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Emerging Era of Nanomedicine and Nanotechnology : Proniosomal Transdermal Drug Delivery System

Ms Saba Khan[1]*, Mrs Jaya Agnihotri[2], MsAlina bi shaikh[3], MsMahnaz sayyed[4], Mr Masnoon Khan[5], Mr Arif Khan[6]

[1]HKCP, Masters Research Student, Department of Pharmaceutics, Mumbai, Maharashtra, India
[2]HKCP, Associate professor, Department of Pharmaceutics, Mumbai, Maharashtra, India
[3,4,5,6]HKCP, Final year Student, Mumbai, Maharashtra, India

Corresponding Author:** ***Ms Saba Khan, *HKCP, Masters Research Student, Department of Pharmaceutics, Mumbai, Maharashtra, India*

Abstract: *Scientists dedicated their efforts to enhancing drug delivery methods while preserving the integrity of these methods' undesirable traits. This dedication ultimately resulted in the creation of proniosomes, a revolutionary medication delivery system. Due to their unique benefits, proniosomes stand out from niosomes and liposomes. These proniosomes are made of non-ionic, water-soluble dry formulations that are added to a carrier system. Upon hydration, these proniosomes transform into niosomes, effectively addressing the instability issues associated with traditional delivery systems. Niosomes, in turn, exhibit tremendous potential for improving the dissolution, accessibility, and absorption of a wide range of medications, whether they are hydrophilic or hydrophobic. Additionally, proniosomes offer a versatile approach to drug delivery, enabling precise medication delivery to the desired target site. The risk of unwanted side effects is reduced by this regulated release technique. Recognizing and understanding the limitations of each study is imperative since each research approach possesses its unique set of advantages and drawbacks. Observational studies can employ a variety of design methodologies, including ecological, prospective, retrospective, case-control, case-crossover, or cross-sectional cohort designs. In the realm of diagnostic research, a critical subset of observational experiments is dedicated to comparing the accuracy of different diagnostic methods and tests against established diagnostic benchmarks. It is essential to underscore that biomedical research heavily relies on data collected through rigorously validated scientific methodologies and employs appropriate statistical methods to derive meaningful insights. Consequently, selecting a robust study strategy is paramount in ensuring an objective and impartial evaluation of research inquiries. This comprehensive review encompasses a wide array of facets related to proniosomes, encompassing their advantages, preparation techniques, mechanisms of action, materials and specifications, study designs, as well as characterization and evaluation parameters.*

Keywords: *Proniosomes, Carrier, Transdermal, skin permeation, Application.*

1. INTRODUCTION

Proniosome

In a dry formulation, proniosomes represent carrier particles coated with surfactants that possess water solubility. When agitated within a hot water solution, these proniosomes rapidly rehydrate, forming a niosomal dispersion suitable for the application. One noteworthy characteristic of proniosomes is their ability to maintain physical stability during storage and transportation.

Medications enclosed within the vesicular structure of proniosomes experience several benefits. They enjoy an extended shelf life within the bloodstream, achieve enhanced tissue penetration, and exhibit reduced toxicity. From a technical standpoint, niosomes emerge as highly appealing drug carriers due to their superior chemical stability and the absence of various drawbacks associated with liposomes, including elevated production costs and variability in phospholipid purity [1-4].

Proniosomes have attracted the attention of researchers since the early 1980s, primarily due to their potential applications as both pharmacological carriers and targets. These applications offer numerous

advantages compared to conventional medication delivery methods while effectively addressing associated disadvantages [5].

2. MECHANISM OF ACTION

Proniosomes are niosomes in an inactive state that must be transformed into active niosomes by a procedure known as hydration. There are two different ways that this hydration can take place:

According to the figure, the proniosome is a stage amidniosome production. There are two strategies to transform the proniosome formulation into niosomes [6–8].

1 **Skin-Driven Hydration:** The proniosome formation and conversion to niosomes are hydrated by the water in the skin. This hydration is accomplished by the skin itself.

2. **Solvent-Mediated Hydration:** Proniosomes are transformed into niosomes using aqueous solutions, such as pure water, saline solution, and buffers, with or without agitation and sonication. [9-11].

