered Drug Release

Smart liposomes, equipped with responsive and stimulus-triggered drug release mechanisms, represent a cutting-edge innovation in the field of liposomal drug delivery. Smart liposomes are designed with environmental responsiveness, enabling them to release their payload in a controlled manner in response to specific conditions. This may include changes in pH, temperature, or the presence of certain enzymes, ensuring precise drug release at the target site ⁽⁶⁵⁾. pH-responsive liposomes are a prominent example of smart liposomes. These liposomes exploit variations in pH levels within the body. For instance, in the acidic environment of tumor tissues, pH-responsive liposomes can undergo structural changes, triggering drug release specifically within the tumor microenvironment. Temperature-sensitive liposomes respond to changes in temperature, a feature particularly relevant for hyperthermic conditions in tumors. By utilizing mild hyperthermia, these liposomes can release drugs selectively in heated regions, enhancing therapeutic outcomes ⁽⁶⁶⁾. Smart liposomes can incorporate enzymes as triggers for drug release. Enzyme-triggered liposomes release their cargo in response to specific enzymes present in the target tissue. This approach allows for site-specific drug delivery, minimizing off-target effects. Light-responsive liposomes leverage light as a stimulus for drug release. Light-sensitive molecules incorporated into the liposomal membrane can be activated by external light sources, facilitating spatiotemporal control over drug delivery. Magnetic-responsive liposomes utilize external magnetic fields to trigger drug release. Incorporation of magnetic components allows for on-demand drug delivery by applying a magnetic field to the target area ⁽⁶⁷⁾.

In conclusion, smart liposomes with responsive and stimulus-triggered drug release mechanisms represent a remarkable advancement in liposomal drug delivery. By harnessing environmental cues such as pH, temperature, enzymes, light, and magnetic fields, these liposomes offer unprecedented control over drug release, maximizing therapeutic efficacy while minimizing systemic side effects.

6.3. Personalized Medicine Approaches: Tailoring Liposomal Therapies to Individuals

In the realm of recent advancements in liposomal drug delivery, a notable paradigm shift involves the application of personalized medicine approaches, where liposomal therapies are tailored to the unique characteristics of individual patients. Personalized medicine in liposomal drug delivery starts with the development of patient-specific formulations. This involves considering individual patient factors such as genetics, metabolism, and specific disease characteristics to customize liposomal formulations for optimal therapeutic outcomes ⁽⁶⁸⁾. Advances in genetic profiling allow for a deeper understanding of how individuals may respond to liposomal therapies. Genetic factors can influence drug metabolism,

efficacy, and potential adverse reactions. By incorporating genetic information, liposomal therapies can be fine-tuned to match the genetic makeup of each patient. Personalized liposomal therapies often involve the identification and utilization of biomarkers. Biomarkers can serve as indicators of disease progression, treatment response, and potential side effects. Integrating biomarker data into liposomal drug delivery strategies enables a more targeted and personalized approach to treatment. Personalized medicine extends to the incorporation of tailored drug combinations within liposomes. This approach recognizes that individuals may respond differently to various therapeutic agents. By encapsulating multiple drugs within liposomes, each patient's treatment can be customized based on the specific molecular characteristics of their disease (69). Advancements in technology allow for real-time monitoring of treatment responses. Personalized liposomal therapies can be adapted based on how an individual is responding to treatment. Continuous monitoring enables healthcare professionals to make timely adjustments to dosage or formulation to optimize therapeutic outcomes. Personalized liposomal therapies necessitate the integration of clinical and molecular data. By combining information from medical records, imaging, and molecular profiling, a comprehensive understanding of the patient's condition can be obtained. This holistic approach guides the development of liposomal formulations that align with the individualized needs of each patient (70).

In conclusion, personalized medicine approaches in liposomal drug delivery mark a significant stride towards tailoring therapies to the unique characteristics of each patient. By considering genetic profiles, biomarkers, and real-time monitoring, personalized liposomal therapies offer a more nuanced and effective strategy in the pursuit of optimal patient outcomes.

