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A Review on – Niosomes Used As a Carrier for Novel Drug Delivery System

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ABSTRACT

A novel drug delivery system (NDDS) that encapsulate the medicine in a vesicle is called a niosome. Niosomes get their name from the bilayer of non-ionic surface-active chemicals that make up the vesicle. The niosomes are tiny, microscopic particles. The nanometric scale shows where their size lies. Despite sharing structural similarities with liposomes, they have a number of benefits over them. Development of an NDDS has been a topic of study interest. The goal of NDDS is to transport the medication to the site of action and administer the active component at a rate determined by the body's requirements over the course of a disease's therapy. Many NDDS have been reported to accomplish targeted and controlled drug delivery using a number of administration techniques. One of the most crucial processes is the encapsulation of the medication in vesicular structures, which, if recommended absorption is successful, may be expected to extend the drug's half-life in systemic circulation and decrease its toxicity. As a result, several vesicular drug delivery systems were created, including pharmacosomes, liposomes, niosomes, and transfersomes. Since then, vesicular drug delivery has developed, resulting in the creation of systems that enable drug targeting and the prolonged or regulated release of traditional medications. This study focuses on the many preparation methods, niosome characterisation, benefits, and highlights the vesicular systems of application.

Keywords – Niosomes, Prolonged delivery, NDDS, Vesicle, Drug targeting.

INTRODUCTION

In 1990 When Paul Ehrlich envisioned a medicine delivery system that would target diseased cells directly, then he launched the field of targeted delivery research. The capacity to accurately direct a medicinal agent to the intended site of action with little to no contact with non-target tissue is known as drug targeting.[1]

Liposomes and niosomes are two well-established drug delivery vehicles among other carriers. The capacity to precisely guide a medicinal agent to the intended site of action with little to no contact with non-target tissue is known as drug targeting.[2]

Niosomes, also known as non-ionic surfactant vesicles, are tiny lamellar structures that are created when cholesterol and non-ionic surfactant belongs to the alkyl or dialkyl polyglycerol ether class are mixed together and then hydrated in aqueous conditions. Niosomes are unilamellar or multilamellar vesicles made of artificial non-ionic surfactants that show great promise as a drug delivery vehicle due to their non-ionic nature.To improve therapeutic targeting at the right tissue location, the drug is integrated into niosomes.[3]

Niosomes are tiny, biodegradable, non-immunogenic, and biocompatible lamellar structures that range in size from 10 to 1000 nm.[4]

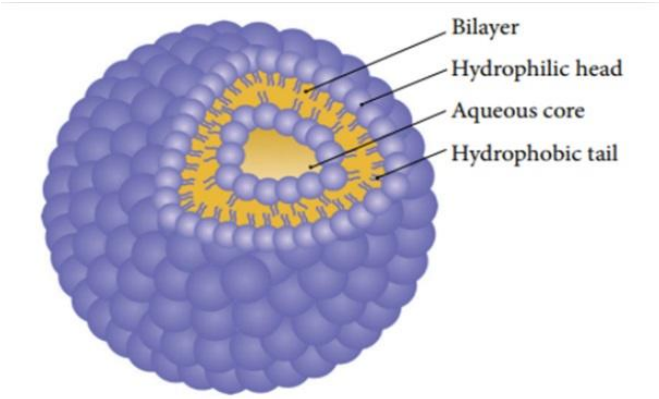

Fig : 1 Structure of niosomes.

Salient Features OfNiosomes [5]

- Niosomes function as liposome substitutes. This eliminates the liposomes' drawbacks.
- Stable and osmotically active.
- The stability of the medication entrapped is increased by niosomes.
- They can be used topically, parenterally, or orally to reach the site of action.
- There are no unique requirements for the surfactant employed in niosomes.
- The surfactants utilized in niosomes are nonimmunogenic, biodegradable, and biocompatible.
- By delaying the medication molecules' clearance from the bloodstream, they enhance their therapeutic efficacy.
- Niosomes are flexible in terms of their size, content, and fluidity, and they may be shaped to fit specific requirements.

Composition Of Niosomes:

The main components of Niosomes are: 1. Non-ionic surfactants 2. Cholesterol

Non-ionic surfactants: - A group of surfactants known as non-ionic surfactants lacks charged groups in their hydrophilic heads. When compared to their anionic or cationic alternatives, they are less poisonous, more stable, more biocompatible. The two distinct sections of non-ionic surfactants are hydrophilic (water soluble) and hydrophobic (organic soluble).

The primary non-ionic surfactants used in the manufacture of niosomes include fatty acids, alkyl ethers, alkyl esters, and alkyl amides.[6]

Cholesterol: cholesterol is a derivative of a steroid that is used to give niosomes their appropriate shape and stiffness. The physical characteristics of niosomes, including their entrapment efficiency, long-term stability, payload release, and biostability, are influenced by their cholesterol concentration. [7,8]

Examples: Spans (span 20, 60, 40, 80, 85)

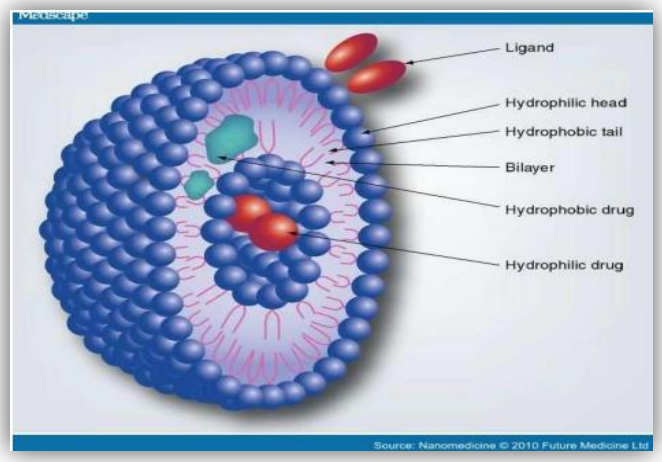

Figure 2 : - Internalstructure of niosomes.

Types of Niosomes

The niosomes are classified as function of the number of bilayer (e.g., SUV, MUV) or as a function of size (e.g., LUV, SUV) or as a function of the method of preparation (e.g., REV, DRV). There are mainly three types of niosomes. The various types of niosomes are described below:

i) Multi lamellar vesicles (MLV),
ii) Large unilamellar vesicles (LUV),
iii) Small unilamellar vesicles (SUV).

Multi lamellar vesicles (MLV): - They are made up of many bilayers that each surround the aqueous lipid compartment in turn. Such vesicles range in diameter from 0.5 to 10 μm. The most popular niosomes are MLV. which are easy to assemble and maintain their mechanical stability over time in storage. These vesicles work best as medication carriers for substances that are lipophilic. [9,10]

Large unilamellar vesicles (LMV): -These niosomes have a high aqueous to lipid compartment ratio, which makes it possible to entrap a significant number of bioactive molecules while using membrane lipids extremely little. Large unilamellar vesicles are larger than 0.10μm in size.[9,11]

Small unilamellar Vesicle (SLV): - These niosomes are often made from multilamellar vesicles using homogenization, French press extrusion, or sonication techniques. Small unilamellar vesicles, with a diameter of 0.025-0.05 μm, are prone to aggregation and fusion due to their thermodynamic instability. Their proportion of an aqueous solute entrapped is modest, and their entrapped volume is minimal as well. [9,12]

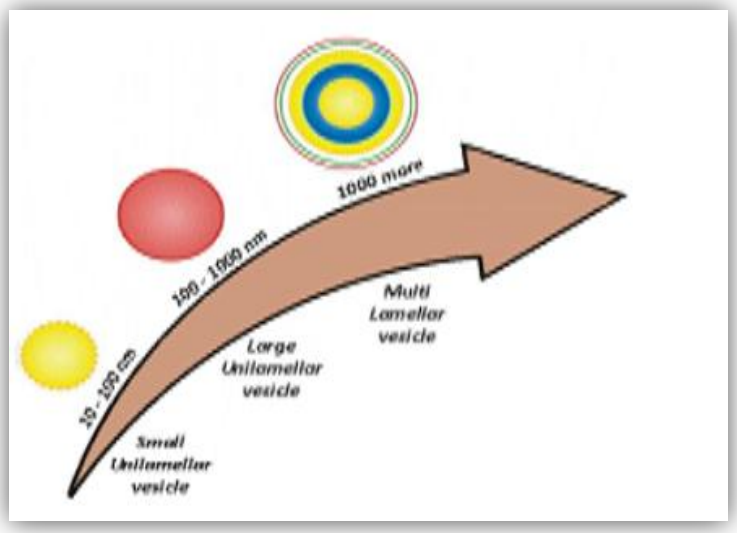

Figure 3: - Types of niosomes.

