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REVIEW ARTICLE OPEN ACCESS

Overview on Proniosomes in Various Drug Delivery System

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Abstract:

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. Drugs that are encased in the vesicular structure of proniosomes have a longer shelf life in the bloodstream, have better tissue penetration, and are less toxic. Technically speaking, niosomes are potential drug delivery systems because they are more chemically stable and lack many of the drawbacks of liposomes, such as their expensive cost and inconsistent phospholipid purity. The focus of this review is on proniosomes' general preparation techniques, characterization, and use in targeted drug action.

Keywords —Proniosomes, types of proniosomes, methods of preparation of proniosomes, advantages and disadvantages, drug carrier, drug delivery system.

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I. INTRODUCTION

Proniosomes are water-soluble carrier particles covered with surfactant in a dry formulation. Immediately prior to agitation in hot aqueous solution, they are rehydrated to create niosomal dispersion. The main goal of developing controlled and targeted release dosage forms is to enhance plasma concentration to boost the therapeutic impact of medications, increase their safety margin, and decrease adverse effects.One method for delivering drugs is through vesicles, such as liposomes, niosomes, transferosomes, pharmacosomes, and provesicles like proniosomes and proliposomes. The fact that liposomes and niosomes are particulate, acting as a drug reservoir, gives them an edge over other conventional dosage forms. A few adjustments can also be made to the pattern and the release of the medicine. Modified vesicles were also discovered to possess characteristics that enabled the delivery of medications into the skin's deeper layers.Proniosomes are promising as drug carriers because they have better chemical stability and share many drawbacks associated with liposomes. Proniosomes are dry formulations of surfactant-coated carrier vesicles that can be rehydrated as needed, and the resulting niosomes are very similar to conventional uniform-sized niosomes. As a dry, free-flowing product, Proniosomes minimize stability issues during storage and sterilization. They also have the advantage of easy transport, distribution, measurement, and storage, making proniosomes a very versatile delivery system.

STRUCTURE OF PRONIOSOMES

Proniosomes are microscopic layered structures. Non-ionic surfactants of the alkyl or dialkyl polyglycol ether class are combined withcholesterol

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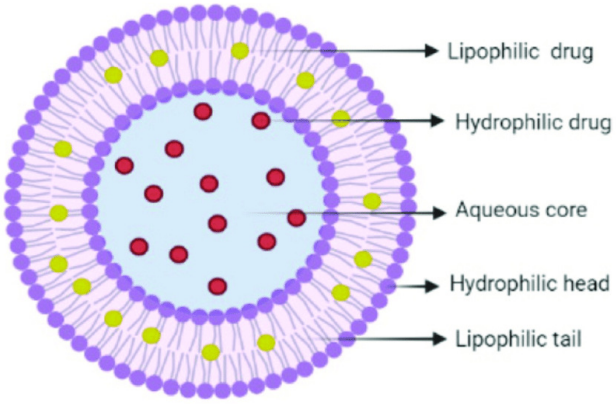
and then hydrated in an aqueous medium. Surfactant molecules are aligned such that the hydrophilic ends of the non-ionic surfactants face outwards, and the hydrophobic ends point in the opposite direction to form a bilayer. Hydrophilic drugs are placed at intervals in the area encircled within the vesicle and the hydrophobic medication is implanted within the bilayer



MATERIALS USED FOR THE PREPARATION OF PRONIOSOMES

1. Surfactant
2. Cholesterol
3. Lecithin
4. Hydration medium
5. Organic Solvent
6. Carrier Material

1. Surfactant: -

Surfactants, especially non-ionic surfactants, are important structural components in the production of proniosomes. These surfactants have a polar head and a non-polar tail, and are therefore uncharged. Its stability and compatibility are superior to other surfactants, non-ionic surfactant has wetting and emulsifying effect, which improves drug solubility and permeability. HLB value is very important for selection, HLB value between 4 and 8 is suitable for vesicle formation by proniosomes.

