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Review

NIOSOMES: CURRENT STATUS AND THEIR PROSPECTS

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Abstract:

A dermal patch that has medicinal properties is painless adhesive patch which puts on the skin surface to convey a particular dose of medicine passing through the skin and into the circulation. Non-Ionic surfactant-based vesicles, otherwise called niosomes, stand out enough to be noticed in drug fields because of their amazing conduct in typifying both hydrophilic and hydrophobic specialists. As of late, it has been found that these vesicles can work on the bioavailability of medications, and may work as another technique for conveying a few normal of remedial specialists, for example, chemical and protein drugs and gene materials with low poisonousness and wanted to focus on efficiency. Compared with liposomes, niosomes are significantly steadier during the plan interaction and storage. The required pharmacokinetic properties can be accomplished by streamlining part sort by surface modification. This original conveyance framework is likewise simple to get ready and scale up with low creation costs. In this paper, we sum up the formulation, method, and characterization of niosome and its applications in skin diseases like Acne dark spots.

Keywords: *Niosome, Cholesterol, Hydrophilic and Lipophilic drugs, Surfactant, Targeted delivery, Bioavailability Improvement, Factors, Applications*

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INTRODUCTION

NIOSOMES, which are formed with un ionized amphiphiles in specific fluid arrangements through self-gather innovation, were first utilized in the improvement of beauty care products. Non-ionic surfactants are typically unilamellar or multi-vesicles with bounded bilayers that house the active agents in hydrophobic shells on the outer layer and hydrophilic cavities on the inside. Lately, with the advancement of nanoscales in the field of pharmaceutics, an ever-increasing number of studies have zeroed in on non-ionic surfactants as nanoparticle carriers for drug conveyance. Unionized surfactants can be an option in contrast to liposomes and polymeric vesicles because of their capacity to typify various types of medications to build their dependability and adequacy. Dissimilar to other nanoparticles, primarily, liposomes, polymeric vesicles, and niosomes have numerous similitudes, and they can be there in every way stacked with both aquaphilic and aquaphobic medications. Along these lines, they could co-convey both hydrophilic and hydrophobic medications in a single vesicle. Non-ionic surfactants, which form niosomes, are more chemically and physically stable than lipids, making them much more stable than lipids.

The Construction and Parts of Niosomes

Understanding the structure of niosomes is critical on account of they may determine which units can made non ionic surfactants and the drug containing process for delivery. Like the lipomeric vesicles, niosomes are un-ionized surfactant vesicles contains a double layer structure (Figure 1). Aquaphilic heads are inverse to watery arrangements and hydrophobic heads are inverse to organic arrangements. Double layer vesicles can be isolated into unilamellar and multilamellar vesicles. Numerous lamellar vesicles are concentric circles built with no less than 2 double layer vesicles or a big vesicle encapsulating at least one little vesicles (Figure 1b,c). Thusly, the molecule size of lamellars vesicles is typically bigger than that of single lamellar vesicles. Concerning (C18-

sorbitan monoester)- cholesterol niosomes, X-beam dissipating information showed a bilayer separating of 15 nm and wreath of 3.3-3.4 nm. Niosomes typically fall into the colloidal (sub-micron) range. The molecule sizes of little single lamellar vesicles (SUV) were around 10-100 nm, enormous single lamellar vesicles (LUV) 100-3000 nm, and (MLV) more prominent than 5 µm, although a couple "goliath" (> 15 um vesicles.

