

Niosomes as Efficient Nanocarriers for Targeted Drug Delivery

Manisha Trivedi¹, Shashi Kiran Misra¹, Smriti Roy², Harsh Pandey³,
Arpit Katiyar⁴, Anupriya Kapoor¹

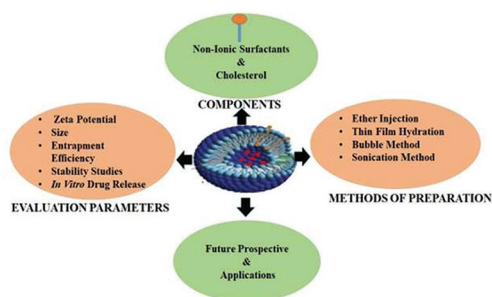
¹Department of Pharmaceutics, School of Pharmaceutical Sciences, CSJM University, Kanpur, Uttar Pradesh, India, ²Department of Legal Studies, Atal Bihari Vajpayee School of Legal Studies, CSJM University, Kanpur, Uttar Pradesh, India, ³Department of Health Research, Ministry of Health, Model Rural Health Research Unit, ICMR RMRIMS Patna, Bihar, India, ⁴Department of Pharmaceutical Chemistry, Sai Meer College of Pharmacy, Chibbramau Kannauj, Uttar Pradesh, India

Abstract

The localization of pharmacological molecules to stick locations is made possible by target-specific drug delivery systems with its bi-layer structure made of non-ionic surfactants, the niosome vesicular system can temporarily increase a drug's bioavailability in a specific location. Scientists who study drug delivery systems have been highly concerned with the creation of vesicles as a means of enhancing medication delivery in recent years. Niosomes' amphiphilic character enhances their ability to effectively encapsulate hydrophilic or lipophilic medications. It is common practice to add additional ingredients, like cholesterol, to preserve the niosomes' structural stiffness. When comparing the great chemical stability and effectiveness of the replacement with niosomes, liposomes use vesicles for medicinal and therapeutic applications, which have several advantages. They boost the therapeutic efficiency of drug molecules by keeping the medicine from exiting circulation too quickly, shielding it from its genetic environment, and lessening its effect on target cells. This research concentrated on current advancements in the distribution of niosomal medications, potential advantages over other delivery systems, building techniques, characterization techniques, and recent research that is noisy. The use of niosomes in nanotechnology has the potential to yield highly targeted, non-infective, and non-cancer agents. Proniosomes and aspasomes are a few examples of novel concepts that have been used to enhance niosomes' drug delivery capabilities. Niosomes are also beneficial as a living component of vaccines and for diagnostic tests. Therefore, further research and development are required in these areas to produce the niosomal preparations that are now on the market.

Key words: Drug release, niosomes, non-ionic surfactants, targeted drug delivery

Graphical Abstract



INTRODUCTION

Niosomes are newly developed vesicular drug delivery systems made of non-ionic surfactants that entrap drugs in particles. These vesicles have bilayer structures made of non-ionic surfactants and lipids, or cholesterol.^[1] They therefore form

lamellae around the drug in its capsule. The niosomes are small and inconsequential in size. They vary in size on a nanoscale, and lipid vesicles are different from niosomes both architecturally as well as in terms of their properties.^[2] As Paul Ehrlich, an investigator, suspected that a drug delivery mechanism could be directed specifically to infectious cells, he began the effort of developing targeted delivery in the year 1909. We'll look into medication targeting right now.^[3]

Address for correspondence:

Dr. Anupriya Kapoor, School of Pharmaceutical Sciences, CSJM University, Kanpur, Uttar Pradesh, India. Mobile: +91-9454739680.
E-mail: anupriya321@gmail.com

Received: 27-03-2024

Revised: 02-08-2024

Accepted: 22-08-2024

The capacity to route a therapeutic substance to a desired, precise spot to demonstrate the activity on targeted tissue may be elucidated as medication targeting. Niosomes are a cutting-edge drug delivery technology that encapsulates the medication inside tiny vesicles comprised of a matrix of polymers.^[4] The term “niosomes” alludes to the two layers of a non-ionic surfactant that are fundamentally present inside these vesicles. Amphiphilic vesicles are frequently stabilized by the addition of cholesterol, a suitable quantity of non-ionic surfactants such as span-60, and an anionic surfactant such as diacetyl phosphate.^[5]

Cholesterol vesicles and non-ionic surfactant, or what is known as a kind of drug delivery system known as a niosome form a closed bilayer by self-assembling in aqueous conditions and structure that satisfies biological requirements.^[6] Due to this delivery system’s solubility, biocompatibility, and versatility in working with both hydrophilic and lipophilic components, researchers are beginning to employ it extensively in the formulation of pharmaceuticals.^[7] Due to their capacity to ensnare hydrophilic and lipophilic elements inside their vesicular matrix, these materials are shielded from the body’s biological milieu. They can regulate a drug’s release and extend its duration of action. Furthermore, niosomes are preferred over liposomes due to their reduced production costs and increased stability.^[8]

By raising the medication’s concentration in the intended tissues and lowering its relative concentration in non-target tissues, targeted medication delivery aims to accomplish these objectives. Consequently, the drug concentrates in the intended area. Consequently, the medication does not affect the surrounding tissues.^[9] Consequently, localization ensures that the medication is administered as effectively as possible and keeps drug loss from happening. Numerous carriers, including erythrocytes, niosomes, liposomes as microspheres, serum proteins, and immunoglobulin, have been used to target drugs.^[10]

The same as liposomes, the kind of layer and the production process define the characteristics of niosomes. Cholesterol intercalation reduces the quantity of cholesterol entrapped during formulation and, thus, the efficiency of the entrapment. Niosomes have been employed to investigate the characteristics of the immune response that antigens elicit.^[11-14]

Niosomes are stiffer than the alternative niosome forms and may be created without the need for complex procedures. Similarly, because they have numerous bilayer membranes, they are appropriate for encapsulating lipophilic medicines.^[15]

ADVANTAGES^[16]

- Niosomes increase pharmacological penetration through the epidermis, thereby enhancing the oral bioavailability of less well-absorbed drugs

- Niosomes are biocompatible, biodegradable, and non-immunogenic surfactants are available
- Niosomes can store a variety of medicinal agents thanks to its structure, which combines hydrophilic and lipophilic elements
- By prolonging clearance from the blood, shielding the medication from its natural surroundings, and enhancing the drug’s actions on the targeted cells, they enhance the therapeutic efficacy of drug molecules
- You can administer them topically, parenterally, or orally to deliver them to the area of action
- The vesicles could serve as a storage mechanism that releases the medication gradually over time
- Niosomes increase the quantity of drug entrapped and are osmotically sensitive and stable.

