Available online on 15.08.2023 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research

Open Access

Review Article

Overview on Niosome

Kapse Sanket *, Jadhav Prakash, Redasani Vivekkumar

YSPM's YTC Faculty of Pharmacy Wadhe, Satara-415011

A B S T R A C T

Pharmaceutical such achemicals can be administered locally to sick locations using target-specific drug-delivery devices.Some of the carriers used in various drug delivery techniques includesynthetic polymers, serum proteins, and immune globulins, liposomes, and microspheres. Niosomes' vesicular system, which features a bilayer structure made possible by nonionic surfactants, has the capacity to extend the time that a medicine is accessible in a specific region .Capturing hydrophilic molecules in niosomes or lipophilic medicines is enhanced by their amphiphilic character. To keep the niosomes' structure rigid, additional chemicals like cholesterol can be added. The key features of niosomes, such as their structural components, production methods, limitations, and current applications to a range of the narrative review mentions disorders briefly.

Keywords: Niosome, Types of niosomes, Method of preparation of niosome, Route of administration,etc.

A R T I C L E I N F O: Received 16 April 2023; Review Complete 24 June 2023; Accepted 14 July 2023; Available online 15 Aug. 2023

Cite this article as:

Sanket K, Prakash J, Vivekkumar R, Overview On Niosome, Asian Journal of Pharmaceutical Research and Development. 2023; 11(4):143-154. DOI: http://dx.doi.org/10.22270/ajprd.v11i4.1295

*Address for Correspondence:
Kapse Sanket, YSPM's YTC Faculty of Pharmacy Wadhe, Satara-415011

INTRODUCTION:

A method of administering medications to ill areas of people or animals at a controlled rate in order to have a therapeutic effect while also reducing the concentration of the medication in healthy tissues. The effectiveness of the medicine is increased by localised drug activity, which also lessens systemic tissue toxicity[1]. The "magic bullet" approach was first put up by Paul Ehrlich in 1909 and has since been known as focused delivery straight to the afflicted cell without harming healthy cells[2]. Since then, numerous forms of medication delivery methods have been created, including serum proteins, liposomes, microspheres, niosomes, immune globulins, synthetic polymers, and serum immune globulins[1]. Liposomes and niosomes are well-known vesicular drug delivery mechanisms among these[3-4]. A vesicular system, in general, is a drug-delivery platform that permits effective bioavailability of pharmaceuticals through monitored therapeutic drug release over an extended period of time[5–6]. Bilayer amphiphilic molecules encircle a water chamberin the vesicles [7, 8, 9.]Drugs that are amphiphilic and lipophilic can be transported via niosomes, which are vesicles made of cholesterol and a nonionic surfactant (such as alkyl ester and alkyl ether) [7,8,10,11]. By shielding drug molecules from abrasive biological surroundings, niosomes improve the efficacy of treatment of drug molecules that have been encapsulated [12.]The process of creating novel medications requires a lot of time and resources. A new drug's development is projected to cost $120 million, and it takes years to get approved by the regulatory body after discovery, clinical testing, and development [13–14]. By enhancing drug selectivity and the therapeutic index while reducing the effective dose, certain drug-delivery systems reduce the need to rush the introduction of new medications to market. This narrative summary includes details on the composition, production process, properties, and applications of niosomes as a drug delivery system.

Niosomes

Structure of niosomes:

The spherical niosomes in Figure 1 contain the miniature lamellar (single or many lamellae) structures.Nonionic the bilayer is produced using surfactants, either with or without cholesterol, and a charge inducer[15, 16]. Niosomes are created by combining various surfactant types in different molar ratios and combinations[17]. Surfactants come in a variety of forms, including sorbitan fatty acid esters, fatty acid esters made by polyoxyethylene, alkyl ethers, and alkyl glyceryl ethers[7]

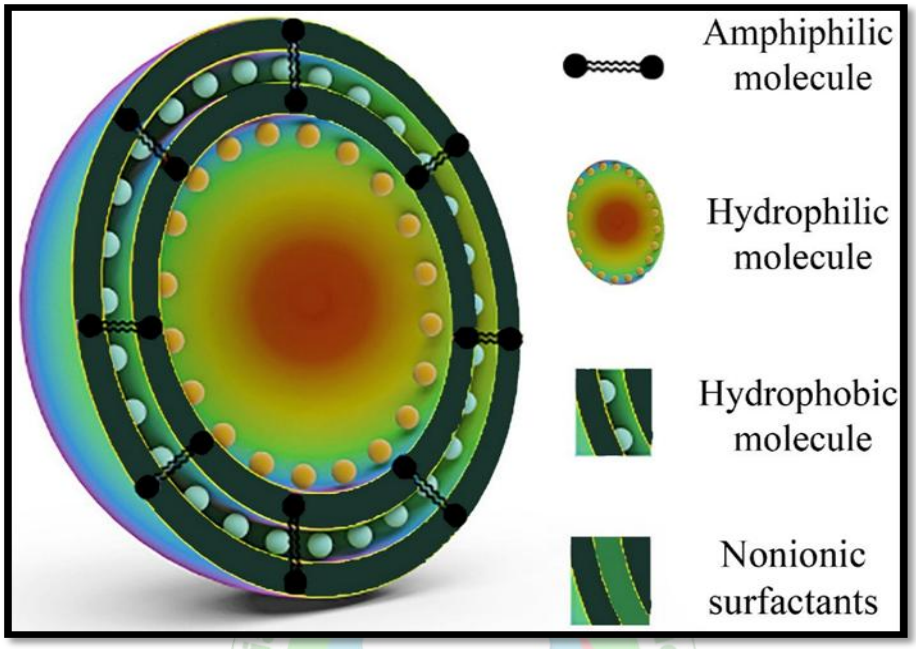

Figure 1: Structure of Niosome

Cholesterol addition keeps the bilayer firm, resulting in fewer leaky niosomes .Charge inducers, on the other hand, give the vesicles a charge and increase their size, enhancing the efficiency of drug entrapment. By using positive charge inducers, the vesicles are stabilised. Such stearylamine and cetylpyridinium negative charge-inducing substances and chloride like trihexadecyl phosphate, dicetyl phosphate, and lipoamino[18–19].Nonionic surfactants in niosomes commonly have their hydrophilic ends facing outward (towards the liquid phase) and their hydrophobic ends facing inward to one another in orderto create a closed bilayer that encloses solutes in a water solution[15]. As a result, a lipophilic gap separates the exterior and internal hydrophilic sides of the niosomes' tight bilayer structure [7, 19].Energy is required to create theheated or physically agitated closed bilayer structure. It was discovered the vesicular structure is maintained by a number of forcesvan der Waals is among themand repulsive forces between the surfactant molecules. The characteristics of the resulting niosomes will probably change if the vesicle's components (such as kind, makeup, and concentration);dimensions, surface charge, or volumeare changed [15, 16, 20]. Three classes the ability to categorise niosomes. According to the size of their vesicles: small unilamellar vesicles (0.025-0.05 mm), multilamellar vesicles (>0.05 mm), and the enormous unilamellar vesicles (>0.10 mm)[20].

