

**"NIOSOME:- NOVEL PHARMACEUTICAL DRUG DELIVERY
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India.**ABSTRACT**

Niosome are a novel drug delivery system, in which the medication is encapsulated in a vesicle. The vesicle is composed of a bilayer of non-ionic surface active agents and hence the name niosomes. Structurally, niosomes are similar to liposomes, in that they are also made up of a bilayer. However, the bilayer in the case of niosomes is made up of non-ionic surface active agents rather than phospholipids as seen in the case of liposomes. Most surface active agents when immersed in water yield micellar structures however some surfactants can yield bilayer vesicles which are niosomes. Niosomes may be unilamellar or multilamellar depending on the method used to prepare them. The niosomes are classified as a function of the number of bilayer (e.g.

MLV, SUV) or as a function of size. (e.g. LUV, SUV) or as a function of the method of preparation (e.g. REV, DRV). Niosomes present a structure similar to liposome and hence they can represent alternative vesicular systems with respect to liposomes, due to the niosome ability to encapsulate different type of drugs within their multienvironmental structure. The technology utilized in niosomes is still greatly in its infancy, and already it is showing promise in the fields of cancer and infectious disease treatments.

LIST OF ABBREVIATIONS

MLV:- Multi Lamellar Vesicles

SUV:- Small Unilamellar Vesicles

LUV:- Large Unilamellar Vesicles

REV:- Reverse Phase Evaporation

DRV:- Dried Reconstituted vesicles

V:- Volume of non-polar group

l_c :- Critical non-polar group length

A_o :- Area of polar head group

INTRODUCTION

In the last few decades, much research has been aimed at prevention and treatment of disease with a significant degree of success. Treatment of an acute disease or a chronic illness has been accomplished by administering various pharmaceutical dosage forms like tablets, capsules, creams ointments, syrups, suppositories and injectables to the patients. Even though these dosage forms ensure a prompt release of drug, it is necessary to administer these conventional dosage forms several times a day to maintain the drug concentration within the therapeutically effective range for the treatment. In the past three decades several advancements in drug delivery systems have been made. As a result new techniques have been developed as delivery systems. These techniques are capable of controlling the rate of drug delivery. Sustaining the duration of therapeutic activity and targeting the delivery of a drug to a tissue. New carrier systems have been designed to procure site-specific pharmacological action of a drug or controlled release of drug or prolonged duration of action of the drug, thus enhancing efficacy while diminishing undesirable side effects. Novel drug delivery systems are being developed rapidly so as to overcome the limitations of conventional dosage forms. Improving the effectiveness of an existing drug by optimizing the delivery and dosage, minimizing the side effect and finding the therapeutic uses may be a better investment and more effective for patients than creating a brand new drug. The objective is to encourage research to develop technologies for targeted controlled and sustained delivery of drug with reduced side effects that efficiently deliver drugs into cells.

The goal of any drug delivery system is to provide a therapeutic amount of drug to proper site in the body to maintain the desired drug concentration. That is the drug delivery system should deliver the drug at a rate dictated by the needs of the body over a specified period of treatment. The development of several novel drug delivery systems of medication provides a number of therapeutic benefits. The novel drug delivery system may be broadly grouped into two types namely:

- Spatial drug delivery system and
- Temporal drug delivery system

1. Spatial drug delivery system

It relates to targeting a drug to a specific organ or tissue.

2. Temporal drug delivery system

It relates to controlling the rate of drug delivery to the target tissue

Present scenario and future of NDDS: In India major thrust area of research and development for NDDS are:

- Liposomes
- Niosomes
- Nanoparticles
- Transdermal drug delivery
- Oral system 8
- Microencapsulation or microcapsules
- Polymer in drug delivery

Novel drug delivery system can be broadly divided into two classes. They are as Follows

Sustained release drug delivery system

Controlled release drug delivery system

Sustained release drug delivery system includes any drug delivery system that Releases the drug over an extended period of time. If the system is successful in Maintaining constant drug level in the drug or target tissue, it is considered as a Controlled release system. If it extends only the duration of action over the Conventional delivery system, it is considered as prolonged release system.

Sustained Release Drug Delivery System

Sustained release drug delivery system is described as a pharmacological Dosage form, formulated to retard the release of a therapeutic agent such that its Appearance in the systemic circulation is delayed and / or prolonged and its plasma Profile is sustained in duration. The onset of its pharmacological action is often Delayed and its duration of the therapeutic effect is extended and therefore the action Is sustained e.g. coated granules.