DISADVANTAGES^[17]

- While niosomal administration has several benefits, stability in the aqueous solution of niosomes may be a problem due to the possibility of drug hydrolysis. Drug diffusion through the trapping site and niosomes aggregation development are potential issues
- Niosomes’ dispersion shape increases the possibility that the medicine it contains will settle, collect, fuse, or leak while being stored
- Certain formulation methods take a long time and call for specialized tools
- Niosomes a potential that surfactant won’t hydrate completely during the procedure
- There may be vesicle fusion and aggregation.

STRUCTURE OF NIOSOMES

Niosomes are bi-layered structures that are used by non-ionic surface-active chemicals. Only when cholesterol and surfactants are properly combined and the resulting temperature exceeds the gel-to-liquid changeover threshold can such thermodynamically resistant bilayered structures form. Cholesterol with enough quantity of an anionic surfactant, such as diacetyl phosphate, stabilizes the non-ionic surface-acting agent-containing amphiphilic vesicles of the niosomes. The structure of niosomes is depicted in Figure 1.^[18,19]

COMPOSITION OF NIOSOMES

Niosomes are a novel kind of vesicular drug delivery method whereby the drug is encapsulated within a vesicle and is generated from non-ionic surfactants. These vesicles are non-ionic bilayered structures, surface-active compounds, and lipid or cholesterol. As a result, they cluster around the medication within the lamellae. For the production of

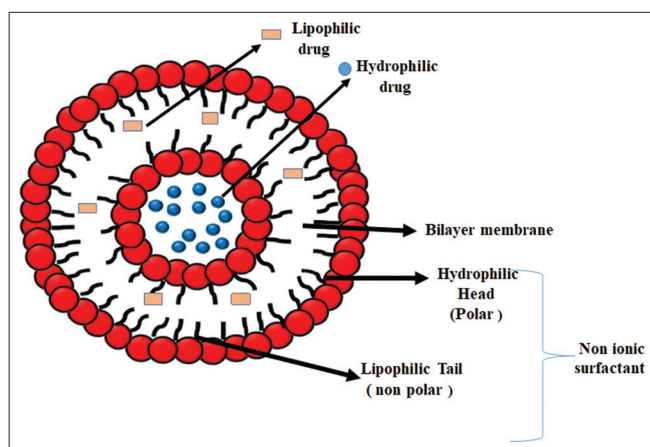


Figure 1: Structure of niosomes

niosomes, many ingredients are employed. They are as follows.

- Non-ionic surfactants
- Cholesterol.

Non-ionic surfactant

A family of surfactants known as non-ionic surfactants lacks charged molecules within their hydrophilic heads. Their nature makes them less toxic, more stable, and more biodegradable than their anionic, amphoteric, or cationic counterparts. They are therefore preferred for the *in vivo* and *in vitro* synthesis of stable niosomes. Amphiphilic molecules are non-ionic surfactants that are divided into two separate sections: A hydrophilic component that is soluble in water and a hydrophobic portion that is soluble in organic matter. Fatty acids, alkyl ethers, alkyl esters, and alkyl amides are the main non-ionic surfactant classes used in the synthesis of ribosomes. Nonionic surfactants self-orient within a two-layer structure, featuring the hydrophilic head or hydrocarbons section constructed thus and a polar or hydrophilic surface positioned on the water body (between). There won't be much interaction in the aquatic environment. Each bilayer folds into itself as a membrane, for example, producing a vesicle, to preserve thermal stability by keeping the hydrocarbon/water interface hidden. To create vesicles, the following categories of nonionic surfactants are often utilized. The hydrophilic head and hydrophobic tail make up the non-ionic surfactant. The types of non-ionic surfactants that are used to prepare niosomes are as follows in Table 1:^[20-24]

Cholesterol

It is an ingredient of steroids that are utilized to give the body the flexibility, stability, and proper form. It is a waxy steroid-based metabolite substance called cholesterol which is essential for the production of vesicular systems, which alter the permeability and fluidity of bilayer structures. To give the bilayer structure of the vesicle systems with the

fluidity, stiffness, permeability, and orientational order, it is often added to the non-ionic surfactants

- The bilayer itself cannot be formed by cholesterol. In most vesicular formulations, it can be added at a higher molar ratio, such as 1:1, to avoid vesicle aggregation. Utilizing repulsive steric/electrostatic forces, such molecules stabilize the vesicular structures and prevent aggregation formation. This leads to the niosomal systems changing from the gel state to the liquid phase. Niosomal systems consequently become less porous in nature. Moreover, cholesterol is an amphiphilic molecule, that adapts its hydroxyl group toward its aqueous state and aliphatic chain as well as toward the chain of hydrocarbons of the surfactants used to form vesicular structures, such as niosomes.^[25-31]

TYPES OF NIOSOMES

Niosomes are categorized according to the quantity of bilayers they contain (multilamellar vesicle [MLV], small unilamellar vesicle [SUV]), their size (Large unilamellar vesicle [LUV], SUV), or their preparation technique (REV, dried reconstituted vesicle). The niosomes types discussed above are as follows:

- SUV - Using the French press extrusion electrostatic stabilization technique in conjunction with the sonication method, little LUVs are produced from big ULVs tiny unilamellar vesicle, ranging in size from 25 to 50 nm or 0.025 to 0.05 μm
- MLV – Multiple bilayers encircling the aqueous lipid compartment individually are present in MLV. MLVs range in diameter from 0.5 to 10 μm on average. Most often, 90 MLV niosomes are utilized to include drugs. The MLV is easier to prepare and more stable over an extended length of time. This vesicle is more suited for medicinal compounds with lipids. Thin film hydration is the primary method used to prepare this sort of niosomes
- LUV – The LUVs have enormous diameters and a single bilayer membrane within their uni-lamellar vesicles. This vesicle has a higher aqueous and lipidic content, which accounts for its larger size.¹⁶ Compared to other varieties, this vesicle has a higher amount of drug entrapment. The LUV has an average size of 100 nm. These vesicles are typically made using the reverse phase evaporation and ether injection methods. LUVs have several advantages over MLVs, including a higher rate of drug encapsulation for water- soluble substances, consistent drug release rates, and lipid economy.^[32,33]

Drug release from niosomes

Targeted release can be achieved by developing niosomes with ligands or surface modifications that specifically interact with the target cells in the superficial layers of the skin. It is important to note that the preparation of niosomal

Table 1: Non-ionic surfactants

S. No.	Non-ionic surfactants	Chemical Designation	IUPAC Name	HLB Value	Appearance	States
1.	Atlas G- 1096	Sorbitan trioleate	Polyoxyethylene (50) sorbitol hexaoleate	16.5	White color	Liquid
2.	Atlas G- 2133	Dodecyl alcohol Ethoxylate	Dodecyl alcohol Ethoxylate	16	White	Liquid
3.	Brij 30	Polyoxyethylene (4) lauryl ether	2(do decyloxy) ethan -1- ol	9.6	White	Solid
4.	Brij 35	Polyoxyethylene lauryl ether	Dodecyl-poly -ethylene-oxide -ether	16.9	Clear colorless	Solid
5.	Brij 52	Polyoxyethylene cetyl ether	Polyoxyethylenecetyl (2) ether	5	White color	Waxy solid
6.	Brij 58	Polyethylene glycol hexadecyl ether	Oxyethylene	15.7	White to faint yellow	Waxy flakes
7.	Brij 72	Polyoxiethylene sorbitan	Polyoxyethylene (2) steryl ether	8.0	Light yellow color	Waxy solid
8.	Emcol PO50	1,2-propanediol monoolete	4-hydroxy 3-methoxy-benzaldehyde	3.4	Yellow	Solid
9.	Myrj 45	Polyoxyethylene sterate	2-hydroxyethyl octadecanoate	7.5	White color	Powder to lump
10.	Myrj 52					
11.	Span 20	Sorbitan monolaurate	(2E)-2-[(2R, 3R, 4S)]-3,4-Dihydroxyoxolan -2-yl]-2-hydroxyethyl dodecanoate	8.6	Amber color	Amber viscous liquid
12.	Span 60	Sorbitan momostearate	(3S)-2-(1,2-dihydroxyethyl) tetrahydrofuran-3,4- diol	4.7	Light cream to tan color hard	Colorless solid

formulations for superficial action involves a balance between factors to achieve optimal drug release, stability, and penetration. Drug release from niosome is depicted in Figure 2.

METHODS OF PREPARATION OF NIOSOMES

Niosome preparation techniques should be selected based on the utilization of tiny particles since the amount of bilayers as well their shape, distribution of size, or entrapment are all factors to take into account. Permeability of the membrane as well as effectiveness in the aqueous phase. The vesicles are made up of various vesicles.

Ether injection method

In this type of method after making a surfactant combination solution, warm water kept at 60°C is gradually added to it. Using a 14-gauge needle, the surfactant combination in ether is injected into the material's aqueous solution. The vaporization of ether results in the formation of single-layered vesicles. Vesicles with dimensions that vary between 50 and 1000 nm are created, depending on the situation.

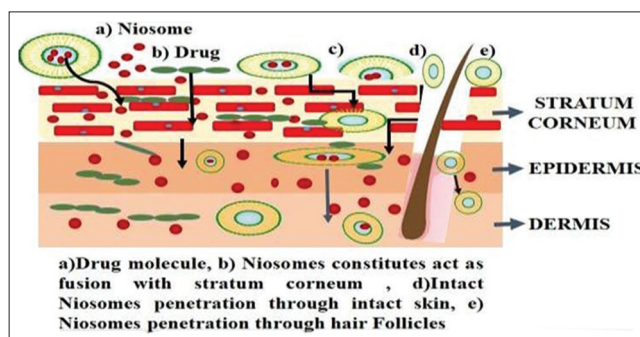


Figure 2: Drug release from niosomes

The biggest disadvantage of such an approach consists of the minimal quantity of ether that usually remains within the vesicle solution and is often difficult to remove. Ether injection method is as shown in Figure 3a.^[34-36]

Reverse phase evaporation method

This method entails mixing a combination of ether and chloroform with cholesterol and surfactant (1:1).^[37] This is blended with a medication-containing aqueous phase, and the two phases are sonicated together at 4–5°C. The transparent gel that has developed above is next subjected to

