

An overview on Niosomes: Novel Pharmaceutical drug delivery system

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Abstract



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

Keywords: Niosomes, Composition, Types, Method of preparation, Characterization, Application.

INTRODUCTION

Poul Ehrlich pioneered the development of targeted drug delivery in 1909. The targeted drug delivery system acts directly on the desired or targeted site. Targeted drug delivery is the ability of a therapeutic agent to act directly on the desired site with little or no interaction with other non-targeting sites. The niosome is composed of non-ionic surfactants containing cholesterol and a small amount of ionic surfactants, such as diacetyl phosphate, which is used for stability. L'Oréal Company created and marketed the first non-ionic surfactant product, which was used for cosmetic purposes. Because of their multi-environmental structure, niosomes can deliver a variety of drugs to specific sites¹. The goal of targeting drug delivery systems is to deliver the drug in the body in such a way that it demonstrates its action to the targeted and desired site to achieve the therapeutic response, i.e. wherever its action is required by limiting undesirable interaction to non-targeted tissues. In 1909, Poul Ehrlich proposed this strategy, which he dubbed "magic bullets." During the last decade, the design of vesicles as a tool to improve drug delivery has piqued the interest of scientists working in the field of drug delivery systems. Liposomes, niosomes, transferosomes, pharmacosomes, and ethosomes are examples of vesicular systems that can be used to improve drug delivery. Among these various carriers, niosomes are highly efficient drug delivery systems. Niosomes are a vesicular, novel drug delivery system that can be used for long-term, controlled, and targeted medication delivery with high stability². Niosomes are a novel drug delivery system that

entraps hydrophilic drugs in the core cavity and hydrophobic drugs in the non-polar region of the bilayer, allowing both hydrophilic and hydrophobic drugs to be incorporated into the niosome. Chemical stability, biodegradability, biocompatibility, low production cost, easy storage, easy handling, and low toxicity are the primary reasons for developing a niosomal system. Niosome can be administered via a variety of routes, including oral, parenteral, topical, and ocular administration^{3,4,5}. The medication is encapsulated in a vesicle in the niosome drug delivery system. The vesicle is made up of a bilayer of non-ionic surfactants, thus the name niosomes⁶. Niosomes are one of the most effective carriers. Niosomes are structurally similar to liposomes and have the same drug delivery potential, but their high chemical stability and economy make them superior to liposomes. Both are made up of the bilayer, which is composed of a non-ionic surfactant. Liposomes contain phospholipids in the case of niosomes and phospholipids in the case of liposomes. Niosomes are microscopic lamellar structures with sizes ranging from 10 to 1000 nm that are made up of biodegradable, non-immunogenic, and biocompatible surfactants. Because niosomes are amphiphilic in nature, hydrophilic drugs can be entrapped in the core cavity and hydrophobic drugs can be entrapped in the non-polar region present within the bilayer, allowing both hydrophilic and hydrophobic drugs to be incorporated into niosomes⁷. Niosomes are one of the techniques used to create a controlled release system. Niosomes have a multilamellar or unilamellar structure that is formed by combining a nonionic surfactant, cholesterol, and diethyl ether, followed by hydration in

aqueous media. Niosomes outperform liposomes in terms of surfactant chemical stability, as opposed to phospholipids, which are easily hydrolyzed due to the ester bond, and cost-effectiveness⁸.

ADVANTAGES^{9, 10, 11, 12, 13}

- Side effects are reduced, and the activity lasts as long as possible.
- When compared to alternative delivery systems, patient compliance is higher.
- The amount of medicine required to provide the desired effect is extremely little.
- Bilayer protects the active component or constituent in the preparation from numerous influences both inside and outside the body.
- As a depot formulation, the drug is released slowly and steadily.
- First-pass metabolism and gastrointestinal degradation are not a problem for this drug.
- Even in emulsion form, they have a stable structure.
- Niosomes can be used orally, topically, or intravenously.

- Niosomes can hold a wide range of drug moieties, including hydrophilic, lipophilic, and amphiphilic medicines.
- The drug can be released in a controlled and continuous manner.
- No special conditions required for handling and storage of surfactants.
- Drug defense against enzyme metabolism.
- They can improve drug penetration through the skin. Due to prolonged clearance from the circulation, they increase the therapeutic profile of drug molecules.

DISADVANTAGES^{14, 15, 16}

- The procedure takes a long time.
- Processing necessitates the use of specialized equipment.
- Due to the limited shelf life
- Cohesion
- Compilation
- Entrapped drug leakage
- Drugs that have been encapsulated are hydrolyzed.

