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A REVIEW ON PERSPECTIVE OF NIOSOMES IN DRUG DELIVERY SYSTEM

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Abstract

Niosomes are a novel drug delivery system that have been used in treatments for antineoplastics, leishmaniasis, peptide drug delivery, transdermal drug delivery systems, cosmetics, immunological peptide drug application, hemoglobin carriers, sustained release, etc.The drug is enclosed in a vesicle, which is known as well as a niosome since it is made up of a bilayer of non-ionic surface-active chemicals. Three types of niosomes have been determined: MLV (Multi-Lamellar Vesicle), LUV (Large Uni-lamellar Vesicle), and SUV (Small Uni-lamellar Vesicle). Different methods are used to prepare niosomes. Such as the hand shaking method, sonication, microfluidization, and ether injection method for the various niosome types.these review article also present the structure , components, and application of noisomes.

Index Term: noisomes , novel Drug delivery system , structure and components, methods of preperation , application.

1.INTRODUCTION

A novel form of drug delivery called niosomes encapsulates the medication within a vesicle. The vesicle is referred to as a niosome because it is made up of a bilayer of non-ionic surface-active substances.[1] Niosomes can be ranging in size from 10 to 1000 nm, being tiny lamellar structures. Both hydrophilic and hydrophobic drugs can be integrated into niosomes since niosomes are amphiphilic in nature. Hydrophilic pharmaceuticals can be entrapped in the core cavity, while hydrophobic drugs can be entrapped in the non-polar region found inside the bilayer.[2] In the 1970s, L'Oréal was the first company to develop an oil-in-water antiaging emulsion skincare product using niosomes.[3,4,5]The niosomal system were chemical stability, biodegradability, and low toxicity. There are several ways to give niosomes, including oral, parenteral, topical, and ocular Formulation.So that the contact between water and hydrocarbons is no longer exposed.[6,7,8]

2.STRUCTURE OF NIOSOME

A niosome is a spherical, bilayered structure made of cholesterol and a non-ionic surfactant. This results in a closed lipid bilayer that surrounds solutes in the aqueous phase, which appears to be the outer and inner surfaces of the hydrophilic area that sandwiched the lipophilic area in between them. The non-ionic surfactant is present in such a way that the hydrophobic end faces inward (toward the lipophilic phase) and the hydrophilic end faces outward (toward the aqueous phases.[9,10]

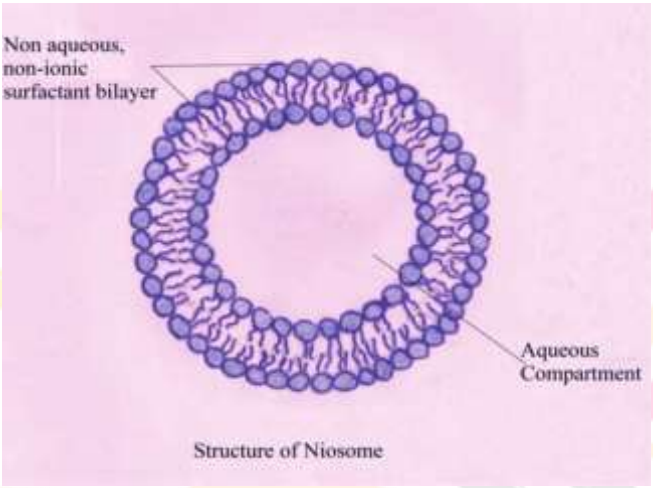


fig no.1 structure of niosomes

3.COMPONENTS OF NIOSOME

Niosomes mainly contains following types of component

3.1**Non-ionic Surfactants**: Non-ionic Surfactants In order to reduce interaction with the media, the hydrophobic head or hydrocarbon segments organize themselves in a bilayer lattice with the polar or hydrophobic heads aligned facing the aqueous bulk (media). Every bilayer creases into a continuous membrane, or vesicles, in order to achieve thermodynamic stability.So that the contact between water and hydrocarbons is no longer exposed.[11]

Mainly following types of non-ionic surfactants are used for the formation of niosomes

a)Alkyl Ethers L'Oreal listed the following surfactants:

1)Surfactant-I (molecular weight (MW 473)) is C16 monoalkyl glycerol ether with an average of three glycerol units. This surfactant is used to create niosomes containing medications or chemicals.

