IJMPR 2025, 9(5), 62-72

International Journal of Modern Pharmaceutical Research

www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Review Article
SJIF Impact Factor: 6.669

COMPREHENSIVE INSIGHTS INTO NIOSOME TECHNOLOGY: FORMULATION, CHARACTERIZATION AND APPLICATIONS

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Article Received on: 11/03/2025

Article Revised on: 01/04/2025

Article Accepted on: 20/04/2025

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ABSTRACT

Niosomes is self-assembled vesicles produced from non-ionic surfactants with or without cholesterol, are a promising drug delivery system. This review comprehensively explores the composition, preparation methods, characterization techniques, and applications of the niosomal drug delivery system. The essential components of niosomes are cholesterol, charge-inducing compounds, hydration media, and non-ionic surfactants. Number of factors, including the nature of the medication, cholesterol content, surfactant properties, and preparation conditions, influence the characteristics and performance of niosomes. Several methods are employed for niosome preparation, including thin film hydration, ether injection, reverse phase evaporation, sonication method, multiple membrane extrusion, transmembrane pH gradient, bubble method, and the microfluidization. Each technique has its advantages and limitations in terms of scalability, reproducibility, and vesicle size distribution. Characterization of niosomes involves evaluating vesicle size, size distribution, morphology, surface charge, entrapment efficiency, in-vitro release, and stability. Niosomes have diverse applications in targeted drug delivery, transdermal and ocular drug delivery, cancer therapy, vaccine delivery, and cosmeceuticals. They have been successfully utilized for the encapsulation and delivery of various drugs, such as antibiotics, anticancer agents, peptides, and radiopharmaceuticals. This review highlights the potential of niosomes as a versatile and effective drug delivery system, with promising prospects for future research and development in the field of nanomedicine.

KEYWORD: Niosomes, Composition, Methods of preparation, Characterization, Applications.

INTRODUCTION

In 1909, Paul Ehrlich was a first person who involved in the development of targeted delivery of drug. The system is based on a method that delivers a certain amount of a therapeutic agent for a prolonged period of time to a targeted diseased area within the body. This helps maintain the required plasma and tissue drug levels in the body, therefore avoiding any damage to the healthy tissue via the drug.[1] Nanotechnology refers to study and manipulation of materials at sizes ranging from 0.1 to 100 nanometers. This field focuses on producing, characterizing, and designing devices and systems by controlling their shape and size at the nanoscale. At this scale, materials exhibit distinct chemical, physical, and biological properties compared to their larger counterpart, primarily due to quantum mechanical interactions at the atomic level. Vesicles are widely used as drug delivery methods for many active substances. Vesicles are ideal drug carriers due to their nanometric size, high surface volume ratio, and easy drug-release manipulation. Niosomes are self-assembled vesicles generated by non-ionic surfactants in aqueous environments, resulting in closed bilayers.[2] In 1975, L'Oréal developed and patented the first niosome formulations.[3] Different carrier system have been used for targeting the drug. Niosomes are highly effective drug carriers. Their formation, through the self-assembly of non-ionic surfactants into vesicles, was first documented in the 1970s by cosmetic industry researchers. These non-ionic surfactant vesicles, formed by hydrating surfactants from the alkyl or dialkyl polyglycerol ether class with cholesterol, result in microscopic lamellar structures that enhance drug delivery.[4] Niosomes are novel drug delivery carriers similar to liposomes. They consist of bilayers which are made from non-ionic surfactants, while liposomes are made from phospholipids. Niosomes are typically sized between 10 to 100 nm and offer high chemical stability, and cost-effectiveness, and are biodegradable, non-immunogenic, and biocompatible. These properties make niosomes an attractive option for drug delivery applications.[5]

Structure and Composition of Niosome

Figure 1 is created using biorender shows that niosomes are spherical and composed of microscopic lamellar structures, either unilamellar or multilamellar. Niosome are amphiphilic in nature which can entrap both hydrophilic drug in aqueous compartment and lipophilic drug in non-aqueous compartment. The bilayer is formed by nonionic surfactants, with or without cholesterol and a charge inducer.

