

NIOSOMES – A NOVEL PROMISING SELF ASSEMBLED NANOSTRUCTURES

Abstract

Niosomes represent a promising and versatile platform for drug delivery, with the potential to overcome limitations associated with traditional drug delivery systems. Niosomes are indeed novel and promising self-assembled nanostructures that have gained attention in the field of drug delivery. These structures are similar to liposomes but are composed of non-ionic surfactants, such as Span and Tween, instead of phospholipids. The unique structure of niosomes allows them to encapsulate both hydrophilic and hydrophobic drugs, providing a versatile platform for drug delivery. Despite these advantages, challenges also exist in the development of niosomal drug delivery systems. Issues such as scalability, reproducibility, and long-term stability need to be addressed for widespread clinical applications. Ongoing research continues to explore their applications in various therapeutic areas.

Keywords: The unique structure of niosomes allows them to encapsulate both hydrophilic and hydrophobic drugs, providing a versatile platform for drug delivery.

Authors

Dr. M. Mothilal

Professor
Department of Pharmaceutics
SRM college of Pharmacy
SRM Institute of science and Technology
Kattankulathur, Tamilnadu, India
mothilam@srmist.edu.in
mothipharma78@gmail.com

Dr. T. S. Saraswathi

Assistant Professor
Department of Pharmaceutics
SRM college of Pharmacy
SRM Institute of science and Technology
Kattankulathur, Tamilnadu, India.
saraswas1@srmist.edu.in
sarassaaicharan@gmail.com

I. INTRODUCTION

Niosomes are a type of liposome-like vesicle that are composed of non-ionic surfactants. They are similar in structure to liposomes, which are spherical vesicles composed of phospholipids. Niosomes, however, are made from non-ionic surfactants, typically containing a hydrophilic head and a hydrophobic tail.

Niosomes can be used as drug delivery systems to encapsulate and deliver various types of drugs. They are particularly useful for delivering drugs with poor water solubility or those that are sensitive to enzymatic degradation. The hydrophobic core of niosomes can encapsulate lipophilic drugs, while the hydrophilic head provides stability and allows for interaction with aqueous environments. The advantages of niosomes include their biocompatibility, ease of preparation, ability to encapsulate a wide range of drugs. They can be tailored to control drug release kinetics and can be surface-modified to target specific tissues or cells. Niosomes also have the potential to enhance drug stability, reduce toxicity, and improve drug bioavailability.

II. STRUCTURAL COMPONENTS OF NIOSOMES

Surfactants

A wide range of surfactants and their various combinations in different molar ratios may entrap many drug moieties in niosomes of varying features such as size. Nonionic surfactants have a high level of interfacial activity and are made up of both polar and nonpolar segments. The hydrophilic-lipophilic balance (HLB) of the surfactant, the chemical makeup of the constituents, and the critical packing parameter (CPP) all affect whether bilayer vesicles or micelles develop. As demonstrated in Fig. 1, the sort of vesicle that a surfactant would generate can be anticipated based on its CPP. The formula for determining CPP from the surfactant's hydrophobic group's volume, hydrophilic head group's surface area, and lipophilic alkyl chain length is also shown in Fig. 1.

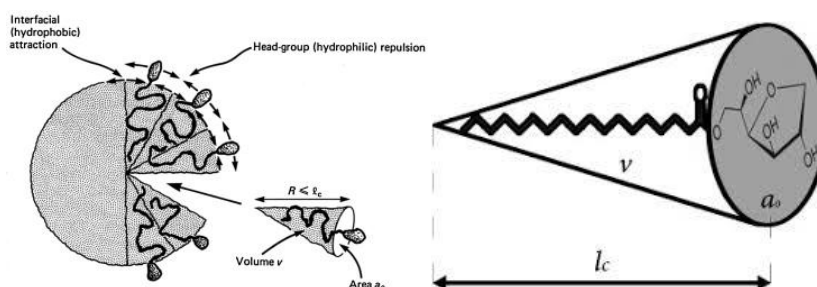


Figure 1 : Critical packing parameter of Niosomes

Critical packing parameter can be determined by the self-assembly of surfactants to vesicles.

$$CPP = V/Ica$$

V = Hydrocarbon chain volume

a = Hydrophilic head group

I_c = Hydrocarbon chain length

CPP between 0.5 to 1	Surfactant form vesicles
CPP < 0.5	Spherical micelles
CPP > 1	Inverted micelles

The size of the hydrophilic head group and the chain length of the nonionic surfactant greatly affect the entrapment efficiency of drug. The stearyl (C18) chains of nonionic surfactants showed higher entrapment efficiency compared with lauryl (C12) chains. The surfactants of tween series bearing a long alkyl chain and a large hydrophilic moiety in combination with cholesterol of water soluble drugs in a 1:1 ratio had the highest entrapment efficiency.

1. **Ether linked surfactants:** These are polyoxyethylene alkyl ethers that are connected with ether and contain both hydrophilic and hydrophobic moieties. This group's general formula is (C_nE_O_m), where n can range from 12 to 18 and m from 3 to 7. There have also been reports of the employment of polyhydroxyl-headed surfactants and ethylene oxide units in the production of niosomes.
2. **Ester linked surfactants:** These surfactants were investigated for their potential use in the formulation and delivery of sodium stibogluconate to the experimental marine visceral leishmaniasis. They have ester linkage between hydrophilic and hydrophobic groups.

