



## Review Article

# Niosomes As Novel Drug Delivery System

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### ABSTRACT

Niosomes are vesicles composed of non-ionic surfactants that are produced by the hydration of a mixture of cholesterol and non-ionic surfactants that can be used as carriers for amphiphilic and lipophilic drug. Niosomes are a delivery system that encapsulates the medication within the vesicles. Niosomes possess a range of properties including being biodegradable, biocompatible, non-immunogenic and flexible in their structure. This review's preparation is crucial because it aims to educate various uses of niosomes in treating a variety of illnesses. This review article also provide us with a goal to study various aspects of niosomes like their mode of preparation, mechanism of action ,How niosomes aids in drug permeation and their use as permeation enhancers and their application and What are the ways in which niosomes can be used to treat various diseases and their toxicity with the aid of surfactants. The stability and economical properties of niosome make it a well-preferred drug delivery system compared to liposome.

### INTRODUCTION

When Paul Ehrlich, a researcher, come up with a drug delivery method that would target infectious cells directly in 1909, he began the process of establishing targeted delivery. We shall now examine the concept of drug targeting. The capacity to direct a therapeutic medication to a desired precise spot to demonstrate the action on

targeted tissue can be expanded upon as drug targeting. Niosomes are a unique drug delivery system in which the medication is enclosed in a polymer matrix in the form of vesicles<sup>1</sup>.The term "niosomes" refers to these vesicles since they essentially contain two layers of non-ionic surfactant. Amphiphilic vesicles include non-surfactant ones like span-60, which are often

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stabilised by the addition of cholesterol and plenty of anionic surfactant<sup>2</sup>.

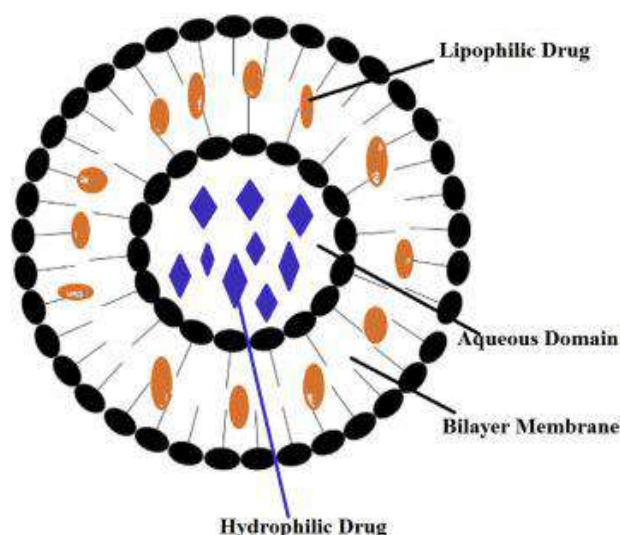
### ADVANTAGES

1. To get the desired effective result, a lower dose is more effective.
2. Depending on the need, a vesicle's size, lamellarity, and other properties can be changed.
3. The medicine can be released gradually and under control using the vesicles as a depot.
4. Niosomes can be employed for a range of medications since its structure allows for the accommodation of hydrophilic, lipophilic, and amphiphilic chemical moieties.
5. Compared to methods that use oil, the water-based vesicle suspension provides better patient compliance.
6. They are stable and osmotically active.
7. It can improve a drug's penetration through the skin.

### DISADVANTAGES

1. The drawbacks of hydrolysis on the pharmaceuticals that are encapsulated lead to a reduction in the specific formulation's shelf life.
2. possibly need specific equipment
3. high cost of production
4. Unstable physical state
5. Leakage of drug entrapped
6. Fusion
7. Aggregation

### STRUCTURE OF NIOSOMES



A typical niosome vesicle would be composed of a tiny quantity of an anionic surfactant, like dicetyl phosphate, which also aids in stabilizing the vesicle, and a vesicle-forming amphiphilic surfactant, such as Span-60, which is often stabilized by the addition of cholesterol.

### COMPOSITION OF NIOSOMES

The following are the different ingredients that are utilized to prepare niosomes.

1. Cholesterol
2. Non-ionic surfactants

#### 1. CHOLESTEROL

A steroid derivative called cholesterol is added to niosome preparations to provide them stiffness and the right shape and the surface acting agent that is non ionic. Examples of specific non-ionic surfactants used in the niosome preparation process are Spans (Span20,40,60,80,85), the tweens (20, 40, 60, 80), Brij's (30, 35, 52, 58, 72, 76) The hydrophilic head and hydrophobic tail make up the non-ionic surfactant.

### PREPARATION OF NIOSOMES

#### 1. Sonication Method:

The drug sample is added to the buffer system, and the resulting mixture of drug and buffer is added to the cholesterol or surfactant mixture in a 20 ml glass vial. To produce niosomes, the mixture is

sonicated for three minutes at 60°C using a sonicator with a titanium probe.

