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Review Article

PRONIOSOMES: A FUTURE REVOLUTIONARY DRUG DELIVERY SYSTEM

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ABSTRACT

The present article provides an insight to provesicular carrier system for various pharmaceutical and cosmeceuticalapplications. Vesicular drug delivery reduces the cost of therapy by improved bioavailability of medication, especially in case of poorly soluble drugs. They can incorporate both hydrophilic and lipophilic drugs. Approaches to stabilize niosomal drug delivery system without affecting its properties of merits have resulted in the development of promising drug carrier,proniosomes .These proniosomes minimize the problems of aggregation, fusion and leakage of drugs and provides additional convenience in transportation, distribution, storage and dosage. It prolongs the existence of drug in systemic circulation .Proniosomes are dry formulation of water soluble carrier particles that are coated with surfactants and can be hydrated to form a niosomal dispersion immediately before use by brief agitation in hot aqueous media.

Keywords: Proniosomes, Provesicularsystem, Niosomes.

INTRODUCTION

In the past decades considerable attention has been focused on the developmentof new drug delivery system .Different carriers are also being used, they may be polymeric, particulate, macromolecular etc. These may include lipid particles ,microspheres and nanospheres. In the recent years vesicles have been choice in drug delivery lipid vesicles have been a valuable tool in genetic engineering, immunology and diagnostic purposes.[7] Awide varieties of drug delivery systems have been developed like liposomes transferosomes, pharmacosomes , niosomes etc.

Even though the structure and properties of niosomes are similar to that of liposomes ,the relatively low cost and chemical stability makes niosomes more useful than liposomes for industrial manufacturing .But due to the problems that the both faces in the aqueous suspension such as aggregation ,fusion, leaking of entrapped drugs limits the shelf life .Thus to overcome this a dry product could be formulated which on hydration immediately before use would avoid the above said problems .The additional benefits of transportation ,distribution ,storage would make the 'dry niosomes ' a promising industrial product [8].

Types of proniosomes[1]

There are two types of proniosomes

1. Dry granular proniosomes
2. Liquid crystalline proniosome

1. Dry granularproniosomes

These involves the coating of water soluble carrier such as sorbitol and maltodextrin with surfactant resulting in the formation of a dry formulation in which each water soluble particle is covered with a thin film of surfactant .

a. Sorbitol based proniosomes

It is a dry formulation which involves sorbitol as a carrier .these are made by spraying surfactant mixture prepared in organic solvent into sorbitol powder and then evaporating the solvent .useful in case where active ingredient is susceptible to hydrolysis .

b. Maltodextrin based proniosomes

These are prepared by slurry method. Maltodextrinis a polysaccride easily soluble in

water and is use as a carrier material in formulation and its morphology is preserved .hollow blown maltodextrin particles are used to increase in gain in surface area .the higher surface area results in thinner surfactant coating which is suitable for rehydration process.

2. Liquid crystallineproniosomes

When surfactant molecules are made in contact with water there are three ways in which the lipophilic chains of surfactants arebeing transformed into a disordered liquid state .The three ways are as follows;

1) Increasing temperature at Kraft's point
2) Addition of solvents
3) Using both temperature and solvent

Components of proniosomes[2]

The main components for the delivery system are as follows

1. Surfactants

These are surface active agents contains organic compounds that are ampiphilic in nature ,thereby it can function as solubilizers ,wetting agents ,emulsifiers and permeability enhancers .Egs of non ionic surfactants used are alkyl esters, alkylethers and esters of fatty acids.

2. Carrier Materials

Many varieties of carrier materials are now being currently investigated and used .The carrier when used in the preparation of proniosomes permits flexibility in ratio of surfactants and other components that are in cooperated .further more it increase surface area and hence efficient loading,all carriers used must be safe and nontoxic, freeflowing, must have poor solubility in the loaded mixture and good water solubility for ease of hydration .

Carriers used are maltodextrin, sorbitol, manitol, spray dried lactose, glucosemonohydrate, lactose monohydrate and sucrose stearate.

3. MembraneStabilizers

Steroids are a vital components of cell membrane and their presence in membrane brings about a change in bilayer stability, fluidity and permeability. Mainly used membrane stabilizers are cholesterol and lecithin.

Cholesterol is a naturally occurring steroids which prevents aggregation by inclusion of molecules which stabilisesthe system against the formation of aggregates by repulsive steric or electrostatic effects, it helps in transition from gel to liquids phase in niosomal system

Phosphatidylcholineis a major components for lecithin .it has low solubility in water and depending upon the source from which they are obtained they are named as soyalecithin or egg lecithin .It acts both as a stabilising and penetration enhancer.

4. Solvent and Aqueous Phase

Alcohols giveprofound effects on vesicle size and drug permeation rate. Different alcohols produce different sized vesicles and thus follow the order.

Ethanol >butanol>Isopropranol

Ethanol has greater solubility in water and form the highest size of vesicles compared to Isopropranol which forms smallest vesicles due to the branched chain present.

Phosphate buffer pH 7.4, 0.1% glycerol and hot water is used as aqueous phase in preparation of proniosomes.

5. Drug

Drug selection is based on the following criteria,

1) Low aqueous solubility of drugs.
2) High dosage frequency of drugs.
3) Short half life.
4) Controlled drug delivery suitable drugs.
5) Higher adverse drug reaction drugs.

