https://doi.org/10.48047/AFJBS.6.Si3.2024.2971-2987

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

AI-Driven Engineering of Liposomes for Targeted Drug Delivery of Marine Bioactive Peptides

Archana Sharma[1], Khushboo Gupta[2], Lakshmi[3], Raghav Dixit[4], MeenakshiTyagi[5], Alisha khurana[6], Sakshi Garg[7*]

[1]KIET Group of institutions Ghaziabad
[2]Associate professor, IIMT college of Pharmacy, Greater Noida
[3]Guru RamdasKhalsa Institute of Science and Technology (Pharmacy), Barela, Kukrikheda, Jabalpur, Madhya Pradesh, Pin Code: 483001
[4]Assistant Professor, Department of Pharmaceutical Sciences, GurukulaKangri (Deemed to be University), Haridwar, Uttarakhand, 249404.
[5]Associate Professor, Quantum University Roorkee-247667, India
[6]Gandhi college of pharmacy, bypass karnal
[7*]KIET School of Pharmacy, KIET Group of Institutions, Ghaziabad
Corresponding author: Sakshi Garg, KIET School of Pharmacy, KIET Group of Institutions, Ghaziabad

Article Info

Volume6, Issue Si3,July2024
Received: 14 May2024
Accepted:21 June 2024
Published:10 July2024
DOI:
10.48047/AFJBS.6.Si3.2024.2971-2987

ABSTRACT:

The integration of artificial intelligence (AI) into liposome engineering represents a groundbreaking advancement in the field of targeted drug delivery, particularly for marine bioactive peptides. Liposomes, as versatile drug carriers, offer numerous benefits, including enhanced bioavailability, reduced toxicity, and the ability to encapsulate both hydrophilic and hydrophobic drugs. Marine bioactive peptides, with their unique therapeutic properties, hold significant potential in pharmaceutical applications. However, the challenge lies in optimizing liposome formulations for efficient and targeted delivery of these peptides. AI-driven approaches address this challenge by leveraging advanced machine learning algorithms to analyze vast datasets, predict liposome behavior, and optimize formulations. In this review, we explore the synergy between AI and liposome technology, focusing on the methods and types of liposome preparation, such as thin-film hydration and ethanol injection, and their functionalization for targeted delivery through strategies like PEGylation and ligand attachment. We discuss the application of AI models, including neural networks and decision trees, in predicting liposome stability, optimizing formulation parameters, and designing experiments. Additionally, we highlight the current pharmacological applications of marine bioactive peptides and present case studies demonstrating their successful integration into AI-optimized liposome systems. Despite the significant advancements, challenges remain in data availability, model scalability, and reproducibility. Future directions emphasize the need for continuous improvement in AI techniques, integration with multi-omics data, and the development of smart liposomes capable of stimuli-responsive drug release. Ethical and regulatory considerations are also addressed to ensure safe and equitable application of these technologies. AI-driven liposome engineering offers a promising pathway to enhance the delivery and efficacy of marine bioactive peptides, paving the way for innovative therapeutics in personalized medicine. Further research and interdisciplinary collaboration will be crucial in overcoming current limitations and realizing the full potential of this transformative approach.

Keywords: Artificial Intelligence, Liposome Engineering, Targeted Drug Delivery, Marine Bioactive Peptides, Machine Learning, Liposome Functionalization

1. Introduction

Targeted drug delivery represents a significant advancement in the field of medicine, aiming to direct therapeutic agents specifically to the site of disease, thereby minimizing systemic side effects and enhancing drug efficacy[1]. Traditional drug delivery methods often suffer from a lack of specificity, leading to the distribution of drugs throughout the body, which can cause adverse effects and reduce therapeutic efficiency[2]. Targeted drug delivery systems employ various strategies to localize the drug action to diseased cells or tissues, using carriers that can navigate biological barriers and release their payload at the intended site[3]. Techniques such as ligand-receptor interactions, magnetic targeting, and stimulus-responsive release mechanisms have been explored to achieve this specificity. This approach is particularly beneficial in treating diseases like cancer, where targeted delivery can significantly improve therapeutic outcomes by concentrating the drug in tumor tissues while sparing healthy cells[4].

Importance of Marine Bioactive Peptides in Pharmaceuticals

Marine bioactive peptides have garnered attention in recent years due to their diverse biological activities and potential therapeutic benefits. Derived from marine organisms such as fish, algae, and invertebrates, these peptides exhibit a wide range of pharmacological properties, including anti-inflammatory, antimicrobial, anticancer, and antioxidant activities[5]. The unique environmental conditions of marine habitats have driven the evolution of these organisms, resulting in the production of bioactive compounds with novel structures and mechanisms of action[6]. This makes marine bioactive peptides valuable candidates for drug development. Their potential applications in pharmaceuticals include the treatment of chronic diseases, infections, and as functional ingredients in nutraceuticals. The exploration of marine biodiversity and advancements in peptide isolation and synthesis techniques continue to uncover new peptides with promising therapeutic potential[7].

Liposomes as Drug Carriers

Structure and Benefits of Liposomes in Drug Delivery

Liposomes are spherical vesicles composed of one or more phospholipid bilayers, which can encapsulate both hydrophilic and hydrophobic drugs, making them versatile drug carriers. Their structure mimics biological membranes, allowing for biocompatibility and the potential for targeted delivery[8]. The core of a liposome can contain hydrophilic drugs, while hydrophobic drugs can be integrated into the lipid bilayer. This unique structure provides several benefits in drug delivery[9]. Firstly, liposomes can improve the solubility and stability of drugs, protecting them from degradation before reaching the target site. Secondly, they can enhance the bioavailability of drugs, allowing for lower dosages and reduced side effects. Thirdly, liposomes can be engineered to release their payload in response to specific stimuli, such as pH or temperature changes, ensuring controlled and site-specific drug release[10].

Challenges in Engineering Liposomes for Targeted Delivery

Despite their advantages, engineering liposomes for targeted drug delivery presents several challenges. One major challenge is achieving the stability of liposomes in the bloodstream, as they can be rapidly cleared by the mononuclear phagocyte system (MPS)[11]. To address this, liposomes are often coated with polyethylene glycol (PEG), a process known as PEGylation, which helps evade immune detection and prolongs circulation time. Another challenge is ensuring efficient targeting and uptake by diseased cells[12]. This can be accomplished by functionalizing the liposome surface with targeting ligands, such as antibodies, peptides, or small molecules, which can specifically bind to receptors on the target cells. However, this requires careful selection and optimization of the targeting moieties to achieve high specificity and affinity. Additionally, large-scale production and

reproducibility of liposome formulations can be complex, necessitating advanced manufacturing techniques and stringent quality control measures[13].

