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REVIEW ARTICLE

Niosomes: An Overview and Future Aspect

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ABSTRACT

Number of techniques are available to achieve restrained release system, such as niosomes. Association of non-ionic surfactant, dieyhyl ether, cholesterol along with successive hydration in aqueous media results in a mixture which ultimately forms the lamellar structure (uni or multi) of niosomes. Surfactants present are responsible for non-toxic, non-immunogenic biodegradation and biocompatible effects. These preparations may guard the functional portion of drug molecule from biological circulation and from metabolism of enzyme. Niosomes show an assuring drug delivery molecule. The charged drug transporters are moderately poisonous and inappropriate while the transporters for niosomes are safe. Niosomes have studied as a better substitute of liposome. Different advantages over liposomes include their comparatively greater chemical stability, enhanced purity & comparatively less expensive than liposomes.

Keywords: *Niosomes, Non-ionic surfactant, Diethyl ether, Cholesterol.*

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INTRODUCTION

Drug focusing on target may be elucidated as the dexterity to undeviating a pharmcaeutical active moiety at the convenient position of action with least or no intercommunication to other tissues.(1) Number of techniques are available to achieve restrained release system, such as niosomes. Basically niosomes are vesicles having microscopic lamellar bilayer structurewhich are nin-ionic surfactant formation of which are occurred by the assembly of monomers (hydrated). Association of non-ionic surfactant, dieyhyl ether, cholesterol along with successive hydration in aqueous media results in a mixture which ultimately forms the lamellar structure (uni or multi) of niosomes.(2) Generally non-ionic surfactants preferred as they have less potential to cause irritation. Niosomes are having size lies in between 10 to 1000 nm as they having microscopic lamellar structures. The lipophillic components as well as the aqeous solution of solutes can be entrapped in the bilayer itself which make the niosomes amphiphillic in nature in which the inside and outside surfaces of bilayers crop up with hydrophilized area embedded lipophilized area in the middle which enable the niosomes to deliver an ample amount of drugs and extra substances. Basically, Niosomes work as storehouse in the living structure that liberate the active drug in the confined way via their bilayer i.e. multilamellar or unilamellar supplying the confined liberation of the entrapped medicament. Niosomes comprise with biodegradable, non-immunogenic and biocompatible surfactants. They easily hydrolyzed because of the presence of ester bond hence they are better than liposomes(Figure 1) (3).

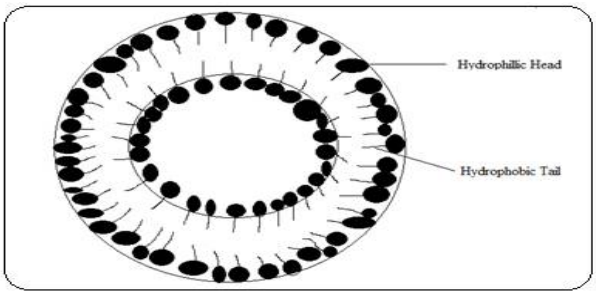

Figure 1. Structure of Niosome

Constitution of Niosomes:

Constituents used (4)

A. Surfactants (Non-ionic):- e.g. tweens, spans, brijs

B. Cholesterol:- it is a steroid derivative, provide proper shape and rigidity to niosome preparation.

Table .1: Various categories of surfactants (Non-ionic)(5)

Category of surfactant (Non-ionic)	Examples
Ethers	Decyl glucoside, brij
Esters	Polysorbates, spans
Alcohol (fatty)	cetostearylalcohol, oleyl alcohol, cetyl alcohol
Copolymers (Block)	Triblock copolymers (poloxamers)

Classification of Niosomes(6)

These are classified as follows:-

- MLV (Multi lamellar vesicles):- having size greater than 0.05µm and prepare by hand shaking method.
- LUV (Large unilamellar vesicles):- vesicles size >0.10µm and reverse phase evaporation method is used to prepare these vesicles.
- SUV (Small unilamellar vesicles):- having vesicles size 0.025-0.05µm and Sonication extrusion method and solvent dilution technique is used to prepare these vesicles.

