Proniosomes: A Novel Drug Delivery System

Mayuri S. Pachpol, Dr. Shivshankar Mhaske, Sanjana Bali
Satyajeet College of Pharmacy, Mehkar

Abstract: Proniosomes are water-soluble carrier particles covered with surfactant in a dry formulation. They rehydrate in hot aqueous media upon agitation, producing niosomal dispersion. Nanotechnology is increasingly used in drug delivery to develop new dosage forms, such as the vesicular drug delivery system. Proniosomes minimize physical stability issues like aggregation, fusion, and leakage, allowing them to be used in various routes, prolonging drug presence and reducing toxicity. They are sconsidered useful for medicinal and cosmetic uses, and their preparation, characterization, in vitro drug release, entrapment efficiency, and applications in the market are discussed.

Keywords: Proniosomes, Drug Carriers, Types, Method of Proniosomes.

INTRODUCTION

Proniosomes are a dry mixture of surfactant-coated, water-soluble carrier particles. Within minutes of being agitated in hot aqueous conditions, they are rehydrated to form niosomal dispersion.

Enhancing plasma concentration is the primary objective of designing controlled and targeted release dosage forms in order to increase the therapeutic impact, increase the safety margin, and reduce side effects of pharmaceuticals.

When used as medication delivery systems, colloidal particle shapes like proniosomes offer clear benefits over traditional dosage forms. Proniosome technology offers a novel method for medications with poor solubility. Both hydrophilic and hydrophobic medications can be entrapped by proneosomes. These are the most sophisticated drug carriers in the vesicular system, and they are composed of cholesterol, non-ionic surfactants, and other compounds. Encapsulation of drugs in any of the vesicular system should increase the length of time a medicine is in the bloodstream, which will improve its bioavailability and therapeutic effectiveness. These technologies are widely used to improve medication penetration, pharmacological targeting, and controlled release. Hydrophilic medications can be encapsulated in the core cavity of proneosomes, also referred to as amphiphilic vesicles, while hydrophobic pharmaceuticals can be encapsulated in the non-polar area of the bilayer. Furthermore, it is a simple method of regularly and extensively producing proniosomes without the use of hazardous solvents. Even protosomes have benefits as drug carriers over liposomes in terms of cost, productivity, and chemical stability, but stability is a key consideration when creating any formulation.

The necessity to get beyond the drawbacks of niosomes—lipid-based vesicles made of non-ionic surfactants—led to the development of the proniosome concept. various carriers—polymeric, particulate, macromolecular, etc.—are being employed. Lipid particles, microspheres, and nanospheres are a few examples. In comparison to niosomes and liposomes, pheniosomes are easier to transport, sterilize, distribute, and store. Both proniosome-derived niosomes and regular niosomes are more stable, according to their release profiles. To maintain the vesicles' chemical and physical integrity, proneosomes were made as a dry powder and reconstitution was performed prior to usage. Proniosomes were created as a gel for transdermal distribution. These gel-like structures offer the benefit of being scalable improved physicochemical stability and the capacity to penetrate the skin. Proniosomes share many of the same problems as liposomes, but they have superior chemical stability, making them attractive as drug carriers. In terms of both size distributions and release performance, proniosome-derived niosomes outperform traditional noisomes. Controlling the release of a medication into the systemic circulation is the main function of these carriers, which can also serve as drug reservoirs. Because of the minimum solvent system, the resulting proniosomes are mixes of many liquid crystal phases, including lamella, hexagonal, and cubic phase liquid crystals (Tiddy, 1980). Compared to traditional dosage forms, colloidal particle shapes like proniosomes provide clear advantages as drug delivery platforms. Because niosomes and liposomes are particulate, they act a They have an advantage over other traditional dose forms because of their drug reservoir.

Drugs are delivered to the target location in the body part, such as a tissue organ, using a variety of carriers, such as niosomes, proniosomes, liposomes, microspheres, electrosomes, phytosomes, etc. The carriers should be free-flowing, non-toxic, and safe. They should also have good water solubility for convenient hydration and poor solubility in the loaded mixed solution. Numerous carrier systems and technologies have been thoroughly investigated recently in an effort to regulate drug release and enhance formulation efficacy and selectivity. Recently, a maltodextrin-based proniosome formulation was created with potential uses in the delivery of hydrophobic or amphiphilic medications. When dry phosphorosomal powder is used, a unit dose of the drug can be delivered with improved drug stability and solubility.

From early 1980s, niosomes (Schreier and Bouwstra, 1994, Baillie et al., 1985) have gained wide attention by researchers for their use as drug targeting agents, drug carriers to have variety of merits while avoiding demerits associated with the conventional form of drugs. Proliposomes are composed of water soluble porous powder as a carrier upon which one may load phospholipids and drugs dissolved in organic solvent. Problems with the physical stability of aqueous suspensions of liposomes have been addressed by Payne et al. (1986a,b) who introduced ‘proliposomes’, a dry free-flowing granular product which could be hydrated imediately before use. K.R. Cho, I. Shih, S. leM, Ovarian cancer, Annu. Rev. Pathol. 4 (2009) 287–313. Proniosomes have drawn a lot of attention from researchers since the early 1980s. because they could be used as carriers and targets for pharmaceuticals. These applications offer several advantages over traditional drug delivery techniques while minimizing drawbacks.

REVIEW OF LITERATURE

1. Bhoomika Malete (2024) In the improvement of new measurements structures, drug conveyance utilizing nanotechnology is assuming a crucial part. Vesicular medication conveyance frameworks have acquired wide consideration in the area of nanotechnology, for example, niosomes , liposomes and proniosomes. Proniosomes address a promising medication conveyance innovations and much exploration must be motivated in this to sift through all the potential in this clever medication conveyance frameworks.

2. Sehrash Ansari (2022) Proniosomes are water-soluble carrier particles covered with surfactant in a dry formulation. They immediately before use, upon agitation in hot aqueous media, rehydrate to produce niosomal dispersion. Proniosomes are physically stable while being transported and stored. They avoid many of the problems associated with aqueous dispersion of contaminants, such as physical stability issues such as aggregation, fusion, and leakage They are known to provide comfort during transport, delivery, storage, and dosing.