Role of AI in Drug Delivery Systems

Artificial intelligence (AI) has revolutionized various fields, including biotechnology, by providing powerful tools for data analysis, predictive modeling, and process optimization. In biotechnology, AI applications range from drug discovery and development to personalized medicine and diagnostics[14]. Machine learning algorithms, a subset of AI, can analyze vast datasets to identify patterns and make predictions, which are invaluable in understanding complex biological systems and optimizing biotechnological processes[15]. For example, AI can accelerate drug discovery by predicting the biological activity of compounds, optimizing drug formulations, and identifying potential side effects. In personalized medicine, AI can analyze patient data to tailor treatments based on individual genetic profiles, improving therapeutic outcomes. The integration of AI in biotechnology promises to enhance the efficiency and precision of research and development efforts, driving innovations in healthcare[16].

Table 1: Summary of Liposomal Products Approved by FDA and EMA

Product Name	Active Pharmaceutical Ingredient (API)	Approved Year/Area	Dosage Form	Administration Route	Indication	References
Doxil/Caelyx	Doxorubicin	1995/FDA, 1996/EMA	Liposomal Injection	Intravenous	Ovarian cancer, multiple myeloma, Kaposi's sarcoma	[7]
AmBisome	Amphotericin B	1997/FDA, 1990/EMA	Liposomal Injection	Intravenous	Fungal infections, leishmaniasis	[8]
DepoCyt	Cytarabine	1999/FDA, 2001/EMA	Liposomal Injection	Intrathecal	Lymphomatous meningitis	[9]
Marqibo	Vincristine sulfate	2012/FDA	Liposomal Injection	Intravenous	Acute lymphoblastic leukemia (ALL)	[10]
Onivyde	Irinotecan	2015/FDA, 2016/EMA	Liposomal Injection	Intravenous	Metastatic pancreatic cancer	[11]
Vyxeos	Daunorubicin and cytarabine	2017/FDA, 2018/EMA	Liposomal Injection	Intravenous	Acute myeloid leukemia (AML)	[12]
Visudyne	Verteporfin	2000/FDA,	Liposomal	Intravenous	Age-related macular	[13]

		2000/EMA	Injection		degeneration	

Potential of AI in Optimizing Liposome-Based Delivery Systems

The potential of AI in optimizing liposome-based delivery systems lies in its ability to handle complex data and uncover relationships that may not be evident through traditional methods. AI can assist in various stages of liposome engineering, from formulation design to in vivo performance prediction[14]. For instance, machine learning models can analyze the physicochemical properties of lipids and other formulation components to predict the stability and encapsulation efficiency of liposomes[4]. AI can also optimize the functionalization of liposomes by predicting the best combination of targeting ligands and their spatial arrangement on the liposome surface to achieve maximum binding affinity and specificity. Additionally, AI-driven simulations can model the behavior of liposomes in biological environments, predicting their distribution, cellular uptake, and drug release kinetics[2]. By integrating experimental data with AI models, researchers can streamline the development process, reduce experimental costs, and accelerate the translation of liposome-based delivery systems from the lab to clinical applications[15].

2. Marine Bioactive Peptides

1. Sources and Characteristics

Definition and Examples of Marine Bioactive Peptides

Marine bioactive peptides are short sequences of amino acids derived from marine organisms, such as fish, algae, mollusks, and crustaceans[3]. These peptides are produced through the hydrolysis of proteins found in marine species, either by enzymatic action, fermentation, or chemical processes. Due to the diverse and extreme conditions of marine environments, marine organisms have evolved to produce peptides with unique structures and functions that are not typically found in terrestrial organisms[16]. Examples of marine bioactive peptides include those derived from fish collagen, such as collagen peptides, which have been shown to possess antioxidant and anti-inflammatory properties. Another example is the peptide conotoxin from cone snails, which has potent analgesic effects. Seaweed-derived peptides like those from Spirulina are known for their immunomodulatory and antihypertensive properties[17].

Unique Properties and Therapeutic Potential

Marine bioactive peptides exhibit a range of unique properties that contribute to their therapeutic potential. One of the key features is their structural diversity, which allows them to interact with various biological targets and modulate multiple physiological processes[12]. These peptides often have high bioavailability and can be absorbed efficiently in the human body, making them effective as therapeutic agents. They also tend to be more resistant to enzymatic degradation compared to their terrestrial counterparts, which enhances their stability and activity in biological systems[18].The therapeutic potential of marine bioactive peptides is vast, encompassing various pharmacological activities. They have shown promise as antioxidants, capable of neutralizing free radicals and protecting cells from oxidative stress, which is implicated in aging and numerous chronic diseases[16]. Their anti-inflammatory properties make them potential candidates for treating inflammatory conditions such as arthritis and inflammatory bowel disease[7,9]. Additionally, many marine peptides possess antimicrobial activities, providing a natural alternative to traditional antibiotics in combating bacterial, fungal, and viral infections. Their anticancer properties are also noteworthy, with several peptides demonstrating the ability to inhibit tumor growth and induce apoptosis in cancer cells. Furthermore, marine peptides have been explored for their cardiovascular benefits, such as lowering blood pressure and improving lipid metabolism[19].

2. Pharmacological Applications

Current Uses in Medicine and Therapeutics

Marine bioactive peptides are increasingly being incorporated into various therapeutic and medical applications due to their potent bioactivities. In the field of dermatology, peptides derived from marine collagen are widely used in cosmetic and skincare products for their anti-aging and skin-rejuvenating effects[4,9]. These peptides enhance skin elasticity, hydration, and repair by stimulating collagen synthesis and reducing the appearance of wrinkles. Marine peptides are also used in nutraceuticals and functional foods, where they contribute to improved health outcomes. For instance, fish-derived peptides are included in supplements aimed at promoting joint health and reducing the symptoms of osteoarthritis[20].In the pharmaceutical industry, marine peptides are being investigated and developed as therapeutic agents for a range of conditions[12]. Antimicrobial peptides from marine sources are being explored as new antibiotics to address the growing problem of antibiotic resistance. Their unique mechanisms of action and ability to target resistant strains of bacteria make them promising candidates for new antimicrobial therapies[17]. Marine peptides with antihypertensive properties are being developed to manage high blood pressure, leveraging their ability to inhibit angiotensin-converting enzyme (ACE) and regulate blood vessel function. Additionally, some marine peptides are in clinical trials for their anticancer properties, offering new avenues for cancer treatment through mechanisms such as apoptosis induction and inhibition of angiogenesis[21].

