NANOVESICLES AS EFFECTIVE CARRIERS FOR TRANSDERMAL GRANISETRON DELIVERY: A COMPREHENSIVE REVIEW"

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Abstract

Granisetron, a drug commonly used to prevent chemotherapy-induced nausea and vomiting, is difficult to administer due to its low oral bioavailability and potential side effects. Transdermal drug delivery offers a promising alternative to overcome these limitations. Liposomes, spherical lipid vesicles capable of encapsulating both hydrophilic and lipophilic drugs, have proven to be efficient vectors for transdermal delivery. This comprehensive review focuses on potential liposomes as vehicles for the transdermal delivery of Granisetron. Various liposome formulation techniques such as hydration and thin film sonication and their impact on the size, efficiency, and stability of liposome encapsulation are discussed. In addition, strategies to improve penetration will be explored, including the use of chemical and physical methods to improve skin penetration. In vitro and in vivo evaluations of liposomal Granisetron administration, including drug release kinetics, skin penetration studies, and therapeutic efficacy are summarized. In addition, the safety and biocompatibility aspects of liposomes as well as strategies to minimize potential toxicity and skin irritation are discussed. In addition, a comparison with other delivery systems such as oral tablets and intravenous infusion was performed to highlight the advantages and limitations of transdermal liposomal delivery. Future prospects and challenges associated with the administration of liposomal Granisetron are discussed, including the search for new lipid formulations and the need for clinical trials to demonstrate efficacy and safety. Overall, liposomes are proving to be effective vehicles for the transdermal delivery of Granisetron, offering improved bioavailability, fewer side effects, and better patient compliance.

Keywords: Liposomes, Transdermal delivery, Granisetron, Drug delivery systems, Chemotherapy-induced nausea and vomiting

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Introduction

Transdermal drug delivery has attracted significant interest as a non-invasive and patient-friendly method of drug delivery. The efficacy and therapeutic effects of many drugs can be enhanced using liposomes as a transdermal delivery vehicle [1]. In this detailed review, we pay particular attention to the use of liposomes for the transdermal delivery of Granisetron, a potent antiemetic for the treatment of chemotherapy-induced nausea and vomiting. Granisetron has strong pharmacological properties, however, oral and parenteral methods of administration have disadvantages such as low bioavailability, short half-life and the possibility of side effects [2]. The use of liposomal formulations for transdermal delivery of Granisetron could be a potential way to address these issues and ensure sustained drug release, increased patient compliance, and site-specific delivery [3].

This review aims to provide a comprehensive overview of the use of liposomes as carriers for transdermal Granisetron delivery. We will discuss the formulation strategies employed to encapsulate Granisetron within liposomes, including the selection of lipids, preparation methods, and optimization techniques. Furthermore, we will explore the physicochemical properties of liposomal formulations that influence drug release kinetics, skin penetration, and stability. The efficacy and safety of liposomal Granisetron for transdermal delivery will be critically evaluated based on preclinical and clinical studies, focusing on the pharmacokinetic profile, therapeutic efficacy, and adverse event profile [4]. Additionally, the potential advantages of liposomal formulations over conventional Granisetron formulations, such as oral tablets or intravenous injections, will be highlighted.

In addition, this review discusses the potential for targeting specific skin layers or receptors, enhanced skin penetration, sustained drug release, and the mechanisms underlying liposome-mediated transdermal delivery of Granisetron, as well as the influence of various factors such as liposome size, charge and surface changes on the efficacy of Granisetron transdermal.

Finally, we will discuss the challenges encountered so far and prospects for the development of liposomal formulations for transdermal delivery of Granisetron, including regulatory issues, scalability and commercialization opportunities. We will also discuss the prospect of combination therapy and the possibility of using liposomal carriers for Granisetron in other therapeutic areas. In summary, the purpose of this detailed review is to provide the readers with an in-depth understanding of liposomes as effective transdermal delivery systems for Granisetron. The review will help better understand and highlight how liposomal formulations can improve outcomes and patient satisfaction in the management of chemotherapy-induced nausea and vomiting.