Significant characteristics of niosomes[21,22,23]

- Solutes can be trapped by niosomes.
- Niosomes are stable and osmotically active.
- The infra-structure of niosomes is mostly made up between hydrophilic and hydrophobic molecules together, allowing the drug atoms a broad spectrum of dissolvability.
- Niosomes function as a medication storage facility in the body because they release the medication in an orderly fashion by the use of their bilayer, which supports the arrival of the encased medication.
- Targeted medicine delivery can also be achieved using niosomes, which deliver the medication directly to the area of the body where the therapeutic effect is needed. As a result, less measurement will need to be controlled in orderto achieve the intended outcome.
- They increase the skin permeability of pharmaceuticals when applied topically, as well as the solubility and poorly soluble substance oral bioavailability medications.

- Niosomes can be created to fit a variety of conditions thanks to their structural flexibility (composition, fluidity, and size).
- Niosomes can enhance the functionality of drug molecules.
- Improved accessibility to the specific spot simply by shielding the medicine from the biological environment.
- Niosomes make the medicine that is entrapped more stable.

Advantage:

- Fewer side effects and a longer period of action.
- When compared to other distribution systems, patient compliance is higher.
- The amount of medicine required to achieve the required effect is very small.
- The preparation's active ingredient or constituent is shielded by a bilayer from different external and internal influences.
- Serve as a depot formulation, allowing for regulated medication release.
- The drug is guarded against gastrointestinal breakdown and first pass metabolism.
- Be structurally stableeven when it's an emulsion. Niosomes can be administered parenterally, topically, or orally [24,25,26].

Disadvantage:

- Time consuming process.
- For processing, specialised equipment is needed.

Insufficient shelf life because-

1. Fusion
2. Combination
3. Drugs that have been sealed up leak.
4. Drugs in capsules are hydrolysed.

Physically unstable [27, 28, 29]

Niosome composition:

The following essential ingredients are utilised to create niosomes:

1. Non-ionic surfactants
2. Cholesterol
3. Charge inducer
4. Moderate Hydration

1. Non-ionic surfactants:

The surface-active component serves as the main ingredient in the composition of the noisome.They have a polar head and a non-polar tail, making them amphiphilic in nature.[30]. Because they don't carry any charge, these substances are more stable, compatible, and non-toxic than other surfactants like anionic, cationic, and amphoteric surfactants.These chemicals reduce haemolysis and cellular surface inflammation. They may serve as wetting agents and emulsifiers.Nonionic surfactants' key characteristic is their ability to block p-glycoprotein, which enhances medication targeting and absorption[31]doxorubicin, daunorubicin, curcumin, and morusin are examples of anticancer drugs. Hydrocortisone is an example of a steroid. Ritonavir is an example of an HIV protease inhibitor. Digoxin and beta-blockers are examples of cardiovascular drugs.Polar and non-polar groups and segments can be found in non-ionic surfactants, which also exhibit significant interfacial activity.Utilising the hydrophilic lipophilic balance (HLB) scale, the component's chemical makeup, and the critical packing parameter (CPP) are all necessary for the creation of bilayer vesicles. The ability of a medicine to be caught is frequently influenced by the size and length of the hydrophilic head group of a non-ionic surfactant. Larger alkyl chains in non-ionic surfactants demonstrate increased trapping efficiency.

2. Cholesterol:

The primary use of cholesterol, a waxy steroid derivative found in cell membranes, is in the synthesis of niosomes[39].By adding cholesterol to the niosomes' bilayer structurecellular membrane permeability is reduced, frequently increasing the trapping efficiency of the niosomes [40].Cholesterol is typically used as a direction or adjustment to non-ionic surfactants in order to provide the rigidity of the niosomal bilayer and the proper.[41.]Because cholesterol can stop the niosomal system from going from a gel to a liquid phase, niosomes are less likely to leak.[42].

3. Charge inducers:

To boost niosome stability by electrostatic repulsion and prevent Charge-inducing substances are coalescence. Added to the mixture. Phosphatidic acid and diacetyl phosphate (DCP) are the negatively charged substances that are used the most frequently.The positively charged inducers STR and stearylpyridinium chloride are examples of stearyl amines. are both used in niosomal preparations. Since higher concentrations can interfere with the development of niosomes [43, 44], charged inducer concentrations between 2 and 5 mole percentages are tolerated.

4. Medium for hydration:

The hydrating agents employed most frequently in the creation of niosomes is phosphate buffer. These phosphate buffers are used at various pH values. The actual pH of the hydration media is impacted by the solubility of the medication being encapsulated [45.]

Types of niosomes:

The various niosome kinds can be categorised.as follows: (Figure 2).

1. Multilamellar vesicles (MLV)
2. Big unilamellar vesicles (LUV)
3. Small unilamellar vesicles (SUV)

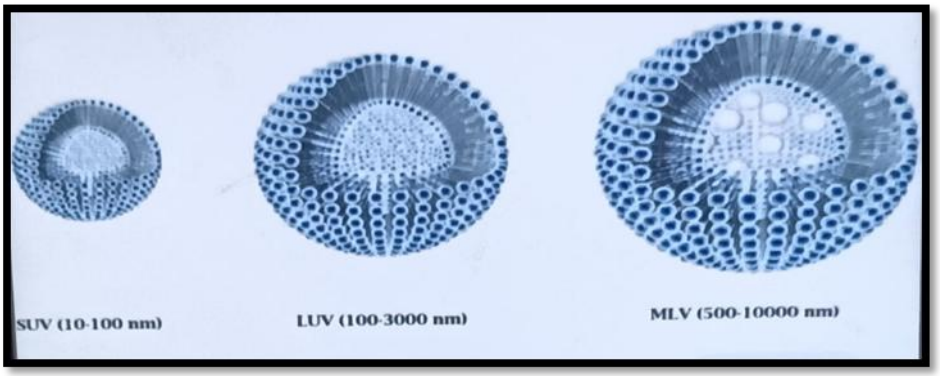

Figure 2: Types of Niosome

1) Multilamellar vesicles (MLV):

Niosomes are most frequently seen in multilamellar vesicles. The vesicles have a diameter that varies between 0.5 and 10 m. The vesicles are easily prepared, and after being stored for a while, they remain mechanically stable. In most cases, each aqueous lipid component is surrounded by a number of bilayers. As medication carriers for lipophilic substances, they are called multilamellar vesicles ideally suited.

2) Big unilamellar vesicles (LUV):

Large unilamellar type niosomes have a high aqueous/liquid compartment ratio, allowing for more bioactive material to be confined in a given volume while using a fraction of the membrane lipids. Large unilamellar vesicles range from 100 to 3000 nm in length in size.

3) Small unilamellar vesicles (SUV):

By using the sonication process, small unilamellar vesicles are often created from multilamellar vesicles. The size of the small unilamellar vesicles has been estimated to be between 10 and 100 nm [46,47.]

Way of preparation:

1. Thin film hydration technique (Hand shaking method)
2. The micro fluidisation method
3. Reverse Phase Evaporation Method (REV)
4. Ether Injection Method
5. Trans-membrane pH-gradient (inside acidic)
6. The Bubble Method
7. The Sonication method
8. Multiple extrusion method
9. Formation of niosomes from proniosomes

1) Thin film hydration technique (Hand shaking method):

Figure 3 illustrates the hand-shaking procedure for dissolving the non-ionic surfactant and cholesterol in a volatile organic solvent (such as diethyl ether, chloroform, or methanol) in a round-bottom flask. A rotary evaporator is used to remove the organic solvent at room temperature (20°C), leaving behind a thin layer of solid mixture that is deposited on the flask wall.Before the dry surfactant layer is hydrated with the drug-containing aqueous phase at 50–60°C, it is gently stirred. Multilamellar niosomes are created using this technique [48, 49.]