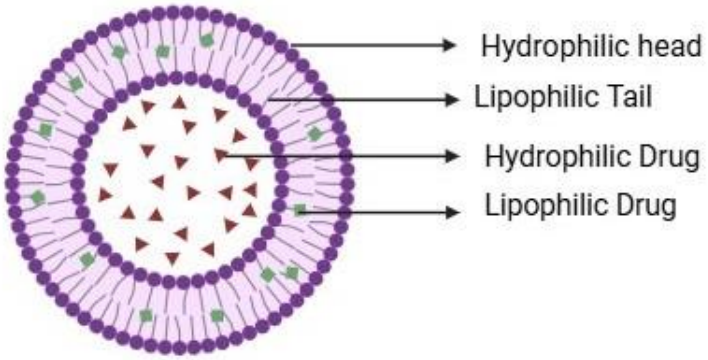


Fig. No. 1: Structure of noisome.

Niosomes are vesicle mainly composed of cholesterol and non-ionic surfactant.

1. Cholesterol: cholesterol is essential in formulation of niosome. It can also influence the membrane's permeability, rigidity, entrapment efficiency, ease of rehydration of freeze-dried niosomes, stability, and storage period. Addition of cholesterol can improve the viscosity of the formulation.[6]

2. Non-ionic Surfactant: The main component in niosome formation is a nonionic surfactant, which is amphiphilic due to its polar head and non-polar tail. Compared to anionic, cationic, or amphoteric surfactants, these uncharged surfactants are typically more stable, compatible, and less harmful.[7] A number of variables, including composition, size aadditives concentration, number of layers (lamellarity) and the surface charge, affect the characteristics of formed niosomes. Niosomes are frequently made with nonionic surfactants, particularly Span (e.g., Span 60, 40, 20, 85, and 80) and the tween (e.g., Tween 20, 40, 60, 85, and 80), which enhance their stability and efficacy.[8]

3. Charges molecule: Charge-inducing molecules are added to niosome formulations to create an electric charge on their surface, which helps to stabilize the niosomes through electrostatic repulsion. This repulsion prevents the niosomes from clumping together (coalescence). For examples dicetyl phosphate and phosphatidic acid (both negatively charged) and stearylamine (positively charged**)**.[9]

4. Hydration medium: The hydration medium is a crucial component in formulating niosomes, Phosphate buffer is commonly used as hydration medium. The pH of the buffer is important as it affects the solubility of the drug being encapsulated, which in turn influences the efficiency and stability of the Niosomes.[10]

Types of Niosomes: Niosomes are classified depending on the number of bilayers (SUV, MUV), size (LUV, SUV), and manufacturing procedure (REV, DRV). Niosomes are divided into three types. The following are descriptions of various types of niosomes: There are three types of vesicles: multi lamellar (MLV), large unilamellar (LUV), and small unilamellar (SUV).[11]

a) Large Unilamellar Vesicles (LUV).

Niosomes with a greater aqueous-to-lipid compartment ratio collect more bioactive chemicals with little membrane lipids. Large unilamellar vesicles have a diameter exceeding 0.10m.

b) Small Unilamellar Vehicles (SUV)

Niosomes are commonly created through solvent dilution, homogenization, French press extrusion, and sonication of multilamellar vesicles. Small unilamellar vesicles (0.025-0.05 μm) are thermodynamically unstable, leading to aggregation and fusion. They entrap a small amount of aqueous solute and have a low entrapped volume.

Some Other Categories of Niosomes

Bola surfactant containing Niosomes:

Omegahexadecylbis-(1-aza-18 crown-6) surfactants with niosomes are known as bolasurfactants.

Aspasomes: Aspasomes are generated by combining acorbyl palmitate, cholesterol, and the highly charged lipid diacetyl phosphate.[12]

Advantage: advantages of Niosomes are following.[13]

1. Niosomes are able to accommodate a variety of the therapeutic moieties, including hydrophilic, lipophilic, and amphiphilic drugs.
2. Vesicle features can be adjusted by adjusting the vesicle composition, size, lamellarity, surface charge, tapped volume, and concentration.

3. The drug can be released in a sustained or controlled manner.
4. Handling and storage of surfactants do not require any particular conditions, which decreases the cost of preparation.
5. Poorly soluble drugs have higher oral bioavailability.
6. Surfactants are biodegradable, biocompatible, and non-immunogenic, hence they are usually allergy-free.
7. They can increase the stability of the entrapped medication.
8. They can improve drug absorption via the skin when applied topically.
9. They improve the therapeutic profile of the drug molecules by delaying their clearance from the blood.
10. Niosomes can be given through various methods, like orally, via injections, or applied to the skin.[14]

Disadvantages

- Aggregation
- Leakage of Drug
- Physical instability
- Time-consuming

Factors affecting Niosomes: The physical and chemical characteristics of niosomes are influenced by numerous factors, which also impact vesicle production.

