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Niosome as a versatile drug carrier

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ABSTRACT

In recent years, numerous research articles have been published relating to the potential of niosomes to serve as a biodegradable, biocompatible carrier for the delivery of various types of drugs. Niosomes are vesicles that are mostly composed of synthetic surfactants and cholesterol. The vesicular system of niosomes, with its bilayer structure assembled by nonionic surfactants, can increase the bioavailability of a drug to a specific area for a set period of time. Niosomes' amphiphilic nature enhances their ability to encapsulate lipophilic or hydrophilic drugs. Other additives, such as cholesterol, can be used to keep the structure of the niosomes rigid. The efficient use can be defined as a lower dose, fewer side effects, fewer dosages, greater patient compliance, and maximum concentration of the drug at the site of action to reduce unnecessary exposure to the entire body. This narrative review discusses the fundamentals of niosomes, such as their structural components and methods.

***Keywords*:** *Niosome,Compositions, Methods Of Preparation, Encapsulation, Surfactants, Vesicles, Application.*

1. INTRODUCTION

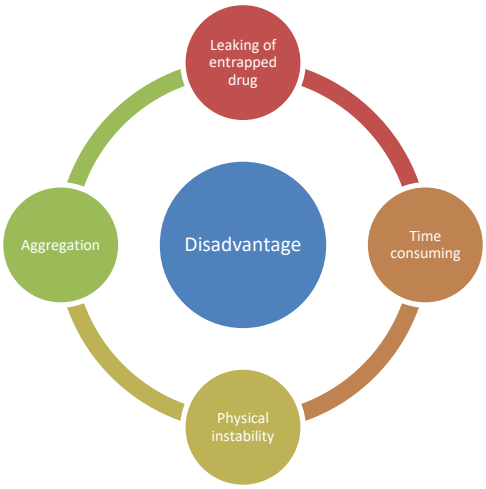
Discover a controlled release pathway. Niosomes play a significanat role in the controlled delivery of drug with poor solubility and bioavailability.(1) Niosomes have smal lamellar bilayer structures that contain chemically soluble monomersin ionic non-ionic vesicles.(2) Niosomes have a multilayer or asymmetricstructure consisting of non-ionic surfactants, cholesterol and diethyl ether in aqueous medium and water transfer. niosomes are cholesterol vesicles andnanonic surfactants (such as alkyl esters and alkyl ethers) that act as carriers of amphiphilic and lipophilic drugs.(3) Hydrophilic compounds are found in the main compound and the hydrophilic compounds are trapped in the polar bilayer so that the hydrophilic and hydrophobic compounds combine into niosomes.(4'5) Niosomes are naturally beneficial and the drug in the vesicle contains a non-ionic surfactant, hence the name. The size of niosomes is very small and not very small. The niosome structure is already established.(6,7,)

Advantage:

1.Niosomes are capable of handling a wide range of hand drugs,including hydrophilic-lipophilic and amphiphilic drugs.
2.Vesicle structure,lamellarity size, charged area, volume tapping, changes in concentration affect vesicle structures.
3. The drug is administered in a controlled and continuous manner.
4. Surfactant does not require special maintenance or storage conditions.
5. Improved bioavailability of soluble drugs.
6. Surfactants are perishable, bio-composite, non-toxic, and immunogenic.
7.They have the ability to inactivate the active zone in the blood
8. They are economical for large scale production.
9. They can protect the drug from enzyme metabolism.
10.They are not only osmotically stable and active but also improve the stability of entrapped drug.
11. They can increase the permeation of drugs through skin.

12. Therapeutic performance of the drug molecules can be improved by tardy clearance from circulation.
13. They can defend the active moiety from biological circulation.
14. They can control the drug delivery rate as aqueous phase niosomal dispersion can be emulsified in the non-aqueous phase and thus normal vesicle can be administered in an external non-aqueous phase.(8 -10)

Disadvantage11



2. COMPONENT OF NIOSOMES:12-14

The following are the two main elements required to create niosomes

* Cholesterol
* Non-ionic surfactants are another type of non-ionic surfactant

1.Cholesterol:cholesterol are most commonly used derivetives it is a waxy steroid metabolite found in cell membranes. It forms vesicles with nonionic surfactants, improving stability and reducing agglomeration. (12)
Non-ionic suractants: A:

a) (span 20, 40, 20, 85, 80)
b) (tween 20, 40, 60, 80)
c) (Brij 30, 35, 52, 58)

Sorbitan esters are an example of an alkyl ester.
(a) Alkyl amides: galactosides and glycosides, for example.
(b) Compounds containing amino acids and fatty acids.