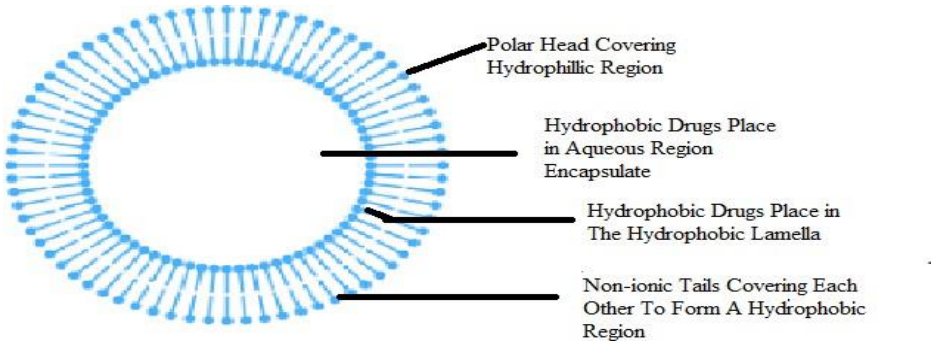


Figure 1: Structure of Niosome

COMPOSITION OF NIOSOMES-

Two components use in niosome preparation are

- Cholesterol
- Non-ionic surfactants

A. Cholesterol is a steroid derivative, which is used to provide rigidity and proper shape, conformation to niosome form.

B. Non-ionic Surfactants are generally used for thepreparation of niosomes.

Examples:

a. Tweens (20, 40, 60, 80)

b. Spans (Span 60, 40, 20, 85, 80)

c. Brijs (Brij 30, 35, 52, 58, 72, 76)

Two parts use in Non- ionic surfactant arrangement are: Cholesterol, Niosome.

Cholesterol is a steroid subordinate used to give inflexibility and legitimate shape,conformity.
Typically, non-ionic surfactants are used in the formulation. Examples: Tweens (20, 40, 60, 80), Ranges (Length 60, 40, 20, 80).

DIFFERENT TYPES OF NON-IONIC SURFACTANTS

Table 1: Different Types of Non-Ionic Surfactants

Type of Non-Ionic Surfactant	Examples
Fatty alcohols	Stearyl alcohol, oleyl alcohol, cetostearylalcohol, cetyl alcohol
Ether	Lauryl glycoside, Decyl glycosides, brije, Octyl glycosides, Nonoxynol-9
Ester	Span
Block copolymer	Poloxamer

Non ionized surfactants: Non ionic surfactant;s are a fundamental part of niosomes. To shape niosomes, different sorts and their mixes are utilized to capture different prescriptions. Non ionized surfactants are normally amphiphilic, recyclable, compatible, and non-immunogenic. The production, centralization of added substances, lamellarity, size and surface charge of vesicles decide the components of formed niosomes. Non-ionized surfactants like range (60, 40, 20, 85, and 80) and Tween (20, 40, 60, and 80) are utilized in the arrangement of niosomes

Cholesterol: It is a pivotal added substance in the plan of niosomes. Not only does cholesterol play a role in the properties of niosomes, but it is also important for theirformation. It impacts the film's porousness, unbending nature, and ensnarement proficiency, simplicity of again hydration of freeze-dried niosomes, security, and capacity period. Assuming itis joined with less HLB surface active agents, it increments vesicles dependability,

and if the HLB esteem is more noteworthy than 6 , it supports the making of double layer vesicles. The expansion of cholesterol works on the consistency and, subsequently, the unbending nature ofthe formulation20.

Charged particle: Niosomes have a very few charged particles added to them to increment strength by giving electric shock to forestall impacts. Phosphotidic and Diacetyl phosphate corrosive are both adversely charged compounds. Also, in niosomes arrangements, stearyl pyridinium and stearyl amine chloride are notable compounds charged 21.

Aqueous medium: Quite possibly the main part in the detailing of niosomes is the aqueous medium. The shock absorber (phosphate) is regularly utilized as a aqueous medium. Bethat as it may, the pH of the not set in stone by the dissolvability of the epitomized medication

TYPES OF NIOSOMES

The various types of niosomes are as:

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

Advantages

Niosomes has a number of benefits. The significant benefits of Niosomes are:

- Niosomes are water based vehicles, consequently they offer high persistent consistence overoily vehicles
- They increment solidness of medication ensnared and makes them stable.
- No extraordinary circumstances are expected for stockpiling and treatment of surface activeagents.
- They improve the bio available drugs that are difficult to absorb and the drugs' ability topenetrate the skin.
- Niosomes safeguard drug from organic climate, postpone the medication leeway and work on the remedial execution.
- Niosomes can be utilized for site focusing through oral, parenteral, and effective courses.

