ISSN 2348-0319 International Journal of Innovative and Applied Research [2024]
(Volume 12, Issue 08)
08-19

Journal home page: http://www.journalijiar.com

INTERNATIONAL JOURNAL
OF INNOVATIVE AND APPLIED RESEARCH

RESEARCH ARTICLE

Article DOI: 10.58538/IJIAR/2106
DOI URL: *http://dx.doi.org/10.58538/IJIAR/2106*

AN OVERVIEWON NIOSOMESAS DRUG DELIVERY

K. Malleswari[1], Dr. D. Rama Brahma Reddy[2], T. Blessi[3], G. Suvarna[4] and B. Sri Lakshmi[5]

1. Associate Professor, Dept. of Pharmaceutics, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli.
2. Principal & Professor, Dept. of Phytochemistry, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli.
3. Student, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli.
4. Student, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli.
5. Student, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli.

Manuscript Info

Manuscript History
Received: 22 July 2024
Final Accepted: 26 August 2024
Published: August 2024

Keywords:
Niosome, Cholesterol, Hydrophilic and Lipophilic Drugs, Surfactant, Targeted Delivery

Abstract

Over the years, researchers have attempted to improve the potency of medicament utilization for the treatment of a variety of diseases. Drug targeting is a phenomenon in which a drug is distributed in the body in such a way that it interacts with the target tissue at a cellular or sub-cellular level to achieve a desired therapeutic response at the desired site while avoiding unwanted interactions at other sites. This can be accomplished using modern drug delivery system targeting methods such as niosomes. Niosomes are a novel drug delivery system that encapsulates the medication in a vesicle. The vesicle is made up of a non-ionic surfactant bilayer. The particle size of the niosome must be in the range of 10 nm -100 nm. Niosomes are preferred over liposomes because they are more stable and less expensive. Niosomes enhance the pharmacological action of drug molecules by delaying the drug's clearance from circulation, protecting the drug from the biological environment, and limiting the effects to the target cells. It has applications in cancer treatment, as a carrier in hemoglobin, delivery of peptide drugs via the oral route, treatment of leishmaniasis, ophthalmic delivery, and as a carrier in dermal drug delivery. This review article focuses on the vesicular system's composition, benefits, types of niosomes, methods of preparation, characterization, and application.

***Corresponding Author:-** **K. Malleswari,** *Associate Professor, Dept. of Pharmaceutics, Nalanda Institute of Pharmaceutical Sciences, Sattenapalli.*

Introduction:-

Niosomes are a novel drug delivery system, which entrapped the hydrophilic drug in the core cavity and hydrophobic drugs in the non-polar region present within the bilayer hence both hydrophilic and hydrophobic drugs can be incorporated into niosomes. The niosomes are ampiphillic in nature, in which the medication is encapsulated in a vesicle which is made by non- ionic surfactant and hence the name niosomes. The niosomes size is a very small and microscopic. The first niosome formulations were developed and patented by L'Oreal in 1975. In the presence of proper mixtures of surfactants and charge inducing agents from the thermodynamically stable vesicles. Niosomes are mostly studied as analternative to liposomes because they alleviate the disadvantagesassociated with liposomes.

Niosomes overcome the disadvantages associated with liposomes such as chemical instability. Chemical instability of liposomes is due to their predisposition to oxidative degradation and variable purity of phospholipids. The main purpose of developing niosomal system is chemical stability, biodegradability, biocompatibility, chemical stability, low production cost, easy storage and handling and low toxicity. Niosomes can be administrated through various routes such as oral, parenteral, topical. Niosomes are used as a carrier to deliver different types of drugs such as synthetic and herbal, antigens, hormones and other bioactive compounds. This article presents some salient features of niosomes along with an overview of the preparation techniques and the current applications of niosomes in encapsulation and delivery of bioactive compounds.[1]

SalientFeaturesof Niosomes

- The niosomes are osmotically active and stable.
- Niosomes surfactants are biodegradable, biocompatible and non-immunogenic.
- Accommodate the drug molesters with a wide range of solubility.
- Niosomes exhibit flexibility in their structural characteristics and can be designed according to the desired situation.
- The bilayers of the niosomes protect the enclosed active pharmaceutical ingredient from the heterogeneous factors present both inside and outside the body.
- So niosomes can be used for the delivery of labile and sensitive drugs.
- Niosomes display adaptability in their basic attributes and can be planned by the ideal circumstance.
- The detailing isaswatery vehicle-based suspension having more prominent patient consistence when contrasted with sleek measurement structures.
- Performance of the drug molecules is increased.
- Niosomal scattering being fluid can be emulsified in a non-fluid stage to direct the medication discharge rate and to control the vesicles in non-fluid stage.
- Protecting drugs from biological environments.[3]

Advantagesof Niosomes

- Niosomes are osmotically active and chemically stable.
- They are non-immunogenic and biodegradable.
- Their surface modification and formation are relatively simple.
- Niosomes have a hydrophilic and hydrophobic architecture that allows them to accommodate medicinal molecules with a wide range of solubility.
- Oral bioavailability of poorly absorbed medicines can be improved by niosomes.
- They have structural qualities that are flexible and may be customized to fit the needs of the circumstance.
- They have a high level of biological compatibility and are low in toxicity.
- Niosomes can let medications penetrate deeper into the skin.
- Niosomes change the organ distribution and metabolic stability of encapsulated drugs by prolonging their circulation.
- They serve as a depot for short-acting peptide medicines, allowing the medicine to be released at a regulated rate.[4]

Disadvantagesof Niosomes

- Due to fusion, aggregation, leakage of entrapped medicines, and hydrolysis of encapsulated medicines, the shelf life of niosome aqueous suspensions may be restricted.
- Extrusion and sonication are two ways for preparing multilamellar vesicles that take time and may require specializedequipment for processing.[4]

Comparison Between Niosomesand Liposomes

Table 1:- Comparison Between Niosomes and Liposomes.

