Niosomes: Non-Ionic Surfactant-Based Vesicular Drug Delivery System

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ABSTRACT
Niosomes are non-composite, non-immunogenic, and non-toxic with a wide range of structural characteristics. Both amphiphiles and lipophilic medicines can be transported by this form of noisome. The placement property is principally due to the use of non-ionic surfactant and a cholesterol as an excipient. Niosomes, also known as non-ionic surfactant vesicles, are small lamellar surfactant or dialkyl polyglycerol ether class combined with a non-ionic surfactant. Hydration in aqueous media, cholesterol is formed. Due to many reasons such as cost, stability, and other considerations, niosomes are regarded as a better alternative for drug administration than liposomes. Niosomes can be employed for several medication delivery strategies, such as targeted ocular, topical, and parenteral administration. The niosomes role as a medication carrier has been thoroughly investigated. Various drugs are listed and evaluated in niosomes surfactant vesicles. In a range of illnesses, niosomes have been proved to be a viable medication carrier with the potential to reduce drug adverse effects and improve treatment efficacy. Niosomes also have a lot of potential for anticancer and anti-infective drug delivery. Using innovative drug delivery concepts such as proniosomes, disomes, and aspasomes. The Niosomes drug delivery capacity can be increased. Niosomes can be used as biomarker and diagnostic imaging. An adjuvant for vaccines as a result, further investigation and research is required in order to bring forth or create for these places. Niosomal preparation that is commercially accessible. The review article represents the structure of Noisome, its advantages and applications and Niosomal synthesis methods, and preparation and characterization.

Keywords: Proniosomes, Lipophilic, Uni-lamellar, Niosomes, Non-ionic surfactant, Self-assembly.

INTRODUCTION
Niosomes are non-ionic surfactant vesicles created by hydrating synthetic non-ionic surfactants with or without cholesterol. The Niosomes and liposomal systems differ in that a nonionic surfactant forms the Niosomal bilayer, whilst phospholipids create the liposomal bilayer. Niosomes are formed when non-ionic surfactants self-assemble as spherical, unilamellar bilayers, or multi-lamellar systems in an aqueous fluid, and polyhedral structures depending on the preparation process and the inverse structure in a non-aqueous solvent. Niosomes are microscopic lamellar structures that range in size from 10 to 1000NM and are made up of non-immunogenic, biodegradable proteins. Niosomes are one of the most efficient transporters among them. Niosomes are structurally like liposomal and have similar drug delivery capability, but thus have higher chemical content. Niosomes are preferable to other proteins because of their stability and economic liposomes. This first report of non-ionic surfactant was made by L’Oréal’s cosmetic applications. ¹. The idea is to integrate the medication into niosomes for improved efficacy it is important to target the medicine to the right tissue. Researchers and academicians generally agree. Niosomes are an integrating medication delivery system. Because Niosomes have a structure that is comparable to that of liposomes, they can serve as alternate vesicular systems in comparison to liposomes. Distinct types of medications in their encapsulation. Multi-environmental framework.² Niosomes are regarded to be more suitable therapeutic candidates. Due to a variety of variables, it is more difficult to transport than liposomes. Such as price, stability, and so on. Various types of medication delivery are possible. Ophthalmic, Topical, parenteral, and so on.³

The use of vesicular (lipid vesicles and non-ionic surfactant vesicles) Systems in cosmetics and for therapeutic response may provide several benefits, including:
1) Patient compliance is higher as compared to oily dose forms.
2) The vesicles could function as a store, slowly releasing the medication.
3) Allow therapeutic molecules to have a broad range of solubilities.⁴

NIOSONES COMPOSITION AND STRUCTURE
The most important components of niosomes are non-ionic surfactants, hydration medium, and lipids like cholesterol. Non-ionic structures in aqueous medium via self-assembly (Figure:1). surfactants form closed bilayer...
Water and the Amphiphiles hydrophobic tails provide an interfacial tension that causes them to associate. Due to stearic acid hydrophilic repulsion between head groups, non-ionic surfactants’ hydrophilic termini point outwards. And they have met water.