2) Diglycerol ether with an average of seven glycerol units is surfactant-II (MW 972)

. 3) Ester linked surfactant (MW 393) is surfactant III. Niosome formulation also uses alkyl glycosides and alkyl ethers with polyhydroxyl head groups in addition to alkyl glycerol.[11,12,13]

b) Alkyl Esters Among this class of surfactants, sorbitan esters are the most commonly used surfactant for niosome synthesis.[14,15,] Compared to other surfactant vesicles, vesicles made using polyoxyethylene sorbitan monolaurate are comparatively soluble.[16] For example, diclofenac sodium has been encapsulated

using polyoxyethylene (polysorbate 60).[17] Cyclosporine-A has been applied topically using a polyoxyethylene-10-stearyl ether:glyceryl laurate:cholesterol (27:15:57) mixture.[11,18]

C) Alkyl amide Niosomal vesicles are made from alkyl amides, such as galactosides and glucosides.[19]

d) Fatty Acid and Amino Acid Compounds Long chain fatty acids and amino acid moieties have also been used in some niosomes preparation.[20]

3.2 Cholesterol Steroids play a significant role in the structure of the cell membrane and have an impact on the permeability and fluidity of the bilayer. One of the main steroid derivatives employed in the formation of niosomes is cholesterol. Its significance in niosome development and the modification of layer properties cannot be discounted, even though it may not play a part in the formation of a bilayer.Niosome characteristics such as membrane permeability, stiffness, encapsulation effectiveness, ease of rehydration of freeze-dried niosomes, and toxicity are generally impacted by the addition of cholesterol. By adding molecules that stabilize the system against the formation of aggregates by repulsive steric or electrostatic forces, which causes the shift from the gel to the liquid phase in niosome systems, it stops the vesicle aggregation. The niosome's inherent leakiness decreases as a result.[21]

3.3 charged molecules Molecule with Charge Niosomes are stabilized by adding specific charged molecules, which inhibit coalescence through electrostatic repulsion. Phosphatidic acid and diacetyl phosphate (DCP) are the negatively charged molecules that are utilized. Similarly, in niosomal preparations, well-known positively charged compounds like stearylamine (STR) and stearyl pyridinium chloride are employed. The primary purpose of these charged molecules is to stop niosomes from aggregating.[22] It is only acceptable to have charged molecules at 2.5–5 mol% concentrations since higher concentrations can prevent the production of niosomes.[23]

4.TYPES OF NIOSOMES

The different types of niosomes can be classified as follows:

1) Multilamellar vesicles (MLV)

2) Large unilamellar vesicles (LUV)

3) Small unilamellar vesicles (SUV)

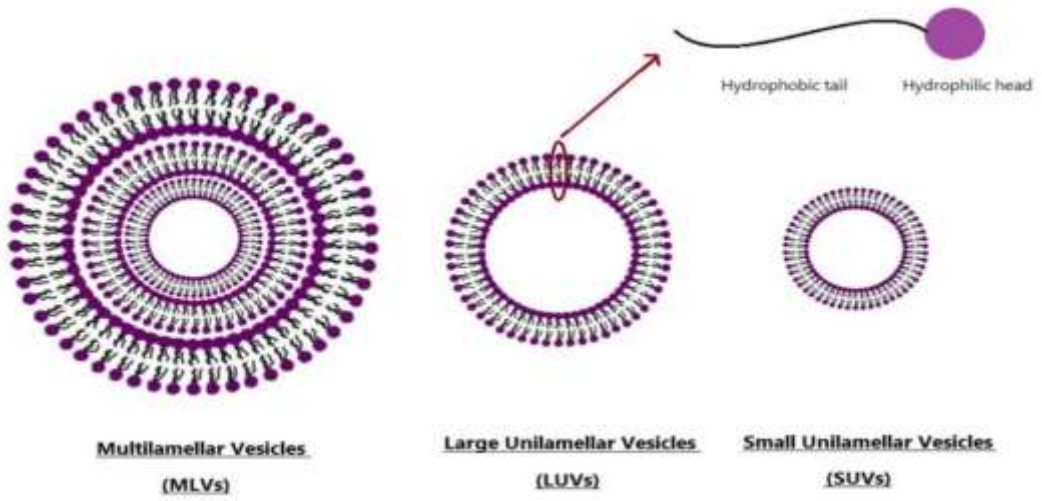


Fig no. 2 Types of niosomes

4.1Multilamellar vesicles (MLV):

Niosomes are most commonly found as multilamellar vesicles. The vesicles have a diameter ranging from 0.5 to 10 µm. The vesicles are simple to prepare and maintain their mechanical stability over extended periods of storage. It typically comprises of many bilayers that each encircle a different aqueous lipid component. These lipophilic compound-containing miltilamellar vesicles are ideal for use as medication carriers.

4.2 Large unilamellar vesicles (LUV):

LUV are a form of niosome that have a high aqueous/liquid compartment ratio. This allows for the cost-effective entrapment of larger volumes of bioactive compounds using membrane lipids. Large unilamellar vesicles have lengths between 100 and 3000 nm.