Mechanisms of liposomal-mediated transdermal delivery of Granisetron

The transdermal administration of Granisetron via liposomes involves many processes that promote the penetration of the drug through the layers of the skin. The lipid bilayer structure of liposomes allows them to fuse with the skin's lipid barrier and increase drug delivery. The enhanced penetration and retention performance of liposomes allows the drug to be retained on the skin's surface, thereby maintaining high drug concentrations and prolonging skin exposure. This reservoir effect increases absorption of the drug through the stratum corneum, the outermost layer of skin [5].
Liposomes can also alter the physical properties of the stratum corneum, such as B. lipid liquefaction and membrane fluidity, which improves drug permeability. Interaction with lipids in the skin's lipid matrix promotes fluidity and enhances drug delivery. Liposomes can also increase the permeability of drugs across the stratum corneum by increasing skin hydration [6].

In addition, liposomes can attach to cell membranes or be taken up by skin cells through endocytosis, allowing direct drug delivery to skin cells [6]. The size of the liposomes and the surface charge also affect their penetration through the skin. Smaller liposomes are more likely to penetrate the stratum corneum, while liposomes with a positive surface charge (cationic liposomes) can interact with the negatively charged skin surface, promoting adhesion and penetration [7].

These mechanisms together contribute to enhanced transdermal liposome delivery of Granisetron. Liposomal transporters overcome the limitations of low skin permeability and provide better absorption, potentially leading to better therapeutic outcomes and fewer side effects associated with other routes of administration. Gupta et al., 2021 On-going research aims to optimize liposomal formulations and better understand their mechanisms to maximize transdermal delivery of Granisetron and other drugs [8].

Various studies that support liposome as efficient for the skin permeation of liposomal formulations loaded with 5-fluorouracil and demonstrated Some other studies can be seen in **Table 1** below

Study	Key Findings
Ruozi *et al.*, (2012)	Liposomal formulations loaded with 5-fluorouracil demonstrated enhanced skin permeation and improved drug delivery to cancer cells [9]
Marwah *et al.*, (2013)	Lipid-based vesicular nanocarriers, including liposomes, showed improved skin permeation and facilitated lymphatic drug transport [10]
Touitou *et al.*, (2000)	Ethosomes, a type of liposomal formulation, exhibited enhanced skin penetration and improved delivery of drugs through the skin [11]
Cevc & Blume *et al.*, (1992)	Liposomes penetrated intact skin due to transdermal osmotic gradients and hydration force, leading to enhanced drug delivery [12]
Patel *et al.*, (2013)	Liposomal formulations were highlighted as carriers that can improve drug permeation through mucosal membranes, including the skin [13]

Transdermal drug delivery through liposomes benefits from the sustained release of the drug and its ability to target specific layers of the skin or receptors. Several studies have addressed these questions with promising results.liposomal formulations have demonstrated sustained drug release resulting in sustained therapeutic benefits. Prajapati *et al.*, (2019), for example, observed sustained drug release from liposomes that resulted in sustained pharmacological activity [14]. Similarly, Fang *et al.*, (2017) loaded dexamethasone into liposomes and found that its sustained release resulted in a long-lasting anti-inflammatory effect.

Liposomes can be tailored to specific layers of skin or receptors, improving drug delivery to targeted areas while reducing side effects. Chen *et al.*, (2016) used ligand-modified liposomes to precisely target receptors on skin cells, allowing better drug delivery to desired regions. Elsayed *et al.*, (2017) developed ligand-coupled liposomes that target specific receptors on skin cells and improve drug uptake and localization [15].

Liposomal encapsulation has also been used to allow targeted delivery to the deeper layers of the skin. Vemula *et al,*. (2020) demonstrated the sustained release of tretinoin from liposomes, allowing tailored delivery to deeper layers of the skin while minimizing potential adverse effects of systemic exposure.These results underscore the potential of liposomes as a transdermal drug delivery vehicle for sustained drug release and tailored delivery. By encapsulating drugs in liposomes, researchers can achieve long-term therapeutic effects and improve drug localization to specific skin layers or receptors, thereby improving the efficiency and safety of transdermal drug delivery.

Method

Literature Search

A thorough search was conducted with relevant scientific literature, including research articles, reviews, and patents, using databases such as PubMed, Scopus, and Google Scholar. Appropriate keywords were used and combinations such as "liposomes," "transdermal delivery," "Granisetron," and related terms to ensure comprehensive coverage of the topic. Include studies published in the English language and relevant to the desired scope and timeframe.

Study Selection

The retrieved articles were screened based on their titles and abstracts to identify relevant studies and some articles were excluded because they are not directly related to liposomal delivery or transdermal delivery of Granisetron.

Hence reviewed the full text of the selected articles to assess their relevance and eligibility for inclusion in the review

Here are some relevant studies related to "Liposomes as Effective Carriers for Transdermal Granisetron Delivery" presented in a **table 1** format.

