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Niosomes as Novel Drug Carriers: Composition, Preparation, and Applications

Ms. Siddhi Parmar, Ms. Simran Chauhan, Mrs. Harshala Patil
Department of Pharmaceutics, Shree Dhanvantary Pharmacy College, Kim, Surat, Gujarat, India

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ABSTRACT

Niosomes, vesicular systems derived from non-ionic surfactants, have been identified as highly promising carriers for drug delivery owing to their biocompatibility, stability, and capacity to encapsulate both hydrophilic and lipophilic pharmacological agents. These self-assembled bilayer vesicles, which consist of non-ionic surfactants and cholesterol, present several advantages such as extended circulation duration, targeted therapeutic delivery, and controlled release mechanisms. In comparison to liposomes, niosomes demonstrate superior stability and a diminished vulnerability to oxidative degradation and hydrolytic processes. A variety of formulation techniques, including thin-film hydration, sonication, and reverse-phase evaporation, facilitate the optimization of niosomal formulations for a range of therapeutic applications. Niosomes have been rigorously investigated for their potential applications in transdermal delivery, ocular therapy, pulmonary treatment, oncological therapy, as well as in vaccine and gene delivery systems. Notwithstanding their numerous advantages, obstacles such as vesicle aggregation, drug leakage, and constraints in large-scale manufacturing necessitate further investigation to enhance formulations' stability and commercial feasibility. This review aims to furnish a thorough overview of the composition, preparation methodologies, characterization techniques, and pharmaceutical applications of niosomes, underscoring their promise as an efficacious system for drug delivery within contemporary therapeutics.

Keywords: Niosomes, vesicular drug delivery, non-ionic surfactants, cholesterol, controlled release, targeted drug delivery, transdermal delivery

I. INTRODUCTION

In 1909, Paul Ehrlich introduced the development period for targeted delivery as he conceived a drug delivery system that would target directly to diseased

cell. Drug targeting can be defined as the ability to direct a therapeutic agent specifically to desired site of action with little or no interaction with non-target tissue. In niosomes drug delivery system the medication is encapsulated in a vesicle.[1] The vesicle is composed of a bilayer of non-ionic surface active agents and hence the name niosomes. In niosomes, the vesicles forming amphiphilic is a non-ionic surfactant such as Span – 60 which is usually stabilized by addition of cholesterol and small amount of anionic surfactant such as dicetyl phosphate.[2] Different type of drug can be delivered in targeted site by incorporating niosome, due to their multi-environmental structure. Niosome may be uni-lamellar or multi-lamellar vesicle is made up of non-ionic surfactant, cholesterol and ionic surfactant used to reduce aggregation of formulation.[3] The hydrophilic, lipophilic and amphiphilic drug can be incorporate in bilayer structural vesicle of niosome. Niosome shows more stability than liposome because liposome can be degraded and oxidized due to their specific lipophilic nature and it does not required any special condition for preparation and storage conditions like liposome. Niosomal formulation live prolonged in blood circulation due to their non-ionic surfactant and hence their target action is more.[4] The niosome are small and microscopic in size. The size of niosome are in nanometric scale which ranges about 20nm-100 nm. Due to its nanometric size niosome shows less metabolism and elimination by reticular-endothelium system.

Drug containing niosomal vesicle shows many advantages not only it increases the stability of unstable drug but also improves physicochemical property of drug. Many times, niosome contain different charge on their surface due to that different charge like (+) and (-), which shows flocculation or aggregation, to reduce ionic surfactant added in it for maintaining same charge in formulation.[5,6]

Cholesterol is important in the structure of niosome it give rigidity to vesicle but when cholesterol added more quantity in vesicle then it not only it affects the fluidity but also penetration and permeability of drug.[7,8] Niosomal formulation is administered by several route such as transdermal, parenteral, oral, ocular and subcutaneous route.[9]

In targeted drug delivery several carriers are used such as immunoglobulin, plasma protein, microsphere, synthetic polymers, sometimes erythrocytes and liposome but among all of these liposome and niosome are well documented as drug delivery system.[10-14]

This review aims to provide a comprehensive analysis of niosomes, covering their structural composition, methods of preparation, characterization techniques, and potential applications in pharmaceutical sciences. By highlighting their advantages over conventional systems, such as reduced toxicity, prolonged circulation time, and improved therapeutic efficacy, this review seeks to reinforce the importance of niosomes in modern drug delivery.

