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NIOSOMES: A Novel Approach In NDDS For Enhanced Drug Delivery

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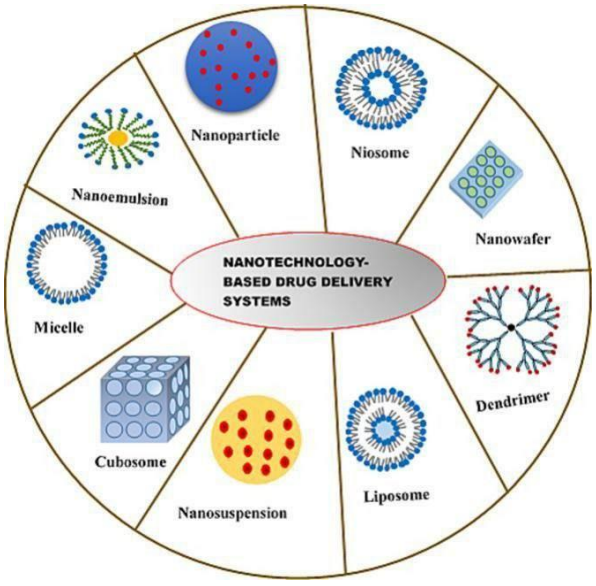
ABSTRACT

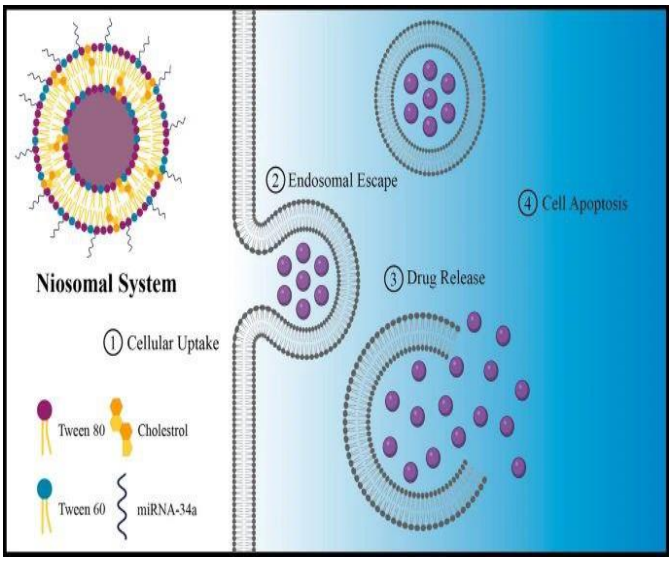
Novel Drug Delivery Systems (NDDS) represent an evolving area of pharmaceutical research aimed at improving drug bioavailability, reducing toxicity, and ensuring targeted delivery. These systems are designed to optimize therapeutic efficacy by controlling the release, distribution, and metabolism of drugs within the body. Traditional drug delivery methods often face limitations such as poor solubility, instability, and a lack of site-specific targeting. To overcome these challenges, vesicular systems like niosomes have gained significant attention. Niosomes, non-ionic surfactant-based vesicles, offer a versatile and efficient platform in NDDS due to their ability to encapsulate both hydrophilic and lipophilic drugs, improving stability and bioavailability. They provide controlled and sustained drug release, enhance permeability through biological membranes, and enable targeted delivery to specific tissues or organs, thus minimizing side effects and maximizing therapeutic impact.