1. Nature of drug: Drugs' molecular weight, chemical structure, hydrophilicity, lipophilicity, and HLB value also affect niosome size. The HLB value influences drug entrapment efficiency. Drug encapsulating in niosomes increases with increasing vesicle size. Hydrophilic or lipophilic nature of drug and the equilibrium between the two can also influence drug entrapment and stability of Niosomes.[15] Drug and surfactant interactions may cause an increase in vesicle size.[16]

2. Effect of Cholesterol: Cholesterol affects the physical properties and structure of niosomes, potentially through interactions with nonionic surfactants. Cholesterol primarily impacts the cohesion and mechanical strength of lipid bilayers, as well as water permeability. The addition of cholesterol dramatically alters the fluidity of niosomes. The amount of cholesterol added is determined by the surfactants' HLB values.[17] As the HLB value exceeds 10, the minimum amount of cholesterol to be added must be increased to compensate for the larger head groups.[18]

3. Nature of Surfactant: A surfactant used to form niosomes must have a hydrophilic head and a hydrophobic tail. The size of the niosome vesicle increases as the HLB value of the surfactant increases, such as from span-85 (HLB-1.8) to span-20 (HLB-8.6), due to an increase in surfactant lipophilicity with a decrease in surface free energy. Using the gel-liquid phase transition temperature (TC), lipid and surfactant can be identified.[19]

4. Hydration Temperature: The shape and size of niosomes are influenced by its hydration temperature. For optimal conditions, it should be higher than the system's gel to liquid phase transition temperature. Temperature changes in the niosomal system affect the assembly of surfactants into vesicles as well as the vesicle shape transformation.[20] The hydration temperature influences the structural features of niosomes. Temperature fluctuations can influence vesicle production.

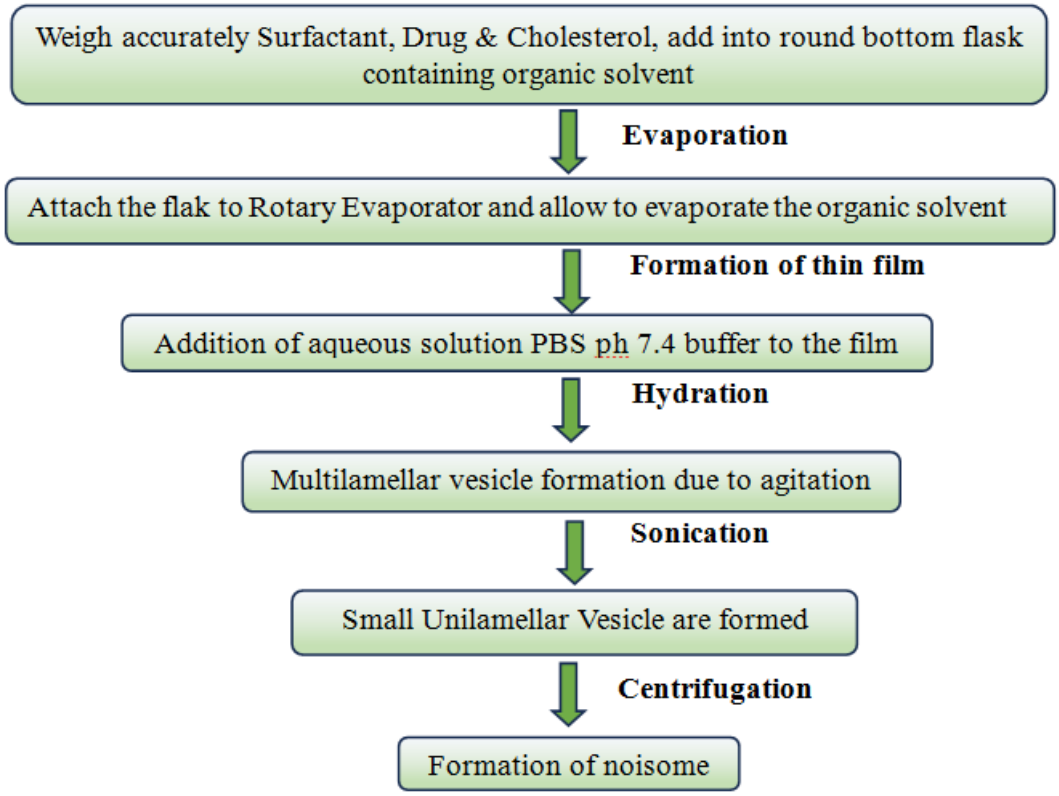
5. Resistance to Osmotic Stress: The size of a niosome suspension decreases when a hypertonic solution is added. First, niosomes enlarge when kept in hypotonic saline, which suggests slow drug release. But this enlargement might result from vesicle fluid elution being suppressed, which would speed up release.[17]

