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Niosomes: An Approach to Current Drug Delivery System

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ABSTRACT

Niosomes composed of non-ionic surfactant vesicles that are prepared by hydrating mixture of cholesterol and non-ionic surfactant. It can be used as carrier of amphiphilic and lipophilic drug. Niosomes is the type of delivery system in which medication is encapsulated in a vesicle. Niosomes exhibit various properties like biodegradable, biocompatible, non-immunogenic and has flexibility in their structure. Niosomes can entangle both hydrophilic and lipophilic medications and can prolong the circulation of the entrapped medication in the body. This review focuses on components of niosomes, types, advantages, preparation methods, factor affecting, characterizations and application of niosomes.

Keywords: Niosomes, surfactants, cholesterol, ether injection.

I. INTRODUTION

For many decades, medication of an acute disease or a chronic illness has been accomplished by delivering drugs to the patients via various pharmaceutical dosage forms like tablets, capsules, pills, creams, ointments, liquids, aerosols, injectables and suppositories as carriers. To achieveand then tomaintain the concentration of drug administered withinthe therapeutically effective range needed for medication, it is often necessary to take this type of drug delivery systems several times in a day. This results in a fluctuated drug level and consequently undesirable toxicity and poor efficiency. To minimize this fluctuation, novel drug delivery systems have been developed, which include niosomes, liposomes, nanoparticles, microspheres, micro-emulsions,impalatable pumps and magnetic microcapsules.[1-2]

Niosomes

Niosomes are one of the best among these carriers. Structurally, niosomes are similar to liposomes and are equative in drug delivery potential but high chemical stability and economy makes niosomes superior than liposomes. Both consist of bilayer, which is made up of non-ionic surfactant in the case of niosomes and phospholipids in case of liposomes. Niosomes are microscopic lamellar structures of size range between 10 to 1000 nm and consists of biodegradable, non-immunogenic and biocompatible surfactants. Theniosomes are amphiphilic in nature, which allows entrapment of hydrophilic drug in the core cavity and hydrophobic drugs in the non-polar region present within the bilayer hence both hydrophilic and hydrophobic drugs can be incorporated into niosomes.[3]

Advantages of niosomes:

1. They help accommodate hydrophilic, lipophilic as well as amphiphilic drug moieties, they can be used for a variety of drugs.
2. They are osmotically active and stable.
3. They increase the stability of the entrapped drug.
4. They can enhance the skin penetration of drugs.[4]

Disadvantages of niosomes:

1. Fusion.
2. Aggregation.
3. Leaking of entrapped drug.
4. Physical instability.[5]

Salient features of niosomes:

- Niosomes can entrap solutes.
- Niosomes are osmotically active and stable.
- Niosomes can improve the performance of the drug molecules.
- Better availability to the particular site, just by protecting the drug from biological environment.[6]

Structure of niosomes:

Niosomes are spherical and consist of microscopic lamellar (unilamellar or multilamellar) structures. The bilayer is formed by a non-ionic surfactant, with or without cholesterol and a charge inducer.

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- surfactants include alkyl ethers, alkyl glyceryl ethers, sorbitan fatty acids esters, and polyoxyethylene fatty acid esters.
- Addition of cholesterol maintain the rigidity of the bilayer, resulting in less leaky niosomes.
- Nonionic surfactants in niosomes tend to orient themselves in such a way that hydrophilic end faces outward (towards the aqueous phase), whereas the hydrophobic end faces inward to each other to form a closed bilayer structure, which encloses solutes in an aqueous solution.