NIOSOMES	LIPOSOMES
Less expensive.	More expensive.
Non-ionic surfactants are neutral.	Phospholipids may be neutral charged.

Non-ionic surfactants are used for stability i.e chemically stable.	Phospholipids are prone to oxidation degradation i.e chemically unstable.
No special methods require for such formulations.	Require special methods for storage and handling of the final formulation.
Niosomes are prepared from uncharged single chain surfactant & cholesterol.	Liposomes are prepared from double chain phospholipids.

Structureof Niosome

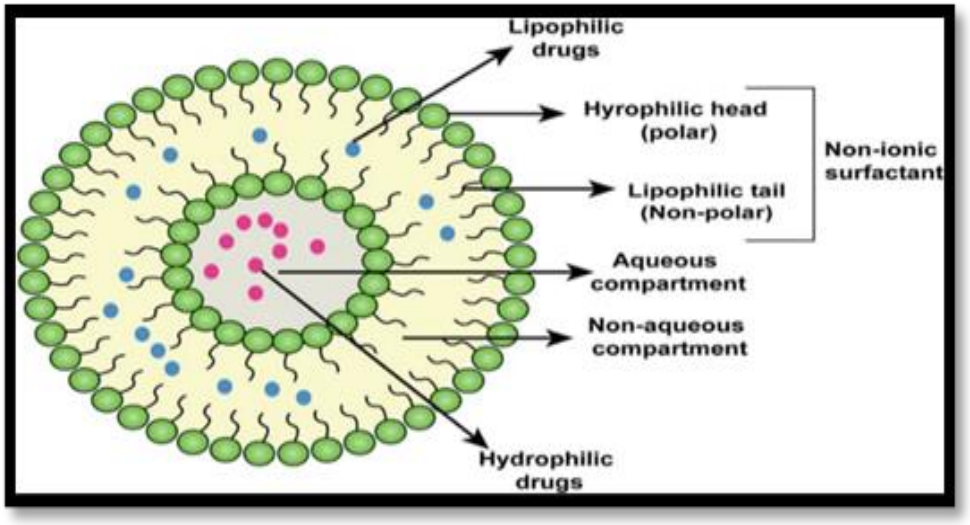

Figure 1:- Structure of Niosomes.

Compositionof Niosomes

Two components use in niosome preparation are: Cholesterol, Non-ionic surfactants.

- Cholesterol is a steroid derivative used to provide rigidity and proper shape, conformation.
- Non-ionic Surfactants are generally used for the formulation.

For Examples: Tweens (20, 40, 60, 80), Spans (Span 60, 40, 20, 80).

1.Non-ionic surfactants: Non-ionic surfactants are an essential component of niosomes. To form niosomes, various types and their combinations are used to entrap various medications. Non-ionic surfactants are naturally amphiphilic, biodegradable, biocompatible, and non- immunogenic. The composition, concentration of additives, size, lamellarity, and surface charge of vesicles determine the properties of formulated niosomes. Non - ionic surfactants such as span (60, 40, 20, 85, and 80) and Tween (20, 40, 60, and 80) are used in the formation of niosomes.

2. Cholesterol: It's a crucial additive in the formulation of niosomes. Cholesterol is not only required for the formation of niosomes, but it also influences many of their properties. It influences the membrane's permeability, rigidity, entrapment efficiency, ease of rehydration of freeze-dried niosomes, stability, and storage period. If cholesterol is combined with low HLB surfactants, it increases vesicle stability, and if the HLB value is greater than 6, it aids in the creation of bilayer vesicles. The addition of cholesterol improves the viscosity and, as a result, the rigidity of the formulation.

3. Charged molecule: Niosomes have some charged molecules added to them to increase stability by providing electric repulsion to prevent collisions. Diacetyl phosphate (DCP) and phosphotidic acid are both negatively charged compounds. Similarly, in niosomal preparations, stearylamine and stearyl pyridinium chloride are well-known charged compounds.

4. Hydration medium: One of the most significant components in the formulation of niosomes is the hydration medium. Phosphate buffer is commonly employed as a hydration medium. However, the pH of the buffer is determined by the solubility of the encapsulated medication. [5]

Typesof Niosomes

The various types of niosomes are as:

- Multi lamellar vesicles (MLV)

- Large unilamellar vesicles (LUV)
- Small unilamellar vesicles (SUV)[2]

Figure 2:- Types of Niosomes.

Table 2:- Types of niosomes.

Parameters	**Multi lamellar Vesicles**	**Small Unilamellar Vesicles**	**Large Unilamellar Vesicles**
Vesicle Size	Greater than 0.05µm	0.025 – 0.05µm	Greater than 0.10µm
Method of Preparation	Hand Shaking Method	Sonication Extrusion Method Solvent Dilution Technique	ReversePhase Evaporation Method

Methodsof Preparationof Niosomes

The preparation methods should be chosen according to the use of the niosomes, since the preparation methods influence the number of bilayers, size, size distribution, and entrapment efficiency of the aqueous phase and the membrane permeability of the vesicles.

1. Ether Injection Method
2. Hand Shaking Method (Thin Film Hydration Technique)
3. Sonication
4. Micro Fluidization
5. Multiple Membrane Extrusion Method
6. Reverse Phase Evaporation Technique (REV)
7. Trans Membrane pH Gradient Drug Uptake Process
8. The Bubble Methods
9. Formation of Niosomes from Proniosomes [3]

1.Ether Injection Method

The ether injection method basically involves slowly injecting Niosomal components in diethyl ether into a heated aqueous phase that is kept at 60°C using a 14-gauge needle at a rate of about 0.25 ml/min. The creation of bigger unilamellar vesicles is likely due to the sluggish vaporisation of the solvent, which creates an ether gradient that extends towards the aqueous–non aqueous boundary. The bilayer structure might have formed because of the former. This method's drawbacks include the fact that a tiny amount of ether is usually present in the vesicle suspension and is challenging to eliminate.[8]