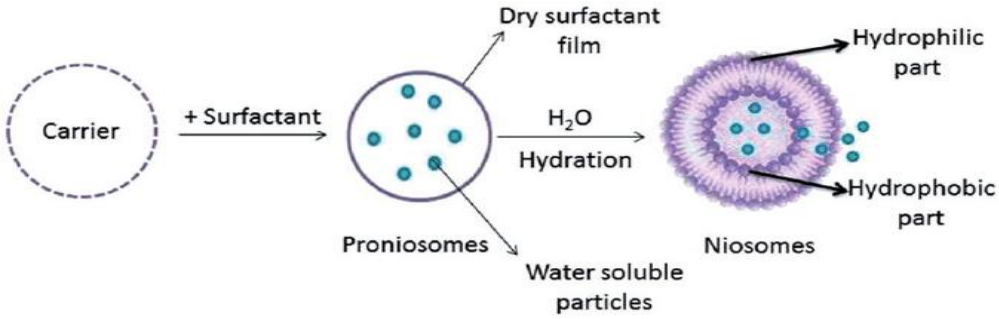

Fig1.

Methods for delivering medication through the skin, known as transdermal delivery methods, utilize various strategies to effectively penetrate the skin. These techniques capitalize on the unique properties of the skin to ensure proper absorption of medications. Here are a few important approaches [12-15]

a) Transfers:

Transfers represent a type of transdermal delivery method that is characterized by their ability to deform without causing harm. This flexibility enables them to navigate through the outer layer of the skin and efficiently deliver medications.

b) Ethosomes:

Ethosomes offer another approach utilized in transdermal drug delivery. These vesicles composed of lipids are specifically designed to disrupt the dense structure of the epidermis upon entry into the body. Through this mechanism, they facilitate penetration of medications, thereby ensuring effective absorption occurs

c) Proniosomes and Niosomes:

Proniosomes and niosomes are innovative delivery systems that utilize surfactants. These surfactants help improve the penetration of medications into the skin. They aid in the transportation of medications through the layers of the skin and improve the solubility of pharmaceuticals.

Any molecule applied topically must first get beyond the skin's barrier, which is made up of the Stratum Corneum (SC) and the viable epidermis, regardless of the precise method used. Successful transdermal distribution hinges on successfully overcoming this barrier, which serves as the first line of defence.

In conclusion, transdermal medication delivery methods employ various techniques to ensure the efficient and safe absorption of drugs through the skin. Each approach has its unique characteristics

and advantages, making them valuable options for delivering medications to the body. However, it is crucial to consider the specific needs of the patient and the medication being administered when choosing the most suitable transdermal method.

3. ADVANTAGES OF PRONIOSOMES TRANSDERMAL DRUG DELIVERY TOOL

4. STRUCTURE OF PRONIOSOMES

a) Lamellar tiny structures make up proniosomes. They mix cholesterol with a non-ionic surfactant of the alkyl or dialkyl polyglycerol ether type, then hydrate it in water. To create the bilayer, the surfactant molecules direct themselves such that the hydrophilic ends of the non-ionic surfactant face outward and the hydrophobic ends face inside. Proniosomes include a bilayer, just like liposomes do. Proniosomes have a bilayer comprised of substances with non-ionic surface activity. [20,21]

b) Proniosomes can be either unilamellar or multi-lamellar depending on the preparation procedure. The proniosome is composed of a surfactant bilayer with hydrophilic ends exposed on the exterior and interior of the vesicles and hydrophobic chains facing one another within the bilayer. Thus, hydrophilic medications are held within the vesicle's confined region, and hydrophobic drugs are incorporated within the bilayer. [22,23].

c) Proniosomal gel has a unique structural makeup and might appear as a transparent, translucent, or semisolid gel. Due to the presence of a small amount of solvent, these proniosomes exhibit a variety of liquid crystal phases, including lamellar, hexagonal, and cubic.

d) Surfactant sheets are arranged in a bilayer configuration during the lamellar phase. While the cylindrical structure of the hexagonal phase is firmly packed and structured in a hexagonal pattern. A continuous, curved lipid bilayer that extends in three dimensions is present in the cubic phase [24].