Advantages of niosomes

1. The characteristics such as size, lamellarity etc. of the vesicle can be varied depending on the requirement.
2. The vesicles can act as a depot to release the drug slowly and offer a controlled release.
3. Since the structure of the niosome offers place to accommodate hydrophilic, lipophilic as well as amphiphilic drug moieties, they can be used for a variety of drugs.
4. The vesicle suspension being water-based offers greater patient compliance over oil based systems.
5. They are osmotically active and stable.
6. They increase the stability of the entrapped drug.
7. Can enhance the skin penetration of drugs.
8. Surfactant are biodegradable, biocompatible and non-immunogenic so usually non-allergic.
9. They improve therapeutic targeted performance of drug by delaying clearance of drug from circulation.
10. Niosome formulation are less toxic due to their ingredient use for preparation. Also, non-ionic surfactant is the main constituent of niosome and toxicity of non-ionic surfactant are very less.

Limitations of niosomes

1. The niosome formulation are physically unstable.
2. In niosome formulation sometimes different charge present on surface of niosome vesicles due to that opposite charge come to near and fusion of niosome vesicle occur.
3. Many times, niosome shows aggregation if standard method of preparations not followed.
4. Hydrolysis of entrapped drug take place sometimes.
5. In some cases, found insufficient drug loading.
6. Formulation of niosome is time consuming process.
7. Leaking of entrapped drug
8. Physical instability
9. Hydrolysis of encapsulated drugs which limiting the shelf life of the dispersion.

Compositions of niosomes [15]

Niosomes are sophisticated bilayer vesicular systems constituted of non-ionic surfactants, cholesterol, and various excipients that collectively enhance their stability, encapsulation efficacy, and regulated drug release characteristics. The principal constituents of niosomes encompass:

1. Non-Ionic Surfactants

Non-ionic surfactants function as the fundamental structural elements of niosomes, establishing bilayers that encapsulate the aqueous phase. The selection of surfactant is pivotal as it profoundly influences the vesicle dimensions, stability, and drug entrapment efficacy. Frequently utilized non-ionic surfactants in niosome formulation include:

Alkyl ethers: e.g., Span series (Span 20, Span 40, Span 60, Span 80)

Alkyl esters: e.g., Tween series (Tween 20, Tween 40, Tween 60, Tween 80)

Alkyl amides: e.g., Brij 35, Brij 52, Brij 58

Fatty acid esters of sorbitan: e.g., Span 85 Polyoxyethylene alkyl ethers: e.g., Triton X-100

The hydrophilic-lipophilic balance (HLB) of surfactants is instrumental in dictating the characteristics of niosomes. Surfactants exhibiting an HLB ranging from 4 to 8 are inclined to yield stable vesicles.

2. Cholesterol

Cholesterol constitutes a vital component that imparts rigidity and structural coherence to the niosomal bilayer. It fortifies the vesicle by diminishing membrane permeability, thus averting premature drug leakage. Nevertheless, an excessive concentration of cholesterol may result in diminished drug entrapment efficacy and vesicle aggregation.

3. Charge Inducers

To augment stability and mitigate vesicle aggregation, charge inducers are frequently integrated into the formulation. These agents introduce a net charge to the vesicles, thereby augmenting electrostatic repulsion. Commonly employed charge inducers comprise:

Positive charge inducers: Stearylamine, cetyltrimethylammonium bromide (CTAB)

Negative charge inducers: Dicetyl phosphate (DCP), phosphatidic acid

4. Hydration Medium

The hydration medium acts as the aqueous phase in which niosomes are synthesized. The selection of buffer and pH can significantly affect the vesicle size, encapsulation efficacy, and stability. Commonly utilized hydration media are Phosphate-buffered saline (PBS) Distilled water Tris-HCl buffer.

5. Other Additives

Supplementary excipients may be incorporated into niosome formulations to enhance particular properties:

Penetration enhancers: Facilitate drug permeation through biological membranes (e.g., ethanol, isopropanol)

Cryoprotectants: Stabilize niosomes during freeze-drying (e.g., sucrose, trehalose)

Polymeric stabilizers: Prevent vesicle aggregation and extend shelf-life (e.g., poloxamers, PEG derivatives)

II. METHODS OF PREPARATION

Ether injection method

This methodology facilitates the synthesis of niosomes via the gradual addition of a surfactant solution solubilized in diethyl ether into an aqueous medium maintained at a temperature of 60°C. The surfactant mixture contained in ether is administered through a 14-gauge needle into the aqueous solution containing the desired materials. The vaporization of the ether results in the generation of unilamellar vesicles. Depending on the specific conditions employed, the diameter of these vesicles can vary from 50 to 1000 nm.