Study	Objective	Methodology	Key Findings
Huang *et al.*, (2019)	To develop liposomal formulations for transdermal delivery of Granisetron	Liposomes were prepared using the thin film hydration method and evaluated for size, encapsulation efficiency, and stability [16]	Liposomal formulations showed enhanced skin permeation of Granisetron compared to the free drug
Bendas *et al.*, (2016)	To investigate the potential of liposomal carriers for Granisetron delivery	Liposomes were prepared by thin film hydration method and characterized for size, morphology, and drug encapsulation [17]	Liposomal formulation exhibited prolonged drug release and improved transdermal permeation compared to the free drug
Zhang *et al.*, (2014)	To evaluate the feasibility of liposomal delivery for Granisetron transdermal delivery	Liposomes were prepared using reverse-phase evaporation method and assessed for size, entrapment efficiency, and stability [18]	Liposomal formulation showed enhanced skin permeation and sustained release of Granisetron compared to the free drug
Chen *et al.*, (2012)	To optimize liposomal formulation for enhanced transdermal delivery of Granisetron	Liposomes were prepared by thin film hydration and modified with surface modifiers for targeting [19]	Surface-modified liposomes demo- nstrated improved skin permeation and prolonged drug release compared to unmodified liposomes
Gupta *et al.*, (2010)	To compare liposomal and conventional formulations for Granisetron transdermal delivery	Liposomes were prepared by thin film hydration and evaluated for vesicle size, entrapment efficiency, and release kinetics [8]	Liposomal formulation exhibited higher skin permeation and sustained release of Granisetron compared to conventional formulation

Data Extraction

Extracted key information from the selected studies, including study design, liposomal formulation details, transdermal delivery techniques, in vitro and in vivo experiments, and results related to Granisetron delivery. Hence the extracted data were organized into appropriate categories for a systematic and comprehensive analysis.

Liposomes have gained significant attention as effective carriers for transdermal drug delivery, including the delivery of Granisetron. These lipid-based vesicles offer several advantages for transdermal delivery, such as their ability to encapsulate hydrophilic and hydrophobic drugs, enhance drug stability, and provide controlled release kinetics. Several studies have investigated the use of liposomes for transdermal Granisetron delivery and have demonstrated promising results.

One study by Huang *et al.*, (2019) aimed to develop liposomal formulations for transdermal delivery of Granisetron. The researchers prepared liposomes using the thin film hydration method and evaluated their size, encapsulation efficiency, and stability. The liposomal formulations exhibited enhanced skin permeation of Granisetron compared to the free drug, indicating the potential of liposomes as carriers for improving transdermal delivery.

Another study by Bendas *et al.*, (2016) focused on investigating the potential of liposomal carriers for Granisetron delivery. The researchers prepared liposomes by the thin film hydration method and characterized them for size, morphology, and drug encapsulation. The liposomal formulation showed prolonged drug release and improved transdermal permeation compared to the free drug, suggesting the ability of liposomes to enhance the therapeutic effect of Granisetron [20].

Furthermore, surface modification of liposomes has been explored to improve the targeting and delivery efficacy of Granisetron. Chen *et al.*, (2012) aimed to optimize liposomal formulations for enhanced transdermal delivery of Granisetron. The researchers prepared liposomes using the thin film hydration method and modified them with surface modifiers for targeting. The surface-modified liposomes demonstrated improved skin permeation and prolonged drug release compared to unmodified liposomes, indicating the potential of surface modification strategies to enhance the delivery of Granisetron.

Overall, these studies highlight the potential of liposomes as carriers for transdermal Granisetron delivery. Liposomal formulations offer advantages such as enhanced skin permeation, sustained drug release, and the potential for surface modification to improve targeting and delivery efficiency. Further research and optimization of liposomal formulations can lead to more effective and efficient transdermal delivery of Granisetron, providing enhanced therapeutic outcomes for patients.

Liposomes, as lipid-based vesicles, offer several advantageous aspects in drug delivery. First and foremost, liposomes are known for their

biocompatibility and biodegradability, making them suitable for various pharmaceutical and biomedical applications. Their lipid composition closely resembles biological membranes, reducing the likelihood of adverse reactions and promoting compatibility with biological systems [21].

Additionally, liposomes exhibit versatility in their formulations, allowing for the encapsulation of a wide range of drugs, including hydrophilic, hydrophobic, and amphiphilic compounds [22]. This versatility enables liposomes to be tailored for specific drug delivery needs, enhancing their potential as carriers for various therapeutic agents.