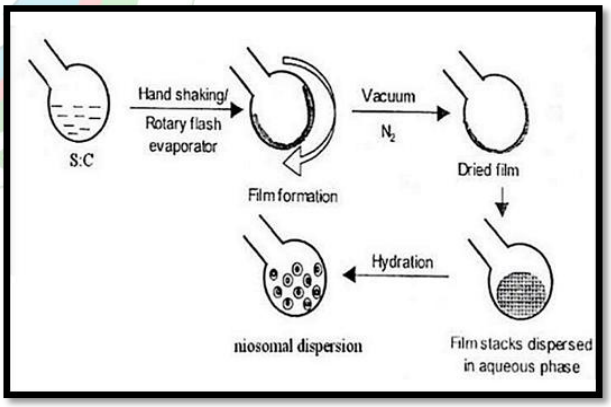

Figure 3: Thin film hydration technique (Hand shaking method)

2) The micro fluidisation method:

The micro-fluidization strategy can be applicable to produce unilamellar vesicles with a certain size distribution, as demonstrated in figure 4.It is based on the submerged jet principle, where two fluidized streams contact at extremely high speeds (100 ml/min) in narrowly defined microchannels inside the interaction chamber. The energy given to the system stays in the area where niosomes are produced because the thin liquid sheet impingement is

arranged along a single front. Niosomes made using this method are more homogeneous, smaller, and repeatable[50, 51].

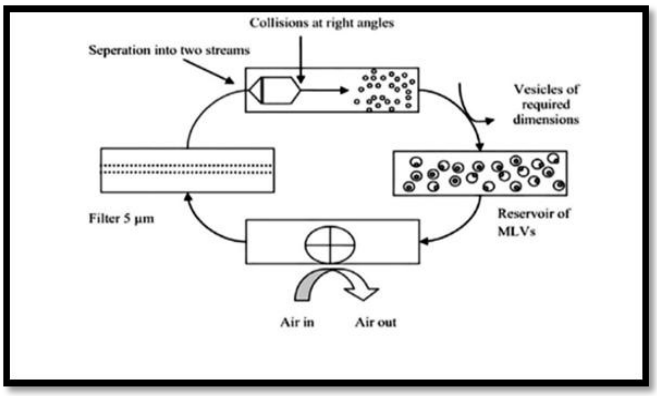

Figure 4: Micro fluidisation Method

3) The Reverse Phase Evaporation (REV):

Reverse phase evaporation calls for a 1:1 ratio of surfactant to cholesterol.The previously described mixture is dissolved in a solution of ether and chloroform. Aqueous phase is where the drug dissolves. At a temperature of 4-6°C, the mixture is sonicated.By employing a water bath and emulsifying the niosome suspension in PBS at 60°C for 10 minutes, niosomes are produced. The resulting product is once more mixed with PBS, then sonicated at low pressure while being held at a temperature of 40 to 45 °C to eliminate the organic phasethe process of making niosomes involves diluting the resultant solution with PBS and heating it on water for 10 minutes at 60°C.[52,53.] depicted in figure 5.

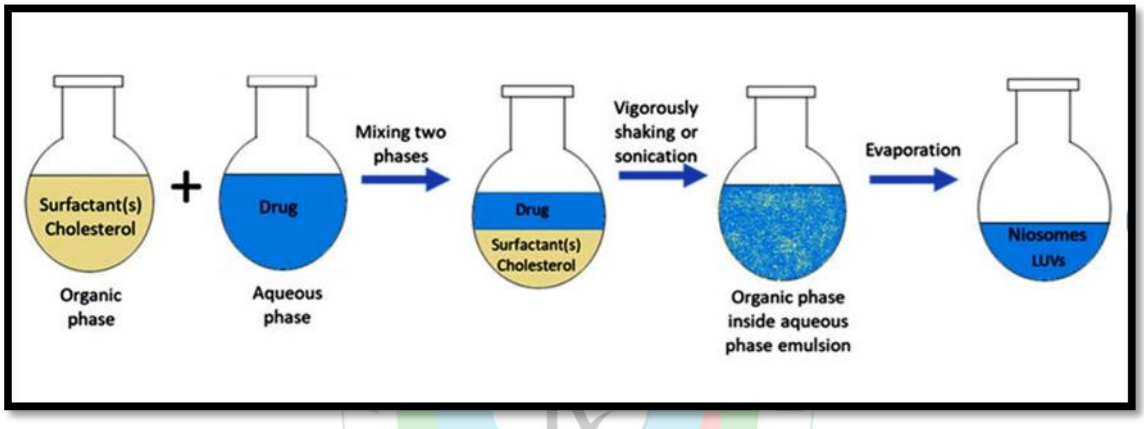

Figure 5: Reverse Phase Evaporation Method (REV)

4) The ether injection method:

By introducing a diethyl ether-dissolved surfactant solution (a volatile organic solvent) into warm water that is kept at 60°C, the niosomes are created using the ether injection method. A 14-gauge needle is used to inject the surfactant solution dissolved in ether into the material's aqueous solution. Ether (a volatile organic solvent) is vaporised to create single-layered vesicles, as shown in figure 6.

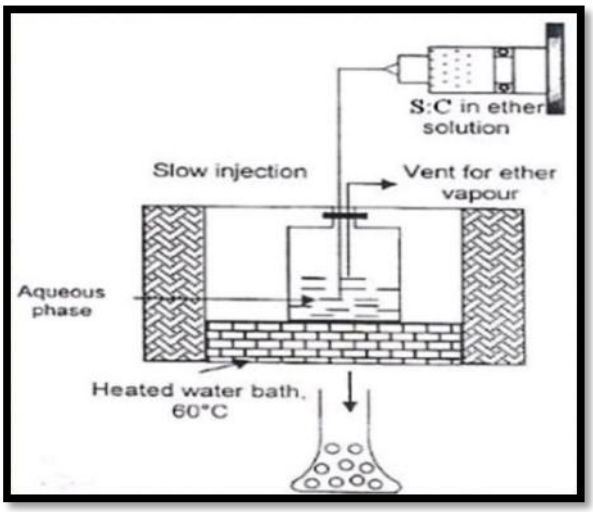

Figure 6: Ether injection method

5) Trans-membrane pH gradient (inside acidic):

This procedure involves mixing/blending cholesterol and surfactant in a round-bottomed flask before dissolving it in chloroform. As the chloroform evaporates at a low pressure, a thin film is created on the flask's wall.The film is hydrated using vortex mixing with 300mM citric acid (pH 4.0). The previously described niosomal suspension is combined with an aqueous solution that has 10 mg/ml of the medicine before being vortexed.The sample's pH is decreased to 7.0–7.2 by adding 1M disodium phosphate, and the mixture is then heated at 60°C for 10 minutes. This technique results in multilamellar vesicles [55, 56, 57].

6) The Bubble method:

The niosomes are made utilising the bubble method, a unique process that does not include organic solvents. This technique makes use of the bubbling unit. This device consists of a flask with three necks and a spherical bottom that is submerged in water to control the temperature. Before the nitrogen is pushed through the third neck, the thermometer and water-cooled reflux are put into the first and second necks, respectively.A buffer solution with a pH of 7.4 and 70 °C is used to mix surfactant with cholesterol. Figure 7. After mixing the solution for 15 seconds in a high-shear homogenizer, nitrogen gas is then utilised to immediately bubble the mixture at 70°C.

