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Niosomes: A targeted drug delivery system

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Abstract

Niosomes are the multilamellar vesicles structure of non-ionic surfactant. Niosomes act as a drug carrier in drug delivery system. Niosomes improved the therapeutic performance of encapsulated drug molecules by protecting the drug from host biological environments resulting in their delayed clearance. In this present review article, we concentrate on the drug Niosomes which is a normal approach for drug delivery system. The niosomes have become the area of interest in the drug delivery system their advantage one liposomes in the field of drug delivery system for being non-toxic makes them more suitable for drug delivery system. Their ability to encapsulate both hydrophilic, lipophilic drugs simultaneously has increased its demand in the present scenario. Niosomes are vesicles made up of non-ionic surfactant, which are biodegradable, nontoxic, more stable and inexpensive and have ability to substitute liposomes but they also flexibility in the route of administration

Thus, in the present articles more focus is made on the development method of niosomes which is used as a novel approach in present scenario So, Niosomes as a drug carrier is of greater Importance in the pharmaceutical field

Keywords: Niosomes; Encapsulated; Lipophilic; Pharmaceutical; Non-Ionic-Surfactant

1. Introduction

Niosomes are multilamellar vesicular shape of nonionic surfactants, just like liposomes and are composed of non-ionic surfactant instead of phospholipids which might be the components of liposomes. So, niosome or non-ionic surfactant vesicles at the moment are widely studied as an opportunity device to liposome. numerous varieties of surfactants had been suggested to shape vesicles, and have the potential to entrap and maintain the hydrophilic and hydrophobic solute debris. Niosomes in particular comprise styles of components i.e., nonionic surfactant and the components. The non-ionic surfactants form the vesicular layer and the components used in niosome preparation are cholesterol and the charged molecules. The presence of the steroidal system (cholesterol) improves the pressure of the bilayer and is vital factor of the mobile membrane and their presence in membrane affects bilayer fluidity and permeability. This provider system protects the drug molecules from the untimely degradation and inactivation because of undesirable immunological and pharmacological outcomes. In recent years, niosomes have been considerably studied for their capacity to serve as a carrier for the shipping of medication, antigens, hormones and other bioactive retailers. except this, niosome has been used to clear up the problem of insolubility, instability and speedy degradation of drugs. (1)

The idea of a drug-transport gadget refers to a procedure of administering pharmaceutical compounds at a predetermined fee to reap a therapeutic effect in humans or animals at a diseased website online, and on the equal time, reducing the attention of the medication in surrounding tissues. Localized drug motion enhances the efficacy of drug

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and decreases systemic toxic consequences to tissues. Paul Ehrlich proposed the idea of centered shipping immediately to the diseased cell without unfavorable wholesome cells in 1909, and this strategy has been called the “magic bullet”. when you consider that then, a number of drug carrier systems have emerged, including immunoglobulins, serum proteins, artificial polymers, liposomes, microspheres, and niosomes, among those systems, liposomes and niosomes are nicely-documented vesicular drug delivery systems. In standard, a vesicular system is a drug-shipping platform that permits powerful bioavailability of medication through controlled launch of therapeutic capsules for an extended length. The vesicles consist of bilayer amphiphilic molecules that surround an aqueous compartment. (2)

Niosomes are vesicles of nonionic surfactant (for example, alkyl ester and alkyl ether) and cholesterol that act as a carrier for amphiphilic and lipophilic drugs. Niosomes improve the therapeutic performance of encapsulated drug molecules by means of protective the drug from harsh biological environments, resulting of their not on time clearance.

Novel drug improvement is both times eating and highly-priced. The development of a brand-new drug prices an expected $one hundred twenty million, and the journey from discovery, medical trying out, and development to regulatory approval takes decades. particular drug-delivery systems alleviate the urgency for bringing new drugs into the marketplace with the aid of increasing drug selectivity and the therapeutic index, even as lowering the effective dose. This narrative evaluation discusses the role of niosomes as a drug-shipping system and information of their shape, practice, homes, and programs

