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Review Article

Niosomes: A Promising Nanocarrier System For Drug Delivery

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ABSTRACT

In 1909, Paul Ehrlich introduced the concept of a medicine delivery system and initiated the development of targeted delivery. Niosomes, consisting of a nonionic surfactant and cholesterol, range in size from 10 nm to 100 nm. Niosomes offer numerous benefits compared to traditional drug delivery methods. Different techniques such as ether injection, thin film hydration, reverse phase evaporation, and sonication are utilized in the preparation of niosomes. Additionally, the applications of niosome-based formulations are explored in comparison to conventional applications. Niosomes are vesicles made up of non-ionic surfactants and cholesterol, used to carry amphiphilic and lipophilic drugs. These vesicles act as delivery systems by encapsulating the medication. The use of targeted drug-delivery systems allows pharmaceutical compounds to be directed specifically to affected areas, improving the effectiveness of treatment Niosomes, featuring a dual-layer structure made from non-ionic surfactants, have the ability to increase the presence of a drug in a specific location over a specific timeframe. Drug targeting is the process through which drugs are distributed in the body so they can interact with specific tissues at a cellular or subcellular level to produce the desired therapeutic effect without causing unwanted effects in other areas. Modern drug delivery systems, like niosomes, can help achieve this targeted delivery. Niosomes are vesicles made up of non-ionic surfactants that, similar to liposomes, have a double-layered structure. These vesicles can trap both water-soluble and fat-soluble drugs within their lipid-based membranes. Niosomes are being extensively researched as a cost-effective alternative to liposomes of non-biological origin, or as carrier systems that closely resemble liposomes in the body. They have unique properties that can be harnessed to achieve specific drug delivery and release patterns.

INTRODUCTION

In the year 1909 the researcher name Paul Ehrlich started the work of establishment of targeted delivery when he thought that a Drug Delivery mechanism that would target directly to infective cells. We will now study what is drug targeting. The drug targeting can be elobrated as the ability to direct a therapeutic agent to a desired specific site to show the action on targeted tissue.[3] A niosome is a type of liposome constructed from a

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nonionic surfactant, with cholesterol typically added as an excipient to facilitate niosome formation.Different excipients can also be utilized in the process. Niosomes have better penetration capabilities compared to previous emulsion formulations. Although structurally similar to liposomes with a bilayer, niosomes are more stable due to their composition, giving them several advantages over liposomes.Niosomes are typically very small, falling within the nanometer range of 10 nm to 100 nm in size.A typical niosome vesicle is composed of a nonionic surfactant like Span 60 for vesicle formation, cholesterol for stability, and a small amount of anionic surfactant like dicetyl phosphate to further stabilize the structure.[4] Niosomes are man-made tiny structures that contain a water center surrounded by a double layer made of cholesterol and nonionic surfactants, forming through the self-assembly of hydrated nonionic surfactant molecules. Niosomes, a new drug delivery approach, encapsulate medications in tiny vesicles comprised of non-ionic surfactants. This innovative method improves bioavailability, addresses drug insolubility, instability, and rapid degradation, thereby lowering therapy costs. The niosomes are extremely small, measuring in the nanometer range. [5]

ADVANTAGES [6,7,8]

1. Using a smaller dose can still achieve the desired effect effectively.
2. The drug is released slowly and in a controlled way.
3. Increases the absorption of the drug through the skin.[6]
4. They can safeguard the active ingredient from being broken down in the body.
5. The drug is shielded from enzyme breakdown.[7]
6. Enhances the stability of the encapsulated drug.
7. They can improve the absorption of drugs through the skin.[8]

DISADVANTAGES [9,10]

1. Fusion.
2. Aggregation.
3. Leaching.
4. Hydrolysis.[9]
5. Time consuming.
6. Physical instability.
7. High production cost.
8. Inefficient drug loading.[10]