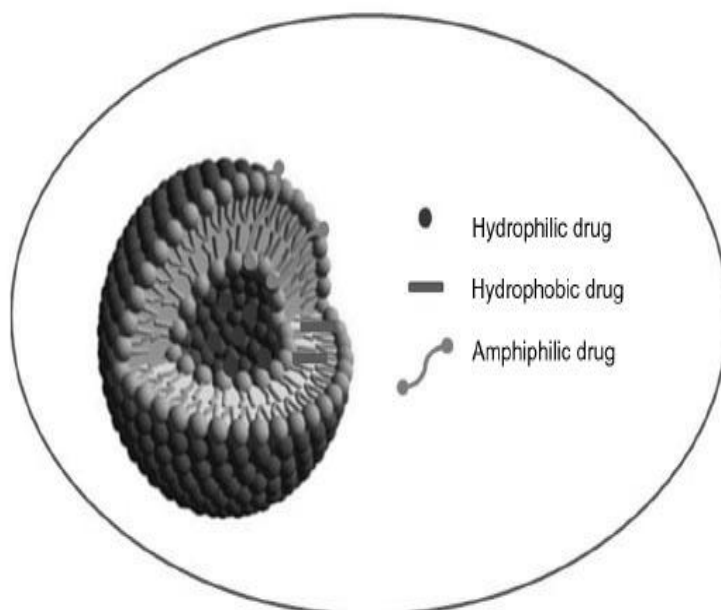


Figure 2: Structure of Niosomes

3. **Sorbitan Esters:** These ester-linked surfactants are the most commonly utilised, particularly in the food business. Commercial sorbitan esters were made by combining oleic acid with sorbitol's mono- and di-anhydrides and their partial esters. These were employed to capture a variety of medicines, including doxorubicin.
4. **Alkyl Amides:** It was discovered that alkyl galactosides and glucosides with amino acid spacers produced vesicles. The alkyl groups are fluorocarbon chains in certain novel

amide compounds, and the alkyl groups are fully or partially saturated C12 to C22 hydrocarbons.

5. Fatty Acids and Amino Acid Compounds: These are closed vesicles comprised of fatty acid bilayers called "Ufasomes" and long chain fatty acids, which are rendered amphiphilic by the addition of hydrophobic alkyl side chains.

- **Cholesterol:** Steroids are a crucial part of cell membranes and modify the fluidity and permeability of the bilayers in observable ways. The non-ionic surfactants are typically supplemented with cholesterol, a waxy steroid metabolite, to enhance stiffness and orientational order. It can be assimilated at high molar ratios but does not contribute to the formation of the bilayer. As an amphiphilic molecule, cholesterol directs its OH group towards the aqueous phase and its aliphatic chain towards the hydrocarbon chain of the surfactant. By preventing the mobility of hydrocarbon carbons in the bilayer, stiff steroidal skeletons alternately positioned with surfactant molecules give rigidity. Additionally, cholesterol is known to stop the transition from the gel to liquid phase, which prevents leaking.
- **Charge Inducers:** By creating a charge on the surface of the manufactured vesicles, charge inducers improve the stability of the vesicles. It works by inhibiting vesicle fusion brought on by repulsive forces of the same charge and by supplying larger zeta potential values. Dicetyl phosphate, dihexadecyl phosphate, and lipoamine acid are often used negative charge inducers, while sterylamine and cetyl pyridinium chloride are positive charge inducers.

6. The advantages of using niosomes as drug delivery systems include:

- **Biocompatibility:** Niosomes are generally considered biocompatible and non-toxic, making them suitable for biomedical applications.
- **Controlled drug release:** Niosomes can be engineered to release their contents in a controlled manner, improving drug efficacy and reducing potential side effects.

III. METHODS OF PREPARATION

There are several methods for the preparation of niosomes, each offering different advantages and suitable for different applications. Some of the commonly used methods are:

1. Thin-Film Hydration Method: In this method, the nonionic surfactant and cholesterol are dissolved in an organic solvent (e.g., chloroform or methanol) to form a thin film on the walls of a round-bottom flask. The solvent is then removed using a rotary evaporator to obtain a thin lipid film. The film is hydrated with an aqueous phase containing the drug of interest and then subjected to gentle agitation or sonication to form niosomal vesicles.