Controlled Release Drug Delivery System

Controlled release drug delivery drug delivery system has a meaning that goes beyond the scope of sustained drug action it implies a predictability and reproducibility in the release kinetics. The release of drug from a controlled release drug delivery system proceeds at a rate profile that is not only predictable kinetically but also reproducible from one unit to another.

The improvement in drug therapy is represented by several potential advantages of controlled release system.

1. Avoid repeated administration and minimize the patient compliance problems
2. Minimize drug accumulation with chronic dosing.
3. Minimize local and systemic side effects.
4. Improve efficiency in treatment by
 - Improving the bioavailability of some drugs.
 - Reducing the fluctuation in drug concentration in blood level.
5. Economical
 - Average cost of treatment over an extended period of time is less.
 - Decrease in nursing time/hospitalization.

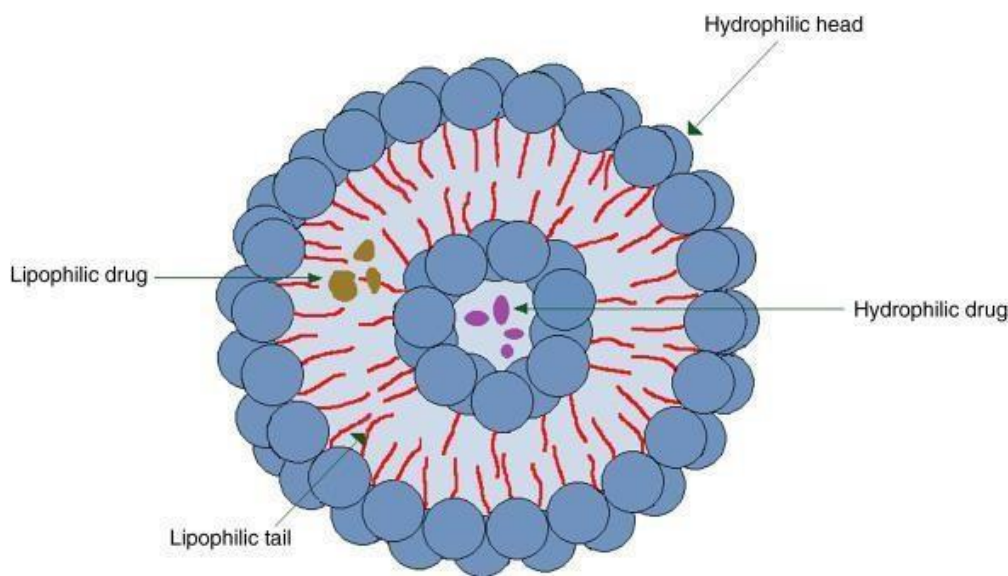
The following drugs are not suitable for formulating a sustained release medication.

- Drugs with long biological half-life (more than 40 hours) e.g. digitoxin.
- Drugs with narrow requirement of absorption.
- Drugs with very short biological half-life (less than 1 hour) e.g. penicillin.
- Drugs which are very insoluble and whose availability is controlled by Controlled release drug system can be classified into four categories
- Rate pre-programmed drug delivery system e.g. Implants.
- Activation – modulated drug delivery system e.g. osmotic pump.
- Feedback – regulated drug delivery system e.g. glucose triggered insulin Delivery system
- Site – targeting drug delivery system e.g. niosomes, liposomes.

NIOSOMAL DRUG DELIVERY

In recent years niosomes received great attention as potential drug delivery Systems for different routes of administration parentally as well as orally. A Tremendous work have been done to formulate drugs in niosomes which serve as Carriers for delivery of drugs, antigens, hormones and other bioactive agents. Niosomes are unilamellar or multilamellar vesicles wherein aqueous solution Is enclosed in highly ordered bilayer structures made up of nonionic surfactant with Or without cholesterol and dicetyl phosphate and exhibit non-toxic, biodegradable, Non-immunogenic and of suitable size and shape to accommodate a variety of Substances. Niosomes are formed by mixing phospholipids, non-ionic surfactant with Aqueous medium. They are microscopic structures consisting of one or more Concentric lipid bilayers

surrounding aqueous compartments. A schematic diagram of A niosome, formed with non-ionic surfactant and cholesterol is shown in figure1 The surfactant and cholesterol form a variety of aggregates from micelles to Large vesicles, which can be used as vehicles for drug delivery. This is in accordance with the observation that a cone shaped and wedge shaped non-Ionic surfactant and cholesterol to form bilayer membranes. These include carriers in Oncology for delivery of anti parasitic agent, cosmetic formulations and as topical Vesicles.