2. Structure of Niosomes

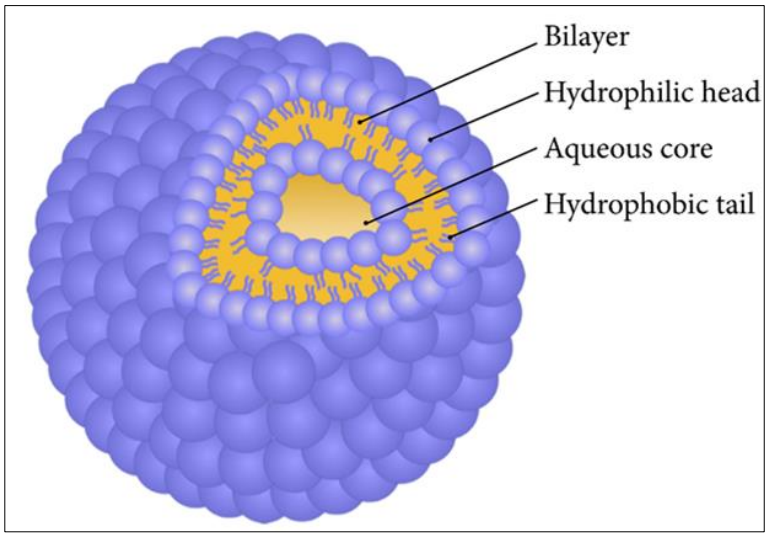


Figure 1 Structure of noisome

as compared to liposomes, niosomes, as shown in determine 1, are non-ionic vesicles which can be composed of two layers. Niosomes are chemically extra stable and much less costly than liposomes. The sizeable feature of the niosome structure is that they incorporate each a hydrophilic head and a hydrophobic tail. It approaches they're capable of entrap a huge variety of drugs (hydrophilic and lipophilic) in their formation. Hydrophilic drugs are loaded into the aqueous core of the niosome, on the identical time that the lipophilic area of the bilayer includes lipophilic tablets [3]. in particular, niosomes are manufactured from non-ionic surfactants, a hydration medium, and lipids, consisting of ldl cholesterol. The efficacy of a vesicular gadget is absolutely dependent on its components. it's also distinctly essential to apprehend the simple structural elements of niosomes prior to training, because it provides popular insight into the mechanism of niosomes and encapsulated tablets. they're taken into consideration unilamellar or multilamellar; unilamellar niosomes are bilayer structures, whilst multilamellar niosomes contain at least 2 bilayer vesicles. the dimensions of the niosome structure is variable from 10 to 1000 nm and they're labeled as small unilamellar vesicles (SUV), massive unilamellar vesicles (LUV), and multi-lamellar vesicles (MLV)[4]. From a thermodynamic factor of view, SUVs are much less solid than other varieties of niosomes, and hiya are able to encapsulate a lower awareness of hydrophilic pills even as tending to form aggregates. LUVs have a big water element that is appropriate for encapsulating hydrophilic tablets. MLVs may be produced without the want for complicated methods and are greater rigid than the alternative styles of niosomes. similarly, they are suitable for the encapsulation of lipophilic drugs due to the existence of multiple bilayer membranes [5,6]:

3. Compositions of niosomes [7]

The two major components used for the preparation of niosomes are,

- Cholesterol
- Non-ionic surfactants

3.1. Cholesterols

Cholesterol is a steroid derivative used to impart rigidity and appropriate shape and conformation to the liposome pre paration.

3.2. Nonionic surfactants [7]

Nonionic surfactants are self-oriented in a two-layer lattice, where the polar or hydrophobic surface is arranged on the water body (between) and the hydrophobic head or hydrocarbon section thus assembled Interaction with the aquatic environment will be minimized. To ensure thermodynamic stability, each bilayer folds onto itself as a membrane, for example by forming a vesicle, so that the hydrocarbon/water interface is not exposed. The following types of nonionic surfactants are generally used to make vesicles

3.3. Alkyl Ethers

L'Oréal discloses some of the surfactants used in the preparation of liposomes containing drug(s) –

- Surfactant-I (molecular weight (MW 473)) C16mono Alkyl Glyceryl Ethers, < br >
- Surfactant-II (MW 972) is a diglyceryl ether with an average of seven glycerol units.
- Surfactant III (MW 393) is an ester-linked surfactant. In addition to alkylglycerols with polyhydroxy head groups, alkyl glycosides and alkyl ethers are also used in liposome production. 4, 6, 7

3.3.1. Alkyl Esters Sorbitan esters are most preferred

This type of surfactant is used in the manufacture of vesicles. 8,9) Vesicles prepared from polyoxyethylene sorbitan monolaurate are more soluble than those from other surfactants. 10) For example, polyoxyethylene (polysorbate 60) was used to encapsulate diclofenac sodium. 11) A mixture of polyoxyethylene-10-stearyl ether: glyceryl laurine: cholesterol (27:15:57) was used to deliver cyclosporine-A.4,12)

4. Classification of Niosomes

The niosomes are classified as a function of the number of bilayer (e.g. MLV, SUV) or as a function of size. (e.g. LUV, SUV) or as a function the method of preparation.

The various types of niosomes are described below:

- Multi lamellar vesicles (MLV, Size=>0.05 um)
- Large unilamellar vesicles (LUV, Size=>0.10 um)
- Small unilamellar vesicles (SUV, Size=0.025-0.05 um).

4.1. Multilamellar vesicles (MLV):

It consists of multiple bilayers surrounding aqueous lipid compartments. The diameter of these vesicles is approximately 0.5-10 microns. Multilayer vesicles are the most commonly used vesicles. These vesicles are well-suited as drug carriers for lipophilic drugs. [8]

4.2. Large unilamellar vesicles (LUV):

This type of vesicle has a balanced water/lipid compartment and therefore allows the capture of large amounts of bioactive substances through the economical use of lipids. [9]

4.3. Small unilamellar vesicles (SUV):

Most small monolayer vesicles are prepared from multilayer vesicles by ultrasonic treatment, French press extrusion, and electrostatic stabilization with such hexadecyl phosphate in charged 5(6)-carboxyluciferin. (CF) In span-based vesicles. [9]

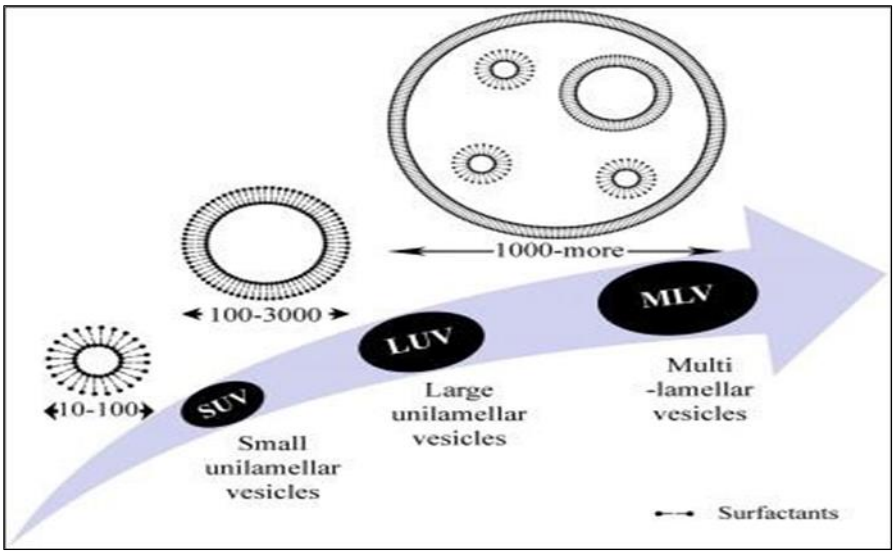


Figure 2 Classification of Niosomes

4.4. Advantages of nisomes[10,11]

- Nanobodies increase the bioavailability of drugs by protecting them from acidic and enzymatic degradation in the intestinal tract, thus increasing the bioavailability of drugs
- Due to its amphipathic structure, we can combine various drugs and use them in various medicines.
- We can increase skin permeability by using nanobodies.
- The therapeutic effect of drug molecules can be enhanced by slowing their elimination from the circulation.
- Surfactants can be used and do not require special storage.
- Vesicles serve as reservoirs from which the drug can be released in a controlled manner.
- Patient compliance is often due to high fuel consumption.