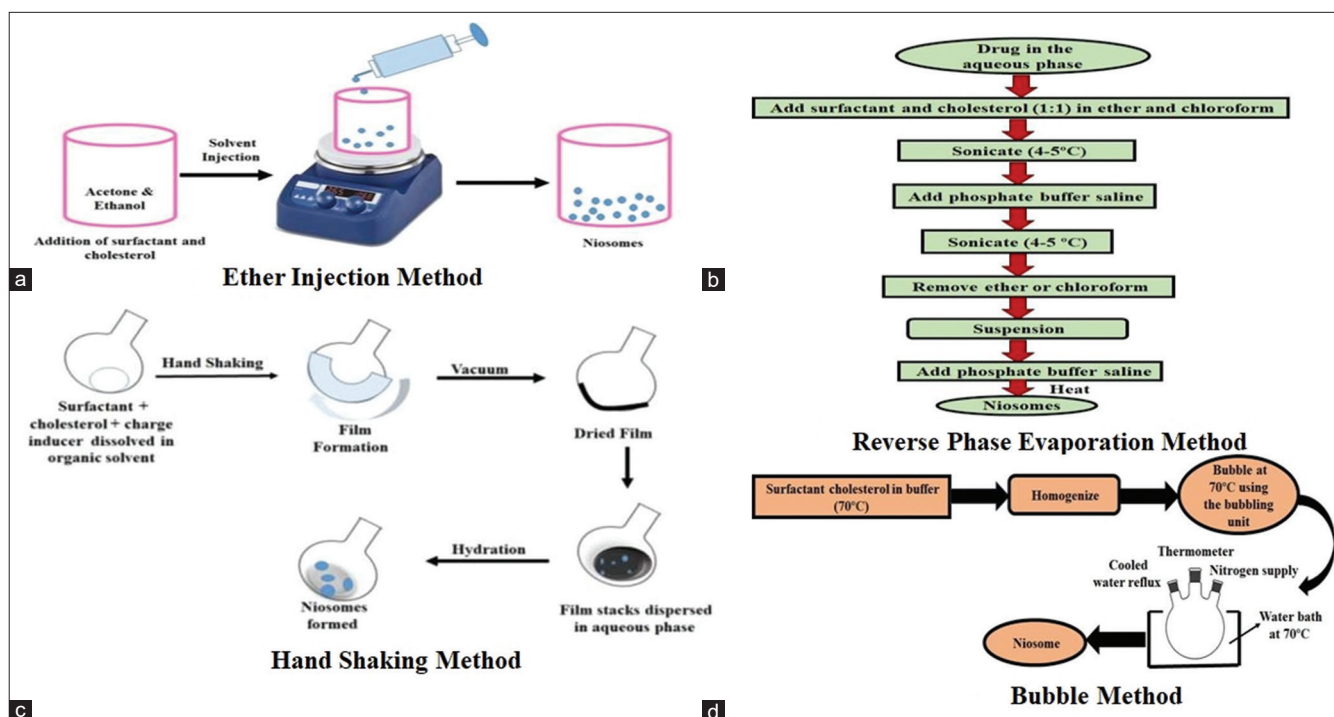


Figure 3: (a-d) Method of preparation of niosomes

sonication following a little addition of saline buffered with phosphate. At 40°C and low pressure, the organic component is destroyed. After mixing phosphate buffer with saltwater to thin the resulting viscous niosome solution, it is heated in a water bath at 60°C for 10 min to generate niosomes. Reverse phase evaporation method is as shown in Figure 3b.^[38,39]

Handshaking method

The method known as the thin-film hydration technique is another name for this process. In another round-bottom flask, vesicles that mix with ingredients such as cholesterol and surfactants disintegrate when exposed to a strongly organic solvent. A revolving evaporator running at a constant temperature (20°C) is used to extract the organic solvent, leaving behind an outer layer of solid mixture that builds up on the flask rim. Between 0 and 60°C and with moderate shaking, the dehydrated surfactant layer can be hydrated again to the phase of water. This process results in typical multilamellar niosomes. Hand shaking method is depicted in Figure 3c.^[40-44]

Micro fluidization method

The idea of immersed jets is the basis for the micro-fluidization process. In this technique, the hydrated stream of drug and surfactant interact at extremely high speeds in a narrowly defined microchannel inside the interaction chamber. Niosomes typically form as a consequence of high-energy collision. Smaller, unilamellar, more homogeneous, and highly repeatable niosomes are created by this technique.^[45-48]

Sonication

The approach states that sonicating a solution is a common step in the veiling process. Using this procedure, a buffered aliquot of medication solution from a 10-mL glass vial is added to the surfactant/cholesterol mixture. To get niosomes, the mix is probe-sonicated for 3 s at 60°C using a titanium probe.^[49]

Multiple membrane extrusion method

A thin layer of diacetyl phosphate, cholesterol, and surfactants is produced in chloroform using a Rotary Evaporator. Through water polycarbonate membranes, the film is hydrated, the film is hydrated. The suspension so formed is extruded via a polycarbonate membrane and into a network of up to eight tunnels. The final product is obtained in the form of niosomes with nearly uniform size. It is a smart move a process for controlling the size of niosomes.^[50]

The bubble method

In this type of technique, the surfactants, chemicals, and buffers are all kept in a clear flask with three necks. The niosome component components are dispersed at 75°C. The dispersion was blended in a homogenizer. The flask is then instantly submerged in a water bath while bubbling the nitrogen gas at a temp of 70°C. Nitrogen gas is employed through the system to power it. As a consequence, you get an amount of homogeneous surfactants. The massive unilamellar vesicle production is shown in Figure 3d.^[51]

EVALUATION OF NIOSOMES

For clinical uses, niosome characterization is crucial. Niosome stability is directly influenced by characterization factors, which also have a major effect on the niosomes' *in vivo* performance. Thus, it is necessary to assess these characteristics, which include size, shape, polydispersity index, the number of lamellae and zeta potential, encapsulation effectiveness, and stability.

Zeta potential

The charge that exists on the surface of a niosomes is known as the zeta potential. This charge is frequently present on the surface of a niosomes and is caused by an ingredient or component that was employed during the manufacturing process.