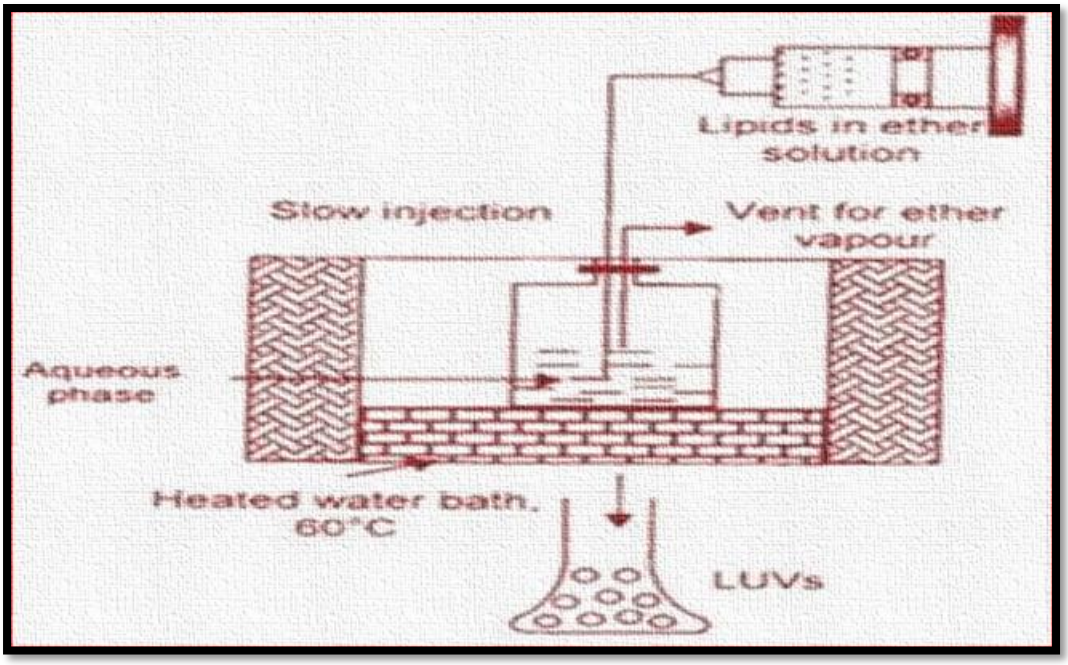

Figure 3:- Ether Injection Method.

2.Hand Shaking Method(Thin Film HydrationTechnique)

Surfactant, cholesterol, and a charge inducer are among the substances used in the mixture. Organic solvent is evaporated at room temperature (20°C) using a rotary evaporator. Creating a thin solid mixed layer. With gentle agitation, the dried surfactant film can be re hydrated with an aqueous phase at 0-60°C. Formation of niosomes. [5]

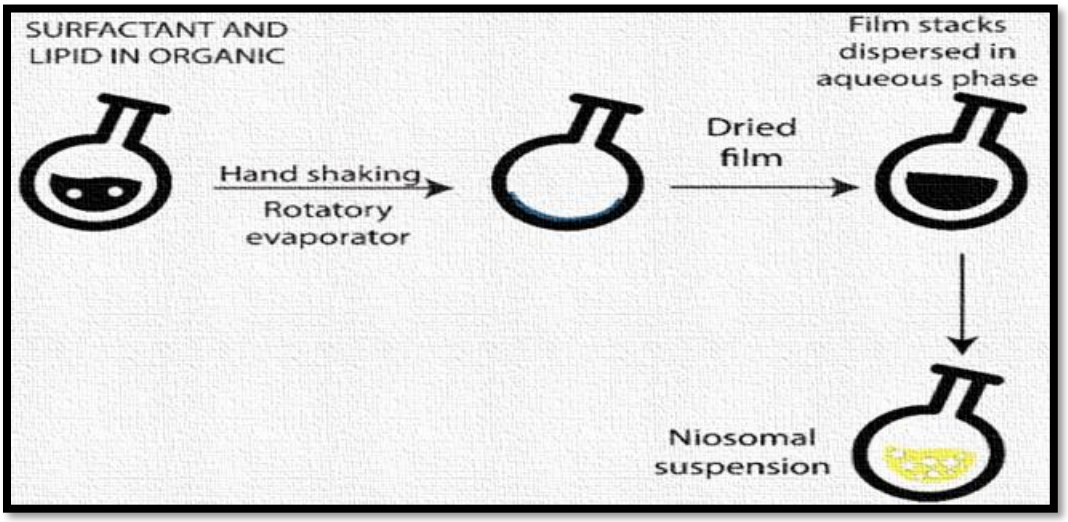

Figure 4:- Hand Shaking Method.

3.Sonication

One common method for creating Niosome vesicles is sonication. The medication, cholesterol, and surfactants are taken out of a 10-ml glass vial and combined with buffer. Subsequently, the mixture is subjected to a titanium probe sonication for approximately three minutes in order to generate Niosomes. The final product has tiny, unilamellar vesicles in it. The most common application of this method is in the creation of tiny vesicles. The two types of sonicators utilised in the sonication process are probe and bath types. Depending on the situation, either type can be employed.[8]