STRUCTURE OF NIOSOME [11

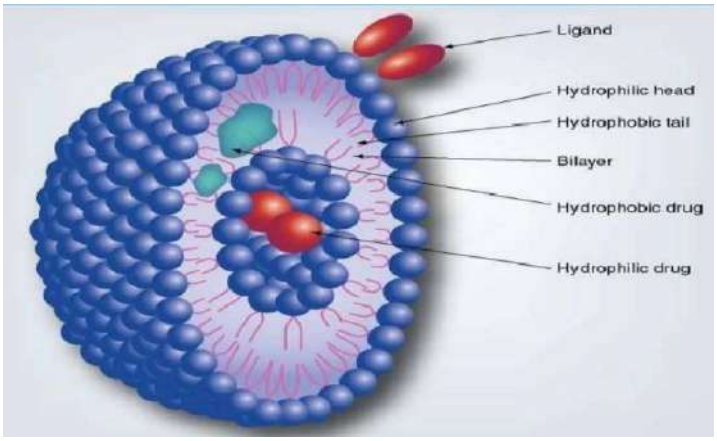

Fig no 1 Structure of Niosome

A new drug delivery method involves having the drug enclosed within a small vesicle made of a dual layer of non-ionic surface active agents, which are very tiny and microscopic. This system is similar to liposomes but has various benefits. The key components are non-ionic surfactant, cholesterol, and a molecule that induces charges.[11]

Composition of Niosome [12]

Two components use in niosome preparation are

1. Cholesterol
2. Non-ionic surfactants

1. Cholesterol :-

Cholesterol, a type of steroid derivative, is essential in giving niosomes their necessary rigidity and shape.

2. Non- ionic surfactant :-

Due to their greater stability, biocompatibility, and lower toxicity as compared to anionic and cationic surfactants, nonionic surfactants are the airface- active agems employed in the synthesis of niosomes.

Ethers:

Brij, Lauryl glucoside, Decyl glucoside, Nanoxynol

Block polymers:

Poloxamers.

Esters:

Glyceryl laurate, Spans, Polysorbate.

Fatty alcohol: \

Stearyl alcohol, Cetyl alcohol, Oleyl alcohol.[12]

Type of Niosome [13]

The various types of niosomes are as:

1. Multi lamellar vesicles (MLV),size=>0.05 μm
2. Large unilamellar vesicles (LUV),size=>0.10 μm
3. Small unilamellar vesicles (SUV).size=0.025-0.05 μm.[13]

Preparation of Niosome [14-20]

Common stages of all Method of Preparation of Niosomes

Cholesterol + Non ionic surfactant

↓ Dissolve in organic solvent

Solution in organic solvent

↓ Drying

Thin film

↓ Dispersion (Hydration)

Niosome suspension.

1. Sonication :-

Mixture of drug solution in the buffer, surfactant and cholesterol

↓

Sonicated with a titanium probe sonicator at 60°C for 3 minutes to yield niosomes.[14]

2.Hand Shaking Method :-

The mixing ingredients surfactant and cholesterol and charge inducer

↓

Dissolves in a volatile organic solvent (chloroform, diethyl ether or methanol) in a round bottom flask

↓

By using a rotary evaporator organic solvent is evaporated at room temperature 20°C

↓

Forming a thin layer of solid mixture

↓

The dry surfactant film can be re-hydrated with an aqueous phase at 0-60°C with gentle agitation

↓

Formation of niosomes [15]