COMPARISON BETWEEN NIOSOME AND LIPOSOME¹⁷

NIOSOMES	LIPOSOMES
Less Expensive	More Expensive
No special methods require for such formulations	Require special methods for storage and handling of the final formulation
Non-ionic surfactant is uncharged.	Phospholipids may be neutral and charged

STRUCTURE OF NIOSOME:

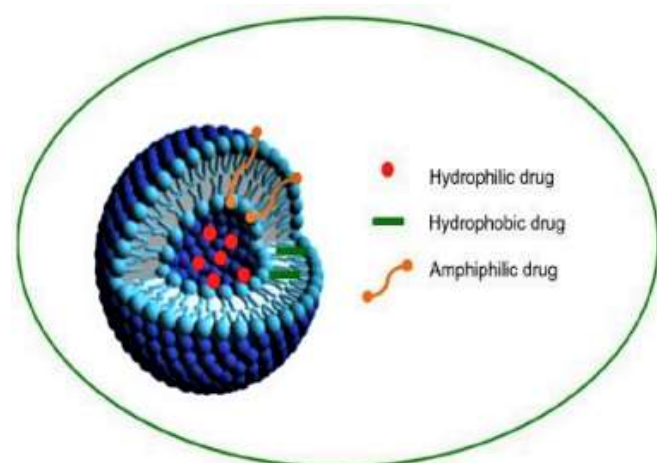


Figure 1: Structure of niosome¹⁸

COMPOSITION OF NIOSOME:

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

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

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

1. **Non ionic surfactants:** Non-ionic surfactants are an essential component of niosomes. To form niosomes, various types and their combinations are used to entrap various medications. Non-ionic surfactants are naturally amphiphilic, biodegradable, biocompatible, and non-immunogenic. The composition, concentration of additives, size, lamellarity, and surface charge of vesicles determine the properties of formulated niosomes. Non-ionic surfactants such as span (60, 40, 20, 85, and 80) and Tween (20, 40, 60, and 80) are used in the formation of niosomes¹⁹.
2. **Cholesterol:** It's a crucial additive in the formulation of niosomes. Cholesterol is not only required for the formation of niosomes, but it also influences many of their properties. It influences the membrane's permeability, rigidity, entrapment efficiency, ease of rehydration of freeze-dried niosomes, stability, and storage period. If cholesterol is combined with low HLB surfactants, it increases vesicle stability, and if the HLB value is greater than 6, it aids in the creation of bilayer vesicles. The addition of cholesterol improves the viscosity and, as a result, the rigidity of the formulation²⁰.
3. **Charged molecule:** Niosomes have some charged molecules added to them to increase stability by providing electric repulsion to prevent collisions. Diacetyl phosphate (DCP) and phosphotidic acid are both negatively charged compounds. Similarly, in niosomal preparations, stearyl

amine and stearyl pyridinium chloride are well-known charged compounds²¹.

4. **Hydration medium:** One of the most significant components in the formulation of niosomes is the hydration medium. Phosphate buffer is commonly employed as a hydration medium. However, the pH of the buffer is determined by the solubility of the encapsulated medication²².

TYPES OF NIOSOMES²³:

The many varieties of niosomes are divided into the following categories:-

- Multi lamellar vesicles (MLV)
- Large unilamellar vesicles (LUV)
- Small unilamellar vesicles (SUV).

Parameters	Multi lamellar vesicles	Small lamellar Vesicles	Large lamellar Vesicles
Vesicle size	Greater than 0.05 um	0.025 – 0.05 um	Greater Than 0.10 um
Method of preparation	Hand Shaking Method	Sonication Extrusion Method Solvent Dilution Technique	Reverse Phase Evaporation Method

METHOD OF PREPARATION OF NIOSOMES:

- A. **Passive Trapping Techniques:** This category includes the majority of the techniques used in niosome preparation in which the medication is incorporated during the niosome preparation process, i.e. during their formation.

1. Ether Injection Method:

- Niosomes are made by progressively introducing a surfactant solution dissolved in diethyl ether into warm water and keeping it at 60 °C.
- A 14-gauge needle is used to inject the ether mixture into an aqueous solution of the substance.
- The production of single layer vesicles is caused by the vaporisation of ether.
- The vesicle's diameter can range from 50 to 1000 nm, depending on the conditions²⁴.

2. Sonication:

- A mixture of medication solution, surfactant, and cholesterol in a buffer
- Niosomes were obtained by sonicating at 60°C for 3 minutes with a titanium probe sonicator²⁵.