Advantages:- (7)

1. These preparations can encompass a diversity of drug elements like hydrophilic lipophilic, and ampiphillic.
2. Vesicles property may be limited to transforming the constitution of various parameters (includes size lamellarity, surface charge, vesicle, concentration and tapped volume).
3. Easy handling so there is no need of special provisions for storage of surfactants used in the preparation.
4. It permits managed release of the drug, as it is the depot formulation.
5. Less soluble drugs can also be delivered with increased bioavailabilty.
6. Surfactants present are responsible for non-toxic, non-immunogenic biodegradation and biocompatible effects.
7. These preparations may guard the functional portion of drug molecule from biological circulation and from metabolism of enzyme.
8. Decrease instability of entrapped drug moiety.
9. Increase dermal permeabililty of drugs.
10. By sustained action these preparations may enhance the therapeutic study of the drug molecules.

Disadvantages(8)**:-**

1. Leaking of enclosed drug 2. Physical instability 3. Aggregation 4. Time consuming

Table. 2: Difference between Niosomes and Liposomes(9)

Liposomes	Niosomes
Costly	Inexpensive
Need special conditions for storage	No special requirements for storage
Not easy to handle	Easy to handle
Phospholipids having charge or neutral	Have uncharged surfactant (non-ionic).

Methods of preparation and evaluation of niosomes:-

Methods

Passive Trapping Techniques- In this technique there is an entrapment of drug molecule during the formation of niosomes. Most methods used to prepare niosomes are generally included in this class. (10).

Sonication – (11)

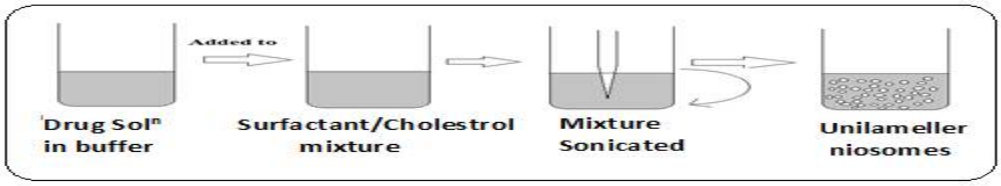

Figure 2: Sonication

Ether injection method- (12)

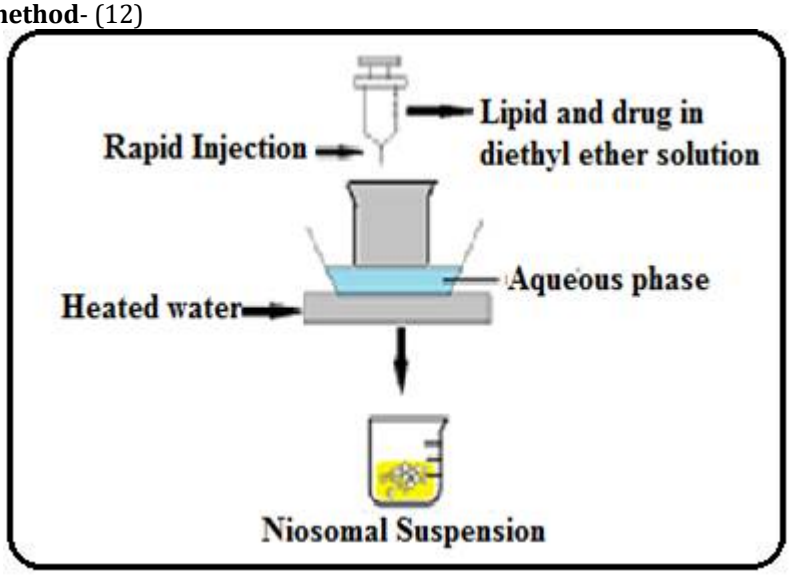

Figure. 3: Ether Injection Method

Reverse Phase Evaporation Technique- (13)

