Indian Journal of Modern Research and Reviews

This Journal is a member of the *'Committee on Publication Ethics'*

Online ISSN: 2584-184X

Review Article

Advancements in Drug Delivery: A Novel Perspective on Proniosomal Gel Systems – Preparation Methods, Applications, and Future Prospects

Dr. K. Parameshwar, Dr. Ravula Parameshwar, Megavath Sravani, Miriyala Akhil Sai, Mobashshira Khatoon, Mucha Aditya, Mukesh.K

Abstract:

This paper presents an innovative drug delivery method using proniosomal gel systems, offering a more stable, easily stored, and effective alternative to traditional vesicular systems such as liposomes. It extensively explores proniosomal gels, covering their formulation, applications in various therapeutic areas, and potential. Key formulation components, such as surfactants, active pharmaceutical ingredients, and stabilizers are detailed, along with preparation methods like film hydration and sonication. The paper examines how factors like surfactant type, hydration time, and gelling agent concentration impact proniosomal gel quality and performance, tailoring them for specific therapeutic needs. It emphasizes their advantages in targeted and controlled drug release, surpassing traditional methods in certain cases. The paper concludes with a forward-looking perspective on proniosomal gels in personalized medicine and as a solution to challenges in conventional drug delivery, making significant contributions to pharmaceutical sciences and patient-centered drug delivery approaches.

Keywords: *Proniosomal Gels; Drug Delivery; Vesicular Systems; Formulation Methods; Controlled Release*

Introduction:

In the dynamic landscape of pharmaceutical research and drug delivery systems, the quest for more efficient, targeted, and patient-friendly methods of medication administration remains a pivotal challenge. The conventional systems, while effective, often grapple with issues such as reduced bioavailability, rapid degradation, systemic side effects, and poor patient compliance. These challenges have catalysed the evolution of drug delivery technology, steering it towards innovative solutions that can overcome the limitations of traditional methods. Among the most promising advancements in this field is the development of proniosomal gel drug delivery systems. Proniosomes, a precursor to niosomes, are dry formulations that, upon hydration, form vesicular systems like liposomes. These novel systems have garnered attention due to their enhanced stability, ease of storage and transportation, and improved drug release profiles.[1] This paper presents a comprehensive exploration of the proniosomal gel as a drug delivery system, delineating its methods of preparation, applications in various therapeutic areas, and the prospective future developments that could reshape pharmaceutical practices. The focus is on understanding how these systems can be optimized for maximum efficacy and patient compliance, especially in chronic treatments where long-term medication administration is pivotal. Proniosomal gels represent a significant leap in addressing the challenges posed by conventional drug delivery methods. By offering a controlled, targeted, and sustained release of therapeutic agents, they Open new avenues for treatment modalities that are not only more effective but also align with the evolving

Article History

- **ISSN**: 2584-184X
- **Received:** 25 Dec 2023
- **Accepted**: 29 Jan 2024
- **Published:** 01 Feb 2024
- **MRR:**2(1) Jan. 2024:34-40

- **Peer Review Process:** Yes
- **Plagiarism Checked**: Yes

Authors Details

Dr. K. Parameshwar
Department of Pharmaceutics, Gurunanak institutions technical campus, School of Pharmacy, Hyderabad, Telangana, India

Dr. Ravula Parameshwar
Department of Pharmaceutical Chemistry, Amity Institute of Pharmacy, Amity University, Gwalior, Madhya Pradesh, India

Megavath Sravani
Department of Pharmaceutics, Gurunanak institutions technical campus, School of Pharmacy, Hyderabad, Telangana, India

Miriyala Akhil Sai
Department of Pharmaceutics, Gurunanak institutions technical campus, School of Pharmacy, Hyderabad, Telangana, India

Mobashshira Khatoon
Department of Pharmaceutics, Gurunanak institutions technical campus, School of Pharmacy, Hyderabad, Telangana, India

Mucha Aditya
Department of Pharmaceutics, Gurunanak institutions technical campus, School of Pharmacy, Hyderabad, Telangana, India

Mukesh.K
Department of Pharmaceutics, Gurunanak institutions technical campus, School of Pharmacy, Hyderabad, Telangana, India