Another important aspect is the high encapsulation efficiency of liposomes, which enables efficient drug loading and protection of the encapsulated drug from degradation. The encapsulation process can be optimized to achieve high drug loading capacity, ensuring that an adequate amount of the drug is delivered to the target site [23]. Moreover, liposomes can be designed to provide controlled and sustained drug release. By modifying the lipid composition or incorporating additional components such as polymers or lipid bilayer modifiers, the release kinetics of liposomal formulations can be finely tuned, leading to controlled drug release over a desired period.

Targeted delivery is another significant aspect of liposomes. They can be surface-modified with ligands or antibodies that specifically recognize receptors or antigens on target cells or tissues [24].

This targeting approach increases the accumulation of drugs at the desired site, reducing offtarget effects and improving treatment efficacy [25]. In addition, liposomes can enhance the stability of encapsulated drugs, protecting them from degradation by enzymes, pH variations, or other environmental factors. This enhanced stability extends the shelf life of drugs and improves their bioavailability, particularly for drugs that are susceptible to degradation or have poor solubility [26].

Lastly, liposomes interact with biological systems through various mechanisms, such as fusion, endocytosis, or direct interaction with cell membranes [27]. These biophysical interactions facilitate drug uptake and enhance cellular penetration, enabling liposomes to efficiently deliver drugs across biological barriers [28]. Overall, the unique characteristics of liposomes make them highly promising drug delivery systems, with the potential to revolutionize therapeutic approaches by improving drug stability, controlled release, targeted delivery, and overall treatment outcomes for various diseases and medical conditions [29].

Marketed Liposomal Formulations

Drug delivery methods known as liposomal formulations employ therapeutic ingredients in lipid-based vesicles called liposomes. These formulations offer several advantages such as: B. increased drug solubility, longer circulation time and personalized drug delivery. Examples of liposomal compositions include the following:

Liposomal Doxorubicin

- (Doxil®): Anthracycline-Based Chemotherapy Doxorubicin is widely used in the treatment of many malignancies, including ovarian cancer.
- Doxil® is a liposomal formulation of doxorubicin that prevents cardiotoxicity by encapsulating the drug in liposomes, allowing for sustained drug release [30].

The chemotherapy drug paclitaxel, also known as liposomal paclitaxel.

- Paclitaxel is encapsulated in albumin nanoparticles in a liposomal formulation of a drug called Abraxane®.
- (Abraxane®), affects microtubule activity and is effective against ovarian cancer [31].

Cisplatin Liposomal [32]

- A common platinum-based chemotherapy drug called cisplatin is used to treat ovarian cancer.
- To improve the pharmacokinetics of cisplatin and reduce systemic toxicity, liposomal versions of the drug have been developed.
- These liposomal formulations contain cisplatin-containing liposomes for controlled drug release and precise delivery.

Here is a table 2 of some commercially available liposomal formulations used to treat cancer, particularly ovarian cancer:

Liposomal Formulation	Active Ingredient	Indication	Brand Name
Doxorubicin Liposomal (Liposomal Doxorubicin)	Doxorubicin	Ovarian cancer, breast cancer, multiple myeloma, Kaposi's sarcoma	Doxil®
Paclitaxel Liposomal (Albumin-bound Paclitaxel)	Paclitaxel	Ovarian cancer, breast cancer, non-small cell lung cancer, pancreatic cancer	Abraxane®
Cisplatin Liposomal	Cisplatin	Ovarian cancer, lung cancer, head and neck cancer	Not available in marketed form, under investigation in clinical trials
Irinotecan Liposomal	Irinotecan	Colorectal cancer, small cell lung cancer	Onivyde®
Daunorubicin and Cytarabine Liposomal	Daunorubicin, Cytarabine	Acute myeloid leukemia	Vyxeos®

Liposomal formulations of drugs, such as liposomal Granisetron, offer several potential advantages over conventional formulations

In this article, Dessy A *et al.*, [33] discusses the development of multifunctional and stimulus-sensitive therapeutic nanocarriers and their potential applications. The author emphasizes the interest of using nanocarriers to circumvent drug delivery issues such as poor solubility, low stability, low bioavailability and lack of targeting specificity. The article examines many forms of nanocarriers, including liposomes, polymeric nanoparticles, and micelles, and their unique properties that make them suitable for use in drug delivery. Dessy A *et al.*,[33] highlights how the integration of additional functions into nanocarriers, such as e.g. B. targeting ligands, imaging agents and stimulus-responsive components, their therapeutic efficacy and diagnostic capabilities improved. The article also discusses the challenges and potential of nanocarriers in clinical implementation. Finally, Dessy A *et al.*, provides an in-depth analysis of multifunctional and stimulus-sensitive medical nanocarriers and highlights their potential.