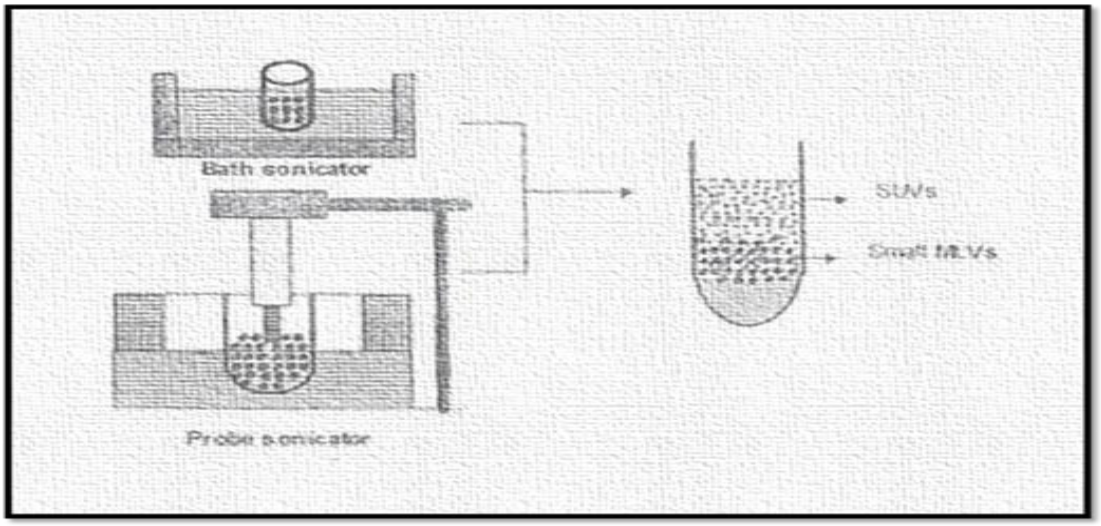

Figure 5:- Sonication Process.

4.Microfluidization

The principle involved in this technique is the submerged jet principle, in which two fluidized streams interact with each other at ultra-high velocities and in micro channels within the interaction chamber. Thin liquid sheet impingements are arranged with a common front so that the energy supplies remain constant within the area of niosome formation, resulting in the formation ofniosomal vesicles with greater uniformity, smaller size, and better reproducibility. [5]

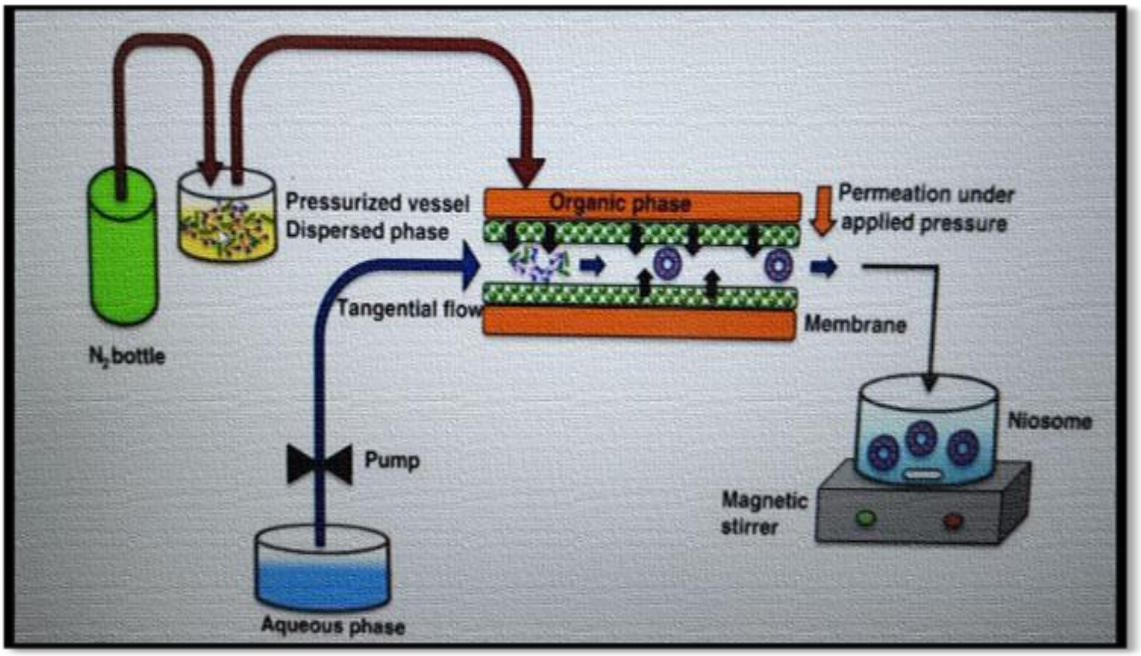

Figure 6:- Microfluidization.

5.Multiple Membrane Extrusion Method

Using a rotary evaporator, a mixture of surfactant, cholesterol, and dicetyl phosphate in chloroform generates a thin layer. Aqueous drug polycarbonate membranes hydrate the film. The solution and its suspension are extruded through a polycarbonate membrane and put in a series of up to eight passageways. It is an effective approach for regulating the size of niosomes. [5]

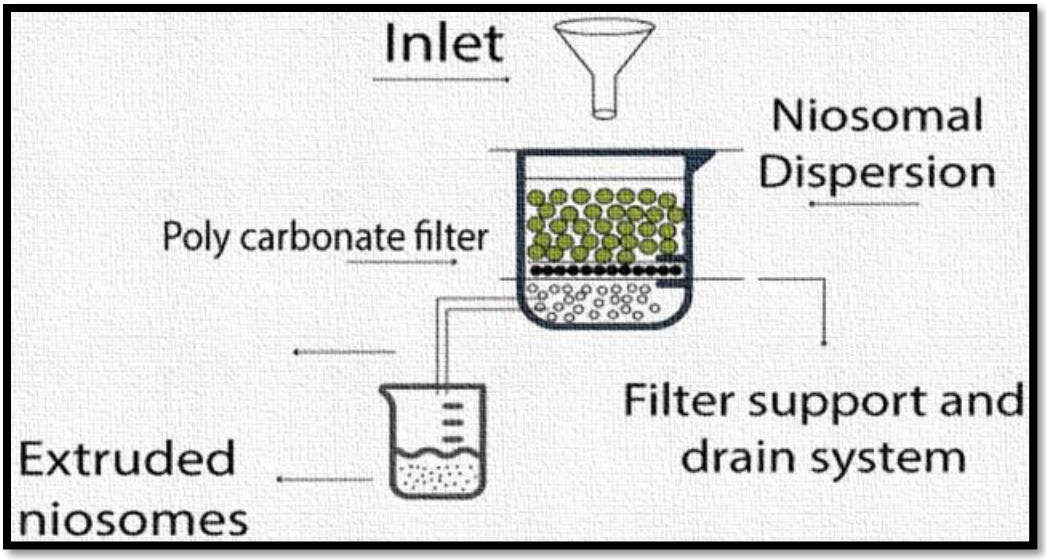

Figure 7:- Multiple Membrane Extrusion Method.