Advantages[13,14,15]

- ✓ Owing to their unique structure, which combines hydrophilic, amphiphilic, and lipophilic components, they are able to accept a broad variety of solubilities in pharmacological molecules.
- ✓ To control the pace of drug administration and provide a normal vesicle in the exterior non-aqueous phase, niosomal dispersion in an aqueous phase can be emulsified in a non-aqueous phase.
- ✓ Biodegradable, biocompatible, and non-immunogenic surfactants are used.
- ✓ They increase drug penetration via the epidermis and increase the oral bioavailability of poorly absorbed medications.
- ✓ The vesicle formulation's properties are changeable and manageable. The properties of the vesicles may be changed by adjusting their concentration, size, lamellarity, tapping volume, surface charge, and composition.
- ✓ They can be administered topically, parenterally, or orally to reach the site of action.

Disadvantage [13,14,15]

- ✓ The niosome formulation are physically unstable.
- ✓ In niosome formulation sometimes different charge present on surface of noisome vesicles due to that opposite charge come to near and fusion of niosome vesicle occur.
- ✓ Many times, niosome shows aggregation if standard method of preparations not followed.
- ✓ Hydrolysis of entrapped drug take place sometimes.
- ✓ In some cases, found insufficient drug loading.
- ✓ Formulation of niosome is time consuming process.

Method Of Preparation

1) Preparation of multilamellar vesicles
2) Preparation of Small unilamellar vesicle
3) Preparation of Large Unilamellar Vesicle

1) Preparation Of Multilamellar Vesicles

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

In a round-bottom flask, the mixture of surfactant and other vesicles-forming ingredients, such as cholesterol, is dissolved in a volatile organic solvent such as diethyl ether, chloroform, or methanol. By removing the organic solvent at room temperature (20°C) with a rotary evaporator, a thin layer of solid mixture is left on the flask wall. Multilamellar Niosomes can be formed by rehydrating the dried surfactant film with an aqueous phase at 60°C and gently stirring it. [16]

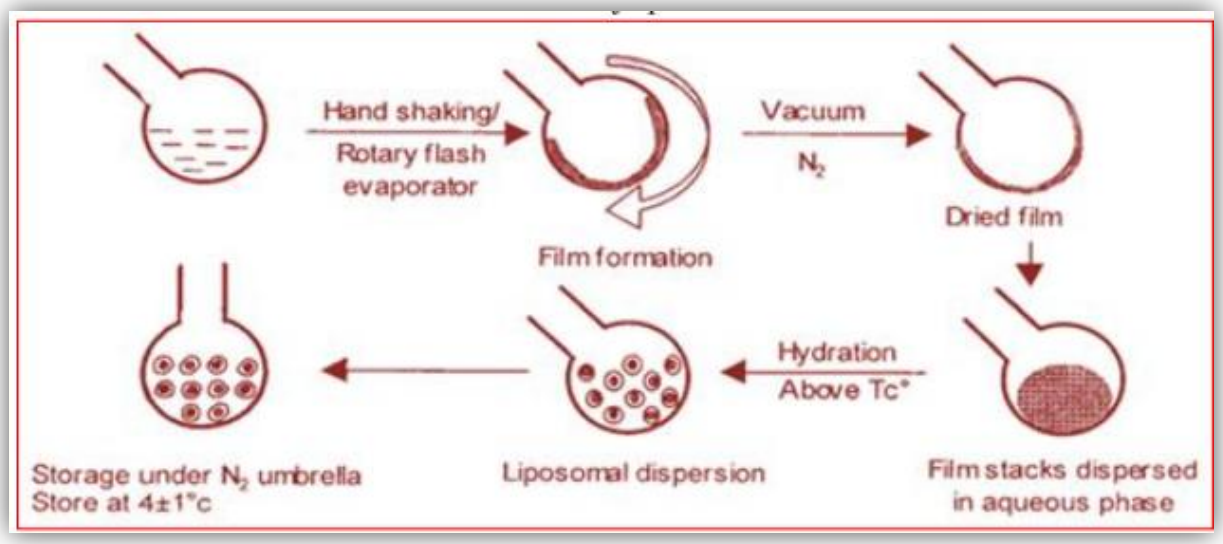

Fig 4: - Hand shaking / thin film hydration technique.

b) Trans-membrane pH gradient (inside acidic) drug uptake process (Remote Loading):

A mixture of surfactant and cholesterol is dissolved in chloroform in a round-bottom flask. The chloroform is then evaporated at low pressure to leave a thin layer on the flask wall. By vortex mixing 300 mM citric acid (pH 4.0) with the film, it is hydrated. After three cycles of freezing and thawing, the multilamellar vesicles are subjected to sonication. This niosomal suspension is mixed with an aqueous solution containing 10 mg/ml of medication, then vortexed. To create the necessary multilamellar vesicles, the pH of the sample is increased to 7.0–7.2 using 1M disodium phosphate. The mixture is then heated at 60°C for 10 minutes. [17, 18]

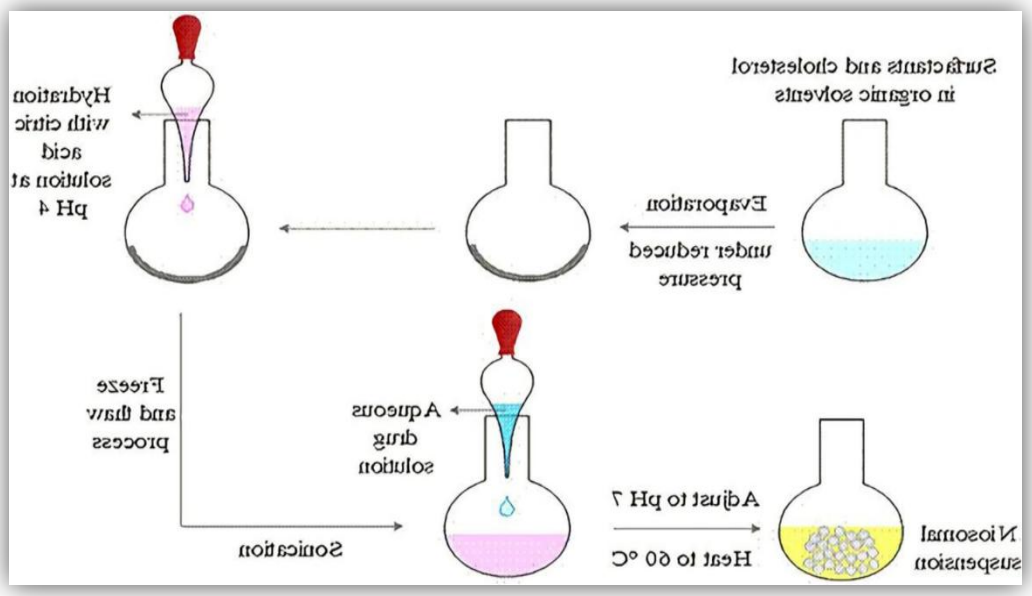

Fig 5: - Trans membrane method.

