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REVIEW ON NIOSOMES: COMPOSITION, PREPARATION

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ABSTRACT
Niosomal vesicle is formed by non-ionic surfactants whereas liposomal vesicles of lipids. Niosomes are superior to liposomes because of higher chemical stability of surfactants than lipids. Niosomes offer superior stability, making them a preferred choice. Non-ionic in nature niosomes offer unique advantages in drug delivery providing a versatile platform for encapsulating various drugs to enhance bioavailability and ensure controlled release. There are several factors like the type of non-ionic surfactant used, method of preparation, the temperature of hydration, etc. which affect the niosome formation.

KEYWORDS: Niosomes, Bioavailability, Non-ionic surfactant, Methods, Applications.

INTRODUCTION

Niosomes are a new drug delivery system (NDDS) with the goal of delivering the medication at a regulated pace dictated by the demands of the body during the course of treatment of an illness to improve absorption and distribute the active substance to the target location.[1] Niosomes are essentially equivalent with liposomes but provide several benefits Because of their tiny size (in nanometers), they can readily pass through all routes of action via the skin. The niosome undergoes less metabolism and removal by the reticular endothelial system due to its nanoscale size. Niosomes are thought to be the ideal drug delivery vehicles since they are non-ionic in nature, have low toxicity, and improve a medicine's therapeutic efficiency by targeting certain cells.[2] Niosomes represent a promising and innovative category of vesicular systems. Non-ionic surfactant vesicles commonly referred to as niosomes. Their size is in the range of 10–1000 nm. They are biocompatible and can be used in drug delivery systems. Niosomes are considered to be the improved vehicle to enhance bioavailability and therapeutic efficiency by acting as a trusted approach for disease treatment and minimizing the side effects. Niosomes are microscopic non-ionic surfactant vesicles formed by the self-assembly of non-ionic surfactant. Niosomes are suggested to be better than liposomes because of the higher chemical stability of surfactants than phospholipids which are easily hydrolyzed due to the ester bond and cost effective.[3]

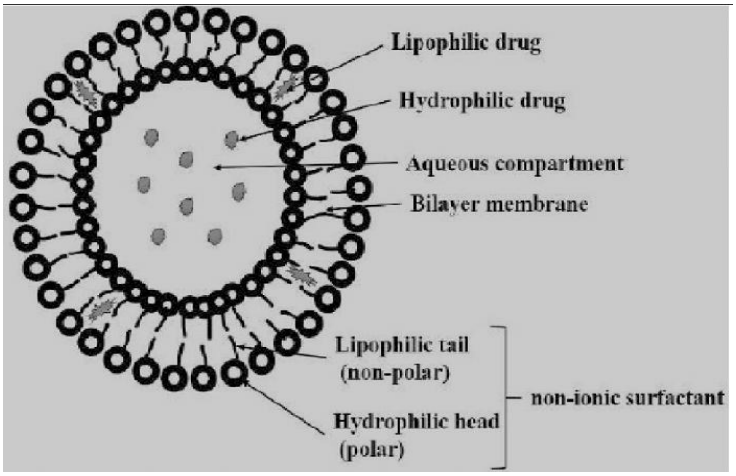

Fig. 1: Structure of Niosomes.

Advantages of Niosomes[4]

- The vesicle suspension being water-based vehicle offers high patient compliance when compared to oily dosage forms.
- Vesicle characteristics can be controlled by altering the composition of vesicle, size lamellarity, surface charge, tapped volume and concentration.
- They can release the drug in sustained/controlled manner.
- Storage and handling of surfactants oblige no special conditions like low temperature and inert atmosphere.
- They can act as a depot formulation, thus allowing the drug release in a controlled manner.
- They enhance the oral bioavailability of poorly soluble drugs.
- They possess stable structure even in emulsion form.

Disadvantages of Niosomes[5]

- Limited shelf life of the aqueous suspensions of niosomes due to fusion, aggregation, leakage of entrapped drugs and hydrolysis of encapsulated drugs.
- Preparation of multilamellar vesicles by extrusion, sonication method is time consuming and requires specialized equipment's for processing.

Types of niosomes[6]

Based on the vesicle size niosomes can be divided into three groups.

1. Small unilamellar vesicles (SUV, size=0.025-0.05 µm)
2. Multilamellar vesicles (MLV, size=>0.05 µm)
3. Large unilamellar vesicles (LUV, size=>0.10 µm).

