**Supporting Information**

**How can ChatGPT benefit pharmacy: a case report on review writing**

Yun Zhu a,1, Dan Han a,1, Shaoqing Chen c,1, Feng Zeng d, Cheng Wang b,\*

a Department of Pharmacy, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, China

b School of Pharmacy, Changzhou University, Changzhou 213164 Jiangsu, China

c Second People's Hospital of Changzhou, Nanjing Medical University, Changzhou, Jiangsu, China

d State Key Laboratory of Materials-Oriented Chemical Engineering, College of Chemical Engineering, Nanjing Tech University, Nanjing 211816, Jiangsu, China

1 These authors have contributed equally to this work.

\* Corresponding author: C. Wang: wangc90@cczu.edu.cn

**History of conversation**

**Author:**

**Please provide a** **concise outline for a scientific mini review article relating to the topic "lipid-based drug delivery systems"**

**ChatGPT:**

Sure, here's a possible outline for a scientific mini review article on lipid-based drug delivery systems:

I. Introduction

Brief overview of the importance of drug delivery systems in medicine

Explanation of why lipid-based drug delivery systems are a promising option

Purpose of the review article

II. Types of lipid-based drug delivery systems

Liposomes

Solid lipid nanoparticles (SLNs)

Nanostructured lipid carriers (NLCs)

Lipid-based microemulsions

Comparison of the different types of systems in terms of drug loading, stability, and release

III. Advantages and limitations of lipid-based drug delivery systems

Advantages, such as biocompatibility, biodegradability, and ability to encapsulate both hydrophilic and hydrophobic drugs

Limitations, such as potential toxicity, difficulty in large-scale production, and susceptibility to degradation

IV. Applications of lipid-based drug delivery systems

Cancer therapy

Treatment of neurological disorders

Delivery of vaccines

Other potential uses

V. Future directions and challenges

Emerging technologies and techniques for improving lipid-based drug delivery systems

Challenges that need to be addressed, such as regulatory hurdles and the need for more clinical studies

VI. Conclusion

Recap of the potential of lipid-based drug delivery systems in medicine

Suggestions for future research and development

Note: This is just one possible outline for a mini review article on this topic. The specific details and sections may vary depending on the author's focus and the scope of the article.

**Author:**

**Please** **write a corresponding scientific Review article based on the above outline with detailed examples**

**ChatGPT:**

Sure! Here's a sample scientific review article based on the outline provided, with examples and details included.

Title: Lipid-Based Drug Delivery Systems: Current Status and Future Directions

I. Introduction

Drug delivery systems play a crucial role in medicine, as they can improve drug efficacy and safety. Among various drug delivery systems, lipid-based drug delivery systems have emerged as a promising option due to their biocompatibility, biodegradability, and ability to encapsulate both hydrophilic and hydrophobic drugs. In this review, we provide an overview of the current status of lipid-based drug delivery systems and discuss the challenges and future directions of this field.

II. Types of lipid-based drug delivery systems

A. Liposomes

Liposomes are spherical structures composed of a phospholipid bilayer that encapsulates drugs. Liposomes can vary in size, charge, and lipid composition, which affect their drug-loading capacity, stability, and release properties. For example, Doxil® is a liposomal formulation of the anti-cancer drug doxorubicin that has been approved by the FDA for the treatment of ovarian and breast cancers.

B. Solid lipid nanoparticles (SLNs)

SLNs are submicron-sized particles composed of a solid lipid core that encapsulates drugs. SLNs have several advantages over liposomes, such as better stability and scalability. However, their drug-loading capacity can be limited by the low solubility of some drugs in lipids. One example of a SLN-based drug delivery system is Visudyne®, which is used to treat age-related macular degeneration.

C. Nanostructured lipid carriers (NLCs)

NLCs are similar to SLNs but have a mixture of solid and liquid lipids in their core, which allows for higher drug loading and better stability. NLCs also have a larger surface area, which can improve drug release. One example of an NLC-based drug delivery system is Emend®, which is used to prevent chemotherapy-induced nausea and vomiting.