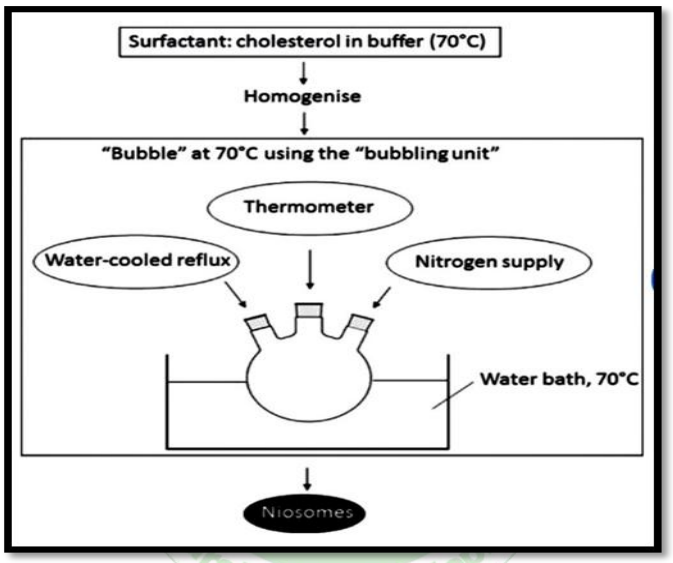

Figure 7: The Bubble method

7) The Sonication:

Sonication is one of the conventional processes for producing niosomes. To make the drug solution in this process, the medication is dissolved in a buffer. The ideal ratio of non-ionic surfactant combination is then added to this buffer medication solution.The combination can be sonicated at a particular frequency, temperature, and duration to produce the required niosomes. It is one of the simple methods for managing niosome particle size. Using this method, the diameter of niosomes with a narrow range of sizes can be decreased. It is also possible to utilise probe sonicators, although they require a lot of energy. This causes a quick rise in temperature and the titanium to discharge, as shown in figure 8 [60].

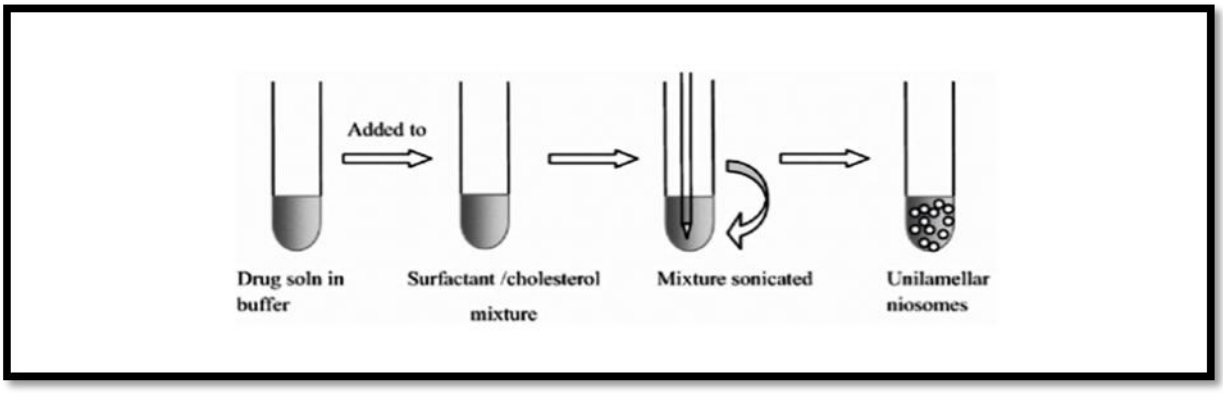

Figure 8: Sonication Method

8) Membrane Extrusion Method:

This process involves mixing diacetyl phosphate, cholesterol, and surfactant with chloroform. Then a thin film is created by evaporating this chloroform mixture.Polycarbonate membranes are hydrated using an aqueous solution. Extrusion of the solution and the resulting suspension occurs through this membrane, which has eight channels. This approach [61,62] is also used to determine the required size of the niosomes, as shown in figure 9

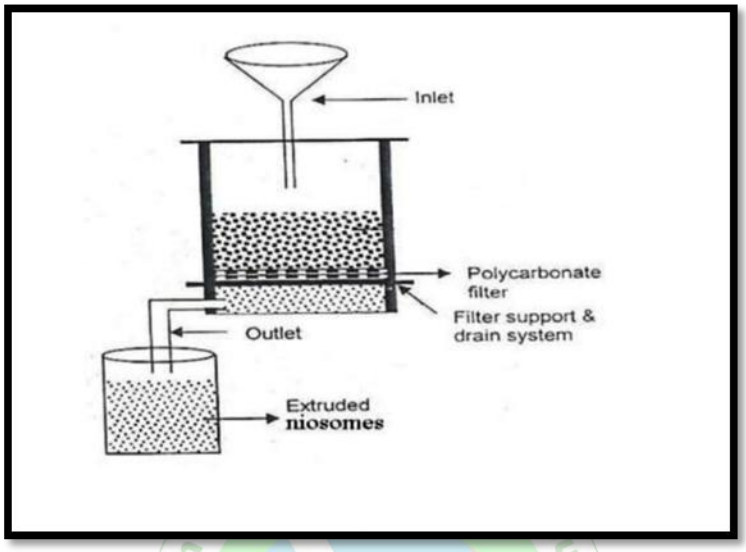

Figure 9: Membrane Extrusion Method

9) Formation of niosomes from proniosomes:

Niosomes are formed by adding aqueous phase with medication to preniosomes with brief agitation at a temperature higher than the surfactant's typical transition phase temperature [63]. T Tm where T is the temperature and Tm is the average phase transition temperature A.I. Blazek-Walsh et al. have documented the creation of niosomes from preniosomes based on malt dextrin. Niosomes can be quickly reconstituted with this formulation, and the amount of leftover/remaining carrier is small. A free-flowing formulation powder was created by drying the malt dextrin and surfactant slurry, which could be rehydrated by adding warm water [64,65].

Separation of unentrapped drug:

1) Dialysis: Using phosphate buffer, glucose solution, or ordinary saline, the aqueous niosomal suspension is dialyzed in dialysis tubing.

2) Gel Filtration: Using a Sephadex-G-50 column and phosphate buffered saline or regular saline as the elution medium, the un-entrapped drug in the niosomal suspension is extracted by gel filtration.

3) Centrifugation: During centrifugation, the liquid supernatant is removed from the niosomal suspension. To create niosomal suspension free of un-entrapped medicine, the pellet and re-suspended solution are washed [66,67].

Liposomal and niosomal differences:

Table 1: An analysis of the variations between liposomes and niosomes.

An analysis of the variations between liposomes and niosomes.[68-69]	
Liposomes	Niosomes
Highly expensive	Less expensive
Phospholipids can degrade by oxidation.	Surfactants that are non-ionic are resistant to oxidative deterioration.
Need for a distinct method for purification, storage, and handling of phospholipid	No unique method is needed
Comparatively more toxic	Less toxic
Size range 10-3000 nm	Size range 10-100 nm

Factors affecting the niosomal formation:

1) Drug:

The physico-chemical properties of the drug that is encapsulated have a direct impact on the charge and rigidity of the niosomal bilayer. The medication is trapped inside the niosomes, and the solute interacts with head groups of surfactants to increase the size of the niosome vesicle.The increase in charge and mutual repulsion between the surfactant bilayers causes the vesicle's size to increase. The degree of entrapment is also influenced by the drug's hydrophilic-lipophilic balance[70, 71].