3. Liposome Technology

1. Liposome Formation and Types

Methods of Liposome Preparation (e.g., Thin-Film Hydration, Ethanol Injection)

Liposome formation involves creating spherical vesicles composed of one or more phospholipid bilayers that can encapsulate drugs. Several methods are used to prepare liposomes, each with its advantages and limitations[5]. One of the most common methods is thin-film hydration. This method involves dissolving lipids in an organic solvent, which is then evaporated to form a thin lipid film on the surface of a round-bottom flask[2]. The film is subsequently hydrated with an aqueous solution, leading to the spontaneous formation of multilamellar vesicles (MLVs). These vesicles can be further processed by techniques such as sonication or extrusion to produce smaller, unilamellarvesicles[22].Another widely used method is ethanol injection. In this process, lipids dissolved in ethanol are injected into an aqueous solution through a fine needle. The ethanol rapidly diffuses into the water, causing the lipids to self-assemble into liposomes. This method is relatively simple and allows for good control over liposome size, but it can be challenging to remove residual ethanol, which may affect the stability and safety of the liposomes[23].Other methods include the reverse-phase evaporation technique, which involves creating a water-in-oil emulsion followed by the removal of the organic phase under reduced pressure to form liposomes, and the detergent removal method, where detergents are used to solubilize lipids and are then removed to allow liposome formation[10]. Each preparation method can impact the size, lamellarity, and encapsulation efficiency of the liposomes, which are critical factors for their application in drug delivery[24].

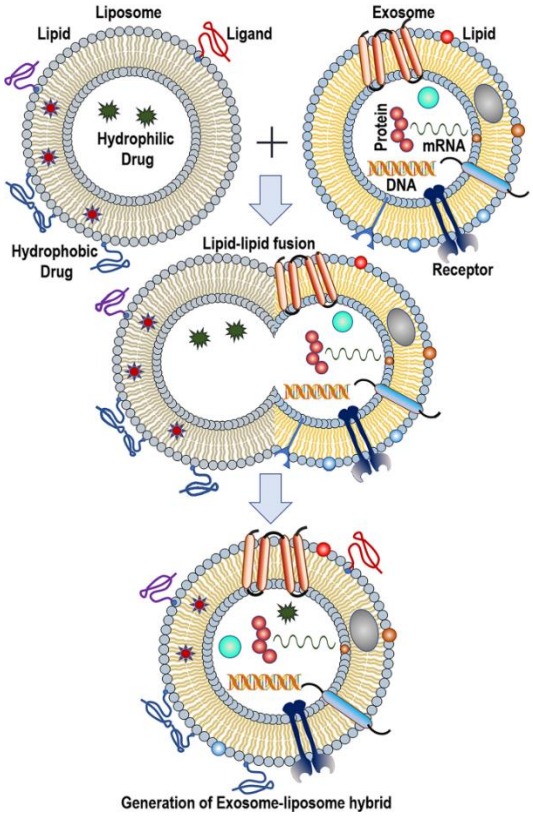

Figure 1: generation of exosome liposome hybrid

Types of Liposomes (e.g., Conventional, Stealth, Targeted)

Liposomes can be categorized into different types based on their composition and surface characteristics, each designed to meet specific therapeutic needs. Conventional liposomes are the simplest form, composed solely of phospholipids and cholesterol[1]. They are biocompatible and can encapsulate both hydrophilic and hydrophobic drugs. However, conventional liposomes are quickly recognized and cleared by the immune system, limiting their circulation time in the bloodstream[25].Stealth liposomes, also known as PEGylated liposomes, are modified to evade the immune system and prolong their circulation time[18]. This is achieved by attaching polyethylene glycol (PEG) chains to the liposome surface, creating a hydrophilic shield that prevents recognition by the mononuclear phagocyte system (MPS). Stealth liposomes can remain in the bloodstream for extended periods, increasing the likelihood of reaching the target site and improving therapeutic efficacy[26].Targeted liposomes are designed to deliver drugs specifically to diseased cells or tissues. This targeting is achieved by attaching ligands, such as antibodies, peptides, or small molecules, to the liposome surface. These ligands can bind to specific receptors overexpressed on the target cells, facilitating receptor-mediated endocytosis and enhancing drug delivery to the desired site. This specificity reduces off-target effects and improves the therapeutic index of the encapsulated drug[27].

2. Functionalization for Targeted Delivery

Strategies for Surface Modification (e.g., PEGylation, Ligand Attachment)

Functionalizing the surface of liposomes is crucial for improving their stability, circulation time, and targeting capabilities[17]. PEGylation involves attaching polyethylene glycol (PEG) chains to the liposome surface, which creates a hydrophilic barrier that reduces protein adsorption and recognition by the immune system. This modification extends the liposomes' half-life in circulation and enhances their stability, making them more effective for drug delivery[28].

Ligand attachment is another key strategy for functionalization, enabling targeted delivery of liposomes to specific cells or tissues[28]. Ligands such as antibodies, peptides, or small molecules are conjugated to the liposome surface to recognize and bind to receptors overexpressed on target cells. For example, antibodies against cancer cell markers can be attached to liposomes to direct them specifically to tumor cells, facilitating targeted therapy. This approach increases the concentration of the drug at the target site, enhancing efficacy while minimizing systemic side effects[29].

Enhancing Stability and Circulation Time

Enhancing the stability and circulation time of liposomes is essential for effective drug delivery. Stability can be compromised by various factors such as aggregation, fusion, or degradation in biological environments. PEGylation is a widely used method to enhance stability by preventing aggregation and fusion, thereby maintaining the integrity of the liposomes in circulation[30].In addition to PEGylation, incorporating cholesterol into the liposome bilayer can improve membrane stability and reduce permeability, preventing premature drug release[27]. The choice of phospholipids with higher transition temperatures also enhances liposome stability, particularly at body temperature.Another strategy involves using cross-linking agents to stabilize the liposome structure, providing additional resistance to destabilizing forces in the bloodstream[15]. Formulating liposomes with cryoprotectants during lyophilization can also improve stability by preventing damage during storage and rehydration.Prolonging circulation time can be achieved by minimizing recognition and clearance by the immune system. Besides PEGylation, other stealth coatings and surface modifications can be used to evade the immune response. Designing liposomes with optimal size and surface charge can also reduce opsonization and uptake by the MPS[31].