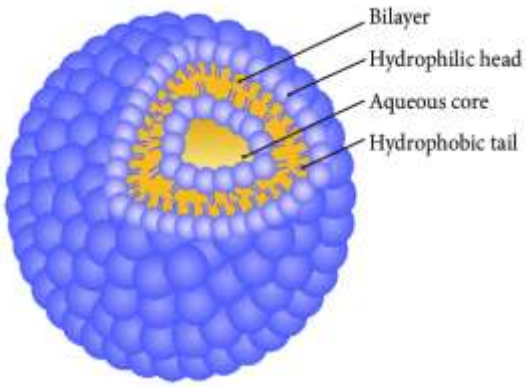

FIGURE 1: STRUCTURE OF NIOSOMES[7]

COMPARISION OF NIOSOMES AND LIPOSOMES

Niosomes are now widely studied as an alternative to liposomes, which exhibit certain disadvantages such as -they are expensive, their ingredients like phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special storage and handling and purity of natural phospholipids is variable. Such vesicular drug carrier systems alter the plasma clearance kinetics, tissue distribution, metabolism and cellular interaction of the drug.
They can be expected to target the drug to its desired site of action and or to control its release.[8]

Table 1: Difference between Liposome and Noisome

Liposomes	Niosomes
More expensive	Less expensive
Phospholipids are prone to unstable due to oxidative Degradation.	Non-ionic surfactants are stable than phospholipid
Required special condition for storage, handling and purification of phospholipids.	Do not required special condition for such formulations as Compare to liposomes.
Phospholipids can be charged or neutral.	Non-ionic surfactants are uncharged.

COMPONENTS OF NIOSOMES:

A) Non-ionic surfactants
B) Cholesterol
C) Charge inducers
D) Hydration medium

A) Non -ionic surfactant: In this non-ionic surfactant contain both hydrophilic head and hydrophobic tail are present. The major of non-ionic surfactants used are Span (20,40,60,65,80, and 85) Tween (20,40,65,80,85), Brij (52,58,35,30), Sorbitan ester, Ester alkyl amide.

B) Cholesterol (Bilayer membrane stabilizer) It offers rigidity, fluidity and permeability to cell membranes and vesicles membranes that are not supplied by the surfactants alone (they are fairly brittle otherwise) and thus integrates cholesterol into the bilayers of the artificial vesicle in order to increase their organized condition. Cholesterol may be included in bilayers, but it does not itself shape bilayers.[9]

C) Charge inducer: Charge inducers are added in the preparation to increase the stability of niosomes by electrostatic repulsion to avoid coalescence.

D) Hydration medium: The most commonly used hydration medium in the preparation of niosomes is phosphate buffer. These phosphate buffers are used at various pH. The actual pH drug being encapsulated.[10]

TYPES OF NIOSOMES:

The niosomes are classified as a function of the number of bilayer (e.g. MLV, SUV) or as a function of size (e.g. LUV, SUV) or as function of the method of preparation (e.g. REV, DRV). The various types of niosomes are described below:

a. Multi lamellar vesicles (MLV)

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b. Large unilamellar vesicles (LUV)
c. Small unilamellar vesicle (SUV)

1.Multi lamellar vesicles (MLV): It consists of a number of bilayers surrounding the aqueous lipid compartment separately. The approximate size of these vesicles is 0.5-10 µm diameter.
2.Large unilamellar vesicles (LUV): Niosomes of this type have a high aqueous/lipid compartment ratio, so that larger volumes of bio-active materials can be entrapped with a very economical use of membrane lipids.
3.Small unilamellar vesicles (SUV): These small unilamellar vesicles are mostly prepared from multilamellar vesicles by sonication method. French press extrusion electrostatic stabilization is the inclusion of diacetyl phosphate in 5(6)-carboxyfluorescein (CF) loaded Span 60 based niosomes.[11]