3. Jadupati Malakar (2011) In last few decades, the thought like proniosome or proniosome derived niosome drug delivery systems have been brought a new dimension in pharmaceutical research and also extensively accepted by the researcher in targeting the particular organ or tissue destination for better treatment. It can be used as non-invasively through transdermal drug delivery system as well as oral drug delivery system. In case of vesicular system, niosomes are well accepted because it has high chemical stability as well as low cost in comparison to conventional liposomal system.

4. Sunitha Reddy M(2020) Nanotechnology is the advancing technology which is based on the study of manipulating the matter on a Nano scale range, and it refers to the constructing and engineering of the functional systems at atomic level. Nanotechnology lead to the development of various types of novel drug delivery systems like liposomes, microparticles, niosomes and proniosomes. Liposomes and niosomes has some demerits like leaking, fusion, aggregation, distribution, transportation and storage.

5. Shakya Deepika(2020) The main aim of drug therapy is to provide therapeutic effect of drug to precise site in the body instantly achieve and then preserve desired drug concentration in order to produce preserve effect. conventional pharmaceutical dosage forms are incapable of controlling the rate of drug delivery to the target site, that result the substantial distribution of drugs in the non- target tissue and body fluids required therapeutic doses that could far exceed the amount necessary in target cells, that was the higher dosage usually lead to dangerous for health during treatment and after treatments

6. Nazim Uddin(2024) Nanotechnology has come a long way, and it has helped a lot in creating new nanocarriers for controlled drug transport. Niosomes were made by proniosomes, which is a lasting predecessor. Their technology has been around for twenty years. Several research papers have been written about the study of how to use Proniosomes to make a controlled drug delivery system (Khatoon et al., 2017). But in order to fully understand and research the many uses of this approach—using prometheosomes as a nasal drug delivery system.

7. Rawia M. Khalil (2016) The vesicles of proniosomal gels fulfill the need for an ophthalmic drug delivery system that has the convenience of a drop that will localize and maintain drug activity at the site of action, also allows for an improved solubility and transport of the drug enclosed in the vesicles through the cornea.

8. Ashwini A. Bachhav (2018) Proniosomes offer a vesicle delivery concept with the potential for drug delivery via the transdermal route.The aim of this work is to search best penetration enhancers in proniosomes as a transdermal delivery system for Piroxicam. Piroxicam is a widely used potent non-steroidal anti-inflammatory drug, with due potential for dermal delivery. This was done with the goal of optimizing the composition of proniosomes as transdermal drug delivery systems.

9. V. Sarovar Reddy (2017) Proniosomes were studied as alternatives to liposomes and other carrier systems for entrapping both polar and nonpolar or hydrophobic and hydrophilic drugs. The additional merits with proniosomes are low toxicity owing to non-ionicnature, no requirement of special precautions and conditions for formulation and preparations.

Niosomes:

These non-ionic surfactant vesicles which are capable of entrapping (or) encapsulating both

hydrophilic and lipophilic drug as similar to that of liposomes.

 They are less toxic due to their non-ionic nature.

 The large-scale production of niosomes does not require any special conditions .

Demerits -

- Aggregation.

- Physical instability.

- Leaking of entrapped drug on storage.

- Time consuming for traditional method of preparation.

- Involves specialized equipment.

- Hydrolysis of encapsulated drugs which reduces the shelf life of the niosomal suspension.

To overcome the demerits of niosomes, proniosomes are prepared and reconstituted to produce

niosomes.

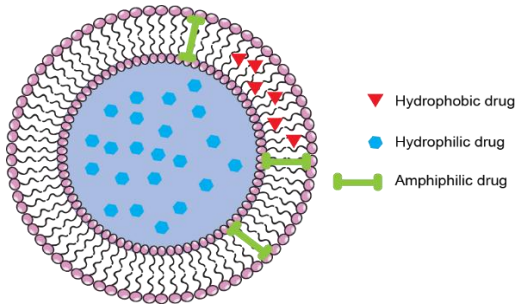
History of Proniosomes:

After over twenty-five years of research to the highest level, Liposome was the first formulation to receive approval for use in humans. Liposomes, however, are not very effective when administered orally and encounter issues with physicochemical stability, including oxidation, phospholipid hydrolysis, fusion, sedimentation, and aggregation. The proliposome technique has made significant progress in dealing with these stability difficulties through the use of a dry, free-flowing product that shows greater stability after sterilization and storage . As more effective drug carriers, niosomes out perform liposomes in terms of chemical stability, drug entrapment efficiency for both hydrophobic and hydrophilic medicines, and reduced toxicity because they are non-ionic. However, niosomes experience physical stability issues such leakage, fusion, aggregation, and sedimentation, much like liposomes do.

Proniosomes can get around these issues. Proliposomes are free-flowing, dry powder formulations that include phospholipid-coated, water-soluble carrier particles that dispersion to create a multilamellar liposomal suspension when water is added. With these benefits, the preparation of proliposomes requires technological challenges such as the need of a nitrogen environment or vacuum during preparation and storage to prevent phospholipid oxidation. Proniosomes are dry, free-flowing formulations of the surfactant-coated carrier, which can be rehydrated by brief agitation in hot water to form a multi-lamellar niosome suspension suitable for administration by oral or other routes.

Structure of Proniosomes:

Proniosomes , a microscopic lamellar structure, is composed of non-ionic surfactants with cholesterol. [El-Laithy HM, Shoukry O, Mahran LG. Novel sugar esters proniosomes for transdermal delivery of vinpocetine: Preclinical and clinical studies. Eur J Pharm Biopharm 2011; (1). Proniosomes are microscopic layered structures. Non-ionic surfactants of the alkyl or dialkyl polyglycol ether class are combined with cholesterol and then hydrated in an aqueous medium. Surfactant molecules are aligned such that the hydrophilic ends of the non-ionic surfactants face outwards, and the hydrophobic ends point in the opposite direction to form a bilayer.Hydrophilic drugs are placed at intervals in the area encircled within the vesicle and the hydrophobic medication is implanted within the bilayer.