2) Preparation Of Small Unilamellar Vesicle.

a) Sonication

A 10-ml glass vial containing a drug solution in buffer is introduced to the combination of surfactant and cholesterol in order to produce the vesicles using a standard procedure. The mixture is then subjected to 3 minutes of probe sonication at 60°C using a titanium probe sonicator in order to produce niosomes. Little, unilamellar vesicles are the finish outcome. [19]

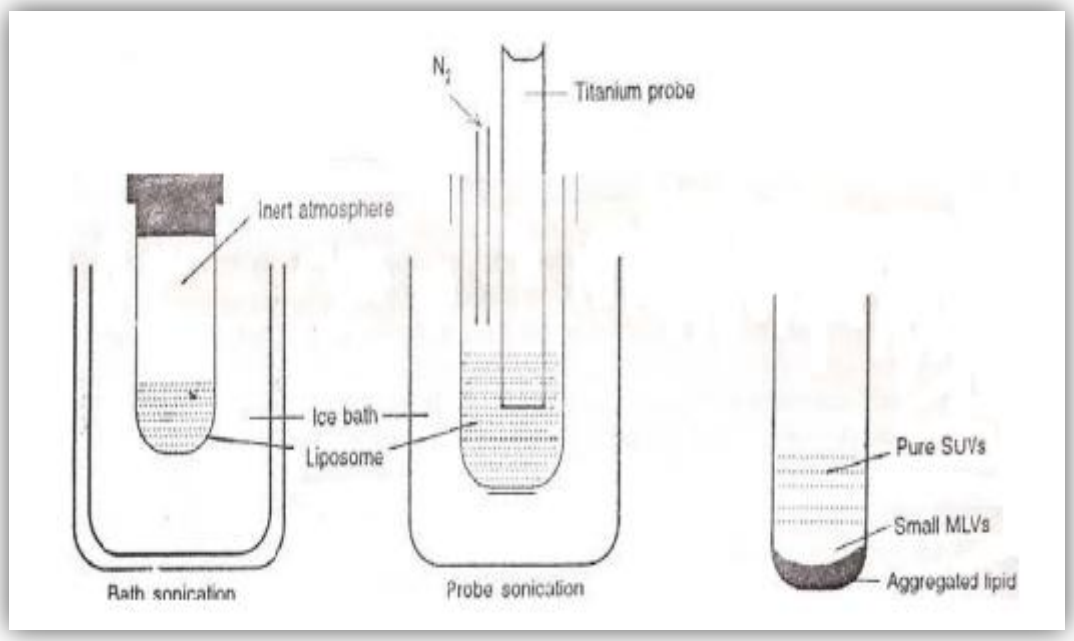

Fig 6: - Sonication method.

a) Micro fluidization

A novel approach for creating unilamellar vesicles with a specified size distribution is called micro fluidization. This technique is based on the submerged jet principle, which involves the ultrahigh-velocity interaction of two fluidized streams in precisely specified microchannels inside an interaction chamber. The arrangement of the thin liquid sheet impingement along a common front ensures that the energy input to the system stays inside the region where niosomes develop. The niosomes that are produced as a result are more homogenous, smaller, and more reproducible. [20]

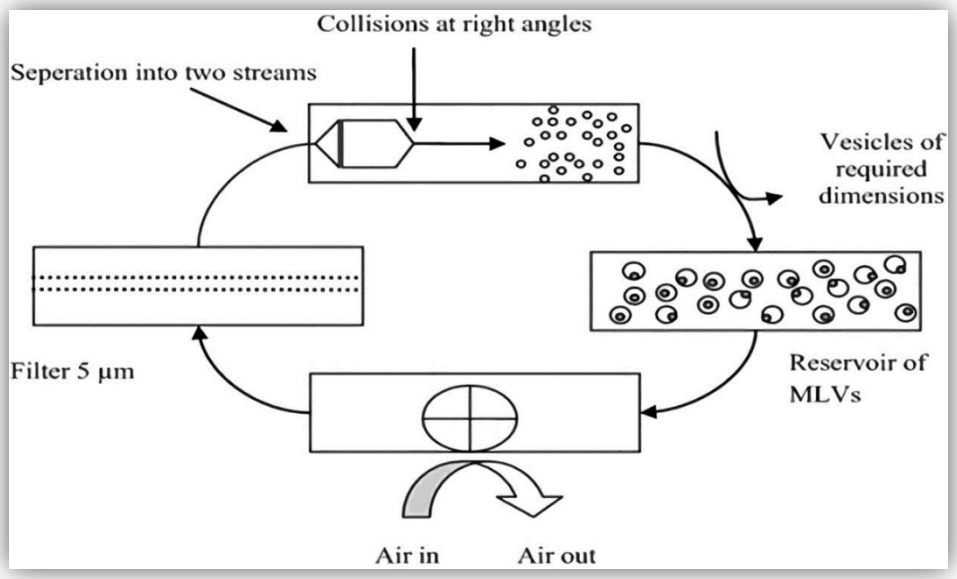

Fig 7: - Micro fluidization method.

3) Preparation Of Large Unilamellar Vesicle

a) **Reverse phase evaporation technique**

Chloroform and ether were used to dissolve cholesterol and surfactant (1:1). After adding a drug-containing aqueous phase, the two resultant phases were sonicated at 4-5°C. Following more sonication of the clear gel that had developed, a little amount of phosphate buffered saline (PBS) is added. At 40°C, low pressure was used to remove the organic phase. To improve niosome yield, the resultant viscous niosome suspension was heated on a water bath at 60°C for 10 minutes after being diluted with PBS. [21]

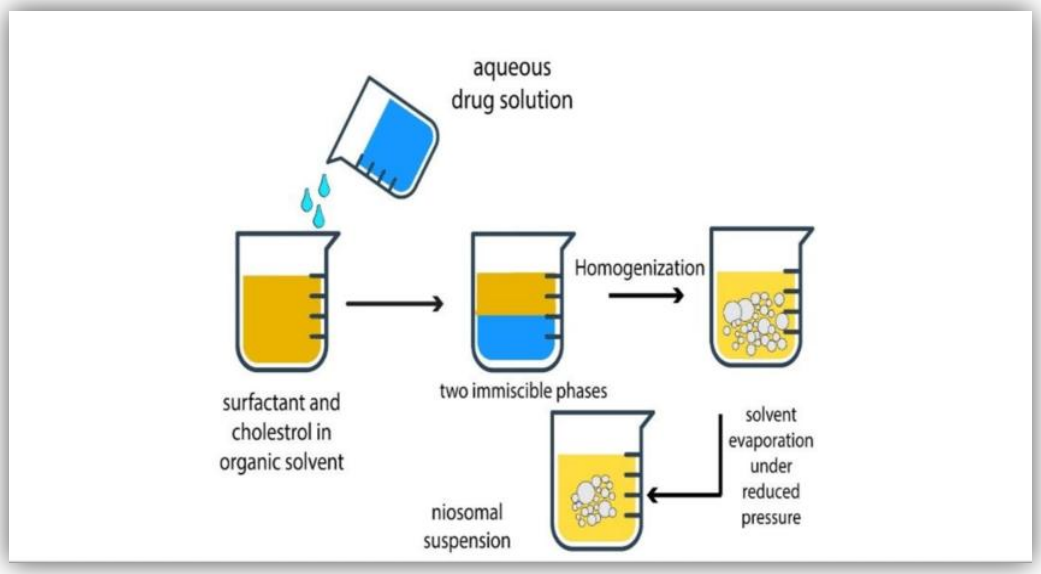

Fig 8: - Reverse phase evaporation method.

b) **Ether Injection Method**

The fundamental principle of the ether injection method is the gradual infusion of noisome components in diethyl ether into a heated aqueous phase maintained at 60°C using a 14-gauge needle at a rate of around 0.25 ml/min. The creation of bigger unilamellar vesicles is likely due to the slow vaporization of the solvent, which creates an ether gradient that extends towards the aqueous-nonaqueous boundary. The bilayer structure may have formed as a result of the former. This method's drawback is that it might be challenging to eliminate the tiny quantity of ether that is usually present in the suspension of the vesicles. [16, 22]

