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A Review on Niosomes Noval Drug Delivery

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ABSTRACT: Niosomes are utilized for drug delivery to specific sites in order to achieve desired therapeutic effects. They provide an alternative to liposomes and are composed of non ionic surfactant-based vesicles that include non-ionic surfactant and cholesterol as excipient which can potentially enhance drug absorption. Structurally, niosomes are similar to liposome as they both consist of a lipid bilayer. However niosome are more stable during the formulation process and storage than liposomes. They can trap hydrophilic and lipophilic drugs, either in an aqueous layer composed of lipid material.The Pharmacokinetic and Pharmacodynamics profile of Niosomal drug delivery system vary for various entrapped drugs. Drugs that are successful in the mitigation or treatment of CNS disorders should cross the BBB to reach the brain, as BBB seems to be an obstacle for a large number of drugs, including CNS active drugs. This article compiles recent techniques for the preparation and characterization of niosomes, the effect of formulation variables on its physicochemical properties and discussed about its effective applications in drug delivery.

KEYWORDS: Niosome, Non-ionic surfactant, Drug delivery-targeted , Preparation

I. INTRODUCTION

Niosomes are microscopic non-ionic surfactant vesicles attained by the hydration of synthetic non-ionic surfactant with or without inclusion of cholesterol.1 They are akin to liposomes. Both Niosomes liposomes act as active carriers of both amphiphilic and lipophilic drugs. Difference in the niosomal and liposomal system is that niosomal bilayer is formed by non-ionic surfactant where as liposomal bilayer made up of phospholipids. Niosomes are formed by the self assembly of non-ionic surfactants in aqueous media as spherical, unilamellar, bilayered, multilamellar system and polyhedral structures depending on the method used to prepare and the inverse structure in case of non-aqueous solvent. The orientation of the surfactant in niosome in hydrophilic ends exposed outwards while hydrophobic ends face each other forming bilayer of the surfactant. The size of the niosomes ranges between 10 to 1000nm. Addition of cholesterol and a small quantity of anionic surfactant for instance dicetyl phosphate stabilizes the niosomal vesicles formed by the non-ionic surfactant.2 Niosomes are suggested to be better than liposomes because of the higher chemical stability of surfactants than phospholipids which are easily hydrolyzed due to the ester bond and cost effective. Niosomes illustrate a promising drug delivery. Various methods of administration of niosomal formulation include intramuscular, intravenous, peroral, and transdermal.

STRUCTURE AND COMPOSITION OF NIOSOME

The selection of surfactant for preparation of niosome mainly depend on the HLB value of surfactant. Vesicle forming ability of surfactant are completely based on hydrophilic-lipophilic balance of surfactant. For proper and compatible vesicle formation of niosome the HLB value of surfactant must be in between 4 to 8.13 .The niosome are circular bilayer structure of non-ionic surfactant, surfactant which must having ability to form micelle. When surfactant concentration are goes above the critical micelle concentration (CMC) then it forms micelles in formation, but non-ionic surfactant has ability to form circular bilayer structure instead of micelles. The cholesterol also added in formulation to give rigidity to vesicle and ionic surfactant reduces aggregation.1 The structure of niosome may be uni-lamellar or multi-lamellar depending on which method used for preparation of niosome. There are all types of drug can be incorporate in structure of niosome such as hydrophilic, lipophilic and amphiphilic drugs. The location of all types of drug in niosome structure are show in Figure 1

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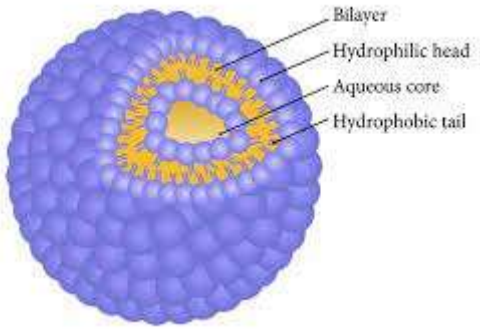
STRUCTURE OF NIOSOME FIG:1



Advantages of Niosomes:

1. The vesicle suspension being water-based vehicle offers high patient compliance when compared to oily dosage forms.
2. Drug molecules of wide range of solubilities can be accommodated in the niosomes provided by the infrastructure consisting of hydrophilic, lipophilic and amphiphilic moieties.
3. Vesicle characteristics can be controlled by altering the composition of vesicle, size lamellarity, surface charge, tapped volume and concentration.
4. They can release the drug in sustained/controlled manner.
5. Storage and handling of surfactants oblige no special conditions like low temperature and inert atmosphere.
6. They can act as a depot formulation, thus allowing the drug release in a controlled manner.
7. They enhance the oral bioavailability of poorly soluble drugs.
8. They possess stable structure even in emulsion form.
9. Surfactants are biodegradable, biocompatible, non-toxic and non-immunogenic.
10. They are economical for large scale production.
11. They can protect the drug from enzyme metabolism.
12. They are not only osmotically stable and active but also improve the stability of entrapped drug.
13. They can enhance the permeation of drugs through skin.
14. Therapeutic concert of the drug molecules can be improved by tardy clearance from circulation.
15. They can protect the active moiety from biological circulation.
16. They can restrict the drug delivery rate as aqueous phase niosomal dispersion can be emulsified in the non-aqueous phase and thus normal vesicle can be administered in an external non-aqueous phase.

Disadvantages of Niosomes:-Limited shelf life of the aqueous suspensions of niosomes due to fusion, aggregation, leakage of entrapped drugs and hydrolysis of encapsulated drugs.

1. Preparation of multilamellar vesicles by extrusion, sonication method is time consuming and requires specialized equipments for processing.

COMPOSITION OF NIOSOMES

The essential components are

1. Cholesterol
2. Non-ionic surfactants
3. Other Additives

1. CHOLESTEROL

In Niosomal systems, cholesterol and its derivatives are the most common additives. It is a waxy steroid metabolite and found in the cell membranes. With non-ionic surfactants it forms the vesicles and provides greater stability and reduces agglomeration. Also, in niosome formation it imparts rigidity and in niosomal bilayer it provides orientational order

2. NON-IONIC SURFACTANTS

It possesses hydrophilic head group and a hydrophobic tail. It is the main component in niosome formation. The hydrophobic moiety consists of 1/2/3 alkyl chains or per fluro group or single stearyl group. Niosomes shows an increased ocular bioavailability when water soluble surfactants such as Tween 20, Tween 80 etc., entrapped because the surfactants act as the penetration enhancer helps to remove the mucus layer and break junctional complexes. Commonly used surfactants are span which having many grades such as span 20, span 40, span 60, span 80 and span 85 and also Tweens such as Tween 20, Tween 40, Tween 60 and tween 80.used are Ether linked surfactant, Di-alkyl chain surfactant, Ester linked, Sorbitan Esters, Poly-sorbates.

3. CHARGE MOLECULE

Some charge molecule is added in niosomal formulation to avoid aggregation of niosome. If same charge present in formulation then repulsion of particle takes place and aggregation not take place. Some of positive and negative charge ionic surfactant added in niosomal formulation. Negative charge molecules- Diacetyl phosphate, phosphatidic acid, lipoamino acid, dihexadecyl phosphate.92 Positive charge

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molecule- Stearyl amine, stearylpyridinium chloride. The charge molecule is also required in optimum concentration, if charge molecule added in more concentration then formation of niosome does not take place. About 2.5-5 mole percentage concentration of charge molecule required for preparation of niosome.

Methods of Preparation: The method of preparation influences the size, size distribution and number of bilayers, entrapment efficiency of the aqueous phase and the membrane permeability of the vesicles.

a) Ether injection method
b) Hand shaking method/thin film hydration method
c) Micro fluidization
d) Multiple membrane extrusion method
e) Reverse phase evaporation technique
f) Sonication
g) Transmembrane pH gradient drug uptake
h) The bubble method
i) Formation from pro-niosomes

a) Ether injection method: This method involves the introduction of surfactant dissolved in diethyl ether into warm water maintained at 60ºC. The ether solution with surfactant is injected into an aqueous solution of material through the 14-guage needle. Single layered needles are formed due to the vaporization of ether 13. The diameter of the vesicle varies from 50-1000nm depending upon the conditions used.