On the basis of method of preparation proniosomes are unilamellar or multi-lamellar. The niosome is made of a surfactant bilayer with its hydrophilic ends exposed on the outside and inside of the vesicles while the hydrophobic chains face each other within the bilayer. Hence the vesicle holds hydrophilic drugs within the space enclosed in the vesicle and the hydrophobic drugs are embedded within the bilayer. Proniosomes are transparent, translucent, or semisolid gel in nature because of containing alimited solvent and these are a mixture of lamellar, hexagonal, and cubic liquid crystals. If the amount of solvent is increased further, a spherical structure is formed which is termed as multi-lamellar and multi-vesicular resulting in complete hydration thereby niosomes are formed.

The structural components present in proniosome are:

Cholesterol (a steroid derivative, which is used to provide rigidity and proper shape, conformation to proniosome form) Non-ionic surfactant, Drug , Solvents, such as – ethanol, propanol, butanol, isopropanol, phosphate buffer, and glycol, etc.

Carrier materials, such as – mannitol, spray-dried lactose, maltodextrin, sorbitol, etc. Charge inducing molecule The non-ionic surfactants used for the preparation of proniosome are- The alkyl or Dialkyl polyglycerol, Alkyl or Dialkyl ethers, Span (64, 20, 85, 80) , Tween (20, 40, 60,80) , Brij (35, 73, 92, 95).

Advantages Of Proniosomes:

1. Avoids stability related issues such as aggregation, fusion, and sedimentation.Avoiding hydrolysis of encapsulated drugs that restricts the dispersion shelf life.
2. They are osmotically active and stable, as well as they increased the stability of entrapped drug Handling and storage of surfactants required no special conditions.
3. Proniosomes were easily prepared and did not require special conditions of storage as like other vesicular systems.
4. They can carry both hydrophilic and hydrophobic drugs.
5. Extensively used in drug targeting for controlled release.
6. Easy to handle, storage, and transportation.
7. Dose uniformity in sterilization, transport, delivery, storage, and scale-up is not difficult.
8. Enhanced bioavailability.
9. Sustained drug release.
10. Biocompatible, biodegradable, and non immunogenic to the body.
11. Enhanced penetration and diffusion of drugs.
12. Proniosomes are not only a convenient way to supply drugs but can also improve the rate of skin barrier recovery.
13. Proniosomes have higher advantages such as additional convenience of dosing, storage, transportation, and distribution.

Mechanism Of Action :

One kind of slowly niosome that requires hydration to change into its dynamic forms is the proneosome. Hydration can be achieved in two ways: first, by exploiting the skin's natural moisture content; second, by employing solvents like water or a support. Transdermal prescription delivery methods employ a variety of skin entrance strategies. Certain ones, like as transfers, may bend and pass through the skin without causing harm. As they enter the body uninjured, some varieties, like ethosomes, disrupt the epidermis's thick structure. Other varieties, such niosomes and proniosomes, pierce the skin more deeply by using surfactants. The SC and practical

epidermis should be the first to be penetrated by the topically controlled particle.

Types Of Proniosomes :

According to the method used for planning proniosomes, there are basically two types.

1. Dry Granular Proniosomes
2. Liquid Crystal Proniosomes

1. Dry Granular Proniosomes

a. Sorbital-based Proniosomes

b. Maltodextrin-based Proniosomes

2. Liquid Crystal Proniosomes

1.Dry Granular Proniosomes :

Dry granular proniosomes encapsulate water-dissolvable transporters like sorbitol and maltodextrin by forming a dry coating, which covers each water-soluble particle with a thin layer of surfactant. The vesicles must be prepared above the proniosomes' progress temperature of the surfactant. For the dry granular type of proteosomes, water-soluble carriers like sorbitol and maltodextrin are coated with a surfactant. A dry formulation with a thin film of surfactant covering each water-soluble particle is the end result of the coating process. The vesicles must be prepared at a temperature greater than the transition temperature of the non-ionic surfactant needed for the formulation (Hu and Rhodes, 1999; Arunothayanun et al., 2000; Blazek-Welsh and Rhodes, 2001a, b).

A.Sorbital -based Proniosomes :

Sorbitol is used as a transporter in sorbitol-based pronesomes, a type of dry plan. After adding hot water and fermenting, the non-ionic surfactant is utilized as a niosome and is additionally coated in sorbitol. Sorbitol-based proniosomes are usually produced by spraying a surfactant mixture including an organic solvent, followed by the solvent's evaporation. Until the desired surfactant coating is obtained, the process must be repeated. Sorbitol-based proniosomes are a kind of dry formulation where sorbitol acts as a carrier. In just a few minutes, it can be used as a noisome by adding hot water and stirring after being further coated with a non-ionic surfactant. Sorbitol is used in the dry formulation of sorbitol-based proniosomes.

B.Maltodextrin -based Proniosomes :

Proniosomes based on maltodextrin Proniosomes containing maltodextrin are made using the slurry process. Maltodextrins are a great solvent in water and are employed as a transporter material in the structure. The surface area is similarly increased by the empty molecule. Maltodextrin-based proneoses can be employed to deliver amphiphilic or hydrophilic drugs. The rapid slurry method is used to manufacture proniosomes based on maltodextrin. The utilization of hollow maltodextrin particles increases the proniosome's surface area, resulting in a thinner surfactant coating that is appropriate for rehydration. The rapid slurry method is used to manufacture proniosomes based on maltodextrin. These formulations involve the addition of maltodextrin and a surfactant solution in an organic solvent to create a slurry. Later, the organic solvent evaporates form a dry powder.

