Current Trends in Pharmacology and Clinical Trials
ISSN: 2642-0848

Academic Strive
Researcher's perception is our reality

Mini Review *Volume 7 Issue 2*

Niosomes: A Short Review

Gunda RK*, Kumar JNS, Anjali VN, Madhuri YR, Renuka TA and Amulya R
Department of Pharmaceutics, Narasaraopeta Institute of Pharmaceutical Sciences India

***Corresponding author:** Raghavendra Kumar Gunda M.Pharm., PhD., FCEM. Associate Professor, Department of Pharmaceutics, Narasaraopeta Institute of Pharmaceutical Sciences (Autonomous), Narasaraopet, Palnadu (Dt), Andhra Pradesh, India, Tel: +91-9666705894; Email: raghav.gunda@gmail.com

Received Date: July 22, 2024; **Published Date:** September 04, 2024

Abstract

Niosomes are the new drug delivery system in which the solution is enclosed in a vesicle that is made of non-ionic surfactant. Niosomes are formations of vesicles by hydrating a mixture of cholesterol and non-ionic surfactants. It can be employed to transport both lipophilic and amphiphilic drugs. Niosomes have a flexible structural characterization and are biodegradable, biocompatible, and non-immunogenic. The primary goal of this review is to examine how noisome technology is applied to treat various diseases like cancer, leishmaniasis, and inflammatory diseases. Niosomes offer promising research opportunities and benefit both the pharmaceutical and research communities. Niosomes are physically and chemically unstable. Niosomes are unilamellar and multilamellar. Niosomes are prepared by the ether injection method, sonication technique, handshaking method, and from proniosomes method etc. Several factors affect the formation of niosomes and the factors are nature and type of surfactant, cholesterol content, and charge, the temperature of hydration, composition of membrane, etc. This review article focuses on the structure and type of niosomes, composition of niosomes, methods to prepare niosomes, factors, and applications of niosomes.

Keywords: Niosomes; Non-Ionic Surfactant; Proniosomes; Cholesterol; Methods of Preparation; Vesicle

Abbreviations

MLU: Multi Lamellar Vesicles; LUV: Large Unilamellar Vesicles; SUV: Small Unilamellar Vesicles.

Introduction

Niosomes are non-ionic surfactant vesicles that can entrap hydrophilic and lipophilic drugs in lipid-based vesicular membranes or aqueous layers [1]. Niosomes are vesicular systems similar to liposomes that can be used as carriers of amphiphilic drugs [2]. A non-ionic surfactant like span-60 which is often stabilized by the addition of cholesterol and a small amount of anionic surfactant like diacetyl phosphate forms are used in niosomes [3]. Since the niosomes are non-ionic and less toxic, they hold promise as a drug delivery vehicle. Additionally, by limiting the medication's action to the target cell, they improve its therapeutic index [4].

Advantages

- Targeted drug delivery can be achieved using niosomes the drug is delivered directly to the body part where the therapeutic effect is required.
- A reduced dose is required to achieve the desired effect.
- Niosomes are amphiphilic i.e. both hydrophilic and lipophilic in nature and can accommodate a large number of drugs with a wide range of solubilities

- Improve the oral bioavailability of poorly soluble drugs.
- Enhance the skin permeability of drugs when applied topically.
- The surfactants used and also the prepared niosomes are biodegradable, biocompatible, and non-immunogenic.
- They are osmotically active and stable.

Disadvantages

Aqueous suspension of niosomes may lead to fusion, aggregation, or hydrolysis of entrapped drugs, thus limiting the self-life of niosomes dispersion.

- Chemical instability
- Physical instability

Structure of Niosomes

Niosomes are non-ionic surfactants in the form of a bi-layered structure. The formation of these thermodynamically stable bilayered structures requires the appropriate proportioning of surfactants and cholesterol as well as the temperature above the gel liquid transition point. There is a hollow area in the middle of this two-layered construction [5].