2. Cholesterol

Cholesterol interacts with non-ionic detergents to modulate the physical and structural properties of proniosomes. improves proniosomes membrane stability and rigidity and controls drug permeation across the membrane. Depending on his HLB value of detergent determines the amount of cholesterol required for proniosomes production. If your HLB value is above 10, you need to increase the amount of cholesterol to cover larger head groups. However, the entrapment efficiency of the prepared formulations decreases above a certain cholesterol level, possibly due to a decrease in volume diameter**.**

3. Lecithin

Lecithin is a phospholipid that acts as a membrane stabilizer in proniosomes formulations. The most common lecithin used in formulations are soybean and egg lecithin, and hydrogenated types of lecithin are reported to be superior to non-hydrogenated lecithin, increasing cholesterol rigidity and providing a firmer, firmer lecithin. Helps form vesicles. The double bonds in uncured lecithin allow the molecular chain to bend (conformational rotation), preventing intimate contact with neighbouring molecules in the formation of niosome membranes. . This makes the membrane less stiff and more permeable

4. Hydration Medium

Typically, the hydration medium used in proniosomes is phosphate buffer. The pH of the buffer is selected according to the solubility of the encapsulated drug. Increasing the amount of hydration medium increased drug efflux, but at the same time, increasing the hydration time from 20 to 45 minutes improved entrapment efficiency.

5. Organic Solvent

Solvents can act as penetration enhancers. It also strongly influences the size of the vesicles formed. The size ofvesicles and the

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permeation rate of drugs in proniosomesformulations are affected by the type of alcohol. Different sized vesicles are formed using different alcohols. This is because the order >> isopropanol < butanol < propanol < ethanol.

6. Carrier Material

The carrier material holds the drug in the proniosomes formulation. Carriers must be safe, non-toxic and free-flowing. should have low solubility in the loading solution, but high solubility in water to facilitate hydration. They increase surface area and give flexibility to proniosomes. Commonly used carrier materials are sorbitol, mannitol.

TYPES OF PRONIOSOMES

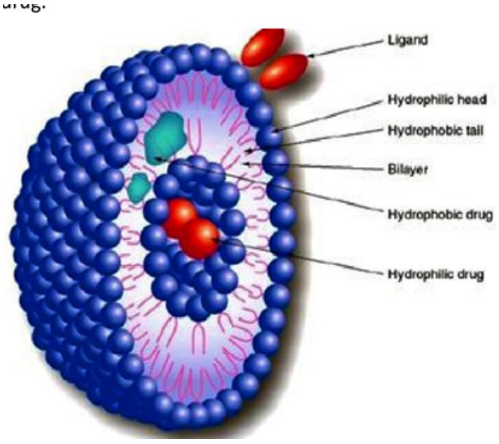
A. Dry Granular Proniosomes
   i. Sorbitol-Based Proniosomes A dry formulation containing sorbitol as a carrier and coated with a non-ionic surfactant by simple agitation using water.
   ii. Maltodextrin-based proniosomes Maltodextrin-based proniosomes were prepared by the Rapid Slurry

B. Liquid Crystal Proniosomes
This type of proniosomes acts as a reservoir for transdermal drug delivery. A transdermal patch contains a backing sheet with a plastic liner. Gel is spread evenly on sheet.

PREPARATION METHOD OF PRONIOSOMES

1. SLURRY METHOD
2. SLOW SPRAY COATING METHOD
3. COACERVATION PHASE SEPRATION METHOD

1. Slurry Method
Proniosomes were prepared by the slurry method using maltodextrin as a carrier. Therefore, the time taken to generate

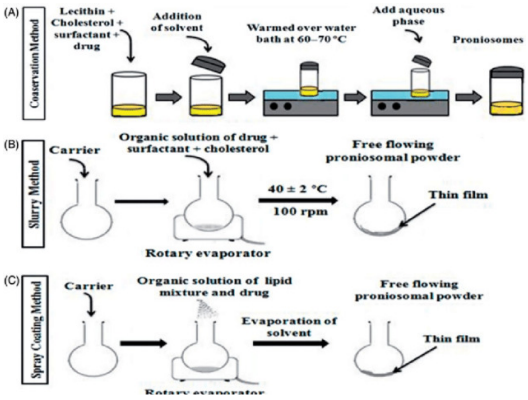


proniosomes is independent of the ratio ofsurfactant solution to support material. In the slurry process, the entire volume of surfactant solution is added to the maltodextrin powder in a rotary evaporator and vacuum is applied until the powder appears dry and free flowing. Drug containing niosomes derived from proniosomes is like the method used for conventional niosomes by adding the drug to the detergent mixture before pouring the solution into the carrier (sorbitol, maltodextrin). It can be prepared by the method of or proniosomes hydration by adding the drug to the aqueous solution.

2. Slow Spray Coating Method
Proniosomes were prepared by spraying sorbitol powder with surfactant in organic solvent and evaporating the solvent. Since the sorbitol carrier is soluble in organic solvents, the process must be repeated until the desired surfactant loading is achieved. The surfactant coating on the support is very thin and hydration of this coating forms multilamellar vesicles.

