

## REVIEW ARTICLE ON NIOSOMES AS NOVEL DRUG DELIVERY SYSTEM

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### ABSTRACT

Niosomes are non-ionic surfactant vesicles obtained by hydrating mixture of cholesterol and nonionic surfactants. It can be used as carriers of amphiphilic and lipophilic drug. In niosomes drug delivery system, the medication is encapsulated in a vesicle. Niosomes are biodegradable, biocompatible non-immunogenic and exhibit flexibility in their structural characterization. The main object of this review is the application of niosome technology is used to treat several diseases, niosomes have good opportunity in research and beneficial for researcher and pharma industries. Niosomes appear to be a well preferred drug delivery system over liposomes as niosomes being stable and economic. Also, niosomes have great drug delivery potential for targeted delivery of anti-cancer, anti-infective agents. Drug delivery potential of niosomes can be enhanced by using novel drug delivery concepts like proniosomes, discosomes and asposomes. Niosomes also serve better aid in diagnostic imaging and as a vaccine adjuvant. Thus, these areas need further exploration and research to bring out or to make for commercially available niosomal preparation.

**Keywords:** Niosomes, Compositions, Methods of Preparation, Encapsulation, Surfactants, Vesicles and Applications.

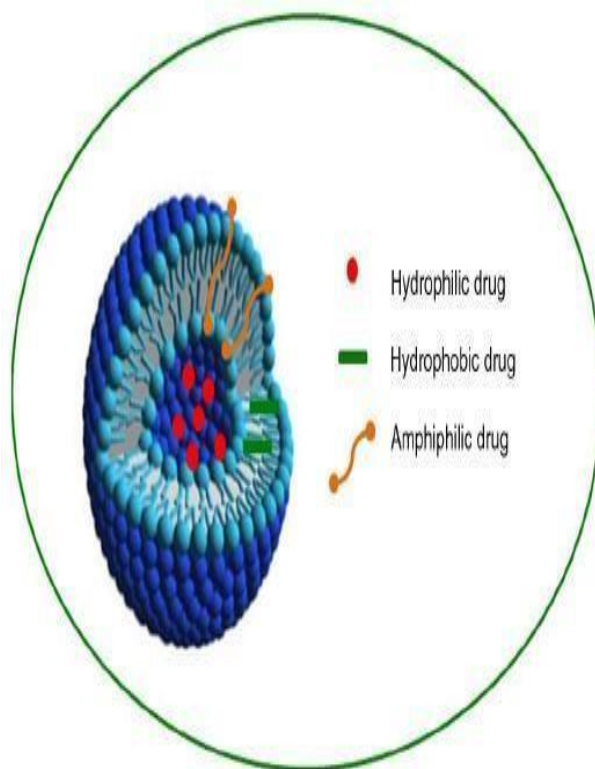
### INTRODUCTION

Paul Ehrlich, in 1909, initiated the era of development for targeted delivery when he envisaged a drug delivery mechanism that would target directly to diseased cells. 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. (Baillie et al., 1985) The vesicle is composed of a bilayer of non-ionic surface- a c t i v e 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 diacetyl phosphate. (Hunter et al., 1988)

### STRUCTURE OF NIOSOME

A typical niosome vesicle would consist of a vesicle forming amphiphilic i.e., a non-ionic surfactant such as Span-60, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as diacetyl phosphate, which also helps in stabilizing the vesicle.



**SALIENT FEATURES OF NIOSOMES:**

- Niosomes are osmotically stable and can entangle the solute and increase the firmness of entangled drug.
- Niosomes are non-ionic surfactants that are biocompatible, non-immunogenic and biodegradable.
- Niosomes possess a framework which comprises of deliquescent and hydrophobic largely along so allows the drug molecules with a large vary of solubility.
- Labile and sensitive medication can be easily delivered by niosomes.
- Niosomes are usually flexible structurally so they can be designed according to the desired situation.
- Availability of the drug at the site is better, just by securing the drug from biological environment.
- Solubility and oral bioavailability of sparingly soluble drugs are improved by niosomes and skin penetrability of drugs which are applied topically is enhanced [10, 11, 12].