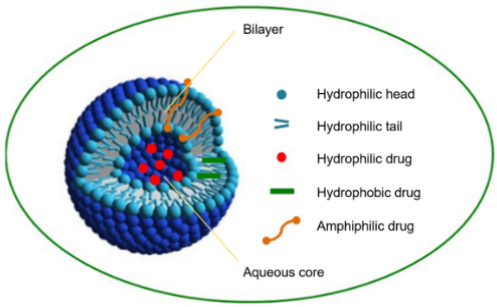

Figure 1: Structure of Niosomes.

Types of Niosomes [6]

Multi lamellar vesicles (MLU)
Large Unilamellar vesicles (LUV)
Small Unilamellar vesicles (SUV)

Multi Lamellar Vesicles (MLV): It is made up of encircle several bilayers each a different aqueous liquid compartment. These vesicles have a diameter of approximately 0.5-10. um. The most commonly used niosomes are multilamellar vesicles. They are easy to build and mechanically stable after extended storage. These vesicles are ideal for delivering lipophilic drugs.

Large Unilamellar Vesicles (LUV): This form of niosomes uses a relatively small amount of membrane lipids to entrap higher quantities of bioactive components due to its high aqueous/lipid component compartment ratio.

Small Unilamellar Vesicles (SUV): Most of the time, the sonication approach is used to create these tiny unilamellar vesicles from multilamellar vesicles. Diacetyl Phosphate is added to 5(6)-Carboxy florescein (Cf) loaded Span 60-based niosomes using French Dress extrusion electrostatic stabilization.

Composition of Niosomes

Two main components are used for the formulation of Niosomes [7].
Cholesterol
Non-ionic Surfactant.

Cholesterol: It is used in the niosomal formulation to provide rigidity, proper shape & Conformation of niosomes. It provides stability, to the Vesicles.

Non-ionic surfactant: The commonly used non-ionic surfactants in the formulation of Niosomes are:
Span: 20,40,60,80 and 85
Tweens: 20,40, 60 and 80
Brij's :30,35,52,58,72 and 76.

Preparation Methods for Niosomes

- Ether injection method
- Handshaking method (thin film hydration method)
- Sonication method
- Micro fluidization method
- Multiple membrane extrusion method
- Reverse phase evaporation technique
- Transmembrane, pH gradient, drug uptake process
- The bubble method
- Formation of niosomes from proniosomes

Ether Injection Method: In the process, the warm water is kept at 60° and it is mixed with surfactant that has been dissolved in diethyl ether. The 14-gauze needle is used to inject an ether solution containing a surfactant added into an aqueous solution of material. As a result, the ether vaporizes and single-layered needles are formed [8].

Hand Shaking Method (Thin Film Hydration Method): A round bottom flask is filled with liquid and non-ionic surfactant which is dissolved in an organic solvent. A rotary evaporator operating at low pressure is used to extract the organic solvent, when an excess amount of aqueous buffer is introduced to a dry liquid & agitated by a hand mixer or a vortex mixer, Multilamellar vesicles are generated, spontaneously. Multilamellar vesicle size and encapsulation are effectively determined by the ionic strength of the aqueous medium, lipid concentration, changes in bilayer chemistry, and the length and intensity of shaking [9].

Sonication Method: The cable describes the vesicle production, which is described by the sonication of the Solution. To the mixture of surfactants in a 10ml glass vial, an aliquot yield buffer solution containing medication is added. Then the mixture is placed in a sonicator fitted with a titanium probe and sonicated at 60° for 5 minutes to generate niosomes [10].

Micro Fluidization Method: To create unilamellar vesicles with a specified Size distribution, a novel approach called micro fluidization is employed. This approach is based on the submerged jet principle, which describes how two fluidized streams interact inside an interaction chamber at extremely high velocities within precisely designed microchannels. The thin liquid sheet impingement along a common front is organized so that the energy input into the system stays in the region where niosomes develop. As a result, the niosomes that are produced have higher uniformity, smaller sizes & improved reproducibility [9].