3. Coacervation Phase Separation Method
In this method, precisely weighed amounts of surfactant, carrier (lecithin), cholesterol, and drug are placed in a clean, dry, wide-mouthed glass vial (5 mL),

solvent is added, and the mixture is simply mixed. To prevent loss of Solvent, cover the open end of the glass vial with cap and heat in a 60-70 °C water bath for 5minutes until the surfactant is completely dissolved. The mixture should be cooled to room temperature until the dispersion is converted to proniosomes.



ADVANTAGES OF PRONIOSOMES

1. Proniosomes avoid physical stability problems such as drug aggregation, fusion, and leakage.
2. Avoid hydrolysis of the encapsulateddrug, which limits the shelf life of the dispersion.
3. Easy storage and handling.
4. In addition, unacceptable solvents are avoided in proniosomes formulations.
5. The system can also be formulated into a transdermal patch, eliminating the need to disperse vesicles in a polymer matrix.
6. Storage makes proniosomes a versatile delivery system with a potential and broad spectrum of active compounds.

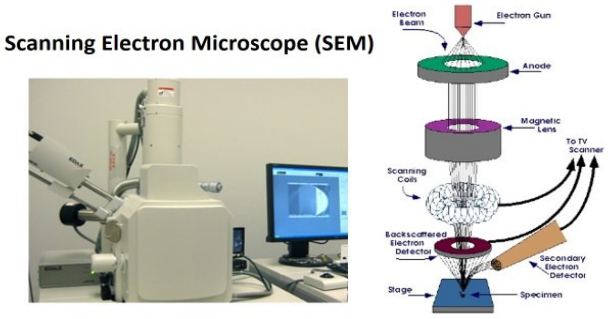
EVALUATION OF PRONIOSOMES

1. Measurement of angle of repose
2. Scanning electron microscopy (SEM)
3. Measurement of vesicle size
4. Drug content
5. Entrapment efficiency
6. In-vivo release studies
7. Stability studies

1. Measurement of angle of repose: -
   The angle of repose of dried proniosomes powder was measured by funnel and cylinder method.

2. Scanning Electron Microscopy

- Particle size of proniosomes is a factor of prime importance.
- The surface morphology and size distribution of proniosomes were studied by SEM.
- A double-sided tape that was affixed on aluminium stubs and the proniosomal powder was spread on it.
- The aluminium stub was placed in a vacuum chamber of scanning electron microscope
- The morphological characterization of the samples was observed using a gaseous secondary electron detector.
- The vesicle formation by the procedure can be confirmed by optical microscopy.



3. Measurement of Vesicle Size

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Vesicle dispersions were diluted approximately 100-fold in the same medium used for their preparation. The size of vesicles was measured with a particle size analyser. The apparatus consists of a 632.8 nm He—Ne laser beam focused with a minimum power of 5 MW to a central point of the multi-element detector using a Fourier lens (R-5), a small volume sample holder and consists of is the focused cell. Samples were agitated with a stirrer prior to vesicle size measurements.

4. Drug Content

- The calibration curve is used to calculate drug content.
- For this, Proniosomes are lysed with methanol in a volumetric flask by shaking for 15 min.
- Then the stock solution is prepared with methanol.
- With the help of phosphate buffer, 10% solution is prepared from the stock solution.
- Aliquots are withdrawn and absorbance is measured followed by a drawing of calibration curve
- Drug Content was calculated from the slope we get from the calibration curve and the absorbance of the various concentration of aliquots

5. Entrapment Efficiency

To study the entrapment efficiency, we need to separate the free drug by several techniques like dialysis, gel filtration, ultracentrifugation, column chromatography, freeze-thawing. Two techniques can be applied to measure entrapment efficiency. One is the destruction of the proniosomal vesicle with propane (50%) or triton (0.1%) and the entrapped drug is determined. Another method is after the destruction of the vesicle, the un-entrapped drug is measuredThe percentage of entrapment is calculated using the following formula:

$$\% \text{ Entrapment} = ED/TD \times 100$$

Where ED is the amount of entrapped drug and TD is the initial amount of drug

6. *In Vivo* Release Studies

The release of the drug from the proniosomal formulations was determined using different techniques such as Franz diffusion cell, Keshary-Chien diffusion cell, Cellophane dialyzing membrane, United states pharmacopeia (USP) dissolution apparatus Type-1, spectator molecular porous membrane tubing. Drug release from proniosomes derived niosomal vesicles can follow any one or more of the following mechanisms; desorption from the surface of vesicles or diffusion of drug from bilayer membrane or a combined desorption and diffusion mechanisms