2. Liquid Crystalline Proniosomes :

The three processes by which water interacts with surfactant molecules to transform their lipophilic chains into a dispersed fluid state known as a lypotropic fluid crystalline state. The three distinct approaches are listed below:-

1) The increasing temperature at Kraft's location

2) The addition of lipid-breaking solvents

3) Making use of both dissolvelable and temperature

These proniosomes serve as reservoirs for the drug's transdermal distribution. Aluminum foil and a plastic sheet are used as baking materials for the transdermal patch. After evenly applying pronesomal gel to the circular plastic sheet, a nylon mesh is placed over it. Aluminum foil is used as the baking material for the transdermal patch, which is then covered with nylon mesh. Among the many benefits of liquid crystalline proniosomes are their stability, high entrapment efficiency, capacity to improve penetration, and ease of scaling up.

Materials Used For The Preparation of Proniosomes :

1. Surfactant

2. Cholesterol

3. Lecithin

4. Hydration medium

5. Organic Solvent

6. Carrier Material

Surfactant :

In the formation of proniosomes, surfactants—especially non-ionic surfactants—play crucial structural roles. Due to their polar head and non-polar tail, these surfactants are uncharged. When compared to other surfactants, the non-ionic surfactant shows better compatibility and stability. Its emulsifying and wetting properties improve the permeability and solubility of medications. The ability of a proniosome to form vesicles is best suited for an HLB value between 4 and 8, which is significant for selection. The high liquid solubility of hydrophilic surfactants makes it challenging for them to reach a high concentration. Consequently, there would be no aggregation to create a proniosomal lamellar structure.

Ex : Polysorbate 80, polyoxyethylene cetyl ethers(Brij 58) , Span 60,tween 20

Cholesterol :

Cholesterol interacts with non-ionic detergents to modify the structural and physical properties of proniosomes. increases the proniosome membranes' stability and flexibility while controlling medication penetration across the membrane. The detergent's HLB value indicates how much cholesterol is required to create periosomes. If your HLB value is greater than 10, you will need to take extra cholesterol to cover larger head groups. However, the entrapment efficacy of the generated formulations decreases at a certain cholesterol level, possibly due to a decrease in volume diameter. It controls drug penetration through the membrane and improves the stiffness and stability of the phosphorosomal membrane.

Lecithin :

A phospholipid called lecithin stabilizes the membrane during proniosome formation. According to reports, hydrogenated lecithins have advantages over non-hydrogenated lecithins, increase the rigidity of cholesterol, and aid in the creation of tight vesicles. The most common lecithins utilized in the formulation are soy and egg lecithin. aids in vesicle formation. Uncured lecithin's double bonds enable conformational rotation, which bends the chemical chain and prevents close contact with nearby molecules during the development of niosome membranes. As a result, the membrane becomes more permeable and less rigid.

Ex: Sunflower seeds ,eggs .

Hydration Medium :

Phosphate buffer is typically utilized as the hydration medium in proniosomes. The solubility of the medicine that is encapsulated determines the pH of the buffer.They discovered that as the hydration duration was increased from 20 to 45 minutes, EE rose, while medication leakage increased as the hydration medium's volume increased.

Ex: distilled water, ethanol-water mixture, phosphate buffer saline, glycerol, and sucrose solution.

Organic Solvent:

It is possible for the solvent to enhance penetration. It also significantly affects the size of the vesicles that develop. In a proniosomal formulation, the kind of alcohol influences the size of the vesicle and the rate at which the medication penetrates. To create vesicles of varying sizes, alcohols are stacked as follows:

Ex: Isopropanol, butanol, propanol, and ethanol.

Carrier Material :

The medicine in the proniosome formulation is held in place by the carrier substance. Carriers ought to be free-flowing, non-toxic, and safe. should be highly soluble in water to aid in hydration but less soluble in the loading solution. They provide proniosomes more surface area and flexibility. Sorbitol and mannitol are frequently used carrier materials.

Stearatel magnesium aluminum silicate, microcrystalline cellulose, spray-dried lactose, glucose monohydrate, lactose monohydrate, and sucrose.

Proniosome As A Drug Carrier:

Proniosomes are extremely promising delivery systems for a variety of pharmaceutical and diagnostic drugs. Proniosomes have been prepared, characterized, and used as medication carriers in a number of papers. They have low toxicity and outstanding biocompatibility due to their non-ionic nature. Proniosomes' distinct structure enables the creation of innovative drug delivery systems that can load both lipophilic and hydrophilic medications. Drugs that are hydrophilic or lipophilic are trapped in the proniosome's aqueous core and membrane bilayer, respectively. Iobitridol, a diagnostic drug used in X-ray imaging, has also been transported via proneosomes. Topical proniosomes can act as a rate-

limiting membrane, a local depot for the prolonged release of dermally active substances, a solubilization matrix, or a penetration enhancer barrier for the modulation of systemic absorption of drugs.

Table 1: Carriers Used For The Preparation Of Proniosomes :

Sr. No.	Carrier materials investigated
1.	Maltodextrin
2.	Sorbitol
3.	Mannitol
4.	Spray dried lactose
5.	Glucose monohydrate
6.	Sucrose stearate

Briefreview of various carriers used in the research work :

Maltodextrin

Sorbitol

Mannitol

Maltodextrin :

When starch is partially hydrolyzed, a mixture of glucose, polysaccharides, and disaccharides is created. Maltodextrin is a flavorless, rapidly absorbed carbohydrate that is made from cornstarch. Controlling the hydrolysis of starch results in the production of maltodextrin. It is a short chain of dextrose (glucose) molecules joined together. powder or granules that are freely soluble in water, white or almost white, and slightly hygroscopic.

Characteristics: White or nearly white powder or granules that are easily soluble in water and mildly hygroscopic.

Application :

Due to their rapid dissolution in water or other aqueous-based systems, maltodextrins are commonly found in consumer products such as dry mixes.

Maltodextrins can be used as a crystallization inhibitor. It can extend the shelf life of sweet and semi-soft sweets and prevent them from spoiling when combined with them. lowering and eliminating the smell of mutton, maintaining the nutritional value, retaining the flavor and character, and improving the quality.

