

REVIEW: NIOSOMAL DRUG DELIVERY SYSTEMS**Rutik Nagnath Ghadge*, Manisha B. Parhad and Dr. Gajanan S. Sanap**

LBYP College of Pharmacy, Pathri, Aurangabad – 431111, Maharashtra, India.

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Corresponding Author*Rutik Nagnath Ghadge**

LBYP College of Pharmacy,

Pathri, Aurangabad –

431111, Maharashtra, India.

ABSTRACT

Niosomes represent a promising medicine delivery module. The vesicle is composed of a bilayer of non-ionic surface active agents and hence the name niosomes. Niosomes are a new medicine delivery system, in which the drug is rephrased in a vesicle. They present a structure analogous to liposome and hence they can represent indispensable vesicular systems with respect to liposomes. Structurally, niosomes are analogous to liposomes, in that they're also made up of a bilayer. Still, the bilayer in the case of niosomes is made up of non-ionic surface active agents rather than phospholipids as seen in the case of liposomes. Niosomes may be unilamellar or multilamellar

depending on the system used to prepare them. Niosomes present a structure analogous to liposome and hence they can represent indispensable vesicular systems with respect to liposomes.

INTRODUCTION

Niosomes are new medicine delivery system (NDDS). Paul Ehrlich, in 1909, initiated the period of development for targeted delivery when he imagined a medicine delivery medium that would target directly to diseased cell. Niosomes in which the drug is rephrased in a vesicle. The vesicle is composed of a bilayer structure composed of amphiphilic moieties girdled by an aqueous compartment of non-ionic surface active agents and hence the name niosomes. The niosomes are veritably small, and tiny in size. Substantially their size is 10- 100 Nanometres. Their size lies in the Nano metric scale. Niosomes have lately been shown to greatly increase transdermal medicine delivery and also can be used in targeted medicine delivery, and therefore increased study in these structures can give new styles for medicine delivery. Among different carriers liposomes and niosomes are well proved medicine delivery. Schematic representation of a medicine targeting through its relation to niosome via antibody. Niosomes are vesicular Nano carriers and have entered important attention as implicit medicine

delivery systems in the last 30 times due to their unique advantages. Nonionic surfactants are preferred because they've less implicit to beget vexation, which decreases in order of cationic, anionic, non-ionic. The unique structures of niosomes as vesicular systems make them able of recapitulating both hydrophilic and lipophilic substances. Hydrophilic medicines are generally reprised in the inner waterless core or adsorbed on the bilayer shells, while lipophilic substances are entangled by their partitioning into the lipophilic sphere of the bilayers. The unique structures of niosomes as vesicular systems make them able of recapitulating both hydrophilic and lipophilic substances. Hydrophilic medicines are usually reprised in the inner waterless core or adsorbed on the bilayer shells, while lipophilic substances are entangled by their partitioning into the lipophilic sphere of the bilayers. These amphiphilic motes, known as surfactants, contain both hydrophobic groups (tails) and hydrophilic groups (heads) and show tone- assembling parcels, adding up into a variety of shapes like micelles or into a planar lamellar bilayer.

STRUCTURE OF NIOSOMES^[20-21]

A typical niosome vesicle would correspond of a vesicle forming amphiphile i.e. a non8ionic surfactant similar as Span860, which is generally stabilized by the addition of cholesterol and a small quantum of anionic surfactant similar as diethyl phosphate, which also helps in stabilizing the vesicle.

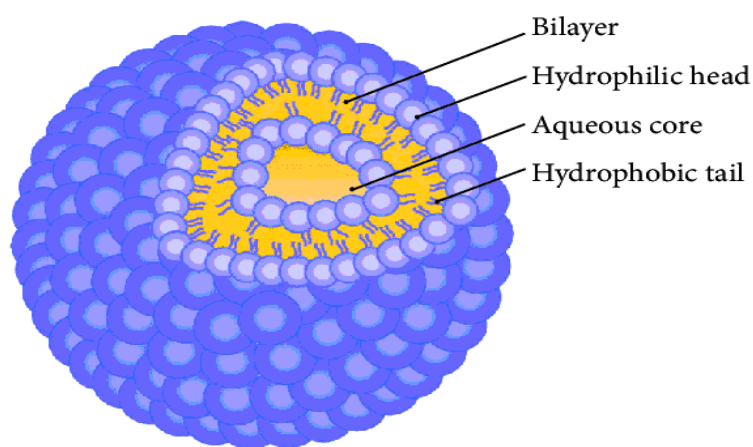


Figure No. 1: Structure of Niosomes.