**ADVANTAGES:**

- Reduced side effects and shows maximum duration of action.
- Patient compliance is more compared to other delivery system.
- Quantity of drug used is very less for achieving its desired effect.
- Active ingredient or constituent present in the preparation is protected by bilayer from various factors present inside and outside the body.
- Act as depot formulation, thus the drug is released in a controlled manner.
- Drug is protected from first pass metabolism and gastro- intestinal degradation.
- Possess stable structure even in emulsion form Niosomes are available in oral, topical as well as parenteral routes [10, 13, 14].

- Niosomal dispersion in an aqueous phase can be emulsified in a non-aqueous phase to regulate the delivery rate of drug and administer normal vesicle in external non- aq media
- The vesicle suspension is water-based vehicle. This offers high patient compliance in comparison with oily dosage forms.
- Niosomes possess an infrastructure consisting of hydrophilic, amphiphilic and lipophilic moieties together and as a result can accommodate drug molecules with a wide range of solubilities.. The characteristics of the vesicle formulation are variable and controllable.
- The vesicles may act as a depot, releasing the drug in a controlled manner.
- They are osmotically active and stable, as well as they increase the stability of entrapped drug.
- They improve oral bioavailability of poorly absorbed drugs and enhance skin penetration of drugs.
- They can be made to reach the site of action by oral, parenteral as well as topical routes.
- The surfactants are biodegradable, biocompatible and non-immunogenic hence can be used safely in preparation of Niosomes.

**DISADVANTAGES:**

- Time consuming process.
- Specialized equipment's are required for processing.
- Limited shelf life due to-
  - 1) Fusion
  - 2) Aggregation
  - 3) Leakage of entrapped drugs
  - 4) Hydrolysis of encapsulated drugs.

Physically unstable [15, 16, 17]

- .1. Physical instability
2. Aggregation
3. Fusion
4. Leaking of entrapped drug
5. Hydrolysis of encapsulated drugs which limits the shelf life of the dispersion

#### **COMPOSITION OF NIOSOMES:**

The vital components used in the niosome formulation are:

- Non-ionic surfactants
- Cholesterol
- Charge inducer
- Hydration medium

##### **1) Non-ionic surfactants:**

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 [18]. 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 p-glycoprotein and thus enhance the absorption and targeting [19] of anticancer drugs (example-doxorubicin, daunorubicin, curcumin, morusin) [20, 21, 22, 23], steroids (example-hydrocortisone) [24], HIV-protease inhibitor (example-ritonavir) [25], cardiovascular drugs (example-digoxin, beta-blockers) [26].

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 [27, 28, 29]. 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 2) and also by the calculation of CPP using certain formula [30].