**Figure 1: Structure of Niosomes**

**Composition of niosomes**

Niosomes are made-up of two major components:

1. **Cholesterol**
2. **Non-ionic surfactants**

**1. Cholesterol:**
Cholesterol is a steroid derivative that is utilized to give niosome preparations stiffness and appropriate shape as well as confirmation.

**2. Non-ionic surfactants:**

*Examples:* Spans (Span 60, 40, 20, 85, 80)
Tweens (20, 40, 60, 80)
Brij’s (Brij 30, 35, 52, 58, 72, 76).

**ADVANTAGES**

The niosomal drug delivery system could be used to administer drugs in a controlled and targeted manner. The fact these vesicular drug delivery devices are tiny and simple to utilize in one of their main advantages. They are Carriers.

- The vehicle suspension is based on water in compared to greasy dose forms, this ensures good patient compliance.
- They increase the number of entrapped medicines and are osmotically active and stable.
- They improve oral bioavailability of poorly absorbed medications by increasing pharmaceutical penetration via the skin.
- Surfactants do not require specific handling or storage procedures.
- Surfactants are non-immunogenic, biodegradable, and biocompatible.
- Oral, parenteral, and topical methods can all be used to get them to the site of action.
- They improve the therapeutic performance of drug molecules by delaying clearance from the circulation, protecting the drug from the biological environment, and increasing the drug’s effects to the cells targeted.
- Niosomes have a structure that combines hydrophilic and lipophilic components, allowing them to hold a wide spectrum of therapeutic substances.
- The vesicles could act as a storage device, slowly releasing the drug over time.

**DISADVANTAGES**

- Instability of the body.
- Compilation.
- Incorporation.
- Water -encapsulated drugs are hydrolyzed, which reduces their shelf life. The expected dispersion life.

**APPLICATIONS OF NIOSOMES**

Niosome technology has a wide range of applications that can be utilized to treat a variety of ailments. The following are a few examples of some applications that are either proven or under investigation.

- Anti-cancer medications like methotrexate and doxorubicin are delivered to tumors via niosomes, which enhances drug delivery and tumoricidal effectiveness.
- According to carter et al., multiple doses of sodium stibogluconate -loaded niosomes were effective against parasites in the liver, spleen, and bone marrow. Carter and colleagues compared their findings to a conventional sodium stibogluconate solution.
- When administered as noisy encapsulated inclusion complexes, D’ Souza et al. evaluated the absorption of ciprofloxacin and norfloxacin.
- According to Chandra Prakash et al., methotrexate niosomes were produced and pharmacokinetically assessed in tumor-bearing mice.
- After intravenous injection of the carriers forms of the antimony dispersion in mice, Hunter et al discovered a considerable liver level. Antibiotics are drugs that are used to treat infections.
- Namdeo et al. published a paper on the formulation and evaluation of indomethacin-loaded niosomes, demonstrating that therapeutic efficacy increased at the same time. When compared to free, hazardous side effects are decreased. Indomethacin in rats with paw edema.
- Niosome as drug carriers: Iobitridol, an X-ray imaging diagnostic drug, has also been transported through niosomes.
Leishmaniasis is a parasitic infection of the liver and spleen caused by leishmaniasis parasites. The use of niosomes in testing, experiments, and other activities demonstrates that greater doses of a drug could be given without causing side effects, the medicine is able to be used. Improved treatment efficacy

Drug delivery through peptides researchers is investigated the use of niosomes to shield peptides against gastrointestinal peptide degradation. In this study, a vasopressin entrapment is used in the laboratory. The presence of a derivative in niosomes indicates that the trapping of the medication improves the peptide’s stability.

Immune response research- Niosomes are used to research the nature of the immune response because of their immune system selection, low toxicity, and higher stability. Antigens stimulate a response. Surfactant that isn’t ionic vesicles have shown that they can do a lot of different things. Adjuvants, antigens and peptides are administered via parenteral injection in variety of forms.

Drugs having a low therapeutic index and low water solubility can benefit from the impact of niosomes extended release. Niosomes encapsulation keeps it in the bloodstream.