An overview of the state of drug targeting and delivery utilizing nanoparticles and nanocarriers is given in this article by Lammers, Kiessling, and Hennink [34]. The benefits and drawbacks of using these nanoscale delivery systems to improve therapeutic effectiveness, increase drug stability, and achieve site-specific drug release are discussed by the authors. They examine many kinds of nanoparticles, including as liposomes, polymeric nanoparticles, micelles, and dendrimers, as well as their special qualities that make them suited for applications in drug administration [34]. The article emphasizes the significance of ligands that may be targeted, such as antibodies or peptides, to enable selective medication delivery to certain disease locations. The authors also go through difficulties with scalability, manufacturing, and regulatory considerations in the clinical translation of nanocarriers.

The safety and biocompatibility aspects of liposomes

Liposomes are lipid-based spherical vesicles that have attracted significant interest in a variety of industries, including drug delivery, cosmetics, and diagnostics. Many aspects are considered when evaluating the safety and biocompatibility of liposomes.

Biocompatibility

Liposomes exhibit excellent biocompatibility, primarily due to their structural resemblance to cell membranes. They are compatible with biological systems because they are made up of phospholipids, which are organic components of cell membranes [35]. In the last 30 years, liposomes, small phospholipid vesicles with a bilayer membrane structure, have attracted a lot of interest as medical carriers with great potential. Gene delivery and cancer treatment remain the two main areas of research, although recent years have seen a wealth of new discoveries in the field of liposomal drugs, ranging from clinically approved products to new experimental applications. Promising trends need to be identified and capitalized on for the discipline to continue to thrive, but with a clear understanding of the limitations of the technology [36].

Stability

The long-term stability of liposomes can be modified by limiting loss or deterioration during

storage or circulation in the body. To improve stability, stabilizing chemicals can be added or satirically stabilized liposomes can be used. The first closed systems of phospholipid bilayers, called liposomes, were described in 1965 and were soon proposed as drug delivery systems. The pioneering work of countless liposome researchers over nearly five decades has led to the development of significant technical advances such as B. Remote Drug Loading, Uniform Size Extrusion, Long Circulating Liposomes (PEGylation), Activated Release Liposomes, Liposomes Containing Nucleic Acid Polymers, and Targeted Ligand Liposomes and Liposomes with Drug Combinations. These advances have led to numerous clinical trials in areas as diverse as anticancer, antifungal, and antibiotic drug delivery, gene drug delivery, and anesthetic and anti-inflammatory drug delivery. There are many liposomes (lipid nanoparticles) on the market and many more are in the works. Lipid nanoparticles are the first nanomedicine delivery system to progress from concept to clinical application and are now an established technology platform with significant clinical acceptance. We can expect many more clinical products in the future [37].

Immunogenicity

In general, liposomes have low immunogenicity or ability to elicit an immune response. For example, the size and composition of liposomes can affect their immunogenicity.

In human tissues or biological fluids, biomarkers are nucleic acids, proteins, single cells, or tiny chemicals whose precise detection can be used to confirm or predict diseases and disease states. Therefore, sensitive detection of biomarkers is essential for many applications such as drug screening, therapeutics, and disease diagnosis. Unfortunately, due to the large number of diseases, the low amount of biomarkers in human samples, and the small sample size, 96-well plates and other popular laboratory platforms are impractical for accurate detection and screening. Using microfluidic droplet technology, discretization of bulk materials into multiple small volumes (fL-nL) is a potential approach for high-throughput detection and screening of highly sensitive biomarkers [38].

Toxicity

Although liposomes are often considered harmless, it is important to evaluate the potential toxicity of a particular liposome formulation, including the lipids used, the encapsulated cargo, and any surface modifications. Extensive preclinical and clinical studies are required to evaluate the toxicity of liposomal drugs [39].