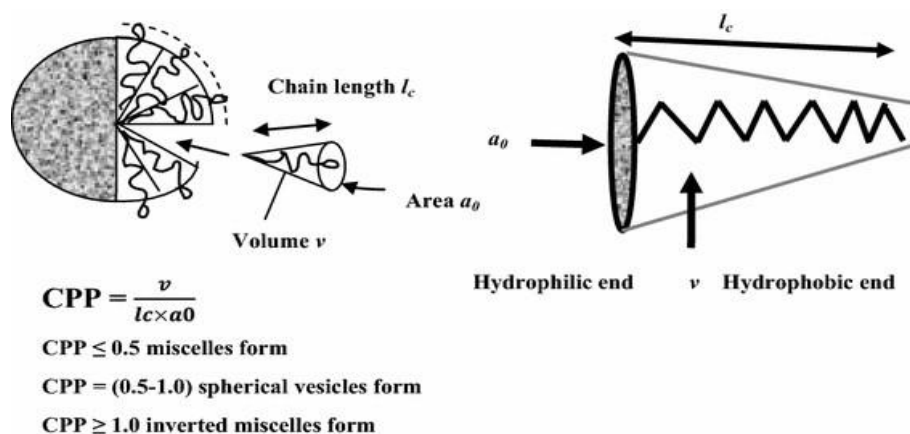


Figure 2: Critical Packing Parameter

**1) 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].

**2) Charge inducers:**

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 phosphotidic acid. Similarly positively charged inducers used in niosomal preparations are stearyl amine (STR) and stearylpyridinium chloride. A concentration of 2-5 mole percentages of charged inducers is bearable because higher concentration can hamper the niosome formation [35, 36].

**3) 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: (Figure 3).

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

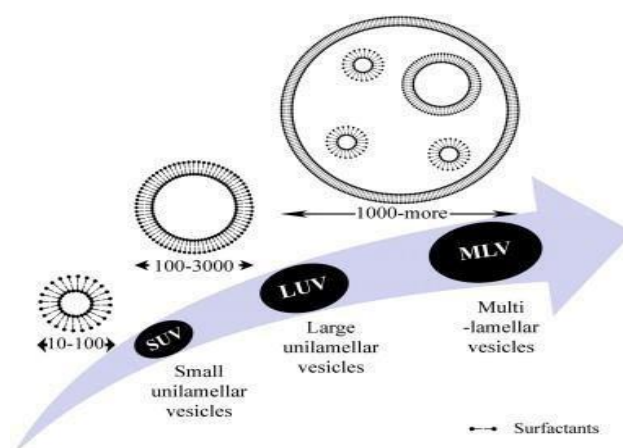


Figure 3: Types of Niosomes

#### 1) Multilamellar vesicles (MLV):

Multilamellar vesicles are most widely niosomes. The size of the vesicles range approximately 0.5-10  $\mu\text{m}$  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 [38, 39]

## PREPARATION METHODS OF NIOSOMES

- 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 [40, 41].

#### 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 [42, 43].

#### 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 [44, 45].

#### 4) Ether injection method:

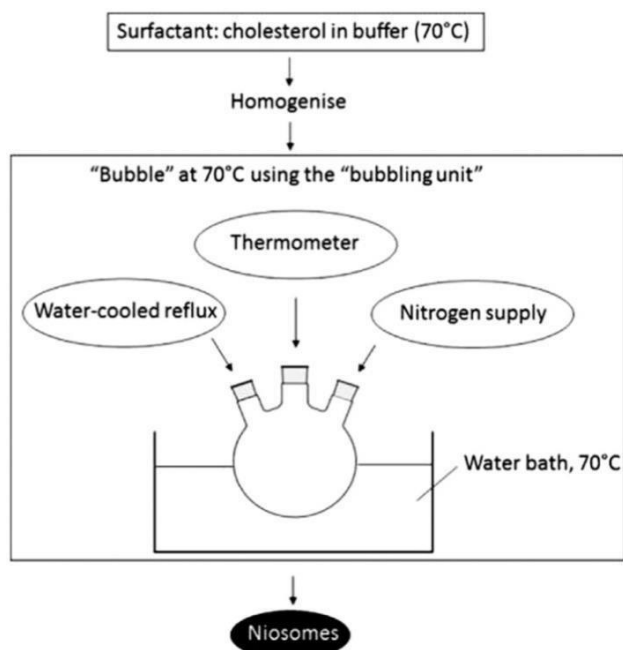
In ether injection method, the niosomes are prepared by introducing a solution of surfactant which is dissolved in diethyl ether (volatile organic solvent) into warm water which is maintained at 60°C. The surfactant mixture in ether is injected into an aqueous solution of material with the help of 14-gauge needle. Single layered vesicles are formed by vapourization of ether (volatile organic solvent) [46].