TYPES OF NIOSOMES

Generally, the niosomes have been classified as a function of the number of bilayer (e.g. MLVs, SULVs) or as a function of size (e.g. LULVs, SULVs) or a function of the method of preparation (e.g. REV – Reverse Phase Evaporation, DRV – Dried Reconstituted vesicles).

1. Multilamellar Vesicles (MLVs)- 1000 to 5000nm
2. Larger Unilamellar Vesicles (LULVs)-100 to 1000nm
3. Small Unilamellar Vesicles(SULVs)-25 to 500 nm

METHODS OF PREPARATION OF NIOSOMES

1. Multi Lamellar Vesicles (MLVs)
 - Thin film hydration method
2. Large Unilamellar Vesicles (LULVs)
 - Reverse Phase Evaporation method
 - Calcium induced method
 - Dehydration / Rehydration of small Unilamellar Vesicles
 - Detergent removal method.

3. Small Unilamellar Vesicles (SULVs) □ Sonication method

- French press method
- Ethanol injection method
- Ether injection method
- Homogenization
- Dried Reconstituted Vesicles

SALIENT FEATURES OF NIOSOMES

- 1) Niosomes are osmotically stable and can entangle the solute and increase the firmness of entangled drug.
- 2) Niosomes are non-ionic surfactants that are biocompatible, non-immunogenic and biodegradable.
- 3) Niosomes possess a framework which comprises of deliquescent and hydrophobic largely along so allows the drug molecules with a large vary of solubility.
- 4) Labile and sensitive medication can be easily delivered by niosomes.
- 5) Niosomes are usually flexible structurally so they can be designed according to the desired situation.
- 6) Availability of the drug at the particular site is better, just by securing the drug from biological environment.
- 7) Solubility and oral bioavailability of sparingly soluble drugs are improved by niosomes and also skin penetrability of drugs which are applied topically is enhanced.

ADVANTAGES

- 1) Reduced side effects and shows maximum duration of Action.
- 2) Patient compliance is more compared to other delivery System.
- 3) Quantity of drug used is very less for achieving its Desired effect.
- 4) Active ingredient or constituent present in the Preparation is protected by bilayer from various factors Present inside and outside the body.
- 5) Act as depot formulation, thus the drug is released in a Controlled manner.
- 6) Drug is protected from first pass metabolism and gastro-Intestinal degradation.
- 7) Possess stable structure even in emulsion form.
- 8) Niosomes are available in oral, topical as well as Parenteral routes.

DISADVANTAGES

- 1) Time consuming process.

- 2) Specialized equipments are required for processing.
- 3) Limited shelf life due to-
 - a) Fusion, b) Aggregation, c) Leakage of entrapped drugs, d) Hydrolysis of encapsulated drugs.
- 4) Physically unstable.

COMPOSITION OF NIOSOMES

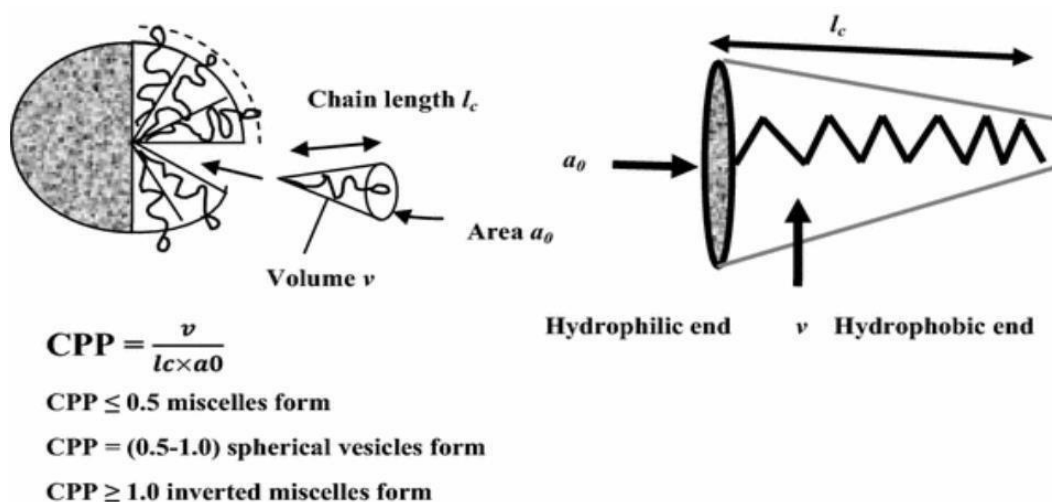
The vital components used in the niosome formulation are:

- 1) Non-ionic surfactants
- 2) Cholesterol
- 3) Charge inducer
- 4) Hydration medium

1. NON IONIC SURFACTANT

The primary component used in the formulation of the Niosome is the surface-active agent. They are amphiphilic in Nature comprising a polar head and a non-polar tail. These agents are more stable, compatible and less toxic When compared to other surfactants such as anionic, Cationic and amphoteric surfactants because they do not Carry any charge. These agents cause less haemolysis and Irritation to cellular surfaces. They can be used as wetting Agents and emulsifiers. The important characteristic of non-Ionic surfactant is that they inhibit pglycoprotein and thus Enhance the absorption and targeting of anticancer Drugs (exampledoxorubicin, daunorubicin, curcumin, Morusin), steroids (example-hydrocortisone), HIVprotease inhibitor (example-ritonavir),Cardiovascular drugs (example-digoxin, betablockers). Non-ionic surfactant exhibit high interfacial activity and are Comprised of both polar and non-polar groups/segments. The bilayer vesicles formation depends on hydrophilic Lipophilic balance (HLB) scale, chemical structure of Components and critical packing parameter (CPP). The Entrapment efficiency of drug are usually altered by chain Length and size of hydrophilic head group of non-ionic Surfactant. Non-ionic surfactant with larger alkyl chain Shows higher entrapment efficiency. The Tween sequence of Surfactants possessing an extended alkyl chain and an Outsized hydrophilic moiety together with cholesterol During a ratio 1:1 have the very best entrapment efficiency Of water soluble drugs. The HLB value of a surfactant plays a vital role in managing drug entrapment of the vesicle it forms Critical packing parameter (CPP) value of a surfactant can be Calculated from the area of the polar head group and volume And length of the non-polar group. Using CPP values the type Of vesicle going to be formed can be determined (Figure) And also by the calculation of CPP

using certain formula.



$$CPP = V/l_c \times a_0$$

Where, V = Volume of non-polar group l_c = Critical non-polar group length a_0 = Area of polar head group.

2. CHOLESTEROL

Cholesterol is a waxy steroid derivative found within the cell membrane that is principally employed in the preparation of niosomes.^[31] Leakiness of the cell membrane is decreased by stabilizing the membrane by incorporating cholesterol into the bilayer constitution of niosomes; this frequently increases the entrapment efficiency of the niosomes.^[32] Cholesterol is usually added to non-ionic surfactants to give hardness and proper direction/adjustment to niosomal bilayer.^[33] Cholesterol is renowned to get rid of gel to liquid phase transition of niosomal system leading to niosomes that are less leaky.^[34]

3. CHARGE INDUCER

Charge inducers are added in the preparation to increase the stability of niosomes by electrostatic repulsion to avoid coalescence. The negatively charged molecules mostly used are diacetyl phosphate (DCP) and phosphatidic acid. Similarly positively charged inducers used in niosomal preparations are stearyl amine (STR) and stearylpyridinium A concentration of 2-5 mole percentages of charged inducers is bearable because higher concentration can hamper the niosome formation.^[35,36]

4) HYDRATION MEDIUM

The most commonly used hydration medium in the preparation of niosome is phosphate buffer.

These phosphate buffers are used at various pHs. The actual pH of the hydration medium depends on the solubility of the drug being encapsulated.^[37]

TYPES OF NIOSOMES

The different types of niosomes can be classified as follows:

- 1) Multilamellar vesicles (MLV)
- 2) Large unilamellar vesicles (LUV)
- 3) Small unilamellar vesicles (SUV)

1) Multilamellar vesicles (MLV)

Multilamellar vesicles are most widely niosomes. The size of the vesicles range approximately 0.5-10 μm diameter. The method of preparation of the vesicles is easy and it is mechanically stable upon storage for longer periods. It usually consists of number of bilayer surrounding the aqueous lipid component separately. These multilamellar vesicles are highly suited as drug carrier for lipophilic compounds.