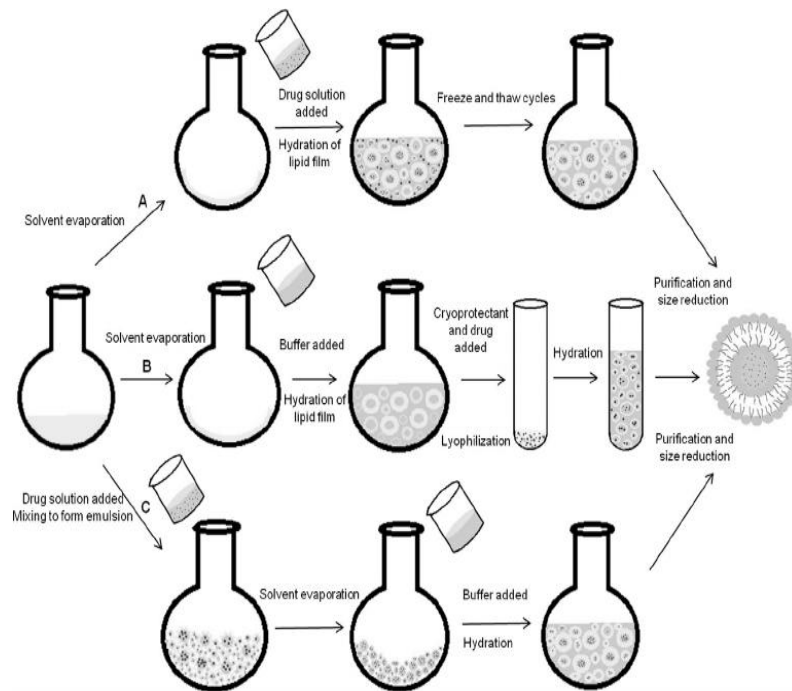


Figure 3

- 2. Reverse Phase Evaporation Method:** This method involves dissolving the nonionic surfactant and cholesterol in an organic solvent and then adding an aqueous phase containing the drug. The mixture is sonicated to form an emulsion. The organic solvent is then evaporated under reduced pressure to form niosomes.
- 3. Ether Injection Method:** In this method, the nonionic surfactant and cholesterol are dissolved in diethyl ether or ether-ethanol mixture. The organic phase is injected into an aqueous phase under continuous stirring or sonication. The solvent is allowed to evaporate, leading to the formation of niosomes.
- 4. Hand-Shaking Method:** This is a simple and less sophisticated method where the nonionic surfactant and cholesterol are mixed in an organic solvent. The mixture is transferred into an aqueous phase and then shaken vigorously to form niosomes.
- 5. Microfluidization Method:** This method involves the use of a microfluidizer to prepare niosomes. The nonionic surfactant and cholesterol are dissolved in an organic solvent, and the resulting solution is mixed with an aqueous phase containing the drug. The mixture is passed through a high-pressure homogenizer, which disrupts the lipid bilayers and forms niosomes.
- 6. Dehydration-Rehydration Vesicles (DRV) Method:** In this method, the nonionic surfactant and cholesterol are dissolved in a small volume of water-miscible organic solvent. The drug is added to the solution, and then the organic solvent is removed by evaporation or freeze-drying. The resulting lipid film is rehydrated with an aqueous solution, leading to the formation of niosomes.

These are some of the common methods used for the preparation of niosomes. The choice of method depends on the desired characteristics of niosomes, the nature of the drug to be encapsulated, and the intended application. Each method has its advantages and limitations, and researchers often select the most suitable method based on their specific requirements. It's worth noting that the choice of method depends on various factors, including the physicochemical properties of the drug, desired niosome characteristics, and scalability of the preparation process. Each method has its advantages and limitations, and the selection should be based on the specific requirements of the formulation.

7. Requirements:

- **Stability:** The presence of cholesterol in niosomes enhances their stability and prevents premature drug release.
- **Easy preparation:** Niosomes can be easily prepared using standard laboratory equipment and techniques.
- **Versatility:** Niosomes can encapsulate both hydrophilic and hydrophobic drugs, allowing for the delivery of a wide range of therapeutic agents.

Niosomes have been explored in various fields of medicine, including targeted drug delivery, vaccine delivery, and gene therapy. They offer promising potential for improving the bioavailability and therapeutic efficacy of drugs while reducing their side effects. However, further research is needed to optimize their formulation and understand their behavior in vivo for practical clinical applications.

IV. APPLICATIONS

Niosomes are widely used in the pharmaceutical, cosmetic, and biomedical fields. Here are some of the common applications of niosomes.

1. **Drug Delivery Systems:** Niosomes are extensively used as drug delivery systems due to their ability to encapsulate both hydrophilic and hydrophobic drugs. They can protect drugs from degradation, improve their stability, and control their release kinetics. Niosomes have been employed for the delivery of various drugs, including anticancer agents, antibiotics, antifungals, and anti-inflammatory drugs.
2. **Topical Delivery :** Niosomes can be formulated into topical creams, gels, or lotions for the localized delivery of drugs to the skin. They enhance the penetration of drugs through the skin barrier, allowing for targeted treatment of skin disorders such as acne, psoriasis, and fungal infections.
3. **Gene Delivery:** Niosomes can be modified to serve as carriers for gene delivery. They can protect nucleic acids, such as DNA or siRNA, from degradation and facilitate their efficient delivery into target cells. This application is particularly useful in gene therapy, where genetic material is delivered to correct genetic disorders or modulate gene expression.
4. **Vaccines:** Niosomes have been explored as vaccine delivery systems. They can encapsulate vaccine antigens and enhance their stability and immunogenicity. Niosomal

vaccines have shown potential in stimulating both humoral and cellular immune responses, making them valuable for infectious disease prevention and immunotherapy.

5. **Diagnostic Imaging:** Niosomes can be utilized as carriers for contrast agents in diagnostic imaging techniques, such as magnetic resonance imaging (MRI) or ultrasound. They enhance the solubility and stability of the contrast agents and help target specific tissues or cells, improving the imaging quality.
6. **Cosmetics:** Niosomes find applications in the cosmetic industry as carriers for cosmetic ingredients. They can encapsulate active compounds, such as vitamins, antioxidants, or skin-whitening agents, improving their stability and enhancing their delivery to the skin.
7. **Agricultural Applications:** Niosomes have been explored for the delivery of agrochemicals, such as pesticides or herbicides. They can improve the targeted delivery of these chemicals to specific plant tissues, reducing the environmental impact and enhancing their efficacy.
 - **Nutraceuticals:** Niosomes are utilized in the encapsulation and delivery of nutraceuticals and dietary supplements. This enables improved bioavailability and targeted delivery of these compounds to specific sites in the body.

These are just a few examples of the diverse applications of niosomes. Ongoing research continues to explore new ways to utilize niosomes in various fields, taking advantage of their versatility as drug and active ingredient carriers.