4. AI in Liposome Engineering

1. Machine Learning Models

Types of AI Models Used in Liposome Research (e.g., Neural Networks, Decision Trees)

In the realm of liposome engineering, machine learning (ML) models have become indispensable tools for predicting outcomes, optimizing formulations, and understanding complex biological interactions. Several types of AI models are utilized in this field, each offering unique strengths[28].Neural networks are among the most powerful and versatile AI models used in liposome research. These models are particularly effective for capturing non-linear relationships between variables, which is essential given the complexity of liposome behavior and their interactions with biological systems[11]. Convolutional neural networks (CNNs) and recurrent neural networks (RNNs) are specific types of neural networks that can process structured and time-series data, respectively. Neural networks can predict how changes in liposome composition and preparation methods impact their stability, encapsulation efficiency, and drug release profiles[32].Decision trees are another popular type of ML model used in liposome research. These models are easy to interpret and can handle both categorical and continuous data[19]. Decision trees work by recursively splitting the dataset based on the value of input features, leading to a tree-like model of decisions. This approach is particularly useful for identifying key factors that influence liposome characteristics, such as lipid composition, hydration techniques, and surface modifications[2,6]. Random forests, an ensemble method combining multiple decision trees, further enhance predictive accuracy and robustness[33].Other ML models, such as support vector machines (SVMs) and k-nearest neighbors (k-NN), are also employed in liposome research. SVMs are effective for classification tasks and can identify optimal conditions for liposome formulation. k-NN, on the other hand, is useful for regression tasks, predicting continuous outcomes based on the similarity of input data points[34].

Training Datasets and Feature Selection

The performance of ML models heavily relies on the quality and quantity of training datasets. In liposome research, training datasets are compiled from experimental data, literature, and high-throughput screening results[18]. These datasets typically include information on lipid types, preparation methods, physicochemical properties, encapsulated drugs, and biological performance metrics. A comprehensive and diverse dataset ensures that the model can generalize well to new, unseen data.Feature selection is a critical step in building effective ML models[12,8]. It involves identifying the most relevant variables (features) that influence the target outcome. In liposome engineering, features may include lipid composition, particle size, zeta potential, encapsulation efficiency, and drug release kinetics. Selecting the right features reduces model complexity, enhances predictive performance, and provides insights into the underlying mechanisms governing liposome behavior[2].Various feature selection techniques, such as correlation analysis, principal component analysis (PCA), and recursive feature elimination (RFE), are employed to identify the most informative features. These techniques help eliminate redundant or irrelevant features, ensuring that the ML model focuses on the most significant variables[35].

2. Applications of AI

Predicting Liposome Behavior and Stability

AI models are instrumental in predicting the behavior and stability of liposomes under various conditions[12]. By analyzing historical data and identifying patterns, these models can forecast how liposomes will interact with biological environments, how stable they will be over time, and how they will release their encapsulated drugs. For instance, neural networks can predict the degradation rates of liposomes in different pH environments, while decision trees can identify the critical factors that influence liposome stability during storage[36].Predictive models help researchers design more robust liposomes by anticipating potential issues and adjusting formulations accordingly. This leads to more efficient and cost-effective development processes, reducing the need for extensive trial-and-error experiments[10].

Optimizing Liposome Formulation and Functionalization

AI plays a crucial role in optimizing liposome formulations to achieve desired properties and performance[4]. Machine learning algorithms can analyze vast amounts of data to identify optimal combinations of lipids, solvents, and preparation methods that maximize encapsulation efficiency, stability, and targeted delivery capabilities. For example, optimization algorithms like genetic algorithms and Bayesian optimization can explore the formulation space to find the best set of parameters that meet specific criteria[22,12].Functionalization, such as the attachment of targeting ligands or surface modifications, can also be optimized using AI. By modeling the interactions between liposomes and target cells or tissues, AI can suggest the most effective ligands and surface modifications to enhance targeting specificity and drug delivery efficiency. This accelerates the development of tailored liposome-based therapies for specific diseases[37].

Designing Experiments and Analyzing Complex Datasets

AI assists in designing experiments by suggesting the most informative experiments to conduct next, based on previous results and model predictions. This approach, known as active learning, helps researchers prioritize experiments that will yield the most valuable data, thereby accelerating the research process and reducing resource consumption[14].Moreover, AI excels in analyzing complex datasets generated from high-throughput screening, omics technologies, and clinical studies[19]. Machine learning algorithms can uncover hidden patterns, correlations, and causal relationships within these datasets, providing new insights into the factors that influence liposome performance. For instance, clustering algorithms can

group liposome formulations with similar properties, while regression models can quantify the impact of individual features on liposome efficacy[38].

5. Integration of AI and Liposome Technology

1. Design and Optimization Process

Workflow from Data Collection to Model Deployment

The integration of AI into liposome technology follows a systematic workflow that begins with data collection and culminates in model deployment. This process is iterative and involves several key stages:

1. **Data Collection**: The foundation of any AI-driven approach is robust and comprehensive data. In liposome engineering, data is collected from various sources, including experimental results, literature, and high-throughput screening[2]. This data encompasses information on liposome composition, preparation methods, physicochemical properties, encapsulation efficiency, drug release profiles, and biological performance metrics. Ensuring data quality and diversity is critical for developing reliable AI models[39].
2. **Data Preprocessing**: Once collected, the data undergoes preprocessing to remove noise, handle missing values, and normalize the variables[10]. This step may involve data cleaning, transformation, and standardization. Feature extraction and selection are also part of this stage, where relevant features that significantly influence the liposome characteristics are identified[22].
3. **Model Selection and Training**: Based on the nature of the data and the specific objectives, appropriate machine learning models are selected[3,9]. Common models used in liposome research include neural networks, decision trees, support vector machines, and ensemble methods like random forests. These models are then trained on the preprocessed data, learning the relationships and patterns that dictate liposome behavior and performance[40].
4. **Model Validation and Testing**: After training, the models are validated using a separate dataset that was not involved in the training process[4,8]. This step ensures that the models generalize well to new data and do not overfit the training data. Metrics such as accuracy, precision, recall, and mean squared error are used to evaluate model performance. Cross-validation techniques are often employed to enhance reliability[30].
5. **Model Optimization**: Hyperparameter tuning and optimization are conducted to refine the model and enhance its predictive accuracy. Techniques such as grid search, random search, and Bayesian optimization can be employed to find the best hyperparametersettings[12].
6. **Model Deployment**: Once validated and optimized, the AI models are deployed for practical use in liposome engineering[20]. This involves integrating the models into existing workflows and systems where they can be used to make predictions, optimize formulations, and guide experimental designs. Deployment also includes creating user-friendly interfaces and ensuring the models are scalable and maintainable[41].
7. **Continuous Monitoring and Updating**: Post-deployment, the models are continuously monitored to ensure they maintain their performance over time. New data is periodically incorporated to update and retrain the models, ensuring they remain accurate and relevant[19].