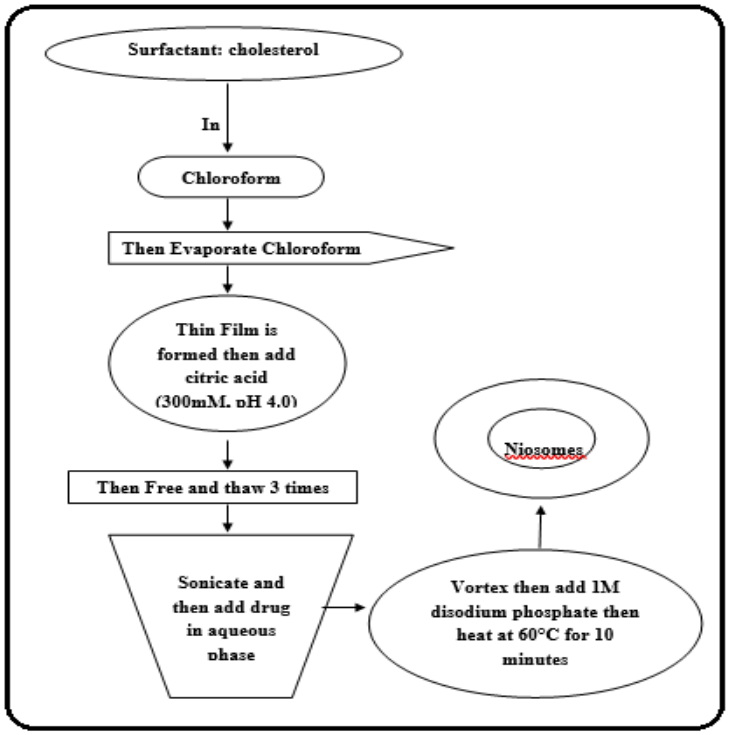

Figure. 4: Reverse Phase Evaporation Technique

The "Bubble" Method-(14)

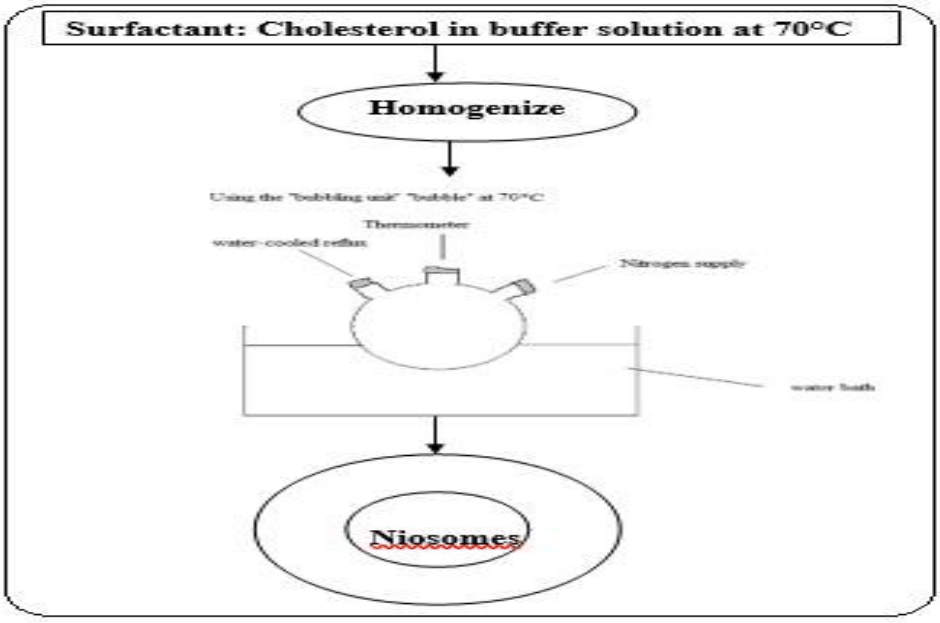

Figure 5: The "Bubble" Method

Hand Shaking Method/Thin Film Hydration Technique/Rotary Evaporator-(15)