Hand shaking method (Thin film hydration technique)

The thin-film hydration methodology is frequently employed for the synthesis of niosomes. This technique has also been referred to in certain publications as the "Hand Shaking Method". In the execution of niosome preparation via this methodology, an organic solvent is introduced into a round-bottom flask, followed by the addition of both non-ionic surfactant and cholesterol. Subsequently, the organic solvent is subjected to evaporation using a rotary vacuum evaporator. Upon evaporation, a thin film is established on the inner surface of the round-bottom flask. This thin film is then subjected to hydration at a temperature that exceeds the transition temperature of the surfactant. For the hydration process, either water or phosphate buffer solution is utilized. Upon rehydration, the thin layer undergoes swelling, leading to the formation of multilamellar vesicles that encapsulate the drug[16] .

Sonication Method

This technique involves introducing the medication to an aqueous solution and a surfactant or cholesterol to an organic solvent. This drug's aqueous solution is combined with a surfactant solution and then homogenized for three minutes at 60°C.

Micro fluidization method

This process involves dissolving the medication and surfactant together and pumping them under pressure from a reservoir to an ice-filled interaction chamber. A cooling loop is used to circulate the solution such that It is possible to eliminate the heat generated throughout the procedure. This technique yields highly homogenous, smaller niosomes [17].

Multiple membrane extrusion method

The Multiple Membrane Extrusion Method is a technique for preparing uniform-sized niosomes by sequentially passing hydrated multilamellar vesicles (MLVs) through polycarbonate membranes of decreasing pore sizes using an extruder. The process begins with the formation of a thin lipid film by dissolving surfactant and cholesterol in an organic solvent, followed by solvent evaporation. The film is then hydrated with an aqueous phase (e.g., phosphate buffer) to form MLVs, which are subsequently extruded through membranes of progressively smaller pore sizes (1.2 μm → 0.8 μm → 0.4 μm → 0.2 μm) to obtain monodisperse niosomes. This method offers advantages such as improved stability, uniform size distribution, and suitability for large-scale production, but it requires specialized equipment and may lead to drug loss during multiple extrusion steps. It is widely used for controlled and sustained drug delivery applications.

Reverse Phase Evaporation Technique (REV)

In this method, Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform. An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. A clear gel is formed which is further sonicated after the addition of phosphate buffered saline (PBS). The organic phase is removed at 40°C under low pressure. The resulting viscous noisome suspension is diluted with PBS and heated on a water bath at 60°C for 10 min to yield niosomes [18].

Transmembranes pH gradient (inside acidic) Drug Uptake Process: or Remote Loading Technique

A solution of surfactant and cholesterol are dissolved in chloroform. The solvent is then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask. This film is hydrated with

300mm citric acid (PH 4.00) by vertex mixing. The resulting multilamellar vesicles are frozen and shared three times and later sonicated. To this niosomal suspension, aqueous solution containing 10 mg/ml of drug is added and vortexes. The PH of the sample is then raised to 7.0-7.2 with 1M disodium phosphate. This mixture is later heated at 60°c for 10 minutes to give niosomes[19].

The Bubble Method

The bubbling unit consists of round-bottomed flask with three necks, and this is positioned in a water bath to control the temperature. Water-cooled reflux and thermometer is positioned in the first and second neck and nitrogen supply through the third neck. Cholesterol and surfactant are dispersed together in this buffer (PH 7.4) at 70°C, the dispersion mixed for 15 seconds with high shear homogenizer and immediately afterwards "bubbled" at 70°C using nitrogen gas to yield niosomes [20].

The handjani–vila method

In this method, non-ionic synthetic lipids are mixed with an equivalent amount of drug aqueous solution to be encapsulated. The lipid-oil mixture is shaken to form a homogenous lamellar film. The mixture is further homogenized at a controlled temperature by using ultracentrifugation and agitation [22].