2) Large unilamellar vesicles (LUV)

Large unilamellar type of niosomes have high aqueous/ liquid compartment ratio, so that larger volumes of bio- active materials can be entrapped with a very economical use of membrane lipids. The size of large unilamellar vesicles are in the range of 100-3000 nm length.

3) Small unilamellar vesicles (SUV)

Small unilamellar vesicles are mostly prepared from multilamellar vesicles by sonication method. It has been reported that the size of the small unilamellar vesicles are in the range of 10-100 nm.

METHOD OF PREPARATION

- 1) Hand shaking method (Thin film hydration technique)
- 2) Micro fluidisation
- 3) Reverse Phase Evaporation (REV)
- 4) Ether Injection Method
- 5) Trans-membrane pH-gradient (inside acidic)
- 6) The Bubble Method
- 7) Sonication
- 8) Multiple extrusion method

9) Formation of niosomes from proniosomes

1) Hand shaking method (Thin film hydration technique)

In hand shaking method, round bottom flask is used in which non-ionic surfactant and cholesterol are dissolved in a volatile organic solvent (such as diethyl ether, chloroform, or methanol). The organic solvent is removed using rotary evaporator at room temperature (20°C) leaving a thin layer of solid mixture which is deposited on the wall of the flask. With gentle agitation the dried surfactant film is hydrated with aqueous phase containing drug at 50-60°C. By this method multilamellar niosomes are formed.

2) Micro fluidisation

Micro-fluidisation is a technique in which unilamellar vesicles of defined size distribution are prepared. It is based on submerged jet principle in which two fluidized streams interact at ultra-high velocities (100 ml/min), in precisely defined micro channels within the interaction chamber. The impingement of thin liquid sheet along a common front is arranged in such a way that the energy supplied to the system remains within the area where niosomes are formed. Niosomes formed by this method have greater uniformity, smaller size and better reproducibility.

3) Reverse Phase Evaporation (REV)

In reverse phase evaporation, the cholesterol and surfactant is taken in the ratio 1:1 ratio. The above mixture is dissolved in ether and chloroform mixture. Drug is dissolved in aqueous phase. Both the mixture is sonicated at the temperature 4-6°C. The suspension of niosomes is diluted in the PBS at 60°C using water bath for 10 minutes, which yields the niosomes. PBS is again added to the obtained product and sonicated at low pressure and temperature is maintained at 40-45°C and organic phase is removed at this temperature. The resultant suspension is diluted with PBS and heated on water at 60°C to 10 minutes to yield niosomes.

4) Ether injection method

In ether injection method, the niosomes are prepared by introducing a solution of surfactant which is dissolved in diethyl ether (volatile organic solvent) into warm water which is maintained at 60°C. The surfactant mixture in ether is injected into an aqueous solution of material with the help of 14-gauge needle. Single layered vesicles are formed by vapourization of ether (volatile organic solvent).

5) Trans-membrane pH gradient (inside acidic)

In this method, the surfactant and cholesterol is mixed/ blended in round bottom flask and dissolved in chloroform. On the wall of the flask, a thin film is formed by evaporating the chloroform under reduced pressure. Hydration of film is done by vortex mixing with 300mM citric acid (pH 4.0). To the above niosomal suspension, aqueous solution containing 10mg/ml of drug is added and vortexed. The pH of the sample is adjusted to 7.0-7.2 by adding 1M disodium phosphate and this mixture is heated at 60°C for 10 minutes. Multilamellar vesicles are produced by this method.

6) The Bubble method

The bubble method is a novel technique in which the niosomes are prepared without using organic solvents. The bubbling unit is used in this method. This unit consist of round bottom flask with 3 necks positioned in water bath by which the temperature is controlled. Water-cooled reflux is placed in first neck, thermometer is placed in second neck and the nitrogen is passed through the third neck. Cholesterol and surfactant are mixed together in buffer solution (pH-7.4) at 70°C. High shear homogenizer is used for mixing the solution for 15 seconds, and then this solution is immediately bubbled at 70°C by the use of nitrogen gas.