b) Hand shaking method/thin film hydration method: Surfactant and cholesterol are dissolved in a volatile organic solvent such as diethyl ether or chloroform or menthol. Using the rotary flash evaporator, the organic solvent is removed at room temperature of 20ºc which leaves a thin layer of solid mixture on the wall of the flask. The dried surfactant film is then rehydrated with aqueous solution of drug at the temperature of surfactants used for specified period of time (time of hydration) with gentle agitation. Multilamellar niosomes are formed by this method14. Thermo sensitive niosomes are prepared by evaporating organic solvent at 60ºC leaving a thin film on the wall of rotary flask evaporator and then the aqueous solution with drug is added slowly by shaking at room temperature followed by sonication.

c) Micro fluidization: Micro fluidization is the technique which forms unilamellar niosomes of defined size distribution, uniformity and better reproducibility. The principle involved in this technique is submerged jet principle in which two fluidized streams interact with each other at ultra high velocities, in the micro channels within the interaction chamber. The impingements of thin liquid sheet along with common front are arranged such that the energy supplied remains same within the area of niosomes formation. It results in the formation of niosomal vesicles of greater uniformity, smaller size and better reproducibility

d) Multiple membrane extrusion method: Desired size of the vesicles can be prepared by this method. It can be achieved by placing polycarbonate membranes in series up to 8 passages. Thin film of the surfactant, cholesterol and dicetyl phosphate mixture is made by evaporation. The film is then rehydrated with the aqueous solution containing drug16. The resultant solution is extruded through poly carbonate membrane (0.1µm nucleophore) by using C16G12.

e) Reverse phase evaporation technique: Cholesterol and surfactant in the ratio of 1:1 are dissolved in the mixture of ether and chloroform. Aqueous drug solution is added to this. The two phases are sonicated at 4-5ºc. Small amounts of phosphate buffered saline (PBS) are added to the clear gel and sonicate it again. The organic phase is removed at 40ºc and lower pressure. The viscous niosomal suspension is further diluted with PBS and heated on a water bath at 60ºc for 10min to yield niosomes.

f) Sonication: The production of vesicles by the sonication of solution is described by cable. An aliquot of buffer solution containing drug is added to the mixture of surfactant/cholesterol mixture in a 10ml glass vial. Then the mixture is subjected to sonication at 60ºc for 3min in a sonicator with titanium probe to produce niosomes

g) Transmembrane PH gradient drug uptake: Surfactant and cholesterol are dissolved in chloroform in a round bottomed flask. The solvent evaporation is done under reduced pressure to get the thin film on the wall of the flak. The film is then hydrated with 300mm citric acid (PH 4.0) by vortex mixing. It results in the formation of multilamellar vesicles. Then they are frozen and thawed 3 times and later sonicated to get niosomes.

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To this niosomal suspension, aqueous drug solution is added and vortexed. To maintain the PH between 7.0-7.2, phosphate buffer is used. Then the mixture is heated at 60ºc for 10 minutes to yield niosomes

h) The bubble method: It is the novel technique used for the one step preparation of niosomes without the use of organic solvents. The bubbling unit has round-bottomed flask with three necks positioned in water bath to control the temperature. In the first neck, water cooled reflux; thermometer in the second and nitrogen supply through the third neck is provided. Cholesterol and surfactant are dispersed in PH 7.4buffer at 70ºc. The dispersion is mixed for 15 seconds using high shear homogenizer. Then nitrogen gas is bubbled at 70ºc immediately.

Evaluation studies

Particle size:

The size of the formulation was analyzed using a Malvern Zetasizer Version.6.2.The formulation was placed in the sample holder and the particles size was measured.

Zeta potential analysis:

Zeta potential of the niosome was measured using Malvern Zetasizer Version,6.2.The zeta analysis, software produces a frequency spectrum from which the electrophoretic mobility hence the zeta potential calculated. The surface charge of the vesicle plays an important role in the in-vivo performance of niosome. The significance of the zeta potential is that its value can be related to the stability of vesicular formulations. The zeta potential indicates the degree of repulsion between adjacent, similarly particles in the dispersion system.