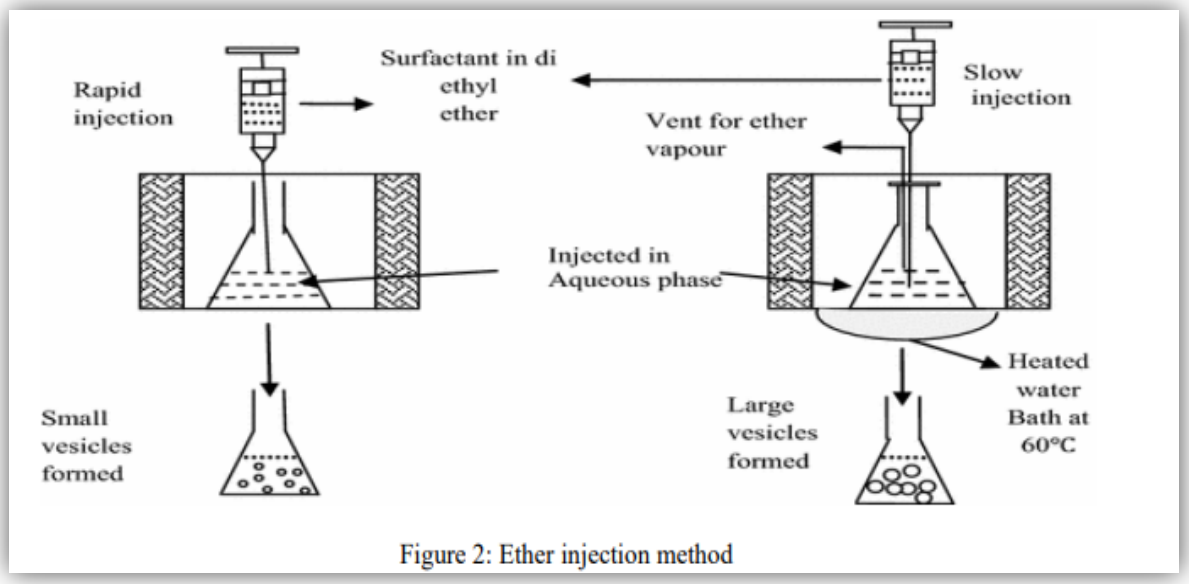

Fig 9: - Ether injection method.

4) Miscellaneous

a) **The 'Bubble' method**

This innovative method eliminates the need for organic solvents and allows for the one-step synthesis of liposomes and niosomes. The bubbling unit is made up of a flask with a circular bottom and three necks that are positioned in a water bath to regulate temperature. The nitrogen supply passes via the third neck, while the water-cooled reflux and thermometer are located in the first and second necks. In this buffer (pH

7.4), the cholesterol and surfactant are combined and stirred for 15 seconds with a high shear homogenizer. The mixture is then "bubbled" at 70°C with nitrogen gas to produce niosomes. [23]

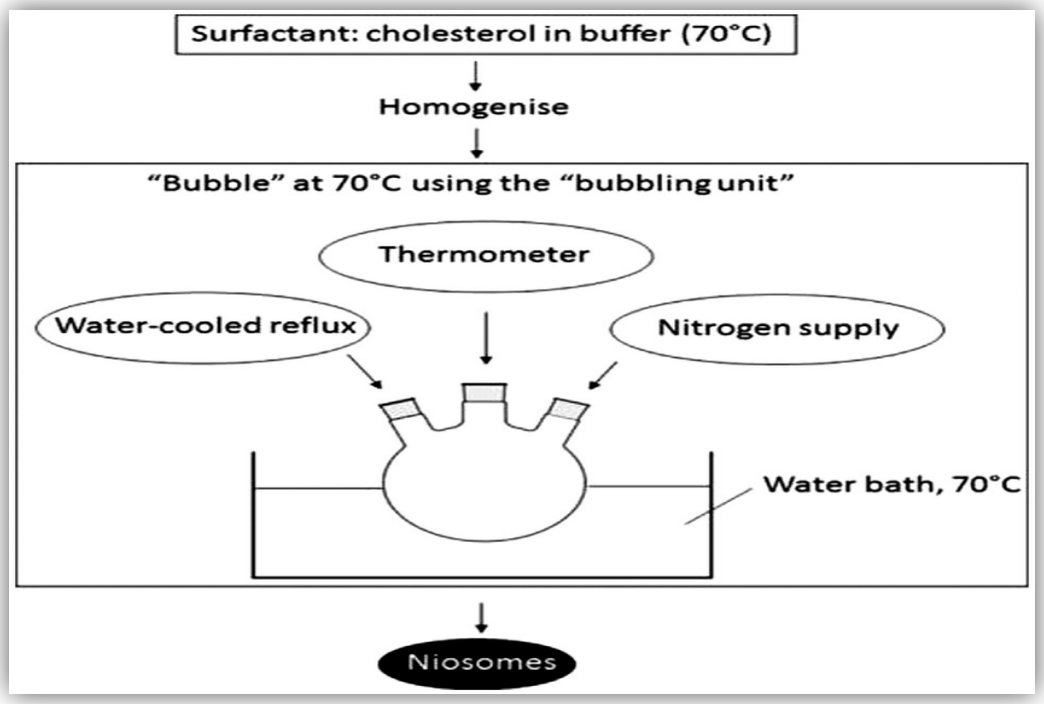

Fig 10: - The bubble method.

b) **Multiple membrane extrusion method**

A mixture of diacetyl phosphate, cholesterol, and surfactant is dissolved in chloroform, and when the solvent is removed, a thin layer is created. The film is hydrated with an aqueous drug solution, and the resulting suspension is then extruded through a sequence of polycarbonate membranes that may accommodate up to eight passes. This is the most effective way to regulate niosome size. [24]

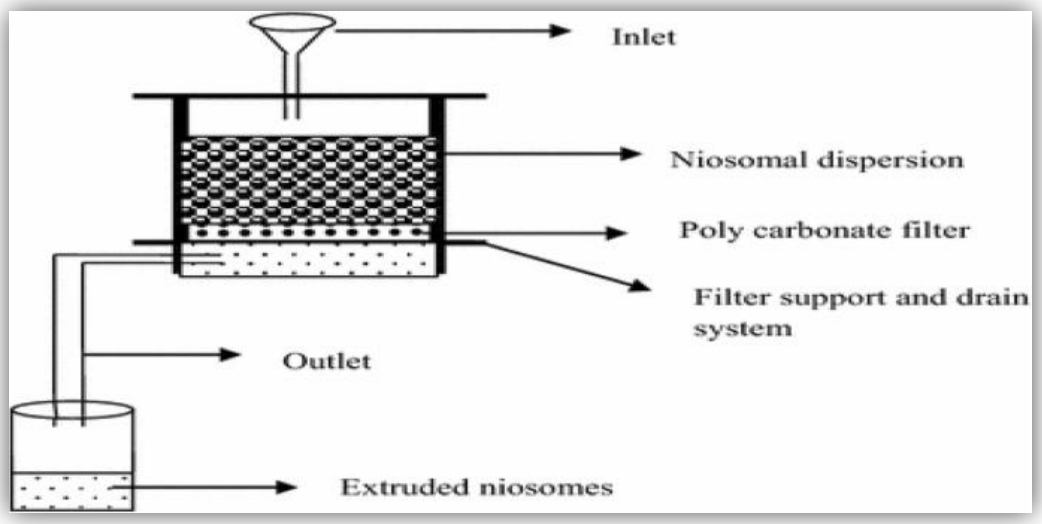

Fig 11: - Multiple membrane extrusion method

c) **Formation of niosomes from proniosomes**

Coating a water-soluble carrier, such sorbitol, with a surfactant is another way to make niosomes. Every water-soluble particle in the dry formulation produced by the coating process has a thin layer of dry surfactant covering it. We refer to this preparation as "proniosomes." The niosomes are recognized by the addition of aqueous phase at T > Tm and brief agitation.[25]

Where, T = Temperature

Tm = Mean phase transition temperature.