8. **Ocular delivery of niosomes:** This refers to the use of niosomal vesicles as a drug delivery system for ophthalmic applications. Niosomes have gained attention in ocular drug delivery due to their ability to improve the bioavailability and therapeutic efficacy of drugs targeting various ocular conditions.
Here are some key aspects of ocular delivery of niosomes:
 9. **Drug Encapsulation:** Niosomes can encapsulate both hydrophilic and hydrophobic drugs within their lipid bilayers. This versatility allows the delivery of a wide range of therapeutic agents, including antibiotics, anti-inflammatory drugs, antivirals, and antiglaucoma medications. The drug is protected within the niosomal vesicles, enhancing its stability and facilitating controlled release.
 10. **Enhanced Drug Penetration:** The unique structure of niosomes allows them to adhere to the ocular surface and release the encapsulated drug over an extended period. This enables improved drug penetration through the ocular tissues, including the cornea, conjunctiva, and sclera. Enhanced drug penetration can be particularly beneficial for treating diseases involving the posterior segment of the eye, where drug penetration is often limited.
 11. **Prolonged Drug Residence Time:** Niosomes can provide prolonged residence time on the ocular surface, thereby increasing the contact time of the drug with the target tissues. This can improve the bioavailability of the drug and reduce the frequency of administration.

- 12. Reduction of Systemic Side Effects:** By delivering drugs directly to the eye, niosomes can minimize systemic exposure and potential side effects associated with systemic drug administration. This localized delivery approach can enhance the safety profile of ophthalmic drugs.
- 13. Targeted Drug Delivery:** Niosomes can be modified or functionalized to achieve targeted drug delivery to specific ocular tissues or cells. Surface modifications, such as the attachment of ligands or antibodies, can enable the active targeting of diseased tissues, improving the therapeutic outcome and reducing off-target effects.
- 14. Sustained and Controlled Drug Release:** Niosomes can be designed to provide sustained and controlled drug release, allowing for a prolonged therapeutic effect with reduced dosing frequency. The release kinetics can be tailored by selecting appropriate lipids, surfactants, and manufacturing methods.
- 15. Stability and Biocompatibility:** Niosomes used in ocular delivery should exhibit good stability in tear fluid and ocular environment. The choice of lipids, surfactants, and formulation parameters can influence their stability and compatibility with ocular tissues. Ocular delivery of niosomes has been investigated for various ocular conditions, including dry eye syndrome, glaucoma, infections, macular degeneration, and inflammatory disorders. The formulation and optimization of niosomes for ocular delivery require consideration of factors such as the desired drug release profile, ocular surface compatibility, patient comfort, and ease of administration.

It's worth noting that while niosomes show promise in ocular drug delivery, further research and development are ongoing to optimize their formulation, stability, and therapeutic efficacy.

V. PRONIOSOMES

These are dry, free-flowing powders that serve as precursors to niosomes. They are composed of a mixture of nonionic surfactants, usually in the presence of a carrier material, which can be easily rehydrated to form niosomal vesicles. Proniosomes offer several advantages over conventional niosomes, including improved stability, ease of handling, and extended shelf life.

Proniosomes are precursor formulations that offer a convenient and stable alternative to traditional niosomes. They are dry, free-flowing powders that contain a mixture of nonionic surfactants, cholesterol, and sometimes other excipients. Proniosomes are designed to self-assemble into niosomes upon reconstitution with water or an aqueous medium, making them useful for drug delivery applications.

VI. ADVANTAGES OF PRONIOSOMES

The main advantages of proniosomes over conventional niosomes include:

- 1. Improved Stability:** Proniosomes are stable in their dry powder form, making them easier to store and transport compared to liquid niosome formulations. This enhanced

stability eliminates concerns about aggregation, fusion, or leakage of the vesicles during storage.

- 2. Ease of Use:** Proniosomes are easy to handle and can be reconstituted into niosomes simply by adding an aqueous medium. This eliminates the need for complex and time-consuming preparation methods involved in traditional niosome formulations.
- 3. Increased Flexibility:** Proniosomes allow for the encapsulation of a wide range of hydrophilic and hydrophobic drugs, similar to traditional niosomes. This versatility enables them to be used for various drug delivery applications.
- 4. Controlled Drug Release:** Proniosomes can be designed to provide controlled and sustained drug release, similar to niosomes. The release kinetics can be tailored based on the specific formulation and the desired therapeutic effect.
- 5. Biocompatibility:** Like niosomes, proniosomes are generally considered biocompatible and well-tolerated, which is crucial for ocular and other sensitive drug delivery applications.

The reconstitution of proniosomes can be achieved through simple methods, such as vortexing or shaking the powder with an aqueous medium, or by using specialized devices like spray drying techniques. Upon rehydration, the nonionic surfactants and cholesterol self-assemble into niosomes, forming lipid bilayers with an aqueous core, which encapsulates the drug.

Proniosomes have found applications in various drug delivery systems, including oral, topical, and ocular delivery. Their stability, ease of use, and potential for controlled drug release make them a promising option for improving drug delivery efficiency and patient compliance. As with any drug delivery system, the selection of appropriate excipients and optimization of the formulation are essential to achieving the desired therapeutic outcomes.

VII. PREPARATION OF PRONIOSOMES

The preparation of proniosomes involves the formulation of dry, free-flowing powders that can self-assemble into niosomes upon reconstitution with water or an aqueous medium. Here is a general method for the preparation of proniosomes:

- 1. Selection of Ingredients:** Choose nonionic surfactants, cholesterol, and other excipients suitable for the desired application and drug. Common nonionic surfactants used in proniosomes include Span and Tween series.
- 2. Weighing and Mixing:** Weigh the appropriate amounts of nonionic surfactants, cholesterol, and any additional excipients according to the desired formulation. The excipients may include stabilizers, antioxidants, or permeation enhancers. Thoroughly mix the ingredients using a mortar and pestle or a suitable blending technique until a homogenous powder is obtained.