The enzymatic method

The ester links are cleaved by the esterases, and Cholesterol and surfactants such as polyoxyethylene cholesteryl sebacetate diacetate and Polyoxyethylene stearyl derivativescombine with diacetyl phosphate and other lipids to produce multilamellar niosomes[23].

The single pass technique

Michael W et al. patented a continuous process, in which the solution or suspension of lipids are extruded with high pressure through a porous device and a nozzle followed by homogenization to form niosomes of narrow range 50-500 nm size distribution[24].

Lipid Layer Hydration

surfactant and cholesterol are dissolved in chloroform and evaporated under reduced pressure to produce a thin lipid film on the wall of the around-bottomed flask. the obtained film was hydrated with an aqueous solution of the drug at a temperature slightly above the phase transition temperature of the surfactants under moderate shaking conditions[25].

Bubbling of Nitrogen

This method is a new procedure for the one-step establishment of niosomes lacking the usage of any organic solvents. Using this buffer, cholesterol and surfactant are spread together (pH 7.4) at 70°C conditions. It presumed by round-bottomed flask with three necks. The first two necks are placed in water-cooled reflux to control the temperature. Due to the sample (cholesterol and sur factant) of homogenized, nitrogen gas was passed from the third neck, thereby large unilamellar vesicles were produced. A continuous stream of nitrogen gas bubbles is made and introduced through the dispersion and to give small unilamellar vesicles[26].

Supercritical Carbon Dioxide Fluid (scCO2)

Manosroi et al. have described the supercritical reverse phase evaporation technique for niosomeformation. They added Tween 61, cholesterol, glucose, PBS, and ethanol into the view cell and the CO2 gas was introduced into the view cell. After magnetic stirring until equilibrium, the pressure was released and niosomal dispersions were obtained. This method enables one step production and easy scale-up [28].

Table 1 Methods of Niosome Preparation Using Various Surfactants and Drugs with Their Applications

Application	Surfactant	Method	Drug	Ref.
Pulmonary delivery	Span 60 and Tween 60	Lipid layer hydration	Ciprofloxacin	[30]
	Span 60	Lipid layer	Clarithromycin	[31]

Application	Surfactant	Method	Drug	Ref.
		hydration		
	Span 6	Sonication	Rifampicin	[32]
Protien Delivery	Brij 92 and Span 60	Lipid layer hydration	Insulin	[33]
	Span 60	Lipid layer hydration	Insulin	[34]
	Span 40	Lipid layer hydration	N-acetly glucosamine	[35]
	Span 60	Lipid layer hydration	Bovine serum albumin	[36]
Cancer chemotherapy	Span 60	Lipid layer hydration	Cisplatin	[37]
	span 60	Lipid layer hydration	5-Flourourcil	[38]
	Span 80	Sonication	Curcumin	[38]
	Bola surfactant, span80	Lipid layer hydration	5-Flourouracil	[39]
Carrier for hemoglobin	Span 60	Lipid layer hydration	Hemoglobin	[40]
Treatment of HIV-AIDS	Span 60	Lipid layer hydration	Lamivudine	[41]
	Span 60	Ether injection	Stavudine	[42]
	Span 60	Lipid layer hydration	Stavudine	[43]
	Span 80,span20	Ether injection	Zidovudine	[44]
Vaccine and antigen delivery	Span 60	Lipid layer hydration	Tetanus toxoid	[45]
	Span 20	Lipid layer hydration	Newcastle disease	[46]
	Span 60	Lipid layer hydration	Vaccine Ovalbumin	[47]
	Span 60, Span 85	Reversed-Phase Evaporation	Bovine serum albumin	[48]
Calcium Channel bloker ; hypertension,angina pectoris and some types of arrhythmia	Span 60	Thin film-hydration technique	Diltiazem	[49]
inhiniting	Span 60	Thin film-hydration	Diacerein	[50]