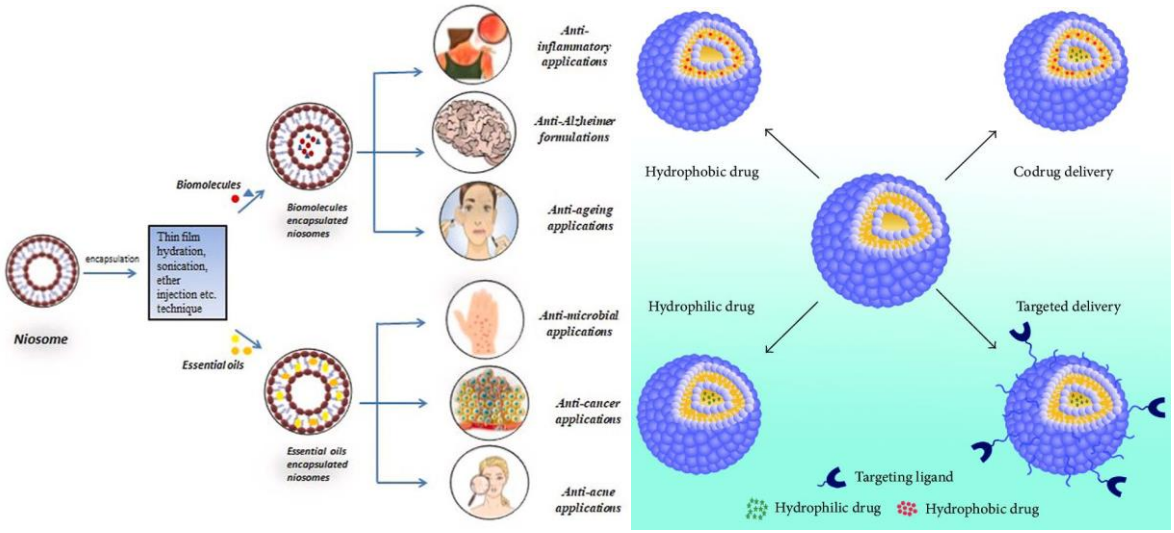
This article explores the role of niosomes as emerging nanocarriers in NDDS, detailing their structural advantages, formulation methods, and their promising future in the development of more effective and targeted therapeutic strategies. The growing interest in niosomes within NDDS is also driven by their ability to overcome biological barriers, such as the blood-brain barrier (BBB) and gastrointestinal barriers, which pose significant challenges in conventional drug delivery. Moreover, niosomes have shown potential in gene delivery and as carriers for macromolecules like proteins and nucleic acids, expanding their application beyond small-molecule drugs. The versatility of niosomes makes them a critical component in the future landscape of nanomedicine, offering a flexible and efficient platform for developing advanced therapeutic solutions in various medical fields, including oncology, infectious diseases, and chronic conditions.

(**KEYWORDS**: Novel Drug Delivery Systems (NDDS), nanocarriers, niosomes, targeted drug delivery, controlled release, biocompatibility, non-ionic surfactants, encapsulation, nanomedicine.)

Graphical Abstract :







INTRODUCTION :

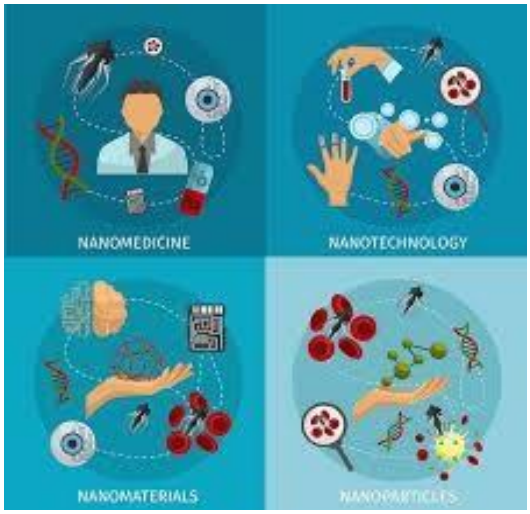
In recent years, there has been an increasing interest in developing methods for the controlled and targeted administration of medications. This interest stems from the need to enhance the efficacy of drugs while minimizing side effects and reducing the frequency of dosing. Traditional drug delivery methods often result in significant drug loss due to degradation, rapid metabolism, or non-specific distribution in the body, which can lead to reduced therapeutic effectiveness and increased side effects. To address these challenges, researchers have turned to advanced drug delivery systems that can improve the precision and efficiency of delivering medications.

Medical nanotechnology has played a crucial role in advancing drug delivery systems, leading to the development of multifunctional nanoparticles that act as drug carriers. These nanoparticles are designed to carry drug molecules and deliver them directly to the desired site of action in the body. They offer several advantages over conventional drug delivery methods, such as:

Protection from Degradation: Nanocarriers can protect drugs from enzymatic degradation and other metabolic processes, ensuring that the therapeutic agent remains intact until it reaches its target.

Controlled Release: Many nanoparticles are engineered to release the drug in a controlled manner, which helps maintain steady therapeutic levels over time and reduces the need for frequent dosing.

Targeted Delivery: Nanocarriers can be designed to recognize specific cells or tissues, allowing for targeted delivery and reducing the risk of side effects associated with systemic drug distribution.