Drug entrapment study

1ml of the sample and 10 ml PBS buffer was taken and centrifuged at 5000 RPM at 40 ˚C for 60 minutes by using eppendrof centrifuge. Supernatant was separated without disturbing the sediment layer by using micropipette. Then, the supernatant layer (free drug) was diluted using phosphate buffer solution pH 7.4 and analyzed by using UV Spectrophotometer.

Drug content

1ml of Niosome preparation was taken in a 100ml volumetic flask. 2ml of acetone was mixed and volume was made upto 100ml with phosphate buffer pH7.4.Sample were filtered through whatman filter paper number 40 and diluted with Phosphate buffer pH 7.4. Drug content was determined spectrometrically at nm.

In-vitro drug release studies

The in-vitro release of niosome was studied by using open end cylinder apparatus. The open end cylinder apparatus consist of a glass tube with an inner diameter of 2.5cm open at both ends. One end of the tube is tied with cellophane membrane, which serves as a donor compartment. Niosomes equivalent to 100mg of drug as taken in a dialysis tube and placed in 200ml of phosphate buffer pH 7.4. The medium was stirred by using magnetic stirrer and the temperature was maintained at 37 ±2˚C. periodically 1ml of samples was withdrawn and after each withdrawal same volume of medium was replaced to maintain sink condition. Then the samples were assayed spectrometrically at using buffer as a blank.

Niosomes use other delivery:

Immuno-niosomes

Niosomes conjugation to antibodies forms immune-niosomes on their surface. Incorporation of cyanuric chloride derivatized Tween 61 in the noisome formulation was done through monoclonal IgG antibodies conjugated to the vesicle surfaces, and are prepared using thin film hydration techniques followed by sonication.

Magnetic niosomes

Niosomes show its effective magnetic targeting in a combination of drug delivery for various applications especially in cancer therapy. Encapsulation of both anti-tumoral model drug and magnetic-EMG 707 ferrofluids into the aqueous core of niosome, lead to the development of Doxorubicin-loaded magneto-niosomal formulations without any additional toxicity

Gene delivery

Niosomes are utilized as a cutaneous gene delivery system for the treatment of skin diseases. In a study by Raghavachariand Fahl, nonionic liposomes in rat skin cells; affords a competent delivery of beta-galactosidase/luciferase DNAs and it is illustrated as that generally DNA is a sequence of base-pairs of four different nucleotide bases .

Anticancer drug delivery

Niosomes comprising a non-ionic surfactant, cholesterol and dicetyl phosphate encapsulating methotrexate (MTX) lead to the increased absorption from the gastrointestinal tract with subsequent oral ingestion. Excessive uptake of MTX into the liver following the intravenous

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administration of the niosomes as compared to MTX, administered either orally or intravenously. Other anticancer agents such as vincristine bleomycin and paclitaxel show reduced toxicity with improved anticancer activity.

Transdermal delivery

Stratum corneum, the intracellular lipid barrier is significantly looser and more permeable for the particles such as niosomes. Niosomes were used as a carrier for the transdermal delivery of ketorolac–a potent nonsteroidal anti-inflammatory drug with significant improvement in drug permeation with reduced lag time .Ammonium glycyrrhizinate, niosomes of the natural compound, having effective anti-inflammatory activity formulated with the help of a new nonionic surfactant.(bola surfactant)–span 80 and cholester in ratio

In ophthalmic drug delivery

Gentamicin sulphate, a water-soluble antibiotic shows an extensive alteration in the release rate during its experimental studies. Moreover, in contrast to the regular drug sample solution, niosomal formulation of drug exhibit sluggish release .Timolol maleate (0.25%) niosomes, formulated via coating with chitosan shows more effect on intraocular tension with fewer side effects as compared to the marketed products

In the treatment of localized psoriasis

The limited applications of Methotrexate for the treatment of psoriasis were because of its manufacturing difficulties. It was then overcome by methotrexate niosomes, using chitosan as the polymer, with the promising results