3. **Reverse Phase Evaporation Technique:** Cholesterol and surfactant (in a 1:1 ratio) dissolve in an organic solvent mixture (ether and chloroform). The aqueous drug solution is added to this, and oil in oil emulsion is formed; two phases are sonicated at 4-5 degrees Celsius. To generate a semisolid gel of big vesicles, the emulsion is dried in a rotary evaporator at 40°C. The clear gel is sonicated again with small volumes of phosphate- buffered saline (PBS). At 40°C and reduced pressure, the organic phase is eliminated. To create niosomes, a viscous niosomal suspension is diluted with phosphate- buffered saline and heated on a water bath at 60°C for 10 minutes²⁶.

4. The Bubble Method:

- To adjust the temperature, a bubbling unit uses a round-bottomed flask with three neck positions in a water bath. The first neck has a water-cool reflux system, the second neck
- thermometer and the third neck has a nitrogen supply.

- At 70°C, cholesterol and surfactant are dispersed in a buffer with a pH of 7.4.
- 15 seconds of dispersion mixing with a high shear homogenizer.
- Nitrogen gas was used to create "bubbles" at 70°C²⁷.

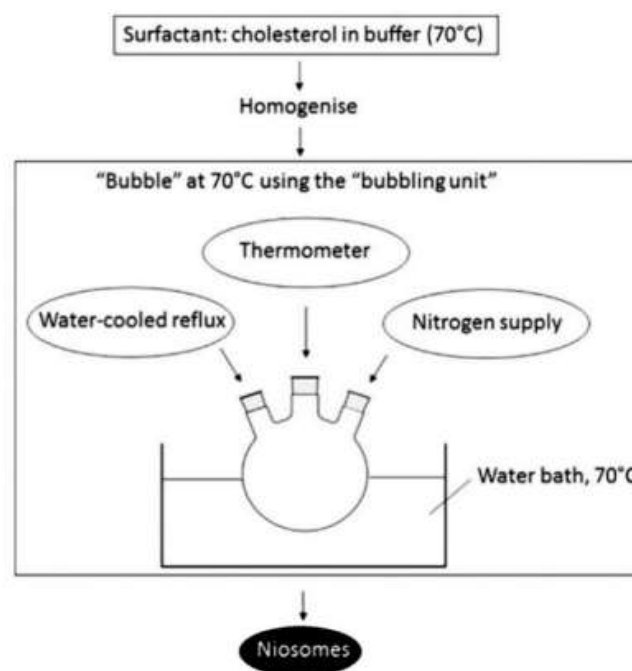


Figure 2: Bubble Point Method²⁸

5. Hand Shaking Method (Thin Film Hydration Technique/Rotary Evaporator)

- Surfactant, cholesterol, and a charge inducer are among the substances used in the mixture.
- Organic solvent is evaporated at room temperature (20°C) using a rotary evaporator.
- Creating a thin solid mixed layer
- With gentle agitation, the dried surfactant film can be re-hydrated with an aqueous phase at 0-60°C.
- Formation of niosomes²⁹.

6. **Multiple Method Extrusion Method:** Using a rotary evaporator, a mixture of surfactant, cholesterol, and dicetyl phosphate in chloroform generates a thin layer. Aqueous drug polycarbonate membranes hydrate the film. The solution and its suspension are extruded through a polycarbonate membrane and put in a series of up to eight passageways. It is an effective approach for regulating the size of niosomes³⁰.

7. Ethanol Injection Method:

- A tiny needle is used to inject a surfactant ethanol solution quickly.
- Having too much saline or another aqueous
- Vaporization of ethanol
- Formation of vesicles³¹.

8. **Micro Fluidization:** The principle involved in this technique is the submerged jet principle, in which two fluidized streams interact with each other at ultra high velocities and in micro channels within the interaction chamber. Thin liquid sheet impingements are arranged with a common front so that the energy supplies remain constant within the area of niosome formation, resulting in the formation of niosomal vesicles with greater uniformity, smaller size, and better reproducibility³².

B. **Active Trapping Techniques:** This includes drug loading after the formation of niosomes. The niosomes are prepared, and the drug is loaded while maintaining a pH gradient or ion gradient to facilitate drug uptake into the niosomes. The advantages of the niosome form include complete entrapment, high drug lipid ratios, no leakage, cost effectiveness, and suitability for labile drugs.

Trans Membrane pH Gradient Drug Uptake Process:-

- Surfactants and cholesterol are dissolved in an organic solvent during the remote loading process (chloroform)
- Under reduced pressure, the solvent evaporates, leaving a thin film on the round bottom flask's wall.
- By vortex mixing, the film hydrates with 300 mM citric acid (pH4.0).
- Multilamellar vesicles are frozen and thawed three times before being sonicated.
- Aqueous solution containing 10 mg/ml of drug is added for niosomal suspension, and vortexing is performed
- With 1M disodium phosphate, the pH of the sample is raised to 7.0-7.2.
- The mixture is then heated for 10 minutes at 60°C to produce³³.