Examples of AI-Driven Optimization in Liposome Engineering

Several case studies demonstrate the successful application of AI-driven optimization in liposome engineering:

1. **Optimization of Liposome Composition**: Researchers have utilized machine learning models to optimize the composition of liposomes for enhanced drug encapsulation and stability[26]. For instance, neural networks have been employed to predict the optimal lipid-to-drug ratio and the type of lipids that maximize encapsulation efficiency and minimize leakage. By analyzing historical formulation data, the models can suggest new compositions that are likely to perform better, reducing the need for extensive trial-and-error experimentation[42].
2. **Surface Functionalization for Targeted Delivery**: AI models have been used to optimize the functionalization of liposome surfaces with targeting ligands[4]. For example, decision trees and genetic algorithms have been applied to identify the best combination of ligands and their densities on the liposome surface that result in maximum binding affinity and specificity to target cells. This approach has been particularly useful in designing liposomes for targeted cancer therapy, where precise delivery to tumor cells is crucial[43].
3. **Predicting Drug Release Profiles**: AI has been instrumental in predicting the drug release kinetics from liposomes under various physiological conditions[33]. Machine learning algorithms can analyze data from in vitro release studies to forecast how different formulations will behave in vivo. This predictive capability allows researchers to design liposomes that release their payload in a controlled manner, matching the desired therapeutic profile[22].
4. **Scaling Up Production**: AI-driven models have also been applied to optimize the scale-up of liposome production processes. By analyzing data from pilot-scale and commercial-scale production runs, machine learning models can predict the impact of scale-up on liposome characteristics and identify the critical parameters that need to be controlled to ensure consistent product quality[44].
5. **Personalized Medicine**: In the realm of personalized medicine, AI has been used to tailor liposome formulations to individual patient profiles. By integrating patient-specific data, such as genetic information and disease biomarkers, machine learning models can recommend customized liposome formulations that are likely to be most effective for a particular patient, enhancing therapeutic outcomes and minimizing adverse effects[45].

6. Challenges and Future Perspectives

Limitations of Current AI Models and Data Availability

While AI has significantly advanced the field of liposome engineering, there are notable limitations and challenges[29]. One major challenge is the quality and availability of data. AI models require large, high-quality datasets for training to achieve accurate and reliable predictions. However, in the realm of liposome engineering, data can be scarce, fragmented, and inconsistent. Experimental data from different studies may vary in quality and methodology, making it difficult to compile comprehensive datasets. Additionally, proprietary data from pharmaceutical companies are often not publicly available, limiting the scope of AI model training[46,47].Another limitation lies in the current AI models themselves. Despite their capabilities, models like neural networks and decision trees can suffer from overfitting, where they perform well on training data but poorly on unseen data[32]. This issue arises when models become too complex and capture noise rather than underlying patterns. Furthermore, many AI models operate as "black boxes," offering limited interpretability. Understanding why a model makes certain predictions is crucial for gaining insights and ensuring trust in its recommendations, especially in a sensitive field like drug delivery[48,34].

Issues in Scalability and Reproducibility

Scalability and reproducibility are critical issues when integrating AI with liposome technology. Scalability refers to the ability to apply AI models effectively across different scales of liposome production and various types of formulations[16]. While AI can optimize small-scale laboratory experiments, translating these optimizations to large-scale industrial production can be challenging[12]. The parameters that work well at a small scale may not directly apply to larger scales due to differences in equipment, environmental conditions, and processing times. Ensuring that AI-driven optimizations are scalable requires extensive validation and adjustment, which can be resource-intensive[49].Reproducibility is another significant concern. Scientific research and industrial applications rely on the ability to reproduce results consistently. Variability in liposome preparation methods, raw materials, and environmental factors can lead to inconsistent outcomes[33]. AI models must account for this variability and provide robust solutions that are reproducible across different settings and batches. However, achieving this level of robustness is challenging due to the inherent complexity and variability in biological systems and experimental conditions[50].

Future Directions

Advances in AI and Machine Learning Techniques

The future of AI in liposome engineering will likely see significant advances in AI and machine learning techniques. Emerging approaches such as transfer learning and few-shot learning can address data scarcity by leveraging knowledge from related fields or requiring fewer data points to train models effectively[22]. Explainable AI (XAI) is another promising area, aiming to make AI models more interpretable and transparent. By understanding how models arrive at their predictions, researchers can gain deeper insights and trust the outcomes more confidently[51].Integration of AI with multi-omics data (genomics, proteomics, metabolomics) can also enhance liposome engineering by providing a comprehensive view of biological systems[16]. This integration can lead to more accurate models for predicting drug delivery and therapeutic efficacy. Additionally, advances in AI hardware, such as quantum computing, could significantly accelerate the processing and analysis of complex datasets, opening new avenues for research and optimization[52].

Potential Breakthroughs in Liposome Technology and Marine Bioactive Peptide Delivery

Future breakthroughs in liposome technology and the delivery of marine bioactive peptides will likely focus on enhancing specificity, efficacy, and safety. Smart liposomes, capable of responding to specific stimuli (e.g., pH, temperature, enzymes), can provide controlled and targeted drug release. AI can play a crucial role in designing these smart systems by predicting optimal stimuli-response mechanisms and ensuring precise control over drug release profiles[53].The combination of liposomes with marine bioactive peptides holds immense potential for creating novel therapeutics with enhanced bioactivity and reduced side effects. Advances in peptide synthesis and modification, guided by AI models, can lead to the development of peptides with improved stability, bioavailability, and therapeutic efficacy[3]. AI can also help in identifying new bioactive peptides from marine organisms by analyzing large-scale genomic and proteomic data, thus expanding the repertoire of available therapeutic agents[54].