2.Other additives: Charge inducers play an important role in the development of niosome. Diacetyl phosphate (DCP), Stearyl amine were two commonly used charge inducers.14

3. CLASSIFICATION

Acording to their size and number of bilayers niosomes are classified into three catagories:

1. Small Unilamellar Vesicles (SUV)
2. Large Unilamellar Vesicles (LUV)
3. Multi-Lamellar Vesicles (MLV)

- **SMALL UNILAMELLAR VESICLES (SUV):** it can be prepared by Sonication method, extrusion method and French press method.
- **LARGE UNILAMELLAR VESICLES (LUV):** It can entrap larger volume of bioactive materials as it having high aqueous/lipid compartment ratio.
- **MULTI-LAMELLAR VESICLES (MLV):**They are most usually used niosomes. It contains number of bilayers. They are easily to formulate and having size range of 0.5-10µm diameter. They are mechanically stable for long period of time on storage(15-16)

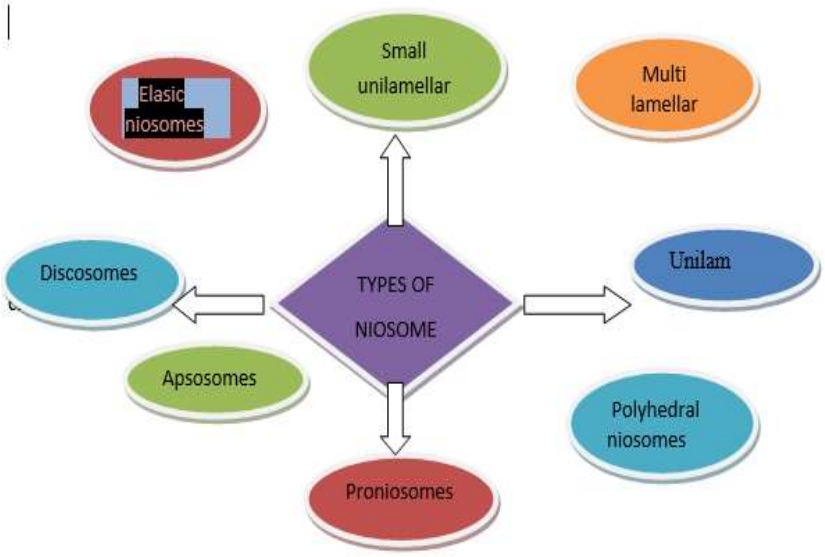
4. TYPES OF NIOSOMES

Proniosomes: Proniosomes have been prepared using maltodextrin, sorbitol, mannitol, glucose monohydrate, lactose monohydrate, and sucrose stearate (17,18). Proniosomes can be made using a variety of techniques, including the slurry method, slow spray coating, and coacervation phase separation. They found in two catagory, depending on there preparation : dry granular proniosomes and liquid crystalline proniosomes (19,20, 21-23
Bola–surfactant niosomes: Bola-surfactant niosomes are prepared from omhexadecyl- bis- (1-aza-18-crown-6): span-80: cholesterol in a molar ratio of 2:3:1. (24)
Aspasomes: Aspasomes were formed when acorbyl palmitate, a highly charged lipid, and diacetyl phosphate were combined. Niosomes were created by hydrating aspasomes with water/aqueous solution and then sonicating them.. Because of their inherent antioxidant properties, aspasomes have also been used to reduce disorder caused by reactive oxygen species. (25)
Discomes: Discomes are large disc-shaped niosomes. Previously, Uchegbu and colleagues used mechanical agitation and sonication to prepare discomes from hexadecyl diglycerol ether, cholesterol, and dicetyl phosphate (25). In the study, they

discovered that discomes were m) in size and grew even larger after sonication. Discomes are also large (11 to 60 8 thermoresponsive; their structure becomes less organised as the temperature rises above 37 degrees Celsius.

Elastic noisome: Elastic niosomes are flexible niosomes that can pass through pores smaller than their size without losing their structure. Surfactants, cholesterol, water, and ethanol are all components of these vesicles Because of their ability to pass through small pores and thus improve penetration through the skin barrier, they are commonly used in topical or transdermal drug delivery.(26)

Polyhedral Niosomes: This type of niosomes were formed by hexadecyl diglycerol ether replacing cholesterol with any type of the non-ionic surfactants and polyoxyethylene 24 cholesteryl ether without cholesterol.