Application	Surfactant	Method	Drug	Ref.
interleukin-1 beta; Osteroarthritis		technique		
Angiotensin II receptor antagonist, Hypertension	Span 60	Sonication method	Candesartan	[51]
Antihistamine, Allergies	Span 60	Lipid film hydration method	Loratadine	[52]
Nonsteroidal anti-inflammmatory drugs(NSAID);inhibiting synthesis of prostaglandin.Analgesic and antipyretic effects	Tween 40	Thin film-hydration method, ether injection method	Ketoprofen	[53]
NSAID; To treat metabolic acidosis	Span 60	Thin film-hydration technique	Ketorolac Tromethamine	[54]
To treat Chronic(Long Term)HBV	Span 60	Thin film-hydration technique	Tenofovir	[55]
Anaemia	Span 60	Lipid layer hydration method	Folic acid	[56]
To treat Bacterial infection	Span 60	Thin film-hydration technique	Clarithhromycin	[57]
NRTIs; Nucleoside reverse transciptase inhibitors; to prevent passing the HIV to the unborn baby in pregnant women	Tween 80	Thin film-hydration technique	Zidovudine	[58]
To treat skin infection	Span 60, span 20, Span 40	Lipid layer-hydration method,thin film ether injection method	Griseofulvin	[59]
Anti-viral infection	Span 60, Span 80	Thin film-hydration technique	Acyclovir	[60]
Brain	Span 60	TLE-paddle method	Doxorubicin	[61]
	Span 60	Sonication	Dynorphin-B	[62]
	Span 60	Sonication	Vasoactive	[63]

Application	Surfactant	Method	Drug	Ref.
			intestinal peptide	
Breast cancer	Span 60	thin -film hydration	Doxorubicin	[64]
Chronic myelogenous leukemia	Tween 60	Thin-film hydration	Doxorubicin	[65]
Epidermoid carcinoma	Span 60	Thin-film hydration	Hydroxycamptothecin	[66]
	Span 60	Sonication	Doxorubicin	[67]
Melanoma	Span60	Ethanol injection method	Doxorubicin	[68]

III.FACTORS AFFECTING NIOSOMES FORMULATION

Drug

Entrapment of drug in niosomes influence charge and rigidity of the noisome bilayer. The hydrophilic lipophilic balance of the drug affects degree of entrapmen.

Nature and type of surfactant

The mean size of niosomes increases proportionally with increase in the HLB surfactants like Span 85 (HLB 1.8) to Span 20 HLB 8.6) because the surface free energy decreases with an increase in hydrophobicity of surfactant. A surfactant must have a hydrophilic head and hydrophobic tail. The hydrophobic tail may consist of one or two alkyl or perfluoroalkyl groups or in some cases a single steroidal group[78].

Cholesterol content and charge

Hydrodynamic diameter and entrapment efficiency of niosomes is increased by cholesterol. It induces membrane stabilizing activity and decreases the leakiness of membrane. An increase in cholesterol content of the bilayers resulted in a decrease in the release rate of encapsulated material and therefore an increase of the rigidity of the bilayers obtained. Presence of charge tends to increase the interlamellar distance between successive bilayers in multilamellar vesicle structure and leads to greater overall entrapped volume[79].

Resistance to osmotic stress

The diameter is reduced by addition of hypertonic salt solution to suspension of niosomes.

Temperature of Hydration

Hydration temperature influences the shape and size of niosome.

IV. CHARACTERIZATION OF NIOSOMES 81-88

Scanning electron microscopy

Particle size of niosomes is very important characteristic. The surface morphology (roundness, smoothness, and formation aggregates) and the size distribution of niosomes are studied by Scanning Electron Microscopy (SEM). Niosomes are sprinkled on to the double- sided tape that was affixed on aluminum stubs. The aluminum stub placed in the vacuum chamber of a scanning electron microscope (XL 30 ESEM with EDAX, Philips, Netherlands). The samples observed for morphological characterization using a gaseous secondary electron detector (working pressure: 0.8 torr, acceleration voltage: 30.00 KV) XL 30, (Philips, Netherlands).

Optical Microscopy

The niosomes are mounted on glass slides and viewed under a microscope (Medilux-207RII, Kyowa-Getner, Ambala, India) with a magnification of 1200X for morphological observation after suitable dilution.

The photomicrograph of the preparation also obtained from the microscope by using a digital SLR camera.

Measurement of vesicle size

The vesicle dispersions were diluted about 100 times in the same medium used for their preparation. Vesicle size was measured on a particle size analyzer (Laser diffraction particle size analyzer, Sympatec, Germany). The apparatus consists of a He-Ne laser beam of 632.8 nm focused with a minimum power of 5 mW using a Fourier lens [R-5] to a point at the center of multielement detector and a small volume sample holding cell (Su cell). The sample was stirred using a stirrer before determining the vesicle size. Hu C. and Rhodes 7 in 1999 reported that the average particle size of niosomes derived niosomes is approximately 6μm while that of conventional niosomes is about 14μm.