3. **Particle Size Reduction** (Optional): If desired, the proniosome powder can be further processed to reduce particle size and enhance reconstitution kinetics. This can be achieved by techniques such as milling or sieving.
4. **Reconstitution:** To use the proniosomes, they need to be reconstituted into niosomes. This can be done by adding an appropriate amount of water or an aqueous medium to the proniosome powder. The exact amount of reconstitution medium depends on the desired concentration of the final niosomal suspension.
5. **Hydration and Vesicle Formation:** The proniosome powder and reconstitution medium are mixed by vortexing, shaking, or using specialized devices like spray drying techniques. This allows the nonionic surfactants and cholesterol to hydrate and self-assemble into niosomes, forming lipid bilayers with an aqueous core. The resulting suspension contains the reconstituted niosomes ready for use.

It's important to note that the specific method for proniosome preparation may vary depending on the chosen nonionic surfactants, excipients, and the desired application. Therefore, it's recommended to refer to scientific literature, formulation guides, or consult with experts in the field to optimize the preparation process for your specific needs.

Additionally, it's crucial to conduct thorough characterization and stability studies of the proniosomes to ensure their quality, stability, and performance as drug delivery systems.

VIII. APPLICATION OF PRONIOSOMES

Proniosomes have a wide range of applications in drug delivery and related fields. Some of the key applications of proniosomes include:

1. **Oral Drug Delivery:** Proniosomes can be used for oral drug delivery, particularly for drugs with poor solubility or bioavailability. Upon reconstitution in the gastrointestinal tract, proniosomes can form niosomes that protect the encapsulated drug, enhance its absorption, and improve therapeutic outcomes.
2. **Topical Drug Delivery:** Proniosomes are also utilized in topical drug delivery formulations. They can encapsulate drugs for dermatological applications, such as anti-inflammatory agents, antifungals, or antioxidants. Proniosomes enhance drug penetration into the skin, provide controlled release, and improve the stability and efficacy of the delivered drugs.
3. **Transdermal Drug Delivery:** Proniosomes can be formulated for transdermal drug delivery, allowing drugs to penetrate the skin and enter systemic circulation. By encapsulating drugs with suitable properties, proniosomes enable controlled release and enhance drug permeation across the skin barrier.
4. **Ocular Drug Delivery:** Proniosomes find applications in ocular drug delivery, similar to conventional niosomes. They can be used to deliver drugs to the eye, providing controlled release, enhanced bioavailability, and prolonged residence time on the ocular surface.

Proniosomes can be reconstituted into niosomal suspensions for direct application to the eye.

5. **Pulmonary Drug Delivery:** Proniosomes can be utilized for pulmonary drug delivery, particularly for inhalation therapy. By encapsulating drugs within niosomes, proniosomes improve the stability, solubility, and lung deposition of the drugs. This delivery route is commonly used for the treatment of respiratory conditions like asthma and chronic obstructive pulmonary disease (COPD).
6. **Vaccine Delivery:** Proniosomes have shown promise as carriers for vaccine delivery. They can encapsulate antigens, enhancing their stability and immunogenicity. Proniosomal vaccine formulations can improve antigen delivery to immune cells and stimulate a robust immune response.
7. **Nutraceutical Delivery:** Proniosomes can be used to encapsulate and deliver nutraceuticals and dietary supplements. This enables improved bioavailability and targeted delivery of these compounds, enhancing their therapeutic effects.
8. **Personal Care Products:** Proniosomes are also utilized in the formulation of various personal care products, including creams, lotions, and sunscreens. They can improve the delivery of active ingredients to the skin, enhancing their efficacy in cosmetic and skincare applications.

It's worth noting that while proniosomes offer several advantages in drug delivery and related applications, their use and optimization depend on the specific drug, target site, and desired release profile. Further research and development are ongoing to explore and expand the potential applications of proniosomes in various fields.

IX. ADVANTAGES OF PRONIOSOMES

Proniosomes offer several advantages as drug delivery systems, making them a promising alternative to traditional niosomes and other drug delivery platforms. Here are some key advantages of proniosomes:

1. **Enhanced Stability:** Proniosomes are dry, free-flowing powders that have improved stability compared to liquid niosome formulations. The dry powder form eliminates concerns about vesicle aggregation, fusion, or leakage, enhancing the shelf life and storage conditions of the formulation.
2. **Ease of Handling:** Proniosomes are easy to handle and transport due to their dry powder form. They can be conveniently stored, measured, and transported without the need for specialized equipment or stringent temperature controls.
3. **Improved Patient Compliance:** Proniosomes offer improved patient compliance due to their ease of use. The dry powder can be reconstituted into niosomes by simply adding water or an aqueous medium, making the formulation ready for administration. This ease of reconstitution simplifies the administration process and may improve patient acceptance and adherence to the treatment.

4. **Versatile Drug Encapsulation:** Proniosomes can encapsulate a wide range of drugs, including hydrophilic and hydrophobic compounds. This versatility allows for the delivery of diverse therapeutic agents, including poorly soluble drugs, peptides, proteins, and lipophilic compounds. Proniosomes can be customized to suit the specific drug properties and requirements.
5. **Controlled Drug Release:** Proniosomes can be designed to provide controlled and sustained drug release, tailoring the release kinetics to the desired therapeutic effect. The lipid bilayers of niosomes formed upon reconstitution allow for controlled release of the encapsulated drug over an extended period, resulting in prolonged therapeutic activity and reduced dosing frequency.
6. **Improved Bioavailability:** Proniosomes can enhance the bioavailability of drugs by protecting them from degradation, increasing their solubility, and facilitating their absorption. The encapsulation of drugs within niosomes improves drug stability, prevents enzymatic degradation, and promotes their transport across biological barriers, such as the gastrointestinal tract or the skin.
7. **Targeted Drug Delivery:** Proniosomes can be modified or functionalized to achieve targeted drug delivery to specific tissues or cells. Surface modifications, such as the attachment of ligands or antibodies, enable active targeting of diseased tissues, improving the therapeutic efficacy and reducing off-target effects.
8. **Biocompatibility:** Proniosomes are generally considered biocompatible and well-tolerated, minimizing the risk of adverse reactions or toxicity. The choice of nonionic surfactants and other excipients can further enhance their biocompatibility.
9. **Scalability and Cost-effectiveness:** The production of proniosomes can be easily scaled up to meet larger manufacturing requirements. The dry powder formulation simplifies manufacturing processes and reduces costs compared to more complex and resource-intensive methods.