D. Lipid-based microemulsions

Lipid-based microemulsions are thermodynamically stable liquid mixtures of oil, water, and surfactant that can encapsulate drugs. They have several advantages, such as easy production and high drug-loading capacity. However, their stability can be affected by changes in temperature or pH. One example of a lipid-based microemulsion is Sandimmune®, which is used to prevent organ rejection after transplantation.

III. Advantages and limitations of lipid-based drug delivery systems

A. Advantages

Lipid-based drug delivery systems have several advantages over other drug delivery systems. They can improve drug solubility, stability, and bioavailability. They can also protect drugs from degradation, enhance their targeting to specific cells or tissues, and reduce their toxicity. For example, liposomal formulations of the anti-cancer drug paclitaxel have been shown to have lower toxicity and better efficacy than the free drug.

B. Limitations

However, lipid-based drug delivery systems also have some limitations. They can be affected by changes in temperature, pH, or ionic strength. They can also be prone to oxidation or hydrolysis, which can affect their stability. In addition, the production of lipid-based drug delivery systems can be complex and costly. Moreover, their toxicity and immunogenicity need to be carefully evaluated. For example, the liposomal formulation of the anti-fungal drug amphotericin B, although effective, can cause severe infusion-related reactions.

IV. Applications of lipid-based drug delivery systems

Lipid-based drug delivery systems have found various applications in medicine, including:

A. Cancer therapy

Liposomal formulations of several anti-cancer drugs, such as doxorubicin, paclitax

**Author:**

**Please provide scientific information on "Brief overview of the importance of drug delivery systems in medicine" with detailed examples**

**ChatGPT:**

Drug delivery systems (DDS) are crucial for the effective treatment of a wide range of diseases, as they can enhance drug efficacy and safety, reduce toxicity, and improve patient compliance. In traditional drug therapy, drugs are administered systemically, which can result in low drug concentrations at the site of action, as well as off-target effects and toxicity. DDS can address these issues by controlling the rate, duration, and site of drug release, and by targeting specific cells or tissues.

DDS can be classified into several categories based on their composition, structure, and mechanism of action. Some of the most common DDS are nanoparticulate systems, such as liposomes, polymeric nanoparticles, and dendrimers, which can encapsulate drugs and protect them from degradation and elimination. Other DDS include hydrogels, implants, and transdermal patches, which can provide sustained drug release or localized drug delivery.

One example of the importance of DDS in medicine is the treatment of cancer. Anti-cancer drugs can have severe side effects, as they can affect both cancerous and healthy cells. Liposomal formulations of several anti-cancer drugs, such as doxorubicin, have been developed to reduce toxicity and improve efficacy. These formulations can selectively accumulate in tumor tissue, as tumors have leaky vasculature and impaired lymphatic drainage. Moreover, liposomes can shield drugs from the immune system, as well as release drugs in a sustained and controlled manner.

Another example is the treatment of neurological disorders, such as Alzheimer's disease. The blood-brain barrier (BBB) is a highly selective barrier that prevents most drugs from entering the brain. DDS that can bypass the BBB or enhance drug transport across it are needed to treat these disorders. Lipid-based nanoparticles, such as SLNs and NLCs, have shown promise in delivering drugs to the brain. For example, a SLN-based delivery system has been developed for the anti-Alzheimer's drug memantine, which can improve drug efficacy and reduce side effects.

DDS can also be used for the delivery of vaccines. Traditional vaccines can elicit immune responses, but they may require multiple doses and adjuvants to achieve optimal efficacy. DDS can enhance the stability, immunogenicity, and delivery of vaccines, as well as enable targeted and sustained antigen release. For example, liposomes have been used to deliver vaccines against infectious diseases, such as hepatitis B, influenza, and malaria.

In summary, DDS are essential for the effective treatment of various diseases, as they can overcome the limitations of traditional drug therapy and improve patient outcomes. Ongoing research and development of novel DDS are needed to address the challenges and opportunities in this field.

**Author:**

**Please provide scientific information on "Explanation of why lipid-based drug delivery systems are a promising option" with detailed examples**

**ChatGPT:**

Lipid-based drug delivery systems (LBDDS) are a promising option for drug delivery due to their versatility, biocompatibility, and ability to enhance drug solubility, bioavailability, and stability. LBDDS include a variety of lipid-based formulations, such as liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and lipid-drug conjugates. In this response, I will provide some scientific information on why LBDDS are a promising option, as well as detailed examples of their applications.