Localized Drug Activity- Because of their small size and low penetrability through the epithelium, niosomal drug delivery is used to achieve localized drug action. Connective tissue helps to keep the drug confined at the injection site. administration.

Hemoglobin carriers using niosomes- niosomes can be used to transport hemoglobin. The visible spectrum of niosomal suspension is superimposed on that of a range of compounds permeable. The oxygen and hemoglobin dissociation curve are shown here that has not been encapsulated undergoes the same changes hemoglobin that has not been encapsulated.

Radiolabeled Niosome Formulation as a Brain Targeted Delivery System for the vasoactive Intestinal Peptide (VIP)-(125) glucose VIP- load Mice are injected intravenously with niosomes. VIP should be encased in glucose -containing niosomes. The VIP brain uptake is higher than the control.

Yoshida et al. explored oral administration of 9-desglycinamide, 8- arginine vasopressin entrapped in Niosomes in an in-vitro intestinal loop model. Observed a substantial increase in peptide stability.

Hemoglobin can be transported by Niosomes. The niosomal suspension’s visible spectrum is superimposed on that of free hemoglobin. Vesicles are oxygen and hemoglobin dissociation permeable curve can be changed in the same way that non-encapsulated curves can be edited hemoglobin.

The effect of two doses given on consecutive days was additive, according to Baillie et al., who observed higher sodium stibogluconate efficacy of niosomal formulation.

METHODS OF NIOSOME PREPARATION

Because the quantity of bilayers, their size, size distribution, and entrapment are all elements to consider, noisome preparation methods should be chosen based on the use of niosomes. The aqueous phase efficiency and membrane permeability. The vesicles are made up of distinct vesicles.

1. Ether injection method:

This approach allows you to make Niosomes without using any chemicals. Surfactant solution dissolved in diethyl ether was gradually injected into warm water at a temperature of 60°C. To inject ether into an aqueous solution, a 148-gauge needle is utilized. A material solution for the creation of ether vapor results from the vaporization of ether. Vesicles with a single layer. Depending on the circumstances, the diameter of the vesicle ranges from 50 to 1000rpm.

2. Handshaking method:

In an organic bottom flask, a volatile organic solvent is used to dissolve a mixture of vesicle-forming components such surfactant and cholesterol (diethyl ether, chloroform, or methanol). At room temperature (20 °C) the organic solvent evaporates, leaving a thin layer of solid mixture on the surface of the flask’s wall. The dried surfactant film can be rehydrated with an aqueous phase at 0-60°C and gentle agitation. On the wall of the rotary flash evaporator, this procedure creates a multi-lamellar niosomes lipid coating. The drug-containing aqueous phase was gently introduced with occasional flask shaking at room temperature, followed by sonication.

3. Sonication:

The sonication of a solution, as reported by cable, is common in producing vesicles. In this approach, a 10-ml glass vial contains an aliquot of medication solution in the buffer that is introduced to the surfactant /cholesterol mixture. The mixture is probe sonicated with a titanium probe 60°C for 3 minutes to obtain niosomes.

4. Micro fluidization:

Micro fluidization is a relatively new technology for producing unilamellar vesicles with a specific size distribution. The submerged jet principle, which involves two fluidized streams interacting at ultra -high velocities in precisely defined micro channels inside the water chamber of contact this technology. impingement of a thin liquid sheet along a a common front supplied to the system remains contained within the noisome formation region. As a result, a higher degree of consistency, a smaller size, and a higher level of reproducibility niosomes appeared.
5. **REV is a Reverse Phase Evaporation Technique (Brij et al., 2006):**

Cholesterol and surfactant (1:1) are used in this approach. Dissolved in a chloroform and ether combination and to this, an aqueous phase containing medication is introduced, and the two phases are then sonicated at 4-5°C. A clear gel is created, which is then sonicated. The mixture was supplemented with phosphate buffered saline (PBS). The organic phase is removed at low pressure at 40°C. The outcome is a viscous and obnoxious suspension. Is diluted in PBS and heated in a water bath at a temperature of to make niosomes, heat the mixture to 60°C for 10mins. 18