4.5. Disadvantages:[12]

- there is more drug aggregation in it
- Some cause physical weakness.
- The medicine inside the vesicles will leak.
- Vesicle hydrolysis reduces the shelf life of encapsulated drugs.
- Long preparation time

5. Types of Niosomes:

5.1. Proniosomes:

Proniosomes are niosomal formulations containing a carrier and surfactant that require hydration before use. Hydration results in the formation of an aqueous dispersion of noisome. Proniosomes reduce the aggregation, leakage, and fusion problems associated with niosomal formulations. [13]

- Carrier + surfactant = proniosomes
- Proniosomes + water = niosomes

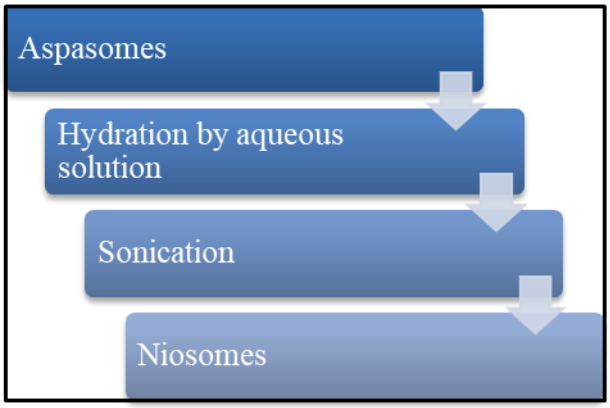
5.2. Bola–surfactant niosomes

Bola surfactant niosomes were prepared from omega-hexadecyl-bis-(1-aza-18-crown-6): span-80: cholesterol in a 2:3:1 molar ratio. Among them, omega-hexadecyl-bis-(1-aza-18-crown-6) is a surfactant. [14]

5.3. Aspasomes

Aspasomes The combination of ascorbyl palmitate, cholesterol, and the highly charged lipid diethyl phosphate leads to the formation of vesicles called aspasomes. Aspasomes are first hydrated with water/aqueous solution and then subjected to sonication to obtain niosomes. Aspasomes can be used to increase the transdermal permeability of drugs. Aspasome is also used to reduce diseases caused by reactive oxygen species due to its antioxidant properties. [15]

5.3.1. Procedure



5.4. Discomes

Discomes are large disc-shaped vesicles. The phase diagram of non-ionic surfactants exists only under certain conditions. When previously spherical vesicles were incubated for 1 h in a shaking bath at 24 and 74 °C, with different rates of respiration, discs of 11-60 μm in size were formed. Discoms are used as vehicles to deliver drugs to the eyes. Abdelkader et al. Ocular delivery formulations of naltrexone were prepared using a modified reverse phase evaporation technique. The temperature used for preparation is 60 °C, which is lower than the previously mentioned temperature and will therefore be beneficial for electrical equipment. [16,17]

5.5. Elastic niosome

They are made using nonionic surfactants, ethanol, and water. They can pass through pores that are larger than the vesicles found in the stratum corneum. They can be used to deliver low and high molecular weight drugs. Their effects last longer than vesicles and their penetration is weaker but depends on trans-epidermal hydration. Manosroi et al., 2013 prepared elastase niosome for scar treatment using Tween 61 and cholesterol in a chloroform/methanol (1:1) mixture. [19]

5.6. Polyhedral niosomes

Polyhedral vesicles are spherical vesicles but are not homogeneous. Polyhedral vesicles have approximately 4 to 12 equal sides. niosomes were prepared by mixing cetyl diglyceryl ether (C16G2) and inhaled C24 by Uchegbu and Florence, 1995; Uchegbu et al., 1997; and Uchegbu and Vyas, 1998. These can be prepared by adding small amounts of cholesterol to the mixture. Polyhedral niosomes can also be prepared by adding mixtures of C16EO5 and solan-C24 into low concentrations of ethanol. [19]

5.7. Vesicles in water and oil system

These vesicles are formed by emulsifying aqueous vesicles in an oily system. If cooled to room temperature, the vesicle system turns into a gel. [20].

6. Method of preparation

6.1. Ether injection method: [21-22]

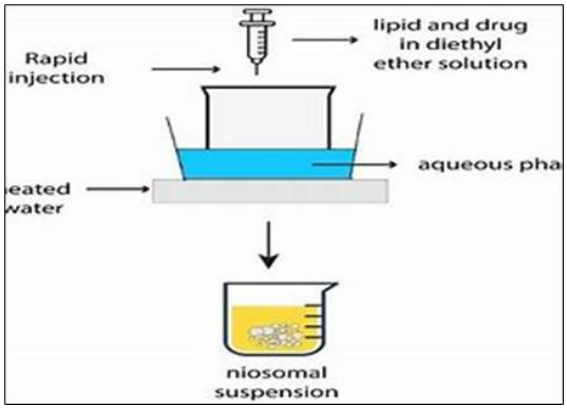
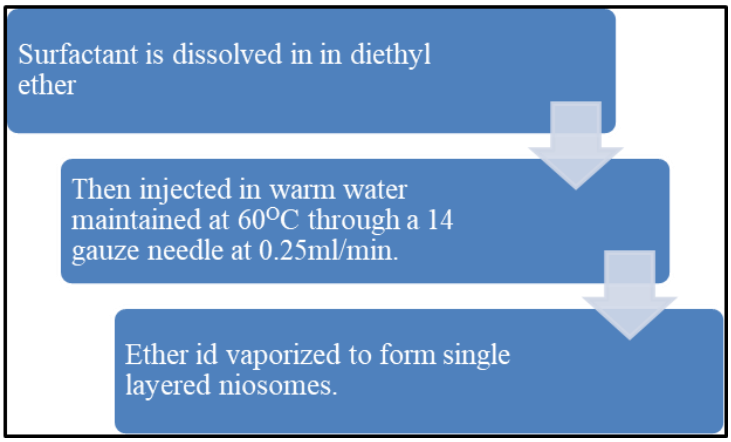