C Miscellaneous Methods:

- **Emulsion Method:** This is a straightforward method for producing niosomes in which oil in water (o/w) emulsion is made from an organic solution of surfactant, cholesterol, and aqueous drug solution. Finally, the organic solvent is removed, leaving the niosomes in the aqueous phase³⁴.
- **Heating Method:** This method is in one-step, scalable and non-toxic and also based on the patent procedure. A suitable aqueous medium such as buffer distilled water, etc. in which mixtures of non-ionic surfactants, cholesterol and/or charge inducing molecules are added in the presence of the polyol like as glycerol. The mixture is heated with (at low shear forces) until the vesicles were formed³⁵.

- **Formation of Niosomes from Proniosomes:** Proniosomes is a dry formulation in which each water-soluble particle is protected by a thin layer of dry surfactant. The niosomes are identified by adding an aqueous phase at $T > T_m$ with brief agitation. T denotes temperature, while T_m denotes the mean phase transition temperature³⁶.

Carrier + surfactant = Proniosomes

Proniosomes + water = Niosomes.

FACTORS AFFECTING NIOSOME FORMATION:

- **Drug:** The charge and rigidity of the niosomal bilayer are directly affected by the physicochemical properties of the encapsulated drug. The vesicle size of the niosomes is increased by entrapping the drug within the niosomes, as well as by solute interaction with surfactant head groups. The increase in vesicle size is due to the enhancement of charge and mutual repulsion between surfactant bilayers. The degree of entrapment is also affected by the drug's hydrophilic-lipophilic balance³⁷.
- **Resistance of osmotic stress:** The addition of hypertonic salt solution to the niosomal suspension causes a decrease in niosomal diameter. Again, the addition of hypotonic salt solution causes slow release with slight swelling of the vesicles due to the inhibition of vesicle elution fluid. The mechanical loosening of the vesicle structure under osmotic stress causes the release to be faster³⁸.
- **Temperature of hydration medium:** The temperature of the hydration medium is critical in the formation of vesicles. This has an impact on their shape and size. The temperature should be kept above the system's gel to liquid phase transition temperature. Temperature also causes changes in the shape of the vesicle. It also influences surfactant assembly into vesicles. The volume of the hydration medium and the duration of the lipid film influence vesicle structure and yield³⁹.
- **Cholesterol:** The presence of cholesterol in niosomes increases their hydrodynamic diameter and entrapment efficiency. It influences the membrane properties of niosomes in the same way that it influences the properties of biological membranes. It reduces the membrane's flexibility and, as a result, the drug's permeation across it. The amount of cholesterol used is determined by the surfactant's HLB value⁴⁰.
- **Amount and Type of Surfactant:** Because the surface free energy of a surfactant decreases with increasing hydrophobicity, the mean size of niosomes increases proportionally with increasing HLB surfactants such as Span 85 (HLB 1.8) to Span 20 (HLB 8.6). Depending on the temperature, the type of surfactant, and the presence of other components such as cholesterol, the bilayers of the vesicles are either liquid or gel. In the gel state, alkyl chains have a well-ordered structure, whereas in the liquid state, the structure of the bilayers is more disordered. The gel-liquid phase transition temperature of surfactants and lipids distinguishes them (TC). The phase transition temperature (TC) of the surfactant also influences entrapment efficiency; for example, Span 60 with a higher TC provides better entrapment⁴¹.
- **Charge:** The vesicle's charge increases the interlamellar distance between successive bilayers in a multilamellar vesicle structure, as well as the overall entrapped volume and stability of niosomes⁴².
- **Nature of encapsulated Drug:** The nature of the drug being encapsulated influences niosomal formulation. The

interaction of the surfactant head groups causes drug entrapment in vesicles and a charge increase. The formation of charge causes mutual repulsion of the surfactant bilayer, increasing vesicle size. The drug's HLB has a similar effect on the degree of entrapment.

- **Composition of the membrane:** The addition of completely different additives to the surfactant mixture can result in the stabilization of niosomes. The main disadvantage of niosome formulation is drug leakage from the vesicles, which may be controlled by the addition of cholesterol. Cholesterol increases the rigidity of the membrane, which reduces drug leakage⁴³.

CHARACTERISATION OF NIOSOMES:

- **Entrapment Efficiency:** The amount of active substances loaded within the niosomal structure is defined as the entrapment efficiency (EE) of vesicular systems. It can be stated as:

$$EE = \text{Amount Entrapped} / \text{Total Amount} \times 100$$

where "total amount" refers to the total amount of drug in the prepared niosomal formulation. Entrapment efficiency is measured spectrophotometrically with a UV-visible spectrophotometer. Gel electrophoresis is performed on genetic material, followed by UV densitometry. Furthermore, the entrapment efficiency can be fluorometrically assessed using a hydrophilic fluorescent dye⁴⁴.