7) Sonication

Sonication is one of the conventional method for the preparation of niosomes. In this method, the drug solution is prepared by dissolving drug in buffer. Then this buffer drug solution is added the mixture of the non-ionic surfactant at optimized ratio. The desired niosomes are obtained by sonicating the mixture at specific frequency, temperature and time. It is one of the easy way in which the particle size of the niosomes can be controlled. This method can be used to decrease the diameters of niosomes with narrow size distribution. Probe sonicators can also be used but they involve high levels of energy. Due to this it leads to sudden increase in temperature and discharge of titanium.

8) Membrane Extrusion Method

In this method the surfactant, cholesterol and diacetyl phosphate is mixed in chloroform. Then this chloroform mixture is evaporated to obtain thin film. Hydration of thin film is done with aqueous drug polycarbonate membrane. Solution and resultant suspension is extruded through this membrane (which consist of 8 passages). Required size of the niosomes is also obtained by this method.

9) Formation of niosomes from proniosomes

By addition of aqueous phase with drug to the proniosomes with short agitation at a temperature greater than mean transition phase temperature of the surfactant results in the formation of the niosomes.

$$T > T_m$$

Where,

T = Temperature

T_m = Mean phase transition temperature

Blazek-Walsh A.I et al has described the formulation of niosomes from maltodextrin based proniosomes. This formulation furnishes rapid reconstitution of niosomes with the minimal left over/ residual carrier. Free flowing powder of formulation was obtained by drying the slurry of maltodextrin and surfactant, which could be rehydrated by addition of warm water.

SEPARATION OF UNENTRAPPED DRUG

1) DIALYSIS

The aqueous niosomal suspension is dialyzed in dialysis tubing by using phosphate buffer or glucose solution or normal saline.

2) GEL FILTRATION

The untrapped drug in the niosomal suspension is removed by gel filtration using Sephadex-G-50 column and elution is done with phosphate buffered saline or normal saline.

3) CENTRIFUGATION

In centrifugation, the niosomal suspension is centrifuged and the supernatant liquid is separated. Niosomal suspension free from untrapped drug is obtained by washing the pellet and the resuspended solution.^[58,59]

NIOSOMES VERSUS LIPOSOMES

The liposomes and niosomes are almost similar in nature. The phospholipids used in liposomes are not stable in nature; whereas niosomes are made up of non-ionic surfactants which are stable. Niosomes are prepared from unchanged single chain non-ionic surfactant, whereas liposomes are prepared from double-chain phospholipids. The size of niosomes ranges from 10-100nm and liposomes from 10-300nm. According to cost, the niosomes are economically cheap compared to liposomes.^[60]

FACTORS AFFECTING THE NIOSOME FORMATION

1) Drug

The physico-chemical properties of encapsulated drug directly affect the charge and rigidity of the niosomal bilayer. The vesicle size of the niosomes is improved by entrapping the drug inside the niosomes, also by interaction of solute with head groups of surfactants. Enhancement of charge and mutual repulsion between the bilayers of surfactant increases the vesicle size. Degree of entrapment is also affected by the Hydrophilic-Lipophilic balance of the drug.^[61,62]

2) Resistance of osmotic stress

The addition of hypertonic salt solution to the niosomal suspension leads the reduction in diameter of niosomes. Again after the addition of hypotonic salt solution, initially it leads to slow release with slight swelling of the vesicles due the inhibition of elution fluid from vesicles. The release becomes faster due to mechanical loosening of vesicle structure under osmotic stress.^[63]

3) Temperature of hydration medium

Temperature of hydration medium plays a vital role in formation of vesicle. This affects their shape and size. The temperature maintained should be above the gel to liquid phase transition temperature of the system. Changes in the vesicle shape are also observed due to the temperature. It also affects the assembly of surfactants into vesicles. Vesicle structure and yield is affected by the volume of hydration medium and duration of the lipid film.^[27,64]

4) Cholesterol content

Cholesterol affects the physical properties and structure of the niosomes. The structure is affected due the presence of non-ionic surfactants. Cholesterol is present in biological membranes it also affects the membrane properties like ion permeation, aggregation, fusion processes, size, shape, elasticity and enzymatic activity. Addition of cholesterol leads to change in fluidity of niosomes. Cholesterol plays an important role during preparation of niosomes because it provides rigidity to vesicles, which is very important during severe stress conditions. The amount of cholesterol to be added depends on the HLB value of the surfactants. As the HLB value increases above 10, the amount of cholesterol should also be increased in order to remunerate for the larger head groups change in value has impact noisome change in HLB value has impact on noisome formulation (Table 1). Inclusion of cholesterol in niosomes increases the hydrodynamic diameter and entrapment efficiency. At high cholesterol

concentration, the gel state is transform liquid ordered phase. An increase in cholesterol content of the bilayers results in a decrease in the release rate of encapsulated material and thereby increases the rigidity of the bilayers obtained.