In leishmaniasis

Generally, leishmaniasis parasite primarily affects the cells of the liver and spleen. Antimonials, the commonly used drug may damage the heart; liver; kidney etc. The incorporation of these drugs like sodium stibogluconate into niosomes improves the efficacy of the drug [82]. The additive effect was observed when two doses were given on successive days. Moreover, the higher level of antimony in the liver after its intravenous (i. v.) administration in mice is found in niosomes drug formulation

In diagnostic imaging

Niosomes-as a carrier for radiopharmaceuticals. It also shows site specificity for spleen and liver using 99mTc labelled DTPA containing niosomes for their imaging studies [84]. Improved tumour targeting of a paramagnetic agent is obtained by conjugated niosomal formulations-gadobenate with (N-palmitoyl-glucosamine, NPG), PEG 4400 and both PEG and NPG

Carrier for haemoglobin

Niosomes being a carrier for haemoglobin plays a major role. A super-imposable curve on free haemoglobin curve is obtained by the niosomal haemoglobin suspension

Cosmetic delivery

L'Oréal developed and patented niosomes in the year 1970s and 1980s who devised the primary report of non-ionic surfactant vesicles for cosmetic applications. And the first product 'Niosome' was introduced in 1987 by Lancôme. Niosomes have intense ability to progress the bioavailability of poorly absorbed substances; raise the stability of entrapped drugs and finally enhances skin penetration, thus paves the way for niosomes in the area of cosmetic and skin care applications

Vaccine delivery

For peroral vaccine delivery system and for topical immunization, niosomes attains good attention. Niosomes for topical DNA delivery of Hepatitis B surface antigen (HBsAg) were formulated, using the reverse phase evaporation method using Span 85 and cholesterol. The immune stimulating activity was investigated and was noted that topical niosomes elicited a comparable serum antibody titer and endogenous cytokines levels as compared to topical liposomes and intramuscular (i. m) recombinant HBsAg.

II. CONCLUSION

From the past few decades, there is a great revolution in development of novel drug delivery system.Niosomes are becoming an efficient and effective move towards a recent drug delivery. These were used in the modern pharmaceutical industry due to their remarkable advantages over conventional vesicular delivery systems. Among all the applications of niosomal technology, the development of a suitable niosomal carrier to encapsulate neuroactive compounds is incredibly promising. The nose to brain delivery route has the potential to become alternative of invasive methods of drug delivery. Niosomes can serve as better diagnostic agents, vaccine delivery system, tumour targeting agents, ophthalmic, nasal and transdermal delivery systems. Research has to be carried out extensively to have commercially available niosomal formulations.

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REFERENCS:

[1]. Saraswathi T. S., Mothilal M., Jaganathan M. K.Niosomes As An Emerging Formulation Tool For Drug Delivery-A Review,Vol 11, Issue 2, 2019

[2]. http://www.pharmainfo.net/reviews/non-ionic-surfactant-based-vesicle-niosome-potential-ocular-drug-delivery-system-overview. [last accessed on 20 sep 2018]

[3]. Rajalakshmi SV, Vinaya OG. Formulation development, evaluation and optimization of medicated lip rouge containing niosomal acyclovir for the management of recurrent herpes labialis. Int J Appl Pharm 2017;9:21-7

[4]. Shinde RL, Devarajan PV.Docosahexaenoic acid-mediated, targeted and sustained brain delivery of curcuminmicroemulsion. Drug Delivery 2017;24:152-6

[5]. R.parthirajan, pradeepkumar, gowrishankaretc. Design and invitro evaluation of voriconozole niosomes. (IJPPS),2013;5(3)604-610

[6]. Imanakbarzadeh, malihehkeramati, amirazadi etc Optimization, physiochemical characterization, and antimicrobial activity of a novel simvastatin nano-somal gel against E.coli, and s.aureus,Journal of Elsevier.2021;105019.

[7]. MohdQumbar, Ameeduzzafar, syedsarim imam etc Formulation and optimaization of lacidipine loaded noisome gel for transdermal delivery: in vitro characterization and in vivo activity. published by Elsevier Masson SAS 2017;93;255-265.