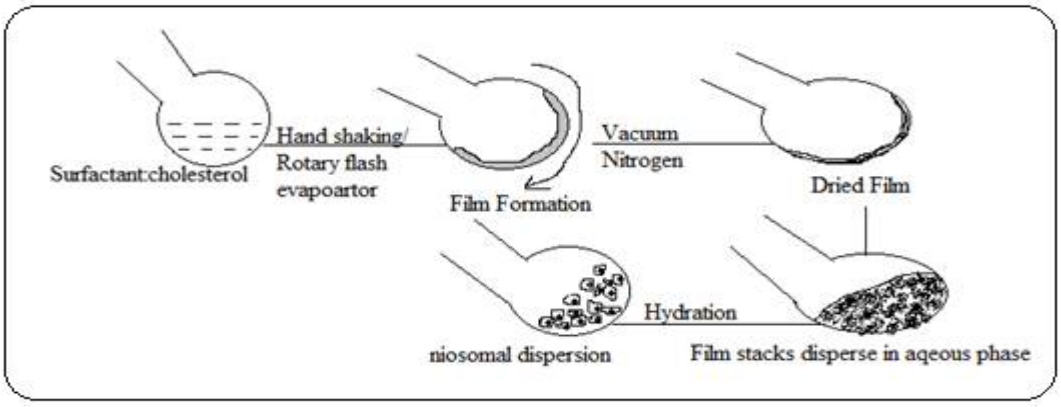

Figure 6: Hand Shaking Method

Micro Fluidization-(16)

Surfactant + Cholesterol + Aqueous solution + Drug

↓

Pass the above mixture through micro fluidizer jet (sample will flow like fluid stream at very high velocity).

↓

At very high velocity when this particle will pass through micro channel system the will interact with each other and produce energy.

↓

This energy will raise the temperature that will cause the folding of surfactant molecule as they are also interacting with aqueous phase.

↓

Thin liquid sheets are formed such that they now fold themselves and form niosomes.

Figure 7: Micro Fluidization

Multiple Membrane Extrusion Method-(17)

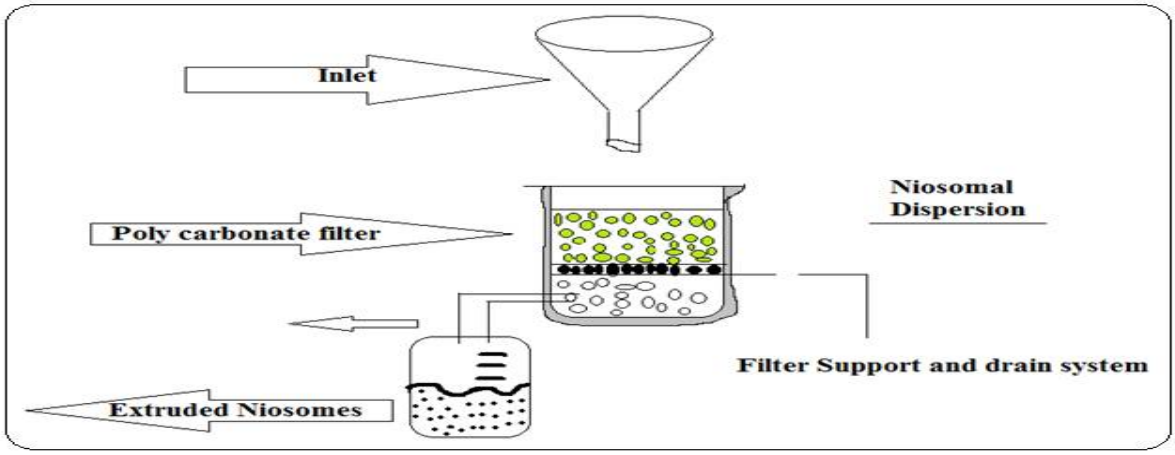

Figure 8: Multiple Membrane Extrusion Method

Ethanol Injection Method-(18)

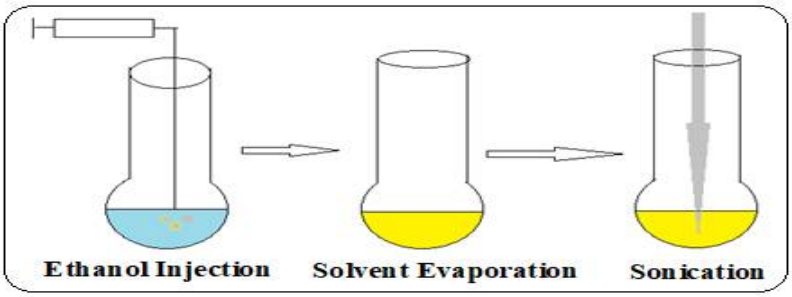

Figure 9: Ethanol Injection Method

Active Trapping Techniques- In this the drug is fill after the formation of niosomes for maintaining a pH slope to aid the assimilation of drug into the formation (niosomes). This technique has some advantages of niosome formation such as high drug lipid proportions, 100% entrapment, lack of leakage, inexpensive and fit for labile drugs.(19)