5. FACTOR AFFECTING THE NIOSOMES

(1)Charge:In a multilamellar vesicle structure, the presence of charge increases the interlamellar distance between successive bilayers, resulting in a larger overall entrapped volume.

(2)Nature of surfactant: A surfactant's HLB value increases the mean size of niosomes due to a decrease in surface free energy with an increase in the surfactant's hydrophobicity. Niosome bilayers can be in either a liquid or a gel state. Temperature, surfactant type, and cholesterol all play a role.

(3) **Cholesterol content:**Incorporation of cholesterol increases the entrapment efficiency and hydro-dynamic diameter of niosomes.

(4)**Nature of the Encapsulated Drug:**The drug is entrapped by interacting with the surfactant head groups, which causes an increase in charge and mutual repulsion of the surfactant bilayer, resulting in a larger vesicle.

(5)**Hydration Temperature:** To facilitate the influences of size and shape of the niosome. The assembly of surfactants into vesicles and the variation of vesicle shape both were affected by temperature changes. The change was also accounted for by the hydration time and volume of the hydration medium.

(6) Resistance to Osmotic Stress: When hypertonic solution was added, vesicle diameter decreases. There was the hang-up of eluting fluid from vesicles causes a slow release at first, followed by a faster release due to mechanical loosening of vesicle structure under osmotic stress. (27-31)

6. NIOSOMES METHOD OF PREPARATION

(a) Ether injection method: Vesicles are formed by injecting or slowly introducing lipids. Nonionic surfactants and cholesterol were placed in a beaker with warm water, and the temperature was kept at 60oC. Phosphate buffer is the aqueous solution used. With the help of a 14-gauge needle, an ether-containing mixture of drug solution is slowly added to the aqueous solution. The ether is then vaporised, resulting in the formation of only one layered niosome vesicle. Niosomes range in size from 50 to 1000nm. (32)

(b) Reverse phase evaporation process: vaporation is used to remove the volatile organic solvent in this method. Disperse cholesterol and surfactant in an equal (1:1) ratio in the ether-chloroform mixture. A drug-containing aqueous phase is added to the above solution, and the resulting two phases are sonicated for a few minutes. The phosphate buffer saline is then added, and sonication results in the formation of a clear gel. Evaporation removes the organic phase at low pressure. The obtained suspension is further diluted with phosphate buffer saline and heated on a water bath at the optimum temperature (45oC) for 10 minutes, resulting in the formation of Niosomes(33)

© Film hydration method: In a round bottom flask, non-ionic surfactant and membrane stabilizer lipid are mixed in organic solvent like chloroform, methanol and diethyl ether. Then evaporation of volatile solvent leads to the formation of thin film of solid mixture on the wall of round bottom flask. Addition of solvent with gentle agitation leads to the rehydration of film. Through this method multi-lamellar vesicles are formed.(34)

(d) Trans membrane PH gradient process: A lipid film formed on the wall of the round bottom flask after dispersing the lipid mixture in the organic solvent. Results in the formation of hydration films and multi-lamellar vesicles.That mixture were subjected to both a freeze-thaw cycle and sonication. The API aqueous solution was then added and stirred. To raise the pH of the mixture, disodium phosphate was used. The mixture is then heated to 65°C to produce niosomes (34).

(e) Sonication: Sonication is a commonly used technique for preparing niosome vesicles. In this method, the drug, surfactant, and cholesterol are mixed with buffer in a 10ml glass vial. The mixture were probe sonicated with a titanium probe for about 3 minutes. (35)
(f) Micro fluidizatin process:The principle of niosme formation was used. When lipids and aqueous phases interact at high speeds, vesicles form (35)
(g)Multiple membrane extrution method: Chloroform was used to dissolve and evaporate nonionic surfactant, cholesterol, and diacetyl phosphate. This results in the formation of a thin film, which is followed by aqueous phase hydration. A polycarbonate membrane is used to filter a niosome suspension. (36)
(h)Bubble method: A round bottom flask with three neck areas is used in this method. One each for the reflux, thermometer, and nitrogen supply inlet. The lipid mixture was dispersed in phosphate buffer saline before being homogenised under high pressure. The addition of nitrogen gas at 65-70 °C causes bubbles.(37)

7. CHARACTERIZATION OF NIOSOMES

1.Size and shape morphology: To determine the size of niosomes, laser light scattering, electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy, optical microscopy, and freeze fracture electron microscopy, among other methods, were used. It is shaped like a sphere. [27] The vesicle size influences the preparation's release rate and shelf life, making it an important parameter. The number of lamellae can be determined using NMR spectroscopy, small angle X-ray scattering, and electron microscopy(38).