Sorbitol :

Glucitol, Sorbogem, and Sorbo are other names for this sugar alcohol, which the human body metabolizes slowly. It can be obtained by reducing glucose, which transforms an aldehyde group into a hydroxyl group. Sorbitol is found in peaches, pears, apples, and prunes. It is synthesized by sorbitol-6-phosphate dehydrogenase and converted to fructose by succinate dehydrogenase and sorbitol dehydrogenase. In the citric acid cycle, a complex of enzymes known as succinate dehydrogenase is involved. Sorbitol is an alternative to sugar.

Application:

As a non-stimulant laxative, sorbitol can be administered as an enema or oral suspension.By attracting water into the large intestine, sorbitol promotes bowel motions and has a laxative effect. Elderly people can safely utilize sorbitol, however it is not advised to do so without first speaking with a clinician. Some dried fruits contain sorbitol, which may help explain why prunes have a laxative effect.

Mannitol:

It is a white, crystalline chemical molecule. This polyol is used as an osmotic diuretic and a moderate kidney vasodilator. Originally called mannite and honey sugar, it was taken from the secretions of the blooming ash. Given its resemblance to the food described in the Bible, it was given the name honey.

Application :

Furthermore, it may be possible to transport drugs directly into the brain with mannitol.Mannitol is commonly used in the heart-lung machine's circuit prime during cardiopulmonary bypass. Mannitol supports renal function in bypass patients during times of low blood pressure and flow. The therapy prevents the enlargement of the kidney's endothelial cells, which may have otherwise reduced blood flow to the region and damaged the cells.Furthermore, mannitol is the basis for bronchitol, a drug developed by the Australian pharmaceutical company Pharmaxis to treat cystic fibrosis and bronchiectasis.

Method Of Preparation Of Proniosomes :

Numerous components, including a membrane stabilizer, coating carriers, and a non-ionic surfactant, make up proniosomes. Desired characteristics of the selected carrier that could be utilized in the production of prionosomes were discussed by Payne et al. (2008). These powdered materials were kept between 2 and 8°C in sealed glass vial containers.These include free flowability, poor solubility in the safety and non-toxicity solution, low

solubility in the loaded mixed solution, and good water solubility for easy hydration. The following are a few techniques for proniosomal preparations that have been documented:

1. Slurry Method

2. Slow Spray Coating Method

3. Coacervation Phase Separation Method

1. Slurry Method :

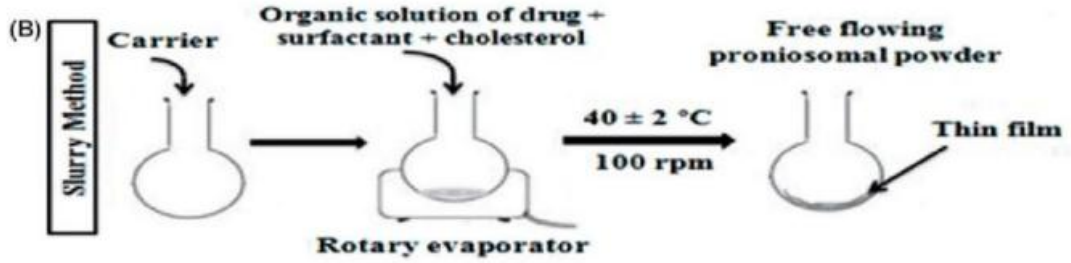
In this procedure, maltodextrin acts as a carrier. A 2:1 ratio of chloroform to methanol was used to create a 250 µ molar stock solution of surfactant and membrane stabilizer. .

A 100 ml round-bottom flask holding the carrier material and a methanol (2:1) solution was filled with the stock solution after a specific amount of the medication had been dissolved in chloroform.

Additionally, an organic solvent solution was added to generate a slurry [25]. A rotary flash evaporator was attached to the flask, which evaporates solvent at 60–100 rpm, 45 ± 2°C, and 600 mmHg of reduced pressure until the bulk inside the flask becomes a dry, free-flowing product.

These materials were placed in a desiccator for a whole night at room temperature after being vacuum-dried. This dry preparation, referred to as "proniosomes," was used in both preparations and further studies on the properties of powder.

The final product, proneosomes, was stored in a tightly sealed container in the refrigerator until further examination was performed.



2. Slow Spray Coating Method :

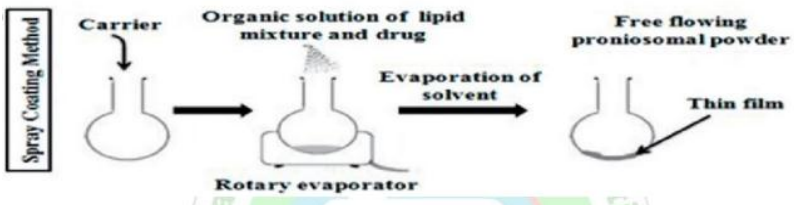
Typically, to create peptidosomes, surfactants in an organic solvent are sprayed upon sorbitol powder, then the solvent is evaporated.

It is possible to attach a 100ml round – Bottom flask with the required amount of carrier to the rotary evaporator.

The revolving evaporator can be attached to a 100 ml round base flagon that contains the desired amount of transporter.

The rotating jar can be rotated in a water shower under vacuum at 65–70°C for 15–20 minutes, once the evaporator has been cleared.

Until the entire surfactant arrangement has been applied, this interaction is repeated. The powder should continue to evaporate until it is totally dry.



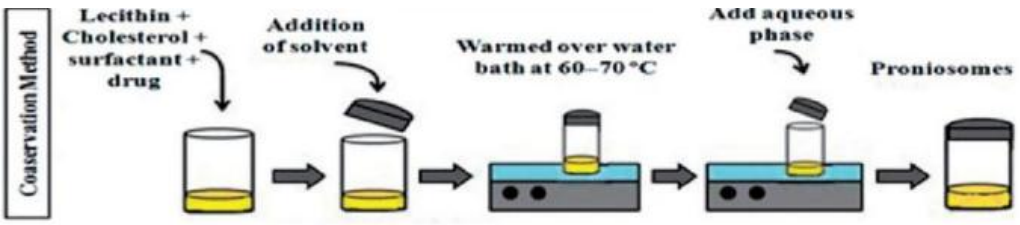
3. Coacervation Phase Separation Method:

Typically, to create peptidosomes, surfactants in an organic solvent are sprayed upon sorbitol powder, then the solvent is evaporated.