Corresponding Author

Dr. K. Parameshwar
Department of Pharmaceutics, Gurunanak institutions technical campus, School of Pharmacy, Hyderabad, Telangana, India

needs have personalized medicine. Figure 1 shows us the Application of Proniosomal gel. This paper aims to shed light on this innovative technology, providing insights into its potential to revolutionize the way drugs are delivered and experienced by patients. [2]

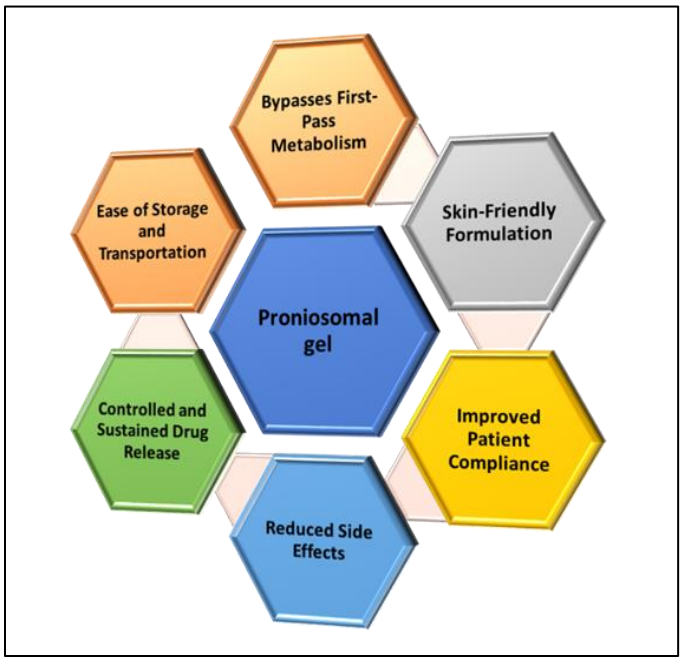

Figure 1: Application of Proniosomal gel

Methods of Preparation

Materials and Components Used [3,4,5]

The formulation of proniosomal gels requires a meticulous selection of materials and components, each playing a crucial role in the efficacy and stability of the final product. The key materials used in the preparation of proniosomal gels include:

Non-Ionic Surfactants

These are the primary components of proniosomes and are responsible for forming the vesicular structure upon hydration. Commonly used surfactants include Span 60, Tween 80, and cholesterol, which aid in stabilizing the vesicle membrane.

Active Pharmaceutical Ingredients (APIs)

The choice of APIs is crucial, as it determines the therapeutic application of the gel. APIs can range across various therapeutic categories, including anti-inflammatory, analgesic, antifungal, and anticancer drugs.

Solvents

Organic solvents such as ethanol, methanol, and chloroform are employed in the initial stages of proniosomal gel preparation to dissolve both the surfactants and the drug. The choice of solvent influences the solubility and encapsulation efficiency of the drug.

Hydrating Medium

Typically, distilled water or phosphate buffer saline (PBS) is used as a hydrating medium to convert the dry proniosomal powder into a gel form, facilitating the formation of niosomes.

Stabilizers and Preservatives

Agents like glycerol, propylene glycol, or PEG (Polyethylene Glycol) may be added to enhance the stability of the gel and prolong its shelf life. Preservatives are also included to prevent microbial growth.

pH Adjusters

The pH of the gel is adjusted to optimize the stability and skin compatibility, using buffering agents as necessary.

Penetration Enhancers

Compounds like limonene or oleic acid are sometimes incorporated to enhance the skin permeation of the drug.

Additional Excipients

Other excipients, such as thickeners or colouring agents, may be added to improve the physical properties and aesthetics of the gel.

Step-by-Step Preparation Process

The preparation of proniosomal gel involves several critical steps to ensure the effective encapsulation and stability of the active pharmaceutical ingredients. The process can be outlined as follows: The **table1** below indicates a combined list of various techniques of Proniosomal gel formation

Solvent Phase Preparation

Begin by dissolving the non-ionic surfactants and cholesterol (if used) in a suitable organic solvent like ethanol or chloroform. This creates a homogenous mixture in which the surfactant molecules are evenly distributed.

Drug Incorporation

The active pharmaceutical ingredient (API) is then dissolved in the solvent phase. Care is taken to ensure complete dissolution of the drug for maximum encapsulation efficiency.