6. Surfactant and Lipid Level: The amount of surfactant/lipid and, as a result, the surfactant/water magnitude relationship are other important properties. Surfactant/lipid ratios typically range between 10 to 30 millimetre's (1-2.5% w/w). If the surfactant/lipid level is excessively high, increasing it will result in more medicine being encapsulated. Changes in the surfactant/water ratio during the association process may have an impact on the system's microstructure and consequently its properties.[21]

7. Membrane composition: The niosome can be made by adding surfactants, drugs, and other additives. Niosomes have a number of permeability, stability, and morphological properties, all of which can be altered by adding different additives. Drug leakage from the vesicles is the fundamental disadvantage of niosome formulation; however, this can be addressed by adding cholesterol. Cholesterol makes the membrane more rigid which decreases drug leakage.[22]

Methods of Preparation

1. Thin Film Hydration Method: Thin film hydration is most common method used for formulation of noisome it is easy procedure and direct method.[23] The process of preparation of niosomes has been shown in the flow diagram. 1



Flow Diagram 1: Showing the thin film hydration method.

Advantages

a) Compared to other methods, this method is straightforward and cost-effective, requiring only basic laboratory equipment.

b) Thin film hydration may encapsulate a variety of molecules, such as small hydrophilic, hydrophobic, and amphiphilic compounds, making it more versatile for drug delivery applications.

c) Vesicles have high encapsulation capacity, allowing for substantial drug entrapment.

d) This approach is easily scalable from laboratory to large-scale manufacturing. Niosomes have high physicochemical stability and can be stored for extended periods.

e) Formulation scientists can change the type and composition of lipid bilayers by using thin film hydration techniques. This makes it possible to alter the noisome size.

Disadvantages

a) The method of thin film hydration involves multiple steps, including extrusion, hydration, and film creation. They take a long time, are complex, and need experienced operators to produce high-quality niosomes.

b) Niosomes generated through thin film hydration may leak during storage, leading to content loss and instability.

2. Ether injection method: The ether injection method is a technique for creating niosomes, which are tiny vesicles made from surfactants. In this process, a solution of surfactant dissolved in diethyl ether is slowly injected into warm water at about 60°C using a 14-gauge needle. As the ether evaporates, it causes the surfactants to form single-layered vesicles. The size of these vesicles can vary from 50 to 1000 nanometers, depending on the specific conditions used during the process.[24]

Advantages

a) This procedure is easy and cost-effective, as it does not require sophisticated equipment.

b) Effective encapsulation of hydrophilic and hydrophobic bioactive substances.

c) Scalability to the industrial level is possible.

Disadvantages

a) Using ether poses a safety issue due to its extreme flammability. Proper handling and disposal practices are necessary for safety.

b) Even if organic solvents are removed, remnants may still cause harm after intake.

c) This approach may yield unstable niosomes over time.

3. Sonication: A common approach for generating vesicles involves sonication. In this procedure, a portion of the drug solution in buffer is combined with a surfactant/cholesterol mixture in a 10-ml glass vial. The resulting mixture is subjected to probe sonication at 60°C for 3 minutes using a titanium probe sonicator, resulting in the formation of niosomes.[25]

Advantages

a) Sonication method breaks down bigger aggregates into smaller. which can improve the stability and performance of the formulation.

b) The sonication method often requires less complicated equipment compared to other procedures, making it more cost-effective and easier to implement in various laboratory settings.

Disadvantages

a) Sonication for a long duration of time can damage niosome structures.

b) The sonication method can not be easily scalable for large-scale production, because it often involves small batch sizes.

c) Maintaining an appropriate temperature during sonication is crucial, but it can be challenging and may require additional equipment.

