

Proniosome Gel: An Effective Novel Therapeutic Topical Delivery System

Alli malarkodi S*, Srilakshmi.Ch, Ganesan. G

Dept. of Pharmaceutics, The Erode College of pharmacy, Perundurai Main Road,
Vallipurathanpalayam (po), Veppampalayam,
ERODE – 638112, TN, India.

*Corres.author: alli68@rediffmail.com
Contact no: +91-9443433093

Abstract: Skin has become an impressive and idealistic platform for the delivery of drugs compared to other routes. However, the stratum corneum “dead, impermeable barrier devoid of biological activity” to skin had challenged the development of transdermal product, which delivers the drugs directly to the systemic circulation at a controlled rate. Recent literature suggests the old doctrine, which states that compounds with a molecular weight 500 Da cannot cross the skin, need some amendment owing to the availability of novel methods that might enhance the transport of large molecular weight compounds into or through the skin. Several approaches put forward to enhance the penetration of drug through skin for transdermal drug delivery and one among them are provesicular niosomes (Proniosomes), which ideally possess the sole property of reversibly reducing the barrier resistance of the horny layer, allowing the drug to reach the living tissues at a greater rate. The provesicular niosome (non-ionic surfactant based vesicles); colloid carrier is still in its infancy and need to exploit more in field of drug delivery. Basically, proniosomal gel is a compact semi-solid liquid crystalline (gel) product of non-ionic surfactants easily formed on dissolving the surfactant in minimal amount of acceptable solvent and the least amount of aqueous phase. This compact liquid crystalline gel can be readily converted into niosomes on hydration. This review provides an important overview of preparation, formulation, evaluation and application of proniosome gel as a drug carrier.

Keywords: Provesicular systems, proniosomal gel, non-ionic surfactant, penetration, entrapment efficiency, transdermal.

INTRODUCTION:

For many decades treatment of an acute disease or a chronic illness¹ has been mostly accomplished by deliverance of drugs to patients using a variety of pharmaceutical dosage forms including tablets, capsules², pills, suppositories, ointments, injectables as drug carriers. Therefore to achieve as well as to sustain the drug concentration within the therapeutic effective range wanted for treatment, it is often necessary to take this type of drug delivery system several times a day.³

The transdermal route is extensively used now days as it is convenient over the conventional dosage forms. Transdermal route bypasses the GI tract hence avoiding the gastric irritation, reduces number of doses, improved patient compliance, and enhanced bioavailability and can preserve suitable plasma concentration.⁴

At present, not a single drug delivery system fulfils all the criteria but, attempts have been made through new approaches. In recent years it has been shown that the skin is a useful route for drug delivery to the system

circulation⁵⁻⁶. Increasing numbers of drugs are being added to the list of therapeutic agents that can be delivered to the systemic circulation *via* skin⁷.

Proniosome are dry product which could be hydrated immediately before use would avoid many of the problems associated with aqueous niosome dispersions and problems of physical stability (aggregation, fusion, leaking) could be minimized.⁸ These dry formulations of surfactant-coated carrier can be measured out as needed and rehydrated by brief agitation in hot water.⁹ They are water-soluble carrier particles that are coated with surfactant and can be hydrated to form a niosomal dispersion immediately before use on brief agitation in hot aqueous media. Reported methods for preparation of proniosomes are the spraying of surfactant on water soluble carrier particles and the slurry method¹⁰. This dry, free-flowing, granular product, on addition of water, disperses or dissolves to form a multilamellar niosome suspension suitable for administration by oral or other routes.

Proniosomes are normally made by spraying surfactant in organic solvent onto carrier (sorbitol/maltodextrin powder) and then evaporating the solvent. Because the carrier is soluble in the organic solvent, it is necessary to repeat the process until the desired surfactant loading has been achieved. The surfactant coating on the carrier is very thin and hydration of this coating allows multilamellar vesicles to form as the carrier dissolves.