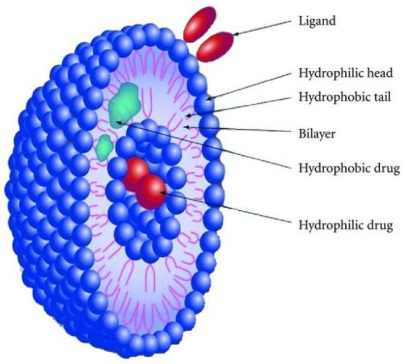

Figure2.

5. APPLICATION

Sr no	Application	REFERENCE
1	**Niosomes in Cosmetics** Niosomes have shown superior efficacy in delivering enoxacin compared to liposomes or standalone active components. This suggests that niosomes can be a valuable tool for delivering larger molecules to the skin, particularly when the skin's barrier function is slightly compromised.	Wu, X.eta l [2]
2	**Niosomes for the Delivery of Ingredients to Prevent Scarring** In terms of improving papain penetration, promoting transdermal absorption, and lessening scarring, elastic noisome particles fared better than normal nanomaterials. Gallic acid's chemical stability and epidermal penetration were both improved by these annoying particles, indicating their viability as anti-ageing drug carriers.	Chen, S et al[26],Cerqueira-Coutinho, C et al [27]
3	**Application on the Hair** The utilization of niosomes not only ensures that the hair maintains a healthy, non-greasy, and silky feel but also aids in the repair of damaged hair. Furthermore, it restores the hair's natural tone, resulting in a shinier and more vibrant appearance.	Abu Hajleh et al [28]
4	**Prolonged release** Niosomal encapsulation can be used to provide medications that have a poor therapeutic index and low water solubility with the prolonged release action of pronisome so that the drugs remain in circulation for a longer period.	Biju SS et al [29]
5	**Uses For Understanding Immunological Response** Niosomes were used for an immune response investigation because of their immunological selectivity, low toxicity, and higher stability. The greatest tools for examining the nature of the immune response triggered by antigens are niosomes and protoniosomes.	Kakr R et al [30],Chandra A et al [31]
6	**Peptide medication delivery** Niosomes were used to circumvent a significant problem of oral peptide medication delivery—bypassing the enzymes, which causes a breakdown of peptide and protein bonds. It was successful in preventing gastrointestinal peptide breakdown and preserved the peptides.	Akhilesh D et al [32]
7	**Proniosomes as haemoglobin carriers** Niosomes can also be used as carriers for haemoglobin inside the blood, according to research (Moser P. and Marchand Arvier M. in 1989). The niosomal vesicle can be used as a carrier of haemoglobin in anaemic patients since it is oxygen permeable.	Sudhamani T [33], Kakar R 34,Sankar V et al [35]
8	**Hormone delivery** Work has been done on the transdermal delivery of the emergency contraceptive levonorgestrel using proniosomes. The corpora lutea was blocked and endometrial samples were tested as part of the bioassay study's progestational activity.	Vora B et al [36]
9	**Proniosomes in phytochemical drugs (curcumin)** Proniosomes encapsulated Curcumin for transdermal administration Curcumin offers diverse therapeutic benefits, but its poor solubility in acidic environments hinders oral absorption and bioavailability. Transdermal drug delivery, specifically using SPAN80-based proniosomal systems, can address these issues and enhance Curcumin's therapeutic effects. Cholesterol aids in dissolving Curcumin and improves drug penetration, while higher SPAN-80 concentrations boost encapsulation efficiency.	Kumar K and Rai AK et al [37]
10	**Anti-neoplastic Treatment** The encapsulation of drugs like Doxorubicin and Methotrexate in niosomes has shown significant benefits compared to unentrapped or uncoated drugs. These advantages include a slower rate of body clearance, higher plasma drug levels, and a slower rate of tumour multiplication.	Sudhamani Tet al [33],Kakar R et al 34,Sankar V et al [35]

6. Material And Methodology

Material:

Sr no	Material	Role	Action	References
1.	Span, tween	Non-ionic surfactant	Maintains the Hydrophilic-Lipophilic Balance (HLB) level, increases the rate at which drugs are absorbed via the skin	Vora B et al[36],Politis S et al[38],Friston KJ et al[39]
2.	Cholesterol ,Soya lecithin	Stabilizers	The permeability and stability of vesicles are significantly modulated by cholesterol. Soya Lecithin serves as an enhancer for penetration. Lecithin's primary function is to maintain the stability, permeability, and structural integrity of vesicles, resulting in improved penetration properties.	Solanki AB et al [40], Amaro E et al [41]
3.	Glucose monohydrate, lactose monohydrate,Sucrose stearate, Mannitol, Polyols, and Maltose	Carriers	It holds the drug	Solanki AB et al [40],Amaro E et al [41]
4.	Methanol, chloroform, ethyl alcohol	Organic solvent	Impact drug vesicle and penetration	Solanki AB et al [40]

Various Method used for Preparation [42-46]

1) Method of Coacervation Phase Separation

To generate a transparent dispersion, a mixture of lipids, a surfactant, and medication is blended with a solvent and subjected to heating in the temperature range of 60 to 70°C using a water bath.

Product type Translucent gel

2) Slurry Technique

An organic solution is prepared by combining cholesterol, surfactants, and medication. This mixture is then poured over a carrier medium to generate a slurry. To achieve proniosomes with optimal flow properties, it is advisable to employ rotary evaporators for efficient solvent evaporation.

Product type powder

3) Method of Spray Coating

A rounded-bottom flask connected to a rotary evaporator is utilized to sequentially spray organic solutions containing cholesterol, surfactants, and medication onto a carrier material.

Product type powder

7. Evaluation of Proniosomes

Sr no	Parameters	Technique	References
1.	Angle of repose	Funnel approach Cylinder approach	Raymond CR et al [47],Radha GV et al [48]
2.	Particle/vesicle size and size distribution	The Malvern master size, Coulter submicron size analyzer, optical microscopy, photon correlation, laser diffraction particle size analyzer	Sankar V et al [35], Nasr M [49]
3.	Aerodynamic behavior	Twin stage impingement	Abd-Elbary Aet al [50]
4.	entrapment efficiency	Using alcohol and propylene glycol to lyse vesicles	Sankar V et al [35]
5.	Shape and surface morphology	Transmission electron microscopy, optical microscopy, and scanning electron microscopy	Sankar V et al [35]

6.	Sieve fractionation	Fritsch analysts sieve shaker	Waghmode M et al [51]
7.	Spontaneity	Neubauer chamber	Parthibarajan R et al [52]
8.	Separation of unentrapped drug	Centrifugation, ultracentrifugation, gel filtration, and exhaustive dialysis	Yadav K, Yadav D et al [53]
9.	In vitro drug release studies	Keshary-chein diffusion cells, Franz diffusion cells, Dialyzing membrane made of cellophane, molecular porous membrane tubing called Spectarpor, USP dissolving device, in vitro skin permeation studies	Prakash SG et al [54]
10.	In vivo studies	Different types of animals, such as rats, mice, rabbits, and guinea pigs, can be used for in vivo investigations.	Fang SCet al [55],Raymond CR et al [56]
11.	Stability studies	According to ICH recommendations, at various temperatures including refrigeration (2°-8°C), room temperature (25°C 0.5°C), and increased temperature (45°C 0.5°C) for a period of one to three months.	AnchalSankhyan et al [56]

8. Conclusion

Proniosomes are surfactant-coated carrier particles that dissolve in water. Just before use, they can be immediately hydrated, producing an aqueous niosomal dispersion. Compared to niosomes and liposomes, pheniosomes are more stable. They have several outstanding qualities that make them useful for transdermal medication delivery, including the capacity to encapsulate both lipophilic and hydrophilic medicines. Due to their simple and affordable production scaling procedure, proniosomes have become a popular dosage form for transdermal medication administration. Proniosomes have successfully solved stability issues, such as fusion and aggregation during storage, that are frequently encountered with niosomes and liposomes.

9. Future Scope

Proniosome-derived niosomes have revolutionized pharmaceutical research, offering targeted therapeutic benefits. The potential for these carriers extends to nutraceuticals, herbal compounds, cosmetics, and peptide delivery, addressing enzymatic degradation challenges. Proniosomes also hold promise for vaccines, minimizing adverse drug effects, and treating anaemia. To realize their full potential, further research and industrial-scale studies are needed, but challenges must be met to establish their suitability for diverse drug and product deliveries.

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