One of the most promising types of bilayer drug carriers is niosomes. Niosomes are spherical vesicles made of non-ionic surfactants and cholesterol in an aqueous medium. They can encapsulate hydrophilic and hydrophobic drugs, making them a versatile option in Novel Drug Delivery Systems (NDDS). Niosomes improve drug stability and bioavailability and provide controlled release, making them suitable for targeted drug delivery.

Components:

- Non-Ionic Surfactants: Form the bilayer structure (e.g., Span, Tween).
- Cholesterol: Provides rigidity and stability to the membrane.

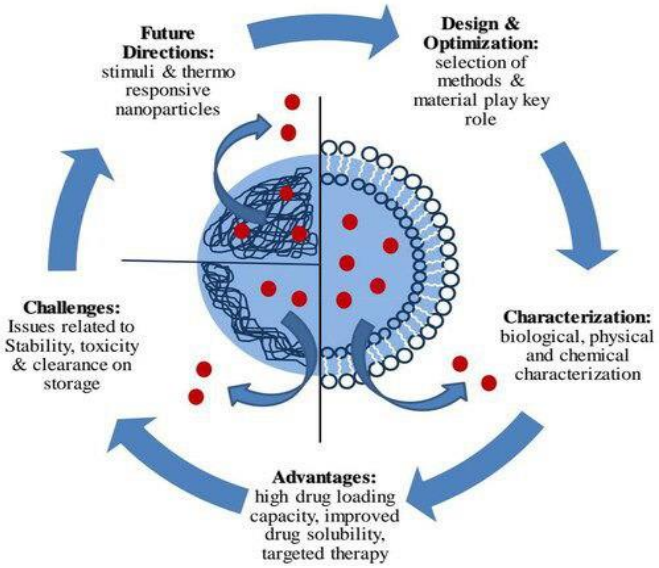
- Charge Inducers (Optional): Prevent aggregation and enhance stability.
- Aqueous Phase: Encapsulates hydrophilic drugs.

Advantages:

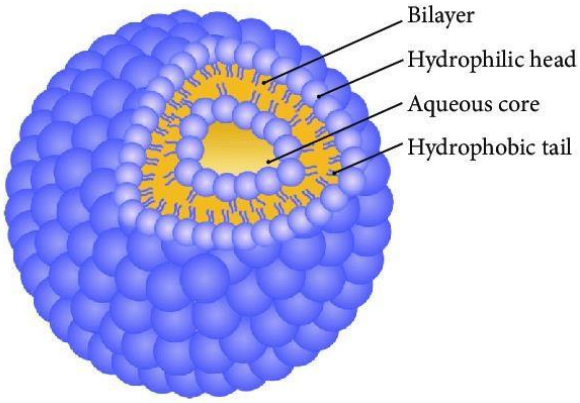
- Enhance drug stability and bioavailability.
- Biocompatible and biodegradable with low toxicity.
- Allow for controlled, sustained drug release.
- Suitable for targeted delivery.
- Cost-effective compared to other vesicular systems like liposomes.

Composition:

Typically 60-70% surfactant, 30-40% cholesterol, and an aqueous phase, with optional charge inducers to stabilize the structure.
Niosomes are a promising approach in NDDS, offering improved therapeutic efficiency and patient-friendly drug delivery.



STRUCTURE AND COMPONENTS OF NIOSOMES :



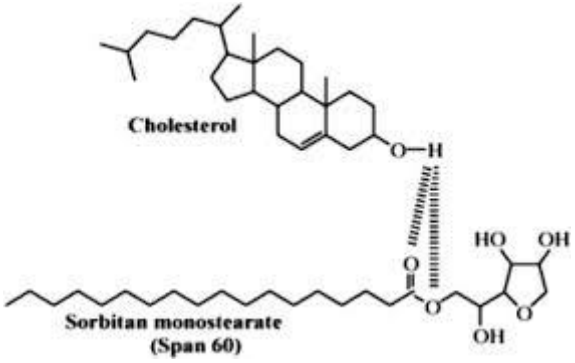
Niosomes are tiny vesicles formed when nonionic surfactants self-assemble in a watery environment, often with the addition of cholesterol and other stabilizing agents. These vesicles act as carriers for both hydrophilic and lipophilic drugs, improving drug stability and allowing for targeted and controlled release. The composition of niosomes is important for their function as drug delivery systems, as it affects their stability, how well they encapsulate drugs, and how drugs are released. Here are the main components and structural aspects of niosomes:

1. Nonionic Surfactants:
Role: Nonionic surfactants are the primary building blocks of niosomes, forming the bilayer structure by self-assembling in water.