Figure 3 Ether injection method

6.1.1. Procedure



6.2. Hand shaking method (Thin film hydration technique) [22, 23]

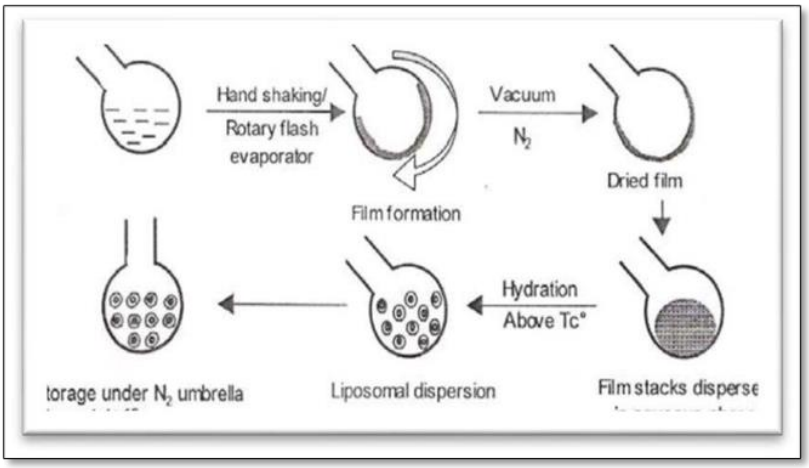
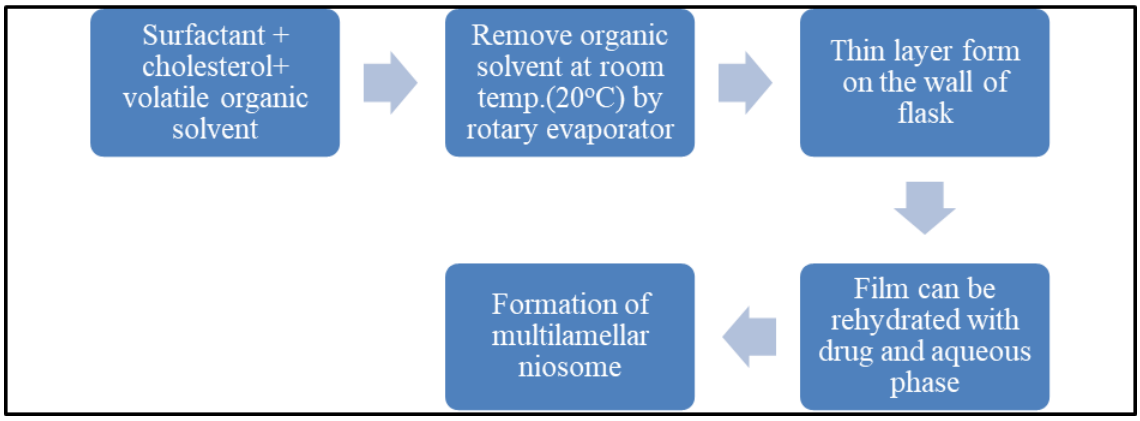
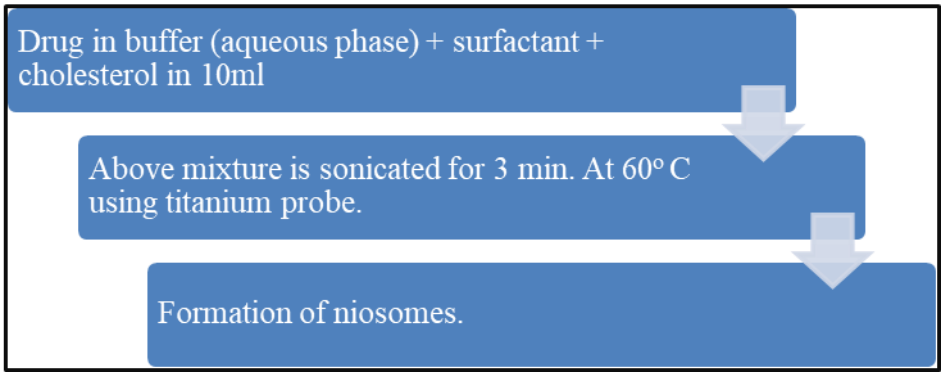