It is possible to attach a 100 ml round-bottom flask with the required amount of carrier to the rotary evaporator.

The evaporator must be removed, and the flask can be rotated for 15 to 20 minutes at 65 to 70 degrees Celsius while under vacuum in a water bath.

Until all of the surfactant solutions have been used, this procedure is repeated. The powder should continue to evaporate in order for multicellular vesicles to develop and for the powder to become entirely dry.



Evaluation Parameters In Proniosomes:

1. Particle size and shape analysis: An optical microscope and a stage micrometer with an accuracy of 0.01 nm were used to determine the particle size of proniosome powder.

2. Angle of repose measurement: The dried proniosome powder's angle of repose was ascertained using the funnel and cylinder method.

3. Vesicle Size Measurement: The size distribution and mean particle size diameter (polydispersity index, PI) were determined using Malvern Zetasizer nano.

4. Stability Study:

Stability studies are standard practices performed on medications and related products at various stages of product development. To investigate the drug's dissemination, a study on medicine release from Proniosome was carried out. For 30 days, pheniosomal dispersion stability was examined at room temperature and at temperatures ranging from 2 to 80 degrees Celsius. The response obtained for different periosomal dispersion settings across the stability period.

Stability tests for dry periosome powders meant for reconstitution should be carried out for accelerated stability at 40°C/75% RH (relative humidity) in accordance with international climatic zones and conditions (WHO, 1996). According to ICH standards, countries in zones I and II should have a temperature of 25°C/60% RH for long-term stability studies, while countries in zones III and IV should have a temperature of 30°C/65% RH.The appearance, color, assay, pH, amount of preservative, particle matter, sterility, and pyrogenicity of the product should all be assessed.

5. Efficiency of Entrapment:

To assess the entrapment efficiency, we must separate the free drug using a range of techniques, such as dialysis, gel filtration, ultracentrifugation, column chromatography, and freeze-thawing.

6. Zeta Potential:

By measuring the zeta potential of vesicles, one can ascertain the stability of niosomes.Proniosomes' zeta potential can influence the properties of drug loading, stability, and release.

7. In vitro research:

1. Shape and surface morphology:

Using techniques from optical microscopy, transmission electron microscopy (TEM), and scanning electron microscopy (SEM), spherical and round shapes are observed once aggregation begins.

2. Angle of repose measurement: Two methods for determining the angle of repose with manufactured dried pronisomes are described below.

Techniques A) the funnel method, B) the cylinder method.

A) Funnel method: A pile is formed when proniosome powder enters the cylinder powder using the cylinder method. To find the angle of repose, measure the pile's height and radius.

B) Cylinder method : Build a pile whose height and radius can be measured to find its angle of repose by pouring dried plasters into a funnel that has been positioned at a height.

8. In Vivo Release Studies :

The drug release from the proniosomal formulations was assessed using a number of techniques, such as the spectator molecular porous membrane tubing, the Franz diffusion cell, the Keshary-Chien diffusion cell, the Cellophane dialyzing membrane, and the United States Pharmacopeia (USP) dissolving equipment Type-1. Drug diffusion from a bilayer membrane, drug desorption from the vesicle surface, or a mixture of desorption and diffusion processes are the three possible ways that drugs can be released from niosomal vesicles made by periosomes.

Application Of Proniosomes :

1. Targeted Delivery: By altering proniosome composition, drugs can be delivered to particular tissues or organs with greater therapeutic efficacy and fewer systemic side effects.

2. Transdermal Drug Delivery: Proniosomes improve skin permeability and offer regulated release for drugs such as hormones (e.g., testosterone, estradiol) and analgesics (e.g., fentanyl).

3. Cancer Treatment: Systemic toxicity can be decreased by targeted chemotherapy administration. Proniosomes aid in drug concentration at tumor locations, increasing treatment efficacy and reducing adverse effects.

4. Antihypertensive Drug administration: By offering regulated release and enhanced bioavailability, periosomes can improve the transdermal administration of antihypertensive drugs, assisting in the maintenance of stable blood pressure levels.

5. Insulin administration: By enhancing the transdermal administration of insulin, periosomes can improve patient compliance and offer a non-invasive substitute for injections.

6. Oral Antidiabetic Drugs: These medications can be used to more efficiently administer oral hypoglycemic medicines, such as glibenclamide and metformin, increasing their absorption and lowering gastrointestinal adverse effects.

Future Prospective :

Another strategy to target and deliver the loaded medications is to use proniosomal formulations. However, in the fields of cosmetics, nutraceuticals, herbal actives, and other synthetic formulations, novel delivery methods utilizing proniosomes must be discovered. Therefore, more extensive study should be conducted to create scale-up batches for natural and pharmaceutical products.

CONCLUSION

Recent developments in science have led to the use of proniosomes as a drug carrier for improved drug targeting at a particular tissue destination. This is because proniosomes are composed of non-ionic surfactants, which make them less toxic and allow them to load hydrophilic, lipophilic, or both types of drugs. According to the pertinent research, proniosomes allow for targeted distribution to a particular tissue type, lower dosage, and increase the stability of the drug that is entrapped. They are known to prevent the dispersion of toxic fluids and a number of issues pertaining to actual stability, including aggregation and leakage.

REFERENCE

[1] Santosh Kumar, Harikesh mouray.(An overview on advance vesicles formulation as a drug carrier for N.D.D.S) European journal of biomedical and pharmaceutical science, 2018; 5(2): 292-303.

[2] Santosh Kumar, Harikesh mouray.(An overview on advance vesicles formulation as a drug carrier for N.D.D.S) European journal of biomedical and pharmaceutical science, 2018; 5(2): 292-303.

[3] Raju J, Karthik YJ, Ashok V, et al. Bioavailability enhancement of zaleplon via proliposome: Role of surface charge. European Journal of Pharm BioPharma, 2012; 80: 347–57.