Overall, proniosomes offer advantages in terms of stability, ease of handling, drug encapsulation, controlled release, bioavailability, targeted delivery, biocompatibility, and cost-effectiveness. These advantages make proniosomes an attractive option for various drug delivery applications and provide opportunities for improving therapeutic outcomes and patient experiences.

However, it's important to note that the availability of specific niosome-based products may vary by country and can change over time due to new product launches and discontinuations.

10. **Niosomal Doxorubicin:** Doxosome (Doxorubicin HCl liposome/niosome) is a niosomal formulation of the chemotherapeutic drug doxorubicin. It is marketed for the treatment of various types of cancers, including breast cancer, ovarian cancer, and multiple myeloma.
11. **Niosomal Amphotericin B:** AmBisome (Amphotericin B liposome) is a niosomal formulation of the antifungal drug amphotericin B. It is used for the treatment of severe systemic fungal infections, such as invasive aspergillosis and cryptococcal meningitis.

12. Niosomal Tacrolimus: Tacrosolv (niosomal tacrolimus) is a niosomal formulation of the immunosuppressive drug tacrolimus. It is indicated for the treatment of moderate to severe atopic dermatitis (eczema) in adults.

13. Niosomal Acyclovir: Zostex (niosomal acyclovir) is a niosomal formulation of the antiviral drug acyclovir. It is marketed for the treatment of herpes zoster (shingles) and recurrent herpes labialis (cold sores).

It's important to consult with healthcare professionals or refer to local pharmaceutical databases and regulatory authorities to obtain the most up-to-date information on marketed niosome-based preparations in your specific region.

X. CONCLUSION

In conclusion, niosomes are versatile lipid-based vesicular systems that offer numerous advantages for drug delivery applications. They are composed of nonionic surfactants and cholesterol, which self-assemble into bilayer structures with an aqueous core. Niosomes can encapsulate both hydrophilic and hydrophobic drugs, improving their stability, solubility, and bioavailability. The unique properties of niosomes allow for controlled and sustained drug release, targeted delivery, and enhanced therapeutic outcomes.

Niosomes have been explored for various routes of administration, including oral, topical, ocular, and pulmonary delivery. They have demonstrated potential in delivering a wide range of drugs, including anticancer agents, antifungals, immunosuppressants, and vaccines. Niosomes can improve drug stability, protect drugs from degradation, and enhance their absorption, resulting in improved drug efficacy and reduced side effects.

Furthermore, the development of proniosomes, which are dry precursor formulations that can self-assemble into niosomes upon reconstitution, has added another dimension to the application of niosomes. Proniosomes offer advantages such as enhanced stability, ease of handling, and improved patient compliance.

While niosomes present several benefits, it's important to consider factors such as formulation optimization, stability, scalability, and regulatory requirements for successful translation into commercial products. Ongoing research and development efforts continue to explore the potential of niosomes in addressing various therapeutic challenges and expanding their applications in the field of drug delivery.

Overall, niosomes represent a promising platform for drug delivery, and their unique properties make them an attractive option for improving the efficacy, safety, and patient acceptability of diverse therapeutic agents.

REFERENCES

- [1] Biju S. S., Talegaonkar S., Mishra P. R., Khar R. K., *Indian J. Pharm. Sci.*, 210, 141—151 (2010).
- [2] Pardridge WM. Blood-brain barrier drugtargeting: The future of brain drugdevelopment. *MolInterv* 2003; 3: 90-105.
- [3] Drug Targeting Organ-Specific Strategies, Edited by G. Molema, D. K. F. Meijer, Chapter 2 Brain-Specific Drug Targeting Strategies, By Ulrich Bickel, Young-SookKang, JörgHuwyler, Pg no. 23-50.