4.3 small unilamellar vesicles (SUV):

The sonication method is primarily utilized to prepare small unilamellar vesicles from multilamellar vesicles. As per reports, small unilamellar vesicles varies in size from 10 to 100 nm., [24,25]

5.METHOD OF PREPARATION OF NIOSOME[26]

5.1Preparation of small unilamellar vesicles

- Sonication method
- Micro fluidization

5.2 preperation of Large unilamellar vesicles

- Reverse Phase Evaporation (REV)
- Ether injection method

5.3 preparation of Multilamellar vesicles

- Hand shaking method (Thin film hydration techniques)
- Trans-membrane pH-gradient (inside acidic)Drug Upake Process: or Remote Loading Technique

5.4 miscellaneous

- Multiple membrane extrusion method
- The Bubble Method
- Formation of niosomes from proniosomes

5.1Preparation of small unilamellar vesicles

Sonication method

Drug in buffer + surfactant/cholesterol in 10 mL

↓

Above mixture is sonicated for 3 mints at 60°C using titanium probe

↓

yielding niosomes[27]

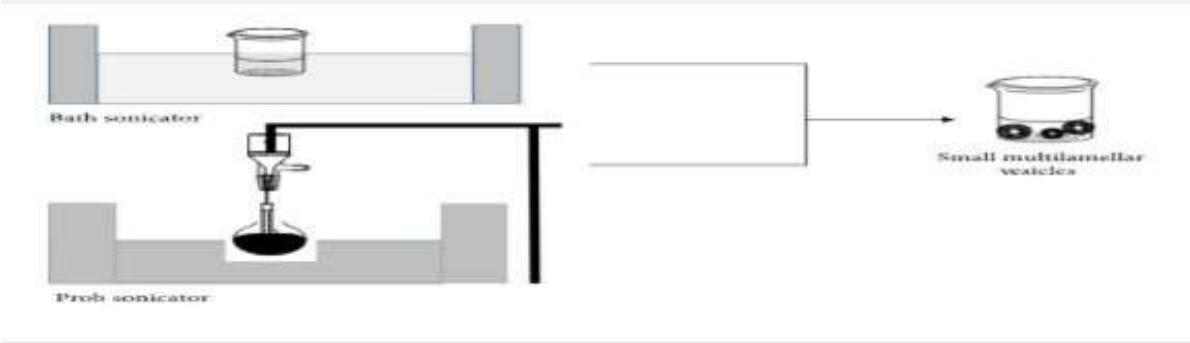


Fig. no: 3 sonication method

micro fluidization

Two ultra high speed jets inside interaction chamber

↓

impingements of thin layer of Liquid in micro channels

↓

High speed impingements and the energy involved

↓

Formation of uniform Niosomes.[28]

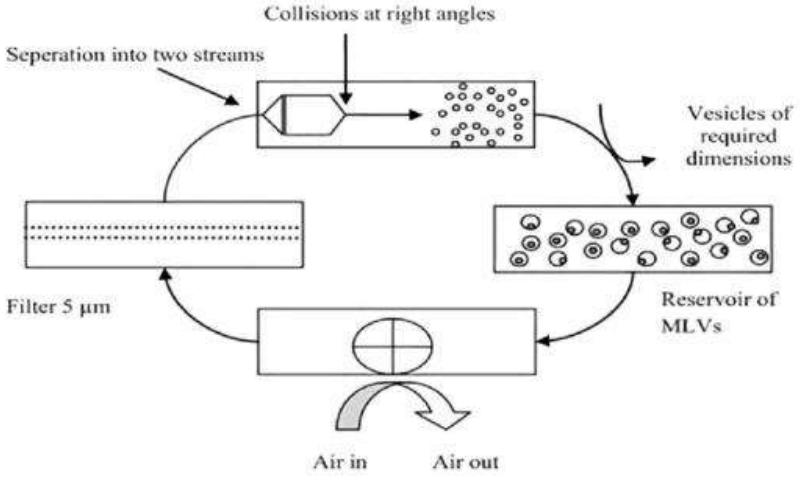


Fig.no: 4. Micro fluidization

5.2 preparation of large unilamellar vesicles

Reverse phase evaporation

Surfactant + cholesterol (1:1) in organic solvents. drug in aqueous phases

↘ ↙

Sonicated at 4-5°

↓

Add phosphate buffer and saline and then sonicated

↓

Organic phase is removed under 40° under low pressure

↓

Viscous niosomes suspension diluted with pbs

↓

Heated on water bath at 60° for 10 minutes

↓

Niosomes is formed.[29]