Multiple Membrane Extrusion Method: This approach can be used to manufacture vesicles of the desired size up to 8 channels of Polycarbonate membranes can be arranged in sequence to achieve this method. Evaporation is used to create a thin coating of the mixture of diacetyl phosphate, cholesterol, and surfactant. After that, the film is rehydrated using the drug-16-containing aqueous solution using C16G12, the final solution is extruded through a polycarbonate membrane (0.1µm nucleophore) [11].

Reverse Phase Evaporation Technique: This process involves dissolving cholesterol and surfactant in an ether and chloroform Combination. After adding a drug containing an aqueous phase, these two phases are sonicated at 4-5°c after adding a tiny quantity of Phosphate buffered Saline, the transparent gel that has formed is subjected to more Sonication At 40% &, low pressure, and the organic phase is eliminated. The resulting viscous niosomes suspension is heated in a water bath at 60%-for 10min to yield niosomes after which it is diluted with phosphate-buffered Saline [12].

Transmembrane pH Gradient Drug Uptake: In a round-bottomed flask, surfactant and cholesterol are dissolved in chloroform. To achieve the thin film on the flak wall, the solvent evaporation is carried out at a lower pressure. Next, by vortex mixing 300mm of Citric acid (PH 4.0) is added to hydrate the film. Multilamellar vesicles are the endpoint of it. They are then 3 times frozen and thawed before being sonicated to extract niosomes. An aqueous drug solution is vortexed and added to this niosomal suspension. Phosphate buffer is utilized to keep the pH between 7.0 and 7.2. To produce niosomes, the mixture is then heated for 10 minutes at 60°C [13].

The Bubble Method: It is a unique process for producing niosomes in a single step without the use of organic solvents. Here the temperature is controlled by three necks on a round-bottomed flask that is submerged in water in the bubbling unit. Reflex is cooled by water in the first neck; a thermometer is located in the second neck and a nitrogen supply is supplied through the third neck. At 70°C cholesterol and surfactant are distributed in a pH 7.4 buffers. Using a high-shear homogenizer, the dispersion is combined for 15 seconds. Then the nitrogen gas bubbles up to 70°C [14].

Formation of Niosomes from Proniosomes: Proniosomal powder is placed in a screw-capped vial with water or saline at 80°. After that, it is combined by vortexing and agitated for 2min, which forms the niosomal suspension. The addition of the aqueous phases T>Tm with brief agitation to generate the niosomes [15].

(T = Temperature; Tm = mean phase transition temperature)

Niosome Formulation- Considerations

- Drug
- Nature and type of surfactant
- Cholesterol content and charge
- Resistance to osmotic stress
- Temperature of hydration
- Composition of membrane

Drug: The entrapment of drugs in niosomes causes an increase in vesicle size, most likely as a result of the solute interacting with the head groups of the surfactant, which raises the charge and mutual repulsion of the surfactant bilayers. The long PEG, chains in polyoxyethylene glycol (PEG) coated vesicles trap part of the medication, so decreasing the inclination to enlarge. The drug's hydrophilic, and lipophilic balance influences the level of entrapment [16].

Nature and Type of Surfactant: Since the surface free energy of surfactant reduces with increasing the hydrophobicity, the mean size of niosomes increases correspondingly with an increase in HLB surfactants such as span 85 (HLB 1.8) to span (HLB 8.6). Hydrophobicity head and hydrophobicity tail are essential components of a surfactant one or two alkyl, perfluoroalkyl, or occasionally a single steroidal group might make up the hydrophobic tail [17].

Cholesterol Content and Charge: An increase in the cholesterol content of the bilayers led to a decrease in the release rate of encapsulated material and consequently an increase in the rigidity of the bilayers obtained. multilamellar vesicle structure & leads to greater overall entrapped volume. Cholesterol increases the hydrodynamic diameter and entrapment efficiency of niosomes. It. induces membrane stabilizing activity and lowers the leakiness of the membrane [18].