2) Resistance of osmotic stress:

Niosome diameter decreases when hypertonic salt solution is mix up in the niosomal suspension. Once more, after the addition of hypotonic salt solution, the vesicles first release slowly with some swelling from the inhibition of fluid elution from the vesicles. Due to the vesicle structure's mechanical weakening under osmotic stress, the release accelerates [72].

3) Temperature of hydration medium:

The hydration medium's temperature is a key factor in vesicle formation. This has an effect on their shape and size.The temperature must always be greater than the temperature at which the system transitions from the gel to liquid phase.The temperature is also seen to affect the vesicle's form. Additionally, it influences how surfactant vesicles are put together. Vesicle structure and yield are influenced by the hydration medium's volume and the lipid film's length [73, 74].

4) Cholesterol content:

Niosome structure and physical characteristics are impacted by cholesterol. Non-ionic surfactants' presence has an impact on the structure. Biological membranes contain cholesterol, which also impacts the membrane's ion permeability, aggregation, fusion processes, size, shape, elasticity, and enzymatic activity, among other features. The fluidity of niosomes changes when cholesterol is added. Because it gives vesicles stiffness, which is crucial under extreme stress circumstances, cholesterol is crucial during the creation of niosomes.How much cholesterol needs to be added is determined by the surfactants' HLB value. To compensate for the larger head groups, it is necessary to increase the amount of cholesterol when the HLB value rises over 10 [75]. Change in HLB value affects the formulation of noisy systems (Table 1). Cholesterol improves the hydrodynamic diameter and trapping effectiveness of niosomes. The gel state transforms into an organised liquid phase when cholesterol levels are high. Bilayers become stiffer as a result of a decline in the encapsulated material's rate of release brought on by an increase in the cholesterol content of the bilayers.[76]

5) Amount and type of surfactant:

HLB surfactants such as Span 85 (HLB 1.8) to Span 20 (HLB 8.6) enhance the mean size of niosomes in a proportionate manner because the surface free energy reduces as the surfactant's hydrophobicity increases.Depending on the temperature, the type of surfactant, and the presence of additional elements like cholesterol, the bilayers of the vesicles can either be liquid or gel.While the structure of the bilayers is more disorganised in the liquid state, alkyl chains are present in the gel state in a well-ordered form. The temperature at which a substance transitions from a gel to a liquid (TC) describes the surfactants and lipids. The phase (TC) transition temperature of the surfactant has an impact on entrapment effectiveness as well; for instance, Span 60 with a higher TC provides better entrapment [77].

6) Membrane Composition:

The stable development of niosomes results from the addition of different chemicals, medicines, and surfactants. Niosomes are produced in a range of morphologies, and their permeability/porousness and stability qualities can be changed by modifying the properties of the membrane with entirely new additions. The polyhedral niosomes made from C16G2 retain their polyhedral structure because only a little amount of solulan C24 (cholesterol poly-24-oxyethylene ether) solution is added, preventing aggregation brought on by the creation of steric[78].

Niosomal characterization:

Angle of repose measurement:

Using a funnel approach, the angle of repose of dried niosome powder was determined. A funnel with a 13mm output aperture that was positioned such that it was 5 cm above a flat, dark surface received niosome powder.After the powder falls down from the funnel to form a cone on the surface, the height of the cone and the diameter of its base were measured to determine the angle of repose.

Scanning electron microscopy:[79]

An essential feature is the particle size of the niosomes. The size distribution of niosomes and the surface morphology (roundness, smoothness, and aggregation formation) were examined using scanning electron microscopy (SEM). Double-sided tape that was applied to aluminium stubs was sprayed with niosomes. The vacuum chamber of a scanning electron microscope (XL 30 ESEM with EDAX, Philips, Netherlands) was filled with the aluminium stub. The samples were investigated for morphological characterisation using a gaseous secondary electron detector (XL 30, Philips, Netherlands) with a working pressure of 0.8 torr and an acceleration voltage of 30.00 KV.

Optical Microscopy:

After appropriate dilution, the niosomes were placed on glass slides and observed morphologically using a microscope (Medilux-207RII, KyowaGetner, Ambala, India) at a magnification of 1200X. Using a digital SLR camera, the photomicrograph of the preparation was also taken under the microscope.

Measurement of vesicle size [79]

The identical media that was utilised to create the vesicle dispersions was diluted approximately 100 times. To determine the size of the vesicles, a particle size analyser (Laser diffraction particle size analyser, Sympatec, Germany) was used.. The system consists of a point-focused He-Ne laser beam at 632.8 nm, a multielement detector, and a small volume sample holding cell (Su cell). With a minimum 5 mW of power utilising a Fourier lens [R-5]. The material was agitated with a stirrer before the vesicle size was calculated. According to Hu C. and Rhodes 7, the typical size of niosome particles generated from niosomes is roughly 6 m, compared to 14 m for typical niosomes.

Entrapment efficiency[79]

To determine how much of the drug is still trapped in niosomes, complete vesicle rupture with 50% n-propanol or 0.1% Triton X-100 is utilised, followed by examination of the resulting solution using the right test method for the drug. By using gel filtration or dialysis centrifugation, as previously mentioned, the un-entrapped medication can be separated.

Osmotic shock [79]

Osmotic investigations can determine how the vesicle size changes. Three hours are spent incubating niosome formulations withthe three isotonic, hypotonic, and hypertonic solutions. Then, using optical microscopy, the variations in vesicle size in the formulations are examined.

Stability studies[80]

The optimised batch was kept in hermetically sealed vials at various temperatures to gauge the stability of niosomes.Surface characteristics and the proportion of drug maintained in niosomes and niosomes produced from proniosomes were chosen as measures for evaluating the stability since instability of the formulation would reflect in drug leakage and a deterioration.. in terms of the medication retention rate. The niosomes were collected at predetermined intervals of time (0, 1, 2, and 3 months), examined for colour change and surface characteristics, assessed for the amount of medication form niosomes, and then analysed using the proper analytical techniques (UV spectroscopy, HPLC methods, etc.).

Zeta potential analysis[81]

To ascertain the resulting compositions' colloidal properties, zeta potential analysis is carried out. Utilising an electrophoretic light scattering and laser-based zeta potential analyser (Zeta plusTM, Brookhaven Instrument Corporation, New York, USA) retained after hydration. Doppler velocimetry approach, the appropriately diluted niosomes formed from proniosomes dispersion were found. At 25 °C, the temperature was fixed. Directly from the measurement, the charge on the vesicles and their mean zeta potential values with standard deviation were acquired.

Application of niosomes:

1) Targeting of bioactive agents:

a) To the reticulo-endothelial system (RES):

The RES cells accept the vesicles preferentially. It is employable to treat liver parasite infestations as well as animal tumours that are known to metastasis to the liver and spleen.

b) To organs other than RES:

It has been suggested that the carrier system employs antibodies to go to a specific location in the body. Immunoglobulin makes it simple to target the drug's delivery system [82].

2) For the treatment of Leshmaniasis:

The parasite invades the liver and cells to cause leishmaniasis. Most people prefer antimonials over other medications. Two doses administered on succeeding days exhibited an additive effect on the sodium stibogluconate efficacy of the niosomal formulation, according to a mouse antimony research.As drug-loaded liposomes, niosomes are also efficacious in experimental leishmaniasis[83].