The resulting niosomes are very similar to those produced by conventional methods and the size distribution is more uniform. It was suggested that this formulation could provide a suitable method for formulating hydrophobic drugs in a lipid suspension without concerns over instability of the suspension or susceptibility of the active ingredient to hydrolysis. It was also observed, however, that certain solutes were affected by the presence of dissolved carrier. Although conventional niosome suspensions would include only the multilamellar surfactant particles in buffer, a typical formulation derived from sorbitol/maltodextrin carrier based proniosomes would consist of multilamellar surfactant particles in buffer and dissolved carrier. The residual sorbitol concentration in the formulation observed to affect entrapment efficiency. Specifically, dissolved carrier could decrease entrapment efficiency to less than one half of that observed without carrier. Because the dissolved carrier can exert such an influence on entrapment behavior, one of the primary goals of subsequent research was to reduce the proportion of carrier to surfactant so that the amount of carrier in the final niosome suspension would be minimal. Although not an issue in the process of making niosomes from proniosomes, it was difficult to coat carrier (sorbitol/maltodextrin) particles because they are soluble in chloroform and other organic solvents. If the surfactant solution was applied too quickly, the carrier particles would degrade and the sample became viscous slurry. To avoid this constraint, several methods of making proniosomes were attempted, but most proved to be time consuming and had narrowly constrained limits on acceptable production conditions. Here, experiments are described in which maltodextrin is used as the carrier material in the proniosome preparations. A proniosome formulation based on maltodextrin was recently developed that has potential applications in delivery of hydrophobic or amphiphilic drugs. The better of these formulations used a hollow particle with exceptionally high surface area. The principal advantage with this formulation was the amount of carrier required to support the surfactant could be easily adjusted, and proniosomes with very high mass ratios of surfactant to carrier could be prepared. Because of the ease of production of proniosomes using the maltodextrin-based slurry method, hydration of surfactant from proniosomes of a wide range of compositions can be studied.

This proniosomal drug delivery have concerned towards transdermal delivery because surfactants themselves act as penetration enhancers and are biodegradable, non-toxic, amphiphilic, possess property of encapsulation and they can entrap both hydrophilic as well as lipophilic drugs. Proniosomes can be converted into niosomes in-situ by absorbing water from the skin.¹¹

These "proniosomes" minimize problems of niosomes physical stability such as aggregation, fusion and leaking and provided additional convenience in transportation, distribution, storage and dosing.¹² Stability of dry proniosomes is probable to be more stable than a pre manufactured niosomal formulation. In release studies proniosomes become visible to be equivalent to conventional niosomes. Size distributions of proniosome derived niosomes are fairly better than those of conventional niosomes so the release performance in more significant cases turns out to be superior.¹³ The advancements in the niosome direct to the evolution of proniosomal delivery systems.¹⁴

Proniosomes are non-ionic based surfactant vesicles which may be hydrated instantly before use to yield aqueous niosome dispersions. Proniosomes are currently used to enhance drug delivery in addition to conventional niosomes. They are converted into niosomes respectively upon simple hydration or by the hydration of skin itself after application.¹⁵

Proniosomes exist in two forms

i) Semisolid liquid crystal gel.

ii) Dry granular powder¹⁶

Of these two forms the proniosomal gel is mainly used for topical / transdermal application.

PRONIOSOMAL GEL:

Proniosomes are vesicular systems, in which the vesicles are made up of non-ionic based surfactants, cholesterol and other additives. Semisolid liquid crystal gel (proniosomes) ready by dissolving the surfactant in a minimal quantity of an acceptable solvent, namely ethanol and then hydration with slightest amount of water to form a gel.¹⁷ These structures are liquid crystalline dense niosomes hybrids that can be converted into niosomes instantly upon hydration or used as such in the topical/transdermal applications. Proniosomal gels are generally present in transparent, translucent or white semisolid gel texture, which makes them physically stable throughout storage and transport.¹⁸

ADVANTAGES OF PRONIOSOMAL GEL:

Liposomes and niosomes are well known drug/cosmetic delivery systems. But these delivery systems have been reported to have many disadvantages in terms of preparation, storage, sterilization, etc. The disadvantages of liposomes and niosomes are given below, which can be overcome by proniosomes.