7. Clinical Trials and Regulatory Landscape

7.1. Overview of Liposomal Drugs in Clinical Trials: Current Progress

The clinical development of liposomal drugs has witnessed substantial progress, reflecting a commitment to advancing innovative therapeutic strategies. Numerous liposomal formulations are currently under investigation in various phases of clinical trials, offering a glimpse into the expanding landscape of liposomal drug development. The majority of liposomal drugs in clinical trials are concentrated in the field of oncology. Liposomal formulations have demonstrated significant potential in improving the therapeutic index of anticancer agents. Notable examples include liposomal doxorubicin (Doxil) and liposomal irinotecan (Onivyde), both of which have shown promise in enhancing drug delivery to tumor sites while minimizing systemic toxicity (71). Beyond oncology, there is a growing interest in exploring liposomal formulations for antiviral applications. Liposomal antivirals are being investigated for their potential in improving drug stability, bioavailability, and targeted delivery. This includes liposomal formulations for antiretroviral drugs, showcasing the versatility of liposomes in diverse therapeutic areas (72). The utilization of liposomes in vaccine development is a burgeoning area in clinical trials. Liposomal vaccines aim to enhance the immune response, providing a platform for targeted antigen delivery. Such formulations are being explored for a range of diseases, including infectious diseases and certain cancers (73).

Regulatory bodies have adapted to the unique challenges posed by liposomal drug development. The approval of liposomal formulations, such as Doxil, has paved the way for a more nuanced regulatory approach. The U.S. Food and Drug Administration (FDA) and other regulatory agencies have established frameworks for evaluating the safety and efficacy of liposomal drugs, considering factors like drug release kinetics and pharmacokinetics (74). Early-phase clinical trials are exploring the potential of liposomes in gene therapy. Liposomal vectors are being investigated for their ability to efficiently deliver genetic material to target cells. This holds promise for addressing genetic disorders and advancing the field of personalized medicine (75). Despite the progress, challenges persist in optimizing liposomal drug design, scalability, and cost-effectiveness. Future directions include refining formulations for specific patient populations, exploring combination therapies, and leveraging advancements in nanotechnology for improved targeting and controlled release. In conclusion, the clinical trials landscape for liposomal drugs is dynamic and multifaceted. From the dominance of liposomal oncology drugs to emerging applications in antivirals, vaccines, and gene therapies, the versatility of liposomal formulations is increasingly evident. Regulatory frameworks are adapting to accommodate the unique attributes of liposomal drugs, reflecting a collaborative effort to bring innovative and targeted therapeutics to the forefront of medical treatment.

7.2. Regulatory Considerations and Approval Processes: Navigating Regulatory Frameworks

The development and approval of liposomal drugs necessitate a comprehensive understanding and adherence to regulatory considerations. Navigating these frameworks is crucial for ensuring the safety, efficacy, and eventual market availability of liposomal therapeutic agents. Liposomal drugs present unique challenges for regulatory approval due to their complex formulations. The encapsulation of therapeutic agents within liposomes introduces novel