6.Reverse Phase Evaporation Technique

Cholesterol and surfactant (in a 1:1 ratio) dissolve in an organic solvent mixture (ether and chloroform). The aqueous drug solution is added to this, and oil in oil emulsion is formed; two phases are sonicated at 4-5 degrees Celsius. To generate a semisolid gel of big vesicles, the emulsion is dried in a rotary evaporator at 40°C. The clear gel is sonicated again with small volumes of phosphate- buffered saline (PBS). At 40°C and reduced pressure, the organic phase is eliminated. To create niosomes, a viscous niosomal suspension is diluted with phosphate - buffered saline and heated on a water bath at 60°C for 10 minutes.[5]

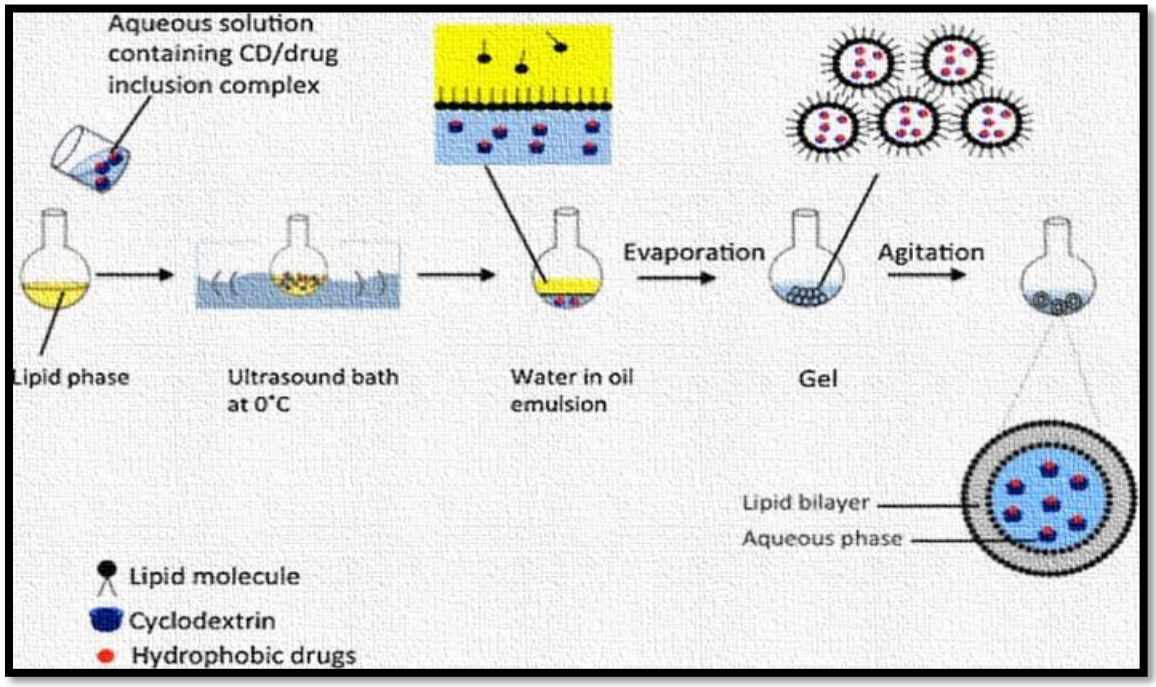

Figure 8:- Reverse Phase Evaporation Method.

7.Trans MembranepH Gradient Drug Uptake Process

Surfactants and cholesterol are dissolved in an organic solvent during the remote loading process (chloroform). Under reduced pressure, the solvent evaporates, leaving a thin film on the round bottom flask's wall. By vortex

mixing, the film hydrates with 300 mM citric acid (pH4.0). Multilamellar vesicles are frozen and thawed three times before being sonicated. Aqueous solution containing 10 mg/ml of drug is added for niosomal suspension, and vortexing is performed. With 1M disodium phosphate, the pH of the sample is raised to 7.0-7.2. The mixture is then heated for 10 minutes at 60°C to produce. [5]

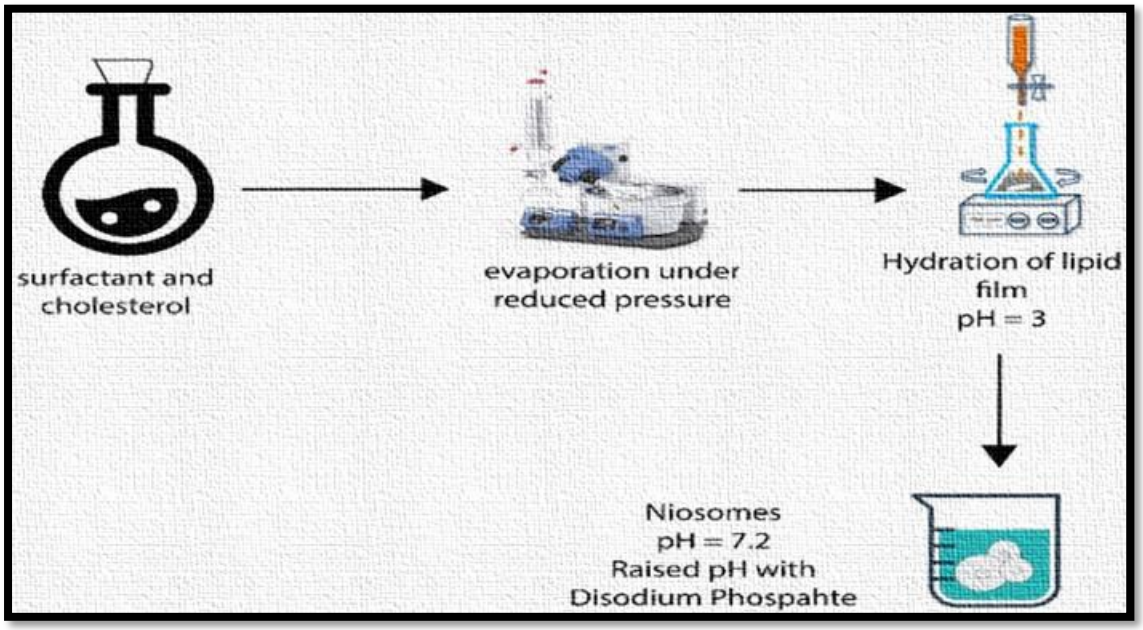

Figure 9:- Trans Membrane pH Gradient Drug Uptake Process.