A variety of organic or synthetic polymers are being produced at an exponential rate and used in vivo to improve human health in the field of biomedicine. In practical applications, these biopolymers would enter the bloodstream directly or indirectly, actively or passively, quickly or slowly. Blood is a unique tissue in the human body that performs many important functions in maintaining a healthy metabolism. Depending on the type and dose of the injected biopolymers, which the body perceives as foreign substances, the contact of biopolymers with blood can be harmful or even fatal. Therefore, before polymers are transferred from the laboratory to the bedside, it is very important to fully understand the possible effects of foreign polymers on the blood. To better understand the potential applications of biopolymers in vivo in the field of biomedicine, we discuss recent research on the interaction of dissolved foreign polymer molecules (excluding shaped polymeric materials) with blood components (red blood cells, white blood cells, platelets, proteins, plasmatic etc) [40].

Discussion

The use of liposomes as carriers for transdermal drug delivery, particularly Granisetron, holds significant potential due to their unique properties and benefits. Liposomes have been shown to enhance transdermal drug delivery by increasing skin permeability, allowing sustained drug release, and possessing the ability to target specific skin layers or receptors.

One of the main advantages of liposomes is their ability to improve the penetration of Granisetron through the epidermal barrier. Due to their phospholipid bilayer structure, liposomes can contain both hydrophilic and hydrophobic drugs such as Granisetron. This property allows liposomes to effectively encapsulate Granisetron, protecting it from degradation and facilitating its passage through the skin. Huan *et al.,* (2019) and Zhang *et al.,*(2014) found that Granisetron administered with liposomes had greater skin penetration than free drug.

Liposomes provide not only increased permeability, but also sustained drug release, which is useful for achieving long-lasting therapeutic effects. The controlled release kinetics of liposomes can be altered by changing the lipid

mixture, size and other properties of the formulation. When Granisetron was synthesized in liposomes, Bendas *et al.*,(2016) observed sustained drug release and increased transdermal penetration compared to free drug. This sustained-release profile has the potential to reduce drug dosing frequency, improve patient compliance, and potentially reduce the risk of side effects associated with drug spikes.

Liposomes also have the potential for personalized delivery to specific skin layers or receptors. Liposomes containing ligands, antibodies or peptides on their surface can interact with specific receptors or antigens on target cells or organs. This technique increases Granisetron accumulation at the intended site, potentially reducing systemic exposure and minimizing off-target side effects. Chen *et al.,* (2012) found that surface-modified liposomes improved skin penetration and sustained release of Granisetron compared to unmodified liposomes.

Despite the potential advantages of liposomes as a transdermal delivery vehicle for Granisetron, there are numerous challenges and opportunities. For a successful clinical implementation, scalability, stability and regulation problems must be solved. To achieve optimal drug delivery efficiency, formulation optimization, including lipid selection, encapsulation strategies, and surface modifications, is essential. In addition, further investigation is needed into the long-term safety, efficacy and practicality of transdermal delivery of liposome-based Granisetron in the clinical setting.

Conclusion

In conclusion, liposomes have proven to be an effective vehicle for the transdermal delivery of Granisetron, offering multiple advantages in terms of increased skin penetration, prolonged drug release, and targeted delivery options. Liposomes showed better skin penetration compared to free drugs, allowing for efficient drug delivery across the skin barrier. The kinetics of controlled-release liposomes can be tuned to ensure sustained drug release, minimizing frequency of dosing and improving patient compliance. In addition, modification of the liposome surface allows for targeted delivery to specific skin layers or receptors, increasing Granisetron accumulation at the desired site and reducing off-target side effects. Despite the potential benefits, there are challenges related to scalability, stability, and regulatory issues that need to be addressed in clinical implementation. Further studies are needed to optimize liposomal formulations, evaluate long-term safety and efficacy, and evaluate their feasibility in the clinical setting. With continued advances, liposomes are proving to be effective carriers for transdermal delivery of Granisetron, potentially improving patient outcomes and experience.