5) Amount 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. The bilayers of the vesicles are either in the liquid state or in gel state, depending on the temperature, the type of surfactant and the presence of other components like cholesterol. Alkyl chains are present in a well-ordered structure in the gel state, while in the liquid state, the structure of the bilayers is more disordered. The surfactants and lipids are characterized by the gel-liquid phase transition temperature (TC). Phase transition temperature (TC) of surfactant also affects the entrapment efficiency i.e. Span 60 having higher TC, provides better entrapment.^[67]

6) Membrane Composition

Addition of various additives along with surfactants and drugs leads to the stable formation of niosomes. Niosomes formed have a variety of morphologies and their permeability/porousness and stability properties will be altered by manipulating membrane characteristics by totally different additives. Just in case of polyhedral niosomes formed from C16G2, the shape of these polyhedral niosome remains unaffected due to the addition of low quantity of solution of solulan C24 (cholesterol poly-24-oxyethylene ether), that prevents aggregation due to development of steric.^[6]

CHARACTERIZATION OF NIOSOMES

1) Entrapment Efficiency

1. The entrapment efficiency (EE) of vesicular systems can be defined as the amount of active substances loaded within the niosomal structure. It can be expressed as

$$EE = \frac{\text{Amount entrapped}}{\text{Total amount}} \times 100$$

Where, the "total amount" is the total amount of drug in the prepared in the niosomal formulation. The entrapment efficiency is determined spectrophotometrically by using UV-visible spectrophotometer. In case of genetic material, gel electrophoresis is done followed by UV densitometry. In addition, the entrapment efficiency can also be fluorometrically evaluated using a hydrophilic fluorescent.

2) Vesicle size and shape

The shape of niosomal vesicles is assumed to be spherical, and their mean diameter can be determined by using laserlight scattering method. Also, the diameter of these vesicles can be determined by using electron microscopy, molecular sieve chromatography, ultracentrifugation, photon microscopy and optical microscopy and freeze fracture electron microscopy. Freeze thawed niosomes increase the vesicle diameter, which might lead to the fusion of vesicles during the cycle.

3) In-vitro release

In in-vitro release study dialysis membrane method is generally used. In this method small amount of niosomes are taken into dialysis bag and are tied at both the ends. Another beaker containing suitable dissolution media is maintained at 37 °C and the dialysis bag is put into the dissolution medium and stirred by a magnetic stirrer. A sample solution is taken from the beaker at specified time intervals and replaced with fresh dissolution media. The samples were analyzed for the concentration of drug at specified wave length reported in the respective monograph of that particular drug.

4) Number of lamellae

Number of lamellae in niosomes can be determined by using electron microscope, NMR spectroscopy or X-ray scattering method.

5) Membrane rigidity

Membrane rigidity of the niosome is measured by means of mobility of fluorescence probe as function of temperature.

6) Bilayer formation

Assembly of non-ionic surfactants to form bilayer vesicle is characterized by the formation of X-cross under light polarization microscopy.

7) Stability study

The stability of niosomes can be evaluated by determining mean vesicle size, size distribution, and entrapment efficiency over several month storage periods of niosomal suspension at different temperatures. During storage the niosomes are sampled at regular intervals of time and the percentage of drug which is retained into the niosomes is analyzed by UV spectroscopy or HPLC methods.

8) Vesicular surface charge

Niosomes are generally prepared by the inclusion of charged molecules in the bilayer to prevent the aggregation of formed vesicles. When dicetyl phosphate like charged molecule was incorporated in vesicles, a reduction in aggregation of vesicle was observed. The charge on vesicles is expressed in terms of zeta potential and calculated using the Henry's equation.

