

## Review Article



## NIOSOMES: A NOVEL DRUG DELIVERY SYSTEM

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## ABSTRACT

On admixture of non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol with subsequent hydration in aqueous media, microscopic lamellar structures formed are known as niosomes or non-ionic surfactant vesicles. Method of preparation of niosome is same as of liposome technology i.e. hydration by aqueous phase of the lipid phase which may be either a pure surfactant or a mixture of surfactant with cholesterol. After preparing niosomal dispersion, untrapped drug is separated by dialysis centrifugation or gel filtration. A method of *in-vitro* release rate study includes the use of dialysis tubing. Niosomes are unilamellar or multilamellar vesicles formed from synthetic non-ionic surfactants. Niosomal drug delivery is potentially applicable to many pharmacological agents for their action against various diseases.

**Keywords:** Niosomes, Encapsulation, Surfactants, Vesicles.

## INTRODUCTION

At present no available drug delivery system achieves the site specific delivery with controlled release kinetics of drug in predictable manner. 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 cell. Since then, numbers of carriers were utilized to carry drug at the target organ/tissue, which include immunoglobulins, serum proteins, synthetic polymers, liposomes, microspheres, erythrocytes, niosomes etc<sup>1</sup>. Among different carriers liposomes and niosomes are well documented drug delivery. 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 nontarget tissue<sup>2</sup>. Niosomes or non-ionic surfactant vesicles are microscopic lamellar structures formed on admixture of non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol with subsequent hydration in aqueous media<sup>3</sup>. In niosomes, the vesicles forming amphiphile 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<sup>4</sup>. Schematic representation of a drug targeting through its linkage to niosome via antibody is shown in figure 1.

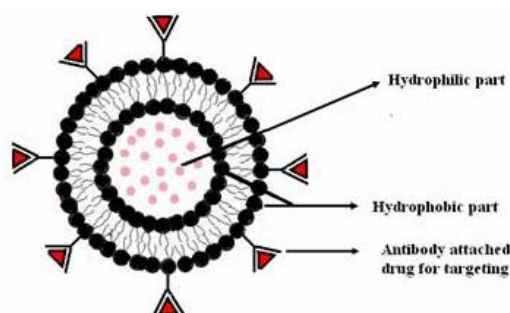


Figure 1: Showing structure of Niosome<sup>4</sup>

## ADVANTAGES OF NIOSOMES

L'Oreal devised the first report of non-ionic surfactant vesicles came from the cosmetic applications<sup>4</sup>. The application of vesicular (lipid vesicles and non-ionic surfactant vesicles) systems in cosmetics and for therapeutic purpose may offer several advantages:

- 1) The vesicle suspension is water-based vehicle thus offers high patient compliance in comparison with oily dosage forms.
- 2) Due to the unique infrastructure consisting of hydrophilic, amphiphilic and lipophilic moieties together they, as a result can accommodate drug molecules with a wide range of solubilities.
- 3) The characteristics of the vesicle formulation are variable and controllable. Altering vesicle composition, size, lamellarity, tapped volume, surface charge and concentration can control the vesicle characteristics.
- 4) The vesicles may act as a depot, releasing the drug in a controlled manner.

## Additional Advantages of Niosomes

- 1) They are osmotically active and stable, and also they increase the stability of entrapped drug.
- 2) Handling and storage of surfactants requires no special conditions.
- 3) They improve oral bioavailability of poorly absorbed drugs and enhance skin penetration of drugs.
- 4) They can be made to reach the site of action by oral, parenteral as well as topical routes.
- 5) The surfactants are biodegradable, biocompatible and non-immunogenic.
- 6) They improve the therapeutic performance of the drug molecules by delayed clearance from the circulation,



protecting the drug from biological environment and restricting effects to target cells.

### Comparison of Niosomes Vs Liposome's

**a)** Niosomes are now widely studied as an alternative to liposome's, which exhibit certain disadvantages such as – they are expensive, their ingredients like phospholipids are chemically unstable because of their predisposition to oxidative degradation, they require special storage and handling and purity of natural phospholipids are variable.

**b)** Differences in characteristics exist between liposome's and niosomes, especially since niosomes are prepared from uncharged single-chain surfactant and cholesterol whereas liposome's are prepared from double-chain phospholipids (neutral or charged)<sup>5</sup>. Handjani-Vila *et al*<sup>6</sup> were first to report the formation of vesicular system on hydration of mixture of cholesterol and a single-alkyl chain non-ionic surfactant.