pharmacokinetic and pharmacodynamic considerations. Understanding and addressing these complexities are pivotal for regulatory success ⁽⁷⁶⁾. Over the years, regulatory bodies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), have evolved their approaches to accommodate the distinctive features of liposomal formulations. The approval of pioneering liposomal drugs like Doxil has contributed to refining regulatory pathways for subsequent liposomal candidates. Regulatory assessments emphasize Critical Quality Attributes (CQAs) in liposomal drug development. Parameters such as particle size, drug encapsulation efficiency, and stability play a pivotal role. The elucidation and control of CQAs are fundamental for ensuring reproducibility and consistency in liposomal drug manufacturing ⁽⁷⁷⁾. Non-clinical assessments play a crucial role in the regulatory evaluation of liposomal drugs. Toxicology studies are essential to delineate the safety profile and potential adverse effects. These studies aid in establishing the safety margins and informing subsequent clinical trial designs. Regulatory scrutiny extends to the design and endpoints of clinical trials. Rigorous clinical trial design, incorporating appropriate controls and endpoints, is imperative for generating robust data on the safety and efficacy of liposomal drugs. This information forms the basis for regulatory decision-making ⁽⁷⁸⁾. The regulatory journey extends beyond approval to post-marketing surveillance. Continued monitoring of liposomal drugs in real-world settings is essential for detecting rare adverse events and ensuring long-term safety. This iterative process contributes to ongoing risk-benefit assessments ⁽⁷⁹⁾. In conclusion, navigating regulatory frameworks is integral to the successful development and commercialization of liposomal drugs. Acknowledging the unique challenges of liposomal formulations, regulatory bodies have adapted their approaches, underscoring the importance of addressing critical quality attributes, conducting thorough non-clinical assessments, and implementing robust clinical trial designs.

8. Comparative Analysis with Other Drug Delivery Systems

8.1. Liposomal vs. Conventional Drug Delivery: Efficacy and Safety Comparisons

The juxtaposition of liposomal and conventional drug delivery systems is pivotal for discerning their impacts on efficacy and safety, shedding light on the advantages and limitations inherent in each approach. The encapsulation of therapeutic agents within liposomes provides a crucial advantage in terms of efficacy. This protective mechanism against premature degradation and clearance leads to prolonged circulation times, resulting in improved drug delivery to the target site. This enhanced stability is associated with superior therapeutic efficacy in comparison to conventional drug delivery methods ⁽⁸²⁾. The targeted release capability of liposomal drug delivery, facilitated by surface modifications, is a distinctive feature that minimizes exposure to healthy tissues. This targeted approach significantly reduces side effects compared to conventional drug delivery, where non-specific distribution may lead to off-target effects and increased toxicity ⁽⁸¹⁾. Liposomal drug delivery systems excel in providing controlled release kinetics, ensuring sustained and prolonged drug release. This controlled release aligns with optimal pharmacokinetics, maintaining a consistent therapeutic effect over an extended period. In contrast, conventional drug delivery systems may exhibit rapid release profiles, potentially impacting efficacy ⁽⁸²⁾. Liposomal formulations exhibit the capability to overcome biological barriers, including the blood-brain barrier (BBB). This property facilitates effective drug delivery to anatomically challenging locations, particularly significant in neuropharmacology. Studies have shown the efficacy of liposomes in delivering drugs to the central nervous system, enhancing therapeutic outcomes ⁽⁸³⁾. Despite the advantages, challenges persist in liposomal drug delivery, encompassing issues related to stability, scalability, and manufacturing complexity. Overcoming these challenges is imperative for the widespread adoption and commercial success of liposomal formulations, emphasizing the need for ongoing research and innovation ⁽⁸⁴⁾. Conventional drug delivery systems, such as oral tablets and intravenous injections, are associated with limitations like poor bioavailability, non-specific distribution, and rapid clearance. These limitations can impact therapeutic efficacy, necessitating higher doses and potentially leading to increased side effects ⁽⁸⁵⁾. In conclusion, the comparative analysis between liposomal and conventional drug delivery systems underscores the enhanced efficacy and targeted delivery advantages of liposomal formulations. While challenges exist in liposomal drug delivery, ongoing research aims to overcome these hurdles, positioning liposomes as promising candidates for the future of drug delivery.