Structure: Each surfactant molecule has a hydrophilic (water-attracting) head group and a hydrophobic (water repelling) tail group. In aqueous solutions, these molecules arrange themselves such that their hydrophobic tails face inward, away from water, while the hydrophilic heads face outward, forming a stable bilayer structure.

Selection Criteria: The choice of surfactant affects niosome properties like size, lamellarity (number of bilayers), and drug entrapment efficiency. The surfactant's hydrophilic-lipophilic balance (HLB) is critical; those with an HLB value between 4 and 8 are typically used to form stable niosomes.

Examples: Common surfactants used in niosome preparation include Span (sorbitan esters) and Tween (polysorbates). Span 60, known for its high phase transition temperature, helps form more stable vesicles, while Tween 20 and 80 are used to create smaller, more fluid vesicles.



2. Cholesterol

Role: Cholesterol is an essential component in niosomal formulations, serving to stabilize the bilayer membrane.

Function in Bilayer: It interacts with the hydrophilic head groups of surfactants through hydrogen bonding, inserting itself between the surfactant molecules. This interaction strengthens the bilayer and decreases membrane permeability, thereby preventing drug leakage.

Effects on Properties:

Stability: Cholesterol increases the rigidity and mechanical strength of niosomes, making them more stable and resistant to external environmental changes.

Entrapment Efficiency: The presence of cholesterol can enhance the ability of the bilayer to encapsulate drugs, but excessive cholesterol may disrupt the membrane, leading to reduced encapsulation efficiency.

Optimal Concentration: Typically, cholesterol is used in a 1:1 or 2:1 molar ratio with surfactants, but the optimal concentration depends on the desired vesicle characteristics and the type of surfactant used.

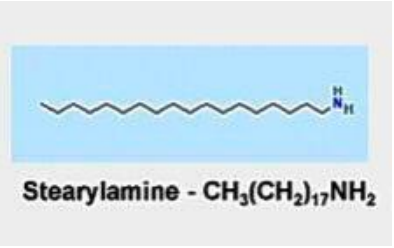
S. N.	Formulation Code	Drug (% w/v)	Surfactant	Surfactant: Cholesterol ratio (µ mol)	Surfactant Quantity (mg)	Cholesterol Quantity (mg)
1	F1	0.5	Span 40	0.5:1	0.194	0.386
2	F2	0.75	Span 40	1.0:1	0.388	0.386
3	F3	1	Span 40	1.5:1	0.582	0.386
4	F4	1.25	Span 40	2.0:1	0.776	0.386
5	F5	1.5	Span 40	1.0:2	0.388	0.772
6	F6	0.5	Span 60	0.5:1	0.215	0.386
7	F7	0.75	Span 60	1.0:1	0.431	0.386
8	F8	1	Span 60	1.5:1	0.646	0.386
9	F9	1.25	Span 60	2.0:1	0.862	0.386
10	F10	1.5	Span 60	1.0:2	0.431	0.772

Charged Molecules:

Role: Adding charged molecules to niosomes helps prevent aggregation by introducing electrostatic repulsion between vesicles, thereby enhancing their stability.

Types of Charged Molecules:

Positively Charged Agents: Stearylamine is often used to impart a positive charge, enhancing the interaction of niosomes with negatively charged cell membranes.



Negatively Charged Agents: Dicetyl phosphate is a common choice for imparting a negative charge, which helps stabilize the niosomes by preventing aggregation.

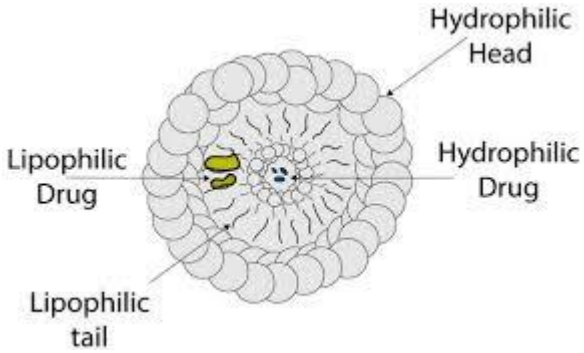
Usage: These agents are typically used in small concentrations (2.5–5 mol %) to modify the surface charge, which can also influence the biodistribution and interaction of niosomes with biological tissues.