Structure of niosomes[7]

Niosomes are the bi-layered structure of non-ionic surface-active agents. These thermodynamically stable bilayered structures are formed only when surfactants and cholesterol are mixed in a proper proportion, and the temperature is above the gel liquid transition temperature. This bi-layered structure contains a hollow space in the center. Because of their special geometry niosomes can encapsulate hydrophilic as well as a hydrophobic drug in their structure

COMPONENTS OF NIOSOMES[8]

The niosome composition is a determinative factor in the fabrication, pharmacokinetic behavior, and application of drug-loaded niosomes. In general, a niosome comprises non-ionic surfactants, lipids such as cholesterol, charge-inducing agents, and hydration medium, which are relatively biocompatible and nontoxic

Non-ionic surfactants

Non-ionic surface-active molecules are the fundamental elements in the preparation of niosomes. They are amphiphilic molecules with a polar head and a non-polar tail. These uncharged surfactants are more stable and less toxic than anionic, cationic, and amphoteric surfactants. These non-ionic surface-active agents, wetting agents, and emulsifiers have diverse capabilities including inhibiting p-glycoprotein, causing less haemolysis and irritation to cellular surfaces, enhancing permeability, and improving solubility.

Cholesterol

Cholesterol can affect membrane permeability and stiffness, drug trapping efficiency, rehydration of dried niosomes, stability, storage condition, and toxicity.[35] [36], In addition to protecting the drugs from premature degradation, cholesterol also inhibits unwanted immunological and pharmacological effects.

METHODS OF PREPARATION

The method of preparation influences the size, size distribution and number of bilayers, entrapment efficiency of the aqueous phase and the membrane permeability of the vesicles. a) Ether injection method.

Ether injection method

This method involves the introduction of surfactant dissolved in diethyl ether into warm water maintained at 60ºC. The ether solution with surfactant is injected into an aqueous solution of material through the 14-guage needle. Single layered needles are formed due to the vaporization of ether. The diameter of the vesicle varies from 50-1000nm depending upon the conditions used.[9]

b) Hand shaking method/thin film hydration method

Surfactant and cholesterol are dissolved in a volatile organic solvent such as diethyl ether or chloroform or menthol. Using the rotary flash evaporator, the organic solvent is removed at room temperature of 20ºc which leaves a thin layer of solid mixture on the wall of the flask. The dried surfactant film is then rehydrated with aqueous solution of drug at the temperature of surfactants used for specified period of time (time of hydration) with gentle agitation. Multilamellar niosomes are formed by this method. Thermo sensitive niosomes are prepared by evaporating organic solvent at 60ºC leaving a thin film on the wall of rotary flask evaporator and then the aqueous solution with drug is added slowly by shaking at room temperature followed by sonication.[10]

c) Micro fluidization

Micro fluidization is the technique which forms unilamellar niosomes of defined size distribution, uniformity and better reproducibility. The principle involved in this technique is submerged jet principle in which two fluidized streams interact with each other at ultra high velocities, in the micro channels within the interaction chamber. The impingements of thin liquid sheet along with common front are arranged such that the energy supplied remains same within the area of niosomes formation. It results in the formation of niosomal vesicles of greater uniformity, smaller size and better reproducibility.[11]

d) Multiple membrane extrusion method

Desired size of the vesicles can be prepared by this method. It can be achieved by placing polycarbonate membranes in series up to 8 passages. Thin film of the surfactant, cholesterol and diacetyl phosphate mixture is made by evaporation. The film is then rehydrated with the aqueous solution containing drug. The resultant solution is extruded through poly carbonate membrane (0.1µm nucleophore) by using C16G12.[12]

e) Reverse phase evaporation technique:

Cholesterol and surfactant in the ratio of 1:1 are dissolved in the mixture of ether and chloroform. Aqueous drug solution is added to this. The two phases are sonicated at 4-5ºc. Small amounts of phosphate buffered saline (PBS) are added to the clear gel and sonicate it again. The organic phase is removed at 40ºc and lower pressure. The viscous niosomal suspension is further diluted with PBS and heated on a water bath at 60ºc for 10min to yield niosomes.[12]

f) Sonication

The production of vesicles by the sonication of solution is described by cable. An aliquot of buffer solution containing drug is added to the mixture of surfactant/cholesterol mixture in a 10ml glass vial. Then the mixture is subjected to sonication at 60ºc for 3min in a sonicator with titanium probe to produce niosomes.[13]

g) Transmembrane PH

Gradient drug uptake:

Surfactant and cholesterol are dissolved in chloroform in a round bottomed flask. The solvent evaporation is done under reduced pressure to get the thin film on the wall of the flak. The film is then hydrated with 300mm citric acid (PH 4.0) by vortex mixing. It results in the formation of multilamellar vesicles. Then they are frozen and thawed 3 times and later sonicated to get niosomes. To this niosomal suspension, aqueous drug solution is added and vortexed. To maintain the PH between 7.0-7.2, phosphate buffer is used. Then the mixture is heated at 60ºc for 10 minutes to yield niosomes.[14]

h) The bubble method

It is the novel technique used for the one step preparation of niosomes without the use of organic solvents. The bubbling unit has round-bottomed flask with three necks positioned in water bath to control the temperature. In the first neck, water cooled reflux; thermometer in the second and nitrogen supply through the third neck is provided. Cholesterol and surfactant are dispersed in PH 7.4buffer at 70ºc. The dispersion is mixed for 15 seconds using high shear homogenizer. Then nitrogen gas is bubbled at 70ºc immediate.[15]