Figure 4 Hand Shaking Method of Niosome

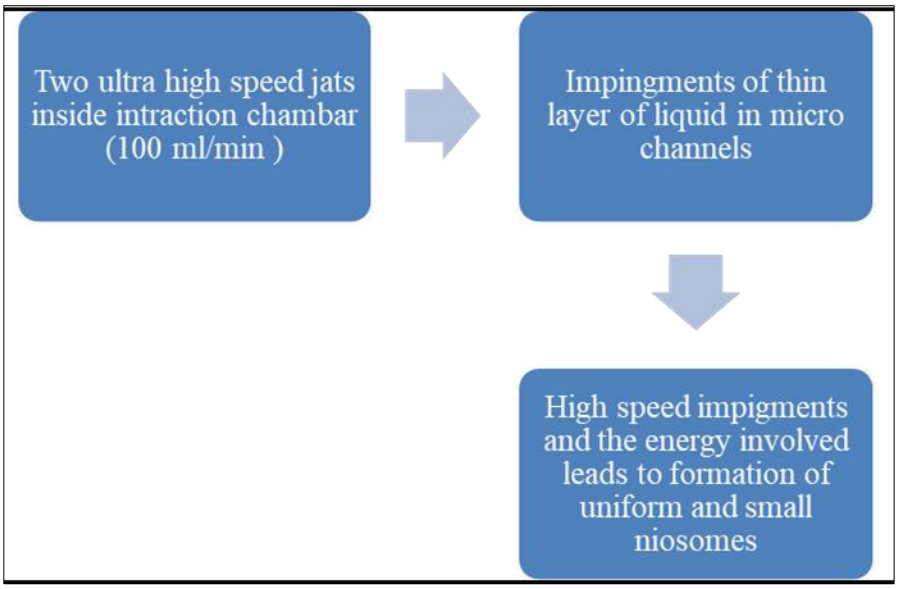
6.2.1. Procedure



6.3. Sonication [22, 24]



6.4. Microfluidization



6.5. Multiple membrane extrusion method: [25]

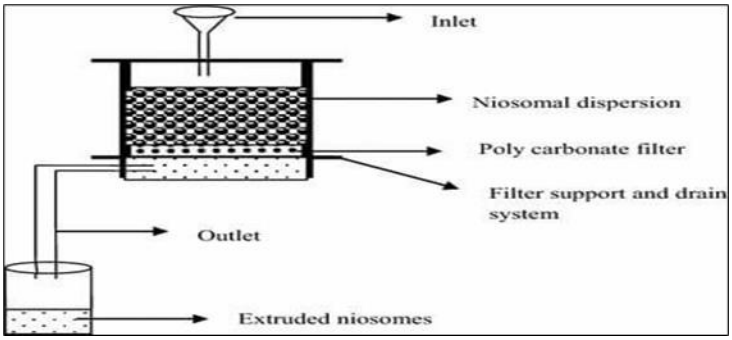
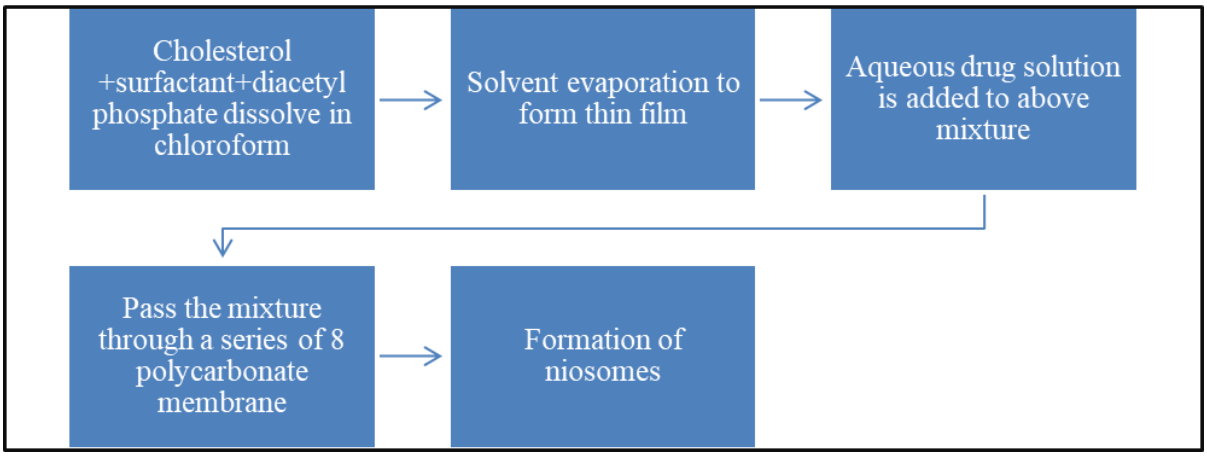
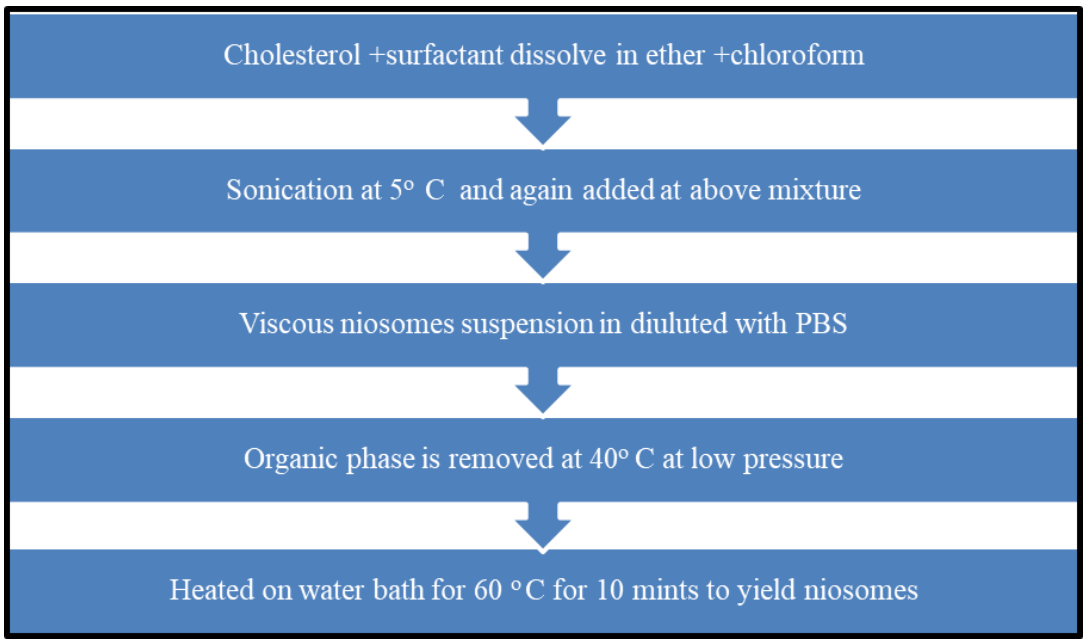