Aqueous Phase:

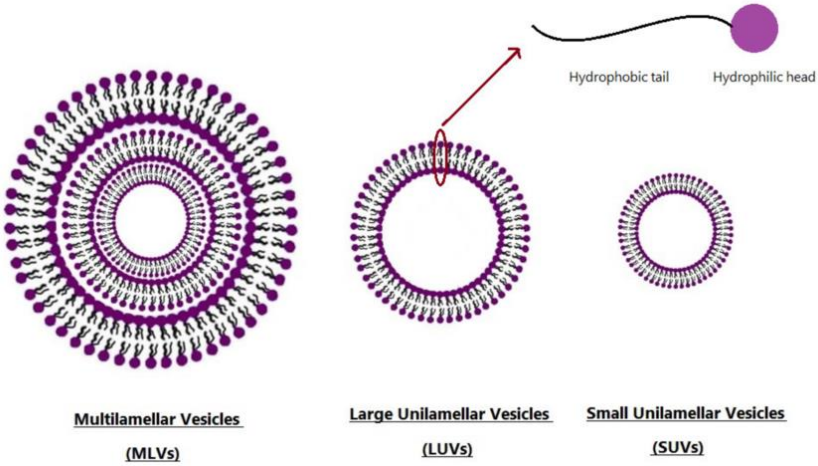
Role: The core of niosomes is filled with an aqueous solution, making them suitable for encapsulating hydrophilic (water-soluble) drugs within the internal cavity.

Function: Hydrophilic drugs are trapped inside the inner aqueous core, while lipophilic drugs can integrate into the bilayer itself. This dual encapsulation ability makes niosomes versatile carriers.

Encapsulation: The drug's solubility profile and its compatibility with the surfactant determine its placement within the niosome, either in the aqueous core or within the bilayer.



Structural Formation and Types of Niosomes :



Niosomes can be classified into several types based on their size, structure, and method of preparation. Small Unilamellar Vesicles (SUV) range from 10 to 100 nm in size and have a single lipid bilayer, making them suitable for drugs that require rapid release due to their small size and large surface area. Large Unilamellar Vesicles (LUV), which are larger (100-1000 nm) and also consist of a single lipid bilayer, are ideal for encapsulating larger molecules, such as proteins and nucleic acids. Multilamellar Vesicles (MLV), with a size ranging from 500 nm to several micrometers, have multiple concentric lipid bilayers. These "onion-like" structures allow for sustained drug release, often used in controlled drug delivery applications.

Another type, Vesicles Prepared by Reverse Phase Evaporation (REV), typically range from 200 to 500 nm and have a large internal aqueous space enclosed by a single lipid bilayer, making them suitable for high-volume hydrophilic drug encapsulation. Multiple Vesicular Niosomes (MVN) consists of several smaller vesicles within a larger one, enabling compartmentalized drug delivery, particularly useful for delivering multiple drugs simultaneously. Each type of niosome has specific compositions and structural characteristics that make it suitable for various drug delivery applications. By adjusting the non-ionic surfactants, additives, and methods of preparation, niosomes can be tailored for targeted delivery, sustained release, and improved stability of therapeutic agents.

Critical Parameters for Niosome Formation

1. Hydrophilic-Lipophilic Balance (HLB):

The Hydrophilic-Lipophilic Balance (HLB) value is an important parameter in formulating niosomes, as it indicates the balance between the hydrophilic and lipophilic portions of surfactants used in their composition. Generally, HLB values range from 0 to 20, with lower values indicating lipophilic

characteristics and higher values indicating hydrophilic characteristics. Surfactants with HLB values between 4 and 8 tend to form stable vesicles, as they strike a balance between being too water-soluble or too hydrophobic.

Non-Ionic Surfactant	HLB Value
Span 40	6.7
Span 80	4.3
Tween-20	16.7
Tween-80	15.0
Sucrose ester (S-1570)	15.0
Sucrose ester (S-1170)	11.0

2. Critical Packing Parameter (CPP):

The Critical Packing Parameter (CPP) is a key concept in the formulation of niosomes, as it helps predict the behavior of surfactants and their ability to form vesicular structures. The CPP is defined as the ratio of the volume of the hydrophobic tail of a surfactant (or amphiphile) to the product of the length of the tail and the area occupied by the head group. It is expressed mathematically as:

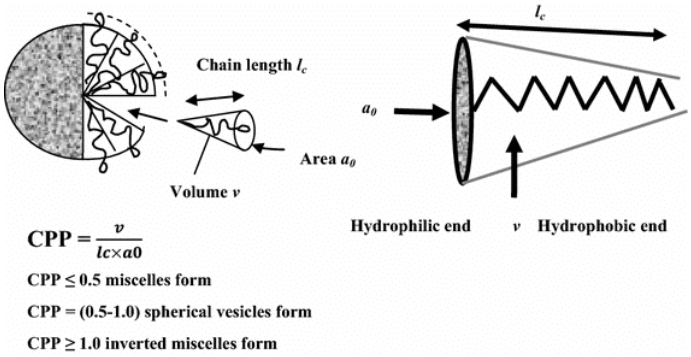
$$CPP = l \times aV$$

Where:

V = volume of the hydrophobic tail

l= length of the hydrophobic tail

a= area of the head group



METHODS OF PREPARATIONS :

Niosomes are prepared by different methods based on the sizes of the vesicles and their distribution, number of double layers, entrapment efficiency of the aqueous phase, and permeability of the vesicle membrane.

Preparation of small unilamellar vesicles

Sonication

The aqueous phase containing the drug is added to the mixture of surfactant and cholesterol in a scintillation vial. The mixture is homogenized using a sonic probe at 60°C for 3 minutes. The vesicles are small and uniform in size.

Micro fluidization

Two fluidized streams move forward through precisely defined microchannels and interact at ultra-high velocities within the interaction chamber. Here, a common gateway is arranged such that the energy supplied to the system remains within the area of niosomes formation. The result is greater uniformity, smaller size, and better reproducibility.

Preparation of multilamellar vesicles

Handshaking method (Thin film hydration technique)

In the hand-shaking method, surfactant and cholesterol are dissolved in a volatile organic solvent such as diethyl ether, chloroform, or methanol in a rotary evaporator, leaving a thin layer of solid mixture deposited on the wall of the flask. The dried layer is hydrated with an aqueous phase containing the drug at normal temperature with gentle agitation.

Trans-membrane pH gradient (inside acidic) drug uptake process (remote Loading)

Surfactants and cholesterol are dissolved in chloroform. The solvent is then evaporated under reduced pressure to obtain a thin film on the wall of the round-bottom flask. The film is hydrated with 300 mM citric acid (pH 4.0) by vortex mixing. The multilamellar vesicles are frozen and thawed three times and later sonicated. To this niosomal suspension, an aqueous solution containing 10 mg/ml of the drug is added and vortexed. The pH of the sample is then raised to 7.0-7.2 with 1M disodium phosphate. This mixture is later heated at 60°C for 10 minutes to produce the desired multilamellar vesicles.

Preparation of large unilamellar vesicles

Reverse phase evaporation technique (REV)

In this method, cholesterol and surfactant are dissolved in a mixture of ether and chloroform. An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. The clear gel formed is further sonicated after the addition of a small amount of phosphate-buffered saline. The organic phase is removed at 40°C under low pressure. The resulting viscous niosome suspension is diluted with phosphate-buffered saline and heated in a water bath at 60°C for 10 min to yield niosomes.

Ether injection method

The ether injection method is essentially based on slow injection of niosomal ingredients in ether through a 14-gauge needle at the rate of approximately 0.25 ml/min into a preheated aqueous phase maintained at 60°C. The probable reason behind the formation of larger unilamellar vesicles is that the slow vaporization of solvent results in an ether gradient extending towards the interface of the aqueous-nonaqueous interface. The former may be responsible for the formation of the bilayer structure. The disadvantages of this method are that a small amount of ether is frequently present in the vesicle suspension and is difficult to remove.

Formulation Method	Components	Structures Size (nm)	Zeta Potential (mV)	Encapsulate Rate (%)
Proniosomes	Span 60	Unilamellar 4400 ± 210	/	99.2 ± 5.1
	Sugar esters	1620 ± 170	/	98.74 ± 0.51
	Span 40 and chol or DCP or lecithin	multi-lamellar more than 20 μm	/	16.7 ± 1.01 (highest)
Sonication	Span 60 cholesterol	Multi-lamellar 35.77	(probably higher zeta potential)	29.2 %
Micro fluidization	Monopalmitin glycerol cholesterol dicetyl phosphate	From 60.96 ± 0.36 to 168.40 ± 2.26 in different buffer	From −76.83 ± 0.81 to −30.63 ± 2.06 in different buffer	/
Thin-film hydration method (TFH)	Polyoxyethylene alkyl ethers or sorbitan monoesters	From 214 to 1368	From −26.73 to −41.31	79.8 ± 3.5% (Span 40) 76.56 ± 2.1% (Span 20)
	Span 60 and cholesterol	5000 ± 1500	/	2.05 ± 0.043/210 Entrapment level (mg)/total lipid (mg)
Reversed phase evaporation (REV)	Span 40 or Span 60	3460, 3610	/	26.27% ± 1.96 (highest)