1. Liposomes and niosomes are dispersed aqueous systems and have a problem of degradation by hydrolysis or oxidation.
2. Liposomes and niosomes require special storage and handling.
3. Sedimentation, aggregation or fusion on storage is usually seen.
4. In liposomes, purity of natural phospholipids is also variable.
5. Difficulty in sterilization, transportation,
6. Distribution, storage uniformity of dose and scale up. Incomplete hydration of the lipid/surfactant film on the walls during hydration process.¹⁹

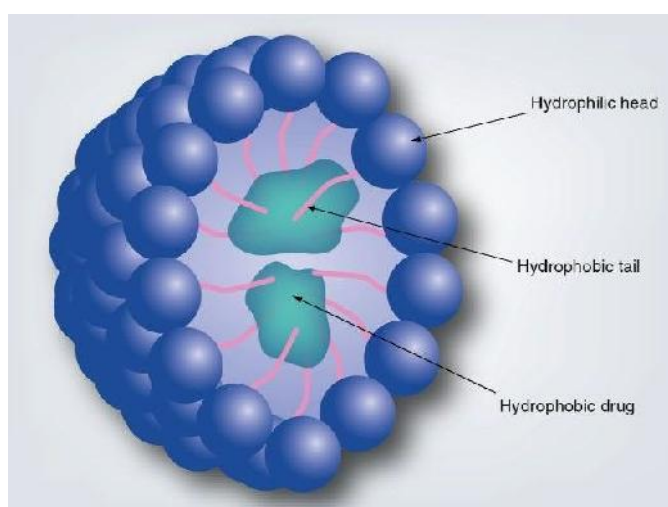
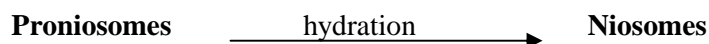


Fig No. 1 Niosomes

Action of Proniosomes:

Proniosomes show their action after they are converted to niosomes on hydration.



The hydration may occur either by the skin or by the addition of aqueous solvents. Proniosomes can entrap both hydrophilic as well as lipophilic drugs.

FORMATION OF NIOSOMES FROM PRNOSOMES²⁰⁻²³:

The niosomes can be prepared from the proniosomes by adding the aqueous phase with the drug to the proniosomes with brief agitation at a temperature greater than the mean transition phase temperature of the surfactant.

$$T > T_m$$

Where,

T = Temperature

T_m = mean phase transition temperature.

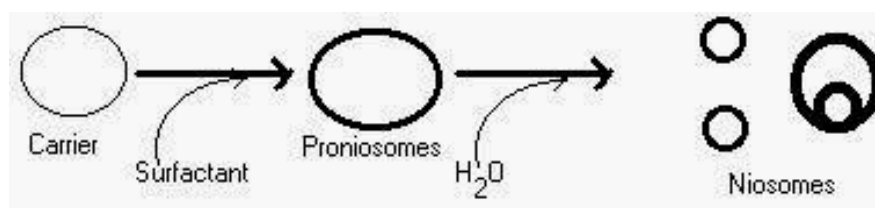


Fig 2: Formation of Niosomes from Proniosomes.

Blazek-Walsh A.I. *et al* has reported the formulation of niosomes from maltodextrin based proniosomes. This provides rapid reconstitution of niosomes with minimal residual carrier. Slurry of maltodextrin and surfactant was dried to form a free flowing powder, which could be rehydrated by addition of warm water²⁴.

PERCUTANEOUS DRUG ABSORPTION: FICK'S FIRST LAW OF DIFFUSION

Percutaneous drug absorption can be defined by Fick's first law of diffusion²⁵ as in Eqn 1:

$$\frac{dQ}{dt} = J_{ss} = \frac{K_s \cdot D}{h} \cdot C_v \cdot A$$

Where, dQ/dt = amount of drug diffused per unit time (i.e. drug flux), J_{ss} = drug flux, K_s = partition coefficient, D = diffusion coefficient, h = diffusional path length (thickness of SC), C_v = concentration gradient of drug and A = skin surface area treated.

In order to achieve enhanced drug delivery changes can be made at two basic levels – First approach - Chemical modifications in drug molecules in order to increase drug flux through the production of derivatives with optimum lipid solubility's, but a major setback to this technique is that it seems to be a failure when the candidate is protein or DNA. Second approach - Structural alterations made within the skin by suitable agents or drug carriers²⁶.

In order to enhance the drug delivery through the transcellular route (a polar pathway) swelling of the intracellular protein matrix, alteration of protein structure within the corneocytes can be attempted. On the other hand in the case of the intercellular route (lipoidal pathway or the aqueous pathway) of penetration of the drug could be enhanced by altering the crystallinity of the intercellular lipid bilayer through an increase in hydration of the lipid polar head groups. Instead, the lipid hydrophobic tails could be disordered to pull off the same effect. Amplified drug partitioning could also be facilitated in the aqueous spaces between the lipid bilayers through a local enrichment of enhancer molecules. Finally, drug penetration can also occur through skin appendages such as hair follicles.