Figure 5 Multiple membrane extrusion



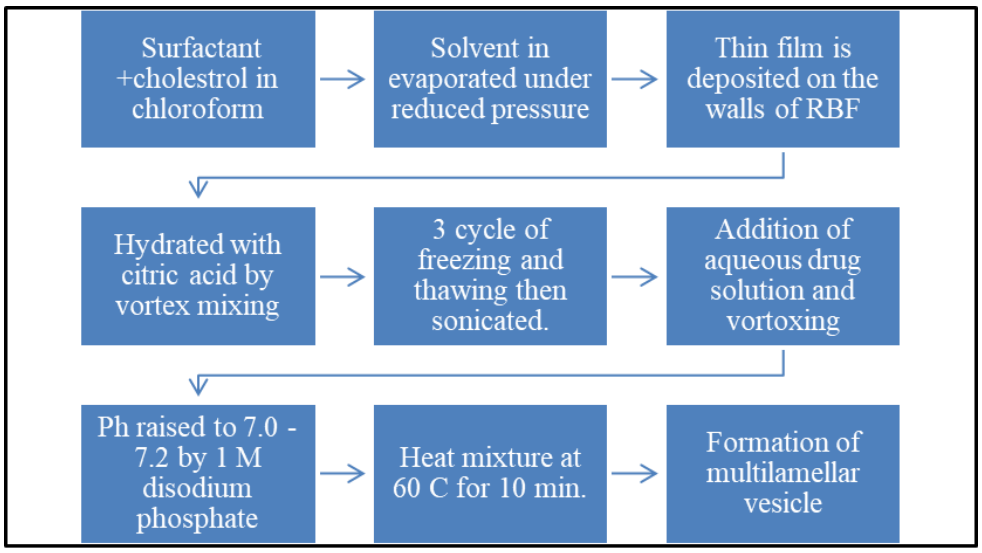
6.6. Reverse Phase Evaporation Technique [23]

6.6.1. Procedure



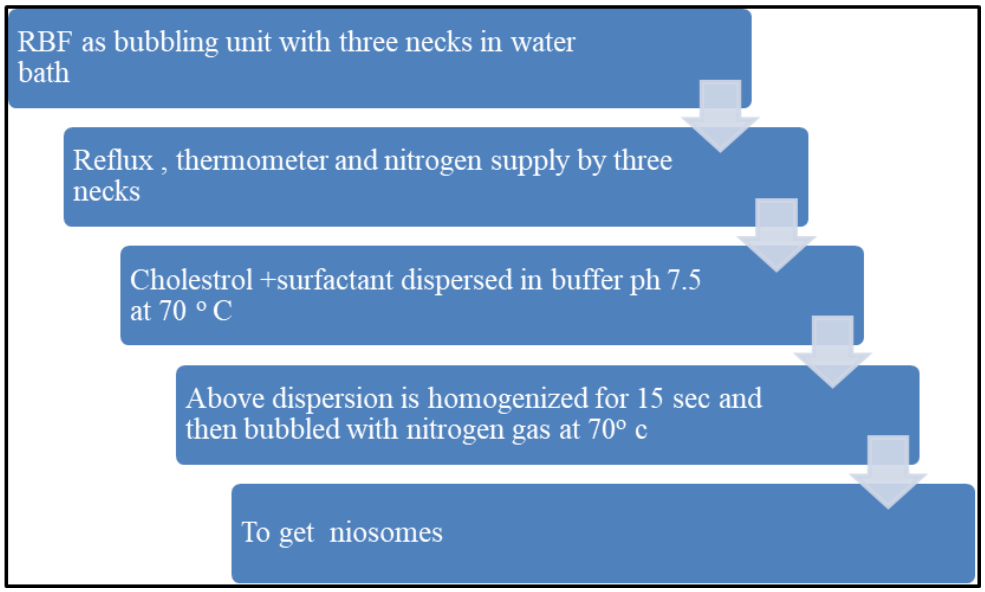
6.7. Trans membrane pH gradient Drug Uptake Process: [26]

6.7.1. Procedure



6.8. The "Bubble" Method: [27]

6.8.1. Procedure



6.9. Formation of niosomes from proniosomes:

Another method of producing niosomes is coating with a water-soluble surfactant such as sorbitol. The result of the outer layer is dry structure. All water-soluble particles are coated with a thin film of dry surfactant. These preparations are called "Proniosomes". Vesicle body was determined by adding the aqueous phase at T > Tm and mixing briefly.

T = temperature. Tm = interphase transition temperature. [28]

Niosomes are reported to consist of maltodextrin-based proniosomes. This allows rapid reorganization with a minimal vector to the vesicles. The slurry of maltodextrin and surfactant is dried to form a white powder that can be rehydrated by adding warm water.