Resistance to Osmotic Stress: The addition of a hypertonic solution results in a decrease in the diameter of the Vesicles; in a hypotonic solution, the mechanical loosening of the vesicle structure under osmotic stress causes an initial delayed release, which is then followed by a rapid release [19].

Temperature of Hydration: The temperature of hydration has an impact on the noisome's size and shape. The temperature at which gel liquid phases change should be higher than the hydration temperature. The assembly of surfactants into vesicles and the modulation of vesicle shape are impacted by temperature changes. The alteration is also explained by the hydration time and medium volume. Drug leakage issues and fragile niosomes are produced when the hydration temperature, duration, and medium volume are

not chosen properly [20].

Composition of Membrane: To stabilize the niosomes, different additives are added to the surfactant and drug.

Forex: Adding cholesterol improves membrane rigidity and decreases drug leakage Adding a small amount of solulan C24 (cholesteryl poly-24-oxy ethylene ether) to the polyhedral niosomes formed from C16G2 stops them from aggregating because steric hindrance develops [21].

Applications of Niosomes

Niosomes as Drug Carriers: Niosomes have been employed as carriers of the symptomatic operator iobitridol, which is used in X-ray imaging. Topical niosomes can act as a rate-restricting layer blockage to adjust foundational medicine intake, as an entry booster, as a neighborhood station for sustained arrival of dermally dynamic mixers, or as a Solubilization grid [22].

Niosomes as Transdermal Delivery of Drugs: When a medication is combined with noisome for transdermal delivery, the drug's penetration through the skin is increased [23].

Anti-Neoplasia: Anthracyclic antibiotics, like doxorubicin, have a dose-dependent, anti-reversible cardiotoxic impact in addition to their broad spectrum antitumor action. When given by niosomal administration into mice with S-180 tumors, this medication increases their lives and slows the rate at which Sarcomas proliferates [24].

Anti-Inflammatory Agents: Diclofenac sodium in niosomal form, which has 70% less cholesterol than the free medication, has more anti-inflammatory effects when compared to the free medication exhibits stronger anti-inflammatory action. [25].

Anti-Fungal Therapy: The span-60 liposomal oral solution of fluconazole was developed by Sharma et al. (2009) to treat fungal infections. When compared to Capsules and pills, it is more effective [26].

Immunological application: The nature of the immunological response triggered by antigens has been studied using niosomes. According to Brewer and Alexander, niosomes are a powerful adjuvant with low toxicity, immunological specificity, and durability [27].

Leishmaniasis: To target therapy for diseases where the contaminating organism resides in the reticuloendothelial framework, niosomes can be employed. One such infection that targets the liver and spleen cells is leishmaniasis [28].

References

1. Kazi KM, Mandal AS, Biswas N, Guha A, Chatterjee S, et al. (2010) Niosome: A future of targeted drug delivery systems. J Adv Pharm Technol Res 1(4): 374-380.

2. Tamizharasi S, Dubey A, Rathi V, Rathi JC (2009) Development and Characterization of Niosomal Drug Delivery of Gliclazide. J Young Pharm 1(3): 205-209.

3. Malhotra M and Jain NK (1994) Niosomes as drug carriers. Ind drug 31(5): 81-86.

4. Baillie AJ, Coombs GH, Dolan TF (1986) Non-ionic surfactant vesicles, niosomes as a delivery system. J Pharm Pharmacol 38(7): 502-505.

5. Gadhiya P, Shukla S, Modi D, Bharadia P (2012) Niosomes in targeted drug delivery- A review. Int J Pharm Res Sch 1(2): 59-72.

6. Raghavendra KG, Suresh Kumar JN, Sandhya B, Satyaprasad A, Bhargavi G, et al. (2023) Niosomes: A Novel drug Delivery System. Pharm Sci 3(2): 88-93.

7. Srinivas S, Anand Kumar Y, Hemanth A, Anitha M (2010) Preparation and evaluation of niosomes containing aceclofenac. Dig J Nano Mat and Biostr 5(1): 249-254.