METHODS FOR PREPARING PRNOSOMES²⁸:

Proniosomal formulations may be prepared by

- Slurry method.
- Slow spray coating method.
- Coacervation phase separation method.

Slurry Method:

Proniosomes can be prepared from a stock solution of surfactants and cholesterol in suitable solvent. The required volume of surfactant and cholesterol stock solution per gram of carrier and drug should be dissolved in the solvent in 100 ml round bottom flask containing the carrier (maltodextrin). Additional chloroform can be added to form the slurry in case of lower surfactant loading. The flask has to be attached to a rotary flash evaporator to evaporate solvent at 50- 60 rpm at a temperature of 45 ± 20 C and a reduced pressure of 600mm Hg until the mass in the flask had become a dry, free flowing product. Finally, the formulation should be stored in tightly closed container under refrigeration in light.

Slow Spray Coating Method:

100 ml round bottom flask containing desired amount of carrier can be attached to rotary flash evaporator. A mixture of surfactants and cholesterol should be prepared and introduced into round bottom flask on rotary evaporator by sequential spraying of aliquots onto carrier's surface. The evaporator has to be evacuated and rotating flask can be rotated in water bath under vacuum at 65-70°C for 15 – 20 min. This process has to be repeated until all of the surfactant solution has been applied. The evaporation should be continued until the powder becomes completely dry.

Coacervation Phase Separation Method:

Accurately weighed or required amount of surfactant, carrier (lecithin), cholesterol and drug can be taken in a clean and dry wide mouthed glass vial (5 ml) and solvent should be added to it. All these ingredients have to be heated and after heating all the ingredients should be mixed with glass rod. To prevent the loss of solvent, the open end of the glass vial can be covered with a lid. It has to be warmed over water bath at 60-70°C for 5 minutes until the surfactant dissolved completely. The mixture should be allowed to cool down at room temperature till the dispersion gets converted to a proniosomal gel.

Table 1: Ingredients used for the preparation of Proniosomal gel

Sr.	Ingredients used	Example	Use
1	Surfactants (Non-ionic)	Spans 20, 40, 60, 80, 85, Tween 20,40, 80	To increase rate of permeation
2	Stabilizers	Cholesterol	To prevent leakage of drug formulation
3		Lecithin	Penetration enhancer
4	Solvent	Ethanol, methanol	For solubilising drug, surfactant.
5	Carriers	Maltodextrin	Provide flexibility in surfactant and other
6		Sorbitol	Alters the drug distribution