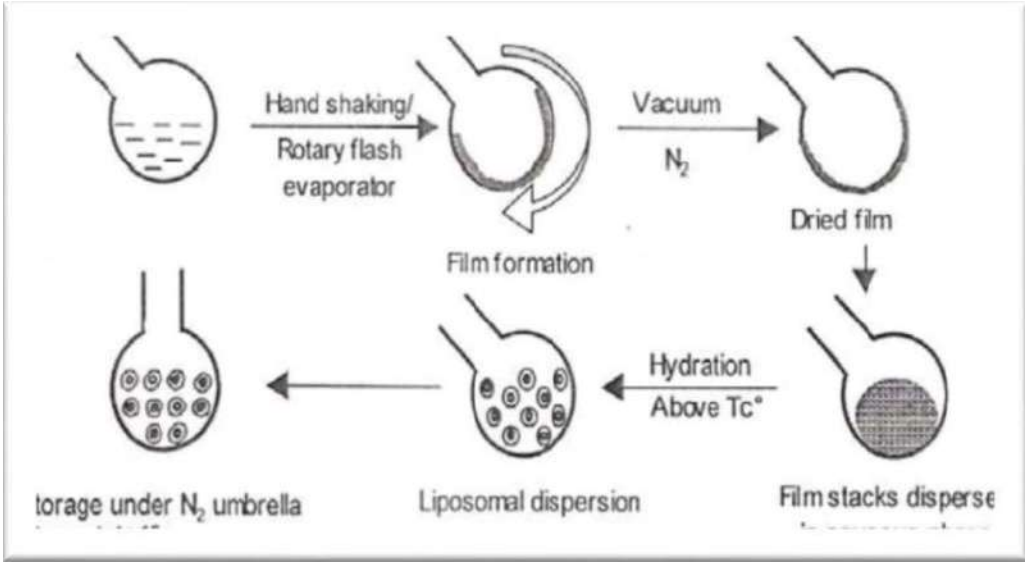

Fig no 3 Hand Shaking Method

3. Reverse Phase Evaporation Technique :-

Drug in aqueous phase

↓

Surfactant: cholesterol (1:1) in ether or chloroform

↓

Sonicate (4-5°C)

↓

+ Phosphate buffered saline

↓

Sonicate (4-5°C)

↓

Remove ether or chloroform

↓

Suspension

↓

+ Phosphate buffered saline

↓

Heat (60°C, 10 minutes)

↓

Niosomes [16]

4. Micro fluidization:-

Two ultra high-speed jets inside interaction chamber

↓

Impingement of thin layer of liquid in micro channels

↓

High speed impingement & the energy involved

↓

Niosomes [17]

5. The Bubble Method :-

The bubbling unit consists of a round-bottomed flask with three necks, placed in a water bath to regulate temperature.

↓

The first neck holds a water-cooled reflux, the second neck has a thermometer, and the third neck is used for nitrogen supply.

↓

Cholesterol and surfactant are mixed in a buffer at pH 7.4 and heated to 70°C.

↓

The mixture is then homogenized for 15 seconds with a high shear homogenizer

↓

Bubbled at 70°C using nitrogen gas.[18]