DISADVANTAGES

Other than a few benefits, there are a few weaknesses of Niosomes.

- Timeframe of realistic use of Niosomes is restricted in view of spillage of medication fromthe vesicles.
- Total and combination of vesicles can happen.
- There might be little physical and substance flimsiness issues.
- In fluid suspensions, the medication might go through hydrolysis which influences thesolidness.
- The process of making niosomes takes a long time.

FORMULATION AND EVALUATION OF NIOSOMES

Handshaking Method (Thin film hydration technique)

A second round bottom flask is used to dissolve the blend of different vesicles that form components like surfactants and cholesterol using a vaporascent organic fluid. The organic solvent is collect by means of a rotary evaporator at temperature (20-30 °C), leaving behind alayer of concrete mixture on the rim of flask. To delicate unsettling, its dried surface-active agent film may be hydrated again at 0-60 ◦C to the fluid stage. Standard multilamellar niosomes structure this strategy.

Ether injection strategy

This approach offers the probability of assembling niosomes by dynamically presenting a compound of the surfactant lowered in ether at 60 ◦ C in warm water. A needle of 14-guage isworn to inject this ether-surface active agent blend into an aqua solution. Ether vaporization adds to single-layered vesicles being framed. The vesicle's size ranges between 49-50 to 1000nm, upheld the condition.

Trans-membrane pH gradient process

Through ether, surface active agent and cholesterol are consumed. Under lower pressure, the dissolvable will then disintegrate and lay out a slim layer on the lower part of round base

Flask. An impact blending corrosive (pH 4.0) saturates the film. The MLV is frozen and warmed multiple times

then sonicated. Aq. Sol. of 9-10 mg/ml of medications is add to the present niosome deferment and gulfed there to. The example pH would then be multiplied to7.0-7.2 including 1 M of disodium phosphate

Sonication

A standard method of vesicle improvement is by arrangement sonication as depicted in Link. During this strategy, a substance arrangement aliquot inside the cushion is presented during a 10-ml glass vial to the surfactant/choleste combination. To obtain niosomes, the response is sonicized for three minutes at 600C using only a sonicator and a titanium sample.

Reverse (phase) evaporation method

For this strategy, the surface active agent and cholesterol are broken up in the combination of ether. A watery stage contains drug is mixed with this and the subsequent more than one stage are sonicated at the temperature of 4-5°C. A reasonable straightforward gel is framed. After the hydration medium has been added, it is then sonicated once more. The above natural stage is eliminated at 40°C. Niosomes are produced by diluting the result of niosome cessation with phosphate buffer saline and heating it for ten minutes at 60°C.

Micro- fluidization strategy

This strategy, the double fluidized streams (one contains drug and other surface-active agent) connect at ultrahigh speed, in exactly characterized miniature passages inside the cooperation block so that the power given to the framework stays in the place of niosomes arrangement. It is called lowered fly standard. Niosomes formation becomes more consistent, smaller,and reproducible as a result.

Expulsion strategy

In the method, the combination of ether and dicetyl phosphate is ready the dissolvable of the blend is dissipated utilizing rotating vacuity evaporator to frame a flimsy film. The film is now hydrolyzed with the medication arrangement and the subsequent deferral is gotten to expelled by the polycarbonate layer and afterward positioned in grouping up to eight entriesto get same size