8.The Bubble Method

Niosomes are made using the bubble process without the use of organic solvents. After combining the surfactants and additives in an aqueous phase, like PBS, the mixture is moved to a flask with three necks and a round bottom.[8]

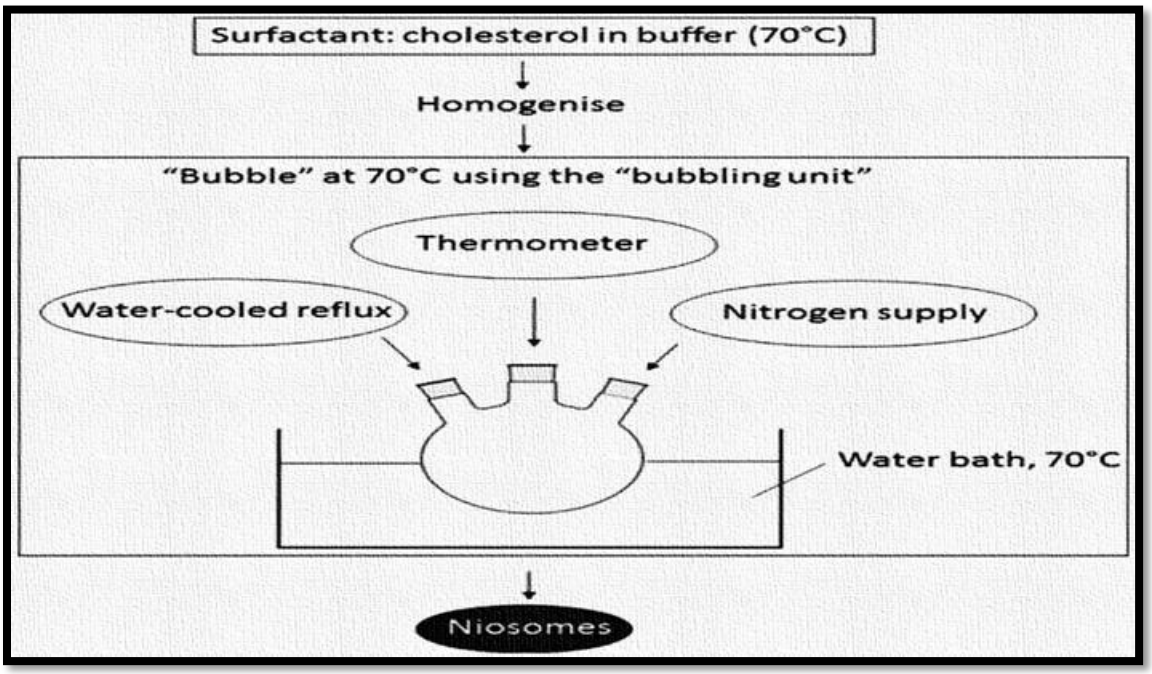

Figure 10:- The Bubble Method.

9.Formationof Niosomesfrom Proniosomes

Proniosomes is a dry formulation in which each water-soluble particle is protected by a thin layer of dry surfactant. The niosomes are identified by adding an aqueous phase at T > Tm with brief agitation. T denotes temperature, while Tm denotes the mean phase transition temperature.[5]

Carrier + surfactant = Proniosomes

Proniosomes + water = Niosomes

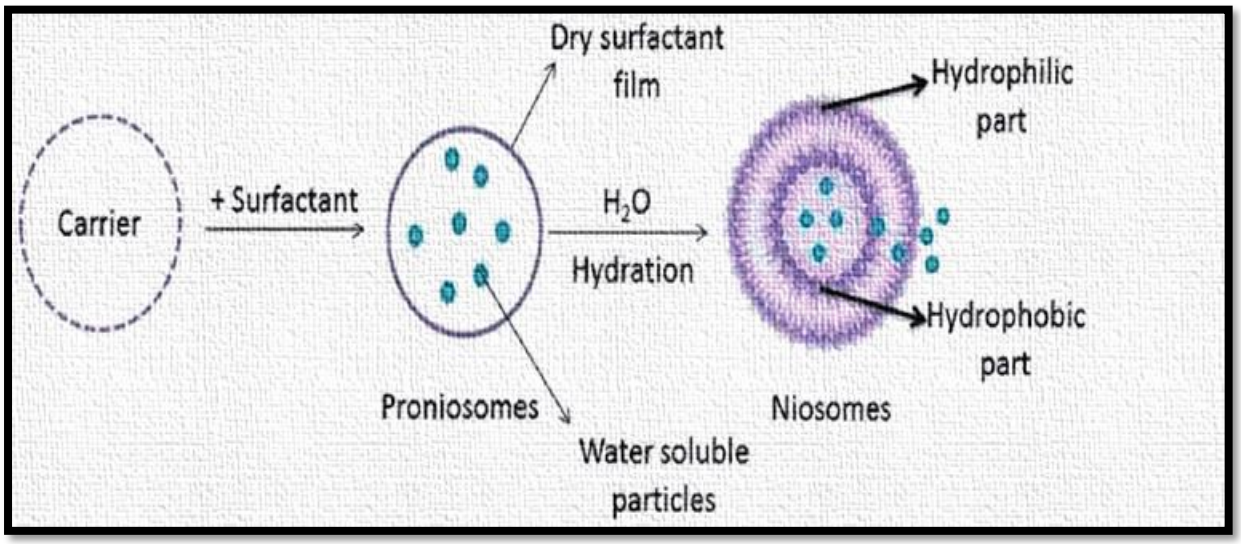

Figure 11:- Formation of Niosomes from Proniosomes.