Trans Membrane pH Gradient Drug Uptake Process-(20)

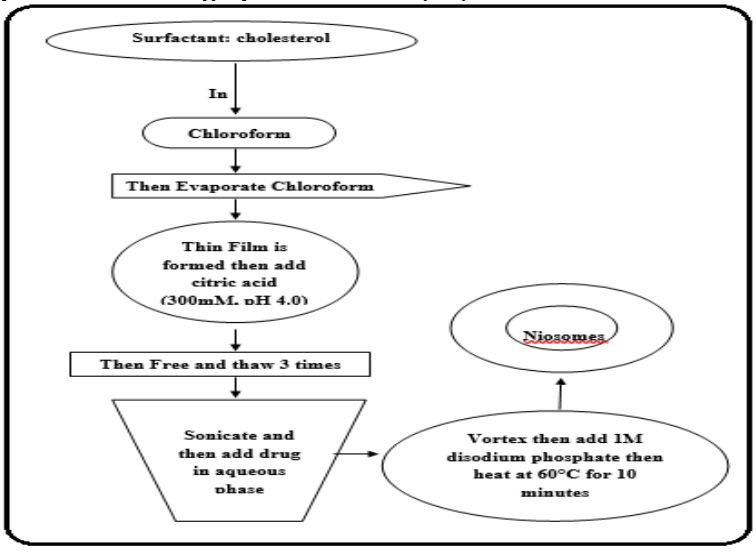

Figure 10: Trans Membrane pH Gradient Drug Uptake Process

Miscellaneous Methods-

Heating Method(21)-

It is one step method and non-toxic.