Every niosome in the formulation has to have some charge on its surface to prevent particle coagulation and all niosome particles from repelling to one another. The niosomes zeta potential was measured using a Zetasizer device with Malvern software. Sample analysis was performed at 25°C and a 90° angle of detection. It is necessary to have a zeta potential value that falls between +30 and -30 mV. This range inhibits niosomal particle agglomeration range of zeta potential, as shown in Table 2.^[52,53]

Size

Niosomal vesicles are thought to have a spherical shape. Their mean diameter can be measured using a variety of methods, including electron microscopy, laser light scattering, freeze-fracture electron microscopy, photonic correlations microscopy, optical microscopy, molecular sieve chromatography, and ultracentrifugation. For scanning electron microscopy (SEM) to examine niosomes, the SEM was employed. They had been set up with double-sided tape applied directly to the SEM sample, stub adhesion tape, and an excellent film with a thickness of 200 nm at a pressure of 0.001 mmHg. Adequate magnification was used for taking the pictures.^[54-56]

Entrapment efficiency

As previously mentioned, following the preparation of the niosomal dispersion, the drug that is not entrapped is

separated using centrifugation, gel filtration, dialysis, and/or finished vesicles impairment utilizing 50% n-propanol or 0.1% Triton X-100. The amount of drug that is still entrapped in the niosomes is then estimated, and the reaction solution is analyzed using the proper assay technique to detect the drug.

Whereby the definition of entrapment efficiency (EF) is

$$\text{Entrapment Efficiency} = \left(\frac{\text{Amount of encapsulated drug}}{\text{Total drug added}} \right) \times 100^{[57-59]}$$

Stability studies

A standard practice for ensuring the preservation of pharmaceutical product safety, effectiveness, and quality throughout the course of the shelf life is stability studies. The regulations set out by regulatory organizations such as the WHO, ICH, and other regulatory authorities are adhered to in the case of pharmaceutical formulations. For 3 months, niosomal formulations are kept in a thermostatic oven at 4, 25, and 37°C as part of stability tests. After a month, the drug content of each formulation is examined. Using appropriate analytical techniques, such as ultraviolet (UV) spectroscopy and high-performance liquid chromatography (HPLC) procedures, the efficiency parameter is measured.

The long-term stability of niosomes under various storage circumstances was investigated. As per the ICH stability criteria, stability was assessed in two distinct situations. The niosomal preparations were kept in clear containers at 4–8°C in a refrigerator and 24 ± 2°C in a climate room. Samples were collected for up to three months at the proper intervals. The stability profile was assessed by evaluating the vesicle size, entrapment, and zeta potential. To assess any variations in formulation color, a visual inspection was also conducted.^[60,61]

In vitro drug release

The cholesterol and surfactant together can reduce permeability and improve membrane stiffness, particularly cholesterol, which might affect the fluidity of the bilayer chain, thereby lowering permeability. To forecast the mechanism of drug release from niosomes, the *in vitro* release data were fitted to several release kinetics models. The rate of release *in vitro* was investigated.^[62]

Dialysis tubing

The dialysis sac is cleaned with distilled water. A dialysis tubing bag is pipetted with the vesicle suspension tube consisting of dialysis tubing. The bag closes safely. After that, the vesicles are put in a 250 mL beaker with 200 mL of buffer solution and continuously shaken at 25°C. An examination of

Table 2: Range of zeta potential

S. No.	Zeta potential (mV)	Stability behavior of the colloid
1.	0±5	Flocculation
2.	±10–±30	Incipient instability
3.	±30–±40	Moderate stability
4.	±40–±60	Good stability
5.	±60	Excellent stability

Table 3: Application of niosomes^[71-74]

S. No.	Surfactant Used	Drug (API)	Method of preparation	Application	Route of administration
1.	Span 40	Docetaxel	Thin layer evaporation technique	DTX niosomes provide an approach for the solubility enhancement, toxicity reduction, and stability enhancement of the anticancer drug DTX.	Oral administration
2.	Span 60	Lecidipine	Ultrasonic method	It provided an alternative to existing delivery systems for this drug	Transdermal administration
3.	Span 80	Cetirizine	Thin film hydration method	Treatment of androgenic alopecia	Topical route of administration
4.	Span 60	Nintedanib	Thin film hydration method	Lung cancer	Nasal route
5.	Span 60, tween 80	Dexamethasone	Thin film hydration method	Topical delivery	Transdermal route of Administration
6.	Span 40	Luliconazole	Thin film hydration method	Used in the treatment of fungal infection	Transdermal route
7.	Span 80	Doxycycline	Thin film hydration method	Its concludes that niosomal-containing drug have potential application	Topical route of administration
8.	Span 60	Azithromycin	Ether injection method	Used as an alternative route of administration for ex- transdermal routes.	Transdermal route of administration
9.	Span 40, 60	Propranolol	Conventional film hydration method	The application of a new topical dosage form of drug shows results for the treatment of infantile hemangioma	Topical route of administration
10.	Span 20, tween 40	Glutathione	Thin film hydration method	Investigate the pharmacokinetic barrier	Oral route of administration

the medication throughout different periods is provided by the Buffer creation of an appropriate test methodology.^[63]

the use of methods such as UV spectrometry, HPLC, and others.^[65-67]

Reverse dialysis

A multitude of small dialysis units, each holding 1 mL of dissolving media, are packed into pseudosomes. Subsequently, the periosomes are transferred into the medium to dissolve the water dilution directly. Proniosomes may be manufactured fast using this method. It is not possible to quantify using the reverse dialysis method.^[64]

Franz diffusion cell

The Franz diffusion cell is used for *in vitro* diffusion investigations. Franz donor chambers are used to inject niosomes. There was a diffusion of cells surrounded by a cellophane membrane. Next, the lysosomes are dialyzed against a desired protein. The materials were dissolved in a dissolving solvent at room temperature at 25°C. They are removed from the medium at regular intervals, and an appropriate method is employed to screen for drug content. Sinks are kept in excellent operating condition by