Method of Preparation

Proniosomes can be prepared by the following methods,

a) Slurry Method

Proniosomes can be prepared by using a stock solution of surfactants and cholesterol in suitable solvents in a round bottom flask containing carriers. The surfactant solution is added to form slurry. The required volume of surfactants and cholesterol stock solution per grams of carrier and drug must be dissolved in the solvents in 100mL round bottom flask containing carrier (maltodextrin or lecithin) additional chloroform.

b) Slow Spray Coating Method

A 100mL roundbottom flask containing desired amount of carrier is attached to rotary flash evaporator. The surfactant solution in organic solvent is sprayed onto the sorbitol powder and the solvent is evaporated. This process is repeated until desired surfactant loading is been achieved.

c) Coacervation Phase Separation Method

All the required ingredients like surfactants, carriers, cholesterol are taken in a clean and dry wide mouth glass vial(5mL) and solvent should be added to it. These ingredients are all heated

and after heating, all ingredients should be mixed with glass rod. The open end of glass vial must be covered with a lid, to prevent loss of solvents, and then it is being needed over water bath at 60 – 70^0 c for 5min until surfactants dissolves completely then the mixture must be cooled at room temperature till dispersion gets converted into proniosomal gel[6]

Advantages of Proniosomes

1) Avoiding the problems of physical stability like fusion, aggregation, sedimentation and leakage on storage.
2) Avoiding the hydrolysis of encapsulated drugs which limiting the shelf life of the dispersion.
3) Ease on storage and handling.
4) No difficulty in sterilization, transportation, distribution, storage uniformity of dose and scale up.
5) Drug delivery with improved bioavailability, reduced side effects.
6) Entrapment of both hydrophilic and hydrophobic drugs.
7) Shows controlled and sustained release of drugs due to depot formation.
8) Biodegradable, biocompatible and non immunogenic to the body.
9) Shape, size, composition, fluidity of niosomes drug can be controlled as and when required.[4]

Characterisation of proniosomes

The characterisation of proniosomes are carried out by different ways

a) Scanning electron microscope(SEM)
b) Fourier transform infrared(FT-IR) spectroscopy
c) Measurement of angle of repose
d) Optical microscopy
e) Measurement of vesicle size
f) Drug content
g) Entrapment efficiency
h) Stability studies

a) Scanning electron microscope

By using scanning electron microscopy the surface morphology and size distribution of proniosomes can be studied .proniosomes were sprinkled on to the double sided tape that was affixed on aluminium stubs .the aluminium stub was placed in vacuum chamber of a scanning electron microscope and was made electrically conductive by coating a thin layer of gold and SEM images were recorded at 15ev accelerating voltage[3].

b) Fourier transform infrared(FT-IR) spectroscopy

Infrared spectrum of the optimised proniosomes powder was obtained using Fourier transform infrared(FT-IR) spectrophotometer by conventional potassium bromide pellets method .the scanning range between 4000-500cm^{-1}

c) Measurement of angle of repose

There are two methods in which the angle of repose of dried proniosomes was measured.

1. Funnel method

The proniosomalpowder was poured into a funnel which was fixed at a position 10cm above the alevel surface .the powder is flowed down from funnel to form a cone on the surface, and the angle of repose was then calculated by measuring the height of the cone and **d**iameter of its base.

2. Cylinder method

The proniosomalpowder was poured into a cylinder which was fixed at a position 10cm above a levelled surface .the powder is flowed down in a cylinder to form a cone on the surface, and the angle of repose was then calculated by measuring the height of the cone and diameter of its base.

Angle of repose is calculated by the equation

$$\mathbf{Ø - Tan^{-1} X (h/r)}$$

d) Optical microscopy

The proniosomal powder was evaluated for number of vesicles formed after hydration .the proniosomal powder was subjected to hydration with phosphate buffer (ph 7.4) and the formed niosomes were counted by optical microscope using haemocytometer. The niosomes in 80 small squares were counted and

Total number of niosomes per cubic mm

$$= \frac{\text{total number of niosomes counted} \times \text{dilution factor} \times 4000}{\text{Total number of squares counted}}$$

e)Measurement of vesicles size

Mainly used for the characterisation of vesicle size and shape .the proniosomal powder were hydrated with phosphate buffer (pH7.4) and subjected to bath sonication for 3 minutes and the resultant dispersion was used for determination of size[5].

f)Drug Content

Proniosomal formulation equivalent to 250mg of drug was taken in a standard volumetric flask .they were lysed with 50 mL propanol by shaking and 1 mL of mixture was then diluted with phosphate buffer (pH 7.4). the absorbance was measured spectroscopically at 281 nm and drug content was calculated from the calibration curve of drug in phosphate buffer 7.4.

g) Entrapment efficiency

The prepared niosomes were separated from entrapped drug by centrifugation .In this method hydrated proniosomes were centrifugation at 14000rpm for 5 minutes using the refrigerated centrifuge and the supernatant were analysed for free drug content .entrapment efficiency was calculated using the given formula ,

$$\text{Entrapment efficiency} = \frac{\text{Total drug loaded} - \text{free drug} \times 100}{\text{Total drug}}$$

h) StabilityStudies

To determine the stability of proniosomes the optimised batches was stored in air tight sealed vials kept at threedifferent temperatures(refrigerated 2-8^{0}c,room ,and 40^{0}c) at definite time intervals (0,30,60,90 days). Samples from each batch were withdrawn after definite time interval, converted into niosomes and residual amount of drug in vesicles determined. Surfacecharacteristics and percentage drug retained in proniosomes and parameters for evaluation of stability, since instability of the formulation would indicate a leakage of drug and decrease in drug retained.

CONCLUSION

Proniosomes represents a significant advance over conventional vesicular system. They are osmotic ally active and stable. Proniosomal systems appears to be efficient drug carrier for future with both physical and chemical stability and potentially scalable for commercial viability. Proniosomes are effective tool for targeting of drugs and have potential to provide better treatment than conventional drug delivery system. Moreover future experiments should be explored with a wide range of drugs having drawbacks so as for improved andeffective therapy. Therefore proniosomes serves as a potential candidate for newer industrial revolutionary works

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