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PRONIOSOMES:- A NOVEL DRUG CARRIER FOR TRANSDERMAL DRUG DELIVERY

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ABSTRACT

The purpose of the current study was to investigate the feasibility of proniosomes as a novel drug carrier for Transdermal drug delivery. This article describes the proniosome- derived niosomes. Niosomes are non-ionic surfactant vesicles that can entrap a solute in a manner analogous to liposomes. Niosomes have been prepared from several classes of non- ionic surfactants. Niosomes may be unilamellar or multilamellar depending on the method used to prepare them. In recent years, niosomes have been extensively studied for their potential to serve as carrier for delivery of drugs, antigen, hormone and other bioactive agents. The basic aim in developing the delivery system is controlling the release of drugs from the carrier system, in order to achieve an extended uptake in the body. Proniosomes 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. This review presents an overview about proniosomes regarding their preparation, characterization and transport of various drugs through skin.

Key words: Niosomes, Proniosomes, Transdermal drug delivery, Vesicles, Non-ionic.

INTRODUCTION

The goal of controlled release dosage form is to establish relatively constant plasma drug concentrations, avoiding the peak and valleys associated with conventional dosage forms. Controlled delivery of drugs by the transdermal route provides unique opportunity in order to maintain constant plasma level of drug [1]. Transdermal delivery of drugs offers several advantages over conventional delivery including oral and injection methods like elimination of gastrointestinal absorption problems hepatic first pass effect, reduction of dosage and dose interval, predictable and extended duration of activity and improved patient compliance [2]. Increasing number of drugs are being added to the list of therapeutic agents that can be delivered to the systemic circulation via skin [3].

Proniosomes

Proniosomes are promising drug carriers, because they are dry product which could be hydrated immediately before use, would avoid many of the problems associated with aqueous niosomes dispersions and problems of physical stability could be minimized. These dry formulations of surfactant- coated carrier can be measured out as needed and rehydrated by brief agitation in hot water [4]. Niosomes are non-ionic surfactant vesicles having potential applications in the delivery of Hydro phobic as well as hydrophilic drugs [5] and are biodegradable, biocompatible and non- immunogenic in nature and exhibit flexibility in their structural characterization [6]. Thus, this proniosomes are minimizing the problems using dry, free flowing product which is more stable during storage and sterilization and it has additional merits of easy of transfer, distribution, measuring and storage make proniosomes a pronouncing versatile delivery system [7].

Composition

Proniosomes can be prepared by using some materials like

1) Surfactants eg: Span 20, 40, 60, 80, 85, Tween 20,40, 80 which is used to increase drug flux rate across the skin [8].
2) Cholestrol used to prevent leakage of drug formation [9].
3) Lecithin as penetration enhancer [10], maltodextrin which provides flexibility in surfactant and other component ratio [11].

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4) Sorbitol which alters the drug distribution [12].

METHOD OF PREPARATION OF PRONIOSOMES

Proniosomes can be prepared by following three methods.

1) Slurry method:- Proniosomes can be prepared from a stock solution of surfactants and cholesterol in suitable solvent. The requires 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. The flask has to be attached to a rotary flask evaporator to evaporate solvent at 50-60 rpm at a temperature of 45 ± 2^0 C and a reduced pressure of 600mm Hg until the mass in the flask had become a dry, free flowing product [13,14].

2) Coacervation phase separation method:-This method is widely adopted to prepare proniosomal gel. Precisely weighed amount of surfactant, lipid and drug are taken in a clean and dry wide mouthed glass vial of 5.0 ml capacity and alcohol of 0.5 ml is added to it. After warming, all the ingredients are mixed well with a glass rod, the open end of the glass bottle is covered with a lid to prevent the loss of solvent from it and warmed over water bath at $60\text{-}70^0$C for about 5 minutes. Then the aqueous phase (0.1% glycerol solution) is added and warmed on a water bath till a clear solution was formed which is then converted into proniosomal gel on cooling [15].