- **Vesicle size and shape:** The spherical shape of niosomal vesicles is assumed, and their mean diameter can be determined using the laser light scattering method. Electron microscopy, molecular sieve chromatography, ultracentrifugation, photon microscopy, optical microscopy, and freeze fracture electron microscopy can also be used to determine the diameter of these vesicles. The vesicle diameter of frozen thawed niosomes increases, which may lead to vesicle fusion during the cycle⁴⁵.
- **In vitro release:** The dialysis membrane method is commonly used in in-vitro release studies. In this method, a small amount of niosomes is placed in a dialysis bag and tied at both ends. Another beaker containing suitable dissolution media is kept at 37 °C, and the dialysis bag is placed in it and stirred with a magnetic stirrer. At predetermined intervals, a sample solution is removed from the beaker and replaced with fresh dissolution media. The drug concentration in the samples was determined at the specified wavelength reported in the drug's respective monograph⁴⁶.
- **Number of lamellae:** Using an electron microscope, NMR spectroscopy, or X-ray scattering, the number of lamellae in niosomes can be determined⁴⁷.
- **Membrane rigidity:** The niosome's membrane rigidity is measured using the mobility of the fluorescence probe as a function of temperature⁴⁸.
- **Bilayer Formation:** Under light polarisation microscopy, the formation of X-crosses characterises the assembly of non-ionic surfactants to form bilayer vesicles⁴⁹.
- **Stability Study:** The stability of niosomes can be assessed by measuring mean vesicle size, size distribution, and entrapment efficiency over several months of niosomal suspension storage at various temperatures. During storage, niosomes are sampled at regular intervals and the percentage of drug retained in the niosomes is determined using UV spectroscopy or HPLC methods⁵⁰.
- **Vesicle charge:** The surface charge of niosomes plays an important role in their stability; charged niosomes are

generally more stable than uncharged vesicles. It is calculated using the electrophoresis method or a zeta sizer⁵¹.

APPLICATIONS OF NIOSOMES:

1. Targeting of bioactive drugs:

- **To reticulo - endothelial system [RES]:** RES cells preferentially take vesicles. It can be used to treat animal tumors that have metastasized to the liver and spleen, as well as parasitic infestations of the liver.
- **To organs other than RES:** It has been proposed that the carrier system uses antibodies to reach specific sites in the body. Immunoglobulin is a convenient method for drug carrier targeting⁵².
- 2. **For the treatment of leishmaniasis:** Leishmaniasis is a disease that occurs when the parasite infiltrates cells and the liver. Antimonials are the most commonly used drugs. The antimony study on mice concluded that increased sodium stibogluconate efficacy of niosomal formulation, the effect of two doses on consecutive days was additive. In experimental leishmaniasis, niosomes are also effective as drug-loaded liposomes⁵³.
- 3. **Anti neoplastic treatment:** The majority of antineoplastic drugs have severe side effects. Niosomes can alter the metabolism of drugs, extending their circulation and half-life and reducing their side effects. Niosomes slow tumor proliferation and increase plasma levels by slowing elimination⁵⁴.
- 4. **Use in studying immune system:** Niosomes are used to study the nature of the immune response elicited by antigens due to their immune system selection, low toxicity, and greater stability⁵⁵.
- 5. **Niosomes as carrier for hemoglobin:** Niosomes are used to transport hemoglobin. Vesicles are easily permeable to oxygen, and the hemoglobin curve can be altered in the same way that non-capsulated hemoglobin can. The visible spectrum of niosomal suspension can be superimposed on that of free haemoglobin⁵⁶.
- 6. **Antibiotics:** Non-ionic surfactant vesicles (niosomes) are used as a carrier for the ophthalmic administration of a water-soluble local antibiotic. Gentamicin sulphate was studied, and the results showed that niosomes are promising ophthalmic carriers for gentamicin sulphate topical application⁵⁷.
- 7. **Delivery of peptide drug:** - Researchers are looking into using niosomes to successfully protect peptides from gastrointestinal peptide breakdown. An in-vitro study using an oral delivery of a vasopressin entrap derivative in niosomes demonstrates that drug entrapment increases the peptide's stability⁵⁸.
- 8. **Transdermal delivery:** Niosomes were investigated as a transdermal drug delivery system, as well as their ability to improve drug permeation and reduce skin irritation through the intact stratum corneum. Using Franz diffusion cells, researchers investigated the permeation of ketorolac (a potent NSAID) across excised rabbit skin from various proniosomes gel formulations. The prepared proniosomes significantly improved drug permeation and lag time⁵⁹.
- 9. **Cosmetics:** The first report of non-ionic surfactant vesicles came from L'Oreal's cosmetic applications. L'Oréal invented and patented niosomes in the 1970s and 1980s. Lancôme launched its first product, 'Niosome,' in 1987. The ability of niosomes to increase the stability of entrapped drugs, improve bioavailability of poorly

absorbable ingredients, and improve skin penetration are all advantages in cosmetic and skin care applications⁶⁰.