Enhanced drug solubility and bioavailability: Many drugs have poor water solubility and low oral bioavailability, which can limit their therapeutic efficacy. LBDDS can increase drug solubility by encapsulating drugs in lipid vesicles or nanoparticles, which can also protect them from degradation and metabolism. Additionally, LBDDS can improve drug absorption and bioavailability by increasing their residence time in the gastrointestinal tract, promoting their uptake by enterocytes, and bypassing efflux transporters. For example, a liposomal formulation of the anti-fungal drug amphotericin B (AmBisome) has been developed, which has higher efficacy and lower toxicity than the free drug.

Controlled drug release: LBDDS can control the rate and duration of drug release, which can improve drug efficacy, reduce side effects, and enhance patient compliance. This can be achieved by modifying the lipid composition, size, surface charge, and encapsulation efficiency of LBDDS, as well as by incorporating stimuli-responsive moieties. For example, a SLN-based formulation of the anti-inflammatory drug curcumin has been developed, which can sustain drug release over 48 hours and reduce inflammation in a rat model of arthritis.

Targeted drug delivery: LBDDS can enable targeted drug delivery to specific cells, tissues, or organs, which can increase drug concentration at the site of action and minimize off-target effects. This can be achieved by modifying the surface of LBDDS with targeting ligands, such as antibodies, peptides, or carbohydrates, that can bind to specific receptors or antigens. For example, a liposomal formulation of the anti-cancer drug irinotecan (Onivyde) has been developed, which can target cancer cells that overexpress the folate receptor.

Imaging and diagnosis: LBDDS can also be used for imaging and diagnosis, as they can encapsulate imaging agents or contrast agents and enhance their accumulation at specific sites. For example, a liposomal formulation of the MRI contrast agent gadolinium (Gd-DO3A-BSA) has been developed, which can target the lymphatic system and improve lymph node imaging.

In summary, LBDDS are a promising option for drug delivery due to their ability to enhance drug solubility, bioavailability, stability, controlled release, targeted delivery, and imaging capabilities. LBDDS have been applied to various therapeutic areas, such as cancer, inflammation, infectious diseases, and neurological disorders, and have shown significant benefits in terms of efficacy, safety, and patient outcomes. Ongoing research and development of LBDDS are expected to expand the range of drug candidates that can be delivered by this approach and improve their clinical translation.

**Author:**

**Please give the purpose of the review article related to "lipid-based drug delivery systems" based on the outline you give above**

**ChatGPT:**

The purpose of the review article related to "lipid-based drug delivery systems" based on the outline I provided above is to provide a concise overview of the current state-of-the-art in lipid-based drug delivery systems, highlighting their importance in medicine, the underlying principles of their design and development, and their potential applications in drug delivery. The review article aims to provide a comprehensive understanding of the advantages and limitations of different types of lipid-based drug delivery systems, including liposomes, solid lipid nanoparticles, nanostructured lipid carriers, and lipid-drug conjugates. The review article will also present detailed examples of the applications of lipid-based drug delivery systems, including their use in enhancing drug solubility, bioavailability, stability, controlled release, targeted delivery, and imaging capabilities. The review article aims to provide an up-to-date and concise resource for researchers, students, and clinicians interested in the field of lipid-based drug delivery systems.

**Author:**

**Please provide scientific information on "Types of lipid-based drug delivery systems" based on the outline you give above with detailed examples**

**ChatGPT:**

There are several types of lipid-based drug delivery systems (LBDDS), each with unique properties and applications. In this response, I will provide scientific information on the different types of LBDDS, as well as detailed examples of their characteristics and uses.

Liposomes: Liposomes are spherical vesicles composed of one or more lipid bilayers that can encapsulate hydrophilic or hydrophobic drugs. Liposomes can vary in size, charge, and composition, which can affect their stability, drug loading capacity, and targeting ability. Liposomes are biocompatible, biodegradable, and can protect drugs from degradation and clearance. Liposomes can be used for both systemic and local drug delivery, as well as for imaging and diagnosis. For example, Doxil is a liposomal formulation of the anti-cancer drug doxorubicin, which has shown higher efficacy and lower toxicity than the free drug.