FORMATION OF NIOSOMES FROM PRONIOSOMES^[22]

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

$T > T_m$

Where,

T = Temperature

T_m = mean phase transition temperature

Blazek & Walsh A.I. et al has reported the expression of niosomes from maltodextrin grounded Proniosomes. This provides rapid-fire reconstitution of niosomes with minimum residual carrier. Slurry of maltodextrin and surfactant was dried to form a free flowing powder, which could be rehydrated by addition of warm water.

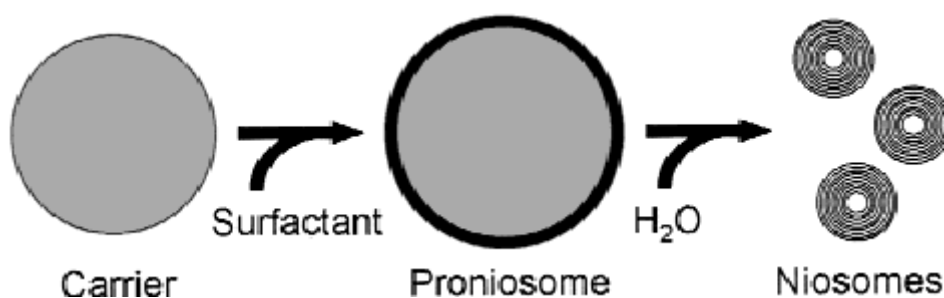


Figure no. 2:-FORMATION OF NIOSOMES TO PRONIOSOMES.

Salient features of niosomes^[4]

1. Niosomes can entrap solutes in a manner similar to liposomes.
2. Niosomes are osmotically active and stable.
3. Niosomes retain an infra-structure conforming of hydrophobic and hydrophilic substantially together and so also accommodate the medicine moles with a wide range of solubility.
4. Niosomes exhibits inflexibility in their structural characteristics (composition, fluidity and size) and can be designed according to the asked situation.
5. Niosomes can ameliorate the performance of the medicine moles.
6. Better vacuity to the particular point, just by guarding the medicine from natural terrain.
7. Niosomes surfactants are biodegradable, biocompatible and non-immunogenic.

TYPES OF NIOSOMES^[5]

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 a function of the system of medication (e.g. REV, DRV). The colorful types of niosomes are described below. 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 a function of the system of medication (e.g. REV, DRV). The colorful types of niosomes are described below.

i) Multi lamellar vesicles (MLV)

ii) Large unilamellar vesicles (LUV),

iii) Small unilamellar vesicles (SUV)

i) Multi lamellar vesicles (MLV)

It consists of a number of bilayer girding the waterless lipid cube independently. The approximate size of these vesicles is 0.5- 10 μm periphery. Multilamellar vesicles are the most extensively used niosomes. It's simple to make and are mechanically stable upon storehouse for long ages. These vesicles are largely suited as medicine carrier for lipophilic composites.

ii) Large unilamellar vesicles (LUV)

Niosomes of this type have a high waterless/ lipid cube rate, so that larger volumes of bio-active accoutrements can be entangled with a veritably provident use of membrane lipids.

iii) Small unilamellar vesicles (SUV)

These small unilamellar vesicles are substantially prepared from multilamellar vesicles by sonication system, French press extrusion electrostatic stabilization is the addition of dicetyl phosphate in 5(6)- carboxyfluorescein (CF) loaded Span 60 grounded niosomes.

Method of preparation of niosomes^[6-7]

Niosomes can be prepared by a number of styles which are as follows

1. Ether Injection system
2. Hand Shaking Method (Thin Film Hydration fashion)
3. Sonication
4. Rear Phase Evaporation fashion (REV)
5. The "Bubble" Method
6. Multiple Membrane Extrusion system
7. Micro fluidization
8. Transmembrane pH grade medicine Uptake Process (Remote lading)

1. Ether Injection system

In this system, a result of the surfactant is made by dissolving it in diethyl ether. This result is also introduced using an injection (14 hand needle) into warm water or waterless media

containing the medicine maintained at 60°C. Vaporization of the ether leads to the conformation of single layered vesicles. The flyspeck size of the niosomes formed depend on the conditions used, and can range anywhere between 50- 1000 µm.

2. Hand Shaking Method(Thin Film Hydration fashion)

In this system a admixture of the vesicle forming agents similar as the surfactant and cholesterol are dissolved in a unpredictable organic detergent similar as diethyl ether or chloroform in a round bottom beaker. The organic detergent is removed at room temperature using a rotary evaporator, which leaves a thin film of solid admixture deposited on the walls of the beaker. This dried surfactant film can also be rehydrated with the waterless phase, with gentle agitation to yield multilamellar niosomes.

3. Sonication

A typical system of product of the vesicles is by sonication of result as described by Cable. In this system an aliquot of medicine result in buffer is added to the surfactant/ cholesterol admixture in a 10- ml glass vial. The admixture is inquiry sonicated at 60 °C for 3 twinkles using a sonicator with a titanium inquiry to yield niosomes.