- [4] Shadab A. Pathan, ZeenatIqbal, Syed M. A.Zaidi, SushmaTalegaonkar, DivyaVohra,et. al., CNS Drug Delivery Systems: NovelApproaches, Recent Patents on DrugDelivery & Formulation, Bentham SciencePublishers Ltd, 2009; 3: 71-89
- [5] Giddi H. S., Arunagirinathan M. A., Bellare J. R. Self-assembled surfactant nano-structures important in drug delivery: A review. *Indian J Exp Biol.* 2007; 45: 133-159.
- [6] Uchegbu I. F., Double J. A., Kelland L. R., Turton J. A., Florence A. T. The activity of doxorubicin niosomes against an ovarian cancer cell line and three in vivo mouse tumour models. *J Drug Target.* 1996; 3: 399-409.
- [7] Arunothayanun P, Bernard MS, Craig DQ, Uchegbu IF, Florence AT. The effect of processing variables on the physical characteristics of non-ionic surfactant vesicles (niosomes) formed from a hexadecyl diglycerol ether. *Int J Pharm* 2000;201:7–14
- [8] Vyas SP and Khar RK. Targeted and Controlled Drug Delivery Novel Carrier Systems. CBS Publishers and Distributors, New Delhi (2011) 249 -279
- [9] Hunter C. A., Dolan T. F., Coombs G. H., Baillie A. J. Vesicular systems(niosomes and liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. *J Pharm Pharmacol.* 1988; 40: 161-165.
- [10] Dahiya N. K., Rao R., Nanda S. Preparation and characterization techniques in niosomal vesicular systems- A review. *J. Pharm. Biomed. Sci.* 2011; 5:1-8.
- [11] Bandyopadhyay P., Johnson M. Fatty alcohols or fatty acids as niosomal hybrid carrier: effect on vesicle size, encapsulation efficiency and in vitro dye release. *Colloids Surf B Biointerfaces.* 2007; 58: 68-71
- [12] Baillie A. J., Coombs G. H., Dolan T.F., Laurie J. Non-ionic surfactant vesicles, niosomes, as a delivery system for the anti-leishmanial drug, sodium stibogluconate. *J Pharm Pharmacol.* 1986; 38: 502-505
- [13] Palozza P., Muzzalupo R., Trombino S., Valdannini A., Picci N. Solubilization and stabilization of beta-carotene in niosomes: delivery to cultured cells. *Chem Phys Lipids.* 2006; 139: 32–42
- [14] Yasin M. N., Hussain S., Malik F., Hameed A., Sultan T., Qureshi F., Riaz H., Perveen G., Wajid A. Preparation and characterization of chloramphenicol niosomes and comparison with chloramphenicol eye drops (0.5% w/v) in experimental conjunctivitis in albino rabbits. *Pak J Pharm Sci.* 2012; 25: 117-121.
- [15] Guinedi A. S., Nahed D. M., Samar M., Rania M. H. Preparation and evaluation of reverse-phase evaporation and multilamellar niosomes as ophthalmic carriers of acetazolamide. *Int J Pharm.* 2005; 306: 71–82.
- [16] Khandare J. N., Madhavi G., Tamhankar B. M., *The Eastern Pharmacist*, 37, 61—64 (1994).
- [17] Vyas S. P., Khar R. K., “Targeted and Control Drug Delivery,” 1st ed., Chap. 6, CBS Publishers and Distributors, New Delhi, 2002, pp. 249—276
- [18] Baillie A. J., Florence A. T., Hume L. R., Muirhead G. T., Rogerson A., *J. Pharm. Pharmacol.*, 37, 863—868 (1985).
- [19] Chauhan S., Luorence M. J. The preparation of polyoxyethylene containing non-ionic surfactant Vesicles. *J Pharm Pharmacol.* 1989; 41: 6.
- [20] Udupa, N. (2004). Niosomes as drug carriers. In: N. K. Jain. *Controlled and Novel Drug Delivery* (pp. 292-303). New Delhi: CBS Publishers & Distributors.
- [21] Mayer L. D., Bally M. B., Hope M. J., Cullis P. R. Uptake of antineoplastic agents into large unilamellar vesicles in response to a membrane potential. *Biochem Biophys Acta.* 1985; 816: 294-302
- [22] Blazek-Walsh AI, Rhodes DG. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. *Pharm Res.* 2001; 18: 656-661.
- [23] Junyaprasert VB, Teeranachaideekul V, Supaperm T. Effect of Charged and Non-ionic Membrane Additives on Physicochemical Properties and Stability of Niosomes. *AAPS PharmSciTech.* 2008; 9(3): 851-859.
- [24] Almira I, Blazek-welsh IA, Rhodes GD. Maltodextrin – Based proniosomes. *AAPS PharmSciTech.* 2001;3:1–8.
- [25] Biswal S, Murthy PN, Sahu J, Sahoo P, Amir F. Vesicles of Non-ionic Surfactants (Niosomes) and Drug Delivery Potential. *Int J Pharm Sci Nanotech.* 2008;1:1–8
- [26] The effect of non-ionic surfactant vesicle (niosome) entrapment on the absorption and distribution of methotrexate in mice, Azmin MN, Florence AT, Handjani-Vila RM, Stuart JF, Vanlerbergh G, Whittaker JS ; *J Pharm Pharmacol.* 1985 Apr; 37(4):237-42.
- [27] Manosroi A, Wongtrakul P, Manosroi J, Sakai H, Sugawara F, Yuasa M, et al. Characterization of vesicles prepared with various non-ionic surfactants mixed with cholesterol. *Colloids Surf .* 2003; 30:129–38
- [28] Biswal S., Murthy P. N., Sahu J., Sahoo P., Amir F., *International Journal of Pharmaceutical Sciences and Nanotechnology*, 1, 1—8 (2008).