APPLICATIONS

- Niosomes are used for delivering anti-cancer drugs like methotrexate and doxorubicin to tumors, improving both drug delivery and tumoricidal efficacy
- Multiple dosages of niosomes loaded with sodium Streptogluconate were found to be effective against infections in the spleen, bone marrow, and liver contrasted their results with an ordinary sodium Stibogluconate solution
- Investigated the absorption of norfloxacin and ciprofloxacin when they were given as noisy encapsulated inclusion complexes
- Established a significant liver level in mice after injecting the carrier forms of the antimony dispersion intravenously. Drugs called antibiotics are used for the treatment of bacterial infections
- In peptide drug delivery for a long time, oral peptide medication administration has struggled to avoid enzymes that would break down the peptide. Research

is being done on the effective use of niosomes to shield peptides from gastrointestinal peptide degradation. The long-term stability of the peptides was shown to be greatly enhanced by the trapping of a vasopressin derivative in niosomes, as demonstrated by an oral administration method used in an *in vitro* investigation

- Niosomes have been used for investigating the nature of the immune response triggered by antigens due to their immunological selectivity, low toxicity, and increased stability. The capacity of non-ionic surfactant vesicles to act as an adjuvant after parenteral delivery of various antigens and peptides has been well shown, as shown in Table 3.^[68-70]

CONCLUSIONS

One of the most notable instances of the rapid advancement in drug delivery technology is the niosomal drug delivery system. Scholars and researchers generally agree that drugs may be incorporated into niosomes and that niosomes can be directed to a certain location. They are substitute vesicular systems for liposomes, and they have several benefits over liposomes, including affordability and stability.

To fully realize the promise of this innovative drug delivery system, considerable study needs to be done on niosomes, an exciting new drug delivery technique. Niosomes are more cost-effective and safe than liposomes as a medication delivery mechanism. Niosomes can potentially be used in drug development to deliver non-infectious, non-cancer drugs with great precision. These days, proniosomes, pain, and aspasome are among the newest methods used to improve niosomal medication delivery. Niosomes function as an adjuvant to the vaccination and as a more significant therapeutic assistance. Therefore, further study and investigation are required in these areas to provide widely accessible niosomal preparation.

FUTURE PROSPECTIVE

A potential molecule for medication delivery is niosomes. Niosomes offer a great deal of potential as drug carriers because they can encapsulate toxic anti-cancer, anti-infective, anti-AIDS, anti-inflammatory, antiviral, and other medications. This will improve the drugs' bioavailability and targeting while also lowering their toxicity and side effects. Niosomal drug carriers are safer than ionic ones, which are more hazardous and inappropriate. Niosome handling and storage do not call for any unique circumstances.

This fact stems from the fact that, as revealed from the examined data, niosomes technology is necessary for the manufacture of cosmeceutical products to provide a superior effect on the skin and hair due to their tiny size and high penetration rate. Improved cosmeceutical outcomes lead

to higher-quality products, which increase sales of these products and produce a more successful marketing strategy.

AUTHORS' CONTRIBUTIONS

MT is the main author of the article having conceptualized the review topic and writing the article. APK has participated in data analysis and provided expertise and insights into specific sections of the reviews and she was involved in the corresponding article. SKM, SR, HP, and AK have contributed to the designing the concept. All the authors have read and approved the article.

REFERENCES

1. Devi SG, Udupa N. Niosomal sumatriptan succinate for nasal administration. *Indian J Pharm Sci* 2000;62:479-81.
2. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes-non-ionic surfactant vesicles. *J Pharm Pharmacol* 1985;37:863-8.
3. Hunter CA, Dolan TF, Coombs GH, Baillie AJ. Vesicular systems (niosomes and liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. *J Pharm Pharmacol* 1988;40:161-5.
4. Van Hal DA, Bouwstra JA, Junginger HE. Nonionic surfactant vesicles containing estradiol for topical application. *Drugs Pharm Sci* 1996;73:329-47.
5. Handjani-Vila RM, Ribier A, Rondot B, Vanlerberghie G. Dispersions of lamellar phases of non-ionic lipids in cosmetic products. *Int J Cosmet Sci* 1979;1:303-14.
6. Moghtaderi M, Mirzaie A, Zabet N, Moammeri A, Mansoori-Kermani A, Akbarzadeh I, *et al.* Enhanced antibacterial activity of *Echinacea angustifolia* extract against multidrug-resistant *Klebsiella pneumoniae* through niosome encapsulation. *Nanomaterials (Basel)* 2021;11:1573.
7. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. *Int J Pharm* 1998;172:33-70.
8. Mavaddati MA, Moztaizadeh F, Baghbani F. Effect of formulation and processing variables on dexamethasone entrapment and release of niosomes. *J Cluster Sci* 2015;26:2065-78.
9. Mokhtar M, Sammour OA, Hammad MA, Megrab NA. Effect of some formulation parameters on flurbiprofen encapsulation and release rates of niosomes prepared from proniosomes. *Int J Pharm* 2008;361:104-11.
10. Kapoor A, Mishra SK, Verma DK, Pandey P. Chemical penetration enhancers for transdermal drug delivery system. *J Drug Deliv Ther* 2018;8:62-6.
11. Allen TM. Liposomal drug formulations. Rationale for development and what we can expect for the future. *Drugs* 1998;56:747-56.
12. Szoka F Jr., Papahadjopoulos D. Comparative properties and methods of preparation of lipid vesicles (liposomes).