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CONCLUSION:

Niosomes are a novel and promising drug delivery technology. They are drug carriers who help to design an efficient drug delivery system. They provide an excellent opportunity for combining hydrophilic, lipophilic, or both drugs. Improved bioavailability, sustained release, controlled release, long circulation time, reduced dosage regimen, site-specificity, and targeted delivery are all advantages of drug encapsulation in niosomes. Niosomes appear to be a better drug delivery system than liposomes because they are more stable and cost-effective. This system is widely accepted by academics and researchers alike. Niosomal formulations can be administered via oral, topical/transdermal, parenteral, and ocular routes to achieve both systemic and local effects. Niosomes have a high drug delivery potential for anticancer, anti-infective, anti-inflammatory, and transdermal drug delivery, as well as recently as a vaccine adjuvant and diagnostic agents. Based on the benefits listed above, we can conclude that niosomes are a very promising vesicular drug delivery system that can improve the overall therapeutic performance of drugs.

REFERENCES:

- Umbarkar MG. Niosome as a Novel Pharmaceutical Drug Delivery: A Brief Review Highlighting Formulation, Types, Composition and Application. *Indian Journal of Pharmaceutical Education and Research*. 2021; 5(1). <https://doi.org/10.5530/ijper.55.1s.34>
- Bhavani GD, Lakshmi PV, "Recent advances of non-ionic surfactant-based nano-vesicles (niosomes and proniosomes): a brief review of these in enhancing transdermal delivery of drug FJPS. 2020; 6(1):1-18. <https://doi.org/10.1186/s43094-020-00117-y>
- Shakya V. Niosomes: A Novel Trend in Drug Delivery. *International Journal of Research and Development in Pharmacy & Life Sciences*. 2014; 3: 1036- 1041.
- Bagheri A, Chu B, Yaakob H. Niosomal Drug Delivery Systems: Formulation, Preparation, and Applications. *World Applied Sciences Journal*. 2014; 32: 1671-1685.
- Islam J, Ganesh NS, Uday Kumar KR, Chandy V. Review on niosome as novel drug delivery system. 2021; 10(5):715-724.
- Sharma D, Ali AAE, Aate JR; Niosomes as Novel Drug Delivery System: Review Article; *PharmaTutor*. 2018; 6(3):58-65. <https://doi.org/10.29161/PT.v6.i3.2018.58>
- Mehta A: Niosomes. www.pharmainfo.net, 2009.
- Handjani-Vila RM, Dispersion of Lamellar Phases of Nonionic Lipids In Cosmetic Products, *Int J Cosmetic Sci*, 1979; 1(5):303-14. <https://doi.org/10.1111/j.1467-2494.1979.tb00224.x>
- Keshavshetti GG, Shirsand SB. Recent advances in niosomal drug delivery - a review. *Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences*, 2019; 5(3):514-531.
- Kalra N, Jeyabalan G. Niosomes: A versatile drug delivery system. *Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences*, 2016; 2(4):44-54.
- Bhat MI, Ganesh NS, Majeed T and Chandy V. Niosomes a controlled and novel drug delivery system: A brief review.
- Vadlamudi HC, Sevukarajan M, Niosomal Drug Delivery System-A Review, *Indo American Journal of Pharmaceutical Research*. 2012;2(9)
- Muzzalupo R, Tavano L, Niosomal Drug Delivery for Transdermal Targeting: Recent Advances, Research and Reports In *Transdermal Drug Delivery*, 2015:423-33. <https://doi.org/10.2147/RRTD.S64773>