Separationof Untrapped Drug

The removal of unentrapped solute from the vesicles can be accomplished by various techniques which include:

1. Dialysis: The aqueous niosomal dispersion is dialyzed in a dialysis tubing against phosphate buffer or normal saline or glucose solution.

2. Gel Filtration: The unentrapped drug is removed by gel filtration of niosomal dispersion through a Sephadex-G-50 column and elution with phosphate buffered saline or normal saline.

3. Centrifugation: The niosomal suspension is centrifuged and the supernatant is separated. The pellet is washed and then resuspended to obtain a niosomal suspension free from unentrapped drug.[3]

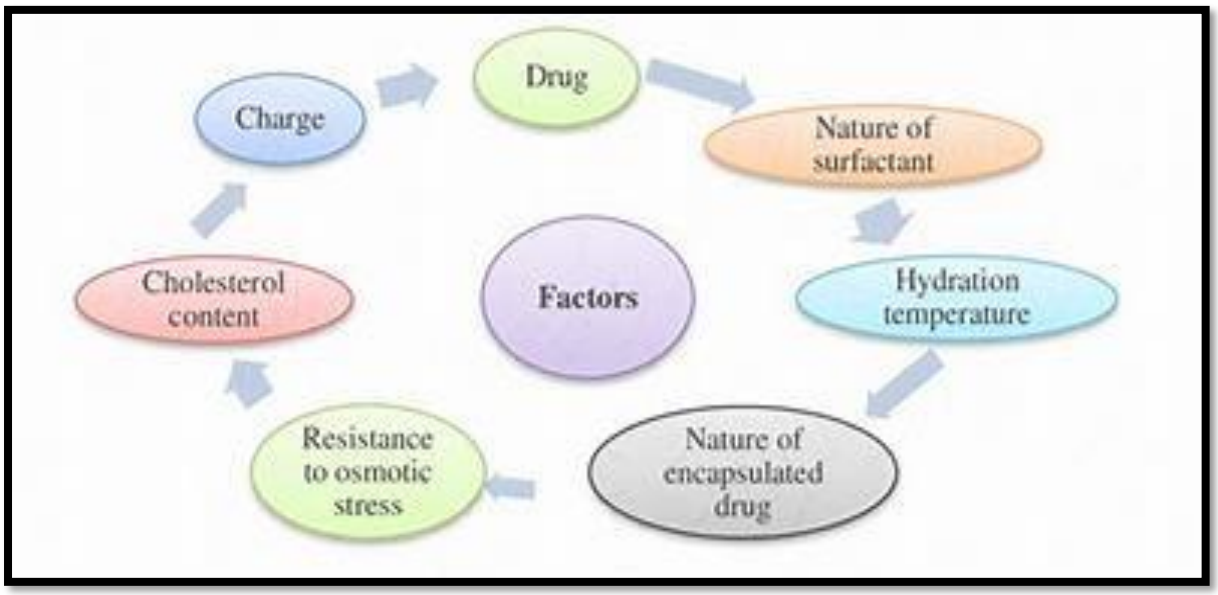

Figure 12:- Factors affecting Niosomal Formulation.

Factors Affecting Niosome Formation

1. **Nature of Surfactants:** A surfactant has a hydrophilic head and hydrophobic tail. The hydrophobic tail may consist of one or two alkyl or perfluoro alkyl groups or in some cases a single steroidal group. The ester type surfactants are chemically less stable than ether type surfactants and the former is less toxic than the latter due to ester linked surfactant degraded by esterase's to triglycerides and fatty acid in vivo. The surfactants with alkyl chain length from C12-C18 are suitable for preparation of niosomes.
2. **Osmotic stress:** Addition of a hypertonic salt solution to a suspension of niosomes brings about reduction in diameter. In hypotonic salt solution, there is initial slow release with slight swelling of vesicles probably due to inhibition of eluting fluid from vesicles, followed by faster release, which may be due to mechanical loosening of vesicles structure under osmotic stress.
3. **Temperature of Hydration:** Hydration temperature influences the shape and size of the niosome. For ideal condition it should be above the gel to liquid phase transition temperature of system. Temperature change of niosomal system affects assembly of surfactants into vesicles and also induces vesicle shape transformation.
4. **Nature of Encapsulated Drug:** The drug interacts with surfactant head groups and develops the charge that creates mutual repulsion between surfactant bilayers and hence increases vesicle size. The aggregation of vesicles is prevented due to the charge development on bilayer.
5. **Membrane Composition:** Niosomes can be prepared with addition of different additives along with surfactants and drugs. Addition of cholesterol molecule to niosomal system provides rigidity to the membrane and reduces the leakage of drug from niosome. Inclusion of cholesterol in niosomes increases its hydrodynamic diameter and entrapment efficiency. In general, the action of cholesterol is two folds; on one hand, cholesterol increases the chain order of liquid-state bilayers and on the other, cholesterol decreases the chain order of gel state bilayers. An increase in cholesterol content of the bilayers leads to decrease in the release rate of encapsulated material and therefore an increase of the rigidity of the bilayers obtained. Presence of charge tends to increase the interlamellar distance between successive bilayers in multilamellar vesicle structure and is responsible for increase in entrapped volume.[4]