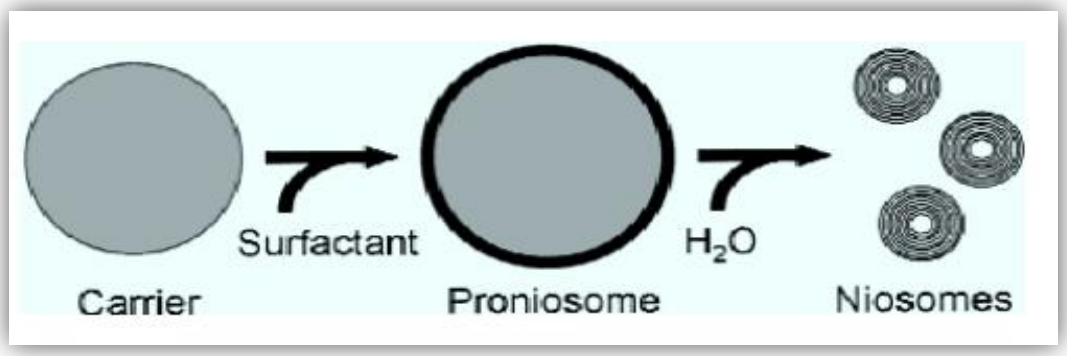

Fig 12: - Formation of niosomefrom proniosome.

Factors Affecting Physico Chemical Properties Of Niosomes.

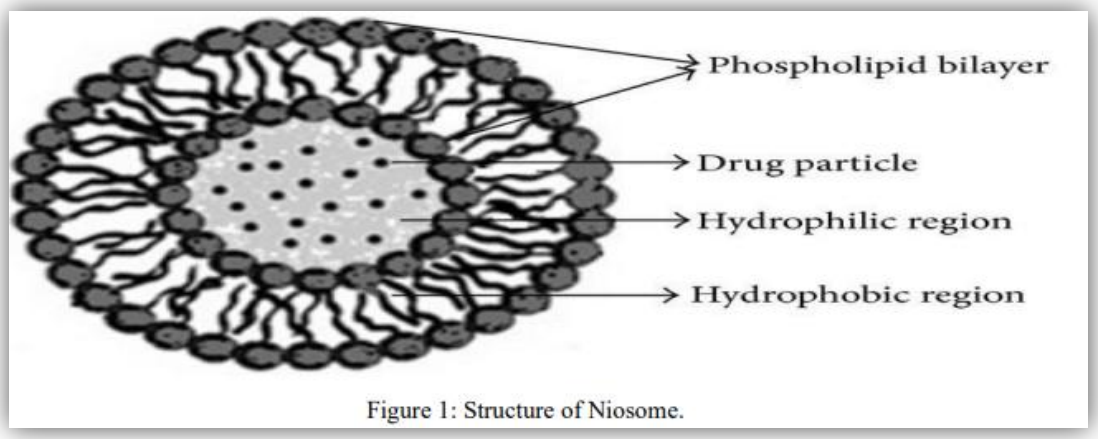

Fig 13:- Structure of niosomes.

1) **Cholesterol content and charge**

Steroids are essential parts of cell membranes, and their presence modifies the fluidity, permeability, and bilayer stability of the membrane in important ways. Additionally, cholesterol increases the diameter and entrapment efficiency.[26]Increased vesicle rigidity and a slower rate of drug release from the encapsulated form result from higher cholesterol content added to the formulation. There are two ways that cholesterol acts: first, it increases the lipid state bilayer order; second, it decreases the gel state bilayer order. High concentrations of cholesterol caused the gel state to change into a liquid order state. The interlamellardistance between successive bilayers in a multilamellar vesicle (MLV) increases if cholesterol has any charge.[27]

2) **Nature of surfactant:**

Table illustrates how the hydrophilicity and lipophilicity of the surfactant affect the niosome. The size of the niosome vesicle increases as the surfactant's HLB value rises, from span-85 (HLB-1.8) to span-20 (HLB-8.6), as the surfactant's lipophilicity increases and its surface free energy decreases. Depending on the kind of lipid and surfactant, temperature, and other factors like cholesterol, the visible bilayer can be liquid or gel-like. Alkyl chains are present in the gel phase properly, however the bilayer structure is not present in the liquid state. Gel-liquid phase transition temperature (TC) is a useful tool for identifying lipids and surfactants. The phase transition temperature of the surfactant affects the entrapment efficiency as well. For instance, span-60, which has higher TC, exhibits higher entrapment. When preparing niosomes, surfactants with an HLB value between 14 and 17 are not recommended.[28]

3) **Drug properties**

The charge and stiffness of the niosome bilayer are influenced by the physico-chemical characteristics of the medication that is encapsulated. The medication interacts with the head groups of surfactants and builds the charge that causes surfactant bilayers to repel one another, increasing the size of the vesicles. The drug's entrapment efficiency is influenced by the HLB value as well. As vesicle size increases, drug trapping in niosome also increases. The drug's trapping in the niosome causes the solute charge and surfactant head group to interact, increasing the vesicle's size in the process. A medication applied to polyethylene glycol-coated vesicles decreases the vesicle's tendency to enlarge. [29]

Table 1:- Relation of drugs nature with stability.

Nature of drug	Leakage from Vesicles	Stability
a) **HydrophobicDrugs**	Decrease	Increase
a) **Amphiphilic Drugs**	Decrease	----------
b) **Hydrophilic Drugs**	Increase	Decrease
c) **Macromolecules**	Decrease	Increase

4) Membrane composition

Drugs, surfactants, and other additions can be used to create niosomes. Various morphological, stability, and permeability properties of niosomes may be changed by using various additives. By preventing the aggregation of niosomes that happens as a result of stearic unhyndrance, C16G2 produce a polyhedral niosome that is unaffected by the addition of low concentrations of solulan C24 (cholesterol poly-24-oxyethylene ether). A spherical niosome is formed by the ratio of C16G2:cholesterol:solution (49:49:2). The composition of the membrane influences the size of the niosome. Polyhedral niosomes formed by C16G2: solution C24(91:9) have a size of around 8.0 ± 0.03 mm, while spherical niosomes formed by C16G2: cholesterol: solution (49:49:2) have a size of approximately 6.6 ± 0.2 mm. [29,30]

5) Temperature of hydration

The noisome's shape and size are influenced by the temperature of the hydration. It should be above the system's gel to liquid phase transition temperature for optimal conditions. The synthesis of surfactants into vesicles and the induction of vesicle shape change are both affected by temperature changes in the niosomal system. [31]

6) Resistance to osmotic stress: -

The diameter of a suspension of niosomes decreases when a hypertonic salt solution is added. The slow release of vesicles in hypotonic salt solution is likely caused by the inhibition of fluid eluting from the vesicles. This is followed by a rapid release, which might be the result of mechanically loosening the vesicles' structure under osmotic stress.[32]

7) Structure of surfactant: -

The shape and size of niosome vesicle are depends on Critical Packing Parameter (CPP), according to CPP we can predict the geometry of niosome vesicle.

Critical Packing Parameter (CPP)= v / lc. a0

Where, v= hydrophobic group volume, lc= the critical hydrophobic group length, a0 = the area of hydrophilic head group.

CPP is helpful in predicting the structure of niosome vesicles in following way;

- Spherical micelles formed if CPP less than 1/2.
- Bilayer micelles are formed if CPP between 0.5 to 1.
- Inverted micelles are formed if CPP more than 1. [33]

Separation Of Un- Entrapped Drugs[30,34,35]

a) Dialysis

Using the appropriate dissolving media, the aqueous niosomal suspension is dialyzed at room temperature in dialysis tubing, dialysis membrane, or cellulose bag. After the sample was removed from the medium at an appropriate period, it was centrifuged and its drug content was determined using either UV spectroscopy or HPLC.