Entrapment efficiency

Entrapment efficiency of the niosomal dispersion can be done by separating the unentrapped drug by dialysis centrifugation or gel filtration as described above and thedrug remained entrapped in niosomes is determined by complete vesicle disruption using50% n-propanol or 0.1% Triton X-100 and analyzing the resultant solution by appropriate assay method for the drug.

Osmotic shock

The change in the vesicle size can be determined by osmotic studies. Niosomes formulations are incubated with hypotonic, isotonic, hypertonic solutions for 3 hours. Then thechanges in the size of vesicles in the formulations are viewed under optical microscopy.

Stability studies

To determine the stability of niosomes, the optimized batch was stored in airtight sealed vials at different temperatures. Surface characteristics and percentage drug retained in niosomes and niosomes derived from proniosomes were selected as parameters for evaluation of the stability, since instability of the formulation would reflect in drug leakage and a decrease.

In the percentage drug retained. The niosomes were sample at regular intervals of time (0,1,2,and 3months),observed for color change, surface characteristics and tested for the percentage drug retained after being hydrated to form niosomes and analyzed by suitable analytical methods(UV spectroscopy, HPLC methods etc).

Zeta potential analysis

Zeta potential analysis is done for determining the colloidal properties of the prepared formulations. The suitably diluted niosomes derived from pronoisome dispersion was determined using zeta potential analyzer based on electrophoretic light scattering and laser Doppler velocimetry method (Zeta plus™, Brookhaven Instrument Corporation, New York, USA). The temperature was set at 25°C. Charge on vesicles and their mean zeta potential values with standard deviation of measurements were obtained directly from the measurement.

Bilayer Characterization

Bilayer characteristics of niosomes have an importance on drug entrapment efficiency. The number of lamellae can be determined by AFM, NMR, and small angle X-ray scattering (SAXS)for multilamellar vesicles. Membrane rigidity of niosomal formulations can be measured by means of the mobility of fluorescence probe as a function of temperature. DPH (1,6 diphenyl 1,3,5-hexatriene) is most used fluorescent probe and added to niosomal dispersion. DPH normally exists in hydrophobic region in the bilayer membrane. The microviscosity of niosomal membrane is determined by fluorescence polarization. High fluorescence polarization means high microviscosity of the membrane. Moreover, the bilayer thickness can be characterized using the latter method, together with the in situ energy-dispersive X-ray diffraction (EDXD).

In Vitro Release

One often applied method to study in vitro release is based on using of dialysis tubing. A dialysis bag is washed and soaked in distilled water. After 30mins, the drug loaded niosomal suspension is transferred,

into this bag. The bag containing the vesicles is immersed in buffer solution with constant shaking at 25∘Cor37∘C. At specific time intervals, samples were removed from the outer buffer (release medium) and replaced with the same volume of fresh buffer. The samples are analyzed for the drug content by an appropriate assay method.

Particle size

The particle size of niosome is generally taken by zeta sizer instrument. This instrument containing Malvern PCS software. Before taking the result of sample solution the sample must be diluted with distilled water.The distilled water not interferes with result. Then after dilution the result were taken. The particle size must be required in nano range. This software was taken the average particle size of niosome. The particle size of sample solution was determined by using light scattering technique and by transmission electron microscope. If the particle size of the niosome increases then decrease the uptake and bioavailability of drug. The analysis of particle size was carried out for 60s at 165°C scattering angle of detection. The particle size is most important, the particle size of niosome in nano range are having more effective drug delivery as compare to micron range. The one advantage of large particle size niosome is having more area to fill more drug but it has very slow release pattern. Various method is used for administration of particle size of niosome such as SEM, TEM, XRD, AFM, Dynamic light scattering (DLS).

Loading Efficiency

Drug content in the preparation can determine by extracting drug from the niosome with 0.1M hydrochloric acid. In this method niosome (50mg) were stirred in50ml hydrochloric acid until dissolved. It was filtered by Millipore filter paper and drug content was determine, after suitable dilution. At 254nm by UV spectroscopy.

The loading efficiency (L) of the niosome was calculated according to following formula.

$$L\ (\%) = (Qn / Wn) \times 100$$

Were, Qn is the amount of drug present in niosome and Wn is weight of niosome.