4. Multiple Membrane Extrusion Method: The multiple membrane extrusion technique involves creating a mixture of surfactant, cholesterol, and dicetyl phosphate in chloroform, which is then transformed into a thin film through evaporation. This film is subsequently hydrated with an aqueous drug solution, and the resulting suspension is extruded through a series of polycarbonate membranes for up to eight passes.[26]

Advantages

a) This method enables exact control over the size of niosomes, producing homogeneous vesicles that can improve drug delivery effectiveness and stability.

b) The multiple membrane extrusion technique can be scaled up for larger volumes of production without any changes to the manufacturing process, making it appropriate for commercial manufacture.

Disadvantages

a) Niosomes produced with this method may aggregate or fuse, especially if not closely controlled.

b) The multiple membrane extrusion approach can be time-consuming as it requires a number passages across membranes to obtain target vesicle size and uniformity in production.

5. Reverse Phase Evaporation Technique (REV): the reverse phase evaporation technique (REV) involves dissolving cholesterol and surfactant in a organic phase. An aqueous phase containing the drug is then introduced, and the two phases are sonicated at a temperature of 4-5°C. The clear gel that forms is further sonicated after adding a small amount of phosphate-buffered saline (PBS). The organic solvent is subsequently removed at 40°C under reduced pressure. The resulting viscous niosome suspension is then diluted with PBS and heated in a water bath at 60°C for 10 minutes to produce niosomes.[27]

Advantages

a) This procedure is straightforward and doesn't require any expensive equipment. It is cost-effective and accessible to laboratories with minimal resources.

b) This approach can load high amounts of drugs and bioactive ingredients, reducing waste.

c) These methods produce more stable niosomes, resulting in a longer shelf life.

Disadvantages

a) This method takes more time than other approaches.

b) Developing narrow size distribution vesicles is challenging.

c) Niosome sizes may vary from batch to batch.

6. Transmembrane pH Gradient (Acidic Inside) Drug Uptake Process: Remote Loading Technique: In this method, lipids or surfactants are dissolved in one or more organic solvents and then evaporated at low pressure to create a thin film on the inside of a flask with a round bottom. After that, the film is vortexed to create multilamellar vesicles by hydrating it with an acidic solution. After that, freeze-thaw cycles and sonication are applied to the resultant vesicles. This niosomal suspension is then mixed with an aqueous solution containing the drug. Then adjust the pH to 7.0-7.2 using 1M disodium phosphate and set up the RBF as a bubbling unit with three necks in a water bath, incorporating a reflux condenser, thermometer, and nitrogen supply through the three necks. After that, Disperse the cholesterol and surfactant mixture in a buffer at pH 7.4 with maintaining a temperature at 70°C. then Homogenize the dispersion for 15 seconds, then bubble nitrogen gas through it at 70°C to form niosomes.[28 29]

Advantages

a) The transmembrane pH gradient enables high drug-lipid ratios, resulting in increased encapsulation efficiency.

b) Researchers can manipulate the pH gradient to alter the release profile of encapsulated drugs, enabling prolonged or targeted delivery as desired.

Disadvantages

a) The preparation consists of several steps, including the production of a thin film, hydration, and pH correction, which may complicated the process and increase the possibility of errors.

b) The method frequently requires specialized equipment for establishing and keeping the pH gradient, which might not be accessible in all laboratories, possibly limiting accessibility.

7. Micro fluidization Method: This is a recent technique used for preparing unilamellar vesicles. In this method, two fluid streams interact at ultra-high velocities within an interaction chamber. This approach results in greater uniformity, improved reproducibility, and smaller niosome sizes. In the interaction chamber, two ultra-

high-speed jets collide, causing a thin layer of liquid to form in microchannels, which yields uniformly sized niosomes.[30]

Advantages
a) This approach yields a uniform size distribution of niosomes.
b) The drug can be encapsulated with high efficiency.
c) Microfluidization allows for easy scaling up for commercial manufacturing of niosomes.

Disadvantages
a) The equipment is costly compared to other approaches and may not be affordable for all laboratories.
b) Running the equipment requires the expertise of a technician.
c) Microfluidization techniques may present instability issues for heat-sensitive substances due to the heat generated by shear stress.