8.2. Liposomal vs. Polymer-based Delivery: Addressing Key Differences

Comparing liposomal and polymer-based drug delivery systems is imperative for understanding the nuanced differences that influence their performance, safety, and therapeutic efficacy. Liposomes, lipid-based vesicles, and polymer-based delivery systems, composed of synthetic or natural polymers, exhibit distinctive structural differences. Liposomes encapsulate drugs within a lipid bilayer, while polymer-based systems can entrap drugs within the polymer matrix or conjugate them to the polymer backbone. One key differentiator lies in the control over release kinetics. Liposomes generally provide controlled and sustained release due to their lipid bilayer structure. In contrast, polymer-based systems offer tunable release profiles based on factors such as polymer composition and degradation rates ⁽⁸⁶⁾. The biodegradability of polymers introduces a notable distinction. Some polymers undergo gradual degradation,

influencing the clearance of the drug from the system. Liposomes, being lipid-based, may undergo metabolic processes but generally exhibit faster clearance compared to long-lasting polymers⁽⁸⁷⁾. Both liposomal and polymer-based systems offer targeted delivery possibilities. Liposomes can be surface-modified for targeted interactions, and polymers can be functionalized for specific binding. The choice between them depends on factors like target site and desired release kinetics⁽⁸⁸⁾. Stability considerations and manufacturing complexities differ significantly. Liposomes may face challenges related to stability during storage, while polymers can provide enhanced stability. However, polymer-based systems may involve more intricate manufacturing processes due to the synthesis of polymers with specific properties⁽⁸⁹⁾. The clinical translation of liposomal and polymer-based delivery systems is influenced by their regulatory status. Liposomal formulations have witnessed regulatory success, with several approved for clinical use. Polymer-based systems, while promising, may face more rigorous regulatory scrutiny due to variations in polymer types and potential toxicity concerns⁽⁹⁰⁾.

In conclusion, the comparison between liposomal and polymer-based drug delivery systems reveals nuanced differences in structural composition, release kinetics, biodegradability, and manufacturing complexity. Understanding these distinctions is crucial for selecting the most appropriate system based on specific therapeutic goals and regulatory considerations.

9. Future Perspectives and Trends in Liposomal Drug Delivery

9.1. A. Emerging Technologies: Pioneering Approaches on the Horizon

As the landscape of drug delivery continues to evolve, emerging technologies are paving the way for innovative approaches in liposomal drug delivery systems.

9.1.1. Nanostructured Lipid Carriers (NLCs)

One of the promising advancements is the integration of Nanostructured Lipid Carriers (NLCs). These lipid-based nanoparticles, characterized by a mix of solid and liquid lipids, offer improved drug loading capacity and enhanced stability compared to traditional liposomes⁽⁹¹⁾. The structural flexibility of NLCs addresses some challenges posed by conventional liposomes, contributing to improved drug delivery efficiency.

9.1.2. Hybrid Lipid-Polymer Systems

Hybrid lipid-polymer systems represent another frontier in liposomal drug delivery. By combining the advantages of both lipids and polymers, these systems aim to achieve enhanced stability, controlled release, and targeted delivery. This approach is particularly valuable in overcoming the limitations associated with each individual system, providing a synergistic platform for effective drug delivery⁽⁹²⁾.

9.1.3. Exosome-Mimetic Nanovesicles

Leveraging the natural communication mechanisms of cells, exosome-mimetic nanovesicles are gaining attention. These lipid-based vesicles mimic the characteristics of exosomes, facilitating targeted drug delivery and promoting cellular uptake⁽⁹³⁾.

9.1.4. Personalized Liposomal Therapies

The concept of personalized medicine is extending to liposomal drug delivery. Tailoring liposomal therapies to individual patient profiles, considering genetic variations and specific disease characteristics, holds immense potential. This approach aims to optimize treatment outcomes by aligning drug delivery systems with the unique biological makeup of each patient⁽⁹⁴⁾.

9.1.5. Remote-Triggered Liposomal Release

Innovations in remote-triggered drug release mechanisms are reshaping the field. Incorporating stimuli-responsive elements into liposomal structures allows for triggered release at specific sites or in response to external stimuli. This level of control over drug release offers opportunities for precise and on-demand therapeutic interventions⁽⁹⁵⁾.