Ethical and Regulatory Considerations

As AI becomes more integrated into liposome engineering and drug delivery, ethical and regulatory considerations will become increasingly important. Ensuring data privacy and security is paramount, especially when dealing with patient-specific data and proprietary research data. Researchers and developers must adhere to stringent data protection regulations and ethical guidelines to safeguard sensitive information[55,56].Regulatory approval for AI-driven drug delivery systems poses another challenge. Regulatory agencies

require rigorous validation and evidence of safety and efficacy before approving new therapeutics[57,58]. AI models used in the development process must be transparent, interpretable, and validated through extensive testing to meet regulatory standards. Collaborating with regulatory bodies early in the development process can help streamline approval and ensure compliance with regulatory requirements[59].Furthermore, there is a need for ethical considerations regarding the use of AI in healthcare. Ensuring that AI-driven technologies are accessible and equitable is crucial to prevent disparities in healthcare delivery. Ethical frameworks must be established to guide the responsible use of AI, balancing innovation with patient safety and public trust[60].While the integration of AI in liposome engineering presents challenges, ongoing advances in AI techniques, liposome technology, and ethical practices promise a future where AI-driven solutions enhance the efficacy and safety of drug delivery systems. By addressing current limitations and embracing future opportunities, researchers can develop innovative therapeutics that significantly improve patient outcomes[61,62].

7. Conclusion

The integration of AI into the engineering of liposomes for targeted drug delivery of marine bioactive peptides represents a significant advancement in biotechnology. AI-driven liposome engineering leverages sophisticated machine learning models to enhance the design, optimization, and functionality of liposomes, making them more efficient and effective in delivering therapeutic agents. By utilizing vast datasets and advanced computational techniques, AI can predict liposome behavior, optimize formulations, and personalize drug delivery systems. This approach not only improves the precision and efficacy of treatments but also accelerates the development process, reducing the need for extensive experimental trials.The potential of AI-driven liposome engineering extends beyond mere optimization. It offers a transformative impact on targeted drug delivery systems, enabling the development of smart liposomes that respond to specific stimuli, ensuring controlled and precise release of therapeutic agents. The ability to functionalize liposomes for targeted delivery enhances their specificity, reducing off-target effects and improving patient outcomes. Moreover, the integration of marine bioactive peptides, known for their unique properties and therapeutic potential, further expands the scope of applications, offering new avenues for treating a wide range of diseases.The synergy between AI and biotechnology is a driving force behind the rapid advancements in liposome engineering. AI's capability to analyze complex datasets, identify patterns, and predict outcomes complements the experimental rigor of biotechnology, leading to innovations that were previously unattainable. This collaboration is paving the way for the development of highly sophisticated and effective drug delivery systems that can be tailored to individual patient needs, marking a significant step towards personalized medicine.Encouragement for further research and development in this field is paramount. While the progress made so far is commendable, there remains a vast potential for discovery and innovation. Continuous advancements in AI algorithms, coupled with improvements in liposome technology and marine bioactive peptide synthesis, will likely yield even more effective and versatile drug delivery systems. Researchers are encouraged to explore new methodologies, embrace interdisciplinary collaborations, and strive for innovations that push the boundaries of what is currently possible.

Conflict of interest

None

8. References

1. D. Kalyane, N. Raval, R. Maheshwari, V. Tambe, K. Kalia, and R. K. Tekade, "Employment of enhanced permeability and retention effect (EPR): Nanoparticle-based precision tools for targeting of therapeutic and diagnostic agent in cancer," *Mater. Sci. Eng. C Mater. Biol Appl.*, vol. 98, pp. 1252–1276, 2019. doi: 10.1016/j.msec.2019.01.066.
2. F. Danhier, A. L. Breton, and V. Preat, "RGD-based strategies to target alphav beta3 integrin in cancer therapy and diagnosis," *Mol. Pharm.*, vol. 9, pp. 2961–2973, 2012. doi: 10.1021/mp3002733.
3. T. Kang, X. Gao, Q. Hu, D. Jiang, X. Feng, X. Zhang, Q. Song, L. Yao, M. Huang, X. Jiang, et al., "iNGR-modified PEG-PLGA nanoparticles that recognize tumor vasculature and penetrate gliomas," *Biomaterials.*, vol. 35, pp. 4319–4332, 2014. doi: 10.1016/j.biomaterials.2014.01.082.
4. H. Liang, F. Zou, Q. Liu, B. Wang, L. Fu, X. Liang, J. Liu, and Q. Liu, "Nanocrystal-loaded liposome for targeted delivery of poorly water-soluble antitumor drugs with high drug loading and stability towards efficient cancer therapy," *Int. J. Pharm.*, vol. 599, p. 120418, 2021. doi: 10.1016/j.ijpharm.2021.120418.
5. Q. Chen, M. Gao, Z. Li, Y. Xiao, X. Bai, K. O. Boakye-Yiadom, X. Xu, and X.-Q. Zhang, "Biodegradable nanoparticles decorated with different carbohydrates for efficient macrophage-targeted gene therapy," *J. Control. Release.*, vol. 323, pp. 179–190, 2020. doi: 10.1016/j.jconrel.2020.03.044.
6. B. S. Pattni, V. V. Chupin, and V. P. Torchilin, "New Developments in Liposomal Drug Delivery," *Chem. Rev.*, vol. 115, pp. 10938–10966, 2015. doi: 10.1021/acs.chemrev.5b00046.
7. T. Kim, J. Kim, and S. Kim, "Extended-release formulation of morphine for subcutaneous administration," *Cancer Chemother. Pharmacol.*, vol. 33, pp. 187–190, 1993. doi: 10.1007/BF00686214.
8. Y. Fan, M. Marioli, and K. Zhang, "Analytical characterization of liposomes and other lipid nanoparticles for drug delivery," *J. Pharm. Biomed. Anal.*, vol. 192, p. 113642, 2021. doi: 10.1016/j.jpba.2020.113642.
9. N. Wang, M. Chen, and T. Wang, "Liposomes used as a vaccine adjuvant-delivery system: From basics to clinical immunization," *J. Control. Release.*, vol. 303, pp. 130–150, 2019. doi: 10.1016/j.jconrel.2019.04.025.
10. S. Beiranvand, A. Eatemadi, and A. Karimi, "New Updates Pertaining to Drug Delivery of Local Anesthetics in Particular Bupivacaine Using Lipid Nanoparticles," *Nanoscale Res. Lett.*, vol. 11, p. 307, 2016. doi: 10.1186/s11671-016-1520-8.
11. M. Richter, E. Waterfield, A. K. Jain, A. J. Canaan, B. A. Allison, and J. G. Levy, "Liposomal delivery of a photosensitizer, benzoporphyrin derivative monoacid ring A (BPD), to tumor tissue in a mouse tumor model," *Photochem. Photobiol.*, vol. 57, pp. 1000–1006, 1993. doi: 10.1111/j.1751-1097.1993.tb02962.x.
12. R. Alving, Z. Beck, G. R. Matyas, and M. Rao, "Liposomal adjuvants for human vaccines," *Expert Opin. Drug Deliv.*, vol. 13, pp. 807–816, 2016. doi: 10.1517/17425247.2016.1151871.
13. Z. Li, W. Perkins, and D. Cipolla, "Robustness of aerosol delivery of amikacin liposome inhalation suspension using the eFlow® Technology," *Eur. J. Pharm. Biopharm.*, vol. 166, pp. 10–18, 2021. doi: 10.1016/j.ejpb.2021.05.021.
14. "Myocet," *European Medicines Agency*. Available: https://www.ema.europa.eu/en/medicines/human/EPAR/myocet-liposomal-previously-myocet. Accessed: Jun. 1, 2021.