[4] R Rao, R Kakar, G Anju, N Sanju. Proniosomes: An Emerging Vesicular System in Drug Delivery and Cosmetics. Der Pharmacia Lettre 2010; 2(4): 227-239.

[5] Tiddy, G.J.T., 1980. Surfactant-water liquid crystal phases. Phys. Rep., 57: 1-46.

[6] Kapil and Rai, AK (2011), "Development and evaluation of proniosomes as a promising drug carrier to improve TDDS", IRJP, Volume 2(11), 71-74.

[7] Mir M, Ishtiaq S, Rabia S, et al. (2017). Nanotechnology: from in vivo imaging system to controlled drug delivery. Nanoscale Res Lett 12:500.

[8] Uchegbu, I.F., Florence, A.T., Non-Ionic Surfactant Vesicles (Niosomes) Physical And Pharmaceutical Chemistry. Adv. Coll. Interf. Sci., 1995; 58: 1-55.

[9] U Havelikar*, A Patel, V Sharma, et al, A Comprehensive Review On Proniosomes: A New Concept In Ocular Drug Delivery. International Journal of Current Pharmaceutical Research. 2023; Vol. 15(5): 1-9.

[10] Hu, Chengjiu, and David G. Rhodes. "Proniosomes: a novel drug carrier preparation." International journal of pharmaceutics 185.1 (1999): 23-35.

[11] Alekhya Gurrapu A, RajuJukanti B, Sharan Reddy Bobbala B, Swetha Kanuganti B and Jyothi B Jeevana. Improved Oral Delivery Of Valsartan From Maltodextrin Based Proniosome Powders. 2012;23:583–590.

[12] Aswathy Sadanandan, Boby Johns George, Jeny Samuel, Praveen Raj, et al. (A review on proniosomes: an innovative approach to vesicular drug delivery) world journal of pharmacy and pharmaceutical sciences, 2017; 6(3): 1039-1053.

[13] HuC. (2000). RhodesD.G., Proniosomes: A novel drug carrier preparation. International Journal of Pharmaceutics, 206, 110–122.

[14] El Maghraby, G. M., & Williams, A. C. (2009). Vesicular systems for delivering conventional small organic molecules and larger macromolecules to and through human skin. Expert Opinion on Drug Delivery, 6(2), 149–163. doi:10.1517/17425240802691059.

[15] Raju J, Karthik YJ, Ashok V, et al. Bioavailability enhancement of zaleplon via proliposome: Role of surface charge. European Journal of Pharm BioPharma, 2012; 80: 347–57.

[16] Tiddy, G.J.T., 1980. Surfactant-water liquid crystal phases. Phys. Rep., 57: 1-46.

[17] Santosh Kumar, Harikeshmouray.(An overview on advance vesicles formulation as a drug carrier for N.D.D.S) European journal of biomedical and pharmaceutical science, 2018; 5(2): 292-303.

[18] Navya M. N., Parthiban S., Adlin Jino Neasalin, Vikneswari A.(Niosomes as novel vesicular drug delivery system-A review)Asian journal of research in biology and pharmaceutical sciences, 2014; 2(2): 62-68.

[19] Almira I. Blazek-Welsh and David G. Rhodes Maltodextrin-Based Proniosomes. AAPS Pharmsci. 2001;3(1).

[20] Schereie H, Bouwstra J; Liposomes and niosomes as topical drug carriers- dermal and transdermal drug delivery; J. Control. Release, 1994; 30: 1-15.

[21] Almira, I., Blazek-Welsh1., Rhodes, D. G. SEM Imaging Predicts Quality of Niosomes from Maltodextrin-Based Proniosomes Pharmaceutical Research. 2001,18, 5, 656-661.

[22] Paolino D, Celia C,Trapasso E (2012) Paclitaxel-loaded ethosomes: potential treatment of squamous cell carcinoma, malignant transformation of actinic keratoses. Eur J Pharma Biopharm 81: 102-112.

[23] Ijeoma F, Uchegbu, Vyas PS; Non-ionic surfactant based vesicles (niosomes) in drug delivery; Int. J. Pharm., 1998; 172: 33-70.

[24] Agarwal,R.Katare,O.P.Vyas,Preparation and in vitro evaluation of liposomal/nioosmal delivery systems for antipsoriatic drug dithranol. Int. J. Pharm.2001, 228, 43–52.

[25] Paolino D, Celia C, Trapasso E (2012) Paclitaxel-loaded ethosomes potential treatment of squamous cell carcinoma, a malignanttransformation of actinic keratoses. Eur J Pharma Biopharm 81: 102-112.

[26] Uchegbu IF, Florence AT. Non-ionic surfactant vesicles (niosomes): physical and pharmaceutical chemistry. Adv Coll Int Sci 1995; 58: 1–55.

[27] Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. Int J Pharm G.V. Radha, T. Sudha Rani, B. Sarvani. A review on proniosomal drug delivery system for targeted drug action. JBCP 2013; 4-2: 42-48.1998; 172: 33–70.

[28] Raju J, Karthik YJ, Ashok V, et al. Bioavailability enhancement of zaleplon via proliposome: Role of surface charge. European Journal of Pharm BioPharma, 2012; 80: 347–57.

[29] Katare O, Vyas S, Dixit V. Effervescent granule based proliposome of Ibuprofen. Journal of Microencapsulation, 1990; 7(4): 455-62.

[30] Solanki AB, Parikh JR, Parikh RH. Formulation and optimization of piroxicam proniosomes by 3-factor, 3-level box-Behnken design. AAPS Pharm Sci Tech 2007; 8(4):1–7.

[31] Navya M. N., Parthiban S., AdlinJinoNeasalin, VikneswariA.(Niosomes as novel vesicular drug delivery system-A review)Asian journal of research in biology and pharmaceutical sciences, 2014; 2(2): 62-68.

[32] Walve JR, Rane BR, Gujrathi NA. Proniosomes: A surrogate carrier for improved transdermal drug delivery system. Int J Res Ayurveda Pharm., 2011; 2: 743–50.