Film Formation

The solvent is evaporated under reduced pressure using a rotary evaporator at a controlled temperature. This process results in the formation of a thin film of the surfactant and drug on the inner walls of the flask.

Hydration and Vesicle Formation
The thin film is hydrated with a suitable aqueous medium, such as phosphate-buffered saline or distilled water, at a specific temperature. This hydration leads to the swelling of the surfactant film and the formation of multilamellar vesicles.The hydration process is often accompanied by gentle agitation to facilitate uniform vesicle formation.

Size Reduction and Homogenization
To achieve the desired vesicle size, the vesicular suspension is subjected to mechanical processes like sonication or high-pressure homogenization. This step is crucial for ensuring uniformity in vesicle size and enhancing the stability of the formulation.

Conversion to Gel
The vesicular suspension is then mixed with a gelling agent, such as Carbopol or HPMC, under continuous stirring to achieve a homogenous gel consistency.
The pH of the gel is adjusted to be compatible with skin pH, using suitable buffering agents.

Encapsulation Efficiency Check
The encapsulation efficiency of the drug within the vesicles is assessed using techniques like centrifugation or dialysis, followed by drug content analysis.

Quality Control and Stability Testing
The final proniosomal gel is subjected to quality control tests including pH measurement, viscosity analysis, and spreadability tests.Stability testing is conducted under various conditions to assess the shelf life and robustness of the formulation Table 2, Table 3.

Factors Affecting the Quality of Proniosomal Gel [6,7]

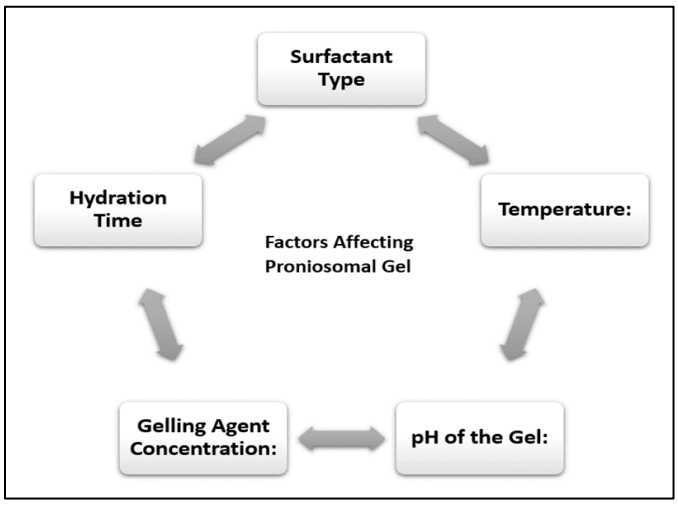

Figure 2: Factors affecting Proniosomal gel

Surfactant Type
The choice of surfactant significantly impacts the stability and encapsulation efficiency of proniosomes. Surfactants with different hydrophilic-lipophilic balance (HLB) values can lead to variations in vesicle size and drug release profiles. For instance, a surfactant with a higher HLB value may form smaller vesicles with a faster drug release rate.

Hydration Time
The time allowed for hydration of the surfactant film affects vesicle formation and size. Insufficient hydration time may result in incomplete vesicle formation, while excessive hydration can lead to larger, potentially unstable vesicles. Optimal hydration time ensures uniform vesicle size and effective drug encapsulation.

Gelling Agent Concentration
The concentration of the gelling agent used to convert the vesicular suspension into a gel plays a vital role in determining the gel's viscosity and spreadability. Higher concentrations of gelling agents typically increase the viscosity, which can affect the skin permeability and release rate of the drug. Conversely, too low a concentration may result in a gel that is too fluid, impacting its stability and application.

pH of the Gel
The pH of the proniosomal gel is crucial for skin compatibility and stability of both the vesicles and the encapsulated drug. A pH that is too acidic or alkaline can lead to drug degradation or vesicle destabilization. Figure 2 shows us the Factors affecting Proniosomal gel

Temperature
The temperature during preparation, especially during the hydration step, can influence the size and distribution of vesicles. Higher temperatures generally increase the fluidity of the surfactant film, potentially leading to larger vesicle sizes.

Drug-Surfactant Interaction
The interaction between the drug and surfactant can affect the drug's encapsulation and release. Drugs with high affinity for the surfactant may show higher encapsulation efficiency but potentially slower release.

