Review Article

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AN UPDATED REVIEW ON NIOSOMES: A PROMISING DRUG CARRIER

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Abstract

Nowadays, advancement in nanocarrier technology gain interest of researchers because it offered various advantages in term of safety and efficacy like enhanced delivery of therapeutics with diverse pharmacological effects, featuring improved targeting capabilities and minimized adverse effects over other carrier systems. Similarly, Niosomes proved as a promising and novel drug carrier. Niosomes are vesicular drug carrier approach which provides controlled and targeted drug delivery. It consist non-ionic surfactants, cholesterol or its derivatives and charged molecules and can be unilamellar, oligolamellar or multilamellar. Their distinctive attributes include the ability to encapsulate both hydrophilic and lipophilic components. This review article illustrates all the basic details of niosomes like structure of niosomes, types of niosomes, its merits and demerits, routes of administration, methods of preparation, factors affecting their formation, evaluation criteria for niosomes as well as their applications and existing marketed formulations.

Keywords: Nanocarrier, lamellar, niosomes, surfactants.

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Introduction

Niosomes referred as non-ionic surfactant vesicles. These tiny lamellar structures are formed when non-ionic surfactants (alkyl or dialkyl polyglycerol ether class) and cholesterol are mixed together [1] [2]. These vesicular systems closely resemble liposomes but liposomes have several disadvantages like toxicity, low cost and stability issues at different pH [3]. Due to the disadvantages of liposomes, research interest shifted towards niosomes. Both niosomes and liposomes serve as carriers for both amphiphilic and lipophilic drugs [4]. Niosomes are considered as best vehicles for drug delivery as niosomes are non-ionic in nature and exhibit lower toxicity and enhance a drug's therapeutic effectiveness by targeting specific cells.

Drug delivery via niosomes is significantly applicable to numerous therpeutical agents for their therapeutic action against various diseases or disorders. It serves as vehicle for poorly absorbable drugs to design the novel formulations. It improves the bioavailability of drugs by crossing the barrier of GIT via transcytosis [5].

Structure of Niosomes

Niosomes are thermodynamically stable, comprising bi-layered structure of non-ionic surface-active agents & formed only when surfactants and cholesterol are mixed in a proper ratio at temperature is above the gel liquid transition temperature [6] [7] [8]. Centrally, its - contains a hollow space where hydrophilic as well as hydrophobic drugs are encapsulated.

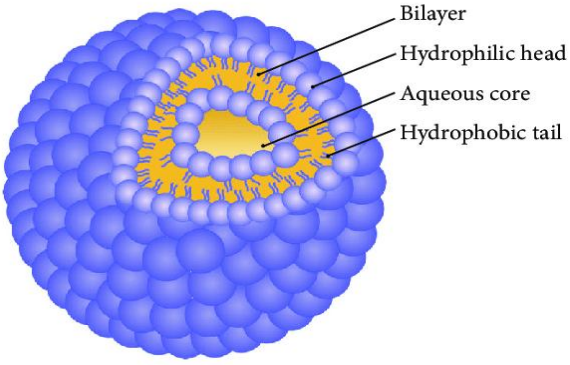

Figure 1: Structure of Niosomes.

Types of Niosomes

Niosomes offer a highly promising platform for drug transportation. Based on the vesicle size, niosomes can be divided into three groups:

1. Small Unilamellar Vesicles (SUV, size=0.025-0.05µm),

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2. Multilamellar Vesicles (MLV, size=>0.05µm),
3. Large Unilamellar Vesicles (LUV, size=>0.10µm).

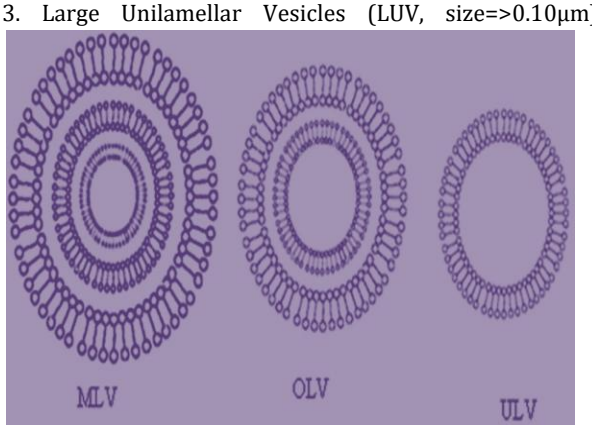

Figure 2. Types of niosomes, MLV (multilamellar vesicles), OLV (oligolamellar vesicles) and ULV (unilamellar vesicles).