8. Bubble Method: This is a novel method for preparing liposomes and niosomes without the use of organic solvents. The setup includes a round-bottom flask with three necks, which is placed in a water bath to regulate the temperature. The water-cooled reflux condenser and thermometer are connected to the first and second necks, while nitrogen gas is supplied through the third neck. The surfactant and cholesterol are combined in a buffer at pH 7.4 and heated to 70°C for 15 seconds using a high-shear homogenizer. Immediately afterward, nitrogen gas is bubbled through the mixture at 70°C.[31]

Advantages
a) The procedure is straightforward and cost-effective.
b) These methods can be scaled up with minimal adjustments.
c) Requires less energy than other procedures like sonication or microfluidization.
d) It is possible to achieve uniform size distributions.

Disadvantages
a) Bubble methods require longer than other processes to formulate niosomes, hence from an economic perspective, large-scale production might not be possible.
b) Batch-to-batch fluctuation is uncontrollable with bubble methods. Therefore, in comparison to other methods, reproducibility is low.

Separation of Unentrapped Drug: Separation of unentrapped drugs from the finished product during niosome preparation is crucial in ensuring the formulation's stability and efficacy. For this, a variety of techniques can be used.[32]

1. Dialysis: The aqueous niosomal suspension is dialyzed at room temperature using the appropriate dissolving medium in cellulose bags, dialysis tubing, or dialysis membranes. At the appropriate interval, the sample is removed from the medium, centrifuged, and examined for drug content using HPLC or UV spectroscopy.

2. Centrifugation: The unentrapped medication is separated by cooling centrifugation, which involves rotating at 7000 g for 30 minutes at 4°C. It is dependent upon the component's molecular weight. Two layers form as a result: niosomal pellets and liquid supernatant. To get rid of the unentrapped medication, the supernatant is removed and niosomal pallets are washed with phosphate buffer or distilled water. Once more, this niosomal pallet slurry is centrifuged, and the unentrapped medication is completely removed.

3. Gel filtration or Column chromatography: The unentrapped medication in niosomal solution can be eluted and analyzed using an appropriate analytical procedure with a sephadex-G-50 column and a suitable mobile phase (phosphate buffer or regular saline)

Characterization of niosomes
1. Vesicle Size- Niosomal vesicles are typically spherical, and their mean diameter can be assessed using various techniques. The size of niosomes can be measured using an electron microscope, ultracentrifugation, molecular sieve chromatography, laser light scattering, optical microscopy, freeze fracture electron microscopy, and photon correlation microscopy. Light polarization microscopy is used to characterize bilayer vesicles. Furthermore, small angle Xray scattering, NMR spectroscopy, and electron microscopy can be used to determine the number of lamellar layers. the Particle size is essential, niosomes in the nanoparticle range deliver drugs more effectively than those in the micron range. Although a large particle size niosome has the advantage of having more space to hold drugs, its release pattern is very slow.[33]

2. Size Distribution: The degree of non-uniformity in a particle size distribution is called "polydispersity" (or "dispersity" according to IUPAC recommendations). PDI, also referred to as the heterogeneity index, is an index that is determined by fitting the correlation data (the cumulants analysis) with two parameters. Values less than 0.05 are mostly observed with highly monodisperse standards due to the dimensionlessness of this index's scaling. In simple terms, the PDI represents the distribution of population sizes within a certain sample. When a sample is extremely polydisperse, meaning it has several populations of different particle sizes, the numerical value of PDI is 1.0; otherwise, it is 0.0 for a perfectly uniform sample with regard to particle size.[34] Consequently, obtaining a specific particle size along with a low polydispersity index (PDI) is an essential factor to consider when designing an effective nanocarrier.[35]

3. Morphology of Niosomes: Niosome morphology is studied through the use of microscopic methods. Scanning electron microscopy (SEM) is used for solid

samples, whereas electronic microscopic techniques such as transmission electronic microscopy (TEM), negative-staining transmission electronic microscopy (NS-TEM), and freeze-fracture transmission electronic microscopy (FFTEM) are preferred for liquid state samples. In 1982, Binnig's group employed scanning tunneling microscopy (STM) and atomic force microscopy (AFM) to characterize micro- and nanoscale structures. Because of its capacity for vertical axis analysis, STM is helpful in evaluating the bilayer thickness of liposomes and Niosomes respectively.[36 37]