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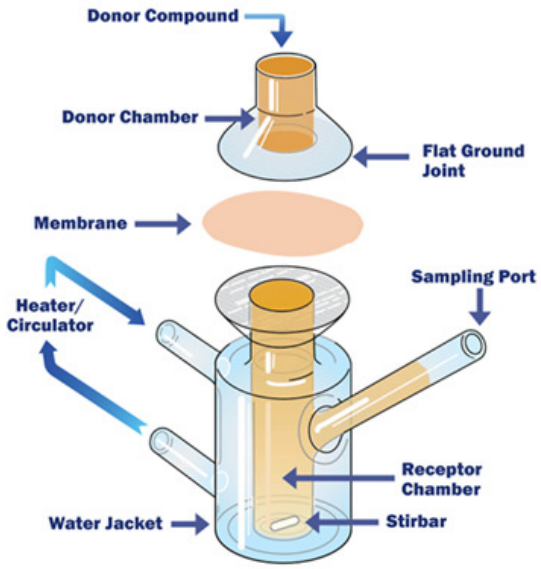

7. Stability Studies

- Stability studies were carried out by storing the prepared proniosomes at various temperature conditions such as refrigeration temperature (2°-8°C), room temperature (25° ± 0.5°C) and elevated temperature (45° ± 0.5°C) from a period of 1 month to 3 months.
- Drug content and variation in the average vesicle diameter were periodically monitored.
- International conference on harmonization (ICH) guidelines suggests stability studies for the dryproniosomes powders meant for reconstitution should be studied for accelerated stability at 40°C/75% relative humidity as per international climatic zones and climatic conditions.
- For long term stability studies, the temperature is 25°C/60% RH for the countries in zone I and II and for the countries in zone III and IV the temperature is 30°C/65% Relative humidity (RH).
- Product should be evaluated for appearance, colour, assay, pH preservative content, particulate matter, sterility, and pyrogenicity

DRUG TARGETING APPLICATION

a. CARDIOVASCULAR
Applications of proniosomes are used as carriers for transdermal drug delivery of the Captopril for the treatment of hypertension. The studies showed the sustained release effect of the drug when formulated into proniosomes. As the drug is encapsulated using carriers such as cholesterol, lecithin, etc.

b. DIABETIS
Here the drug used is furosemide which is formulated as proniosomes which gives non invasive effect of the drug. Here the skin permeation effect is seen using the DCP, lecithin, Span and Tween of different grades.

c. HORMONAL THERAPY
Work had been performed on proniosomes based transdermal delivery of levonorgestrel the emergency contraceptive. The structure of the niosome was liquid crystalline compact hybrid. The system was tested for particle size, encapsulation efficiency, stability study, in vivo and in vitro study. Bioassay for pregestational activity was also performed.

d. CARRIER FOR HAEMOGLOBIN
Blood has many carrier proteins present in it. Proniosomes be used as carriers for haemoglobin within the blood. The niosomal or the proniosomal vesicle is permeable to oxygen and hence it acts as a carrier for haemoglobin in patients.

e. DELIVERY OF PEPTIDE DRUGS
Oral peptide drug delivery has a drawback of bypassing the enzymes, which would breakdown the peptide and protein bonds. Niosomes were used to successfully protect the peptides from gastrointestinal peptide breakdown.

f. SUSTAINED RELEASE
Sustained release action of Proniosomes can be applied to drugs with low

therapeutic index and low water solubility since those could be maintained in the circulation via niosomal encapsulation

g. OCULAR DRUG DELIVERY

Proniosomes gel ocular drug delivery bridges the problems encountered in ocular drug delivery and preserves drug activity. This solves the metabolic problem and avoids degradation of the drug by metabolic enzymes available on the surface of the tear fluid and corneal epithelium, another advantage is increased contact time and improved drug retention. is to also improved. Lomefloxacin proniosomal gel suitable for bacterial conjunctivitis is compared to conventional eye drops.

CONCLUSION

Recently, there has been a significant increase in drug delivery technologies, of which proniosomes are one of the widely used sterile drug delivery systems in cancer therapy. From the above article, we conclude that the concept of incorporating drugs into niosomes for better targeting of drugs to appropriate tissue target sites is widely accepted by researchers and scholars. Proniosomes-derived niosomes are promising modules for drug delivery. 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.Proniosomes not only provide a promising means of delivering drug, but also have the potential to improve the recovery rate of theskin barrier. Proniosomes represent a promising drug delivery technology, and much research needs to be encouraged to fully reveal the potential of these new drug delivery systems. All this makes proniosomes, or "dried niosomes", promising industrial and research products.

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