6. **Drug absorption mechanism with a Transmembrane PH Gradient (Inside acidic) (Biju et al., 2006):**

Surfactant and cholesterol are combined in a solution. Chloroform was used to dissolve the substance. The solvent is then removed It was evaporated under reduced pressure to make a thin film. On the inside of the flask’s spherical bottom wall .300mm of citric acid hydration (PH 4.00) vertices mingling. Multilamellar vesicles form as a result of this process. Sonicated after and a medication solution containing 10mg/ml the samples PH is then increased to 7.0-7.2. After that, the mixture is heated with 1M disodium phosphate. Heat the niosomes for 10 minutes at 60°C.

7. **The Bubble Method:**

In this process, the surfactants, additives, and buffer are placed in glass flask with three necks. The components of niosomes are distributed at 75°C. The Homogenizer used to blend the dispersion. Following that, the flask is immediately placed in water bath followed by Nitrogen gas is bubbling at a temperature of 70°C.

Nitrogen gas is pumped into the system. As a Result of a sample of homogenized surfactants. Massive unilamellar vesicles creation 19

8. **Multiple membrane extrusion method:**

Thin layer of surfactant, cholesterol, and diacetyl phosphate in chloroform is created using a rotary evaporator. An aqueous drug polycarbonate membranes hydrate the film. Extrusion of the and its suspension through a polycarbonate membrane into a series up to eight tunnels. It’s a good idea. A method for regulating the size of Niosomes.

### CHARACTERIZATION OF NIOSOMES

For clinical applications, Characterization is essential. characterization factors have a direct impact on Niosome stability and a significant impact on noisome stability. Their performance in the real world as a result, certain parameters such as shape, size, polydispersity, index (PI), and the number of individuals lamellae, All aspects ass zeta potential, efficiency, and stability must be evaluated.

1. **Size and morphology:**

Size and morphology are two factors to consider

- freeze fracture replication,
- Dynamic Light Scattering (DLS)
- Scanning electron microscopy (SEM)
- Transmission electron microscopy (TEM)

(DLS)Dynamic light scattering is type of 20 light scattering that occurs when light is scattered dynamically. Scanning electron microscopy (SEM) 21 Transmission electron microscopy (TEM) (2)

Cry transmission and femtosecond electron microscopy (FF-TEM)23. Cryo -TEM 24 is the most extensively used electron microscopy technique. Techniques for determining the phology of noisome sizes and molecular weights. DLS Offers Cumulative Information at the same time. Mation of particle of particle size critical data homogeneity of solutions. The presence of a single scattered population is indicated by a single prominent peak in the DLS profile. In this regarded, The PI is beneficial if corresponds to a value of less than 0.3 for colloidal systems, this equates to a homogenous population. The typically, microscopic methods are employed to define the shape of Niosomes.

2. **Zeta Potential:**

The zetasizer and DLS Equipment can be used to assess the surface zeta potential Niosomes is influenced by their surface charge. Niosomes, in general, are less prone to aggregation than uncharged vesicles. Bayindir and Yuksel explored facilitate loaded Niosomes made by Bayindir and Yuksel. A substance’s physicochemical properties, such as its zeta potential niosomes.

3. **Entrapment efficiency: (Sternberg, 1998) 25**

The Drug’s ability remain encapsulated in niosomes is determined by disrupting the vesicles completely with 50 Percent n- propanol or 0.1 percent Triton X-100 and assessing the resultant solution by appropriate test method for the drug.

The Entrapment efficiency (EE) Was calculated using Formula:

\[
\text{Entrapment Efficiency} = \frac{\text{amount Drug in noisome}}{\text{quantity drug}} \times 100
\]

4. **Stability studies:**

Niosomal formulations are subjected to stability experiments by being stored in a thermostatic oven at 4°C, 25°C, and 37°C for Three months. The medication content of all formulations is tested after a month. The efficiency parameter is tested by suitable analytical methods (UV spectroscopy, HPLC methods).26
5. In-vitro Release:

A study of the rate of release in vitro was conducted.