3) Tumour targeting:

Chemotherapy is only effective if a considerable amount of an anticancer agent is present at the tumour site. This reduces the drug's concentration in other tissue compartments of the body, which lessens the negative effects. Numerous research teams have examined niosomes for improved transport of anticancer drugs to local lymphatic's. To produce cytarabine hydrochloride niosomes with smaller vesicles, researchers used a lipid hydration approach without dicetyl phosphate. The vesicles that were producedsize between 600 and 1000nm.The formulation with Span 60 produced the slowest rate of release out of the four surfactants chosen(Tween 20, Tween 80, Span 60, Span 80). An initial burst release that lasted for 2–6 hours was followed by a steady release that continued for at least 16 hours [84].

4) For the treatment of AIDS:

Human immunodeficiency virus (HIV), which results in a severely compromised immune system, is what causes AIDS. Zidovudine (AZT), an anti-HIV drug, serves as a treatment AIDS. It may be administered alone or in conjunction with antiviral medications. A substantial percentage of the AZT medication was shown to be imprisoned in the noisome created by the addition of Tween 80 in one study, where the addition of diacetyl phosphate caused a delay in the drug release of 88.72% over 12 hours. The molecular ratios of the non-ionic surfactant with a constant ratio of cholesterol were altered during the formation of the niosomes, changing the entrapment efficiency and resulting in the observation of a AZT is released under control[85].

5) Niosome as carrier for haemoglobin:

The transporter for haemoglobin is a niosome. Similar to non-capsulated haemoglobin in vesicles, which is easily permeable to oxygen, the haemoglobin curve can be modified. You can overlay the visible spectra of free haemoglobin with niosomal suspension [86].

6) Antibiotics:

A topical antibiotic that is water soluble is delivered to the eyes using the non-ionic surfactant vesicles (niosomes). The investigation into gentamicin sulphate revealed that niosomes are the most promising ocular transporters for topical gentamicin sulphate administration [87].

7) Protein and peptide:

For the transportation of peptides and proteins, niosomes can be employed as an oral formulation with sustained release [88].

8) Transdermal delivery:

Niosomes have been investigated as transdermal drug delivery systems, as well as their capacity to improve drug absorption and lessen skin irritation through the intact stratum corneum. Using Franz diffusion cells, it was determined whether ketorolac (a strong NSAID) permeated through excised rabbit skin from different proniosome gel formulations. The produced proniosomes greatly reduced lag time and improved medication penetration[89]

Route of application of niosome drug[90]:

Table 2: Route of application

Route of administration	Examples of drugs
Intravenous route	Doxorubicin, comptothecin, insulin, zidovudine, cisplatin, rifampicin
Inhalation	All trans-retonic acids
Transdermal route	Piroxicam, estradiol, nimesulide
Ocular route	Timolol maleate,cyclopentol
Nasal route	Sumatriptan, influenzaviral vaccines

CONCLUSION:

One of the clearest illustrations of the rapid advancement in nanotechnology and drug delivery systems is the niosomal drug delivery system. Niosomes are largely stable in nature and economically, thus it is clear that they are favoured over other dosage forms as a method of drug delivery. There is a lot of room for toxic anti-cancer, anti-infective, anti-AIDS, anti-inflammatory, anti-viral, and other drugs to be encapsulated in niosomes and used as promising drug carriers in order to increase the drugs' bioavailability and targeting properties while lowering their toxicity and side effects. Therefore, more comprehensive analysis and study are needed in these areas to develop economically viable niosomal preparations. In order to better target the treatment at the right tissue destination, researchers and academicians typically support the idea of inserting the drug into or niosomes.Ionic drug carriers, which are more poisonous and unsuitable, are less safe than niosomal carriers. Niosomes

can be handled and stored without any special guidelines. Niosomes are a potential drug delivery system.The niosome can serve as an alternative vesicular system to liposomes due to its structural similarities and degree of property similarity, which allows them to encapsulate a variety of medications within their multienvironmental framework. Because of many considerations like cost, stability, and others, niosomes are regarded to be a better candidate for drug administration than liposomes. In many drug delivery methods, including targeted, topical, ocular, and parenteral, niosomes play a crucial and significant function. The pharma industry have a bright future thanks to niosomes. Only animal testing of this targeted medication delivery method has been documented thus far, but additional clinical studies in human volunteers as well as pharmacological and toxicological research in both animals and humans may help to fully utilise niosomes as effective drug carriers for treating conditions like cancer, infection, and AIDS, among others.

REFERENCES:

1. Allen TM. Liposomal drug formulations: rationale for development and what we can expect for the future. Drugs. 1998; 56:747–56.
2. Strebhardt K, Ullrich A. Paul Ehrlich's magic bullet concept: 100 years of progress. Nat Rev Cancer. 2008; 8:473–80.
3. Chen X, Huang W, Wong BC, Yin L, Wong YF, Xu M, et al. Liposomes prolong the therapeutic effect of anti-asthmatic medication via pulmonary delivery. Int J Nanomedicine. 2012; 7:1139–48.
4. Moazeni E, Gilani K, Sotoudegan F, Pardakhty A, Najafabadi AR, Ghalandari R, et al. Formulation and in vitro evaluation of ciprofloxacin containing niosome for pulmonary delivery.
5. Kumar GP, Rajeshwarrao P. Nonionic surfactant vesicular systems for effective drug delivery—an overview. Acta Pharm Sin B. 2011; 1:208–19.
6. Bhaskaran S, Lakshmi PK. Comparative evaluation of niosome formulations prepared by different techniques. Acta Pharma Sci. 2009; 51:27–32.
7. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. Int J Pharm. 1998; 172:33–70.
8. Negi LM, Garg AK, Chauhan M. Ultra deformable vesicles: concept and execution. Pharma Times. 2009; 41:11–4.
9. Sankar V, Ruckmani K, Jailani S, Ganesan KS, Sharavanan SP. Niosome drug delivery system: advances and medical applications – an overview. Pharmacologyonline. 2009; 2:926–32.
10. Uchegbu IF, Florence AT. Non-ionic surfactant vesicles (niosomes): physical and pharmaceutical chemistry. Adv Colloid Interface Sci. 1995; 58:1–55.
11. Bouwstra JA, van Hal DA, Hofland HEJ, Jun ginger HE. Preparation and characterization of nonionic surfactant vesicles. Colloids Surf A: Physicochemical Eng Aspects. 1997; 123–124:71–80.
12. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes—non-ionic surfactant vesicles. J Pharm Pharmacology. 1985; 37:863–68.
13. Tiwari G, Tiwari R, Sriwastawa B, Bhati L, Pandey S, Pandey P, et al. Drug delivery systems: an updated review. Int J Pharma Investing. 2012; 2:2–11. [17] Thacharodi D, R.
14. Bhatt M, Shenoy DS, Udupa N, Srinivas CR. Optimization of delivery of betamethasone-dipropionate from skin preparation. Indian Drugs. 1995; 32:211–4.
15. Diljyot K. Niosomes: a new approach to targeted drug delivery. Int J Pharm Phytopharm Res. 2012; 2:53–9.
16. Malhotra M, Jain NK. Niosomes as drug carriers. Indian Drugs. 1994; 31:81–6.
17. Giddi HS, Arunagirinathan MA, Bellare JR. Self-assembled surfactant nano-structures important in drug delivery: a review. Indian J Exp Biol. 2007; 45:133–59.
18. Biju SS, Talegaonkar S, Mishra PR, Khar RK. Vesicular systems: an overview. Indian J Pharm Sci. 2006; 68:141–53.
19. Gandhi A, Sen SO, Paul A. Current trend in niosome as vesicular drug delivery system. Asian J Pharm Life Sci. 2012; 2:339–53.
20. Kazi KM, Mandal AS, Biswas N, Guha A, Chatterjee SA, Behera M, et al. Niosome: a future of targeted drug delivery systems. J Adv Pharm Tech Res. 2010; 1:374–80.
21. Makeshwar K, Wasankar S. Niosomes: a novel drug delivery system. Asian J. Pharm. Res. 2013; 3: 16-20.
22. Sankhyan A, Pawar P. Recent Trends in Niosome as Vesicular Drug Delivery System. Journal of Applied Pharmaceutical Science. 2012; 2: 20-32.
23. Gurjar P. Niosome: A Promising Pharmaceutical Drug Delivery. Int. J. Pharm Anal. 2014; 2: 425-431.
24. Keshavshetti GG, Shirsand SB. Recent advances in niosomal drug delivery - a review. Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences, 2019; 5(3): 514-531.
25. Kalra N, Jeyabalan G. Niosomes: A versatile drug delivery system. Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences, 2016; 2(4): 44-54.
26. Bhat MI, Ganesh NS, Majeed T and Chandy V. Niosomes a controlled and novel drug delivery system: A brief review. World journal of Pharmaceutical sciences, 2019; 3(8): 481-497.
27. Usman MRM, Ghuge PR and Jain BV. Niosomes: a novel trend of drug delivery. European Journal of Biomedical and Pharmaceutical Sciences, 2017; 4(7): 436-442.
28. Sharma D, Ali AAE, aate JR. Niosomes as novel drug delivery system: review article. PharmaTutor, 2018; 6(3): 58-65.
29. Sudheer P, Kaushik K. Review on niosomes – a novel approach for drug targeting. Journal of Pharmaceutical Research, 2015; 14(1): 20-25.
30. Hadjizadeh A, Moghassemi S. Nano-niosomes as nanoscale drug delivery systems: an illustrated review. Journal of Controlled Release, 2014; 185: 22–36.
31. Zhang S, Morris ME. Efflux transporters in drug excretion. In: Wang B, Siahaan T, Soltero R, editors. Drug Delivery: Principles and Applications, New Jersey, John Wiley &Sons publishers, 2005 .p. 381–398.
32. Bhatt P, Lalani R, Vhora I, Patil S, Amrutiya J, Misra A, et al. Liposomes encapsulating native and cyclodextrin enclosed paclitaxel: Enhanced loading efficiency and its pharmacokinetic evaluation. International journal of pharmaceutics. 2018;536(1):95-107.
33. Shtil AA, Grinchuk TM, Tee L, Mechenter EB, and Ignatova TN. Overexpression of P-glycoprotein is associated with a decreased mitochondrial transmembrane potential in doxorubicin selected K562 human leukaemia cells. International Journal of Oncology, 2000; 17: 387–392.
34. Kumar SD, Agarwal S, Sheikh MM, Raveendran S, Rochani AK, Maekawa T. Formulation, characterization and evaluation of morusin loaded niosomes for potentiation of anticancer therapy. Royal Society of Chemistry Advances, 2018; 8: 32621- 32636.
35. Amoabediny G, Naderinezhad S, Haghiralsadat F. Co-delivery of hydrophilic and hydrophobic anticancer drugs using biocompatible pH-sensitive lipid-based nano-carriers for multidrug-resistant cancers. Royal Society of Chemistry Advances, 2017; 7: 30008–300019.
36. Ueda K, Okamura N, Hirai M, Tanigawara Y, Saeki T,Kioka N, Komano T and Hori R. Human P-glycoprotein transports cortisol, aldosterone, and dexamethasone, but not progesterone. The Journal of Biological Chemistry, 1992; 267(34): 24248- 24252.
37. Greenblatt DJ, Perloff MD, Moltke LLV, Marchand JE. Ritonavir induces P-glycoprotein expression, multidrug resistance associated protein (MRP1) expression, and drug transporter mediated activity in a human intestinal cell line. Journal of Pharmaceutical Sciences, 2001; 90(11): 1829-1837.
38. Kumar GP, Rajeshwarrao P. Nonionic surfactant vesicular systems for effective drug delivery—an overview. Acta Pharmaceutical Sinica B, 2011; 1(4):208-219.
39. Nasir A, Harikumar SL and Kaur A. Niosomes: An excellent tool for drug delivery. International Journal of Research in Pharmacy and Chemistry's, 2012; 2(2): 479-487.
40. De S, Girigoswami A, Das S. Fluorescence and dynamic light scattering studies of niosomes membrane mimetic systems. Spectrochimica Acta Part A, 2006; 64: 859-866.
41. Rogerson A, Cummings J, Florence AT. Adriamycin-loaded niosomes-drug entrapment, stability and release. Journal of Microencapsulation, 1987; 4(4): 321– 328.