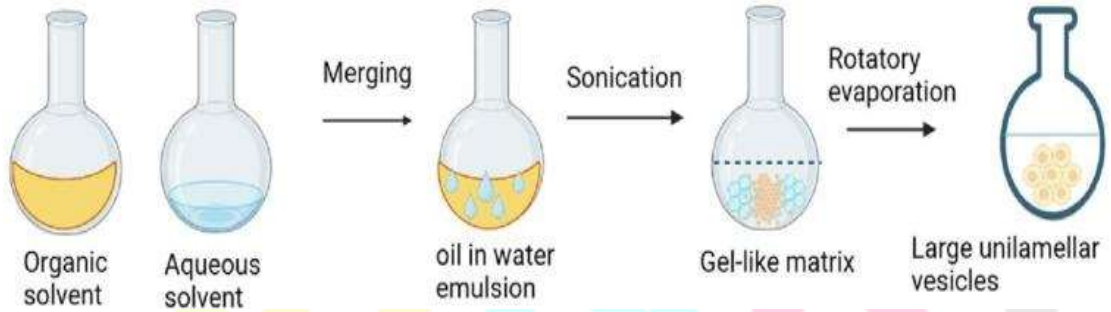


Fig .no:5 reverse Phase evaporation

Ether injection method

Diethyl ether dissolves in the surfactant.

↓

Then injected using a 14-gauge needle into warm water that was kept at 60 degree

↓

The vaporized ether is used to produce single-layered niosomes.[30]

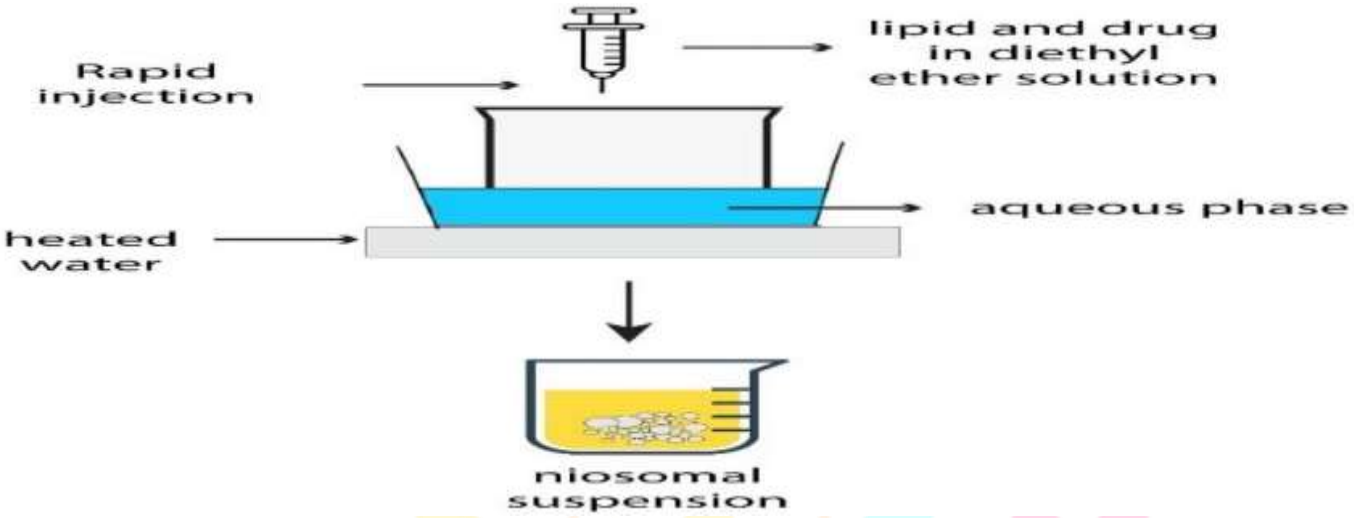


Fig.no : 6. Ether injection method

5.3 preperation of Multilamellar vesicles

Hand shaking method (Thin film hydration technique)

Surfactant +cholesterol+ volatile organic solvent

↓

Remove organic solvent at room temperature by rotary evaporator

↓

Thin layer formed on the wall of flask

↓

Film can be rehydrated with drug and aquous phase

↓

Multilamellar vesicles .[31,32]