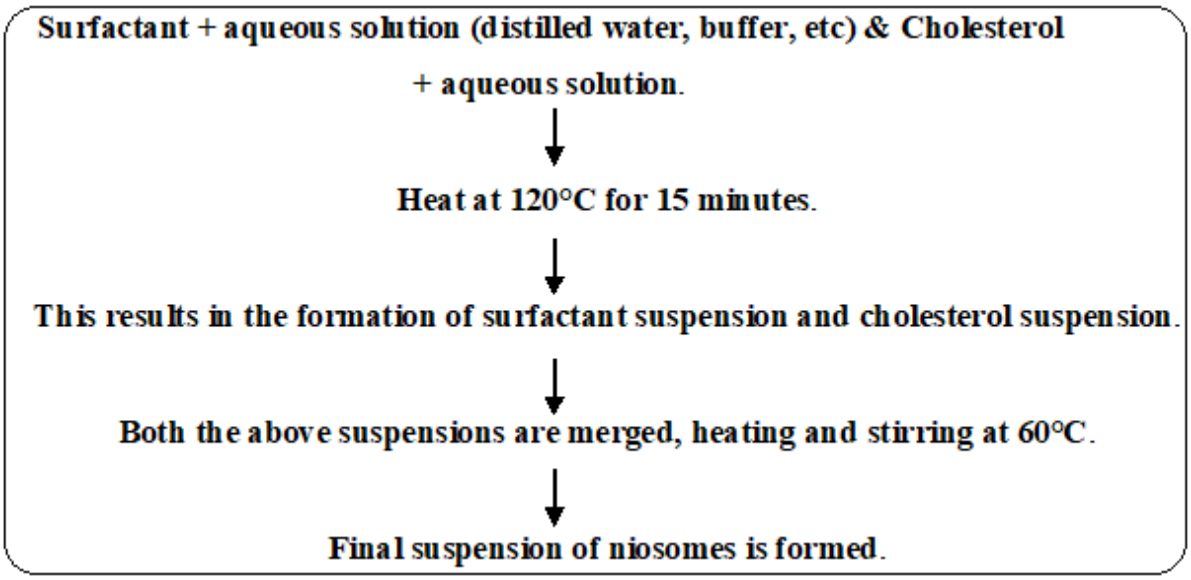

Figure 11: Heating method

Emulsion Method-

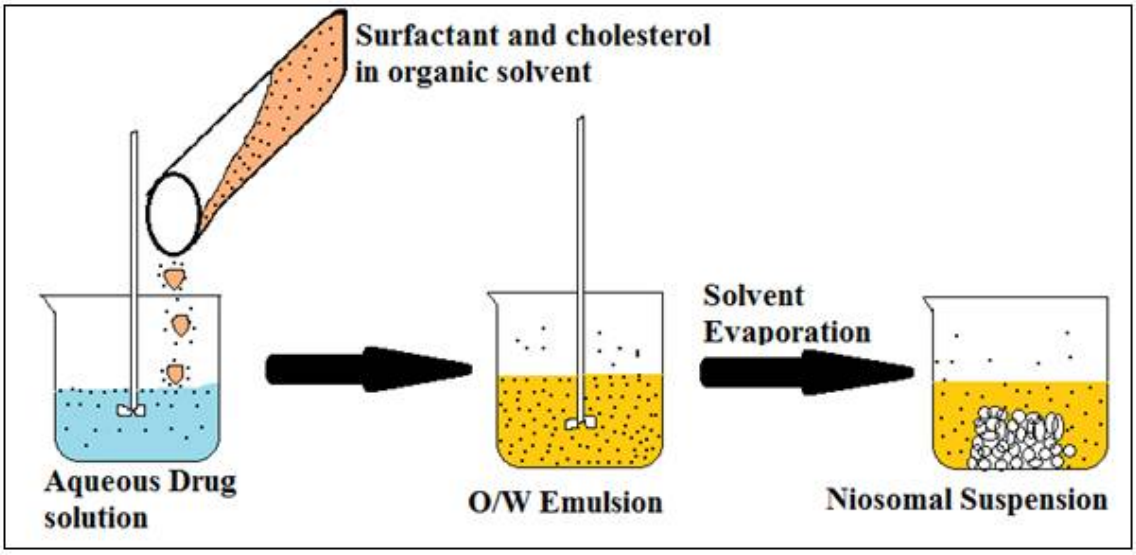

Figure 12: Emulsion Method

Lipid Injection Method-

Step I: Firstly, the melted mixture of lipids and surfactant is taken.

Step II: Then this mixture injected into an excessively agitated & heated aqueous phase in which the drug is dissolved.

Step III: Drug then dissolves in melted lipid and the mixture will be injected into the agitated, heated aqueous phase having surfactant.(22)

Formation of Proniosomes and niosomes from Proniosomes-

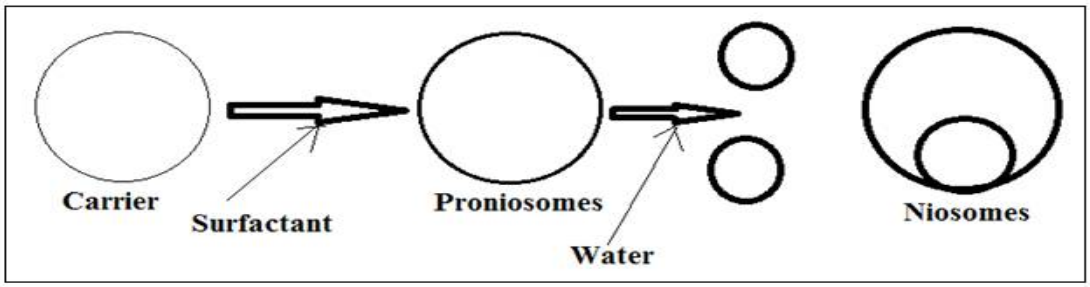

Figure 13: Formation of Proniosomes and niosomes from Proniosomes

Factors Affecting Niosomes(23)**:**
This includes following Factors:

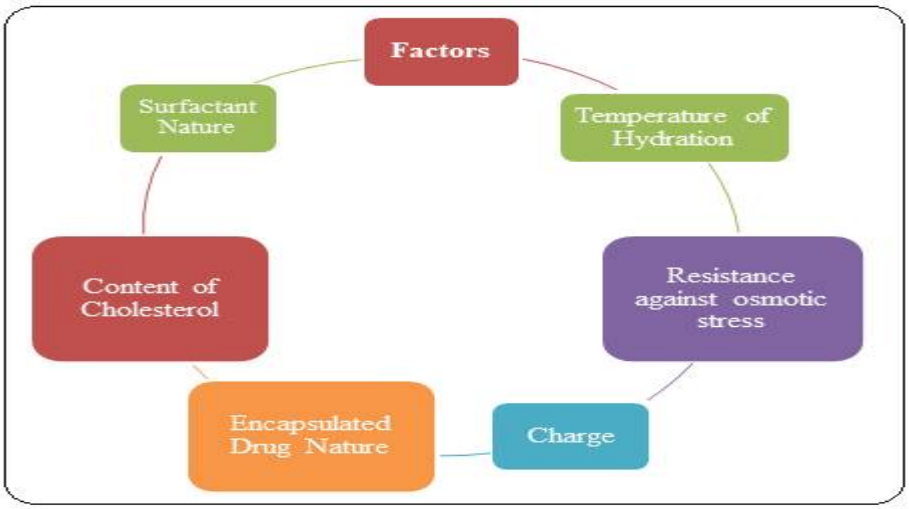

Figure 14: Factors Affecting Niosomes

Surfactant nature: HLB value positively affects the mean size of the niosome i.e. an increment in the HLB value increases the average dimension of Niosomal preparation due to the surface free energy with a hike in the hydrophobicity of the surfactant. Liquid phase, gel and transformation temperature influence the Entrapment efficiency of the surfactant.E.g. span 60 with high transition temperature of the surfactant.

Temperature of Hydration: Temperature of hydration effect the dimensions and appearance of niosomes. The amendment can be done via time and volume of hydration.

Content of cholesterol: The trapping ability and effective diameter of niosomes is increased by the addition of cholesterol.

Resistance against osmotic stress: The vehicle diameter is ameliorated by incorporation of solution (hypertonic). Inhibition of fluid coming out of vesicle results in slow release at initial point. It is followed by a faster release because of mechanical wear out of vesicle assembly under the influence of osmotic stress.

Enclosed Drug Nature: trapping of drug moiety take place by interrelating the surfactant head groups which is leading to the increase in charge and creates reciprocal repugnance of the bilayer of surfactant and thus grows the dimensions of vesicle.

Removal of unenclosed Drug:

The separation of unenclosed drug particles from the vesicles may be achieved via different techniques namely:

Centrifugation: Supernatant is separated after Niosomal suspension is centrifuged. Then to get a Niosomal suspension unaffected by the un-enclosed drug the pellet is washed and then resuspended.

Dialysis: The liquid Niosomal suspension is purified in the tube of dialysis against glucose solution, normal saline, or phosphate buffer.

Gel filtration: Sephadex G-50 column is used through which the enclosed drug is separated by gel filtration of Niosomal dispersion which further eluted by pouring normal saline or phosphate buffer.

Characterization of niosomes: (24)

Size & Shape: Various techniques are utilized for the resolution of average diameter such as molecular sieve chromatography apart from it laser light scattering, electron microscopy, photon correlation microscopy, optical microscopy, are also used to resolve size & shape.

Stability study: Niosomal preparations are stored at 4ºC, 25ºC & 37ºC for three months in thermostatic oven. Afterwards (one month), using entrapping efficiency parameter the drug content of entire preparations are measured.

Bilayer Rigidity & Homogeneity: Differential Scanning Calorimetry (DSC), P-NMR & Fourier Transform-Infrared Spectroscopy (FT-IR) techniques. Could be used to recognize Homogeneity which may exist both within niosome structures as well as among niosomes in dispersion. The effect of firmness of the bilayer is responsible for the Biodistribution & Biodegradation of niosomes.

In-line SEM (Scanning Electron Microscopy): The niosomes are perceived under a SEM (Scanning Electron Microscope). These are arranged instantaneously onto the SEM sample remnant by dual sided

adhering tape & layered with gold film of thickness of 200nm under decreased pressure of 0.001 mm Hg, photographs are taken at appropriate intensification.

Charge on vesicle: The surface charge on vesicle can take part in the way of acting of niosomes in vitro & in vivo. Aggregation & fusion is less stable then charged niosomes. Sequentially to achieve an estimation of the potentials (surface and zeta) of each niosomes may be determined by the microelectrophoresis. Recently, dynamic light scattering as well as pH-sensitive fluorophores are being used to calculate zeta potential of niosomes.