EVALUATIONNIOSOME

Evaluation of Niosomes. There are a few Evaluation methods for niosomes

1. **Size, structure, and size arrangement:** Numerous methods like microscopy, photon relationship spectroscopy, electron infinitesimal investigation, SEM, TEM (transmission electron magnifying lens), light dispersing, and zeta potential can be utilized to concentrate on their anatomy and decide the size of Niosomes. The molecule size estimated by the conduction electron magnifying instrument is more modest than the powerful light dissipating (DLS) strategy as a result of the different estimation standards utilized by the two procedures
2. **Transmission Electron Microscopy (TEM):** TEM is utilized in the assurance of the form, size, and lamellarity of Niosomes. The pre- arranged suspension is blended in with 1% phosphotungstic corrosive (in required sum) and afterward a drop of this resultant was now utilized on carbon covered matrix, then, at that point, the framework was seen in the wake of depleting off the overabundance. Following complete drying, the images are taken using TEM at a suitable magnification [6].
3. **Optical Microscopy Technique:** This method is likewise utilized for the perception of the shape and size of the Niosomes. The molecule is not entirely set in stone; almost 100 niosomes are utilized for molecule size assurance. The size of the Niosomes is still up in the air by harmonizing stage micrometer and eyepiece micrometer and working out the estimations.
4. **Ensnarement proficiency:** Capture productivity can be determined by taking away how much-dumped drug from the aggregate sum of medication added. The dumped medication can be resolved utilizing strategies like filtration, thorough dialysis, centrifugation, or gel chromatography. The convergence of stacked medications can be determined by mixing niosome in half n- propanolol or 0.1-0.2% Triton X - 100 and the subsequent arrangement be tested utilizing a particular technique. The accompanying condition can be utilized to work out the % ensnarement effectiveness.

   $$\%\text{Capture Effectiveness} = \frac{\text{Amount of medication} - \text{stacked in the noisome Absolute amount of medication in the suspension}}{\text{x } 100}$$

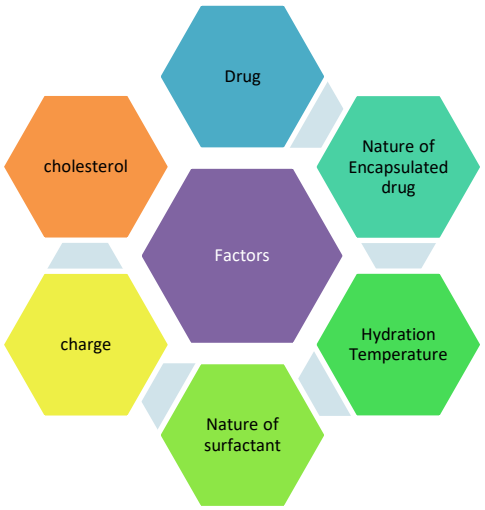
5. **Zeta Potential:** The Niosomes resist one another as of the charge they carry. This electrostatic shock forestalls total and combination and keeps them steady. It is used to decide the Niosome surface charge. The zeta sizer, mastersizer, and DLS instrument all decide the potential. The condition used to ascertain zeta potential is Henry's condition

   $$£ = \mu E \pi \eta / \Sigma$$

   Where £ = Zeta potential. μE = Electrophoretic portability η = Thickness of medium Σ = Dielectric consistent

6. **Number of lamellae:** Different methods like NMR, little point X-beam spectroscopy, electron microscope can be utilized for assurance of the amount of lamellaes. For the portrayal of the width of the double layer, little point x-beam dissipating can be utilized through the in-situ energy-scattered x- beam diffraction.
7. **Film inflexibility:** Bio conveyance and biodegradation of not entirely set in stone by the double layer's unbending nature. Degree of differentiation Calorimetry Scanning (DSC) and FTIR methods can be used to define dispersion within niosome frameworks and between Niosomes in homogeneity.
8. **Osmotic shock:** The adjustment of the vesicle size is not entirely settled by osmotic examinations when they are exposed to various constitution conditions. The formed Niosomes are brood with hypotonic, isotonic, and hypertonic answers for 3 hours optical microscopy is utilized to decide the progressions in the size of vesicles in the definitions.
9. **Strength Review:** Niosomes are regularly put away at 4±1 °C and 25±2 °C to lead to soundness tests. One can look at the dimension, form, and number of vesicles per cubic millimeter of definition when 30 days of capacity. Additionally, after 14 and 30 days, remaining drug can be measured. Light microscopes can determine the dimension of vesicles, and haemocytometers can measure the number of vesicles per cubic mm. Number of Niosomes for each cubic mm = absolute number of Niosomes x weakening component complete x 400/all-out number of little squares count
10. **In Vitro Release:** Concentrate By and large dialysis film strategy is utilized in this review. In this technique, dialysis sacks containing a modest quantity of Niosomes are united at both closures. The dialysis bag is then stored at 37 °C in a beaker containing the appropriate dissolution medium. It and mixed by an attractive stirrer. At determined periods, test arrangement is taken from the measuring utensil and supplanted with new disintegration media. The examples are dissected for how much medication is at a frequency determined in the monograph of that specific medication.
11. **Tissue Distribution/In Vivo Study:** Animal models are utilized for concentrating on tissue drug dispersion. In-vivo examinations for Niosomes rely upon the course of conveyance, a grouping of medication, impact, and home season of the medication in tissues like the lung, liver, spleen, and bone marrow. The kidney, liver, heart, spleen, and lungs of sacrificed animals is removed to study the distribution pattern. Buffer is used to wash these tissues. These tissues are then homogenized and centrifuged. The medication content is investigated from the supernatant.