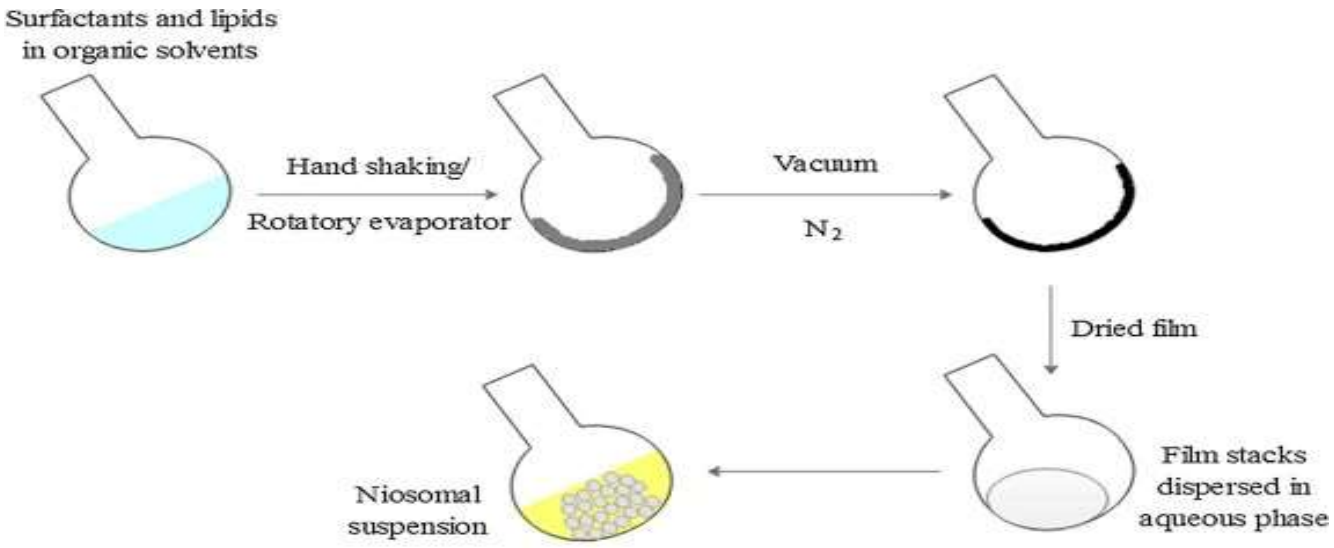


Fig.no : 7 hand shaking method

Trans membranes PH gradient (inside acidic) Drug Upake Process: or Remote Loading Technique

Surfactant+ cholesterol in chloroform

↓

Thin film deposited on the wall of the flask

↓

Hydrated with citric acid by vortex mixing

↓

Freezing and thawing and then sonication

↓

Addition of aquous drug solution and vortexed

↓

pH raised to 7 to 7.2 by 1M disodium phosphate

↓

Multilamellar niosomes[33]

Fig.no: 8 Trans membranes PH gradient (inside acidic) Drug Upake Process: or Remote Loading Technique

5.4 Miscellaneous

Multiple extrusion method

Cholesterol + surfactant dissolved in ether + chloroform

↓

Sonicated at 50c° and again sonicated after adding PBS

↓

Drug in aqueous phase is a added to above mixture

↓

Viscous niosomes suspension is diluted with PBS

↓

Organic phase is removed at 40c°at low pressure

↓

Heated on a water bath for 60c° for 10 mints to yield niosomes. [34]