Applications of Niosomes :

Niosomes have versatile applications across various fields due to their unique ability to encapsulate a wide range of drugs, improve stability, and enable controlled release. Here are some key applications along with specific examples:

1. Drug Delivery

Targeted Drug Delivery: Niosomes can deliver drugs directly to target sites, such as tumors or infected cells, minimizing side effects and enhancing therapeutic efficacy.

Doxorubicin-loaded niosomes have been investigated for targeting cancer cells, reducing cardiotoxicity while improving drug accumulation at the tumor site.

Controlled Release: Niosomes provide sustained or controlled release, improving bioavailability and reducing dosing frequency.

Niosomal formulations of acyclovir have shown improved sustained release, making it more effective for treating herpes infections.

2. Gene and Vaccine Delivery

Gene Therapy: Niosomes can encapsulate DNA, RNA, and other genetic materials, protecting them from degradation and allowing targeted delivery to cells.

Niosomes have been studied for delivering siRNA (small interfering RNA) to silence specific genes in cancer cells, showing promise in gene therapy.

Vaccine Delivery: Niosomes can enhance immune responses by protecting antigens, making them suitable for vaccine delivery.

Niosomal formulations have been explored for hepatitis B vaccines, enhancing the immune response and providing better stability than traditional formulations.

3. Cosmetic and Dermatological Applications

Topical Delivery: Niosomes enhance the permeation of active ingredients through the skin, making them valuable in cosmetics and skincare.

Niosome-encapsulated retinol is used in anti-aging creams to improve skin penetration and reduce irritation, offering more effective results.

Transdermal Drug Delivery: Niosomes enable deeper penetration through the skin and controlled release of drugs.

Niosomal gel formulations of ketoprofen have been developed for pain relief, providing sustained release and better skin absorption.

4. Anti-Cancer Therapy

Enhanced Efficacy and Reduced Toxicity: Niosomes can target chemotherapy drugs to cancer cells, enhancing drug accumulation at the tumor while reducing side effects.

Methotrexate-loaded niosomes have shown promise in treating lung cancer, with improved targeting and reduced systemic toxicity.

Multidrug Resistance (MDR): Niosomes can be engineered to bypass resistance mechanisms in cancer cells, increasing the effectiveness of chemotherapy.

Niosomes loaded with paclitaxel have been used to overcome resistance in breast cancer cells, improving therapeutic outcomes.

5. Anti-Fungal and Anti-Bacterial Delivery

Antimicrobial Agents: Niosomes can deliver antifungal and antibacterial drugs more effectively.

Amphotericin B-loaded niosomes have been used for treating fungal infections like candidiasis, showing reduced toxicity compared to conventional formulations.

Improved Penetration: Niosomes enhance drug penetration through skin and mucous membranes, making them effective for localized treatments.

Ciprofloxacin-loaded niosomes have been studied for topical application, showing better penetration for skin infections.

6. Ophthalmic Drug Delivery

Niosomes can improve drug retention time in the eye, making them useful for treating ocular conditions.

Niosomal formulations of timolol have been used for glaucoma treatment, improving drug absorption and reducing intraocular pressure more effectively than conventional eye drops.

7. Pulmonary Drug Delivery

Inhalable Formulations: Niosomes can be formulated for inhalation, directly delivering drugs to the lungs.

Niosomal formulations of rifampicin have been studied for tuberculosis treatment, providing better delivery to lung tissues.

8. Anti-Inflammatory Applications

Niosomes are effective in delivering anti-inflammatory drugs, providing targeted action and reducing systemic side effects.

Niosomal formulations of diclofenac have been developed for treating arthritis, offering localized pain relief with sustained release.