4. Rear Phase Evaporation fashion (REV)

This system involves the creation of a result of cholesterol and surfactant (11 rates) in a admixture of ether and chloroform. An waterless phase containing the medicine to be loaded is added to this, and the performing two phases are sonicated at 4- 5 °C. A clear gel is formed which is farther sonicated after the addition of phosphate softened saline (PBS). After this the temperature is raised to 40 °C and pressure is reduced to remove the organic phase. This results in a thick niosome suspense which can be adulterated with PBS and hotted on a water bath at 60 °C for 10 mins to yield niosomes.

5. The “Bubble” system

It's a fashion which has only lately been developed and which allows the medication of niosomes without the use of organic detergents. The washing unit consists of a round bottom beaker with three necks, and this is deposited in a water bath to control the temperature. Water- cooled influx and thermometer is deposited in the first and alternate neck, while the third neck is used to supply nitrogen. Cholesterol and surfactant are dispersed together in a buffer (pH7.4) at 70 °C. This dissipation is mixed for a period of 15 seconds with high shear

homogenizer and incontinently latterly, it's gurgled at 70 °C using the nitrogen gas to yield niosomes.

6. Multiple Membrane Extrusion system

Admixture of surfactant, cholesterol and dicetyl phosphate in chloroform is made into thin film by evaporation. The film is doused with waterless medicine polycarbonate membranes result and the attendant suspense extruded through which are placed in series for over to 8 passages. It's a good system for controlling niosome size.

7. Micro fluidization

Micro fluidization is a recent fashion used to prepare unilamellar vesicles of defined size distribution. This system is grounded on submerged spurt principle in which two fluidized aqueducts interact at ultra-high rapidity, in precisely defined micro channels within the commerce chamber. The smash of thin liquid distance along a common front is arranged similar that the energy supplied to the system remains within the area of niosomes conformation. The result is a lesser uniformity, lower size and better reproducibility of niosomes formed.

8. Transmembrane pH grade medicine Uptake Process (Remote lading)

In this system, a result of surfactant and cholesterol is made in chloroform. The detergent is also faded under reduced pressure to get a thin film on the wall of the round bottom beaker, analogous to the hand shaking system. This film is also doused using citric acid result by whirlpool mixing. The performing multilacellar vesicles are also treated to three snap thaw cycles and sonicated. To the niosomal suspense, waterless result containing 10mg/ ml of medicine is added and vortexed. The pH of the sample is also raised to 7.0-7.2 using 1M disodium phosphate and admixture is latterly hotted at 60 °C for 10 twinkles to give niosomes.

Advantages of niosomes^[18]

- Surfactants used to prepare niosomes are biodegradable, biocompatible, and not immunogenic.
- The system used for routine and large- scale product of niosomes doesn't involve use of inferior detergents.
- Niosomes are suitable to synopsise a large quantum of material in a small vesicular volume.

- Due to the chemical stability of their structural composition, the running and storehouse of niosomes doesn't bear any special conditions.
- Niosomes ameliorate the remedial performance of medicine moles by delaying concurrence from the rotation and confining goods to target cells.
- The structure of niosomes cover medicine constituents from miscellaneous factors present both inside and outside the body, so niosomes can be used for the delivery of labile and sensitive medicines.

Disadvantages of Niosomes^[19]

1. Physical instability
2. Aggregation
3. Fusion
4. Leaking of entrapped drug
5. Hydrolysis of encapsulated drugs which limiting the shelf life of the dispersion.

Physical properties of Niosomes^[8]

Particle size

The particle size of niosomes was measured by dynamic light scattering (DLS) outfit (NICOMP 380 ZLS, flyspeck Sizing Systems, Santa Barbara, CA). The dissipations were adulterated to about 100 times with Dulbecco's PBS. The time-dependent correlation function on the scattered light intensity was measured at a scattering angle of 90^0 and wavelength at 535 nm.^[8]

Morphology

The dissipation of niosomes was fleetly firmed in liquid propane using cry preparation outfit (Leica EM CPC, LeicaCo., Vienna, Austria). The frozen sample was fractured in snap-replica- making outfit (FR- 7000A, Hitashi ScienceCo., Tokyo, Japan) at -150^0C . The fracture face was replicated by sinking platinum at an angle of 45^0C and followed by carbon to strengthen the replica. It was placed on a 150 mesh bobby grid after washing with acetone and water. The vesicles were observed under a transmission electron microscope (JEM-1200EX, JEOLCo.)^[8]

Evaluation

Entrapment efficiency

After preparing niosomal dispersion, untrapped medicine is separated by dialysis centrifugation and gel filtration. The medicine remain entangled in niosomes is determined by complete vesicle dislocation using 50 n- propanol or 0.1 TritonX-100 and anatomized attendant result by applicable assay system using following equation.^[9-10]