- Usman MRM, Ghuge PR and Jain BV. Niosomes: a novel trend of drug delivery. *European Journal of Biomedical and Pharmaceutical Sciences*, 2017; 4(7):436-442.
- Sharma D, Ali AAE, Aate JR. Niosomes as novel drug delivery system: review article. *PharmaTutor*, 2018; 6(3):58-65. 17. <https://doi.org/10.29161/PT.v6.i3.2018.58>
- Sudheer P, Kaushik K. Review on niosomes - a novel approach for drug targeting. *Journal of Pharmaceutical Research*, 2015; 14(1):20-25. <https://doi.org/10.18579/jpcrk/2015/14/1/78376>
- Debnath A, Kumar A, Structural And Functional Significance of Niosome And Proniosome In Drug Delivery System, *International Journal of Pharmacy And Engineering*, 2015; 3(3):621-637.
- Kemps J and Crommelin DA. Hydrolyse van fosfolipiden in watering milieu. *Pharm Weekbl*, 1998; 123: 355-363.
- Usman M, Ramdas K, Baviskar K, "Pesticides: an overreview." *JDDT*, 2017; 7(4):1-5. <https://doi.org/10.22270/jddt.v7i4.1462>
- Bhardwaj P, Tripathi P, Gupta R, Pandey S, "Niosomes: a review on niosomal research in the last decade" *JDDST*, 2020; 56:101581. <https://doi.org/10.1016/j.jddst.2020.101581>
- <https://doi.org/10.1016/j.jddst.2020.101581>
- Rao N, Chowdary P, Divya Y, Lakshmi T, Latha K, Sirisha P, "Niosomes: a vesicular drug delivery system" *RJPT*, 2018; 11(8):3731- 3736. <https://doi.org/10.5958/0974-360X.2018.00684.4>
- Kamal M, Maher M, Ibrahim A, Louis D, "An overview on niosomes: a drug nanocarrier" *DDIPIJ*, 2018; 1(5):1-9. <https://doi.org/10.32474/DDIPIJ.2018.01.000125>
- Kaur D*, Kumar S, Niosomes: Present Scenario and Future Aspects, *Journal of Drug Delivery & Therapeutics*. 2018; 8(5):35-43 <https://doi.org/10.22270/jddt.v8i5.1886>
- Rogerson A, the Distribution of Doxorubicin In Mice Following Administration In Niosomes, *J Pharm, Pharmacol*, 40(5):337-42. <https://doi.org/10.1111/j.2042-7158.1988.tb05263.x>
- Sankhyan A, Pawar P, Recent Trends In Niosome as Vesicular Drug Delivery System, *Journal of Applied Pharmaceutical Science* 2012; 02(06):20-32.
- Singh G, Dwivedi H, Saraf SK, Saraf SA, Niosomal Delivery of Isoniazid - Development And Characterization, *Tropical J Pharm Res*. April 2011; 10(2):203-210. <https://doi.org/10.4314/tjpr.v10i2.66564>
- Lohumi A, Rawat S, Sarkar S, Sipai AB, Yadav MV, Review Article A Novel Drug Delivery System: Niosomes Review. *J of Drug Delivery & Therapeutics* 2012; 2(5):129-135. <https://doi.org/10.22270/jddt.v2i5.274>
- Navya MN, Parthiban S, Neasalin JAJ, Vikneswari A. Niosomes as novel vesicular drug delivery system- a review. *Asian Journal of Research in Biological and Pharmaceutical Sciences*, 2014; 2(2):62-68.
- Madhav NVS, Saini A, Niosomes: A Novel Drug Delivery System, *International Journal of Research in Pharmacy and Chemistry*. 2011; 1(3)
- Chandu VP, Arunachalam A, Jeganath S, Yamini K, Tharangini K, Chaitanya G, Niosomes: A Novel Drug Delivery System, *International Journal of Novel Trends in Pharmaceutical Sciences*, 2012; 2(1).
- Gurjar P, Naik N, Chouksey S, Niosome: A Promising Pharmaceutical Drug Delivery, *Int. J. Pharm Anal*, 2(5):425- 436.
- Shakya V, Bansal BK, Niosomes: A Novel Trend In Drug Delivery, *International Journal of Research And Development In Pharmacy And Life Sciences*, 2014, 3(4):1036-1041.