4. Vesicle Charge: The surface charge of vesicles significantly influences the behaviour of niosomes both *in vivo* and *in vitro*. The zeta potential refers to the charge present on the surface of niosomes. This charge arises from the components or ingredients used during their production.[38] The zeta potential of the niosomes was measured using a Zetasizer instrument equipped with Malvern software. The analysis was conducted at 25°C with a detection angle of 90°. An optimal zeta potential value should be the range of greater than+30mV and smaller than -30 mV, as this range helps prevent the aggregation of niosomal particles.[39]

The charge on vesicles is expressed in terms of zeta potential and calculated using the Henry's equation.[40]

$$£ = \mu E \pi \square \ / \ \sum$$

where,
£ = Zeta potential
μE = Electrophoretic mobility
μ = Viscosity of medium
Σ = Dielectric constant

5. Entrapment Efficiency: The amount of medication present in the transparent supernatant after centrifugation was measured using a UV spectrophotometer in order to determine drug entrapment. For this, a standard medication calibration curve was plotted. The total amount of drug added during the preparation (Wi) was then deducted from the amount of drug in the supernatant. (Wi-Wf) will efficiently indicate the quantity of medication trapped in the noisome.[41]

$$EE\% = Wi - Wf \div Wi \times 100$$

6. *In-vitro* Release Study: One approach to studying the *in-vitro* release rate involves the use of dialysis tubing. First, a dialysis bag is thoroughly washed and soaked in distilled water. Next, the vesicle suspension is carefully pipetted into the tubing bag, which is then sealed. This bag, containing the vesicles, is submerged in 200 mL of buffer solution placed in a 250 mL beaker, where it is kept in constant motion at a temperature of either 25°C or 37°C. At specified time intervals, samples of the buffer are taken and analyzed for drug content using an appropriate assay method.[42]

7. Stability study: Niosomal stability is crucial for formulation development. The preparation process, drug loading, and membrane-forming material selection all have an impact.[43] Calculating particle size, zeta potential, morphology, and loaded product leak risk can help assess package stability. To test the safety of niosomes during circulation, drug-loaded vesicles can be incubated at 37°C in serum or under severe circumstances to duplicate in vivo conditions. The stability of niosomes is substantially affected by their size and surface charge.[44]

Application

Niosomes can be used for drug delivery and cosmetics. They can be administered via oral, topical, transdermal, ocular, intravenous, pulmonary, and transmucosal routes. Formulation design is influenced by the route of administration.

Targeted drug delivery: Niosomes can be employed as nano-carriers in targeted drug delivery systems. It has been observed that niosome formulation is a stable formulation that allows for the encapsulation of antiviral, anti-inflammatory, anti-cancer, and antibacterial medications. Niosomes present a new pathway for administering drugs via nanocarrier technology, enabling improved targeting and bioavailability.[45]

Transdermal drug delivery: Transdermal drug delivery has gained popularity recently as a means of delivering a range of pharmaceuticals that are difficult to administer through traditional routes. Niosomes, vesicular nanocarriers, are gaining popularity for transdermal drug delivery due to their improved drug penetration, sustained sedate discharge by local depot, and ability to limit systemic absorption through the skin's membrane.[46]

Antibiotic: Niosomes, a type of non-ionic surfactant vesicle, are utilized to deliver a water-soluble topical antibiotic to the eye. The study found that niosomes are effective ocular carriers for gentamicin sulphate topical administration.[47]

Cancer therapy: Recent advancements in nanotechnology have allowed for the development of nanomaterials that can specifically target cancer cells. These materials can be engineered to recognize specific biomarkers associated with tumours, enabling precise delivery of therapeutic agents, such as chemotherapy drugs, RNA molecules, or immunotherapies. Recent advancements in cancer treatment include employing niosomal formulations for drug targeting to several types of cancer cells such as breast cancer, skin cancer, lung cancer, prostate cancer, and cervical cancer.[48]

Vaccine delivery: Vaccination through the skin may be favourable because to the prevalence of immune-competent Langerhans cells (LCs) along transdermal penetration pathways. These cells are aligned exactly along the minute pores where pathogens can enter the body.[49] LCs, located near the stratum corneum, are

immune cells that cover 25% of the entire surface area. The immune response to transdermal immunization against TT using niosomes was significantly (p b 0.05) comparable to that obtained by intramuscular injection of the same dose of AATT, indicating that niosomes exhibited a better immunological response than liposomes.[50]