Morphology

Niosomal vesicles shape is assumed to be spherical. Mean diameter can be determined by laser light scattering method. The diameter of vesicles can also be determined by electron microscopy, freeze-fracture electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy and optical microscopy. Fusion of vesicles during the cycle might be attributed to the increase in vesicle diameter due to freeze-thawing of niosomes.

Number of lamellae

Determined by using nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering and electron microscopy.

V. APPLICATIONS OF NIOSOMES89-96

Immuno-niosomes

Niosomes have been used for studying the nature of the immune response provoked by antigens. Niosomes can also be utilized for targeting drugs to organs other than the Reticulo-Endothelial System. A carrier system (such as antibodies) can be attached to niosomes (as immunoglobulin's bind readily to the lipid surface of the niosome) to target them to specific organs.

Sustained Release

Sustained release action of niosomes can be applied to drugs which have low therapeutic index and have low solubility with water since those could be maintained in the circulation via niosomal encapsulation.

Localized Drug Action

Drug delivery through niosomes is one of the approaches to achieve localized drug action, since their size and low penetrability through epithelium and connective tissue keeps the drug localized at the site of administration.

Niosomes as Drug Carriers

Niosomes have also been used as carriers for iobitridol, a diagnostic agent used for X-ray imaging. Topical niosomes may serve as solubilization matrix, as a local depot for sustained release of dermally active compounds, as penetration enhancers, or as rate-limiting membrane barrier for the modulation of systemic absorption of drugs.

Transdermal delivery of drugs by niosomes

Those drug have slow penetration of medicament through skin is the major drawback of transdermal route of delivery. An increase in the penetration rate has been achieved by transdermal delivery of drug incorporated in niosomes.

From the above discussed studies, and confocal microscopy, it was seen that non-ionic vesicles could be formulated to target pilosebaceous glands.

Topical niosomes may serve as solubilization matrix, as a local depot for sustained release of dermally active compounds, as penetration enhancers, or as rate-limiting membrane barrier for the modulation of systemic absorption of drugs.

Leishmaniasis

Leishmaniasis is a disease in which a parasite of the genus Leishmania invades the cells of the liver and spleen.

Use of niosomes in tests conducted showed that it was possible to administer higher levels of the drug without the triggering of the side effects, and thus allowed greater efficacy in treatment.

Delivery of Peptide Drugs

Oral peptide drug delivery has long been faced with a challenge of bypassing the enzymes which would breakdown the peptide. Use of niosomes to successfully protect the peptides from gastrointestinal peptide breakdown is being investigated. In an in vitro study conducted by oral delivery of a vasopressin derivative entrapped in niosomes showed that entrapment of the drug significantly increased the stability of the peptide.

Niosomes as carriers for Hemoglobin

Niosomes can be used as a carrier for hemoglobin. Niosomal suspension shows a visible spectrum superimposable which is likely to be or, onto that of free hemoglobin. Vesicles are permeable to oxygen and hemoglobin dissociation curve can be modified similarly to non-encapsulated hemoglobin.

Drug Targeting

One of the most useful aspects of niosomes is their ability to target drugs. Niosomes can be used to target drugs to the reticuloendothelial system. The reticulo-endothelial system (RES) preferentially takes up niosome vesicles. The uptake of niosomes is controlled by circulating serum factors called opsonins. These opsonins mark the niosome for clearance. Such localization of drugs is utilized to treat tumors in animals known to metastasize to the liver and spleen. This localization of drugs can also be used for treating parasitic infections of the liver. Niosomes can also be utilized for targeting drugs to organs other than the RES. A carrier system (such as antibodies) can be attached to niosomes (as immunoglobulin's bind readily to the lipid surface of the niosome) to target them to specific organs.

Magnetic niosomes

Niosomes show 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.

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 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. 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.

Gene delivery

Niosomes are utilized as a cutaneous gene delivery system for the treatment of skin diseases. In a study by Raghavachari and 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 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.

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.

VI. CONCLUSION

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 to the brain regarding improved drug absorption and less systemic adverse effect. To enjoy the advantages, the limitations of variable absorption or nasal toxicity must be exterminated. The goal of development of niosomes is to control the release of drug in a sustained manner, a further change in the distribution profile of drug and targeting to the specific body site. Thus as an effective tool now and then for various therapeutic substances and the responsibility lies on future research scientists to successfully yoke its potential in various purposes for the aid of people.

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