Solid lipid nanoparticles (SLNs): SLNs are small particles composed of solid lipids that can encapsulate lipophilic drugs. SLNs can improve drug stability, bioavailability, and controlled release. SLNs are biocompatible, biodegradable, and can penetrate biological barriers. SLNs can be used for both topical and systemic drug delivery. For example, Meglumine antimoniate SLNs have been developed for the treatment of visceral leishmaniasis, which can improve drug efficacy and reduce side effects.

Nanostructured lipid carriers (NLCs): NLCs are small particles composed of both solid and liquid lipids that can encapsulate both hydrophilic and lipophilic drugs. NLCs can improve drug loading capacity, stability, and controlled release. NLCs can also enhance drug penetration and targeting. NLCs can be used for both topical and systemic drug delivery. For example, Ciclopirox olamine NLCs have been developed for the treatment of onychomycosis, which can improve drug penetration and efficacy.

Lipid-drug conjugates: Lipid-drug conjugates are covalent complexes of lipids and drugs that can improve drug solubility, stability, and targeting. Lipid-drug conjugates can enhance drug absorption and bioavailability, as well as reduce toxicity and side effects. Lipid-drug conjugates can be used for both systemic and local drug delivery. For example, PEGylated lipid-doxorubicin conjugates have been developed for the treatment of breast cancer, which can improve drug efficacy and reduce cardiotoxicity.

In summary, there are several types of lipid-based drug delivery systems that can improve drug solubility, bioavailability, stability, controlled release, targeted delivery, and imaging capabilities. The choice of LBDDS depends on the physicochemical properties of the drug, the intended route of administration, and the therapeutic indication. Ongoing research and development of LBDDS are expected to expand the range of drug candidates that can be delivered by this approach and improve their clinical translation.

**Author:**

**Please provide scientific information on "Advantages and limitations of lipid-based drug delivery systems" based on the outline you give with detailed examples**

**ChatGPT:**

Lipid-based drug delivery systems (LBDDS) have several advantages over traditional drug delivery methods, but they also have some limitations. In this response, I will provide scientific information on the advantages and limitations of LBDDS, as well as detailed examples of each.

Advantages of LBDDS:

Improved solubility and bioavailability: Many drugs have low solubility in water, which can limit their bioavailability and efficacy. LBDDS can improve drug solubility and bioavailability by encapsulating hydrophobic drugs in lipophilic carriers, which can enhance their absorption and distribution in the body.

Controlled release: LBDDS can provide controlled release of drugs, which can improve their therapeutic effectiveness, reduce toxicity, and enhance patient compliance. LBDDS can be designed to release drugs in a sustained manner over a specific period of time, or in response to certain stimuli such as changes in pH, temperature, or enzymes.

Targeted delivery: LBDDS can be designed to target specific tissues or cells, which can enhance drug efficacy and reduce systemic toxicity. Targeted delivery can be achieved through several mechanisms, such as surface modification with ligands that can bind to receptors on the target cells, or exploiting the unique physiological properties of the target tissues, such as the leaky vasculature of tumors.

Reduced toxicity: LBDDS can reduce the toxicity of drugs by limiting their exposure to healthy tissues and cells. By encapsulating drugs in lipophilic carriers, LBDDS can improve drug pharmacokinetics and biodistribution, which can reduce systemic toxicity and improve drug safety.

Limitations of LBDDS:

Complexity and variability: LBDDS are complex and variable systems that can be affected by several factors, such as drug properties, carrier composition, preparation method, and storage conditions. This complexity and variability can pose challenges for the reproducibility, scalability, and regulatory approval of LBDDS.

Stability and shelf-life: LBDDS can be sensitive to changes in temperature, pH, and other environmental factors, which can affect their stability and shelf-life. LBDDS can also be prone to drug leakage, aggregation, and degradation, which can compromise their efficacy and safety.

Cost and accessibility: LBDDS can be more expensive and less accessible than traditional drug delivery methods, due to the specialized equipment, expertise, and materials required for their development and manufacturing.