[33] ND Shukla, M Tiwari; Proniosomal Drug Delivery System– Clinical Applications. Intenational Journal of Research in Pharmaceutical and Biomedical Sciences 2011; 2 (3):880-887.

[34] Farooqui N, Kar M and Singh RP. Formulation and evaluation of proniosomal gel for transdermal delivery of ketorolac tromethamine. Asian Journal of Pharmaceutics, 2016; 10: 394-400.

[35] Jain, S., Jain, P., Umamaheshwari, R. B., & Jain, N. K. (2003). Proniosomes: A novel drug carrier system. Indian Journal of Pharmaceutical Sciences, 65(3), 261-271.

[36] Arunothayanun P, Bernard MS, Craig DQ, Uchegbu IF, Florence AT. The effect of processing variables on the physical characteristics of non-ionic surfactant vesicles (niosomes) formed from a hexadecyl diglycerol ether. Int J Pharm, 2000; 201: 7-14.

[37] Sayed S, Abdelmotelab M, Amin MM, Khowessah OM. Effect of formulation variables and gamma sterilization on trans corneal permeation and stability of proniosomal gels as ocular platforms for antiglaucomal drug. AAPS PharmSciTech. 2020 Apr;21(3):1-3.

[38] Blazek-Welsh, A.I. and D.G. Rhodes, 2001b. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharm. Res., 18: 656-661.

[39] Satpathy G, Ahmed NH, Nayak N, Tandon R, Sharma N, Agarwal T. Spectrum of mycotic keratitis in north India: sixteen years study from a tertiary care ophthalmic centre. J Infect Public Health. 2019 MayJun;12(3):367-71. doi: 10.1016/j.jiph.2018.12.005, PMID 30600158.

[40] Patil HN, Hardikar SR, Bhosal AV. Formulation and evaluation of proniosomal gel of carvedilol. Int J Pharm Pharm Sci., 2012; 4(1): 191-7.

[41] Abreu CR. On the relationship between the hydrophilic-lipophilic balance and the nano architecture of nonionic surfactant systems. J Surfactants Deterg. 2019 Jan;22(5):1001-10

[42] Biju SS, Talegaonkar S, Mishra PR, Khar RK. Vesicular systems: an overview. Indian J Pharm Sci., 2006; 68(2): 141-53.

[43] Venkatesh ND, Priyanka SV, Tulasi K, Kalyani K, Ali AS, Jilakara H. Proniosomes: A superior drug delivery system. Int J Pharm Sci Drug Res., 2014; 6(3): 178-82.

[44] AswathySadanandan, Boby Johns George, Jeny Samuel, Praveen Raj, et al. (A review on proniosomes: an innovative approach to vesicular drug delivery) world journal of pharmacy and pharmaceutical sciences, 2017; 6(3): 1039-1053.

[45] Sivaprasad SN, Kumar PL, Srinivas M, Brahmaiah B, Nama S. Proniosome: a novel approach to vesicular drug delivery system. Int J Drug Discov. 2013;3:85-90.

[46] Morakul B, Junyaprasert VB. Proniosomes: an effective carrier for dermal and transdermal delivery. Songklanakarin J Sci Technol. 2020;42:1171-1186.

[47] Ruckmani K, Sankar V. Formulation and optimization of zidovudine niosomes. AAPS PharmSciTech. 2010;11:1119-1127.

[48] Kumar K, Rai AK. Development and Evaluation of Proniosome Encapsulated Curcumin for Transdermal Administration. Tropical Journal of Pharmaceutical Research, 2011; 10(6): 697-703.

[49] D. Akhilesh*, G. Faishal and JV. Kamath. Comparative Study of Carriers used in Proniosomes. International journal of pharmaceutical and chemical sciences.2012;1(1),164-173.

[50] T.Sudhamani, V. Ganesan, N.Priyadarsini and M. Radhakrishnan.Formulation and evaluation of Ibuprofen loaded maltodextrin based Proniosome. International Journal of Biopharmaceutics. 2010;1(2):75-81.
[51] Ankur Gupta, Sunil Kumar Prajapati, Balamurugan M, Mamta Singh and Daksh Bhatia (2007). Design and Development of a Proniosomal Transdermal Drug Delivery System for Captopril. Tropical J. Pharm Res., 6(2): 687-693.
[52] Venkata Ramesh yasam, Satya lavanya jakki, Jawahar Natarajan, Gowthamarajan Kuppusamy. (A review on novel vesicular drug delivery proniosomes) journal of liposome reserach, 2016; 21(4): 243-249.
[53] Mishra A, Kapoor A, Bhargava S. Proniosoml gel as a carrier for improved transdermal drug delivery. Asian J Pharm Life Sci, 2011; 1: 370–9.
[54] Karatzas AA, Politis SN, Rekkas DM (2017) Development of rapidly dissolving pellets within the Quality by Design Approach. Drug Dev Ind Pharm 43: 770-779.
[55] Sankar V, Ruckmani K, Durga S, Jailani S. Proniosomes as drug carriers. Pak J PharmSci, 2010; 23: 103–7.
[56] Abd-Elbary A, El-laithy MI, Tadros HM. Sucrose stearatebased proniosome- derived niosomes for the nebulisable delivery of cromolyn sodium. Int J Pharm. 2008; 357:189-198.
[57] Boddy M, Choppri V, Vamshi R. K, Badam M. Formulation and Evaluation of Proniosome of Felodipine. Drug Des, an open access journal, 2017; 6(3): 1-9.
[58] Ramkanth S, Chetty CM, et al. Development, characterization & invivo evaluation of proniosomal based transdermal delivery system of Atenolol. Futur J Pharm Sci. 2018;4(1):80–87.
[59] Aswathy Sadanandan, Boby Johns George, Jeny Samuel, Praveen Raj, et al. (A review on proniosomes: an innovative approach to vesicular drug delivery) world journal of pharmacy and pharmaceutical sciences, 2017; 6(3): 1039-1053.
[60] Jain NK, Ramteke S, Maheshwari U. Clarithromycin based oral sustained release nanoparticle drug deliverysystem. Indian J Pharm Sci. 2006; 4: 479.