42. Cummings J, Rogerson A, Florence AT, Willmott N. The distribution of doxorubicin in mice following administration in niosomes. J. Pharm. Pharmacology., 1988; 40: 337-342.
43. Louis D, Mahmoud K, Mohamed M and Ibrahim A. An overview on niosomes: a drug Nano carrier. Drug Designing and Intellectual Properties International Journal, 2018; 1(5): 143- 151.
44. Uchegbu IF, Lalatsa A, Wong D (2013). Polymeric nanoparticles. In: Uchegbu IF, Schatzlein AG, Cheng WP and Lalatsa A editors. Fundamentals of pharmaceutical Nano science, Springer, New York, USA Publishers, .p. 211-234.
45. Khan R, Irchhaiya R. Niosomes: a potential tool for novel drug delivery. Journal of Pharmaceutical Investigation, 2016; 46(3): 195-204.
46. Dwivedi C, Kumar B, Tiwari SP, Satapathy T, Yadav R, Sahu G, Roy A. Niosomes: an excellent tool for drug delivery. Int.J.of Res. in Pharmacology and Pharmacotherapeutics, 2014; 3(3): 192- 204.
47. Cetinel S, Zarrabi A, Durak S, Rad ME, Yetisgin AA, Sutova HE and Kutlu O. Niosomal drug delivery systems for ocular disease—recent advances and future prospects. Nanomaterials, 2020; 10(6): 1-29.
48. More VV, Gilhotra RM, Manoj M. Nitalikar, Prajakta K. Khule. Niosomal drug delivery - a comprehensive review. Asian Journal of Pharmaceutics, 2018; 12(4): 1159-1164.
49. Baillie AJ, Coombs GH, Dolan TF, Laurie J. Non-ionic surfactant vesicles, niosomes, as a delivery system for the anti-leishmanial drug, sodium stibogluconate. J. Pharm Pharmacol., 1986; 38: 502-505.
50. Chavda VP. Niosome: a vesicular weapon for targeted and controlled drug delivery. Indian Journal of Novel Drug Delivery, 2016; 8(3): 133-156.
51. Frank LS and Huang L. Large scale production of DC-Chol cationic liposomes by microfluidization. International Journal of Pharmaceutics, 1996; 144(2): 131–139.
52. Gowda DV, Jain SC, Gupta NV, Kulkarni PK. A brief review on niosomes. Journal of Pharmacy Research, 2017; 11(5): 450-458.
53. Raja NR, Pillai GK, Udupa N, Chandrashekar G. Antiinflammatory activity of niosome encapsulated diclofenac sodium in arthritic rats. Indian Journal of Pharmacology, 1994; 26(1): 46-48.
54. Sunilkumar MR, AdlinJinoNesalin J, Man TT. Niosome as a novel drug delivery system-review. Internationa Research Journal of Pharmaceutical and Applied Siences, 2015; 5(3): 1-7.
55. Lohumi A, Rawat S, Sarkar Si, Sipai AB, Yadav MV. A novel drug delivery system: niosomes review. Journal of Drug Delivery & Therapeutics, 2012; 2(5): 129-135.
56. Mayer LD, Bally MB, Hope MJ, Cullis PR. Uptake of antineoplastic agents into large unilamellar vesicles in response to a membrane potential. Biochem Biophys Acta, 1985; 816(2): 294- 302.
57. Kuotsu K, Karim MK, Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M. Niosome: a future of targeted drug delivery systems. J Adv Pharm Tech Res., 2010; 4(1): 374-380.
58. Navya MN, Parthiban S, Neasalin JAJ, Vikneswari A. Niosomes as novel vesicular drug delivery system- a review. Asian Journal of Research in Biological and Pharmaceutical Sciences, 2014; 2(2): 62-68.
59. Chauhan S, Luorence MJ. The preparation of polyoxyethylene containing non-ionic surfactant vesicles. J Pharm Pharmacol., 1989; 41(6).
60. Yuan WE, Xuemei Ge, Minyan Wei, Suna H. Advances of nonionic surfactant vesicles (niosomes) and their application in drug delivery. Pharmaceutics, 2019; 11(2): 1-16.
61. Yadav JD, Kulkarni PR, Vaidya KA, Shelke GT. Niosomes: a review. Journal of Pharmacy Research, 2011; 4(3): 632-636.
62. Khanam N, Alam MI, Sachan AK, Gangwar SS, Sharma R. Recent trends in drug delivery by niosomes: a review. Asian Journal of Pharmaceutical Research and Development, 2013; 1(3): 115- 122.
63. Sudhamani T, Priyadarisini N, Radhakrishnan M. Proniosomes - a promising drug carriers. International Journal of PharmTech Research, 2010; 2(2): 1446-1454.
64. Almira I, Blazek-Welsh, Rhodes DG. Maltodextrin-Based Proniosomes. AAPS Pharm SciTec., 2001; 3(1): 1-8.
65. Blazek-Walsh AI and Rhodes DG. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharmceutical Research, 2001; 18: 656-661.
66. Gandhi M, Paralkar S, Sonule M, Dabhade D and Pagar S. Niosomes: novel drug delivery system. International Journal of Pure and Applied Bioscience, 2014; 2(2): 267-274.
67. Akhilesh D, Kamath JV. Review on span-60 based non-ionic surfactant vesicles as novel drug delivery. International journal of research in pharmaceutical and biomedical sciences, 2012; 3(1): 6-12.
68. Kazi KM, Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M, et al. Niosome: A future of targeted drug delivery systems. J Adv Pharm Technol Res. 2010;1(4):374-80. doi: 10.4103/0110-5558.76435, PMID 22247876.
69. Mohamad EA, Aly AA, Khalaf AA, Ahmed MI, Kamel RM, Abdelnaby SM, et al. Evaluation of natural bioactive-derived punicalagin niosomes in skinaging processes accelerated by oxidant and ultraviolet radiation. Drug Des Dev Ther. 2021;15:3151-62. doi: 10.2147/DDDT.S316247, PMID 34321865.
70. Sharma P, Jain AP, Pandey P, Gupta R, Roshan S. Niosome a novel approach for drug delivery system: an overview. Asian Journal of Pharmaceutical science and Research, 2013; 3(5):18- 30.
71. Cummings J, Staurt JF, Calman KC. Determination of adriamycin, adriamycinol and their 7- deoxyaglycones inhuman serum by high performance liquid chromatography. Journal of Chromatography, 1984; 311: 125-33.
72. Vadlamudi CH, Sevukarajan M. Niosomal drug delivery systema review. Indo American Journal of Pharmceutical Research, 2012; 2(9).
73. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. International Journal of Pharmaceutics, 1998; 172: 33-70.
74. Nasseri B. Effect of cholesterol and temperature on the elastic properties of niosomal membranes. International Journal of Pharmaceutics, 2005; 300: 95-101.
75. Mahale NB, Thakkar PD, Mali RG, Walunj DR, Chaudhari SR. Niosomes: novel sustained release nonionic stable vesicular systems - an overview. Advances in Colloid and Interface Science, 2012; 183-184: 46–54.
76. Sarker A, Shimu IJ, Alam SAA. Niosome: as dermal drug delivery tool. IOSR Journal of Pharmacy and Biological Science, 2015; 10(2): 73-79.
77. Sakthivel M, Kannan K, Manavalan, Senthamarai. Non-ionic surfactant vesicles-a review. Research Journal of Pharmaceutical, Biological and Chemical, 2012; 3(1):604-614.
78. Jindal K. Niosomes as a potential carrier system: a review. International Journal of Pharmaceutical, Chemical and Biological Sciences, 2015; 5(4): 947-959.
79. Sternberg B, Uchegbu IF, Florence AT and Murdan S. 1998.
80. Theresa MA. Drugs published by ADIS international Ltd. 1998; 56(5):747-756.
81. Buckton G and Harwood. Interfacial Phenomena in Drug Delivery and Targeting Academic Publishers, Switzerland. 1995;154-155.
82. Mujoriya R, Bodla RB, Dhamande K, Singh D and Patle L. Niosomal drug delivery system: the magic bullet. Journal of Applied Pharmaceutical Science, 2011; 1(9): 20-23.
83. Kalra N, Jeyabalan G, Singh G, Choudhary S. Non- ionic surfactant vesicles and their therapeutics potentials. Journal of Innovations in Pharmaceuticals and Biological sciences, 2016; 3 (2): 193-201.
84. Azeem A, Anwer MK and Talegaonkar S. Niosomes in sustained and targeted drug delivery: some recent advances. Journal of Drug Targeting, 2009; 17(9): 671-689.
85. Koh RY, Yeo PL, Chye SM and Ling APK. Niosome: a mini review on its structure, properties, methods of preparation and medical applications. Journal of Chemical and Pharmaceutical Research, 2016; 8(10): 231-239.
86. Yadav JD, Kulkarni PR, Vaidya KA, Shelke GT. Niosomes: a review. Journal of Pharmacy Research, 2011; 4(3): 632-636.
87. Pawar P, Sankhyan A. Recent trends in niosome as vesicular drug delivery system. Journal of Applied Pharmaceutical Science, 2012; 2(6): 20-32.
88. Lalani R, Misra A, Amrutiya J, Patel H, Bhatt P, Patel V. Challenges in Dermal Delivery of Therapeutic Antimicrobial Protein and Peptides. Current Drug Metabolism. 2017; 18(5):426-36.
89. Abd-el-Kader H, Alani AWG and Alany RG. Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. Drug Delivery, 2013; 21(2): 87-100.
90. Gayatri Devi S, Venkatesh P, Udupa N. Niosomal sumatriptan succinate for nasal administration. Int J Pharm Sci 2000;62:479-81

.