Partical size analysis: - Partical size analysis was done by surveying electronic microscopy (SEM) using JEOL JSM- T330A scanning microscope brass stab. The stabs were placed compactly in a drier and also carpeted with gold in an ion sputter. Filmland of niosomes were taken by arbitrary scanning of the end and count. The periphery is about 30 niosomes was measured from the photomicrographs of each batch. Eventually, average mean compasses were taken into consideration.^[9-11]

In- vitro release study

Mortal corpse skin (HCS) was attained from frontal part of forearm of 35 times old manly cadaver and was stored at 4 °C. HCS membrane was spread and punches it at roughly 3 cm² area. Trimmed down the excess fat and sliced to 500 m consistence using Dew's derma tone. These slices were doused in pH7.4 PBS for 24 hrs. previous to use. The HCS were attached to Khesary cell (K.C. filled with 100 ml of PBS) and add 10 mg niosomal suspense on it. Eventually, cell was immersed into the receptor cube. The dermal face was just flush to the face of saturation fluid (PBS), which was maintain at 37 °C 0.50 ° C and stirred magnetically at 50r.p.m, aliquots were withdraw and replaced with the same volume of fresh buffer, at every slice points and anatomized by U.V. Spectrophotometer system at 294 nm.^[12-13]

Stability Study

All niosomal phrasings were subordinated to stability studies by storering at 4°C, 25°C and 37 °C in thermostatic roaster for the period of three months. After one month, medicine content of all the phrasings were checked by system bandied preliminarily in entangled effectiveness parameter. In- vitro release studies of named phrasings were also carried out.^[14]

Applications of niosomes^[15-16]

The application of niosomal technology is widely varied and can be used to treat a number of diseases.

Niosomes as Drug Carriers

Niosomes have also been used as carriers for iobitridol, a individual agent used for X-ray imaging. Topical niosomes may serve as solubilization matrix, as a original depot for sustained release of dermally active composites, as penetration enhancers, or as rate- limiting membrane hedge for the modulation of systemic immersion of medicines.

Medicine Targeting

One of the most useful aspects of niosomes is their capability to target medicines. Niosomes can be used to target medicines to the reticuloendothelial system. The reticulo- endothelial system (RES) preferentially takes up niosome vesicles. The uptake of niosomes is controlled by circulating serum factors called opsonins. These opsonins mark the niosome for concurrence. Similar localization of medicines is employed to treat excrescences in creatures known to metastasize to the liver and spleen. This localization of medicines can also be used for treating parasitic infections of the liver. Niosomes can also be employed for targeting medicines to organs other than the RES. A carrier system (similar as antibodies) can be attached to niosomes (as immunoglobulin's bind readily to the lipid face of the niosome) to target them to specific organs.

Anti-neoplastic Treatment

Most antineoplastic medicines beget severe side goods. Niosomes can alter the metabolism; protract rotation and half-life of the medicine, therefore dwindling the side goods of the medicines. Niosomes is dropped rate of proliferation of excrescence and advanced tube situations accompanied by slower elimination.

Leishmaniasis

Leishmaniasis is a complaint in which a sponger of the rubric *Leishmania* invades the cells of the liver and spleen. Use of niosomes in tests conducted showed that it was possible to administer advanced situations of the medicine without the triggering of the side goods, and therefore allowed lesser efficacy in treatment.

Delivery of Peptide medicines

Oral peptide medicine delivery has long been faced with a challenge of bypassing the enzymes which would breakdown the peptide. Use of niosomes to successfully cover the peptides from gastrointestinal peptide breakdown is being delved. In an in vitro study

conducted by oral delivery of a vasopressin secondary entangled in niosomes showed that use of the medicine significantly increased the stability of the peptide.

Other Applications^[16-17]

Sustained Release:- Sustained release action of niosomes can be applied to medicines with low remedial indicator and low water solubility since those could be maintained in the rotation via niosomal encapsulation.

Localized medicine Action:- medicine delivery through niosomes is one of the approaches to achieve localized medicine action, since their size and low penetrability through epithelium and connective tissue keeps the medicine localized at the point of administration.

CONCLUSION

The conception of incorporating the medicine into liposomes or niosomes for a better targeting of the medicine at applicable tissue destination is extensively accepted by experimenters and academicians. Niosomes represent a promising medicine delivery module. The technology employed in niosomes is still greatly in its immaturity, and formerly it's showing promise in the fields of cancer and contagious complaint treatments. The system is formerly in use for colorful ornamental products. Niosomes are studied to be better for medicine delivery as compared to liposomes due to colorful factors like cost, stability etc. colorful type of medicine deliveries can be possible using niosomes like targeting, ophthalmic, topical, parenteral, etc.

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