Physical Stability
The physical stability of proniosomal gels, in terms of maintaining vesicle size and preventing aggregation over time, is crucial for consistent drug delivery. This stability can be affected by the overall formulation, including the type and concentration of surfactant and gelling agent.

Characterization of Proniosomal Gel

To ensure the efficacy and safety of proniosomal gel drug delivery systems, a comprehensive characterization of their physical and chemical properties is essential. This section of the paper outlines the various analytical methods employed to evaluate the characteristics of proniosomal gels, including vesicle size, drug encapsulation efficiency, and release kinetics. [8,9,10].

Vesicle Size and Size Distribution

Dynamic Light Scattering (DLS)

This technique is utilized to measure the average size and size distribution of the vesicles in the proniosomal gel. DLS provides insights into the homogeneity of the vesicle population, which is crucial for consistent drug delivery.

Transmission Electron Microscopy (TEM) or Scanning Electron Microscopy (SEM)

These methods offer detailed visualization of the vesicular structures, allowing for the assessment of vesicle morphology and size at a microscopic level.

Drug Encapsulation Efficiency

Centrifugation Method: Following the centrifugation of the proniosomal gel, the supernatant is analyzed to determine the amount of unencapsulated drug. The encapsulation efficiency is calculated by comparing this to the total amount of drug used in the formulation.

UV-Visible Spectrophotometry

This method is used to quantify the drug concentration in the supernatant after centrifugation, providing a precise measurement of encapsulation efficiency.

Release Kinetics

In Vitro Release Studies: These studies are conducted using dialysis bags or diffusion cells to mimic the drug release profile in physiological conditions. The rate and pattern of drug release from the proniosomal gel are monitored over a specific period.

HPLC Analysis

High-Performance Liquid Chromatography (HPLC) is employed to accurately quantify the drug release at various time intervals during the in vitro release studies.

Zeta Potential Measurement

Electrophoretic Light Scattering: The zeta potential of the vesicles is measured to assess their surface charge, which is an indicator of colloidal stability. A higher zeta potential generally implies better stability of the vesicle suspension in the gel.

Rheological Properties

Viscometry

The viscosity of the proniosomal gel is measured to ensure appropriate consistency for application. This factor can influence the drug release and skin permeation rates.

Texture Analysis

This test evaluates the spreadability and extrudability of the gel, which are critical parameters for patient compliance and ease of application.

pH and Stability Testing

pH Meter

The pH of the proniosomal gel is assessed to confirm skin compatibility and stability of the drug and vesicles.

Accelerated Stability Studies

These studies are conducted under various temperature and humidity conditions to predict the shelf-life and long-term stability of the gel formulation.

Applications

The versatile nature of proniosomal gels makes them suitable for a wide array of therapeutic applications. This section discusses various medical conditions and drug delivery challenges where proniosomal gels can be effectively utilized, emphasizing their advantages and potential.[11,12]

Targeted Drug Delivery

Cancer Therapy: Proniosomal gels can be used to deliver chemotherapeutic agents directly to tumor sites, minimizing systemic toxicity. Their ability to encapsulate both hydrophilic and hydrophobic drugs broadens their applicability in various cancer treatments. [13,14,15]

Skin Diseases

Due to their enhanced skin permeation properties, proniosomal gels are ideal for treating skin conditions such as psoriasis and eczema. They offer localized drug delivery, reducing systemic side effects common in oral or injectable forms. Table 4.

Enhanced Bioavailability Oral Drug Delivery

For drugs with poor oral bioavailability, proniosomal gels can enhance absorption through the gastrointestinal tract, ensuring a higher concentration of the drug reaches systemic circulation.

Ocular Applications

The gel's ability to adhere to the ocular surface allows for prolonged retention and sustained release of drugs,

beneficial in treating eye diseases like glaucoma. Controlled Drug Release

Chronic Pain Management
Proniosomal gels can be formulated for the sustained release of analgesics, providing long-lasting relief for chronic pain conditions, and reducing the frequency of dosing.

Hormone Therapy
The controlled release feature is particularly advantageous in hormone replacement therapies, where maintaining consistent hormone levels is crucial. Reduced Systemic Side Effects

Gastrointestinal Protection
For drugs known to cause gastrointestinal irritation, proniosomal gels can facilitate direct absorption through the skin or mucosal tissues, bypassing the GI tract and reducing related side effects.