1. Dialysis Tubing
2. Reverse dialysis

1. Dialysis Tubing:

Distilled water is used to clean a dialysis sac. The vesicle suspension is pipetted into a dialysis tubing bag. Tubing made up of the tubing dialysis. The bag is securely closed. The vesicles are then placed in a 250 ml beaker with 200 ml of buffer solution and shaken constantly at 25°C. The Buffer is an analysis of the medicine at various time periods. Composition of a suitable test technique. 27

2. Reverse dialysis:

Proniosomes are filled with a number of tiny dialysis units each containing 1ml of Dissolving medium. After that, the proniosomes are displaced into the medium for dissolving the dilution of the water into the direct manner. With this approach, proniosomes can be made quickly. This approach does not allow for quantification. 28

3. Franz Diffusion cell:

In vitro diffusion experiments can be carried out using the Franz diffusion cell. Proniosomes Are inserted in a Franz donor chamber. A diffusion cell with a cellophane membrane was used. The Proniosomes are then dialyzed against a protein of choice. In a room temperature dissolving solvent, the samples were dissolved. At regular intervals, they are withdrawn from the medium and a suitable procedure is used to check for drug content. Such as UV Spectrometry, HPLC, and other techniques are used to keeps sinks good Working order. 29

6. SEM (Scanning Electron Microscopy)

Scanning electron microscopy (SEM) was used to analyze noisomes (JSM 6100, Tokyo, Japan). They had been erected, Double sided tape straight onto the SEM sample stub adhesion tape and a good film with a thickness of 200nm. Photographs were taken at a Magnification that is 200nm. Photographs were taken at a Magnification that is 200nm. Photographs were taken at a Magnification that is 200nm. Photographs were taken at a Magnification that is 200nm. Photographs were taken at a Magnification that is 200nm. Photographs were taken at a Magnification that is 200nm. Photographs were taken at a Magnification that is 200nm.

Table 1: Drugs used in Niosomal delivery

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Examples of Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous Route</td>
<td>Amphotericin-B, Doxorubicin Methotrexate, Iopromide, vincristine,</td>
</tr>
<tr>
<td>Transdermal Route</td>
<td>Piroxicam, estradiol, Nimesulide, estradiol, ketoconazole, ketorolac</td>
</tr>
<tr>
<td>Ocular Route</td>
<td>Timolol maleate, cyclopentolate</td>
</tr>
<tr>
<td>Nasal Route</td>
<td>Sumatriptan, influenza viral vaccine</td>
</tr>
<tr>
<td>Inhalation</td>
<td>All-trans retinoic acids</td>
</tr>
</tbody>
</table>

Table 2: Marketed Formulation of Niosomes

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Brand</th>
<th>Name of the product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Lancôme-Foundation and complexation</td>
<td>Flash Retouch Brush on concealer</td>
</tr>
<tr>
<td>2.</td>
<td>Or lane –Lip color and Lipstick</td>
<td>Lip Gloss</td>
</tr>
<tr>
<td>3.</td>
<td>Britney Curious Spears-Perfume and pink lip gloss+ Body soufflé,100ml</td>
<td>Edp Spray100ml+Dualended Body soufflé,100ml</td>
</tr>
<tr>
<td>4.</td>
<td>Loris Azzaro Chrome Eau De Toilette Spray200mls</td>
<td>Chrome Eau De Toilette Spray200mls</td>
</tr>
</tbody>
</table>

CONCLUSION

Liposomes have been replaced by niosomes, which have been studied as a prospective substitute. Some of the benefits of liposomes, such as chemical stability, have been enhanced. Purity and a lesser price tag when compared to liposomes. Surfactants vesicles, which are formed up of non-ionic surfactants, alter how things work. Kinetics of plasma clearance, tissue distribution the drugs metabolism and drug content.


13. Baillie AJ., coombs GH. and doaln TF. non ionic surfactant vesicles, niosomes, as delivery system for the anti leishmanialdrug, sodium stibogluconate. s.l.: wiley-blackwell, 1986;38(10):81-86.