Various Factors Affecting Niosome Preparation



APPLICATIONS NIOSOME

- Niosome helps in reducing acne dark spots.
- It also helps in flaking the skin layer and treat comedones (small bumps due to acne)
- To kill bacteria, reduce irritation, and unplug blocked pores.
- It helps in treating skin conditions like acne, acne scar, melasma, hyperpigmentation, wrinkle lines, and photoaging.
- Acne gels are also effective, easy to transport and use that's why they are popular among consumers.

VARIOUS ROUTE OF PURPOSE OF NIOSOME CONTAINING DRUG

Table 5: DRUG Used in Niosomal deliverance

Route of Administration	Examples of Drug
Transdermal Route	Piroxicam, Estradiol, Nimesulide
Nasal Route	Sumatriptan
Ocular Route	Cyclopentol
Intravenous Route	Doxorubicin, Rifampicin, insulin

CONCLUSION

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, metabolism and cellular interaction of the drug.

FUTURE PROSPECTS

Niosomes symbolize a capable drug release molecule. There is a bunch of possibility to encapsulate toxic anti-infective drug, anti-inflammatory drug, anti-cancer drug, anti-aids drug, etc. in niosome to use them as capable drug carrier to achieve better targeting and bioavailability properties and for skip the toxic and side-effects of the drugs. The ionized drug carrier is comparatively toxic and incompatible while niosome containing carrier is safer. Managing and storage space of niosomes need no out of the ordinary conditions.

Reference-

1. Umbarkar MG. Niosome as a novel Pharmaceutical Drug Delivery: A brief review highlighting formulation, types, composition and application. Indian Journal of Pharmaceutical Education and Research. 2021 Mar 19;55(1s). doi:10.5530/ijper.55.1s.34
2. G DB, P VL. Recent advances of non-ionic surfactant-based nano-vesicles (NIOSOMES and proniosomes): A brief review of these in enhancing transdermal delivery of drug. Future Journal of Pharmaceutical Sciences. 2020 Nov 25;6(1). doi:10.1186/s43094-020-00117-y
3. Ahmad S, Teotia D, Kumar K. Niosomes a promising carrier for Drug Delivery. International Journal of Research and Development in Pharmacy & Life Sciences. 2018 Aug;7(4):3015–21. doi:10.21276/ijrdpl.2278-0238.2018.7(4).3015-3021
4. P. SS. Formulation and evaluation of tetracycline NIOSOMAL topical gel drug delivery system. World Journal of Pharmacy and Pharmaceutical Sciences. 2017 Aug 1;2644–57. doi:10.20959/wjpps20178-9963
5. Ashwini K. Shinde, Bilal Sufi, Rajlaxmi S. Deolekar, Vedika D. Bihade, Achal A. Kale. Review on NIOSOME-a future of targeted drug delivery system. International Journal of Advanced Research in Science, Communication and Technology. 2023 Dec 21;716–24. doi:10.48175/ijarsct-14298
6. Sharma D, Ali AA, Aate JR. NIOSOMES as Novel Drug Delivery System: Review article. Pharmatutor. 2018 Mar 1;6(3):58. doi:10.29161/pt.v6.i3.2018.58
7. Sudarshan Upadhye S, Rafik. IN. Proniosomes: A novel vesicular drug delivery system. American Journal of PharmTech Research. 2020 Apr 7;10(2):260–73. doi:10.46624/ajptr.2020.v10.i2.019
8. Sahu RK, Yadav R, Prasad P, Roy A, Chandrakar S. Adverse drug reactions monitoring: Prospects and impending challenges for Pharmacovigilance. SpringerPlus. 2014 Nov 26;3(1). doi:10.1186/2193-1801-3-695
9. Ag Seleci D, Seleci M, Walter J-G, Stahl F, Scheper T. NIOSOMES as nanoparticular drug carriers: Fundamentals and recent applications. Journal of