- [29] Formulation and in vivo evaluation of niosome-encapsulated daunorubicin hydrochloride. Balasubramaniam A, Kumar VA, Pillai KS; *Drug Dev Ind Pharm.* 2002 Nov; 28(10):1181-93.
- [30] Yoshioka T, Stermberg B, Florence AT. Preparation and properties of vesicles (niosomes) of sobitan monoesters (Span 20, 40, 60, and 80) and a sorbitan triester (Span 85) *Int J Pharm.* 1994;105:1–6.
- [31] Karki R, Mamatha GC, Subramanya G, Udupa N. Preparation, characterization and tissue disposition of niosomes containing isoniazid. *Rasayan J Chem.* 2008;1:224–7.
- [32] Shah BM, Misra M, Shishoo CJ, Padh H (2015) Nose to brain microemulsionbased drug delivery system of rivastigmine: formulation and ex-vivo characterization. *Drug Delivery* 22: 918-930.
- [33] Patel MR, Patel RB, Bhatt KK, Patel G, Gaikwad RV (2016) Paliperidone microemulsion for nose-to-brain targeted drug delivery system: pharmacodynamic and pharmacokinetic evaluation, *Drug Delivery* 23: 346-354.
- [34] Shinde RL, Devarajan PV (2017) Docosahexaenoic acid-mediated, targeted and sustained brain delivery of curcumin microemulsion, *Drug Delivery* 24: 152-161.
- [35] Boche M, Pokharkar V (2016) Quetiapine Nanoemulsion for Intranasal Drug Delivery: Evaluation of Brain-Targeting Efficiency. *AAPS PharmSciTech.*
- [36] Karavasili C, Fatouros DG (2016) Smart materials: In situ gel-forming systems for nasal delivery. *Drug Discovery Today*.8
- [37] Rao M, Agrawal DK, Shirsath C (2017) Thermoreversible mucoadhesive in situ nasal gel for treatment of Parkinson's disease. *Drug Dev and Industrial Pharmacy* 43: 1.
- [38] Sharma S, Lohan, Murthy RSR (2014) Formulation and characterization of intranasal mucoadhesive nanoparticulates and thermo-reversible gel of levodopa for brain delivery. *Drug Dev Ind Pharm* 40: 869-878.
- [39] Parhizkar E, Emadi L, Alipour S (2017) Development and evaluation of midazolam in situ nasal gel properties in presence of solubility enhancers at cilia-friendly pH. *Macromolecular Research*: 1-7.
- [40] Morsi N, Ghorab D, Refai H, Teba H (2016) Ketorolac tromethamine loaded nanodispersion incorporated into thermosensitive in situ gel for prolonged ocular delivery. *International Journal of Pharmaceutics* 506: 57-67.
- [41] Ismail A. A., Sanaa A., Gizawy E., Fouda M. A., Donia M. A., *AAPS PharmSciTech*, 8, E1—E7 (2007).
- [42] "The Physical Chemistry of Membranes," ed. by Silver B. L., Allen & Unwin, Boston-London-Sydney, 1985.
- [43] Haran G., Coben R., Bar L. K., Barenholz Y., *Biophys. Acta*, 1151, 201 (1993).
- [44] Verma S., Singh S. K., Syan N., Mathur P., Valecha V., *J. Chem. Pharm. Res.*, 2, 496—509 (2010).
- [45] Azmin M. N., Florence A. T., Handjani-Vila R. M., Stuart J. F. B., Vanlerberghe G., Whittaker J. S., *J. Pharm. Pharmacol.*, 37, 237—242 (1985).
- [46] Biswal S., Murthy P. N., Sahu J., Sahoo P., Amir F., *International Journal of Pharmaceutical Sciences and Nanotechnology*, 1, 1—8 (2008).
- [47] Mura S., Pirot F., Manconi M., Falson F., Fadda A. M., *J. Drug Target.*,15, 101—108 (2007).
- [48] H.O. Ammar, M.Haider et al., *Invitro and invivo investigation for optimization of niosomal ability for sustainment and bioavailabilty enhancement of diltiazem after nasal administration.*2017, 24(1), 414-421
- [49] Sayedeh Raziye, Mahdevi Moghddam, Abdul ahad et al., *Formulation and optimization of niosomes topical diacerein delivery using 3-factor, 3-level. Box- Behnken design for the management of psoriasis.* 2016, 69:789-797 *Materials science & Engineering*
- [50] Nilufer Yuksel, Zerrin Sezgin bayindir et al., *In situ Niosome forming Maltodextrin proniosome of candesartan cilexetil: Invitro and invivo evaluation of Insitu Niosome forming proniosomes containing candesartan cilexetil.* *International Journal of Biological Macromolecules* 2015, 82:453-463
- [51] Vyshnavi.V, Indira. S et al., 2015 *Formulation and evaluation of Nasal Niosomal insitu Gels of Loratidine* *International journal of Pharmaceutical Sciences and Drug Research* 7 (1) 13-21
- [52] Kaushik Kar, Preethi Sudheer et al., *Formulation and evaluation of niosomal drug delivery system of ketoprofen* *Journal of Pharmaceutical Sciences*, 2015; 5(4):173-180
- [53] Ajay Kuma et al., *Formulation, evaluation and comparison of Ketorolac tromethamine transdermal gel containing natural and synthetic permeation enhancers,* *International Journal of Pharmacy and Pharmaceutical Sciences*, 2014, 6(4), 151-176.
- [54] Sunil Kamboj, Vipin Saini, et al., *Formulation and characterization of drug loaded non-ionic surfactant vesicles (Niosomes) for Oral bioavailabilty enhancement* *The Scientific World Journal*, Volume 2014 (2014), Article ID 959741, 8 pages
- [55] Nagaraju Ravouru, Pallavi Kondreddy, Deepathy korakanchi and Haritha M et al., *Formulation and evaluation of Niosomal nasal drug delivery system of folic acid for brain targeting.* *Current Drug Discovery Technologies*, 2013, 10, 210-282

- [56] V.C. Okore, A. A.Attarna, K.C. Ofokansi, C.O.Esimone et al., Formulation and evaluation of Niosomes Indian journal of pharmaceutical sciences, 2011, 73(3): 323-328
- [57] Pratap S. Jadon, Virendra Gajbhiye, Rajesh S. Jadon et al., Enhanced oral Bioavailabilty of Griseofulvin via Niosomes AAPS Pharmsci Tech, Vol.10, No.4, Dec 2009
- [58] Kadasamy Ruckmani and veintramuthu Sankar et al., Formulation and optimization of Zidovudine Niosomes 2010, AAPS Pharma SciTech, 11(3), 1119-1127.