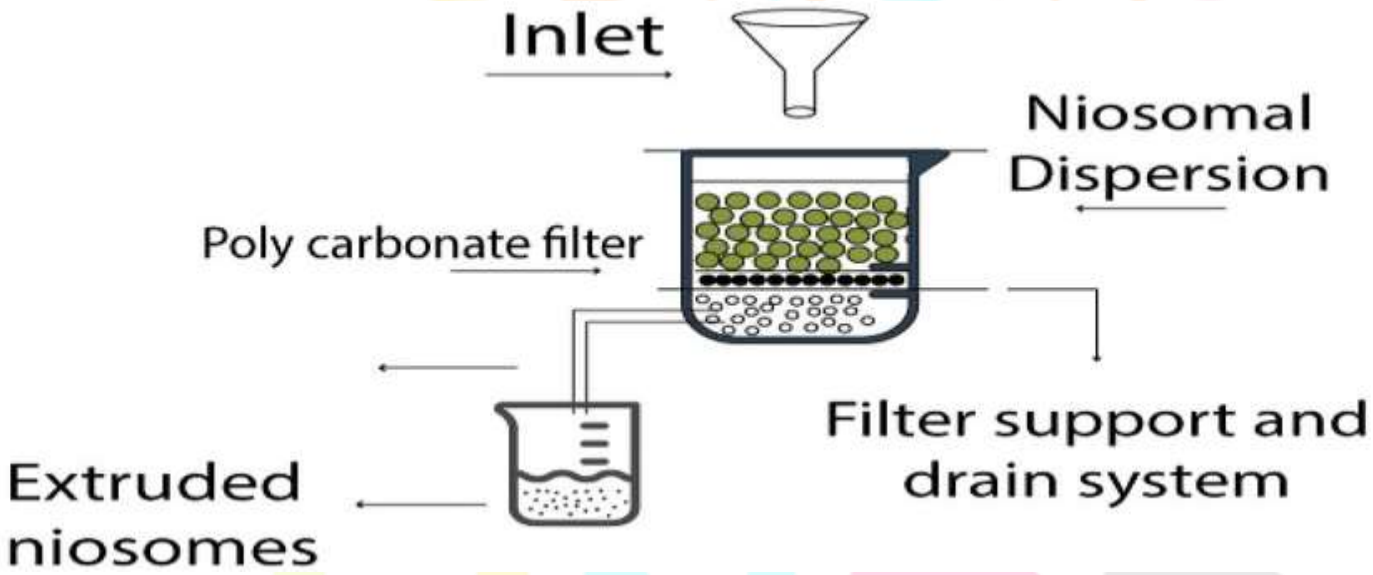
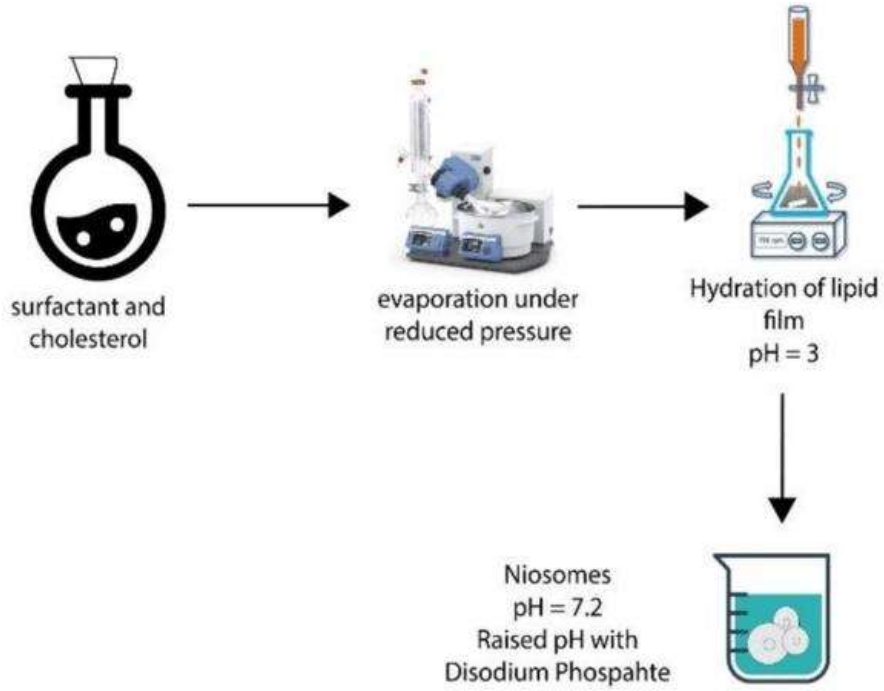


Fig. no: 9 Multiple extrusion method



The Bubble Method

RBF as bubbling unit with three neck in water bath

↓

Reflux , thermometer nitrogen supply by three neck

↓

Cholesterol + surfactants dispersed in buffer pH 7.4 at 70°c

↓

Above dispersion is homogenized for 15 sec and then bubbled With nitrogen gas at 70°c

↓

To get niosomes [35]