15. R. D. Signorell, P. Luciani, D. Brambilla, and J. C. Leroux, "Pharmacokinetics of lipid-drug conjugates loaded into liposomes," *Eur. J. Pharm. Biopharm.*, vol. 128, pp. 188–199, 2018. doi: 10.1016/j.ejpb.2018.04.003.
16. Dharmendra Bhati *et al.*, "FUSED AND SUBSTITUTED PYRIMIDINE DERIVATIVES AS POTENT ANTICANCER AGENTS," *Biochemical and Cellular Archives/Biochemical and cellular archives*, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.749.
17. K. J. Mangala *et al.*, "NANOCELLULOSE: A VERSATILE AND SUSTAINABLE CARRIER FOR DRUG AND BIOACTIVE COMPOUNDS," *Biochemical and Cellular Archives/Biochemical and cellular archives*, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.553.
18. Rohit Kumar Trivedi *et al.*, "REVOLUTIONIZING DRUG DELIVERY THROUGH 3D PRINTING TECHNOLOGY: CURRENT ADVANCES AND FUTURE DIRECTIONS," *Biochemical and Cellular Archives/Biochemical and cellular archives*, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.521.
19. H. Rastogi, P. Bhatt, S. Garg, S. Kamboj, V. Deva, and R. Goel, "EXPLORING THE POTENTIAL OF QUANTUM DOTS AS LUMINOUS PROBES FOR TARGETED DRUG DELIVERY AND BIOIMAGING IN CLINICAL DIAGNOSTICS," *Biochemical and Cellular Archives/Biochemical and cellular archives*, vol. 24, no. 1, Jan. 2024, doi: https://doi.org/10.51470/bca.2024.24.1.457.
20. M. shama, "CRISPR-Cas9 gene editing in pharmaceuticals : Current applications and future prospects," *Biochemical and Cellular Archives/Biochemical and cellular archives*, vol. 23, no. S1, Dec. 2023, doi: https://doi.org/10.51470/bca.2023.23.s1.1655.
21. S. Arora, Saiphali, G. Dharmamoorthy Dharmendra Bhati, T. Gupta, and P. Bhatt, "Advancements in peptide-based therapeutics: Design, synthesis and clinical applications," *Biochemical and Cellular Archives/Biochemical and cellular archives*, vol. 23, no. S1, Dec. 2023, doi: https://doi.org/10.51470/bca.2023.23.s1.1415.
22. M. Singhal et al., "Formulation development and characterization of powder for oral suspension containing H2 blocker drug to combat GERD and peptic ulcer," NeuroQuantology, vol. 20, no. 11, pp. 1258, 2022.
23. S. Ahamed, P. Bhatt, S. J. Sultanuddin, R. Walia, M. A. Haque, and S. B. InayathAhamed, "An Intelligent IoT enabled Health Care Surveillance using Machine Learning," in 2022 International Conference on Advances in Computing, Communication and Applied Informatics (ACCAI). IEEE, 2022.
24. V. Ahmed, S. Sharma, and P. Bhatt, "Formulation and evaluation of sustained release tablet of diltiazem hydrochloride," International Journal of Pharmaceutical Sciences and Research, vol. 11, no. 5, pp. 2193–2198, 2020.
25. A. E. Al-Snafi, S. Singh, P. Bhatt, and V. Kumar, "A review on prescription and non-prescription appetite suppressants and evidence-based method to treat overweight and obesity," GSC biol pharm sci, vol. 19, no. 3, pp. 148–155, 2022.
26. B. Baskar, S. Ramakrishna, and A. Daniela La Rosa, Eds., Encyclopedia of green materials. Singapore: Springer Nature Singapore, 2022.
27. P. Bhatt et al., "Nanorobots recent and future advances in cancer or dentistry therapy- A review," Am J PharmTech Res, vol. 9, no. 3, pp. 321–331, 2019.
28. P. Bhatt et al., "Citrus Flavonoids: Recent Advances and Future Perspectives On Preventing Cardiovascular Diseases," in The Flavonoids, 2024, pp. 131-152.
29. P. Bhatt et al., "Functional and tableting properties of alkali-isolated and phosphorylated barnyard millet (Echinochloaesculenta) starch," ACS Omega, vol. 8, no. 33, pp. 30294–305, 2023.