Characterisation of niosomes

Size

Shape of niosomal vesicles is assumed to be spherical, and their mean diameter can be determined by using laser light scattering method. Also, diameter of these vesicles can be determined by using electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy and optical microscopy[29,30] and freeze fracture electron microscopy. Freeze thawing of niosomes increases the vesicle diameter, which might be attributed to a fusion of vesicles during the cycle.[16]

Bilayer formation

Assembly of non-ionic surfactants to form a bilayer vesicle is characterised by an X-cross formation under light polarisation microscopy.[17]

Number of lamellae

This is determined by using nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering and electron microscopy.[18]

Membrane rigidity

Membrane rigidity can be measured by means of mobility of fluorescence probe as a function of temperature.[19]

Entrapment efficiency

After preparing niosomal dispersion, unentrapped drug is separated and the drug remained entrapped in niosomes is determined by complete vesicle disruption using 50% n-propanol or 0.1% Triton X-100 and analysing the resultant solution by appropriate assay method for the drug.[20] It can be represented as:

Entrapment efficiency (EF) = (Amount entrapped / total amount) × 100

In vitro Release Study

A method of in vitro release rate study was reported with the help of dialysis tubing.[33] A dialysis sac was washed and soaked in distilled water. The vesicle suspension was pipetted into a bag made up of the tubing and sealed. The bag containing the vesicles was then placed in 200 ml buffer solution in a 250 ml beaker with constant shaking at 25°C or 37°C. At various time intervals, the buffer was analysed for the drug content by an appropriate assay method. In another method, isoniazid-encapsulated niosomes were separated by gel filtration on Sephadex G- 50 powder kept in double distilled water for 48 h for swelling.[34] At first, 1 ml of prepared niosome suspension was placed on the top of the column and elution was carried out using normal saline. Niosomes encapsulated isoniazid elutes out first as a slightly dense, white opalescent suspension followed by free drug. Separated niosomes were filled in a dialysis tube to which a sigma dialysis sac was attached to one end. The dialysis tube was suspended in phosphate buffer of pH (7.4), stirred with a magnetic stirrer, and samples were withdrawn at specific time intervals and analysed using high-performance liquid chromatography (HPLC) method.[21]

APPLICATIONS OF NIOSOMES[22,23]

Niosomes as Drug Carriers

Niosomes have also been used as carriers for iobitridol, a diagnostic agent used for X-ray imaging. Topical niosomes may serve as solubilization matrix, as a local depot for sustained release of dermally active compounds, as penetration enhancers, or as rate-limiting membrane barrier for the modulation of systemic absorption of drugs.

Drug Targeting

One of the most useful characteristics of niosomes is their ability to target drugs. Niosomes can be used to target drugs to the reticuloendothelial system. The reticuloendothelial system (RES) preferentially takes up niosome vesicles. Such localization of drugs is utilized to treat tumors in animals known to metastasize to the liver and spleen. This localization of drugs can also be used for treating parasitic infections of the liver. Niosomes can also be utilized for targeting drugs to organs other than the RES.

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. Niosomes are decreased rate of proliferation of tumor and higher plasma levels accompanied by slower elimination.

Leishmaniasis

Leishmaniasis is a disease in which a parasite of the genus Leishmania invades the cells of the liver and spleen. Use of niosomes 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.

Delivery of Peptide Drugs

Oral peptide drug delivery has long been faced with a challenge of bypassing the enzymes which would breakdown the peptide. Use of niosomes to successfully protect the peptides from gastrointestinal peptide breakdown is being investigated. In an in vitro study conducted by oral delivery of a vasopressin derivative entrapped in niosomes showed that entrapment of the drug significantly increased the stability of the peptide.

Use 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. Nonionic surfactant vesicles have clearly demonstrated their ability to function as adjuvant following parenteral administration with a number of different antigens and peptides.

Niosomes 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 haemoglobin in anaemic patients.

CONCLUSION

Niosomes are a suitable, targeted, and effective drug delivery system with the ability to load both hydrophilic and hydrophobic drugs. Niosomes also improve medication stability, decrease drug toxicity, and delay drug release. Niosomes develop a suitable technology for large production because it is a promising targeted drug delivery system. Niosomes can be used for targeted, ocular, topical, parenteral, and other types of drug delivery.

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