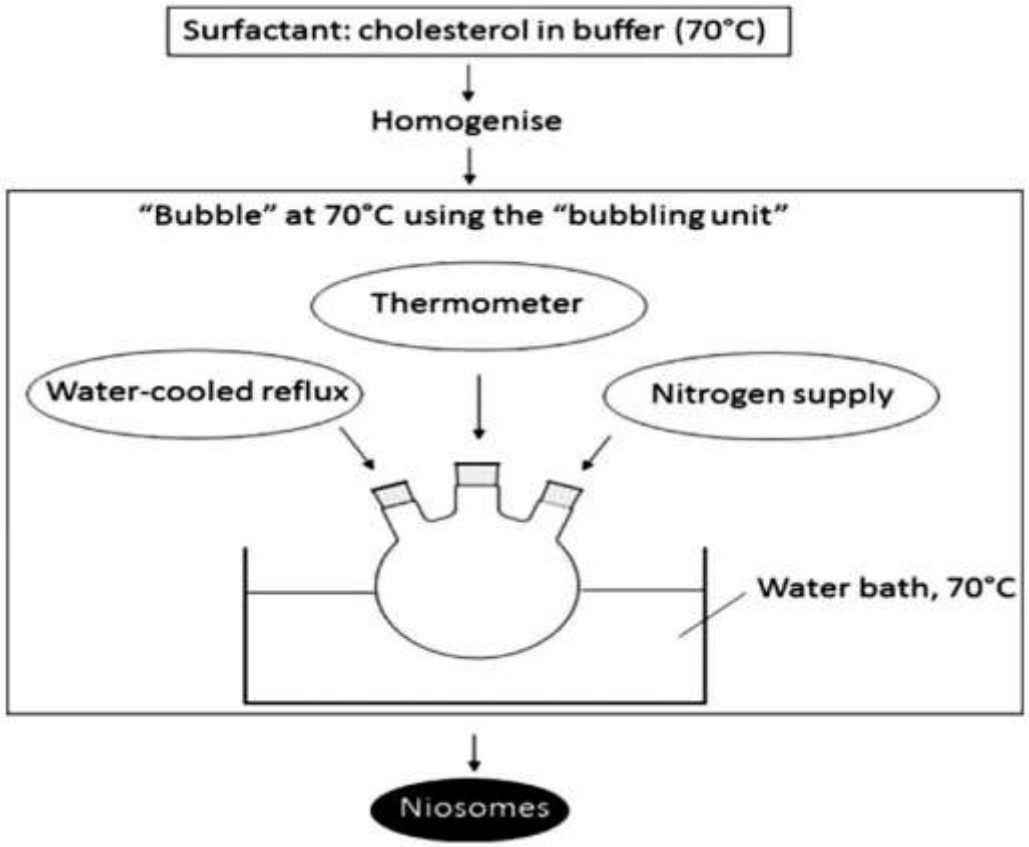


fig.no: 10. The bubble method

Formation of niosomes from proniosomes

By adding the drug-containing aqueous phase to the proniosomes and briefly agitating them at a temperature higher than the surfactant's mean transition phase temperature, niosomes can be synthesized from proniosomes.

T > Tm

Where

T stands for temperature.

Tm stand for Phase transition temperature

Niosomes have been reported to be formulated from maltodextrin-based Proniosomes by Blazek-Walsh A.I. et al. This allows for quick reconstruction of niosomes with little carrier leftover. A free-flowing powder was created by drying a slurry of maltodextrin and surfactant, which could be rehydrated by adding warm water.[36]

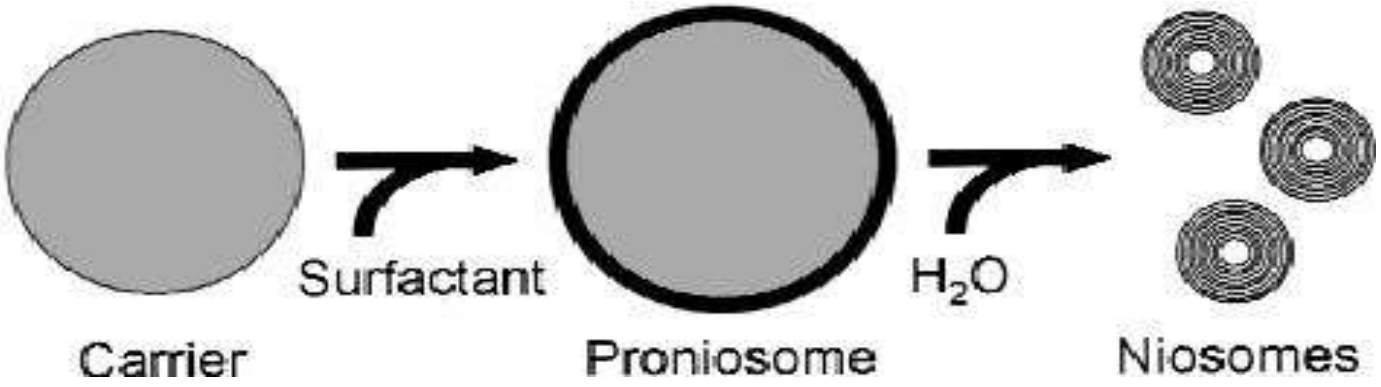


Fig no: 11 Formation of niosomes from proniosomes

6.APPLICATION OF NIOSOMES

6.1Drug targeting: Niosomes have several benefits, one of which is their ability to deliver drugs with precision. The reticuloendothelial system (RES), which has a predilection for niosome vesicles, can be targeted with medications using niosomes. Opsonins are circulating blood factors that flag niosomes for clearance and control niosome uptake. In animals, this targeted medication localization has been applied to tumors that are prone to metastasizing to the spleen and liver. It can also be used to treat parasitic liver-related infections. Niosomes can be used to target medications to organs other than the RES. One method is to attach a carrier system, such antibodies, to niosomes since immunoglobulins bind to niosome lipid surfaces easily and allow for targeted organ delivery.[37,38]