### **2. Hand shaking method (thin film hydration technique)3:**

Using a round-bottom flask and a volatile organic solvent (diethyl chloroform, methanol, or diethyl), the cholesterol and surfactant are dissolved in this method. Using a rotary evaporator, the organic solvent is removed at room temperature (20°C), leaving behind a thin layer of solid mixture that is deposited on the flask wall. Multilamellar niosomes can be produced by rehydrating the dried surfactant film with aqueous phase at 0–60°C while gently stirring.

### **3. Ether injection method:**

The fundamental principle of the ether injection method is to gradually add surfactant-dissolved in diethyl ether to warm water that is kept at 60°C. A 14-gauge needle is used to inject the surfactant mixture in ether into the material's aqueous solution. Single-layered vesicles are formed when ether vaporizes. The conditions under which the vesicle is formed determine the size of the niosomes that form, which can range in diameter from 50 to 1000 nm.

### **4. Micro fluidization method8**

The process of creating unilamellar vesicles with a precisely defined size distribution is a relatively new technology. The principle of two fluidized streams interacting with each other at extremely high velocities drives the micro fluidization approach. The thin liquid sheet impinges along a typical front in such a way that the energy input to the system stays within the range where niosomes form. The end product could be more homogeneous, smaller, and more reproducibly formed niosomes.

### **5. The Bubble Method6:**

The bubbling unit is a three-necked, round-bottomed flask that is submerged in a water bath

to regulate temperature. The nitrogen supply passes through the third neck, and the water-cooled reflux and thermometer are located in the first and second necks. In this buffer (PH 7.4), cholesterol and surfactant are combined and dispersed at 70°C. The mixture is then mixed for 15 seconds with a high shear homogenizer, and right away, using nitrogen gas, the mixture is "bubbled" at 70°C to produce niosomes.

### **6. Reverse Phase Evaporation Technique (REV):**

In this technique, the Cholesterol and surfactant in 1:1 ratio are dissolved in a mixture of ether and chloroform. This is combined with a drug-containing aqueous phase followed by the sonication of resulting two phases at 4-5°C. The addition of phosphate buffered saline (PBS) results in the formation of a clear gel that is further sonicated. Under low pressure and at 40°C, the organic phase is eliminated. In order to produce niosomes, the resultant viscous niosome suspension is diluted with PBS and heated on a water bath at 60°C for 10 min.

## **FACTORS AFFECTING NIOSOMES FORMULATION**

### **1. Drug**

The charge and rigidity of the niosome bilayer are affected by drug entrapment in niosomes. The drug's hydrophilic lipophilic balance influences the level of entrapment.

### **2. Nature and type of surfactant4**

Niosome size is directly correlated with surfactant hydrophobicity (HLB), meaning that as surfactant hydrophobicity increases, so does surface free energy. This means that niosome size will increase as HLB of the surfactant rises, such as span 85. There must always be a hydrophilic head and a hydrophobic tail in a surfactant. In certain cases, the hydrophobic portion of the surfactant may



contain a single steroidal group in addition to one or more alkyl or perfluoroalkyl groups.

### **3. Cholesterol content and charge**

Cholesterol aids in increasing the entrapment efficiency and hydrodynamic diameter of niosomes. It makes membrane stabilizing activity possible and reduces membrane leakiness. Increases in cholesterol may cause the encapsulated material to release at a slower rate, which would increase the stiffness of the resulting bilayers. In a multilamellar vesicle structure, the presence of charge will lengthen the interlamellar distance between succeeding bilayers and increase the total entrapped volume.

### **4. Resistance to osmotic stress**

By adding hypertonic salt solution to the suspension of niosomes, their diameter is decreased.

### **5. Temperature of Hydration**

The temperature of hydration affects the niosomes' size and shape.

## **CHARACTERIZATION OF NIOSOMES**

### **1. Measurement of Angle of repose**

Using the funnel method, the angle of repose of powdered dry niosomes was determined. Powdered niosomes were added to a funnel that was positioned so that its 13mm exit orifice was 5 cm above a level black surface. After the powder flows out of the funnel and forms a cone on the surface, the diameter of the cone's base and its height were measured to determine the angle of repose.

### **2. Scanning electron microscopy**

One of the most significant features of niosomes is their size. Scanning electron microscopy (SEM) was used to examine the size distribution and surface morphology (roundness, smoothness, and formation aggregate) of niosomes. On the double-sided tape that was attached to the aluminum stubs, distribute the niosomes. The scanning

electron microscope's vacuum chamber held the aluminum stub. The sample was examined using a gaseous secondary electron detector to determine its morphological characteristics.

### **3. Osmotic shock**

The osmotic studies can be used to determine whether the vesicles' sizes change. The hypotonic, isotonic, and hypertonic solutions are incubated with the niosome formulation for a duration of three hours. When the vesicles in the formulation are examined under optical microscopy, we can observe changes in their size following the time interval.

### **4. Stability Studies**

In case the stability of the niosomes needs to be determined the optimized batch was preserved at varying temperatures in tightly packed vials. The parameters chosen for assessing stability were the surface features and percentage of drugs retained in niosomes and niosomes derived from proniosomes. Drug leakage may be a result of an unstable formulation.