**c)** Niosomes behave *in-vivo* like liposome's, prolonging the circulation of entrapped drug and altering its organ distribution and metabolic stability<sup>7</sup>. Encapsulation of various anti neoplastic agents in these carrier vesicles has been shown to decrease drug induced toxic side effects, while maintaining, or in some instances, increasing the anti-tumour efficacy<sup>8</sup>. Such vesicular drug carrier systems alter the plasma clearance kinetics, tissue distribution, metabolism and cellular interaction of the drug<sup>7,9</sup>. They can be expected to target the drug to its desired site of action and/or to control its release<sup>10</sup>.

**d)** As with liposome's, the properties of niosomes depends both on the composition of the bilayer and on method of their production<sup>11</sup>. It was observed by Baillie *et al*<sup>10</sup> that the intercalation of cholesterol in the bilayers decreases the entrapment volume during formulation and thus entrapment efficiency. As the concentration of cholesterol increases, entrapment efficiency decreases.

**e)** The entrapment efficiency increases with increase in the concentration and lipophilicity of surfactant<sup>12</sup>. Chandraprakash *et al*<sup>12</sup> made Methotrexate loaded non-ionic surfactant vesicles using lipophilic surfactants like Span 40, Span 60 and Span 80 and found that Span 60 (HLB = 4.7) gave highest percent entrapment while Span 85 (HLB = 9.8) gave least entrapment. They also observed that as HLB value of surfactant decreased, the mean size was reduced.

### Types of Niosome

Niosomes can be divided into three groups on the basis of their vesicles size:

- (i) Small Unilamellar Vesicles (SUV, Size=0.025-0.05  $\mu\text{m}$ )
- (ii) Multilamellar Vesicles (MLV, Size=>0.05  $\mu\text{m}$ )
- (iii) Large Unilamellar Vesicles (LUV, Size=>0.10  $\mu\text{m}$ ).

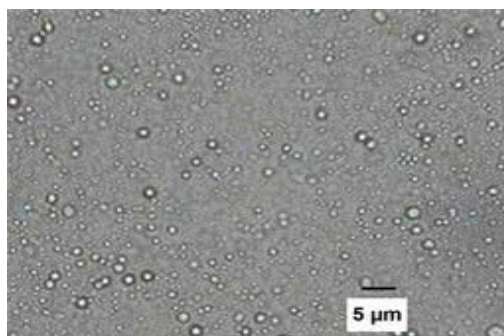
### METHODS OF PREPARATION OF NIOSOMES

Niosomes are prepared by different methods based on the desired sizes of the vesicles and their distribution,

number of double layers, entrapment efficiency of the aqueous phase and permeability of vesicle membrane.

### (i) Preparation of Small Unilamellar Vesicles

**(a) Sonication:** The aqueous phase containing drug is added to the mixture of surfactant and cholesterol in a scintillation vial<sup>13</sup>. The mixture is probe sonicated at 60°C for 3 minutes to produce small and uniform in size niosomes.



**Figure 2:** Photomicrograph of Niosomes after Sonication<sup>13</sup>

**(b) Micro fluidization:** Micro fluidization is a recent technique to prepare unilamellar vesicles of defined size distribution. This method is based on submerged jet principle in which two fluidized streams interact at ultra high velocities, in precisely defined micro channels within the interaction chamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation. The result is a greater uniformity, smaller size and better reproducibility of niosomes formed<sup>14</sup>.

### (ii) Preparation of Multilamellar Vesicles

**(a) Hand shaking method (Thin film hydration technique):** In the hand shaking method, surfactant and cholesterol are dissolved in a volatile organic solvent (such as diethyl ether, chloroform or methanol) in a round bottom flask. The organic solvent is removed at room temperature (20°C) using rotary evaporator leaving a thin layer of solid mixture deposited on the wall of the flask. The dried surfactant film is hydrated with aqueous phase containing drug at 50-60°C with gentle agitation. This process forms typical multilamellar niosomes<sup>13</sup>.

**(b) Trans-membrane pH gradient (inside acidic) drug uptake process (remote loading):** Surfactant and cholesterol are dissolved in chloroform<sup>15</sup>. The solvent is then evaporated under reduced pressure to obtain a thin film on the wall of the round-bottom flask. The film is hydrated with 300 mM citric acid (pH 4.0) by vortex mixing. The multilamellar vesicles are frozen and thawed three times and later sonicated. To this niosomal suspension, aqueous solution containing 10 mg/ml of drug is added and vortexed. 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 produce the desired multilamellar vesicles.