30. P. Bhatt et al., "Plasma modification techniques for natural polymer-based drug delivery systems," Pharmaceutics, vol. 15, no. 8, p. 2066, 2023.
31. P. Bhatt et al., "Comparative study and in vitro evaluation of sustained release marketed formulation of aceclofenac sustained release tablets," Pharma Science Monitor, vol. 9, no. 2, 2018.
32. P. Bhatt et al., "Development and characterization of fast dissolving buccal strip of frovatriptan succinate monohydrate for buccal delivery," Int J Pharm Investig, vol. 11, no. 1, pp. 69–75, 2021.
33. P. Bhatt et al., "Artificial intelligence in pharmaceutical industry: Revolutionizing drug development and delivery," The Chinese Journal of Artificial Intelligence, 2023.
34. P. Bhatt et al., "Blockchain technology applications for improving quality of electronic healthcare system," in Blockchain for Healthcare Systems, 2021, pp. 97–113.
35. P. Bhatt, "Mouth Dissolving Tablets Challenges, Preparation Strategies with a Special Emphasis on Losartan Potassium–A Review," World J. Pharm. Pharm. Sci, vol. 7, no. 9, pp. 271-287, 2018.
36. C. Goyal et al., "Estimation of shelf-life of Balachaturbhadrika syrup containing different sweetening agents," Res J Pharm Technol, pp. 5078–5083, 2022.
37. T. Kaur and S. Singh, "Controlled release of bi-layered malvidin tablets using 3D printing techniques," J Pharm Res Int, pp. 70–78, 2021.
38. M. Kaurav et al., "In-depth analysis of the chemical composition, pharmacological effects, pharmacokinetics, and patent history of mangiferin," Phytomed Plus, vol. 3, no. 2, p. 100445, 2023.
39. A. Kumar, P. Bhatt, and N. Mishra, "Irritable bowel Syndrome with reference of Alosetron Hydrochloride and Excipient profile used in the manufacturing of Alosetron tablet-A review," J Chem Pharm Sci, vol. 12, no. 03, pp. 71–78, 2019.
40. M. K. Malik et al., "Significance of chemically derivatized starch as drug carrier in developing novel drug delivery devices," Nat Prod J, 2022.
41. M. K. Malik et al., "Preclinical safety assessment of chemically cross-linked modified mandua starch: Acute and sub-acute oral toxicity studies in Swiss albino mice," ACS Omega, vol. 7, no. 40, pp. 35506–35514, 2022.
42. M. K. Malik et al., "Phosphorylation of alkali extracted mandua starch by STPP/STMP for improving digestion resistibility," ACS Omega, vol. 8, no. 13, pp. 11750–11767, 2023.
43. Pankaj, "Anti-cancer cyclodextrinnanocapsules based formulation development for lung chemotherapy," J Pharm Res Int, pp. 54–63, 2021.
44. Pankaj, "Cyclodextrin modified block polymer for oral chemotherapy," J Pharm Res Int, pp. 21–29, 2021.
45. V. Raghuwanshi et al., "Recent Advances In Nanotechnology For Combating Against Corona Virus Infection," Journal of Pharmaceutical Negative Results, pp. 1811-1820, 2022.
46. K. K. Sahu et al., "Utility of nanomaterials in wound management," in Nanotechnological Aspects for Next-Generation Wound Management, 2024, pp. 101–130.
47. S. K. Sharma et al., "Combined therapy with ivermectin and doxycycline can effectively alleviate the cytokine storm of COVID-19 infection amid vaccination drive: A narrative review," J Infect Public Health, vol. 15, no. 5, pp. 566–572, 2022.
48. S. K. Sharma and P. Bhatt, "Controlled release of bi-layered EGCG tablets using 3D printing techniques," J Pharm Res Int, pp. 5–13, 2021.
49. S. K. Sharma and S. Singh, "Antimicrobial Herbal Soap Formulation," Journal of Pharmaceutical Research International, vol. 32, no. 36, pp. 82-88, 2022.

50. S. Singh et al., "Cardiovascular comorbidity of COVID-19 disease: A review," WJPMR, vol. 8, no. 4, pp. 216–225, 2022.
51. S. Singh et al., "Phytonutrients, Anthocyanidins, and Anthocyanins: Dietary and Medicinal Pigments with Possible Health Benefits," in Advances in Flavonoids for Human Health and Prevention of Diseases, 2024, pp. 23-46.
52. S. Singh et al., "Digital Transformation in Healthcare: Innovation and Technologies," in Blockchain for Healthcare Systems, 2021, pp. 61–79.
53. S. Singh et al., "Alginate based Nanoparticles and Its Application in Drug Delivery Systems," Journal of Pharmaceutical Negative Results, pp. 1463-1469, 2022.
54. R. Johari et al., "Artificial Intelligence and Machine Learning in Drug Discovery and Development," in 2023 12th International Conference on System Modeling& Advancement in Research Trends (SMART), 2023, pp. 556-561.
55. P. Bhatt et al., “Impact of Cross-Linking on the Physicochemical and Physiological Characteristics of Barnyard Millet (Echinochloafrumentacea) Grains Starch,” Stärke/Starch, May 2024, doi: https://doi.org/10.1002/star.202300285.
56. V. Kumar et al., “Ultrasound assisted techniques for starch modification to develop novel drug delivery systems: A comprehensive study,” Journal of bioactive and compatible polymers, May 2024, doi: https://doi.org/10.1177/08839115241249143.
57. Y. Barenholz, "Doxil®—The first FDA-approved nano-drug: Lessons learned," *J. Control. Release.*, vol. 160, pp. 117–134, 2012. doi: 10.1016/j.jconrel.2012.03.020.
58. M. Dicko, S. Kwak, A. A. Frazier, L. D. Mayer, and B. D. Liboiron, "Biophysical characterization of a liposomal formulation of cytarabine and daunorubicin," *Int. J. Pharm.*, vol. 391, pp. 248–259, 2010. doi: 10.1016/j.ijpharm.2010.02.014.
59. Q. Ye, J. Asherman, M. Stevenson, E. Brownson, and N. V. Katre, "DepoFoam™ technology: A vehicle for controlled delivery of protein and peptide drugs," *J. Control. Release.*, vol. 64, pp. 155–166, 2000. doi: 10.1016/S0168-3659(99)00146-7.
60. D. E. Large, R. G. Abdelmessih, E. Fink, and D. T. Auguste, "Liposome composition in drug delivery design, synthesis, characterization, and clinical application," *Adv. Drug Delivery Rev.*, vol. 176, p. 113851, 2021. doi: 10.1016/j.addr.2021.113851.
61. D. Guimarães, A. Cavaco-Paulo, and E. Nogueira, "Design of liposomes as drug delivery system for therapeutic applications," *Int. J. Pharm.*, vol. 601, p. 120571, 2021. doi: 10.1016/j.ijpharm.2021.120571.
62. Y. He, L. Qin, Y. Huang, and C. Ma, "Advances of Nano-Structured Extended-Release Local Anesthetics," *Nanoscale Res. Lett.*, vol. 15, p. 13, 2020. doi: 10.1186/s11671-019-3241-2.