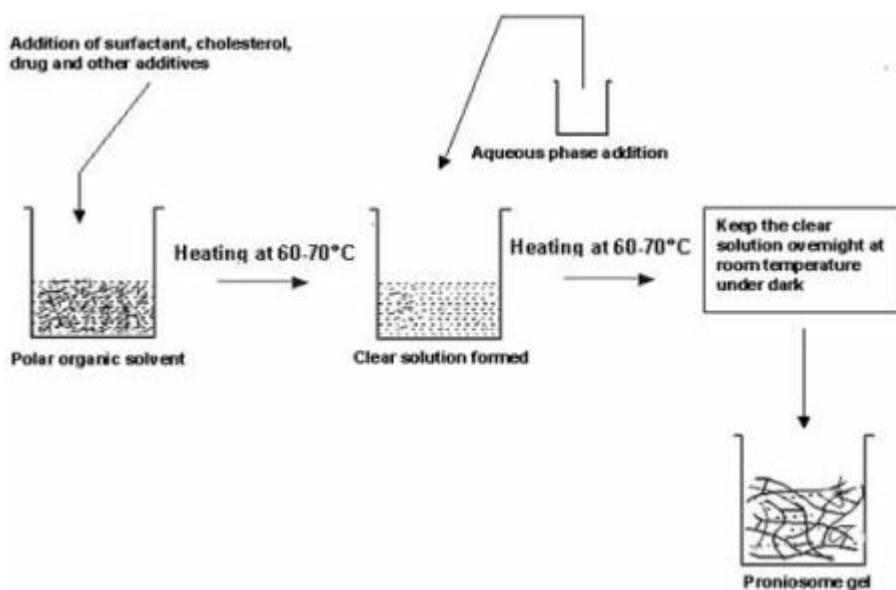


Fig. 3: Coacervation phase separation method

Table 2: Examples of some therapeutic and cosmetic agents used in carrier system

Therapeutic agent	Therapeutic category	Route of delivery	Delivery system
Levonorgestrel	Contraceptive agent	Transdermal	Proniosome gel
Flurbiprofen	NSAID	Transdermal	Proniosome gel
Captopril	Antihypertensive	Transdermal	Proniosome gel
Estradiol	Female hormone	Transdermal	Proniosome gel
Fruzemide	Diuretic	Transdermal	Proniosome gel
Losartan potassium	Antihypertensive	Transdermal	Proniosome gel
Cosmetic composition	Penetration enhancer for NSAIDS	Topical	Proniosome gel
Chlorpheniramine Maleate	Anti-histamine	Transdermal	Proniosome gel
Ketorolac tromethamine	NSAIDS	Transdermal	Proniosome gel

Surfactants: Selection of surfactant should be done on the basis of HLB value. As Hydrophilic Lipophilic Balance (HLB) is a good indicator of the vesicle forming ability of any surfactant, HLB number in between 4 and 8 was found to be compatible with vesicle formation. It is also reported that the hydrophilic surfactant owing to high aqueous solubility

on hydration do not reach a state of concentrated systems in order to allow free hydrated units to exist aggregates and coalesced to form lamellar structure. The water soluble detergent polysorbate 20 also forms niosomes in the presence of cholesterol. This is despite the fact that the HLB number of this compound is 16.7 Degree of entrapment is affected by the HLB of a surfactant. Transition temperature of surfactants also affects the entrapment of drug in vesicles. Spans with highest phase transition temperature provide the highest entrapment for the drug and vice versa. Span 40 and Span 60 produces vesicles of larger size with higher entrapment of drug. The drug leaching from the vesicles is reduced due to high phase transition temperature and low permeability. High HLB value of Span 40 and 60 results reduction in surface free energy which allows forming vesicles of larger size hence large area exposed to the dissolution medium and skin. No significant

difference is observed in the skin permeation profile of formulation containing Span 60 and Span 40 due to their higher phase transition temperature that is responsible for their lower permeability. The encapsulation efficiency of Tween is relatively low as compared to Span. The geometry of vesicle to be formed from surfactants is affected by its structure, which is related to critical packing parameters. On the basis of critical packing parameters of Surfactants can predicate geometry of vesicle to be formed. Critical packing parameters can be defined using following equation,

$$CPP = \frac{V}{l_c \times a^0}$$

CPP 0.5 micelles form

CPP= 0.5 – 1 spherical vesicles form CPP = 1 inverted vesicles form V – hydrophobic group volume l_c = the critical hydrophobic group length, a^0 = the area of hydrophilic head group. Span 60 is the good surfactant because it has CPP value between 0.5 and 1

Stabilizers: Cholesterol is essential component of vesicles. Incorporation of cholesterol influence vesicle stability and permeability. Concentration of cholesterol plays an important role in entrapment of drug in vesicles. There are reports that entrapment efficiency increase with increasing cholesterol content and by the usage of span 60 which has higher transition temperature. It was also observed that very high cholesterol content had a lowering effect on drug entrapment to the vesicles. This could be due to the fact that cholesterol beyond a certain level starts disrupting the regular bi-layered structure leading to loss of drug entrapment. Lecithin also provides stability but to a lesser extent compared to cholesterol.

Carriers: Maltodextrin is a polysaccharide. It has minimal solubility in organic solvent. Thus it is possible to coat maltodextrin particles by simply adding surfactant in organic solvent. The use of maltodextrin as carrier in Proniosomes preparation permitted flexibility in the ratio of surfactant and other components which can be incorporated. Coating sorbitol results in solid cake like mass²⁷.

CLINICAL APPLICATIONS OF PRNOSOMES:

The application of proniosomal technology is widely varied and can be used to treat a number of diseases. The following are the few uses of proniosomes which are either proven or under research.

1. Anti-Neoplastic Treatment:

Most antineoplastic drugs cause severe side effects. Niosomes can alter the metabolism; prolong circulation and half life of the drug, thus decreasing the side effects of the drugs. Entrapment of Doxorubicin and Methotrexate (in two separate studies) showed beneficial effects over the untrapped drugs, such as decreased rate of proliferation of the tumor and higher plasma levels accompanied by slower elimination.