Drugs	Application	Method
Doxirubicin	Anticancer drug delivery	Sonication method
Pilocarpine hydrochloride	Ophthalmic drug delivery	Sonication method
Ammonium glycyrrhiinate	Transdermal drug delivery	Film hydration method
Nefopam	Nasal drug delivery	Film hydration method
Insulin	Peptide drug delivery	Film hydration method
Ketoprofen	Drug delivery	Film hydration method
Ag85B-ESAT-6	Immunological response	Dehydration–rehydration method
Gadobenate	Diagnostic imaging	Hand shaking/Ether injection method
Zanamivir	Pulmonary drug delivery	Thin layer hydration
Paclitaxel	Anticancer/oral drug delivery	Thin layer hydration

Future Prospects :

Advancements in niosome technology focus on enhancing their stability, drug-loading capacity, and specificity for target tissues. Techniques like surface modification (e.g., PEGylation or ligand attachment) are being refined to improve their circulation time and ability to evade the immune system, which is crucial for delivering drugs to sensitive areas like the brain. Additionally, new methods of niosome preparation, including microfluidics and supercritical fluid technology, are enabling more consistent and scalable production of these vesicles. This is paving the way for their potential commercialization in the pharmaceutical industry.

The future of niosomes in drug delivery looks very promising. Ongoing research aims to maximize their potential as versatile nanocarriers. Niosomes are being explored for their ability to deliver a wide range of therapeutic agents, including small molecules, proteins, peptides, and genetic material like DNA and RNA. This makes them suitable for various medical applications such as cancer therapy, gene therapy, vaccine delivery, and treatment of chronic conditions like diabetes.

Moreover, the combination of niosomes with other nanocarriers, such as liposomes or nanoparticles, is being explored to create hybrid systems with synergistic properties. These hybrid systems could further improve drug release profiles and targeting capabilities. With the increasing focus on personalized medicine, niosomes hold the potential to be tailored for patient-specific therapies, optimizing treatment effectiveness and minimizing side effects. As research continues to uncover new possibilities for niosomes in drugs. delivery, their role in shaping the future of nanomedicine and pharmaceutical technology appears increasingly significant.

Conclusion :

Niosomes offers a new and effective way to deliver drugs. They provide a flexible system for improving the stability, availability, and targeting of various drugs. Made from non-ionic surfactants, niosomes can encapsulate both water-soluble and fat-soluble drugs, making them suitable for a wide range of applications, from cancer therapy to vaccine delivery. Their ability to release drugs in a controlled manner allows for better treatment outcomes while reducing side effects, which is especially important for conditions that require precise targeting, such as cancer or neurological disorders. Recent advancements in niosome technology, such as improved preparation methods and surface modifications, have further boosted their potential. These developments have made niosomes more stable in the body and capable of overcoming biological barriers like the blood-brain barrier. This makes them suitable for a variety of delivery routes, including oral, transdermal, and intravenous. Although challenges like large-scale manufacturing and regulatory hurdles remain, the benefits of niosomes in targeted drug delivery are clear. With ongoing research, niosomes are poised to play a key role in the future of drug delivery, offering a more efficient, safe, and patient-specific approach to treatment.

REFERENCES:

1. Azmin MN, Florence AT, Handjani-Vila RM, Stuart JF, Vanlerberghe G, Whittaker JS. The effect of non-ionic surfactant vesicle (noisome) entrapment on the absorption and distribution of methotrexate in mice. *J Pharm Pharmacol.* 1985;37:237–42.
2. Baillie AJ, Coombs GH, Dolan TF. Non-ionic surfactant vesicles: niosomes as delivery system for the anti-leishmanial drug sodium stribogluconate. J Pharm Pharmacol. 1986; 38: 502-505.
3. Malhotra M, Jain NK. Niosomes as Drug Carriers. Indian Drugs. 1994; 31(3): 81-86.
4. Rentel C O, Bouwstra J A, Naisbett B, Junginger H E, Niosomes as a novel peroral vaccine delivery system. Int J Pharm. 1999; 186:161–167.
5. Vyas SP, Khar RK. Controlled drug delivery system: concept and advances. New Delhi: CBS Publishers and Distributors; 2002.
6. Srinivas S, Anand Kumar Y, Hemanth A, Anitha M. Preparation and evaluation of niosomes containing aceclofenac. Dig J Nano Mat and Biostr. 2010; 3(2):199-203.
7. Vijay S Jatav, Santosh K Singh, Pankaj Khatri, Ashish K Sharma, Rambir Singh. Formulation and invitro evaluation of Rifampicin-Loaded Niosomes. J. Chem. Pharm. Res. 2011; 3(2):199-203.
8. Hu C, Rhodes DG. Proniosomes: A Novel Drug Carrier Preparation. *Int J Pharm.* 1999;185:23–35.