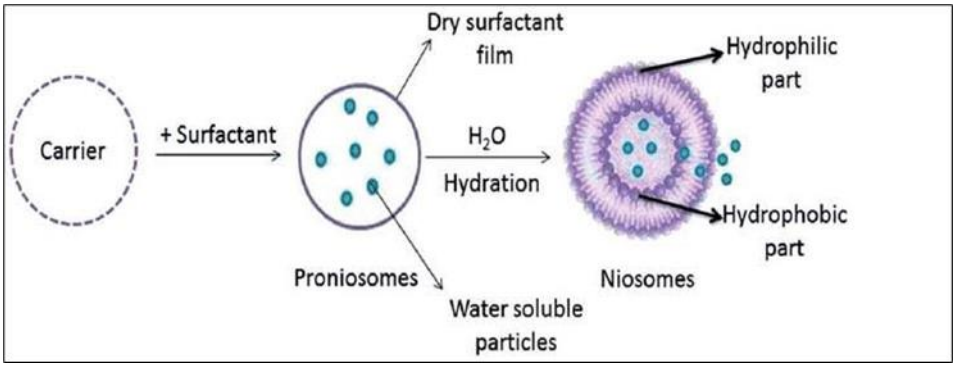


Figure 6 Formation of niosom from proniosom

7. Niosome preparation using Micelle:

Vesicles can also be prepared using enzymes in mixed micellar solutions. The mixed micellar drug contains C16 G2, dicalcium phosphate (DCP), polyoxyethylene cholesteryl hypoacetate (PCSD) as drug moieties when coagulated with esterase. PCSD acts on polyoxyethylene, sebacic acid and cholesterol through its esterase action, and then cholesterol combines with C16 G2 and DCP to form C16 G2 niosomes. [29]

Table 1 Routes of administration with Example

Route of administration	Examples
Inhalations	All-trans retinoic acid
Nasal route	Sumatriptan, Influenza viral vaccine
Ocular route	Timolol maleate, cyclopentolate
Intravenous route	Doxorubicin, Methotrexate, etc.
Peroral route	Proteins, Peptides, etc
Transdermal route	Piroxicam, Ketorolac, etc.

8. Factors influencing the preparation of niosomes

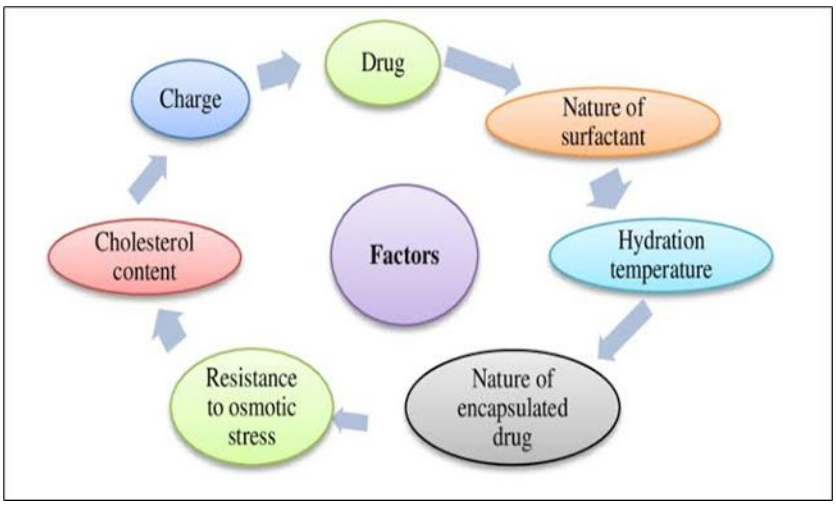


Figure 7 Factor influencing the preparation of niosomes

8.1. Nature of Surfactant: [30 to 34]

Since the inertial force decreases as the hydrophobicity of the surfactant increases, the increase in the HLB value of the surfactant leads to an increase in the center of the niosomes. The double layer of vesicles may exist in liquid or gel form. This depends on temperature, type of surfactant and cholesterol.

Alkyl chains are ordered in the gel state and disordered in the liquid state. Encapsulation efficiency is affected by the gel and liquid phase transition temperature (TC) of the surfactant. Example: Aperture 60 with higher TC indicates better encapsulation effect. Surfactants with HLB values between 14 and 17 are not suitable for use in vesicle formulations. Reducing the HLB value of the surfactant from 8.6 to 1.7 reduced the encapsulation efficiency; The highest encapsulation efficiency occurred at an HLB value of 8.6.

8.2. Nature of Encapsulated Drug

The amount and stiffness of the vesicle bilayer are mainly affected by the physicochemical properties of the encapsula ted drug. Drug degradation results from interactions with the head group of the surfactant, resulting in an increase in charge. And the surfactant increases the size of the vesicles by creating mutual repulsion between the bilayer. The HL B value of the drug will affect the degree of encapsulation

8.3. Hydration Temperature

The size and shape of the vesicle body is affected by the hydration temperature. The water temperature must be higher than the temperature of the gel and the liquid phase change. Changes in temperature can affect the aggregation of surfactants into vesicles and change the shape of the vesicles. Hydration time and volume of hydration medium also contribute to this change. Incorrect selection of hydration temperature, duration, and hydration medium volume can create brittle nanostructures/potentially lead to drug leakage.

8.4. Cholesterol Content

Inclusion of cholesterol increases the efficiency and hydrodynamic diameter of the vesicles. Cholesterol has two effects. Increases the chains of the liquid bilayer. The chain order of the gelled bilayer was reduced. Increasing cholesterol levels increased bilayer stiffness and decreased release of encapsulated substances.

8.5. Charge

The presence of charges causes further distortion of consecutive bilayers in the multilayered vesicle structure and a larger total volume.

9.6 Resistance to Osmotic Stress:

Addition of hypertonic solution reduces the diameter of the bubbles. Inhibition of vesicle eluates in low osmotic pressure solutions occurs with an initial slow release followed by faster release due to mechanical relaxation of the vesicles at high osmotic pressures.

9. Characterization Of Niosomes:-[35 to 41]

9.1. Bilayer Rigidity and Homogeneity

The biodistribution and biodegradation of niosomes are affected by the stiffness of the bilayer. Homogeneity can occur both within the vesicle structure and between dispersed vesicle bodies and can be defined as follows. pNMR, Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared Spectroscopy (FT-IR) techniques.

9.2. Size and Shape

There are many ways to measure average diameter, such as laser light scattering; It can also be measured by electron microscopy, molecular sieve chromatography, photon correlation microscopy and optical microscopy.