Merits: -

i) Inexpensive and easy to performed.
ii) Suitable for highly viscous system
iii) Many time dilutions of niosomal suspension take place.

Demerits: -

i) Tedious and extremely slow process.
ii) Chances of dilution of niosomal suspension

b) Gel filtration or column chromatography

Phosphate buffer or normal saline can be used as a suitable mobile phase together with a sephadex-G-50 column to elute and analyze the unentrapped medication in the niosomal suspension using an appropriate analytical method.

Merits: -

i) It is a Very quick technique.

Demerits: -

i) Pre-treatment of the column with empty niosome required.
ii) Gel are costly when it not re-used.
iii) It not suitable for highly viscous and large particle (>10 – 20 µm).

c) Centrifugation

The process of cooling centrifugation is used to separate unentrapped medication, with a rotating speed of less than 7000g and a temperature of 4°C for 30 minutes. It is dependent upon the component's molecular weight. As a result, two layers appear: the liquid supernatant and the niosomal pallets. To get rid of the unentrapped medication, the supernatant is removed and niosomal pallets are washed with phosphate buffer or distilled water. Once more, the niosomal pallet solution is centrifuged to remove all of the unentrapped medication.

Merits: -

i) It is a Very fast process.
ii) This is inexpensive instrument.

Demerits: -

i) Sub-micron size vesicle fails to sediment.
ii) May leads to destruction of fragile system. The new advancement take place in above method is ultra-centrifugation in which separation of unentrapped drug take place with high speed about 150000 g for 1-1.5 hr.

Strengths And Limitations OfNiosomes In Drug Delivery

When compared to liposomes, one of niosomes' most significant advantages is their chemical stability. In comparison to liposomes, niosomes have a longer storage life and are more durable against oxidation or chemical degradation. The surfactants that are utilized in the niosome production process are nonimmunogenic, biodegradable, and biocompatible. There are no requirements for the handling or storage of surfactants. Furthermore, the kind of manufacturing process, surfactant, cholesterol content, surface charge additions, and suspension concentration may all be used to regulate the composition, size, lamellarity, stability, and surface charge of niosomes. [36]

Niosomes, on the other hand, have issues with physical stability. Niosomes exposed to dispersion may aggregate, fuse, hydrolyze the encapsulated medicines, or release pharmaceuticals. Moreover, niosome sterilization is a costly process. Thus, these areas need further research to produce commercially niosomal preparations.[37]

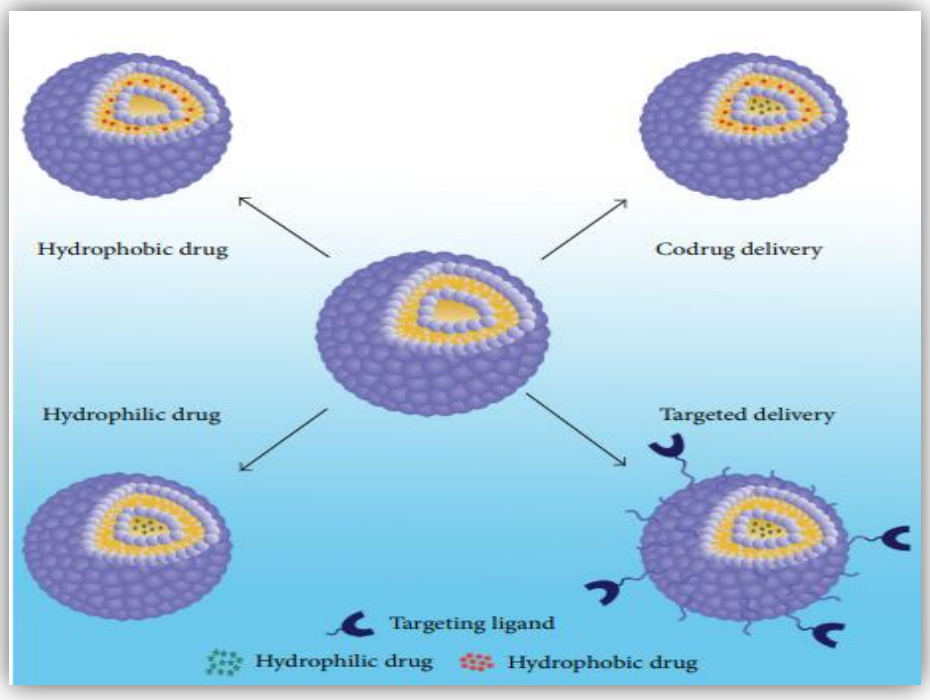

Figure 14: - Niosomes used in drug delivery

Table 2 : - Difference between niosomes and liposomes.

Sr No.	Niosomes	Liposomes
1	Surfactant used	Phospholipid used
2	Size 10 to 100 nm	Size 10 to 3000 nm
3	Inexpensive	Expensive
4	Not required special storage condition	Required special storage condition
5	Surfactant are more stable	Phospholipid are unstable
6	Less toxic	More toxic
7	Non-ionic surfactants are uncharged	Phospholipid may charge
8	Cholesterol Present	Do not contained cholesterol

Evaluation Of Niosomes

1) **Zeta potential**[40]

The charge that exists on the surface of a niosome is known as the zeta potential. The niosome surface has a charge that is present several times. The substance or component that was employed in the production process is what caused this charge.All of the niosomes in the formulation must have some charge on their surface in order to prevent coagulation of the particles and for all of the niosome particles to repel one another. Using a zeta sizer device with Malvern software, the niosome's zeta potential was measured. At 25°C, a 90° angle of detection was used for the sample analysis. It is necessary to have a zeta potential value that falls between +30 and -30 mV. The range in question inhibits the niosomal particles.

2) **Scanning electron microscopy**[41]

The niosomes' particle size is a crucial feature. Using scanning electron microscopy (SEM), the size distribution and surface morphology (roundness, smoothness, and forming aggregation) of niosomes were examined. On the double-sided tape that was attached to the aluminum stubs, niosomes were dispersed. The aluminum stub was inserted into the scanning electron microscope's vacuum chamber (XL 30 ESEM with EDAX, Philips, Netherlands). Using a gaseous secondary electron detector (working pressure: 0.8 torr, acceleration voltage: 30.00 KV) XL 30 (Philips, Netherlands), the samples were examined for morphological characterisation.

3) **Entrapment efficiency**[42]

The drug that is still entrapped in niosomes can be identified by completely disrupting the vesicles with 50% propanol or 0.1% Triton ×100, and then analyzing the resulting solution using the drug's specific assay method. The entrapment efficiency of the niosomal dispersion can be achieved by separating the unentrapped drug by dialysis centrifugation or gel filtration, as previously described.

Where,

$$\text{Percentage entrapment} = \frac{\text{Total drug} - \text{Diffused drug}}{\text{Total drug}}$$

4) In vitro release[43]

A frequently used technique for studying in vitro release is dialysis tubing. After cleaning, distilled water is used to immerse a dialysis bag. The medication-loaded niosomal suspension is put into this bag after 30 minutes. The vesicle-containing bag is submerged in buffer solution at either 25°C or 37°C while being constantly shaken. Samples were taken out of the outer buffer (release medium) and replaced with an equal amount of new buffer at predetermined intervals. The samples are subjected to a suitable assay technique analysis to determine the drug content.

5) **Measurement of vesicle size**[44]

The preparation liquid was used to dilute the vesicle dispersions about 100 times. A particle size analyzer (Laser diffraction particle size analyzer, Sympatec, Germany) was used to measure the size of the vesicles. A small volume sample holding cell (Su cell) and a multielement detector are at the core of the equipment, which is comprised of a He-Ne laser beam with a wavelength of 632.8 nm and a minimum power of 5 mW focused using a Fourier lens [R-5]. Prior to measuring the size of the vesicles, the sample was agitated with a stirrer. According to a 1999 study by Hu C. and Rhodes 7, the typical particle size of traditional niosomes is around 14µm, but that of niosomes derived niosomes is roughly 6µm.