Examples:

An example of the advantage of LBDDS is the liposomal formulation of the anti-cancer drug doxorubicin, known as Doxil or Caelyx. Doxil is designed to encapsulate doxorubicin in a liposomal carrier, which improves its solubility and bioavailability, as well as its pharmacokinetics and biodistribution. Doxil has been shown to be more effective and less toxic than the free drug, and is approved for the treatment of several types of cancer.

An example of the limitation of LBDDS is the variability and complexity of liposomes. Liposomes can be composed of different lipids, with different sizes, charges, and surface modifications, which can affect their stability, drug loading capacity, and targeting ability. The variability and complexity of liposomes can pose challenges for the reproducibility and regulatory approval of liposomal formulations, and require careful characterization and quality control.

In summary, LBDDS have several advantages over traditional drug delivery methods, such as improved solubility and bioavailability, controlled release, targeted delivery, and reduced toxicity. However, LBDDS also have some limitations, such as complexity and variability, stability and shelf-life, and cost and accessibility. These advantages and limitations should be carefully considered when selecting and developing LBDDS for specific therapeutic applications.

**Author:**

**Please provide scientific information on "Applications of lipid-based drug delivery systems" based on the outline you give with detailed examples**

**ChatGPT:**

Lipid-based drug delivery systems (LBDDS) have a wide range of applications in medicine due to their ability to improve drug solubility, bioavailability, and targeting, as well as reduce toxicity and increase patient compliance. In this response, I will provide scientific information on the applications of LBDDS, along with detailed examples.

Applications of LBDDS:

Cancer therapy: LBDDS have been extensively studied as a delivery system for anti-cancer drugs, due to their ability to selectively target tumor cells, improve drug efficacy, and reduce systemic toxicity. Liposomal formulations of drugs such as doxorubicin (Doxil/Caelyx) and paclitaxel (Abraxane) have been approved for the treatment of several types of cancer, and other LBDDS are being developed for targeted delivery of chemotherapy agents and other cancer therapies.

Gene therapy: LBDDS can also be used for the delivery of genetic material, such as DNA and RNA, for gene therapy applications. Lipid-based carriers can protect the genetic material from degradation and enhance its cellular uptake, which can improve the efficiency and specificity of gene therapy. Examples of LBDDS used for gene delivery include lipoplexes, liposomes, and lipid nanoparticles.

Vaccines: LBDDS have shown promise as delivery systems for vaccines, due to their ability to enhance the immune response and induce long-lasting immunity. Lipid-based carriers can encapsulate antigens and adjuvants, which can stimulate the immune system and enhance the efficacy of vaccines. Lipid-based adjuvants such as MF59 and AS03 have been approved for use in influenza vaccines, and other LBDDS are being developed for the delivery of vaccines against infectious diseases and cancer.

Drug delivery to the brain: LBDDS can also be used for drug delivery to the brain, which is challenging due to the blood-brain barrier (BBB) that limits the penetration of drugs into the brain. Lipid-based carriers can be designed to cross the BBB and deliver drugs to the brain, which can improve the treatment of neurological disorders such as Alzheimer's disease, Parkinson's disease, and brain tumors. Examples of LBDDS used for brain drug delivery include liposomes, solid lipid nanoparticles, and nanostructured lipid carriers.

Dermatological applications: LBDDS can also be used for dermatological applications, such as the delivery of drugs for the treatment of skin diseases and the enhancement of skin permeation. Lipid-based carriers can improve the solubility and penetration of drugs in the skin, which can enhance their efficacy and reduce systemic toxicity. Examples of LBDDS used for dermatological applications include liposomes, ethosomes, and transfersomes.

Examples:

An example of the application of LBDDS in cancer therapy is the liposomal formulation of paclitaxel, known as Abraxane. Abraxane is designed to encapsulate paclitaxel in a liposomal carrier, which improves its solubility and bioavailability, as well as its pharmacokinetics and biodistribution. Abraxane has been shown to be more effective and less toxic than the free drug, and is approved for the treatment of several types of cancer.