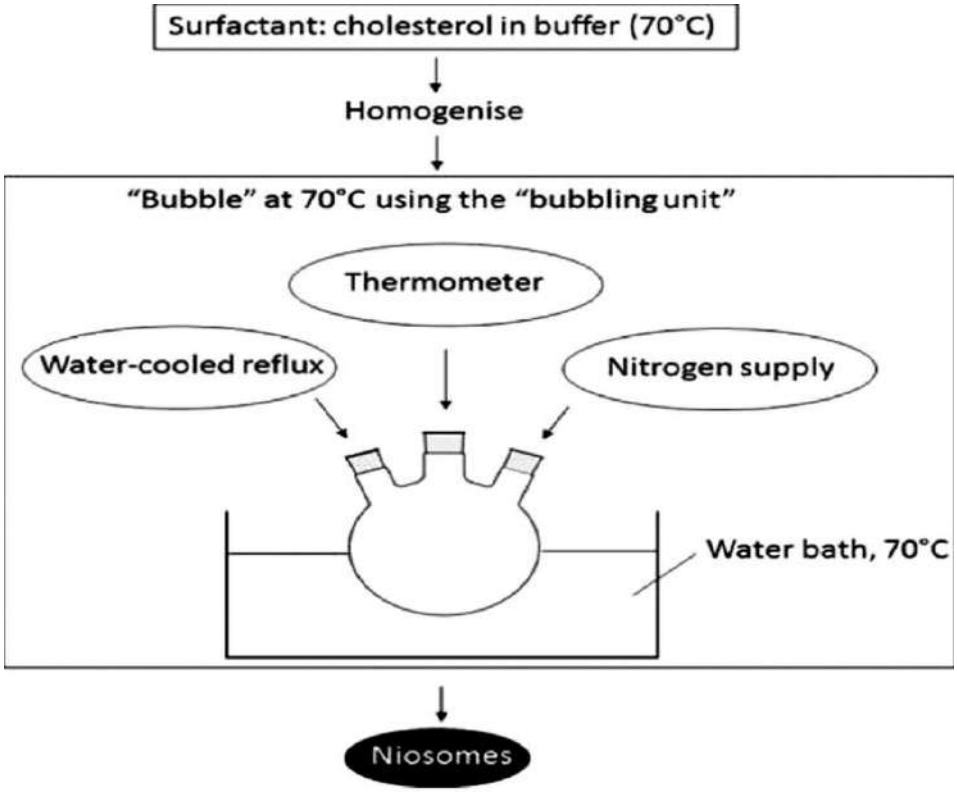

Fig no 4 Bubble Method

6. Ether Injection :-

An ethanol solution of surfactant is injected rapidly through a fine needle

↓

Into excess of saline or other aqueous medium

↓

Vaporization of ethanol

↓

Formation of vesicle.[19]

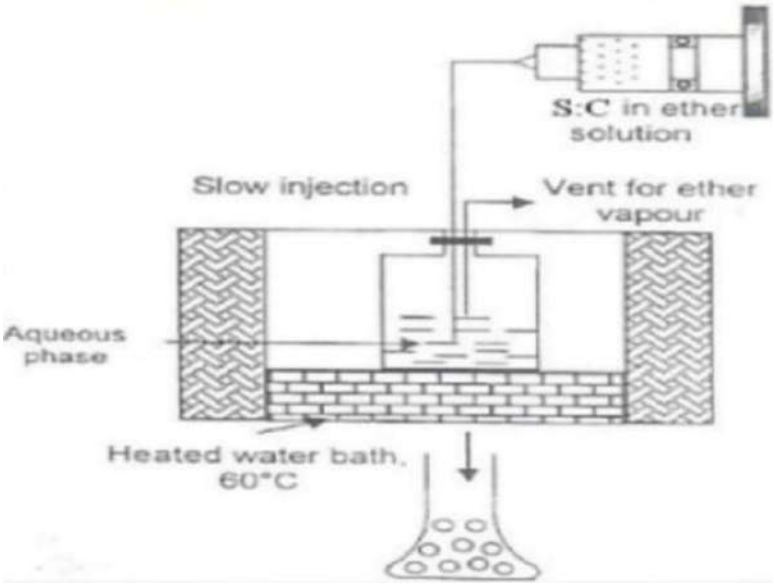

Fig. no 5 Ether Injection

7. Trans Membrane pH Gradient Drug Uptake Process

Surfactant: cholesterol in chloroform

↓

Evaporate chloroform

↓

Thin film

↓

+ Citric acid (300 mM, pH 4.0)

↓

Free and thaw (3 times)

↓

Sonicate

↓

+ Drug in aqueous phase

↓

Vortex

↓

+ Disodium phosphate (1M)

↓

Heat (60°C, 10 minutes)

↓

Niosomes. [20]

Factors Affecting Niosomes Formulation [21-26]