6) **Stability studies**[41,43]

The optimized batch was kept in closed vials at various temperatures to check the niosomes' stability. Since drug leakage and a decline in the percentage of drug kept would result from formulation instability, surface features and the percentage of drug retained in niosomes and niosomes produced from proniosomes were chosen as metrics for evaluating the stability. The proportion of medicine maintained after being hydrated to

form niosomes was evaluated, color changes and surface properties were noted, and appropriate analytical techniques (UV spectroscopy, HPLC procedures, etc.) were used to analyze the niosomes at regular intervals of time (0, 1, 2, and 3 months).

7) **Optical microscopy**[44]
The niosomes were mounted on glass slides and viewed under a microscope with a magnification of ×1200 for morphological observation after suitable dilution. The photomicrograph of the preparation was also obtained from the microscope using a digital SLR camera.

Future Prospectus:
Niosomes are a potential drugs delivery system. Niosomes have been effectively employed as a drug carrier over the past thirty years to address biopharmaceutical issues such medication side effects, insolubility, and poor chemical stability. Toxic anticancer, anti-inflammatory, anti-infective, anti-AIDS, and antiviral medications, among others, can be effectively encapsulated in niosomes to improve bioavailability, target characteristics, and reduce toxicity and side effects. Niosome handling and storage don't call for any unique circumstances. Niosomal drug carriers are more stable and less hazardous than ionic drug carriers.

Applications [45]

I. **Targeting of bioactive agent:** -To the Reticulo-Endothelial System (RES): The vesicles are taken up preferentially by the RES cells. Opsonins are circulating blood factors that regulate niosome uptake. The opsonins indicate the niosome for clearance. However, such localized medication accumulation has been used to treat liver parasite infestation and animal tumors that have been known to spread to the spleen and liver. b) Organs other than RES: Drugs can also be targeted to organs other than RES using niosomes. Since immunoglobulin binds easily to the lipid surfaces of niosomes, a carrier system, such as antibodies, can be linked to niosomes in order to direct them toward particular organs.

II. **Delivery of Anticancer Drugs**: - Chemotherapy is the standard cancer treatment nowadays. Many anticancer medications have severe adverse effects on healthy cells in addition to inadequate penetration into tumor tissue, which limits their therapeutic efficiency. Numerous efforts have been undertaken to address these drawbacks, such as the innovative drug delivery mechanism of niosomes.

III. **Niosome immunological applications**: -Studies on the nature of the immune response triggered by antigens have been conducted using niosomes. Drugs other than those for the Reticulo-Endothelial System can also be targeted with niosomes. Niosomes can be targeted to certain organs by attaching a carrier system, such as antibodies, to them since immunoglobulins bind to the lipid surface of niosomes with ease.

IV. **Sustained Release**: -Since niosomal encapsulation may keep medications with low therapeutic index and poor water solubility in the bloodstream, sustained release niosomes can be used to treat these conditions.

V. **Localised drug action**: -Because of their small size and poor capacity to pass through connective tissue and epithelium, niosomes are one method of delivering drugs that have a localized effect at the site of administration.

VI. **Niosomes as a drug Carrier: -** Iobitridol, a medication used as a diagnostic in X-ray imaging, has also been transported via niosomes. Topical niosomes can work as a solubilization matrix, a local site for the prolonged release of chemicals that are dermally active, penetration enhancers, or a membrane barrier that limits the pace at which medications are absorbed systemically.

VII. **Leishmaniasis**: -The disease known as leishmaniasis is caused by a parasite belonging to the genus Leishmania invading the spleen and liver cells. The use of niosomes in experiments shown that larger dosages of the medication may be given without causing adverse effects, allowing for more effective therapy.

VIII. **Delivery of Peptide drugs: -** The problem of avoiding the enzymes that would break down peptides has long plagued oral peptide medication administration. It is being researched if using niosomes may effectively shield the peptides from gastrointestinal peptide degradation. Entrapment of the medication considerably increased the stability of the peptide in an in vitro investigation using oral administration of a vasopressin derivative entrapped in niosomes.

IX. **Co drug Delivery: -**Many recent research have focused on the co-delivery of various medicines using niosomes for combination treatment. Anticancer medications can have detrimental side effects. The epirubicin and nitric oxide transporting system that Pasut et al. developed simultaneously functions as a sensitizer of anticancer drug therapy as well as a protective reagent against anthracycline-induced cardiomyopathy. They employ branched PEG as the polymer backbone rather than linear PEG in order to improve the Co delivery system's capacity to preserve cardiocytes and increase anticancer effectiveness. In order to administer several drugs to cancer patients, Sharma et al. created niosomes that were dual-encapsulated with hydrophobic curcumin and hydrophilic doxorubicin. Comparing dual drug loaded niosomes to free drug, the results indicated that the former were more cytotoxic to HeLa cells.

CONCLUSION

One of the greatest examples of how drug delivery technologies and nanotechnology have advanced significantly is the niosomal drug delivery system. Due to its mainly stable nature and cost effectiveness, niosomes clearly seem to be a well-liked drug delivery technology over other dosage forms. Many opportunities are present for covering harmful anti-cancer, anti-infective, anti-AIDS, anti-inflammatory, antiviral, and other medications in niosomes and using them as effective drug carriers to improve the drugs' bioavailability and targeting qualities while lowering their toxicity and adverse effects. In order to develop an affordable and useful niosomal preparation, these topics hence need more systematic thought and study.

The concept of encapsulating the medication within niosomes to improve its targeting at the proper tissue site is extensively acknowledged by scholars and researchers. While niosomal carriers are safer, ionic drug carriers are comparatively harmful and inappropriate. Furthermore, processing and storing niosomes is not required for any special conditions. A potential medication delivery mechanism is represented by niosomes. Since they have certain structural similarities with liposomes and may contain a variety of medicines inside their multienvironmental structure, niosomes might be seen of an alternate vesicular system to liposomes. Because of their stability, affordability, and other advantages over liposomes, niosomes are considered superior candidate drugs for distribution.

In several drug delivery systems, including topical, ophthalmic, parenteral, and targeted, niosomes play a crucial and significant role. The pharma industry will find niosomes to be quite beneficial in the future. Niosomes are a lucrative drug carrier that may be used to target drugs more effectively for the treatment of cancer, infections, AIDS, and other conditions. Up until now, only animal experiments with this targeted drug delivery system have been reported; however, additional clinical research in human volunteers, as well as pharmacological and toxicological research in animals and human volunteers, may be helpful.

Declaration
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Availability of data and materials, the datasets generated and analysed during the current study are available from the corresponding author on a reasonable request.
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REFERENCES

[1]. Khandare JN, Madhavi G, Tamhankar BM. Niosomes novel drug delivery system. East Pharm 1994;31:61-4.
[2]. Bhaskaran S, Panigrahi L. Formulation and evaluation of niosomes using different nonionic surfactant. Indian J Pharm Sci 2002;63:186.
[3]. Ravi Kumar, Shivjee Kumar, Shyam Shankar Jha, Amit Kumar Jha, Vesicular System-Carrier for Drug Delivery, Der Pharmacia Sinica, 2011, 2(4), 192-202.
[4]. Handjani-vila RM: Dispersion of lamellar phases of nonionic lipids in cosmetic products. Int J Cosmetic Sci, 1979; 1: 303.
[5]. Surender Verma, S.K. Singh, Navneet Syan, Pooja Mathur, Vinay Valecha, Nanoparticle vesicular systems: A versatile tool for drug delivery, Journal of Chemical and Pharmaceutical Research, 2010, 2(2), 496-509.
[6]. Jiao J, "polyoxyethylated non-ionic surfactants and their applications in topical occular drug delivery," Advanced drug delivery Reviews, vol.60, no.15, pp.1663, 2008.
[7]. Akhilesh D, Bini K. B, and Kamath J. V, “Review on span-60 based non-ionic surfactant vesicles (niosomes) as novel drug delivery,” International Journal of Research in Pharmaceutical and Biomedical Sciences, vol. 3, pp. 6–12, 2012.
[8]. Nasseri B, “Effect of cholesterol and temperature on the elastic properties of niosomal membranes,” International Journal of Pharmaceutics, vol. 300, no. 1-2, pp. 95–101, 2005.
[9]. Sonule M, Gandhi M, Paralkar S, Dabhade D, Pagar S. Niosomes: novel drug delivery system. Int J Pure App Bio Sci. 2014; 2(2):267-74. 9.
[10]. Parmar RP, Parmar RB. Conceptual aspects of vesicular drug delivery system with special reference to niosome. Asian J Pharm Tech. 2013; 3(2):52-59.