2. Leishmaniasis:

Leishmaniasis is a disease in which a parasite of the genus Leishmania invades the cells of the liver and spleen. Use of proniosome in tests conducted showed that it was possible to administer higher levels of the drug without the triggering of the side effects, and thus allowed greater efficacy in treatment.

3. Uses In Studying Immune Response:

Proniosomes are used in studying immune response due to their immunological selectivity, low toxicity and greater stability. Niosomes are being used to study the nature of the immune response provoked by antigens.

4. Proniosomes As Carriers For Haemoglobin:

Niosomes can be used as carriers for haemoglobin within the blood. The niosomal vesicle is permeable to oxygen and hence can act as a carrier for hemoglobin in anaemic patients.

5. Proniosomes Used In Cardiac Disorders:

Proniosomal carrier system for captopril for the treatment of hypertension that is capable of efficiently delivering entrapped drug over an extended period of time. The potential of proniosomes as a transdermal drug delivery system for captopril was investigated by encapsulating the drug in various formulations of proniosomal gel composed of various ratios of sorbitan fatty acid esters, cholesterol and lecithin prepared by coacervation-phase separation method.

6. Antibacterial Therapy:

Amphotericin-B proliposomes could be stored for 9 months without significant changes in distribution of vesicle size and for 6 months without loss of pharmacological activity. Even though physical stability of the preparation can be increased, a vacuum or nitrogen atmosphere is still required during preparation and storage to prevent oxidation of phospholipids.

7. Cosmetics Formulation:

Now a day's large numbers of cosmetic preparations available in the market are utilizing niosomes and liposomes as a carrier for delivery of actives. Liposomes were prepared using unacceptable organic solvents, whose traces in the final preparation can cause harm to the skin. It is proved that proniosomes are as effective as niosomes and liposomes, but their preparation, handling, storage and transportation make them superior over others. The therapeutic agents which can be utilized for incorporation into proniosomal carrier systems include, moisturizing, nutritional, anti wrinkle, anti-ageing, cleansing, sunscreen particles, etc.

Examples of some therapeutic and cosmetic agents used in carrier system are shown in table.2

FACTOR AFFECTING ENTRAPMENT EFFICIENCY AND SIZE OF VESICLES

Entrapment efficiency is the measure of solute retention. High entrapment efficiency means a less time and less effort needed to remove the untrapped drug. Entrapment efficiency and vesicular size are important parameters to predict the stability of the dispersion. If the prepared formulation remains the unchanged vesicular size and entrapment efficiency even after storage, hence the formulation considered stable.

1. Non-Ionic Surfactant

The non-ionic surfactant used act as vesicle forming agent, the amount and its nature will affect the entrapment and vesicular size.

A. Nature of non-ionic surfactant

The entrapment efficiency and vesicular size depends upon the HLB value, chemical nature and phase transition temperature. The surfactant with high or low HLB value has high entrapment efficiency with some approaching 100%. In addition to HLB, the chemical structure of the surfactant i.e., the alkyl chain length will also affect the entrapment, which is directly proportional to the phase transition temperature. The higher the alkyl chain higher will be the entrapment efficiency; as it is having high phase transition temperature thereby it is more likely to form orderly gel form and hence less leaky. While surfactant with lower phase transition temperature are likely to form less orderly liquid. The increase in leakiness means it has less entrapment efficiency. This is evident from the report that, Sorbitan mono oleate (span 20, span 80) and Stearate, Sucrose esters shows higher entrapment efficiency, as their alkyl chain is longer thereby higher phase transition temperature. Whereas, Tween 20 and 80 have higher HLB, value and hence showed lower entrapment compared to span series. While Tween 80 has comparatively higher efficiency than Tween 20, because of higher phase transition temperature due to longer alkyl chain.

B. Amount of surfactant

The increase in surfactant amount will increase the entrapment efficiency because the surfactant being the vesicle forming agent.