Small circles (o) represent polar head group, sticks (–) represents non polar tails of single-chain surfactant molecules and a bilayer membrane represent a circular double surfactant molecules layer oriented in continuous tails-to-tails and polar heads lining the inner and outer circle.

Merits of Niosomes

These non-ionic surfactant vesicles offer several advantages over other drug delivery approaches:

1. Controlled and targeted drug delivery.
2. Stable and osmotically active.
3. Increased dermal penetration and oral bioavailability.
4. Niosomes are non-immunogenic, non-toxic, biocompatible and biodegradable.
5. It can be used for parenteral, oral as well as topical routes.
6. No special condition required for handling and storage of surfactant vesicles.
7. Improved therapeutic performance of drugs.
8. Niosomes have water base, therefore having great patient compliance over oily dosage forms.

Demerits of Niosomes

Conversely, Niosomes posses some disadvantages:

1. May exhibit fusion, leaching or hydrolysis of entrapped drug which limits the shelf life.
2. Insufficient drug loading capacity.
3. Specialized equipment required for manufacturing.
4. Physically instable.
5. Leakage of entrapped drug.
6. Time consuming techniques.
7. Expensive.

Routes of Administration

Niosomes can be utilized to deliver drug via:

1. Ocular delivery (example-tacrolimus, naltrexone HCl)[9,10],
2. Transdermal (example-gallidermin, clomipramine) [11,12],
3. Pulmonary (example-glucocorticoid),
4. Oral (example-cefdinir, Lornoxicam),
5. As well as they can be used to deliver drug across blood-brain barrier (example-temozolomide).

Methods of Preparation

The self-assembly of nonionic surfactants in aqueous media results in closed bilayer structures.

There are numerous methods to formulate lipid-based vesicles, niosomes which are used as drug delivery systems. It includes therapeutically active ingredients, non-ionic surfactants consist of a hydrophilic head and hydrophobic tail [e.g. - Spans (Span 20, 40, 60, 80, 85), Tweens (tween 20, 40, 60, 80)], cholesterol which are the derivative of steroids which is used to provide the flexibility , rigidity and to give appropriate shape, phospholipids (e.g., phosphatidylcholine) and organic solvent (e.g., chloroform or methanol) [14].

1. **Ether Injection Method**
   In this method, solution of the surfactant and other additives (in diethyl ether) is introduced through a needle into warm water (60°C) which contain the drug. Vaporization of organic solvent help to form single layered vesicles [15] [16].
2. **Hand Shaking Method (Thin Film Hydration Technique)**
   In this method, surfactant, cholesterol and other excipients are dissolved in organic solvent such as diethyl ether or chloroform in a RBF. Rotary vacuum evaporator is used to remove organic solvent to obtain a thin film of solid mixture which is deposited on the walls of the flask. After that, an aqueous media is utilised to hydrate this dried surfactant film above transition temperature with gentle agitation for a particular time period in order to get multilamellar niosomes [17].
3. **Reverse Phase Evaporation Technique (REV)**
   In this method, ingredients are dissolved in a mixture of ether and chloroform and added to aqueous phase containing the drug. The resulting mixture is sonicated to get an emulsion and then organic solvent is evaporated by using rotary vacuum evaporator to obtain large unilamellar vesicles [18].
4. **Microfluidization Method**
   This method follow submerged jet principle in which active pharmaceutical ingredient and surfactant fluidized streams react at ultrahigh velocities, in micro channels in reaction chamber. At last, niosomes are formed due to involved high speed impingement and energy [19].
5. **Transmembrane pH gradient**
   Initially, a solution of surfactant is prepared in chloroform is prepared and then solvent is evaporated under reduced pressure to get a thin film on the wall of the round bottom flask. This film is then hydrated using citric acid solution of pH 4 by vortex mixing. The resulting hydrated film is then freeze thawed for noisome formation. Then, aqueous solution containing drug is added to the niosomal suspension and pH of suspension is maintained

between 7.0-7.2 using phosphate buffer and at the end mixture is heated at 60°C for 10 minutes to get niosomes [20].

6. **The Bubble Method**
   In this method, cholesterol and surfactant are dispersed together in a buffer at 70°C using a glass flask with three necks. This dispersion is mixed for a period of 15 seconds with high shear homogenizer and immediately afterwards, nitrogen gas is passed through homogenizer to obtain large unilamellar niosomes [21].