Filling & Encapsulation Efficiency of Niosomal Preparation: The Niosomal aqueous suspension is subjected to ultracentrifuge supernatant is washed two times by distilled water to separate the surface assimilated drug then drug loading & encapsulation efficiency is determined.

Calculation of Niosomal % Recovery:

% Recovery = Total content of niosomes recovered/Content of excipents+polymer+API x 100

% Drug Loading = 1+ Content of drug in niosomes/Content of niosomes x 100

Entrapment Efficiency = Total content of drug in niosomes/Content of drug x 100

Applications: (25)

1. In the release of polymeric drugs: Niosomal preparations protect the peptide drugs from gastrointestinal breakdown thus prove to be an effective means for the delivery of large size peptide drugs.
2. In study of immune system: As we know the toxicity level of niosomes is very limited and they have high stability so they are utilized to determine the response of immune system aggravated by different kind of foreign substances or antigens.
3. In the cancer treatment: Niosomal preparation may vary the reaction process, sustain the half life & circulation of the drug limiting the adverse effect of drug. These overcome the pace of over multiplication of tumor forming cells whether malignant or static.
4. Leishmaniasis: It is a liver disease which is caused by a parasite of liver of genus leishmania. This Parasite occupies the liver and spleen cell. Niosomal preparations can be used to achieve greater efficacy in the treatment with desired targeted action.
5. To organs except Reticulo-Endothelial system: several cells acquire the inherent capability to identify and connect to specific carbohydrate identifiers & it may be subjugated to the straight transporters method to specific cells.
6. To Golgi system: The Niosomal uptake via cells as well as pronins, the circulating serum factors which smear them for clearance such experiment-based values can be used to treat tumor cells known as profuse to the liver and spleen and in bloodsucking invasion of the hepatic organ.
7. In cosmetics: Niosome was first introduced in 1987 in the name of Lancôme. Niosomes benefit in cosmetic and dermal care contain their capability to raise the steadiness of enclosed active pharmaceutical ingredient and often get better bioavailability of weakly absorbable additives and improve dermal permeation.

Miscellaneous Applications:

- Prolonged discharge medication: Prolonged discharge medication have a vital rate dependent on niosomes Prolonged discharge mechanism of action of niosomes may be functional for the drugs which have poor water solubility and minimum therapeutic index.
- Localized Action of Drug: To attain localized drug action niosome is the best choice. Local drug action can be achieved by using niosome approach, while their dimension and poor perfusion via the epithelium and connective tissue hold the drug effective and specific at the administration site.

Tabe 2: Route of Administration of Niosomal drug:

Routes	Drug Used
Ocular	Cyclopentol
Nasal	Sumatriptan
Intravenous	Insulin, Doxorubicin, Rifampicin
Transdermal	Estradiol, Nimesulide, Piroxicam

Table 3: Marketed Niosomal Preparations

S. No.	Brand	Product Name
1	Loris Azzaro – Chrome	Chrome Eau De Toilette Spray 200 ml
2	Orlane – Lipcolor and Lipstick	Lip Gloss
3	Lancôme- Foundation and complexation	Flash Retouch Brush on Concealer
4	Britney Spears – Curious	Curious Coffret: Edp Spray 100 ml+ Dualended Parfum & Pink

FUTURE PROSPECTUS

Niosomes show an assuring drug delivery molecule. The charged drug transporters are moderately poisonous and inappropriate while the transporters for niosomes are safe. There are no special provisions require for storage & handling of niosomes. It has got a great deal of extent to cover poisonous moieties (antiviral, anticancer, anti-aids, anti-inflammatory etc). In Niosomal preparations and to utilize them as assuring drug transporters to get targeting properties & enhanced bioavailability & for decreasing the toxicity & adverse effects of the drugs.

CONCLUSION

Niosomes have studied as a better substitute of liposome. Different advantages over liposomes include their comparatively greater chemical stability, enhanced purity & comparatively less expensive than liposomes. Surfactant (Non-ionic) vesicle Change the tissue distribution, cellular interaction of the drug, metabolism & plasma clearance kinetics.

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