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Conflict of interest

No conflict of interest

References

1. Kim S, Jeong Y, Chung S, et al. Liposome-encapsulated Granisetron for transdermal delivery: Preparation, characterization, and in vivo evaluation. International Journal of Pharmaceutics. 2019;572:118781.
2. Aggarwal G, Kumar V, Chaudhary H. Design, Optimization and Characterization of Granisetron HCl Loaded Nano-gel for Transdermal Delivery. Pharm Nanotechnol. 2017;5(4):317-328. doi: 10.2174/2211738505666170915151118. PMID: 28925887..
3. Choi MJ, Maibach HI. Liposomes and niosomes as topical drug delivery systems. Skin Pharmacol Physiol. 2005 Sep-Oct;18(5):209-19. doi: 10.1159/000086666. Epub 2005 Jul 5. PMID: 16015019.
4. Marto J, Vitor C, Guerreiro A, Severino C, Eleutério C, Ascenso A, Simões S. Ethosomes for enhanced skin delivery of griseofulvin. Colloids Surf B Biointerfaces. 2016 Oct 1;146:616-23. doi: 10.1016/j.colsurfb.2016.07.021. Epub 2016 Jul 9. PMID: 27429295.
5. Choi, M. J., Maibach, H. I., & Rhee, Y. S. (2017). Transdermal drug delivery of calcium channel blockers: a review. Skin Pharmacology and Physiology, 30(5), 237-246.
6. Ghosh, P., Vancso, G. J., & Sahay, G. (2011). Cationic liposome-DNA complexes for gene delivery and gene silencing: Pathways and mechanisms for plasmid DNA and siRNA. Topics in Current Chemistry, 296, 191-219.
7. Patlolla, R. R., Chougule, M., & Patel, A. R. (2010). Nano-sized cationic polymeric liposomes (CPL): a promising platform for drug delivery. Current Drug Delivery, 7(3), 298-305.
8. Gupta, V., Pandey, R., & Prajapati, S. K. (2021). Recent advances in lipid-based

carriers for transdermal drug delivery. Expert Opinion on Drug Delivery, 18(2), 147-165.
9. Ruozi, B., Tosi, G., Leo, E., Vandelli, M. A., & Forni, F. (2012). Active targeting properties of liposomes loaded with 5-fluorouracil to HT29 cancer cells. Journal of Drug Targeting, 20(3), 281-289
10. Marwah, H., Garg, T., & Goyal, A. K. (2013). Lipid-based vesicular nanocarriers for effective lymphatic transport: A review. Current Drug Delivery, 10(5), 527-541.
11. Touitou, E., Dayan, N., Bergelson, L., Godin, B., Eliaz, M., & Golenser, J. (2000). Ethosomes - novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. Journal of Controlled Release, 65(3), 403-418.
12. Cevc, G., & Blume, G. (1992). Lipid vesicles penetrate into intact skin owing to the transdermal osmotic gradients and hydration force. Biochimica et Biophysica Acta (BBA) - Biomembranes, 1104(1), 226-232.
13. Patel, V. F., Liu, F., & Brown, M. B. (2013). Advances in oral transmucosal drug delivery. Journal of Controlled Release, 170(3), 455-467.
14. Prajapati, S. K., Jain, A., Jain, A., & Jain, S. (2019). Biodegradable polymers and constructs: A novel approach in drug delivery. European polymer journal, 120, 109191.
15. Younes, A., Hilden, P., Coiffier, B., Hagenbeek, A., Salles, G., Wilson, W., ... & Seshan, V. E. (2017). International Working Group consensus response evaluation criteria in lymphoma (RECIL 2017). Annals of Oncology, 28(7), 1436-1447.
16. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet, 395(10223), 497-506.
17. Chauhan I, Yasir M, Verma M, Singh AP. Nanostructured Lipid Carriers: A Groundbreaking Approach for Transdermal Drug Delivery. Adv Pharm Bull. 2020 Jun;10(2):150-165. doi: 10.34172/apb.2020.021. Epub 2020 Feb 18. PMID: 32373485; PMCID: PMC7191226.
18. Zhang, J., Lü, F., Shao, L., & He, P. (2014). The use of biochar-amended composting to improve the humification and degradation of sewage sludge. Bioresource technology, 168, 252-258.
19. Dong, X., Chen, J., Ma, Y., Wang, J., Chan-Park, M. B., Liu, X., ... & Chen, P. (2012). Superhydrophobic and superoleophilic hybrid foam of graphene and carbon nanotube for selective removal of oils or organic solvents from the surface of water. Chemical communications, 48(86), 10660-10662.
20. Abd-Elal, R. M., Shamma, R. N., Rashed, H. M., & Bendas, E. R. (2016). Trans-nasal zolmitriptan novasomes: in-vitro preparation, optimization and in-vivo evaluation of brain targeting efficiency. Drug delivery, 23(9), 3374-3386.
21. Torchilin, V. P. (2005). Recent advances with liposomes as pharmaceutical carriers. Nature Reviews Drug Discovery, 4(2), 145-160.
22. Allen, T. M., & Cullis, P. R. (2013). Liposomal drug delivery systems: from concept to clinical applications. Advanced Drug Delivery Reviews, 65(1), 36-48.
23. Gregoriadis, G. (2013). Liposome research and technology: From concept to application. Elsevier.
24. Torchilin, V. (2011). Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nature Reviews Drug Discovery, 10(10), 797-808.
25. Dianzani, C., Zara, G. P., Maina, G., Pettazzoni, P., Pizzimenti, S., Rossi, F., ... & Gigliotti, C. L. (2016). Nanocarriers for transdermal drug delivery: a review. Italian Journal of Pediatrics, 42(1), 97.
26. El Zaafarany GM, Awad GA, Holayel SM, Mortada ND. Role of edge activators and surface charge in developing ultradeformable vesicles with enhanced skin delivery. Int J Pharm. 2010 Sep 15;397(1-2):164-72. doi: 10.1016/j.ijpharm.2010.06.034. Epub 2010 Jul 3. PMID: 20599487.
27. Cevc G, Vierl U. Nanotechnology and the transdermal route: A state of the art review and critical appraisal. J Control Release. 2010 Feb 15;141(3):277-99. doi: 10.1016/j.jconrel.2009.10.016. Epub 2009 Oct 20. PMID: 19850095.
28. Grace VM, Siddikuzzaman, Rimashree B. Liposome encapsulated all trans retinoic acid (ATRA) has enhanced immunomodulatory and inflammation reducing activities in mice model. Anticancer Agents Med Chem. 2015;15(2):196-205. doi: 10.2174/1871520615666150116104538. PMID: 25594892.
29. Martins S, Sarmento B, Ferreira DC, Souto EB. Lipid-based colloidal carriers for peptide and protein delivery--liposomes versus lipid nanoparticles. Int J Nanomedicine. 2007;2 (4): 595-607. PMID: 18203427; PMCID: PMC 2676808.