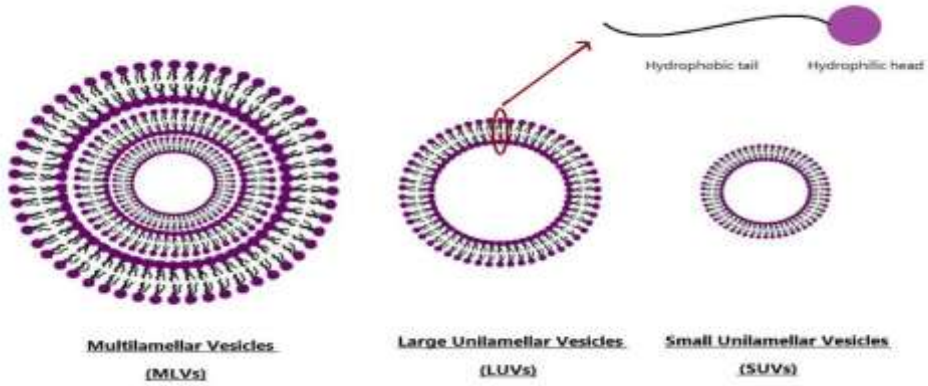

FIGURE 2: TYPICAL VESICLE SIZE OF NIOSOMES [12]

CHARACTERSTICS OF NIOSOMES:
1)Size: Shape of niosomal vesicles is assumed to be spherical, and their mean diameter can be determined by using laser light scattering method.
2)Bilayer formation: Assembly of non-ionic surfactants to form a bilayer vesicle is portrayed by X-cross formation under light polarization microscopy.
3)Number of lamellae: This is determined by utilizing nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering and electron microscopy.
4)Membrane rigidity: Membrane rigidity can be estimated by means of mobility of fluorescence probe as a function of temperature.
5)Entrapment efficiency: The unentrapped medication is separated by dialysis, centrifugation, or gel filtration. Entrapment efficiency = (Amount entrapped / total amount) x 100.
6) pH measurement: The pH of niosomes can be measured by a pH meter. The pH estimation performed at 25°C.
7)Zeta potential measurement: Zeta potential of suitably diluted niosomes dispersion is carried out using zeta potential analyzer which is based on electrophoretic light scattering and laser Doppler velocimetry method. [13]

II. METHOD OF PREPARATION:

A. Passive trapping technique
1. Sonication
2. Ether injection method
3. Reverse phase evaporation technique
4. The bubble method
5. Hand shaking method
6. Multiple membrane extrusion method
7. Ethanol injection method
8. Micro Fluidization
B. Active trapping technique
1. Trans membrane pH gradient drug uptake process
C. Miscellaneous method
1. Emulsion method
2. Heating method
3. Formation of niosomes from proniosomes
4. Lipid injection method .[14]

A. Passive trapping technique
Sonication:
It is a typical method of production of the vesicles in which a 10ml glass vial drug solution in

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buffer is added to the surfactant/cholesterol mixture. Then the mixture is probe sonicated at 60°C for 3 min using a sonicatorwith titanium probe to yield niosomes. The resulting vesicles are small and unilamellar.

Hand shaking method (Thin film hydration technique):

Surfactant and the other vesicles forming ingredients like cholesterol are blended and mixture is dissolved in a volatile organic solvent like diethyl ether, chloroform or methanol in a round bottom flask. Using rotary evaporator, the organic solvent is removed at room temperature (20°C), by this a thin layer of solid mixture deposited on the wall of the flask. The dried surfactantfilm canbe rehydrated with aqueous phase at 60°C with gentle agitation results in formation of multilamellar niosomes[15]

Micro fluidization:

It is a recent technique based on submerged jet principle. In these two fluidized streams interact atultra-high velocities and move forward through precisely defined micro channelwithin the interaction chamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation which results in a greater uniformity, smaller size and better reproducibility of niosomes formed.[16]

The "Bubble" Method:

It is one step technique by which liposomes and niosomes are prepared without the use of organic solvents. Round bottomed flask is used as bubbling unit with its three necks positioned in water bath to control the temperature. Water-cooled reflux and thermometer are positioned in the first and second neck and nitrogen supply through the third neck. At 70°C Cholesterol and surfactant are dispersed together in the buffer (pH 7.4) and mixed with high shear homogenizerfor 15 sec and immediately afterwards "bubbled" at 70°C using nitrogen gas.[17]