33. Karim KM, Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M, Kuotsu K, Niosome: A Future of Targeted Drug Delivery Systems Journal Of Advanced Pharmaceutical Technology & Research, 2010; 1(4). <https://doi.org/10.4103/0110-5558.76435>
34. Jindal K, Niosomes as A Potential Carrier System: A Review, International Journal of Pharmaceutical, Chemical And Biological Sciences, 2015; 5(4):947-959.
35. Sarker A, Shimu IJ, Alam SAA, Niosome: As Dermal Drug Delivery Tool, IOSR Journal of Pharmacy And Biological Sciences, 2015; 10(2):73-79.
36. Nasir A, Harikumar SL, Kaur A, Niosomes: An Excellent Tool For Drug Delivery, IJRPC 2012; 2(2).
37. Sharma P, Jain AP, Pandey P, Gupta R, Roshan S. Niosome a novel approach for drug delivery system: an overview. Asian Journal of Pharmaceutical science and Research, 2013; 3(5):18- 30.
38. Vadlamudi CH, Sevukarajan M. Niosomal drug delivery systema review. Indo American Journal of Pharmceutical Research, 2012; 2(9)
39. Kauslya A, Borawake PD, Shinde JV, Chavan RS, Niosomes: A Novel Carrier Drug Delivery System, Journal of Drug Delivery and Therapeutics. 2021; 11(1):162-170 <https://doi.org/10.22270/jddt.v11i1.4479>
40. Kumavat S, Sharma PK, Koka SS, Sharma R, Gupta A, Darwhekar GN, A Review on Niosomes: Potential Vesicular Drug Delivery System, Journal of Drug Delivery and Therapeutics. 2021; 11(5):208-212. <https://doi.org/10.22270/jddt.v11i5.5046>
41. Sakthivel M, Kannan K, Manavalan, Senthamarai. Non-ionic surfactant vesicles-a review. Research Journal of Pharmaceutical, Biological and Chemical, 2012; 3(1):604-614.
42. Vadlamudi HC, Sevukarajan M, "Niosomal drug delivery- a review" IAJPR, 2012; 2(9).
43. Patel H, .Patel U, "Review on niosomes - a novel approach for drug targeting" IJAP, 2019; 08(01):1-6.
44. Carafa M, Marianecchi C, Marzio LD, Rinaldi F, Celia C, Donatella Paolino D , Alhaique F, Esposito S. Niosomes from 80s to present: the state of the art. Advances in Colloid and Interface Science, 2014; 205:187-206. <https://doi.org/10.1016/j.cis.2013.11.018>
45. Kuotsu K, Karim MK, Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M. Niosome: a future of targeted drug delivery systems. J Adv Pharm Tech Res., 2010; 4(1):374-380. <https://doi.org/10.4103/0110-5558.76435>
46. Singh SK, Rajera R, Nagpal K, and Mishra D. Niosomes: a Controlled and novel drug delivery system. Biological and Pharmaceutical Bulletin, 2011; 34(7):945-953 <https://doi.org/10.1248/bpb.34.945>
47. Gowda DV, Jain SC, Gupta NV, Kulkarni PK. A brief review on niosomes. Journal of Pharmacy Research, 2017; 11(5):450-458
48. Nagalakshmi, Aruljothy M, Shanmuganathan S. An overview on niosome as carrier in dermal sdrug delivery. Journal of Pharmaceutical science and Research, 2015; 7(11): 923-927.
49. Gandhi A, Sen SO, Paul A. Current trends in niosome as vesicular drug delivery system. Asian Journal of Pharmacy and Life Science, 2012; 2 (2):339-353.
50. Stahl F, Selecki DA, Selecki M, Walter JG, and Scheper T. Niosomes as nanoparticulate drug carriers: fundamentals and recent applications. Hindawi Publishing Corporation Journal of Nanomaterials, 2016; 2016: 1-13. <https://doi.org/10.1155/2016/7372306>
51. Suma U S, Parthiban S, Senthil Kumar GP, Tamiz Mani T, Novelty of Niosomal Gel In Tdds Application, Asian Journal Of Research In Biological And Pharmaceutical Sciences. 2015; 3(2):41-48.
52. Mujoriya R, Bodla RB, Dhamande K, Singh D and Patle L. Niosomal drug delivery system: the magic bullet. Journal of Applied Pharmaceutical Science, 2011; 1(9):20-23.
53. Kalra N, Jeyabalan G, Singh G, Choudhary S. Non- ionic surfactant vesicles and their therapeutics potentials. Journal of Innovations in Pharmaceuticals and Biological sciences, 2016; 3 (2):193-201
54. Singh S, Niosomes: A Role In Targeted Drug Delivery System, IJPSR, 2013; 4(2):550-557.
55. Patel SM, Rathod DR, Patel KN, Patel BA, Patel PA, Niosome As An Effective Drug Delivery: A Review, International Journal For Pharmaceutical Research Scholars (IJPRS), 2012; 1(2). <https://doi.org/10.31638/IJPRS.V1.I1.00018>
56. Yadav JD, Kulkarni PR, Vaidya KA, Shelke GT. Niosomes: a review. Journal of Pharmacy Research, 2011; 4(3):632-636.
57. Pawar P, Sankhyan A. Recent trends in niosome as vesicular drug delivery system. Journal of Applied Pharmaceutical Science, 2012; 2(6): 20-32.
58. Gadhiya P, Shukla S, Modi D, Bharadia P, Niosomes In Targeted Drug Delivery - A Review, s Journal For Pharmaceutical Research Scholars, 2012; 1(2).
59. Abdelkader H, Alani AWG and Alany RG. Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. Drug Delivery, 2013; 21(2):87-100. <https://doi.org/10.3109/10717544.2013.838077>
60. Verma NK, Roshan A, Niosomes and Its Application-A Review, IJRPLS, 2014; 2(1):182-184.