2. Cholesterol

Cholesterol that acts as cementing agent, when its concentration is increased which will considerably decrease the entrapment efficiency. It will retard the afflux profile of entrapped drug. The reason behind decrease in the entrapment efficiency due to increase in cholesterol is that with higher amounts of cholesterol may compete with the drug for packing space within the bilayer, hence excluding the drug as the amphiphiles assemble into the vesicles. However, the effect of cholesterol will vary the entrapment efficiency according to the surfactant used. This is evident from the report that, increase in cholesterol content will vary the entrapment efficiency according to the surfactant used. In case of Brij 52(HLB- 5.3) has insignificant effect on the entrapment efficiency as the concentration of cholesterol is increased, but Brij 76 the HLB value is 12.6 indicating low hydrocarbon chain volume in comparison with hydrophilic surface area. Increased cholesterol content will increase the lipophilic character and hence the entrapment efficiency. Whereas, span series the entrapment efficiency was increased with cholesterol to some extent further increase lead to the decreased entrapment efficiency. This can explained to be due to the following fact that a small increase in cholesterol increases bilayer hydrophobicity and stability, thus the permeability is decreases as it efficiently traps the drug in the bilayer as vesicles are formed. However, the cholesterol may compete with the drug as the concentration is beyond certain limit.

3. Stearyl Amine

Stearyl amine when incorporated in the formulation will increase the entrapment efficiency as it produces strong electrostatic interaction between the negative charge drug and positive charged inducer stearylamine²⁹.

EVALUATION³⁰:

Scanning Electron Microscopy:

Proniosome powder is affixed to double sided carbon tape, positioned on an aluminum stub, and excess powder is removed. The stub is stored under vacuum overnight. The samples are sputter-coated with Au/pd under an argon atmosphere at 180 mA for 1 min (polaron E 5100; VG microtech, west swsex, UK). Electron micrographs are obtained using a field emission SEM operating at 1 or 2 kv (Zeiss DSM 982 Gemini, LEO Electron Microscopy Ltd, Cambridge, U.K.).

Transmission Electron Microscopy:

The morphology of hydrated niosome dispersion is determined using transmission electron microscopy. A drop of niosome dispersion is diluted 10-fold using deionised water. A drop of diluted niosome dispersion is applied to a carbon coated 300 mesh copper grid and is left for 1 min to allow some of the niosomes to adhere to the carbon substrate. The remaining dispersion is removed by adsorbing the drop with the corner of a piece of filter paper. After twice rinsing the grid (deionised water for 3-5 s) a drop of 2% aqueous solution of uranyl acetate is applied for 1 s. The remaining solution is removed by absorbing the liquid with the tip of a piece of filter paper and the sample is air dried. The sample is observed with a JEOL 100 CX transmission electron microscope at 80 kv.

Angle Of Repose:

The angle of repose of dry proniosome powder is measured by a funnel method. In this method, the funnel is fixed at a position so that the 13 mm outlet orifice of the funnel is 10 cm above a level black surface. The powder is poured through the funnel to form a cone on the surface, and the angle of repose is then calculated by measuring the height of the cone and the diameter of its base.

Particle Size And Particle Size Distribution:

A small aliquot (100 μ l) of niosome dispersion is dispersed in 50 ml of distilled water and is measured immediately with a Sald-1100 Laser Diffraction particle size analyzer. The particle size range of is set to 0.1-45 μ m and the refractive index range is set to 0.2-1.7 μ m. The particle size distribution of niosome is calculated internally.

Entrapment Efficiency:

Free drug is separated from niosome entrapped drug by centrifugation. When a 1 ml aliquot of niosomes is centrifuged at 18000 \times g, a stiff, floating fraction containing the niosomes is formed at the top of the tube; and a clear niosome-free solvent fraction remained at the bottom. The clear fraction is used for determination of free drug using suitable technique. The entrapment efficiency of the drug is defined as the ratio of the mass of niosome associated drug to the total mass of drug.

Release Of Drug From Proniosome:

In vitro release is determined using dialysis tube. One end of the tube is sealed with cellophane membrane. Measured amount of niosome are placed in the dialysis tube. Dialysis tube is placed into a beaker containing simulated fluid at 37 $^{\circ}$. Beaker is placed on magnetic stirrer and is shaken at 100 rpm at temperature of 37 $^{\circ}$. Aliquots are withdrawn from receptor compartment at certain time intervals. The drug in withdrawn samples is estimated by the suitable analytical method.

CONCLUSION

The concept of incorporating the drug into niosomes for a better targeting of the drug at appropriate tissue destination is widely accepted by researchers. Proniosomes derived niosomes represent a promising drug delivery module. They represent a structure similar to liposome and hence they can represent alternative vesicular systems with respect to liposomes, due to the niosome ability to encapsulate different type of drugs within their multi environmental structure. Proniosomes based niosomes are thoughts to be better candidates drug delivery as compared to liposomes due to various factors like cost, stability etc.

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