[11]. Babu VL, Mathew ST, Jayaveera KN, PrasanthVV. Niosomes – vesicular drug delivery system. Int J Pharm. 2013;3(1):180-85.
[12]. Kazi MK, Asim SM, Nikhil B, Arijit G, Sugata C. Niosome: A future of targeted drug delivery systems. J Adv Pharm Tech Res. 2010; 1(4):374-80.
[13]. Soumya S. Niosomes: A role in targeted drug delivery system. Int J Pharm Sci Res 2013;4:550-7.
[14]. Surender Verma, S.K. Singh, Navneet Syan, Pooja Mathur, Vinay Valecha, Nanoparticle vesicular systems: A versatile tool for drug delivery, Journal of Chemical and Pharmaceutical Research, 2010, 2(2), 496-509.
[15]. Madhav NVS, Saini A, Niosomes: A novel drug delivery system, International Journal of Research in Pharmacy and Chemistry, 2011, 1(3), 498-511.
[16]. Baillie AJ, Coombs GH, Dolan TF: Non-ionic surfactant vesicles, niosomes, as delivery system for the antileishmanial drug, sodium stribogluconate. J Pharm Pharmacol, 1986, (38), 502-505.
[17]. Mayer LD, Bally MB, Hope MJ, Cullis PR: Uptake of antineoplastic agents into large unilamellar vesicles in response to a membrane potential. BiochemBiophys Acta, 1985, (816), 294-302.
[18]. Kazi Masud Karim, Asim Sattwa Mandal, Nikhil Biswas, Arijit Guha, Sugata Chatterjee, Mamata Behera: Niosome: A future of targeted drug delivery systems. J Adv Pharm Tech Res, 2011, (62), 122
[19]. Baillie AJ, Coombs GH, Dolan TF: Non-ionic surfactant vesicles, niosomes, as delivery system for the antileishmanial drug, sodium stribogluconate. J Pharm Pharmacol, 1986, (38), 502-505.
[20]. Khandare JN, Madhavi G and Tamhankar BM. Niosomes: Novel drug delivery system. The Eastern Pharmacist. 1994;37:61-64.
[21]. Chandu VP, Arunachalam A, Jeganath S, Yamini K, Tharangini K, Chaitanya G. Niosomes: a novel drug delivery system. Int J novel trends Pharm Sci. 2012; 2(1):25-31.
[22]. Rogerson A, Cummings J and Willmott N. The distribution of doxorubicin in mice following administration in niosomes. J Pharm Pharmacol. 1988;40:337-342.
[23]. Chauhan S, Luorence MJ. The preparation of polyoxyethylene containing non-ionic surfactant vesicles. J Pharm Pharmacol1989;4:6
[24]. Jayaraman SC, Ramachandran C, Weiner N: Topical delivery of erythromycin from various formulations: An in vivo hairless mouse study. J Pharm Sci, 1996, (85), 1082-1084.
[25]. Blazek-Walsh AI, Rhodes DG. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharm Res 2001;18:656-
[26]. Rogerson A. Adriamycin-Loaded Niosomes –Drug Entrapment, Stability and Release. J Microencap. 1987; 321.
[27]. Baillie AJ. The preparation and Properties of Niosomes-Nonionic Surfactant Vesicles. J Pharm. Pharmacol. 1985;863.
[28]. Malhotra M, Jain NK. Niosomes as Drug Carriers. Indian Drugs. 1994;31(3):881-66.
[29]. Tangri P, Khurana S. Niosome: Formulation and evaluation. International Journal of Biopharmaceutics. 2011;2(1):47-52.
[30]. Chandu VP, Arunachalam A, Jeganath S, Yamini K, Tharangini K, Chaitanya G, et al. Niosome: A Novel Drug Delivery System. International Journal of Novel Trends in Pharmaceutical Sciences. 2012;2(1):27-30
[31]. Uchegbu IF and Florence AT. NonIonic Surfactant Vesicles (niosomes) Physical and Pharmaceutical chemistry. Adv Colloid Interface Sci. 1995; 1
[32]. Kiwada H, Nimura H and Kato Y. Chem Pharm Bull. 1985;33:2475-2482
[33]. Bhaskaran S and Panigrahi L. Formulation and Evaluation of Niosomes using Different Nonionic Surfactant. Ind J Pharm Sci. 2002; 63.
[34]. Rane S, Inamdar Y, Rane B, Ashish J. Niosomes: A Non-Ionic Surfactant Based Vesicles as a Carriers for Drug Delivery. International Journal of Pharmaceutical Sciences Review and Research. 2018;51(1):198-213.
[35]. Blazek-Walsh AI, Rhodes DG. SEM imaging predicts quality of niosomes from maltodextrin-based Proniosomes. Pharm Res. 2001;18(5):656-61.
[36]. I. F. Uchegbu and S. P. Vyas, “Non-ionic surfactant based vesicles (niosomes) in drug delivery,” International Journal of Pharmaceutics, vol. 172, no. 1-2, pp. 33–70, 1998
[37]. Waddad, S. Abbad, F. Yu et al., “Formulation, characterization and pharmacokinetics of Morin hydrate niosomes prepared from various non-ionic surfactants,” International Journal of Pharmaceutics, vol. 456, no. 2, pp. 446–458, 2013.
[38]. Szoka F, Jr, Papahadjopoulos D. Comparative properties and methods of preparation of lipid vesicles (liposomes) Annu Rev BiophysBioeng. 1980; 9:467– 508.

[39]. Azmin MN, Florence AT, Handjani-Vila RM, Stuart JF, Vanlerberghe G, Whittaker JS. The effect of nonionic surfactant vesicle (noisome) entrapment on the absorption and distribution of methoterxate in mice. J Pharm Pharmacol. 1985; 37:237–42.

[40]. Smulders S, Kaiser JP, Zuin S, Landuyt KLV, Golanski L, et al. Contamination of nanoparticles by endotoxin: Evaluation of different test methods. Particle and Fibre Toxicology. 2012;9(41):2-11

[41]. Manosroi A: Characterization of Vesicles Prepared with Various Nonionic Surfactants mixed with Cholesterol. Colloids and surfaces Biointerfaces, 2003.P.129.

[42]. D. Pando, G. Gutierrez, J. Coca, and C. Pazos, “Preparation and ´ characterization of niosomes containing resveratrol,” Journal of Food Engineering, vol. 117, no. 2, pp. 227–234, 2013

[43].] D. Akhilesh, K. B. Bini, and J. V. Kamath, “Review on span-60 based non-ionic surfactant vesicles (niosomes) as novel drug delivery,” International Journal of Research in Pharmaceutical and Biomedical Sciences, vol. 3, pp. 6–12, 2012

[44]. Silver BL. The Physical Chemistry of Membranes. New York: Alan/Unwin and Solomon Press; 1985. p. 209-30.

[45]. 169–176, 2012. g. C. Marianecci, F. Rinaldi, L. D. Marzio, A. Ciogli, S. Esposito, and M. Carafa, “Polysorbate 20 vesicles as multi-drug carriers: in vitro preliminary evaluations,” Letters in Drug Design and Discovery, 2013; 10(3): 212–218.