8. Khandare JN, Madhavi G, Tamhankar BM (1994) Niosomes novel drug delivery system. East Pharm 37: 61-64.

9. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A (1985) The preparation and properties of niosomes Non-ionic surfactant vesicles. J Pharm Pharmacol 37(12): 863-868.

10. Harini Chowdary Vadlamudi, Sevukarajan M (2012) Niosomal drug delivery system- A Review. Indo Amer J Pharm Res 2(9): 1-15.

11. Naresh RA, Chandrashekar G, Pillai GK, Udupa N (1994) Anti-inflammatory activity of niosomes encapsulated diclofenac sodium with tween-85 in Arthitic rats. J Pharmacol 26(1): 46-48.

12. Mayer LD, Bally MB, Hope MJ, Cullis PR (1986) Vesicles of variable sizes produced by a rapid extrusion procedure. Biochem Biophys Acta 858(1): 161-168.

13. Chauhan S, Luorence MJ (1989) The preparation of polyoxyethylene containing Non-ionic surfactant vesicles. J Pharm Pharmacol 41(6): 1-6.

14. Blazek WAI, Rhodes DG (2001) SEM Imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharm Res 18(5): 656-661.

15. Gayatri Devi S, Venkatesh P and Udupa N (2000) Niosomal sumatriptan succinate for nasal administration. Int J Pharm Sci 62(6): 479-481.

16. Kumar A, Lunawat AK, Kumar A, Sharma T, Islam MM, et al. (2024) Recent Trends in Nanocarrier-Based Drug

Delivery System for Prostate Cancer. AAPS PharmSciTech 25(3): 55.

17. Weissman G, Bloomgarden D, Kaplan R, Cohen C (1975) A general method for the introduction of enzymes, using immunoglobulin - coated liposomes, into lysomes of deficient cells. Proc Natl Acad Sci 72(1): 88-92.

18. Shatalebi MA, Mostafavi SA, Moghaddas A (2010) Niosome as a drug carrier for topical delivery of N-acetyl glucosamine. Res Pharm Sci 5(2): 107-117.

19. Schreier H, Bouwstra J (1994) Liposomes and niosomes as topical drug carriers: dermal and transdermal drug delivery. J Contr Rel 30(1): 1-15.

20. Arunothayanun P, Bernard MS, Craig DQ, Uchegbu IF, Florence AT (2000) The effect of processing variables on the physical characteristics of non-ionic surfactant vesicles (niosomes) formed from a hexadecyl diglycerol ether. Int J Pharm 201(1): 7-14.

21. Rogerson A, Cummings J, Florence AT (1987) Adriamycin-loaded niosomes: drug entrapment, stability, and release. J Microencapsul 4(4): 321-328.

22. Maheshwari K, Wasankar S (2013) Niosomes: a novel drug delivery system. Asian J Pharm Res 3(1):16-20.

23. Kaur H, Dhiman S, Arora S (2012) Niosomes: A novel drug delivery system. Int J Pharm Sci Rev Res 15(1): 113-120.

24. Cai W, Chen X, Pan Q, Zhang S, Tan L, et al. (2017) Antitumor activity of yulangsan polysacchrides in mice bearing S180 sarcoma tumors. Mol Clin Oncol 7(4): 716-720.

25. Navya M (2014) Niosomes As novel vesicular drug delivery system- A review. Asian J Res Bio Pharm Sci 2: 62-68.

26. Sharma S (2009) Span-60 Niosomal Oral Suspension of Fluconazole: Formulation and in vitro evaluation. Asian J Pharm Res Heal 1: 142-156.

27. Gandhi A, Sen S, Paul A (2012) Current Trends in Niosomes as vesicular drug delivery system. Asia J Pharm Life Sci 2: 339-353.

28. Kaur D, Kumar S (2018) Niosomes: Present scenario and future aspects. J Drug Deliv Therapeutics 8: 35-43.