Where,

$$\xi = \frac{\mu E \pi \eta}{\Sigma}$$

ξ = Zeta potential

μE = Electrophoretic mobility μ = Viscosity of medium

APPLICATIONS OF NIOSOMES

1) Targeting of bioactive agents

a) To reticulo-endothelial system (RES)

The vesicles are preferentially taken by the cells of RES. It can be used in the treatment of animal tumors known to metastasize to the liver and spleen and in parasitic infestation of liver.

b) To organs other than RES

It has been suggested that carrier system reaches at specific site in the body by the use of antibodies. Immunoglobulin is a convenient means for targeting of drug carrier.

2) For the treatment of Leishmaniasis

Leishmaniasis is a disease state in which the parasite invades cells and liver. Antimonials are most commonly preferred drugs. The antimony study was done on mice and it was concluded that increased sodium stibogluconate efficacy of niosomal formulation, effect of two dose on successive days was additive. Niosomes are also effective as liposomes of loaded drug in experimental leishmaniasis.

3) Tumor targeting

For effective cancer chemotherapy, a high concentration of anticancer agent is required at the tumor site. This minimizes the concentration of the drug in other tissue compartments of the body, thus minimizing their adverse reactions. Niosomes have been studied by several groups for enhanced delivery of anticancer agents to regional lymphatics prepared niosomes of cytarabine hydrochloride by lipid hydration method that excluded dicetyl phosphate to obtain vesicles of smaller size. The size of the vesicles obtained ranged from 600 to 1000nm. Among the different surfactants selected (Span 60, Span 80, Tween 20, Tween 80), Span 60

formulation yielded the slowest release rate. Release occurred in two phases, an initial burst release that lasted for 2-6h, followed by a sustained release that was maintained for at least 16h.

4) For the treatment of AIDS

AIDS is caused by human immunodeficiency virus (HIV), which is characterized by severely damaged immune system. Zidovudine (AZT) is anti-HIV compound which is used for AIDS treatment. It is given alone or in combination with anti-viral drugs. In one of the study, the niosome made by addition of Tween 80 showed high entrapped amount of AZT drug and addition of diacetyl phosphate increased the drug release for prolonged time (88.72% over 12 hours). During preparation of niosomes, the molecular ratios of non-ionic surfactant with constant ratio of cholesterol, the entrapment efficiency was changed and controlled release of AZT was observed.

5) Niosome as carrier for haemoglobin

Niosomes are used as carrier for haemoglobin. Vesicles are easily permeable to oxygen and haemoglobin curve can be modified similarly to non-capsulated haemoglobin. Niosomal suspension shows a visible spectrum which is superimposable onto that of free haemoglobin

6) Antibiotics

The non-ionic surfactant vesicles (niosomes) are used as carrier for ophthalmic delivery of a water soluble local antibiotic. Gentamicin sulphate was investigated and results demonstrated that niosomes are the promising ophthalmic carriers for topical application of gentamicin sulphate.

7) Protein and peptide

Niosomes can be established as sustain release oral formulation for transport of peptide and protein.

8) Transdermal delivery

Niosomes as a transdermal drug delivery systems was studied and also their ability to enhance drug permeation and reduce skin irritation through the intact stratum corneum was also studied. Permeation of ketorolac (a potent NSAID) across excised rabbit skin from various proniosome gel formulation was investigated using Franz diffusion cells. The prepared proniosomes significantly improved drug permeation and reduced and reduced lag time.

FUTURE PROSPECTS

Niosome is a promising drug delivery system. Niosome can be used to encapsulate toxic drugs like anti-cancer, anti-viral, anti-AIDs etc and can increase their bioavailability and targeting properties. Special storage and handling conditions are not required for niosomes.

CONCLUSION

Niosomes represent a promising and novel drug delivery technology. They are drug carriers to design effective drug delivery system. They offer a great opportunity for loading hydrophilic, lipophilic or both drugs together. Many studies have been demonstrated that niosomes improve the stability of entrapped drug, reduce the dose and enable targeted delivery to a specific site. Niosomes appears to be well preferred drug delivery system over liposome as niosomes are stable and economic. This system is widely accepted by the researchers as well as academicians. Niosomes have a great drug delivery potential for targeted delivery of anti-cancer, anti-infective, anti-inflammatory agents, transdermal drug delivery and recently as vaccine adjuvant and as diagnostic agents.

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