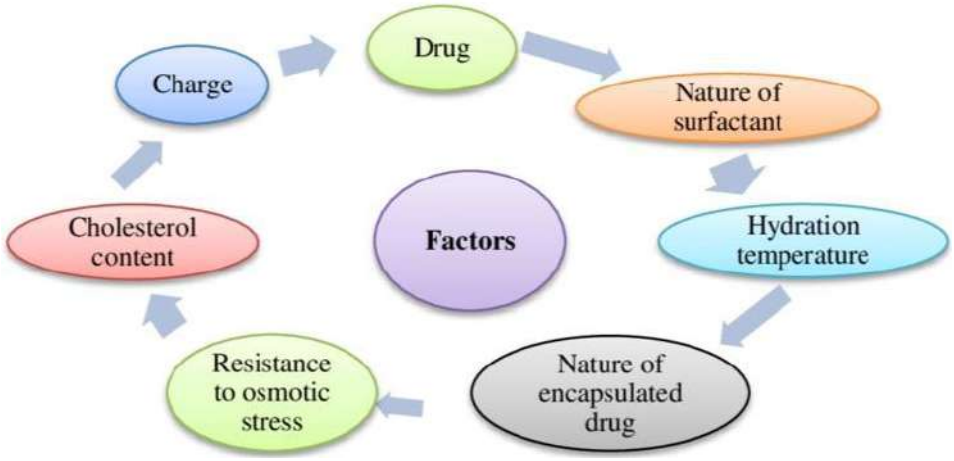

Fig. 6 Factors Affecting Niosomes Formulation

1. Drug :-

The entrapment of drugs in niosomes affects the charge and rigidity of their bilayers, disrupting the balance between hydrophilicity and lipophilicity of the drugs and impacting the degree of entrapment. [21]

2. Natura of Surfactants :-

The charge and the rigidity of the niosomal bilayer are greatly influenced by physical chemical properties of the encapsulated drug.The HLB of drug influences the degree of entrapment.[22]

3. Hydration Temperature :-

The temperature at which niosomes are hydrated plays a significant role in determining their size and shape, with the hydration temperature needing to be higher than the gel-liquid phase transition temperature.[23]

4. Resistance to Osmotic Stress:-

Adding a hypertonic solution makes vesicles smaller. In a hypotonic solution, the release of contents from vesicles is slowed initially due to inhibition, but then speeds up because the vesicle structure loosens under osmotic stress.[24]

5. Cholesterol Content :-

The entrapment efficiency and hydrodynamic diameter of niosornes is increased by the help of cholesterol. It enables membrane stabalizing activity and decrease the leakiness of membrane.[25]

6. Charge :-

Presences of charge leads to an increase in inter lamellar distance between successive bilayers in multi lamellar vesicle structure and greater overall entrapped volume.[26]

Characterizations Of Niosomes [27-33]

- **Size :-**

Shape of niosomal vesicles is presumed to be spherical and their mean diameter can be adamant by using laser light scattering method. As well, diameter of these vesicles can be adamant by using electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy, optical microscopy and freeze fracture electron microscopy .[27]

- **Osmotic shock :-**

If the size of the vesicles changes it can be determined by the osmotic studies. The formulation of niosomes are incubated with the hypotonic. isotonic, hypertonic solution for 3 hours. After the time interval we can see the changes in the size of the vesicles in the formulation are viewed under optical microscopy.[28]

- **Vesicle Charge :-**

The vesicle surface charge can play an important role in the behavior of niosomes in vivo and in vitro. Charged niosomes are more stable against aggregation and fusion then unchanged vesicles.[29]

- **Stability Studies**

To determine the stability of the niosomes, the optimized batch was placed in airtight sealed vials at varying temperatures. The surface properties and the amount of drugs preserved in the niosomes and those obtained from proniosomes were chosen as criteria for assessing stability.[30]

- **Bilayer Rigidity and Homogeneity :-**

The biodistribution and biodegradation of niosomes are influenced by rigidity of the bilayer. In homogeneity can occur both within niosome structures and between niosomes in dispersion and could be identified via.[31]

- **Entrapment Efficiency :-**

After formulating niosomal dispersion, unentrapped drug is separated by dialysis, centrifugation or gel filtration as reported above and the drug remained entrapped in niosomes is determined by complete vesicle disruption using 50% n-propanol or 0.1% Triton X-100 and analyzing the resultant solution by appropriate assay technique for the drug.