Evaluation Parametersof Niosomes

1. **Size:** The mean diameter of niosomal vesicles may be estimated using the laser light scattering technique, and their shape is considered to be spherical. Electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy, optical microscopy, and freeze fracture electron microscopy can also be used to assess the diameter of these vesicles.
2. **Bilayer formation:** Under light polarisation microscopy, the assembly of non-ionic surfactants to create a bilayer vesicle is characterized by an X-cross formation.
3. **Membrane rigidity:** The mobility of a fluorescence probe as a function of temperature can be used to determine membrane stiffness.
4. **Entrapment efficiency:** Unentrapped drug is separated by dialysis, centrifugation, or gel filtration as described above, and the drug that remains entrapped in niosomes is determined by complete vesicle disruption with 50 percent n-propanol or 0.1 percent Triton X-100 and analyzing the resultant solution using the appropriate assay method for the drug.
5. **Number of lamellae:** Nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering, and electron microscopy are used to determine this.
6. **In vitro release study:** Several researchers have used dialysis tubing to conduct in vitro release rate studies. A dialysis sac is immersed in distilled water after being cleaned. The vesicle suspension is pipetted into and sealed in a bag made of tubing. The vesicles are then put in a 200 ml buffer solution in a 250 ml beaker and shaken constantly at 25°C or 37°C. The drug content of the buffer is determined at various time intervals using an appropriate assay technique.[4]

Drugsand Routesof Administration Usedin Niosomes

1. **Intravenous Route:For Example:** Ipromide, Vincristine, Indomethacin, Colchicines, Rifampicin, Transferrin, Zidovudine, amarogentin, Daunorubicin, Amphotericin B.
2. **Transdermal Route:For Example:** Flurbiprofen, Piroxicam, Cisplantin, Levonorgestrol, Nimeluside, Estradiol, Ketoconazole, Enoxacin, DNA loaded noisome, Cyclosporine, Erythromycin, aninterferon.
3. **Oral Route: ForExample:** Vaccine, Polysaccharide Coated noisome, Cipro floxacin, Insulin.
4. **Oncology Route: ForExample:** Methotrexate, Doxorubicin, Adriamycin.
5. **Ocular Route: For Example:** Timolol, cyclopentolate.
6. **Nasal Route: For Example:** Sumatriptan, Influenza.

7. **Immunological Adjuvant: For Example:** Bovine serum albumin, Haemoglobin.
8. **For treatment of Leishmaniasis: For Example:** Stibogluconate.[7]

Applicationsof Niosomes

1. It is used as Drug Targeting.
2. It is used as Anti- Neoplastic Treatment i.e. Cancer Disease.**For Example:**Methotrexate.
3. It is used as Leishmaniasis i.e. Dermal and Mucocutaneous infections.**For Example:** Sodium stibogluconate.
4. It is used act as Delivery of Peptide Drugs.
5. It is used in Studying Immune Response.
6. Niosomes as Carriers for Hemoglobin.
7. Transdermal Drug Delivery Systems Utilizing Niosomes.**For Example:** Erythromycin.
8. It is used in Ophthalmic drug delivery. **For Example:** Cyclopentolate. [8]

Marketed Formulations of Niosomes

Table 3:- Marketed Formulations of Niosomes[2]

S.No.	Brand	Name of the Product
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

Conclusion:-

The idea of encapsulating the medication within Niosomes to improve delivery of the medication to the right tissue location. They resemble liposomes in structure, hence they can be thought of as an alternative to liposomes in vesicular systems. Because of their affordability, durability, and other advantages over liposomes, Niosomes are considered superior options for drug administration. Niosomes can be used for targeted, ocular, topical, parentral, and other types of drug delivery.

Reference:-

1. Sanklecha V.M., Pande V.V., Pawar S.S., Pagar O.B., Jadhav A.C.,"Review on Niosomes",Austin Pharmacology & Pharmaceutics (APP),May 29, 2018, 3(2): 01-07.
2. Kaur Dhanvir, Kumar Sandeep,"Niosomes: Present Scenarioand Future Aspects", Journal of Drug Delivery & Therapeutics (JDDT), 2018, 8(5):35-43.
3. Shreyas V. Desai, Prof. Bhavna Joshi, Dr. Umesh Upadhyay,"An Overview on Niosomes as Novel Drug Delivery Systems",Research Journal of Pharmaceutical Dosage Forms and Technology (RJPDFT), October - December, 2020, 12(4).
4. Patil Abhishek S. et al, "Niosomes: A Promising Drug Delivery Carrier", International Journal of Pharmaceutical Sciences and Medicine (IJPSM), June- 2021, 6(6):15-27.
5. Sharma Riya, Dua J.S, Parsad DN,"An overview on Niosomes: Novel Pharmaceutical drug delivery system", Journal of Drug Delivery & Therapeutics (JDDT),2022, 12(2-s): 171-177.
6. Chhaya Vinayak Atole, Jyoti Jawale, "Niosomes as Targeted Drugs Delivery System– An Overview",International Journal of Creative Research Thoughts (IJCRT), May 2022, 10(5): 914-934.
7. Pardeep Kaur, Ritu Rani, Ajeet Pal Singh, Amar Pal Singh, "An Overview of Niosomes", Journal of Drug Delivery and Therapeutics (JDDT), 2024; 14(3):137-146.
8. Prashant R. Chaudhari, Sulbha G. Patil, Sunil P. Pawar,"Niosomes Review Article", World Journalof Pharmaceuticaland Medical Research (WJPMR), 2024, 10(6): 165-169.
9. Pei Ling Yeo, Chooi Ling Lim, Soi Moi Chye, Anna Pick Kiong Ling, Rhun Yian Koh, "Niosomes: A Review of their Structure, Properties, Methods of Preparation, and Medical Applications", Asian Bio Medicine (ABM), 2017, 11(4):301-14.
10. Anchal Sankhyan, Pravin Pawar, "Recent Trends in Niosome as Vesicular Drug Delivery System", Journal of Applied Pharmaceutical Science (JAPS), 2012, 2(6): 20-32.
11. Mahmoud Kamal, Mohamed Maher, Amr Ibrahim1, Dina Louis, "An Overview on Niosomes: A Drug Nanocarrier", Drug Designing & Intellectual Properties International Journal (DDIPIJ), 2018, 1(5): 143-151.

12. Dharashive VM, Kapse Vidya N, Sonali S Devne, “Niosomes: as a Targeted Drug Delivery System”, International Journal of Research in Pharmacy and Chemistry, 2015, 5(4): 582-589.