- Ann Rev Biophys Bioeng 1980;9:467-508.
13. Brewer JM, Alexander J. The adjuvant activity of non-ionic surfactant vesicles (niosomes) on the BALB/c humoral response to bovine serum albumin. *Immunology* 1992;75:570-5.
 14. Moghassemi S, Hadjizadeh A. Nano-niosomes as nanoscale drug delivery systems: An illustrated review. *J Control Release* 2014;185:22-36.
 15. Marianecci C, Di Marzio L, Rinaldi F, Celia C, Paolino D, Alhaique F, *et al.* Niosomes from 80s to present: The state of the art. *Adv Colloid Interface Sci* 2014;205:187-206.
 16. Bagheri A, Chu BS, Yaakob H. Niosomal drug delivery systems: Formulation, preparation and applications. *World Appl Sci J* 2014;32:1671-85.
 17. Ahuja N, Saini V, Bishnoi VK, Garg A, Hisoria M, Sharma J, Nepali K. Formulation and evaluation of lansoprazole niosome. *Rasayan J Chem* 2008;1:561-3.
 18. Rogerson AC, Cummings J, Willmott N, Florence AT. The distribution of doxorubicin in mice following administration in niosomes. *J Pharm Pharmacol* 1988;40:337-42.
 19. Buckton G. *Interfacial Phenomena in Drug Delivery and Targeting*. United States: CRC Press; 2000.
 20. Ge X, Wei M, He S, Yuan WE. Advances of non-ionic surfactant vesicles (niosomes) and their application in drug delivery. *Pharmaceutics* 2019;11:55.
 21. Mishra A, Kapoor A, Bhargava S. Proniosomal gel as a carrier for improved transdermal drug-delivery. *Asian J Pharm Clin Res* 2011;1:370-9.
 22. Girigoswami A, Das S, De S. Fluorescence and dynamic light scattering studies of niosomes-membrane mimetic systems. *Spectrochim Acta A Mol Biomol Spectrosc* 2006;64:859-66.
 23. Jiao J. Polyoxyethylated nonionic surfactants and their applications in topical ocular drug delivery. *Adv Drug Deliv Rev* 2008;60:1663-73.
 24. Abdelkader H, Ismail S, Kamal A, Alany RG. Preparation of niosomes as an ocular delivery system for naltrexone hydrochloride: Physicochemical characterization. *Pharmazie* 2010;65:811-7.
 25. Liu T, Guo R, Hua W, Qiu J. Structure behaviors of hemoglobin in PEG 6000/Tween 80/Span 80/H₂O niosome system. *Colloids Surf A Physicochem Eng Aspects* 2007;293:255-61.
 26. Agarwal S, Bakshi V, Vitta P, Raghuram AP, Pandey S, Udupa N. Effect of cholesterol content and surfactant HLB on vesicle properties of niosomes. *Indian J Pharm Sci* 2004;66:121-3.
 27. Tangri P, Khurana S. Niosomes: Formulation and evaluation. *Int J* 2011;2229:7499.
 28. Okore VC, Attama AA, Ofokansi KC, Esimone CO, Onuigbo EB. Formulation and evaluation of niosomes. *Indian J Pharm Sci* 2011;73:323-8.
 29. Rogerson A, Cummings J, Florence AT. Adriamycin-loaded niosomes: Drug entrapment, stability and release. *J Microencapsul* 1987;4:321-8.
 30. Griffin WC. Calculation of HLB values of non-ionic surfactants. *Am Perfumer Essent Oil Rev* 1955;65:26-9.
 31. Uchegbu IF, Florence AT. Non-ionic surfactant vesicles (niosomes): Physical and pharmaceutical chemistry. *Adv Colloid Interface Sci* 1995;58:1-55.
 32. Cook EJ, Lagace AP, Inventors; Biotechnology Development Corp, Assignee. Apparatus for Forming Emulsions. United States Patent US 4,533,254; 1985.
 33. Naveen G, Vishal S, Somesh S, Aditya P. Formulation and evaluation of non-ionic surfactant vesicles (niosomes) for ocular delivery of ofloxacin. *Int J Phar Life Sci* 2010;1:413-8.
 34. Kaur H, Dhiman S, Arora S. Niosomes: A novel drug delivery system. *Int J Pharm Sci Rev Res* 2012;15:113-20.
 35. Yadav R, Chanana A, Chawra HS, Singh RP. Recent advances in niosomal drug delivery: A review. *Int J Multidiscip Res* 2023;5:1-10.
 36. Srinivas S, Kumar YA, Hemanth A, Anitha M. Preparation and evaluation of niosomes containing aceclofenac. *Dig J Nanomater Bios* 2010;5:249-54.
 37. Naresh RR, Pillai GK, Udupa N, Chandrashekar G. Anti-inflammatory activity of niosome encapsulated diclofenac sodium in arthritic rats. *Indian J Pharmacol* 1994;26:46-8.
 38. Sharma SK, Chauhan M, Anilkumar N. Span-60 niosomal oral suspension of fluconazole: Formulation and in vitro evaluation. *J Pharm Res Health Care* 2009;1:142-56.
 39. Bhaskaran S, Lakshmi PK. Comparative evaluation of niosome formulations prepared by different techniques. *Acta Pharm Sci* 2009;51:27-32.
 40. Sharma SK, Chauhan M, Anilkumar N. Span-60 niosomal oral suspension of fluconazole: Formulation and in vitro evaluation. *J Pharm Res Health Care* 2009;1:142-56.
 41. Khandare JN, Madhavi G, Tamhankar BM. Niosomes novel drug delivery system. *East Pharm* 1994;37:61.
 42. Mouzam MI, Dehghan MH, Shaikh Samina M. Development and characterization of salmeterol xinafoate niosomes for nasal delivery. *Ind J Pharm Educ Res* 2011;45:121-7.
 43. Zidan AS, Rahman Z, Khan MA. Product and process understanding of a novel pediatric anti-HIV tenofovir niosomes with a high-pressure homogenizer. *Eur J Pharm Sci* 2011;44:93-102.
 44. Verma S, Singh SK, Syan N, Mathur P, Valecha V. Nanoparticle vesicular systems: A versatile tool for drug delivery. *J Chem Pharm Res* 2010;2:496-509.
 45. Prabhu P, Koland M, Vijaynarayan K, Harish NM, Ganesh D, Charyulu RN, *et al.* Preparation and evaluation of niosomes of brimonidine tartrate as ocular drug delivery system. *J Pharm Res Health Care* 2010;2:293-301.
 46. Kapoor A, Gahoi R, Kumar D. In-vitro drug release profile of Acyclovir from Niosomes formed with different Sorbitan Esters. *Asian J Pharm Life Sci* 2011;1:64-70.
 47. Suwakul W, Ongpipattanukul B, Vardhanabhuti N. Preparation and characterization of propylthiouracil niosomes. *J Liposome Res* 2006;16:391-401.