Entrapment Efficiency = (Amount entrapped/total amount)X100 [32]

Measurement Of Angle Of Repose :-

Angle of repose of dry powder niosomes Can be calculated by the help of funnel method. The powder of niosomes is poured into the funnel which was fixed at certain position so that the 13mm outlet orifice of the funnel is 5cm above a level black surface.[33]

Application :- [34,35,36]

A. Drag delivery for the eyes:-

Due to tear formation, brief residence times, and corneal epithelial impemeability, the main disadvantage of ocular dose forms including ophthalmic solutions, suspensions, and ointments is that it is challenging to obtain excellent bioavailability. [34]

B. Transdermal drug delivery :-

Niosomes structural characteristics have a permeation enhancer effect and enable direct vesicle fusion with the stratum corneum (the skin's outer layer), which improves the penetration of loaded medications when applied transdermally, [35]

C. Nasal administration :-

The medication's incorporation into niosomes improved direct transport percentage, brain bioavailability, drug targeting effectiveness, and bruin absorption via the direct nose-to-brain channel, showing improved central nervous system targeting via the direct nasal pathway .[36]

CONCLUSION

The development of niosomal drug delivery system represents a significant advancement in the pharmacy field, showcasing the progress in drug delivery technologies and nanotechnology. The structure of niosome, a relatively new drug delivery method, is two layers of nonionic surfactants. Various medications can be put in niosomes by varying the experiment's parameters and the ratio of surfactant and cholesterol used. Niosomes have been studied as an alternative to liposomes. Some advantages over liposomes, such as their relatively higher chemical stability, improved purity and relatively lower cost in comparison with liposomes. Non-ionic surfactant vesicles alter the plasma clearance kinetics, tissue distribution. Niosomes are being considered as superior drug delivery options compared to liposomes due to factors such as cost and stability. These vesicles are commonly used for delivering various types of medications, specifically in areas such as ophthalmology, oral, and parenteral administration.Scientists typically favor the use of niosomes, which are utilized to target specific tissues with medicine. Niosomes are composed of single-chain uncharged surfactant molecules. They enable the safe delivery of toxic drugs that would otherwise require higher doses.

REFERENCE

1. Kaur D, Kumar S. Niosomes: present scenario and future aspects. Journal of drug delivery and therapeutics. 2018 Sep 6;8(5):35-43.
2. Keshav J. NIOSOMES AS APOTENTIAL CARRIER SYSTEM: A REVIEW. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2015 Oct 1;5(4).
3. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes—non-ionic surfactant vesicles. Journal of pharmacy and pharmacology. 1985 Dec;37(12):863-8.
4. 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 Feb;2(1):25-31.
5. Rogerson AC, Cummings J, Willmott N, Florence AT. The distribution of doxorubicin in mice following administration in niosomes. Journal of pharmacy and pharmacology. 1988 May;40(5):337-42.
6. Singh S. Niosomes: A role in targeted drug delivery system. International Journal of Pharmaceutical Sciences and Research. 2013 Feb 1;4(2):550.
7. Vadlamudi HC, Sevukarajan M. Niosomal drug delivery system-a review. Indo American Journal of Pharmaceutical Research. 2012;2(9).

