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NIOSOMES: THE VERSATILE VESICULAR DELIVERY SYSTEMS-A SYSTEMATIC REVIEW

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ABSTRACT

Niosomes refer to vesicles composed of non-ionic surfactant-based multilamellar or unilamellar structures, where a membrane formed by surfactant macromolecules organizes as a bilayer to encapsulate an aqueous solute solution. The term "Niosomes" originated from "non-ionic surfactants" as these vesicles consist of a bilayer of non-ionic surface-active substances. These Niosomes represent a distinctive drug delivery technology that safely encapsulates medications within vesicles. In contrast to hazardous and unsuitable Ionic drug carriers, Niosomal drug carriers pose lower risks. Moreover, Niosomes exhibit remarkable stability and do not necessitate specific handling or storage conditions. As a drug carrier, Niosomes show promising potential in reducing medication side effects and enhancing therapeutic insolubility, instability, limited bioavailability, and rapid degradation. This review article delves into the advantages, preparation methods, evaluation, and medicinal applications of Niosomes.

KEYWORDS: Niosomes, Compositions, Preparation methods, vesicles, Evaluation, Applications.

INTRODUCTION

Niosomes are a novel drug delivery system. They can direct a therapeutic agent that explicitly targets a desired site to produce an action with little or no interaction with a target tissue. The Aim of any drug delivery system should always be to achieve maximum therapeutic response with Minimum side effects. Researchers employ various carriers for drug targeting, and Niosomes are one of the notable carriers used for this purpose. The Niosomes drug delivery

system evaporates the medication in a vehicle.[1] The Niosome are amphiphilic, in which non-ionic surfactants make Vesicles and have the name Niosomes. The Niosomes' size is minimal and microscopic. The first Niosome formulation was developed and patented by L'Oréal in 1975. The primary purpose of developing the Niosomes system is chemical stability: biocompatibility, low production cost, Easy storage, and handling. Various kinds of routes of administration, such as oral, parenteral, and topical, must be used for administering drugs.[2,4]

SALIENT FEATURES OF NIOSOMES

1. Niosomes can entrap hydrophilic and hydrophobic drugs within their Bilayer for different drug delivery applications.
2. Niosomes are osmotically active and stable.
3. Using Niosomes allows for achieving targeted medication delivery, as they specifically deliver the medication to the intended body part.
4. They improve the solubility and oral bioavailability of poorly soluble drugs. On topical administration, they increase the skin permeability of the drugs.
5. Niosomes improve the performance of the drug molecules.

ADVANTAGES

1. Niosomes increase the bioavailability of drugs by protecting the drug from acidic acid enzymatic degradation in GIT.
2. The vesicles act as a reserve, allowing the controlled release of the drug.
3. The therapeutic efficiency of drug molecules is improved by reducing the clearance rate and targeting specific sites by protecting the encapsulated drug.
4. Niosomes exhibit biodegradable, biocompatible, and non-immunogenic.
5. They have a high level and biological compatibility and are low in toxicity.
6. Niosomes have a hydrophilic and hydrophobic architecture that allows them to accommodate medicinal molecules with a wide range of solubility.
7. Surfactants can be handled and stored easily with no specific condition.

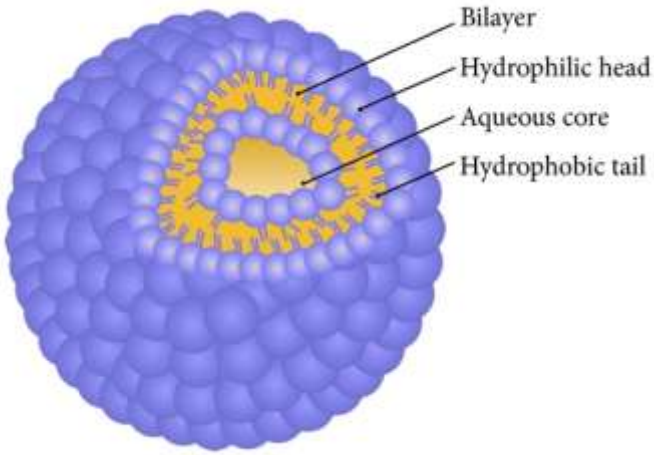
DISADVANTAGES

1. Aggregation, leakage, and hydrolysis of encapsulated medicines may limit the shelf-life of Niosomes aqueous suspension.
2. It is a time-consuming process for preparing multi-lamellar vesicles.
3. It requires specialized equipment for processing.
4. The entrapped drug can leak.