An example of the application of LBDDS in gene therapy is the use of lipid nanoparticles (LNPs) for the delivery of messenger RNA (mRNA) vaccines, such as the COVID-19 vaccines developed by Pfizer-BioNTech and Moderna. LNPs can encapsulate the mRNA and protect it from degradation, while also promoting its cellular uptake and expression of the encoded protein.

In summary, LBDDS have a wide range of applications in medicine, including cancer therapy, gene therapy, vaccines, drug delivery to the brain, and dermatological applications. These applications are based on the ability of LBDDS to

**Author:**

**Please provide scientific information on "Future directions and challenges" based on the outline you give with detailed examples**

**ChatGPT:**

Future directions and challenges of lipid-based drug delivery systems (LBDDS):

Personalized medicine: LBDDS have the potential to enable personalized medicine, by tailoring drug delivery to individual patient needs based on their genetics, lifestyle, and disease state. This can be achieved by designing LBDDS that can selectively target specific cells and tissues, or by incorporating diagnostic and monitoring tools that can provide real-time feedback on drug efficacy and toxicity.

Combination therapies: LBDDS can also be used to deliver multiple drugs or agents, which can improve drug efficacy and reduce the development of drug resistance. Combination therapies can be achieved by encapsulating multiple drugs in a single carrier, or by using different types of carriers to deliver different drugs or agents to different sites in the body.

Biocompatibility and toxicity: The biocompatibility and toxicity of LBDDS remain important challenges that need to be addressed. While LBDDS are generally considered to be safe and well-tolerated, there is a need for further research into their long-term effects and potential toxicity, as well as the development of strategies to minimize toxicity and improve biocompatibility.

Manufacturing and scale-up: The manufacturing and scale-up of LBDDS can also be challenging, due to the complex nature of the lipid-based carriers and the need for precise control over their size, composition, and properties. There is a need for the development of scalable and reproducible manufacturing processes for LBDDS, as well as the optimization of their stability and storage conditions.

Examples:

An example of a future direction for LBDDS is the development of targeted drug delivery systems that can selectively deliver drugs to specific cells or tissues. This can be achieved by using targeting ligands or antibodies that can bind to receptors or antigens on the surface of cells, or by incorporating imaging or diagnostic tools that can guide drug delivery to specific sites in the body. This approach has the potential to improve drug efficacy and reduce toxicity, as well as enable personalized medicine.

An example of a challenge in LBDDS is the need for further research into the long-term effects and toxicity of these carriers. While LBDDS are generally considered to be safe and well-tolerated, there is a need for studies that evaluate their long-term effects on different organs and systems, as well as their potential to accumulate in the body over time. In addition, there is a need for the development of strategies to minimize toxicity and improve biocompatibility, such as the use of biodegradable and biocompatible materials.

In summary, the future directions and challenges of LBDDS include personalized medicine, combination therapies, biocompatibility and toxicity, and manufacturing and scale-up. These areas of research and development have the potential to advance the field of drug delivery and improve patient outcomes, but also require continued innovation and collaboration between researchers and industry.

**Author:**

**Please provide scientific information on "Conclusion" based on the outline you give**

**ChatGPT:**

In conclusion, lipid-based drug delivery systems (LBDDS) have emerged as a promising option for the delivery of a wide range of therapeutic agents, including small molecules, peptides, and nucleic acids. LBDDS offer several advantages over conventional drug delivery systems, including improved bioavailability, reduced toxicity, and the ability to encapsulate hydrophobic and hydrophilic drugs.

There are several types of LBDDS available, including liposomes, solid lipid nanoparticles, and nanoemulsions, each with their unique advantages and limitations. While LBDDS have been successfully applied in the treatment of various diseases, including cancer, cardiovascular disease, and infectious diseases, there are still challenges that need to be addressed.

Future directions for LBDDS include the development of targeted drug delivery systems, personalized medicine, and combination therapies. However, challenges such as biocompatibility and toxicity, manufacturing and scale-up, and regulatory approval remain.

Overall, LBDDS have the potential to transform the field of drug delivery and improve patient outcomes. Continued research and innovation in this area will be necessary to address the current challenges and fully realize the potential of LBDDS for the delivery of therapeutic agents.