Ether injection method: This method provides a means of making niosomes by slowly introducing a solution of surfactant dissolved in diethyl ether into warm water maintained at 60°C. The surfactant mixture in ether is injected through 14-gauge needle into an aqueous solution of material. Vaporization of ether leads to formation of single layered vesicles. Depending upon the conditions used, the diameter of the vesicle range from 50 to 1000 nm (Mayer et al., 1985).[18]

B. Active trapping technique

Trans membrane pH gradient method: Equal proportions of surfactant and cholesterol are dissolved in chloroform and evaporated under reduced pressure to produce a thin lipid film on the wall of a round bottomed flask. The film is hydrated with a solution of an acidic compound, generally citric acid by vortex mixing. The resulting product is subjected to freeze thaw cycles after which an aqueous solution of drug is added and the mixture vortexed. The pH of the sample is then raised to 7–7.2 using disodium hydrogen phosphate solution.[19]

C. Miscellaneous method

Lipid injection method:

In this process, either mixture of lipids and surfactant is first melted and then injected into a highly agitated heated aqueous phase containing dissolved drug, or the drug can be dissolved in molten lipid and the mixture will be injected into agitated, heated aqueous phase containing surfactant. This method does not require expensive organic phase.[20]

III. EVALUATION OF NIOSOMES:

Scanning Electron Microscopy (SEM):

Shape and surface morphology of niosomes was studied using scanning electron microscopy (SEM). The niosomes formed were mounted on an aluminum stub with double-sided adhesive carbon tape. The vesicles were then sputtercoated with gold/palladium using a vacuum evaporator and examined with the scanning electron microscope equipped with a digital camera.[21]

Transmission electron microscopy (TEM) analysis: TEM (Philips CM 200 super twin stem microscope) was used to determine the morphology of the niosomal vesicles. Few drops of the optimized niosomal formulation (CS17) were deposited on a carbon-coated copper grid and examined under a transmission electron microscope. [22]

Visual Observation: All the prepared batches were visually observed for turbidity and flocculation in transparent containers. The selected batches (with good entrapment efficiency) were also observed for sedimentation. The experiment was performed in

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triplicate and results for sedimentation rate were reported on the bases of bottom view of the containers having niosomal preparations.[23]

In-vitro release A method of in-vitro release rate study includes the use of dialysis tubing. A dialysis sac is washed and soaked in distilled water. The vesicle suspension is pipetted into a bag made up of the tubing and sealed. The bag containing the vesicles is placed in 200 ml of buffer solution in a 250 ml beaker with constant shaking at 25° C or 37° C. At various time intervals, the buffer is analysed for the drug content by an appropriate assay method.[24]

Drug content analysis: 1ml of noisome preparation was taken in a 100 ml volumetric flask. 2 ml of acetone was mixed and volume was made up with phosphate buffer pH 7.4. Samples were filtered through Whatman filter paper number 40 and diluted with PBS pH 7.4. Drug content was determined spectrophotometrically at 255 nm.[25]

Drug encapsulation efficiency: After preparing niosomal dispersion, unentrapped drug was separated by centrifugation using pH 6.8 phosphate buffer for 45 min at 17,000 rpm. The resulting solution was analysed by UV spectrophotometer at 204 nm for the total amount of entrapped drug.[26]

IV. CONCLUSION

The present review concludes that niosomes are novel nano drug carrier to assign effective drug delivery system. As niosomes are made of non-ionic surfactants so there are more stable, safe and convenient to handle than other ionic drug carriers. The structural properties and characteristics of the niosomes can be enhanced by using novel preparation, loading, modification method for particular route of administration. Niosomes helps for the sustained and controlled release of the drug. Thus, niosomes present itself as promising tools in commercially available therapeutic.

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