5. Insufficient drug loading.

STRUCTURE

An amphiphilic bilayer containing a non-ionic surfactant, such as span 60, constitutes a Niosome vesicle. We can stabilize the structure by incorporating cholesterol and a small amount of anionic surfactant such as diacetyl phosphate, which also aids in stabilizing the Vesicle.[5-8]



TYPES OF NIOSOMES

1. PRONIOSOMES

After hydrating the Niosomes, we create Pro-Niosomes using the carrier and surfactant mixture.[9-12]

2. ASPASOMES

- A combination of ascorbyl palmitate, cholesterol, and highly changed lipid diacetyl phosphate leads to forming Vesicles called Aspasomes.
- Aspasomes are first hydrated with water/aqueous solution and then sonicated to obtain the Niosomes.
- Aspasomes can be used to increase the transdermal permeation of drugs.

3. VESICLES IN WATER AND OIL SYSTEM

- Reports indicate that aqueous Niosomes emulsify into an oil phase within Vesicles in a water-in-oil emulsion(v/w/o)

 They prepare them by adding a Niosomes suspension from sorbitol monostearate, cholesterol, and solution c24(poly-24 oxyethylene cholesteryl ether) to the oil phase at 60°C. This results in the formation of Vesicles in water in oil gel(v/w/o gel)

 The v/w/o gel thus obtained can entrap proteins/proteinous drugs and protect them from enzymatic degradation after oral administration and controlled release.

4. NIOSOMES IN CARBOPOLGEL

Researchers prepared Niosomes from drug spans and cholesterol, and then they incorporated them into Carbopol, propylene glycol(10%w/w), and glycerol(30%w/w)

5. NIOSOMES OF HYDROXYL PROPYL METHYL CELLULOSE

In this type, they prepared a base containing 10% hydroxy propyl methyl cellulose and glycerin and then incorporated Niosomes.

CLASSIFICATION

Niosomes are also classified accordingly to the number and size of the Bilayer.[13-16]

1. MULTI LAMELLAR VESICLES (MLV)

These are the most widely used Niosomes. It consists of several bilayers. The approximate size of Vesicles is 0.5-10um in diameter.

2. LARGE UNILAMELLAR VESICLES (LUV)

Niosomes of these large Uni-lamellar Vesicles possess a high aqueous/lipid compartment ratio, enabling them to entrap more immense amounts of bioactive materials.

3. SMALL UNILAMELLAR VESICLES(SUV)

These small Uni-lamellar vesicles are primarily prepared from Multi-lamellar vesicles by the Sonication method.

COMPOSITION OF NIOSOMES

Niosomes mainly contains the following types of components.[15-17]

1. NON-IONIC SURFACTANTS

Based on MLB value surfactant selected as HLB(Hydrophilic Lipophilic Balance) is a good indication of the vesicle-forming ability of any surfactant; they formed the HLB number between 4 to 8 to be compatible with Vesicle formation.

A) ALKYL ETHERS

Here are some surfactants used in the formulation of Niosome containing drugs/chemicals:

SURFACTANT-I: It is c16 monoalkyl glycerol ether with an average of three glycerol units.
SURFACTANT-II: Diglycerol ether has an average of seven glycerol units.
SURFACTANT-III: It is Ester linked surfactant.

B) ALKYL ESTERS

Sorbitan esters are the most preferred surfactant for the preparation of Niosomes. Vesicles prepared by polyoxyethylene sorbitan monolaurate are more soluble than other surfactant vesicles.

C) ALKYL AMIDES

Researchers have utilized alkyl amides (such as galactosides and glucosides) to produce Vesicles.

2. CHOLESTEROL

- Steroids are essential components and cell membranes; their presence in the membrane affects bilayer fluidity and permeability.
- In the formation of Niosomes, researchers primarily use cholesterol, a steroid. derivative
- Incorporating cholesterol alters Niosome features such as membrane permeability stiffness and encapsulation efficiency.

3. CHARGED MOLECULE

- Some charged molecules are added to Niosome to increase the stability of Niosomes by electrostatic repulsion, which prevents coalescence.
- Negatively charged molecules are diacetyl phosphate(DCP) and phosphatidic acid.
- Stearylamine and stearyl pyridine chloride are well-known positively charged molecules used in Niosomal preparations.
- These charged molecules prevent the aggregation of Niosomes.

METHODS OF PREPARATION

1. ETHER INJECTION METHOD

In this method, they slowly introduce a solution of surfactant dissolved in Diethyl ether into warm water maintained at 60°C. They inject the surfactant mixture in ether through a needle into an aqueous drug solution.[18-20] Ether, an organic solvent, evaporates using a rotary evaporator, forming single-layered vesicles. The Disadvantage of this method is that a small amount of ether is often present in the vesicle suspension and is difficult to remove.

2. HANDSHAKING METHOD

This approach uses a volatile organic solvent like diethyl ether, chloroform, or methanol to dissolve the surfactant, cholesterol, and selected additives-charged molecules. The process is carried out at a temperature of 20°C using a rotary evaporator, which forms a thin layer of solid mixture deposited on the inner wall of the flask. Rehydrate the dried surfactant film with an aqueous phase at 0-60°C while gently agitating to yield multi-lamellar Niosomes. They slowly added the aqueous-containing drug to the flask with intermittent shaking at room temperature.