9.3. Stability Study

Niosomal formulations were stored in incubators at 4°C, 25°C, and 37°C for three months for safety studies. After 1 month, the drug content of all formulations was evaluated by encapsulation efficiency parameters.

9.4. In-vitro Release

In-vitro release rate study carried out by the use of

- Dialysis Tubing,
- Reverse dialysis and
- Franz diffusion cell.

9.4.1. Dialysis Tubing

Wash the dialysis capsule with distilled water. The removed vesicle is transferred to a bag containing a filter tube and the bag is closed. The bubble bag was then placed in 200 ml of solution in a 250 ml beaker and shaken continuously at 25 °C. At different times, the content of the drug in it was not reviewed with appropriate precautions**.**

9.4.2. Reverse Dialysis

Place a small amount of dialysate, such as a solution containing 1 ml of separation medium, into the proniosomes. The pronosome is then transferred to the dissolution medium. Proniosome can be directly diluted using this method and rapid release cannot be calculated using this method.

9.4.3. Franz Diffusion Cell

In vitro diffusion studies can be performed using Franz diffusion cells Proniosomes were placed in the free chamber of a Franz diffusion cell equipped with a cellophane membrane. Proniosomes are then dialyzed against a suitable dissolution medium at room temperature; Samples are removed from the environment at appropriate times and analyzed for chemical content using appropriate methods (UV spectroscopy, high-performance liquid chromatography, etc.). Tank maintenance is important

9.5. Scanning Electron Microscopy

Niosomes were observed using a scanning electron microscope (SEM) (JSM 6100 JEOL, Tokyo, Japan). They were placed directly on the SEM model stage using double-sided tape and coated with a 200 nm thick gold film at a pressure of 0.001 mmHg. Art. Use images at appropriate scale.

9.6. Vesicle Charge

Vesicle surface charge plays an important role in the behavior of vesicles in vivo and in vitro. Charged vesicles are more stable against aggregation and fusion than uncharged vesicles. To obtain an estimate of the surface potential, the zeta potential of individual niosomes can be measured by microelectrophoresis. Another approach is to use pH-sensitive fluorophores. Dynamic light scattering has recently been used to measure the zeta potential of the vesicle body.

9.7. Entrapment efficiency

It can be calculated by subtracting the suspension from all additives. Uncharged substances can be determined using techniques such as filtration, filtration, gel chromatography or centrifugation. The concentration of the loaded drug can be calculated by dissolving the niosome in 50% n-propanol or 0.1% Triton X-100, and the resulting solution can be determined using a proprietary method. Following the equation P. Bhardwaj et al. Journal of Drug Delivery Science and Technology 56 (2020) 101581 7 % can be used to calculate the encapsulation efficiency – % encapsulation efficiency = amount of drug loading in vesicles/total amount of drug in suspension X 100

10. Application of niosomes

Niosomes as a delivery system can be used for a number of purposes therapeutically.

10.1. Delivery of anticancer drugs

Targeted delivery of antibodies can be achieved using nanobodies. Such a target can be unsuccessful (releasing cysts in the tumor due to special properties of tumor cells not found in the normal body), delivered to the body (delivered to a specific environment such as pH or magnetic fields), or active type (forces liposomes into tumor cells). The primary goal can be achieved by changing the surface properties or by adding ligands to the nanosomes. For ligand binding, cholesterol-PEG-ligand conjugates can be incorporated into liposomes or attached to the ends of cholesterol or polyethylene glycol chains. [42]

10.2. Neoplasia

The antibiotic doxorubicin has a broad spectrum and exhibits uninhibited anti-tumor and anti-inflammatory activity. By entrapping the drug in vesicles, the half-life of the drug is prolonged, its circulation is prolonged, and its metabolism is changed. [43]

10.3. Carrier for haemoglobin

Nanobodies can also be used as carriers for hemoglobin in the blood due to their oxygen-absorbing properties. The vesicle suspension displays a visible spectrum that can be superimposed on the spectrum of free hemoglobin so that it can be used as a carrier for hemoglobin. Vesicles also absorb oxygen and the heme dissociation curve will be similar to that of unencapsulated heme. [43]

10.4. Delivery of peptide drug

Vesicle-encapsulated oral administration of 9-desglycinamide, 8-arginine vasopressin was tested in an in vitro intestinal model and showed an increase in the stability of the peptide. [44].

10.5. Dignostic imaging with niosomes

Niosomes can be used as a diagnostic test. MRI analysis showed that gadobenate dimethicamide and [N-palmitoylglucosamine (NPG)], PEG 4400, and liposomal formulations combining PEG and NPG were more effective against encapsulated paramagnetic drugs. The applications of blistering techniques are wide and varied and can be used to treat many diseases.[45]

10.6. Delivery of anticancer drugs

Targeted delivery of antibodies can be achieved using nanobodies. Such a target can be weak (release of blood vessels in the tumor due to special properties of tumor cells that are not present in normal cells),

physical (conduction properties according to a specific environment such as pH or magnetic fields) or active type (supporting liposomes in tumor cells). Active targeting can be achieved by changing surface properties or by binding ligands to nanosomes. For ligand binding, cholesterol-PEG-ligand conjugates can be incorporated into niosomesss or attached to the ends of cholesterol or polyethylene glycol chains. [46]

11. Conclusion

Nanobodies are a drug delivery system that can be used for the administration, delivery and distribution of drugs. There is interest in nanobodies due to their ability to encapsulate both hydrophilic and hydrophobic drugs. They can be used to encapsulate naturally occurring drugs, enzymes, peptides, genes, vaccines, antibiotics, and virtually any type of drug. They provide change not only in medication but also in management style. Their non-toxic properties make them suitable for drug delivery compared to liposomes. Therefore, it seems that research in the nanobodies business will increase and bring good business to the pharmaceutical industry.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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