8. Muzzalupo R, Tavano L. Niosomal drug delivery for transdermal targeting: recent advances. Research and reports in transdermal drug delivery. 2015 Jul 29:23-33.
9. Hunter CA, Dolan TF, Coombs GH, Baillie AJ. Vesicular systems (niosomes and liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. Journal of pharmacy and pharmacology. 1988 Mar;40(3):161-5.
10. Usman MR, Ghuge PR, Jain BV. Niosomes: a novel trend of drug delivery. European Journal of Biomedical and Pharmaceutical Sciences. 2017;4(7):436-42.
11. Blazek–Welsh AI, Rhodes DG. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharmaceutical research. 2001 May;18:656-61.
12. Kaur D, Kumar S. Niosomes: present scenario and future aspects. Journal of drug delivery and therapeutics. 2018 Sep 6;8(5):35-43.
13. Kaur H, Dhiman S, Arora S. Niosomes: A novel drug delivery system. Int. J. Pharm. Sci. Rev. Res. 2012;15(1):113-20.
14. Sankhyan A, Pawar P. Recent Trends in Niosome as Vesicular DrugDelivery System. Journal of Applied Pharmaceutical Science. 2012 Jun 30(Issue):20-32.
15. Madhav NV, Saini A. Niosomes: a novel drug delivery system. International journal of research in pharmacy and chemistry. 2011;1(3):498-511.
16. Singh G, Dwivedi H, Saraf SK, Saraf SA. Niosomal delivery of isoniazid-development and characterization. Tropical journal of pharmaceutical research. 2011;10(2).
17. Shakya V, Bansal BK. Niosomes: a novel trend in drug delivery. International Journal of Research and Development in Pharmacy & Life Sciences. 2014 Jul 15;3(4):1036-41.
18. Lohumi A. A novel drug delivery system: niosomes review. Journal of drug delivery and therapeutics. 2012 Sep 15;2(5).
19. Rogerson AC, Cummings J, Willmott N, Florence AT. The distribution of doxorubicin in mice following administration in niosomes. Journal of pharmacy and pharmacology. 1988 May;40(5):337-42.
20. Kazi 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 Oct 1;1(4):374-80.
21. Malhotra M, Jain NK. Niosomes as drug carriers. Indian Drugs-Bombay-. 1994;31:81-.
22. Hunter CA, Dolan TF, Coombs GH, Baillie AJ. Vesicular systems (niosomes and liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. Journal of pharmacy and pharmacology. 1988 Mar;40(3):161-5.
23. Yoshida H, Lehr CM, Kok W, Junginger HE, Verhoef JC, Bouwstra JA. Niosomes for oral delivery of peptide drugs. Journal of controlled release. 1992 Jul 1;21(1-3):145-53.
24. Dwivedi C, Sahu R, Tiwari SP, Satapathy T, Roy A. Role of liposome in novel drug delivery system. Journal of drug delivery and therapeutics. 2014 Mar 14;4(2):116-29.
25. Biswal S, Murthy PN, Sahu J, Sahoo P, Amir F. Vesicles of non-ionic surfactants (niosomes) and drug delivery potential. International Journal of Pharmaceutical Sciences and Nanotechnology (IJPSN). 2008 May 31;1(1):1-8.
26. Rastogi B, Nagaich U, Jain DA. Development and characterization of non-ionic surfactant vesicles for ophthalmic drug delivery of diclofenac potassium. Journal of Drug Delivery and Therapeutics. 2014 Jun 23:1-6.

27. Hu C, Rhodes DG. Proniosomes: a novel drug carrier preparation. International journal of pharmaceutics. 1999 Aug 5;185(1):23-35.
28. Sharma D, Ali AA, Aate JR. Niosomes as novel drug delivery system. PharmaTutor. 2018 Mar 1;6(3):58-65.
29. Suma US, 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):41-8.
30. Allen TM. Liposomal drug formulations: rationale for development and what we can expect for the future. Drugs. 1998 Nov;56(5):747-56.
31. Keservani RK, Sharma AK, Ayaz M, Kesharwani RK. International Journal of Research in Controlled Release.
32. Balasubramaniam A, Anil Kumar V, Sadasivan Pillai K. Formulation and in vivo evaluation of niosome-encapsulated daunorubicin hydrochloride. Drug development and industrial pharmacy. 2002 Jan 1;28(10):1181-93.
33. Abhilash N. Preparation, evaluation and optimization of proniosomes containing zidovudine (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
34. Shakya V, Bansal BK. Niosomes: a novel trend in drug delivery. International Journal of Research and Development in Pharmacy & Life Sciences. 2014 Jul 15;3(4):1036-41.
35. Marianecci C, Di Marzio L, Rinaldi F, Celia C, Paolino D, Alhaique F, Esposito S, Carafa M. Niosomes from 80s to present: the state of the art. Advances in colloid and interface science. 2014 Mar 1;205:187-206.
36. Sita VG, Jadhav D, Vavia P. Niosomes for nose-to-brain delivery of bromocriptine: Formulation development, efficacy evaluation and toxicity profiling. Journal of Drug Delivery Science and Technology. 2020 Aug 1;58:101791.

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