9.1.6. Artificial Intelligence in Formulation Design

The integration of artificial intelligence (AI) in formulation design is revolutionizing the development of liposomal drug delivery systems. AI algorithms analyze vast datasets to optimize liposomal formulations, considering factors like drug

compatibility, release kinetics, and pharmacokinetics. This data-driven approach expedites the formulation design process and enhances the chances of successful outcomes ⁽⁹⁶⁾.

In conclusion, the future of liposomal drug delivery is marked by pioneering approaches that leverage cutting-edge technologies. Nanostructured lipid carriers, hybrid lipid-polymer systems, exosome-mimetic nanovesicles, personalized therapies, remote-triggered release mechanisms, and the integration of artificial intelligence collectively represent the horizon of innovation in liposomal drug delivery.

9.2. Potential New Applications: Exploring Uncharted Therapeutic Territories

The trajectory of liposomal drug delivery is poised to venture into unprecedented therapeutic territories, unlocking novel applications that could redefine the landscape of medical interventions. Addressing the intricate challenge of treating neurodegenerative diseases, liposomal drug delivery holds promise in overcoming the blood-brain barrier (BBB). The potential application of liposomes in delivering therapeutic agents to the brain opens avenues for innovative treatments against conditions like Alzheimer's and Parkinson's disease ⁽⁹⁷⁾. The realm of gene therapy and nucleic acid delivery is ripe for exploration with liposomal formulations. Liposomes provide an efficient means to encapsulate and transport genetic material, offering a protective environment for fragile nucleic acids. This application is particularly relevant in the context of advancing treatments for genetic disorders. In the realm of immunotherapy and vaccination, liposomal drug delivery emerges as a versatile platform. Liposomes can serve as carriers for antigens, optimizing their delivery to immune cells and potentially enhancing the effectiveness of vaccines. This holds significant promise for developing vaccines against infectious diseases and certain types of cancers ⁽⁹⁸⁾. Overcoming challenges in ocular drug delivery represents an intriguing application for liposomal formulations. The unique properties of liposomes can potentially enhance drug penetration, prolong release, and improve the treatment of ocular diseases such as macular degeneration and glaucoma ⁽⁹⁹⁾. Liposomal drug delivery may chart new territories in addressing cardiovascular diseases, offering targeted delivery of therapeutic agents to vascular sites affected by conditions like atherosclerosis or thrombosis. Liposomes could serve as carriers for anti-inflammatory or anti-thrombotic agents, providing innovative solutions in cardiovascular medicine. The escalating concern of antimicrobial resistance propels liposomal drug delivery into the spotlight for infectious diseases. Liposomes can encapsulate antimicrobial agents, safeguarding them from degradation and enhancing targeted delivery to infectious sites. This approach holds promise in combating resistant microbial strains ⁽¹⁰⁰⁾.

In conclusion, the evolving landscape of liposomal drug delivery opens doors to pioneering applications in neurodegenerative diseases, genetic therapies, immunotherapy, ocular drug delivery, cardiovascular interventions, and antimicrobial applications, showcasing the diverse potential of liposomes in reshaping therapeutic landscapes.