### 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 [47, 48, 49].

### 1) 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 [50,51] (Figure 4).

**1) 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 [52].

**2) 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 [53, 54]

**8) Formation of niosomes from proniosomes:**

By addition of aqueous phase with drug to the preniosomes with short agitation at a temperature greater than mean transition phase temperature of the surfactant results in the formation of the niosomes [55].

$$T > T_m$$

Where,

T = Temperature

T<sub>m</sub> = Mean phase transition temperature

Blazek-Walsh A.I et al has described the formulation of niosomes from maltodextrin based preniosomes. 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 [56, 57].

#### **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 unentrapped 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 unentrapped 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 [65]. Change in HLB value has impact on niosome formulation (Table 1). Inclusion of cholesterol in niosomes increases the hydrodynamic diameter and entrapment efficiency. At high cholesterol concentration, the gel state is transformed to a 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 [66]. Table 1: HLB value and their impact on niosome formation.

HLB Value	Impact on niosome formation
>6	Need to add cholesterol in formation of bilayer formation.
1.7-8.6	Decreases entrapment efficiency of niosomes.
14-16	Does not produce niosomes.
8.6	Increases entrapment efficiency of niosomes.
Lower value	Need to add cholesterol to increase stability.

#### 1) 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].

## 2) 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 [68].

## CHARACTERIZATION OF NIOSOMES:

### 1) Entrapment Efficiency:

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 [69].



### 2) Vesicle size and shape:

The shape of niosomal vesicles is assumed to be spherical, and their mean diameter can be determined by using laser light 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 increases the vesicle diameter, which might lead to the fusion of vesicles during the cycle [49].

### 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 wavelength reported in the respective monograph of that particular drug [70].

### 1) Number of lamellae:

Number of lamellae in niosomes can be determined by using electron microscope, NMR spectroscopy or X-ray scattering method [44].

### 2) Membrane rigidity:

Membrane rigidity of the niosome is measured by means of mobility of fluorescence probe as function of temperature [60].

### 3) Bilayer formation:

Assembly of non-ionic surfactants to form bilayer vesicle is characterized by the formation of X-cross under light polarization microscopy [71].

**4) 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 [72].

**5) 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: [70].

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

where,

$\xi$  = Zeta potential

$\mu E$  = Electrophoretic mobility  $\mu$  = Viscosity of medium

$\Sigma$  = Dielectric constant

**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 system reaches at specific site in the body by the

use of antibodies. Immunoglobulin is a convenient means for targeting of drug carrier [73].

2) For the treatment of Leshmaniasis:

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 [74].

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 [75].

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 [76].

**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 [53].

**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 [77].

**7) Protein and peptide:**

Niosomes can be established as sustain release oral formulation for transport of peptide and protein [78].

**8) Transdermal delivery:**

Niosomes as a transdermal drug delivery system 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 [79].

#### 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

Niosomal drug delivery system is one of the best examples of great evolution in drug delivery technologies and nanotechnology. It is obvious that niosome appears to be a well preferred drug delivery system over other dosage form as niosome mostly stable in nature and economic. There is lot of scope to encapsulate toxic anti-cancer drugs, anti-infective drugs, anti-AIDS drugs, anti-inflammatory drugs, anti-viral drugs, etc. in niosomes and to use them as promising drug carriers to achieve better bioavailability and targeting properties and for reducing the toxicity and side effects of the drugs. Thus these areas require further systemic consideration and research so as to bring out commercially and valuable available niosomal preparation. The concept of incorporating the drug into or niosomes for a better targeting of the drug at appropriate tissue destination is widely accepted by researchers and academicians. The ionic drug carriers are relatively toxic and unsuitable whereas niosomal carriers are safer. And also handling and storage of niosomes require no special conditions. Niosomes represent a promising drug delivery module. They have similar structure to liposome, to little same in property 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 multi-environmental structure. Niosomes are thoughts to be better candidate drug delivery as compared to liposomes due to various factors like cost, stability etc. Niosomes have very important and key role in various types of drug deliveries; like targeting, topical, ophthalmic and parenteral. Niosomes are very useful in bright future for pharma industries.

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