2.Encapsulation Efficiency: For the separation of unentrapped drugs, centrifugation, dialysis, or gel filtration are used. The medication will remain entrapped in niosomes is determined by complete vesicle interference utilizing 50% *n*-propanol or 0.1% Triton X-100 and examined with a suitable analytical method. Entrapment efficiency increases with surfactant concentration and lipophilicity.(39)

The encapsulation efficiency (EE) percentage is considered according to the following equation:

Entrapment efficincy= (Amount entrapped in niosome / total amount) x 100

3.Bilayer Formation:Under light polarisation microscopy, the assembly of non-ionic surfactants and cholesterol to form a bilayer vesicle is described by X-cross formation. (40)

4.Number of Lamellae: Nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering, and electron microscopy were used to determine these properties (41)5.Membrane Rigidity: The temperature-dependent mobility of a fluorescence probe can be used to estimate membrane rigidity (41)

6.Stability Study: Niosomal formulations are tested for stability by storing them in thermostatic ovens set to 4°C, 25°C, and 37°C for three months. After one month, the drug content of all formulations is checked using the entrapment method. efficiency parameter.(42)

7.In-vitro Release: In-vitro release rate study using
1. Dialysis tubing,
2. Reverse dialysis, and
3. Franz diffusion cell.

a.Dialysis tubing:Shake constantly in a 250 ml beaker with 200 ml of buffer solution at 25°C. The buffer is a drug content analysis carried out at different time intervals using an appropriate assay method. A dialysis sac is cleaned with distilled water. Pipetting the prepared vesicle suspension into a bag lined with dialysis tubing and sealing it. After that, the vesicles are inserted

b.Reverse Dialysis: Proniosomes are filled with a number of small dialysis tubes containing 1ml of dissolution medium for reverse dialysis. After that, the proniosomes were displaced into the evaporating medium.

c.Franz Diffusion Cell: In vitro diffusion studies can be carried out by using the Franz diffusion cell.In this proniosomes were present in the donor chamber of a cellophane-lined Franz diffusion cell. Then samples are then dialyzed at room temperature against a suitable dissolution condition, and the drug content is determined using methods such as UV spectroscopy, HPLC, and others.(43-46)

8. Scanning Electron Microscopy:The niosomes were examined using a scanning electron microscope (SEM). They were double-sided taped to the SEM sample stub and coated with a film with a thickness of 200 nm at a pressure of 0.001 mm Hg.(47)

Applications of Niosomes in Drug Delivery: Niosomes can be used in a variety of applications, including drug delivery systems, drug targeting, and disease treatment. Some examples of niosomes The following tables summarise drug delivery applications from the literature Niosomes use in various drug delivery application.(48-56).

Drug	Categroy	References
Itraconazole	Antifungal	Khazaeli et al., 2014[48]
Doxorubicin	Anticancer Drugs	Lakshmi et al. -2007[49]
Piroxicam	Anti-inflammatory	Reddy et al. -1993[51]
Primaquine	Anti-malarial drug	Varghese et al.-2004[54]
Ketoconazole &	Anti-fungal	Arora and Ajay et al. 2010[53]
Fluconazole		Kumar sharma et al. - 2009[55]
Rifampicin	Antituberculosis drug	Jain et al., 2006[51]
Bleomycin	Anticancer drugs	Naresh et al. -1996[50]
Venlafaxine	Anti-depressant	Negi et al. -2011[56]

8. CONCLUSION

The niosomal drug delivery system is one of the best examples of significant progress in drug delivery technologies and nanotechnology. It's easy to see why niosomes appear to be a preferred drug delivery system over other dosage forms. Niosomes are novel nanodrug carriers that can be used to create effective drug delivery systems. They provide an excellent opportunity for loading hydrophilic, lipophilic, or both drugs simultaneously. There are numerous options for encapsulating toxic anti-cancer, anti-infective, anti-AIDS, anti-inflammatory, anti-viral, and other drugs. Niosomes can also help with diagnostic imaging and as a vaccine adjuvant. To improve bioavailability and targeting, as well as to reduce drug toxicity and side effects, niosomes are being used as promising drug carriers. Thus, niosomes present themselves as a versatile therapeutic tool.

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