48. Gondkar SB, Malekar NS, Saudagar RB. An overview on trends and development of niosomes as drug delivery. *Res J Top Cosmet Sci* 2016;7:79-85.
49. Yasam VR, Jakki SL, Natarajan J, Kuppusamy G. A review on novel vesicular drug delivery: Proniosomes. *Drug Deliv* 2014;21:243-9.
50. Selvaraj S, Niraimathi V, Nappinnai M. Formulation and evaluation of acyclovir loaded chitosan nanoparticles. *Int J Pharm Res Sci Nanotechnol* 2016;5:619-29.
51. Smulders S, Kaiser JP, Zuin S, Van Landuyt KL, Golanski L, Vanoirbeek J, *et al.* Contamination of nanoparticles by endotoxin: Evaluation of different test methods. *Part Fibre Toxicol* 2012;9:41.
52. Tarekegn A, Joseph NM, Palani S, Zacharia A, Ayenew Z. Niosomes in targeted drug delivery: Some recent advances. *Int J Pharm Sci Res* 2010;1:1-8.
53. 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;1:374-80.
54. Biswal S, Murthy PN, Sahu J, Sahoo P, Amir F. Vesicles of non-ionic surfactants (niosomes) and drug delivery potential. *Int J Pharm Sci Nanotechnol* 2008;1:1-8.
55. Azmin MN, Florence AT, Handjani-Vila RM, Stuart JF, Vanlerberghe G, Whittaker JS. The effect of non-ionic surfactant vesicle (niosome) entrapment on the absorption and distribution of methotrexate in mice. *J Pharm Pharmacol* 1985;37:237-42.
56. Tavano L, Aiello R, Ioele G, Picci N, Muzzalupo R. Niosomes from glucuronic acid-based surfactant as new carriers for cancer therapy: Preparation, characterization and biological properties. *Colloids Surf B Biointerfaces* 2014;118:7-13.
57. Mehta SK, Jindal N. Formulation of tyloxapol niosomes for encapsulation, stabilization and dissolution of anti-tubercular drugs. *Colloids Surf B Biointerfaces* 2013;101:434-41.
58. Waddad AY, Abbad S, Yu F, Munyendo WL, Wang J, Lv H, *et al.* Formulation, characterization and pharmacokinetics of Morin hydrate niosomes prepared from various non-ionic surfactants. *Int J Pharm* 2013;456:446-58.
59. Pando D, Gutiérrez G, Coca J, Pazos C. Preparation and characterization of niosomes containing resveratrol. *J Food Eng* 2013;117:227-34.
60. Karki R, Mamatha GC, Subramanya G, Udupa N. Preparation, characterization and tissue disposition of niosomes containing isoniazid. *Rasayan J Chem* 2008;1:224-7.
61. Vaishnav S, Kothavade M, Khairnar K. Niosomes: A promising nanocarrier system for drug delivery. *Int J Pharm Sci* 2024;2:503-14.
62. Keservani RK, Sharma AK, Ayaz M, Kesharwani RK. *Int J Res Control Release* 2022;7:523-34
63. Vishvakrama P, Sharma S. Liposomes: An overview. *J Drug Deliv Therapeut* 2014;4:47-55.
64. Tangri P, Khurana S. Niosomes: Formulation and evaluation. *Int J* 2011;2229:7499.
65. Suma US, Parthiban S, Senthil Kumar GP, Tamiz Mani T. Novelty of niosomal gel in TDDS application. *Asian J Res Biol Pharm Sci* 2015;3:41-8.
66. Kumari R, Verma K, Verma A, Yadav GK, Maurya SD. Proniosomes: A key to improved drug delivery. *J Drug Deliv Ther* 2014;4:56-65.
67. Suma US, Parthiban S, Senthil Kumar GP, Tamiz Mani T. Novelty of niosomal gel in TDDS application. *Asian J Res Biol Pharm Sci* 2015;3:41-8.
68. Namdeo A, Mishra PR, Khopade AJ, Jain NK. Formulation and evaluation of niosome encapsulated indomethacin. *Indian Drugs* 1999;36:378-80.
69. Rossi A, Campo D, Fortuna MC, Garelli V, Pranteda G, De Vita G, *et al.* A preliminary study on topical cetirizine in the therapeutic management of androgenetic alopecia. *J Dermatolog Treat* 2018;29:149-51.
70. Sarisozen C, Vural I, Levchenko T, Hincal AA, Torchilin VP. PEG-PE-based micelles co-loaded with paclitaxel and cyclosporine A or loaded with paclitaxel and targeted by anticancer antibody overcome drug resistance in cancer cells. *Drug Deliv* 2012;19:169-76.
71. Sarisozen C, Vural I, Levchenko T, Hincal AA, Torchilin VP. PEG-PE-based micelles co-loaded with paclitaxel and cyclosporine A or loaded with paclitaxel and targeted by anticancer antibody overcome drug resistance in cancer cells. *Drug Deliv* 2012;19:169-76.
72. Thakkar M, Brijesh S. Opportunities and challenges for niosomes as drug delivery systems. *Curr Drug Deliv* 2016;13:1275-89.
73. Tavano L, Muzzalupo R, Picci N, De Cindio B. Co-encapsulation of antioxidants into niosomal carriers: Gastrointestinal release studies for nutraceutical applications. *Colloids Surf B Biointerfaces* 2014;114:82-8.
74. Marianecchi C, Rinaldi F, Di Marzio L, Ciogli A, Esposito S, Carafa M. Polysorbate 20 vesicles as multi-drug carriers: *In vitro* preliminary evaluations. *Lett Drug Design Discov* 2013;10:212-8.

Source of Support: Nil. **Conflicts of Interest:** None declared.