6.2 Study of Immune Response: Niosomes' immunological selectivity, low toxicity, and increased stability have led to their current use in immune response research. By demonstrating their capacity to function as adjuvants when given parenterally with different antigens and peptides, these non-ionic surfactant vesicles have improved our understanding of the nature of immune responses**.[**38]

6.3 Anticancer Drug Delivery: Anticancer medications such as methotrexate, vincristine, bleomycin, and paclitaxel have been encapsulated in niosomes, which are made of cholesterol, non-ionic surfactants, and diketyl phosphate. Because of this encapsulation, there has been an improvement in anticancer efficacy, less toxicity, and greater absorption from the gastrointestinal tract after oral administration.[37,38]

6.4 Vaccine Delivery: Niosomes are being investigated as vaccine carriers, especially for oral and topical vaccination, since they are not very immunogenic on their own. The effects of varying surfactant, cholesterol, and dicetyl phosphate concentrations on niosome morphology, size of particles, entrapment effectiveness, and in vitro antigen discharge were studied. Topical liposomes and intramuscular recombinant HBsAg both showed similar immune-stimulating properties when applied topically.[37,38]

6.5 Anti-inflammatory agents : When compared to free medications, niosomal formulations containing 70% cholesterol of diclofenac sodium demonstrate stronger anti-inflammatory effects. Niosomal forms of flurbiprofen and nimesulide also have stronger anti-inflammatory effects than the free medications.

6.6 Treatment of Leishmaniasis: Since the infectious organism in disorders like leishmaniasis lives in the reticuloendothelial system (RES), niosomes may be used to target medications for this condition. Niosomal formulations have demonstrated improved effectiveness and decreased negative effects, especially when it comes to sodium stibogluconate, a frequently prescribed medication that has an arsenic connection.[37,38]

6.7 Cosmetic Applications: Niosomes, which are vesicles made of non-ionic surfactant, were initially used in cosmetic applications by Oreal. As a result, Lancôme launched the first niosome product in 1987. Cosmetics using niosomes have several benefits, including better skin penetration, better bioavailability of poorly absorbed substances, and increased stability of entrapped medications.[37,38]

6.8 Prolonged Release Capability of Niosomes: Niosomes' prolonged release characteristic is useful for medications with low therapeutic index and limited water solubility. This is due to the fact that niosomal encapsulation makes it possible for these medications to remain in circulation.[39,40,41,42]

6.9 Hormone Delivery: Researchers have investigated the in vitro penetration of estradiol into the human stratum corneum using niosomes made of non-ionic n-alkyl polyoxyethylene ether surfactants. The mechanisms at play are the impact of vesicular structures at the stratum corneum suspension interface and the penetration-enhancing effect of surfactant molecules.[37,38]

6.10 Tumor targeting: A large concentration of anticancer drug is needed at the tumor site for cancer chemotherapy to be effective. By doing this, the drug's concentration in other bodily tissue compartments is reduced, which lessens the possibility of negative side effects. Several organizations have investigated niosomes for their potential to improve the transport of anticancer medicines to local lymphatics. Cytarabine hydrochloride niosomes were generated using a lipid hydration process that did not include dicetyl phosphate, resulting in smaller vesicles. The vesicles that were formed varied in size from 600 to 1000 nm. Tween 20, Tween 80, Span 60, and Span 80 were the selected surfactants; the Span 60 formulation produced the slowest release rate. Two phases of release took place: a brief initial burst that lasted for two to six hours, and a prolonged release that continued for at least 16 hours.[43]

6.11 Transdermal Drug delivery system: The potential of niosomes to improve drug penetration and lessen skin irritation through the intact stratum corneum has also been investigated, along with their use as a transdermal drug delivery system. Using Franz diffusion cells, the penetration of ketorolac (a strong NSAID) into excised rabbit skin from different proniosome gel formulations was studied. The synthesized proniosomes lowered lag time and greatly enhanced medication penetration [44]

CONCLUSION

Niosomes are vesicles composed of non-ionic surfactants that are biodegradable, relatively non-toxic, more stable, and less expensive compared to liposome . They can be used as carriers to improve the oral bioavailability and delivery of various drugs such as those used for cancer, diabetes, and inflammation treatment.The components of niosomes typically include drugs (both hydrophilic and hydrophobic), cholesterol or its derivatives, non-ionic surfactants, and sometimes charged molecules like dicetyl phosphate or stearylamine. The surfactant type, charge, and concentration can significantly impact the properties and performance of the niosomes.Compared to liposomes, niosomes have advantages like being less expensive, more stable, and less toxic. They can be formulated in different vesicle sizes (small unilamellar, multilamellar, large unilamellar) to suit different applications.Overall, niosomes are a promising drug delivery system that can improve the solubility, bioavailability, and targeted delivery of various therapeutic agents.

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