Characterization of Niosomes

1. Size, Shape and Morphology
   Structure of niosomes has been visualized and examined by microscopy and size of vesicles determine by photon correlation spectroscopy11.
2. **Entrapment efficiency**
   After preparing niosomal dispersion, untrapped drug is separated by dialysis, centrifugation, or gel filtration and the drug remained entrapped in niosomes is determined by following formula-
   Entrapment efficiency (% EF) = (Amount of drug entrapped/ total amount of drug) x 100
3. **Vesicle diameter**
   Niosomes diameter can be determined using light microscopy, photon correlation microscopy and freeze fracture electron microscopy10.
4. ***In-vitro* release**
   A method 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 analyzed for the drug content by an appropriate assay method13.
5. **Vesicle charge**
   Micro-electrophoresis, pH sensitive fluorophores & dynamic light scattering have been used to measure the zeta potential of niosomes and to obtain an estimate of the surface potential15.
6. **Bilayer Rigidity and Homogeneity**
   The Bilayer Rigidity and Homogeneity could be identified via. NMR, differential scanning calorimetry (DSC) and fourier transform-infra red spectroscopy (FT-IR) techniques [16].
7. **Niosomal drug loading and encapsulation efficiency**
   To determine drug loading and encapsulation efficiency, the niosomal aqueous suspension was centrifuged, supernatant was removed and sediment was washed twice with distilled water in order to remove the adsorbed drug [17].

The niosomal recovery was calculated as:

$$\text{Niosome recovery (\%)} = \frac{\text{Amount of niosomes recovered}}{\text{Amount of polymer + Drug + Excipient}} \times 100$$

The entrapment efficiency (EE) was then calculated using formula:

$$\text{Entrapment efficiency (\%)} = \frac{\text{Amount of drug in niosomes}}{\text{Amount of Drug used}} \times 100$$

The drug loading was calculated as:

$$\text{Drug loading (\%)} = \frac{\text{Amount of drug in niosomes}}{\text{Amount of niosomes recovered}} \times 100$$

Table 1: Marketed Formulations of Niosomes.

S.N.		
1	Lancome- Foundation and complexation	Flash Retouch Brush on Concealer
2	Britney Spears – Curious	Curious Coffret: Edp Spray 100ml +Dualended Parfum & Pink Lipgloss + Body soufflé 100 ml
3	Loris Azzaro – Chrome	Chrome Eau De Toilette Spray 200 ml
4	Orlane – Lipcolor and Lipstick	Lip Gloss

Applications of Niosomes

Day-by-day, interest in the use of niosomes has been increasing in various regions such as in the pharmaceutical, cosmetic, and food industries, as niosomal technology is widely varied and can be used to treat a number of diseases.

1. Niosomal carriers are suitable for the delivery of numerous pharmacological and diagnostic agents, including antioxidants, anticancer, anti-inflammatory, antiasthma, antimicrobial, anti-Alzheimer's, and antibacterial molecules, oligonucleotides, and others11.
2. Niosomes have been used for successful targeting of drugs to various organs like the liver and brain or to pathological districts such as tumor, enhancing drugs pharmacological activities while reducing side effects19.
3. Niosomes have been used for studying the nature of the immune response provoked by antigens.
4. It is used as Drug Targeting.
5. Niosomes as Carriers for Hemoglobin.
6. It is used act as Delivery of Peptide Drugs.
7. It is used in ophthalmic drug delivery, Transdermal Drug Delivery Systems [20].

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Conclusion

Nano-carriers present a great approach in drug delivery with promising features such as protection of drug from degradation and cleavage, controlled release, and in case of targeted delivery approaches the delivery of drug molecules to the target sites. Niosomes represent alternative vesicular similar to liposome due to the ability of niosomes to encapsulate different type of drugs within their structure. The niosomal technology is showing significant promise in the fields of cancer and infectious disease treatments. The system is already in use for various cosmetic products. Niosomes represent a promising drug delivery technology various type of drug deliveries can be possible using niosomes like targeting, ophthalmic, topical, parenteral, etc.

In particular, targeted niosomal systems have been designed with different mechanisms of action, including active, passive, and magnetic targeting, leading to more advanced and specific macromolecular drug carriers.

To sum up, in terms of stability and permeability for drug-sized molecules, niosomes exhibit similar characteristics to liposomes and could present a cost-effective and excellent alternative for delivery purposes.

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Conflict of Interest Statement

No conflict of interest.

Ethics Approval and Consent to Participate

Not applicable.

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