Pediatric and Geriatric Use
Their non-invasive nature makes proniosomal gels suitable for pediatric and geriatric patients who may have difficulties with traditional routes of administration.

Personalized Medicine Customizable Formulations
Proniosomal gels can be tailored to meet individual patient needs, such as adjusting dosages or combining multiple drugs in a single formulation.

Gene Therapy
They have the potential to be used in gene therapy, delivering genetic material efficiently to target cells. Proniosomal gels offer a multifaceted approach to drug delivery, addressing various challenges in medication administration. Their ability to enhance bioavailability, ensure targeted and controlled release, and reduce systemic side effects makes them an asset in modern pharmaceutical formulations, with promising applications across diverse therapeutic areas.

Scope and future prospectives of proniosomal gel [16,17,18,19]
Integration with Emerging Technologies
The future of proniosomal gels lies in their integration with cutting-edge technologies such as nanotechnology, smart drug delivery systems, and precision medicine. This integration could lead to even more targeted, efficient, and personalized treatment strategies.

Scale-Up and Commercialization
Research must now focus on scaling up the production process and addressing the challenges of commercialization. The viability of proniosomal gels in the market will depend on their Cost-effectiveness, stability during storage, and ease of manufacturing.

Wider Clinical Trials and Applications
Extensive clinical trials are necessary to validate the efficacy and safety of proniosomal gels in a broader range of therapeutic areas. Exploring their potential in more diverse medical conditions will be critical in understanding their full capabilities.

Regulatory Approvals and Market Acceptance
Gaining regulatory approval and market acceptance is crucial for the widespread adoption of proniosomal gels. This involves demonstrating consistent quality, safety, and therapeutic efficacy in line with regulatory standards.

Conclusion
In this paper, we have delved into the innovative realm of proniosomal gel drug delivery systems, elucidating their preparation methods, applications, and prospects. The research underscores the transformative potential these systems hold for advancing pharmaceutical formulations and enhancing patient care.

Innovative Preparation Methods
The study highlights the advanced techniques in proniosomal gel preparation, displaying how the strategic selection of surfactants, solvents, and active pharmaceutical ingredients (APIs) contributes to the robustness and efficacy of these delivery systems.

Versatile Therapeutic Applications
Proniosomal gels have emerged as versatile vehicles for drug delivery, demonstrating effectiveness across a spectrum of medical conditions. Their applications range from targeted drug delivery in cancer therapy to improved treatment options in dermatology, pain management, and ocular diseases.

Enhanced Drug Delivery
A significant advantage of proniosomal gels is their ability to enhance drug bioavailability while offering controlled and sustained release. This attribute is pivotal in managing chronic conditions and improving therapeutic outcomes.
Patient-Centric Advantages: The research emphasizes the reduced systemic side effects and improved patient compliance associated with proniosomal gels. Their non-invasive nature and ease of application make them particularly beneficial for diverse patient demographics, including pediatric and geriatric populations. Potential Impact on Future Drug Delivery and Patient Care

Proniosomal gels represent a significant stride in the evolution of drug delivery systems. Their potential to offer targeted, efficient, and patient-friendly drug delivery aligns with the ongoing shift towards personalized medicine. The adaptability of these systems to various pharmacological needs presents an opportunity to refine treatment regimens, reduce adverse effects, and improve patient adherence to therapies.

Implications for Future Research

The exploration into proniosomal gels paves the way for further innovation in drug delivery research. Future studies should focus on expanding the range of drugs suitable for proniosomal encapsulation, exploring synergies with other novel drug delivery technologies, and assessing long-term stability and cost-effectiveness for large-scale production. The integration of proniosomal gels with emerging fields like nanotechnology and precision medicine could further enhance their efficacy and applicability. In conclusion, the development of proniosomal gel drug delivery systems marks a significant advancement in pharmaceutical technology, with the potential to profoundly impact patient care and treatment modalities. Their continued research and development promise to open new avenues in effective, efficient, and patient-centered drug delivery.

Acknowledgement: The authors are thankful to their parents.

Conflict of interest: The authors declare that there is no conflict of interest.