10. Conclusion

In navigating the expansive realm of liposomal drug delivery systems, our comprehensive review has unearthed several key findings that collectively underscore the significance and versatility of this innovative approach to drug administration. The structural anatomy of liposomes, defined by their lipid bilayer encapsulating therapeutic agents, provides a dynamic platform for drug delivery. The intricate interplay between liposomal types, their distinct characteristics, and encapsulation techniques unveils a rich tapestry of options in tailoring drug delivery systems to specific therapeutic needs. Exploring the advantages of liposomal drug delivery, our synthesis of insights illuminates the mechanisms behind enhanced bioavailability. Liposomes, by virtue of their lipid-based structure, contribute to improved drug solubility and stability, facilitating optimal therapeutic outcomes. A pivotal revelation from our review lies in the realm of targeted drug delivery. Surface modifications of liposomes, an area of growing significance, enable the precise delivery of therapeutic agents to specific cells or tissues, minimizing off-target effects. Examining experimental and clinical studies, our synthesis emphasizes the potential of liposomal drug delivery in reducing side effects. The evidence, drawn from diverse studies, underscores the importance of liposomal formulations in enhancing therapeutic efficacy while mitigating adverse effects. Addressing challenges in liposomal drug delivery, our review highlights strategies for overcoming instabilities and hurdles in manufacturing. The nuanced discussion sheds light on current practices and future innovations, illustrating the dynamic landscape of overcoming limitations. Our synthesis brings forth the diversification and personalization potential of liposomal drug delivery. From oncology to infectious diseases, the applications extend to gene therapy, immunotherapy, and even ocular drug delivery, marking a paradigm shift in the therapeutic landscape.

In conclusion, the amalgamation of insights from our review underscores the multifaceted nature of liposomal drug delivery. From its foundational principles and mechanisms to targeted applications, reduction of side effects, and strategies for overcoming challenges, the synthesis paints a holistic picture of the past, present, and future of this

dynamic field. As we navigate the complexities and opportunities within liposomal drug delivery, our comprehensive understanding serves as a guiding compass for future advancements and innovations in pharmaceutical sciences.

As we conclude this comprehensive review on liposomal drug delivery systems, the implications for the future of pharmacy emerge as transformative, heralding a paradigm shift in how drugs are administered and therapeutic outcomes are optimized. One of the most profound implications is the advent of tailored and personalized medicine. Liposomal drug delivery allows for the customization of treatments, catering to individual patient needs. This transformative approach aligns with the broader shift towards precision medicine, where therapies are precisely calibrated for maximum efficacy with minimal side effects. Chronic diseases, often requiring prolonged and carefully managed treatment regimens, stand to benefit significantly from liposomal drug delivery. The sustained release and targeted delivery mechanisms offer a new frontier in managing conditions like diabetes, cardiovascular diseases, and autoimmune disorders, potentially improving patient adherence and overall health outcomes. The integration of liposomal drug delivery with nanotechnology opens avenues for groundbreaking therapeutic approaches. The multifunctional nature of nanocarriers allows for simultaneous drug delivery, imaging, and diagnostics, paving the way for theranostic applications. This convergence has the potential to redefine how diseases are diagnosed and treated, marking a revolutionary phase in pharmaceutical sciences. The implications for cancer therapeutics are particularly promising. Liposomal formulations, with their ability to enhance drug accumulation in tumor tissues and reduce systemic toxicity, contribute to the ongoing advancements in oncology. Future cancer treatments may increasingly rely on liposomal drug delivery to improve the effectiveness of chemotherapy while minimizing detrimental side effects. The development of smart liposomes, capable of responding to specific stimuli for triggered drug release, holds great promise. This innovation not only enhances the precision of drug delivery but also minimizes unnecessary exposure, reducing the risk of adverse effects. The advent of responsive liposomes is poised to revolutionize the field, especially in conditions where controlled drug release is paramount. The widespread adoption of liposomal drug delivery systems necessitates a reevaluation of regulatory frameworks. As these technologies become integral to healthcare, regulatory bodies must adapt to ensure the safety and efficacy of these novel approaches. Moreover, the ethical dimensions surrounding personalized medicine and the potential for unequal access to advanced treatments demand careful consideration as we navigate the future landscape of drug delivery.

In conclusion, the future of pharmacy is intricately interwoven with the trajectory of liposomal drug delivery. The implications are far-reaching, ranging from personalized medicine and chronic disease management to nanotechnological integrations, advancements in cancer therapeutics, the advent of smart liposomes, and the imperative for robust regulatory frameworks. As we stand at the threshold of this pharmaceutical evolution, the potential to reshape the landscape of drug delivery and patient care is both exciting and transformative.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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