Nanomaterials. 2016;2016:1–13. doi:10.1155/2016/7372306
10. Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences. 2016 Dec;2(4). doi:10.26479/2016.0204.08
11. Nasef A. Self - emulsifying drug delivery system: A novel approach for oral delivery of poorly water soluble drugs. Records of Pharmaceutical and Biomedical Sciences. 2021 Jan 1;5(1):52–8. doi:10.21608/rpbs.2021.52929.1086
12. Sharma D, Ali AA, Aate JR. NIOSOMES as Novel Drug Delivery System: Review article. Pharmatutor. 2018 Mar 1;6(3):58. doi:10.29161/pt.v6.i3.2018.58
13. Sudheer P, Kaushik K. Review on NIOSOMES - A Novel Approach for drug targeting. Journal of Pharmaceutical Research. 2015 Mar 1;14(1):20. doi:10.18579/jpcrkc/2015/14/1/78376
14. Ahmed A, Karki N, Charde R, Charde M, Gandhare B. Transdermal Drug Delivery Systems: An overview. International Journal of Biomedical and Advance Research. 2011 Oct 9;2(1). doi:10.7439/ijbar.v2i1.21
15. Priya ChS, Mounika K, Srinivas N, Balusu H, Reddy SR. Formulation design and evaluation of Aceclofenac Transdermal Patches. Annals of Phytomedicine An International Journal. 2023 Dec;12(2). doi:10.54085/ap.2023.12.2.116
16. 1. Drais HK. Transdermal delivery of Lornoxicam Hybrid Nanogel: Design, preparation, characterization, and in-vitro diffusion evaluation. Iraqi Journal of Industrial Research. 2023 Oct 20;10(2):98–104. doi:10.53523/ijoirvol10i2id289
17. . RK G. Transdermal drug delivery system: An emphasis on transdermal patches. Pharmaceutical Drug Regulatory Affairs Journal. 2023 Jun 29;6(1):1–5. doi:10.23880/pdraj-16000147
18. Yadav P, Solanki D, Soni A, Jaiswal R. "formulation and evaluation of Transdermal Patch of amlodipin besylate." International Journal of Pharma Professional's Research (IJPPR). 2023 Feb 3;14(1):33–8. doi:10.48165/ijppronline.2023.14115
19. M. N Jalajakshi, Chandrakala V, Srinivasan S. Preparation and evaluation of transdermal patches of an anti-inflammatory drug. International Journal of Pharmaceutical Sciences Review and Research. 2023 Oct;82(2). doi:10.47583/ijpsrr.2023.v82i02.019
20. Kharat R, Bathe RS. A comprehensive review on: Transdermal Drug Delivery Systems. International Journal of Biomedical and Advance Research. 2016 Apr 30;7(4):147. doi:10.7439/ijbar.v7i4.3131
21. Sharma R, Dua JS, Parsad D. An overview on NIOSOMES: Novel pharmaceutical drug delivery system. Journal of Drug Delivery and Therapeutics. 2022 Apr 15;12(2-S):171–7. doi:10.22270/jddt.v12i2-s.5264
22. Ge X, Wei M, He S, Yuan W-E. Advances of non-ionic surfactant vesicles (NIOSOMES) and their application in drug delivery. Pharmaceutics. 2019 Jan 29;11(2):55. doi:10.3390/pharmaceutics11020055
23. KASHYAP V, RANI A. Formulation and evaluation of NIOSOMAL gel of azelaic acid for Antiacne Activity. International Journal of Applied Pharmaceutics. 2023 Sept 7;237–44. doi:10.22159/ijap.2023v15i5.48593