3) Slow Spray- coating method:- A 100ml round bottom flask containing desired amount of carrier can be attached to rotary flask evaporator. A mixture of surfactants and cholesterol should be prepared and introduced into round bottom flask on rotary evaporator by sequential spraying of aliquots into carrier's surface. The evaporator has to be evacuated and rotary flask can be rotated in water bath under vacuum at $65\text{-}70^0$C for 15-20 minutes. 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.

MECHANISM OF SKIN PERMEATION OF PRONIOSOMES

Several mechanisms can be used to explain the ability of niosomes to modulate drug transfer across the skin including [16].

1) Adsorption and fusion of niosomes on to the surface of skin leading to a high thermodynamic activity gradient of drug at the interface, which is the driving force for permeation of lipophillic drugs.

2) The effects of vehicles as the permeation enhancers reduce the barrier properties of stratum corneum.

3) The lipid bilayers of niosomes act on rate limiting membrane barrier for drugs, stratum corneum in transdermal delivery.

CHARACTERIZATION OF PRONIOSOMES

1) Measurement of vesicle size:- The vesicle dispersion was diluted about 100 times in the same buffer, used for their preparation. Vesicle size was measured as MVD on a particle size analyzer. The apparatus consist of a He-Ne Laser beam of 632.8nm focussed with a minimum power of 5mW using a fourier lens (R-5) to a point at the center of multielement detector and a small volume sample holding cell. The sample was stirred using a stirrer before determining the particle size [17].

2) Shape and surface morphology:- Surface morphology means roundness, smoothness and formation of aggregation it was studied by scanning electron microscopy, optical microscopy, Transmission electron microscopy [18].

3) Zeta potential:- Zeta potential was analyzed to measure the stability of niosome by studying its colloidal property. The zeta potential value of the sample was measured by a zeta potential probe model DT-300. A niosomes which gives best results for entrapment efficiency and drug release was determined for Zeta potential [19].

4) Measurement of Angle of Repose:- The angle of repose of drug proniosomes powder was measured by a funnel method it was calculated by measuring the height of the cone and the diameter of its base. It can be denoted by formula [20]

$$\text{Tan } \theta = h/r$$

5) Encapsulation efficiency:- To evaluate the loading capacity of proniosomal system it was dispersed in distilled water and warmed a little for the formation of niosomes. Then the dispersion was centrifuged at 18000rpm for 40 minutes at 5^0C. The clear fraction was used to determine free drug spectrophotometrically [21].

% encapsulation efficiency = [1-(unencapsulated drug) / Total drug)] × 100

6) Stability studies:- Stability of the pronoisomal formulations was determined by storing in glass petridish covered with aluminium foil at room temperature (30 ± 2^0C) and in a refrigerator (4 ± 2^0C). After 5, 15, and 30 days they were observed visually and under optical microscope for changes in consistency and appearance of drug crystals [22].

7) Invitro Drug Release:- It can be determined by

a) Franz diffusion cell:- This cell has a donor chamber fitted with a cellophane membrane, the proniosomes are placed in it and dialysed against a suitable dissolution medium at room temperature, the drug content is analysed using suitable method (UV; HPLC) [23].

b) Dialysis Tubing:- This apparatus has prewashed dialysis tubing which can be thermatically sealed, the proniosomes are placed in it and then dialysed against a suitable dissolution medium at a room temperature, the samples are withdrawn from the medium at suitable intervals centrifuged and analysed for drug content using suitable method (UV; HPLC).

c) Reverse Dialysis:- In this apparatus a number of small dialysis tubes containing 1ml of dissolution medium are placed. Then proniosomes are displaced into the dissolution medium, the direct dilution of the proniosomes is possible with this method. But the rapid release cannot be qualified using this method [24].

8) Statistical Analysis:- Data were expressed as the mean of three experiments ± the standard deviation and were analyzed using one- way analysis of variance, followed by Tukey's multiple comparision post test. Statistical

differences yielding $p < 0.05$ were considered significant [25].

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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