### **5. Zeta potential analysis**

Zeta potential analysis is necessary in order to understand the colloidal characteristics of the formulation we have prepared. With the use of a zeta potential analyzer based on electrophoretic light scattering and laser doppler velocimetry, the diluted Niosomes that are derived from proniosomes dispersion were found. Direct measurements were used to determine the temperature at which vesicles were charged to 25°C, as well as their mean zeta potential values and measurement standard deviations.

## **IN-VITRO METHOD FOR NIOSOMES**

The following methods can be used to study drug release in vitro:

- a. Dialysis Tubing
- b. Reverse dialysis
- c. Franz diffusion cell



### 1. Dialysis Tubing

Dialysis tubing could be used to achieve in vitro drug release. The niosomes are inserted into dialysis tubing that has been previously cleaned and sealed hermetically. After that, the dialysis sac is dialyzed at room temperature against an appropriate dissolving medium. The samples are taken out of the medium at appropriate intervals, centrifuged, and their drug content is examined using an appropriate technique (U.V. spectroscopy, HPLC, etc.). Maintaining the condition of the sink is crucial<sup>5</sup>.

### 2. Reverse dialysis

Several tiny dialysis units, each holding one millilitre of dissolving medium, are inserted into proniosomes using this technique. After that, the proniosomes are moved into the dissolving medium. This method allows for the direct dilution of the proniosomes, but it is unable to quantify their rapid release.

### 3. Franz diffusion cell

The In-vitro diffusion study can also be studied using the Franz diffusion cell method. Proniosomes can be inserted into the Franz diffusion cell's donor chamber, which has a cellophane membrane installed. The proniosomes can be dialyzed against an appropriate dissolving media at room temperature. The sample is taken out and examined for drug content on a regular basis using appropriate techniques (UV, spectroscopy, HPLC, etc.). It is crucial to maintain the sink condition during this process.

## APPLICATIONS OF NIOSOMES<sup>10</sup>

- Niosomes have been employed in research to examine the type of immune response triggered by antigens.
- It serves as a drug targeting tool.
- It treats cancer by acting as an anti-neoplastic agent.

- It is used to treat leishmaniasis, such as sodium stibogluconate, as well as dermal and mucocutaneous infections.
- Niosomes as Haemoglobin Carriers.
- It serves as a means of delivering peptide drugs.
- haemoglobin can be transported by niosomes.
- It's applied to immunological response research.
- Niosome-Based Transdermal Drug Delivery Systems.
- It is applied to the delivery of drugs to the eyes.
- The niosomal system is a useful tool for diagnosis.

### 1. Niosome application in immunology

Studies on the nature of the immune response triggered by antigens have been conducted using niosomes. Drugs other than those for the Reticulo-Endothelial System can also be targeted with niosomes. Niosomes can be targeted to particular organs by attaching a carrier system, such as antibodies, to them because immunoglobulins bind to the lipid surface of niosomes with ease.

### 2. Sustained Release

Since niosomal encapsulation permits the retention of drugs with low therapeutic efficacy and low water solubility in the bloodstream, sustained release niosomes can be used to treat these conditions.

### 3. Localized Drug Action

Niosomes are a modern method of delivering drugs that have a localized effect because of their small size and poor ability to pass through connective tissue and epithelium, which keeps the drug at the administration site.

### 4. Niosomes as Drug Carriers

Niosomes have also been employed as delivery systems for the diagnostic drug iobitridol, which



is used in X-ray imaging. Topical niosomes can act as a solubilization matrix, a local site for the sustained release of chemicals that are dermally active, penetration enhancers, or a membrane barrier that limits the rate at which drugs are absorbed systemically.

### 5. Leishmaniasis

A parasite belonging to the genus *Leishmania* enters the liver and spleen cells, causing leishmaniasis. Niosomes are used to increase the amount of drugs incorporated into the body at a high level without causing adverse effects.

### 6. Transdermal delivery of drugs by niosomes

One of the main disadvantages of transdermal drug delivery is the slow penetration of drugs through the skin. With the aid of niosomes, transdermal drug delivery can be accelerated. Topical niosomes can be used as a local depot for the sustained release of compounds that are dermally active, as well as a solubilization matrix to improve penetration.

### CONCLUSION

One of the best illustrations of the significant advancements in nanotechnology and drug delivery technologies is the niosomal drug delivery system. Given that niosomes are generally stable and affordable, it is clear that they seem to be a well-liked drug delivery system over alternative dosage forms. Niosomes offer a great deal of potential as drug carriers because they can be used to encapsulate toxic anti-cancer, anti-infective, anti-AIDS, anti-inflammatory, antiviral, and other medications. This will improve the drugs' bioavailability and targeting capabilities while also lowering their toxicity and side effects. The notion of encapsulating the medication within niosomes to enhance its targeting at the proper tissue site is extensively acknowledged by scholars and researchers.

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