3. SONICATION METHOD

Add an aliquot of drug solution in a buffer to the surfactant or cholesterol mixture in a 10ml glass vial. The mixture is Sonicated with a titanium probe sonicator at 60°C for 3 minutes, forming Niosomes.

4. MICRO FLUIDIZATION

It is a technique used to prepare unilamellar vesicles. This method bases on a submerged jet principle where two fluidized streams are employed. One stream contains the drug, while the other includes the surfactant.[21-22] These two streams interact at an ultrahigh velocity within precisely defined micro-channels in the interaction chamber, ensuring that the supplied energy remains in the area of Niosomes formation. This method offers excellent uniformity, smaller size, prominent consistency, and high reproducibility in the formulation of Niosomes.

5. REVERSE PHASE EVAPORATION TECHNIQUE

This method dissolves cholesterol and surfactant at a 1:1 ratio in a mixture of ether and chloroform. They add an aqueous phase containing the drug and sonicate the resulting mixture at 4-5°C. After that, they form a clear gel, which they further sonicate after adding phosphate-buffered saline under low pressure. They remove the organic phase at 40°C. Then, they dilute the resulting Niosome suspension with phosphate buffer saline and heat it at 60°C for 10min to form Niosomes.[23]

EVALUATION TESTS

1. SIZE

The shape of the Niosomal Vesicle is assumed to be spherical, and the mean diameter of the Niosomal can be determined using the light scattering method. There are different methods to calculate the diameter of vesicles, i.e., chromatography, photon correlation microscopy,

optical microscopy, molecular sieve chromatography, electron chromatography, ultracentrifugation, and freeze-fracture electron microscopy.[24]

2. BILAYER FORMATION

The formation is essential for drug entrapment efficiency. Non-ionic surfactants assemble to form a bilayer vesicle characterized by an X-cross formation by the light polarization method. Using the latter approach, one can describe the thickness of the Bilayer.

3. FOR ENTRAPMENT EFFICIENCY

- First, they make a Niosome dispersion.[25-26]
- Then Gel filtration and Dialysis centrifugation are done to remove the untrapped drug.
- Determination of the drug, i.e., to be entrapped in Niosomes, is done by using 50% n-propanol
- They perform the analysis using the following equation:

Entrapment efficiency=Amount Entrapped/total amount * 100

4. MEMBRANE RIGIDITY

They measure the mobility of the fluorescent excellent probe as a function of temperature. Researchers widely use the fluorescent probe DPH(1,6diphenyl 1,3,5hexatriene)for analyzing the Niosomal dispersion. DPH is present in the bilayer membrane at the hydrophobic region.[27]

5. STABILITY

The stability is determined with different temperatures by vesicle size, size distribution, and entrapment efficiency. Researchers use UV spectroscopy or HPLC methods to determine the percentage of drugs retained by Niosomes.

6. INVITRO RELEASE

A widely used method to study In-Vitro Release is dialysis tubing.

APPLICATION OF NIOSOMES

1. The new drug system of Niosomes, similar to liposomal capsules, employs tablet forms for oral conditions.[28-31]

2. Niosomes can be used as implants and transdermal patches because they penetrate the skin.

3. Niosomes have both hydrophilic and hydrophobic parts as they can carry /accommodate both H2O soluble and H2O insoluble drugs.

4. As Niosomes can increase the bioavailability of poorly soluble. Drugs-Drugs like lignocaine with the least oral bioavailability can be given by this.

5. One can administer drug like insulin using Niosomes, as they are resistant to acids.

MARKETED PRODUCTS

SR.	Brand	Name of the product
1.	Lancôme foundation and complexation	Flash Retouch Brush on Concealer
2	Britney Spears Curious	Curious coffret: Edp Spray 100 ml + Dualended Parfum & Pink lipgloss + Body souffle 100 ml
3	Loris Azzaro - Chrome	Chrome Eau De Toilette Spray 200 ml
4	Orlane – Lip colour and Lipstick	Lip gloss

CONCLUSION

In conclusion, the review of Niosomes, A novel drug delivery system, has revealed several significant advantages and promising potential. Niosomes are non-ionic surfactant-based vehicles that are a well-preferred drug delivery system over conventional drug delivery methods as they are mostly stable and economical. They can encapsulate hydrophilic and hydrophobic drugs, allowing for a broader range of therapeutic agents to effectively deliver to target issues, enhancing the Versatility of treatment options. Biocompatibility and low toxicity of Niosomes make them suitable for biomedical applications. These Vesicles demonstrate excellent potential in improving drug solubility. Bioavailability and pharmacokinetic profile, thereby enhancing therapeutic outcomes and minimizing adverse effects. Niosomes play a crucial role in various types of drug deliveries, like targeting topical ophthalmic parenteral.

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