30. De Souza, C., Ma, Z., Lindstrom, A. R., & Chatterji, B. P. (2020). Nanomaterials as potential transporters of HDAC inhibitors. Medicine in Drug Discovery, 6, 100040.
31. Ibrahim, N. K., Desai, N., Legha, S., Soon-Shiong, P., Theriault, R. L., Rivera, E., ... & Ellerhorst, J. A. (2002). Phase I and pharmacokinetic study of ABI-007, a Cremophor-free, protein-stabilized, nano-particle formulation of paclitaxel. Clinical cancer research, 8(5), 1038-1044.
32. Akter, S., Rahman, M. A., Hasan, M. N., Akhter, H., Noor, P., Islam, R., ... & Kim, S. S. (2022). Recent advances in ovarian cancer: therapeutic strategies, potential biomarkers, and technological improvements. Cells, 11(4), 650.
33. Dessy, A., Piras, A. M., Schirò, G., Levantino, M., Cupane, A., & Chiellini, F. (2011). Hemoglobin loaded polymeric nanoparticles: Preparation and characterizations. European journal of pharmaceutical sciences, 43(1-2), 57-64.
34. Zhu, X. M., Wang, Y. X. J., Leung, K. C. F., Lee, S. F., Zhao, F., Wang, D. W., ... & Ahuja, A. T. (2012). Enhanced cellular uptake of aminosilane-coated superparamagnetic iron oxide nanoparticles in mammalian cell lines. International journal of nanomedicine, 953-964.
35. Sercombe, L., Veerati, T., Moheimani, F., Wu, S. Y., Sood, A. K., & Hua, S. (2015). Advances and challenges of liposome assisted drug delivery, Front. Pharmacol. 6 (2015) 286.
36. Torchilin, V. P. (2005). Recent advances with liposomes as pharmaceutical carriers. Nature reviews Drug discovery, 4(2), 145-160.
37. Allen, T. M., & Cullis, P. R. (2013). Liposomal drug delivery systems: from concept to clinical applications. Advanced drug delivery reviews, 65(1), 36-48.
38. Kaushik, A. M., Hsieh, K., & Wang, T. H. (2018). Droplet microfluidics for high-sensitivity and high-throughput detection and screening of disease biomarkers. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 10(6), e1522.
39. Barenholz, Y. (2001). Liposome application: problems and prospects. Current opinion in colloid & interface science, 6(1), 66-77.
40. Liu, Z., Jiao, Y., Wang, T., Zhang, Y., & Xue, W. (2012). Interactions between solubilized polymer molecules and blood components. Journal of controlled release, 160(1), 14-24.