References

1. Jangam RP, Thombre AN, Gaikwad NP. A review: proniosomes as a novel drug delivery system. Asian J Pharm Technol. 2017;7(3):166-174.
2. Bandawane A, Saudagar R. A review on novel drug delivery system: a recent trend. J Drug Deliv Ther. 2019;9(3):517-521.
3. Mahomoodally MF, Sadeer N, Edoo M, Venugopala KN. The potential application of novel drug delivery systems for phytopharmaceuticals and natural extracts–current status and future perspectives. Mini Rev Med Chem. 2021;21(18):2731-2746.
4. Gowri SP, Lakshmi HV, Bhanu VN, Brahmaiah B, Nama S, Rao CB. Proniosome: a novel approach to vesicular drug delivery system. Pharma Innovation. 2013;2(3, Part A):166.
5. Deepika S, Rizwana K, Sharma B. A review on proniosomes drug delivery: An innovative approach. World J Pharm Res. 2020;9:1322-33.
6. Pandey N. Proniosomes and ethosomes: New prospect in transdermal and dermal drug delivery system. Int J Pharm Sci Res. 2011;2(8):1988.
7. Suryawanshi SS, Patil PP, Gaikwad RG, Mali SS, Pol SL. Proniosomes: Modern drug delivery system. Pharm Res. 2021;4(1):7-18.
8. Ashara KC, Paun JS, Soniwala MM, Chavda JR, Nathawani SV, Mori NM, Mendapara VP. Vesicular drug delivery system: a novel approach. Mintage J Pharm Med Sci. 2014;3(3):1-14.
9. Kumari R, Verma K, Verma A, Yadav GK, Maurya SD. Proniosomes: a key to improved drug delivery. J Drug Deliv Ther. 2014:56-65.
10. Parameshwar K, Sahoo SK. A review of merely polymeric nanoparticles in recent drug delivery system. Asian J Pharm Clin Res. 2022;15(4):4-12.
11. Reddy MR, Jha SK, Parameshwar K. Role of various natural and synthetic polymers in development and in-vitro characterization of oral controlled drug delivery system of fexofenadine. Pharm Res. 2018;8(03).
12. Vakkalagadda RK, Ravula P, Parameshwar K, Saraswathi K, Sindhuri P, Srikala R, Sandeep K. Protective Potential of Canthium dicoccum Methanolic Extract Against Hepatic Injury in Rats. Pharmacogn J. 2021;13(6s).
13. Suresh C, Parameshwar K, Sandeep K. Formulation and evaluation of colon specific drug delivery of Eterocoxib by using Okra Gum. Asian J Pharm Pharmacol. 2017;3(6):238-246.
14. Rasheed SH, Vakkalagadda RK, Mustak S, Sen S. In silico Based Virtual Screening of Non-polar Phytochemicals obtained From Petroleum Ether Extract of Asparagus racemosus by GC-MS Analysis. Pharmacognosy Res. 2023;16(1).
15. Neelamma G, Rasheed SH, Vinukonda A, Aruna M. In-vitro screening for cytotoxic activity of herbal plant extracts on N2a cell lines. Res J Pharm Tech. 2021;14(4):2009-2012.
16. Ravula P, Babu H, Manichandrika P, Ramanachary N, Narendra Sharath Chandra JN. Microwave assisted synthesis, biological evaluation and docking studies of novel pyrazoline derivatives as potent antiinflammatory and antibacterial agents. Int J Chem Sci. 2016;14(2).
17. Gulipalli KC, Bodige S, Ravula P, Endoori S, Vanaja GR, Babu GS, et al. Design, synthesis, in silico and in vitro evaluation of thiophene derivatives: A potent tyrosine phosphatase 1B inhibitor and anticancer activity. Bioorg Med Chem Lett. 2017;27(15):3558-3564.
18. Suresh C, Kondapuram P, Sandeep K, Rajesh VB. Development, Optimization and Characterization of Orudis Niosomal Drug Delivery System. NeuroQuantology. 2022;20(15):337.
19. Sabareesh M, Yanadaiah JP, Sekhar KC. A novel vesicular approach for transdermal administration of enalapril maleate loaded nanoproniosomal gel: Formulation, ex vivo evaluation and in vivo

antihypertensive study. Int J Appl Pharm. 2020;12(5):190-202.