Delivery of peptide drug: To effectively shield peptides from gastrointestinal peptide breakdown, researchers are investigating the use of niosomes. Drug entrapment improves the stability of the peptide, according to an *in-vitro* study that used oral delivery of a vasopressin entrap derivative in niosomes.[51]

Cosmeceutical: Non-ionic surfactant vesicles were initially reported in cosmetics by L'Oreal. L'Oréal created and patented niosomes in the 1970s and 1980s. Lancôme introduced its first product, 'Niosome,' in 1987. Niosomes offer benefits in cosmetic and skin care applications by improving medication stability, bioavailability, and skin penetration.[52]

Radiopharmaceuticals: In 1996, Erdogan was the first to successfully employ niosomes in this capacity. They produced positive-charged iopromide niosomes tagged 131-I.[53]

Leishmaniasis Treatment: Niosomes can target disease-causing organisms in the reticulo-endothelial system. Leishmaniasis is a disease caused by parasites invading the liver and spleen. Antimonial, similar to arsenic, are routinely prescribed medications that can harm the heart, liver, and kidneys at excessive dose.[54]

Targeting of Bioactive Agents: The vesicles are taken up preferentially by the cells of the RES (Reticulo-Endothelial System). Niosomes are also taken up by the cells by the action of opsonin's, which are circulating serum factors that signal niosomes for clearance.[49]

Hemoglobin carrier. Niosomes may have an important part in the hemoglobin transport mechanism. Niosomal vesicles function as a hemoglobin transporter because they are absorbent of oxygen. Niosomes carry hemoglobin. Vesicles can change the hemoglobin curve similarly to non-capsulated hemoglobin because to their high oxygen permeability. The visible spectrum of niosomal suspension can be compared to that of free hemoglobin.[51]

List of Drug encapsulated in Niosomes

Table No. 2: List of drugs encapsulated in niosomes.

Drug	Route of drug administration	Result	Reference No.
Acetazolamide	Topical	enhances its antibacterial and antibiofilm effects	[55]
Amygdalin	Topical	Enhance permeation into deep skin layers.	[56]
Atorvastatin	Oral	Improve dissolution rate	[57]
Betaxolol	Ocular	Improve ocular retention time	[58]
Bromocriptine	Nasal	Enhance permeation across nasal mucosa	[59]
Buspirone hydrochloride	Nasal	Improve nasal mucosal permeability	[60]
Cilomilast	Pulmonary	Improve lung uptake	[61]
Doxorubicin	Topical	enhances its anticancer activity	[62]
Etodolac	Topical	Improves skin penetration	[63]
Flurbiprofen	Ocular	Prolong contact time with ocular tissues	[64]
Hydrochloride naltrexone	Ocular	Enhance corneal permeability	[65]
Insulin	Oral	Improve solubility	[66]
Ketoprofen	Topical	Improves skin penetration	[67]
Levofloxacin	Oral	Improve gastrointestinal membrane permeability	[68]
Methotrexate	Nasal to brain	Enhance brain concentration of drug	[69]
Nintedanib	Pulmonary	Extend release and enhance cellular internalization	[70]
Nefopam hydrochloride	Nasal	Enhance drug penetration through nasal mucosa	[71]
Olanzapine	Nasal	Improve nasal mucosal permeability	[72]
Paclitaxel	Intravenous	Extend elimination half-life	[73]
Repaglinide	Oral	Improve solubility	[74]
Salbutamol sulfate	Pulmonary	Improve lung deposition and retention	[75]
Telmisartan	Oral	Improve stability and extend release	[76]

CONCLUSION

Niosomes, a nonionic surfactant-based vesicular system, are a unique and effective method of drug administration. A variety of medications can be encapsulated into niosome by including suitable nonionic surfactants and cholesterol into the vesicular membrane. Furthermore, niosomes are more stable and have fewer harmful pharmacological effects, with the encapsulated drug released over time. In addition, unlike other drug-delivery methods such as liposomes, niosomes do not require particular handling or storage conditions. Niosomes can be employed in particular routes of administration by undergoing appropriate modifications, which result in structures such as proniosomes. In

conclusion, niosomes are a highly efficient tool for drug administration in the treatment of a wide range of disorders, with the potential to deliver more effective treatment than traditional drug-delivery systems.

ACKNOWLEDGEMENT

Thank you to Appasaheb birnale college of pharmacy sangli for providing facility to carry out this review work.

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