**(iii) Preparation of Large Unilamellar Vesicles**

**(a) Reverse phase evaporation technique (REV):** In this method, cholesterol and surfactant are dissolved in a mixture of ether and chloroform<sup>16</sup>. An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. The clear gel formed is further sonicated after the addition of a small amount of phosphate buffered saline. The organic phase is removed at 40°C under low pressure. The resulting viscous niosome suspension is diluted with phosphate-buffered saline and heated in a water bath at 60°C for 10 min to yield niosomes.

**(b) Ether injection method:** The ether injection method is essentially based on slow injection of niosomal ingredients in diethyl ether through a 14-gauge needle at the rate of approximately 0.25 ml/min into a preheated aqueous phase maintained at 60°C<sup>13,17</sup>. The probable reason behind the formation of larger unilamellar vesicles is that the slow vaporization of solvent results in an ether gradient extending towards the interface of aqueous-non-aqueous interface. The former may be responsible for the formation of the bilayer structure. The disadvantages of this method are that a small amount of ether is frequently present in the vesicles suspension and is difficult to remove.

**(iv) Miscellaneous**

**(a) Multiple membrane extrusion method:** A mixture of surfactant, cholesterol, and diacetyl phosphate in chloroform is made into thin film by evaporation. The film is hydrated with aqueous drug solution and the resultant suspension extruded through polycarbonate membranes, which are placed in a series for up to eight passages. This is a good method for controlling niosome size<sup>14</sup>.

**(b) Emulsion method:** The oil in water (o/w) emulsion is prepared from an organic solution of surfactant, cholesterol, and an aqueous solution of the drug<sup>18,19</sup>. The organic solvent is then evaporated, leaving niosomes dispersed in the aqueous phase.

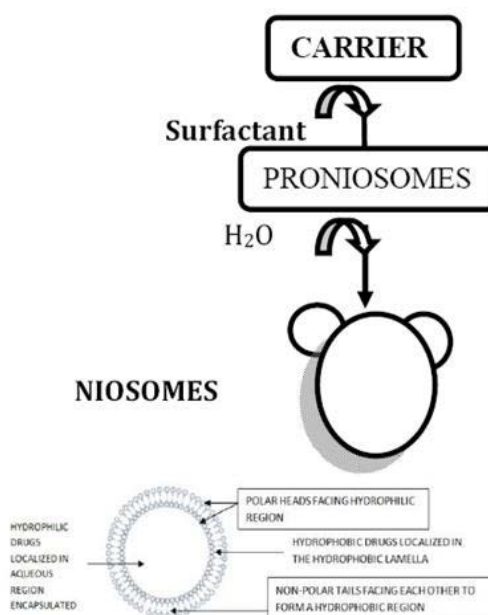
**(c) Lipid injection method:** This method does not require expensive organic phase. Here, the mixture of lipids and surfactant is first melted and then injected into a highly agitated heated aqueous phase containing dissolved drug. Here, the drug can be dissolved in molten lipid and the mixture will be injected into agitated, heated aqueous phase containing surfactant.

**(d) The “bubble” method:** It is novel technique for the one step preparation of liposome's and niosomes without the use of organic solvents. The bubbling unit consists of round-bottomed flask with three necks positioned in 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<sup>20</sup>.

**(e) Formation of Niosomes from Proniosomes:** Another method of producing niosomes is to coat a water-soluble carrier such as sorbitol with surfactant. The result of the coating process is a dry formulation. In which each water-soluble particle is covered with a thin film of dry surfactant. This preparation is termed “Proniosomes”. The niosomes are recognized by the addition of aqueous phase at  $T > T_m$  and brief agitation<sup>21</sup>.

$T$  = Temperature

$T_m$  = Mean phase transition temperature



**Figure 3:** Steps involved in formation of Niosomes<sup>21</sup>

**Table 1:** Drugs Incorporated into Niosomes by Various Methods

| Method of Preparation | Drug Incorporated                       |
|-----------------------|-----------------------------------------|
| Ether Injection       | Sodium stibogluconates <sup>13,22</sup> |
|                       | Doxorubicin                             |
| Hand Shaking          | Methotrexate <sup>23</sup>              |
|                       | Doxorubicin                             |
| Sonication            | 9-desglycinamide                        |
|                       | 8-arginine                              |
|                       | Vasopressin                             |
|                       | Oestradiol <sup>21</sup>                |

**Separation of Untrapped Drug**

The removal of untrapped solute from the vesicles can be accomplished by various techniques, which include:

**(i) Dialysis**

The aqueous niosomal dispersion is dialyzed in dialysis tubing against phosphate buffer or normal saline or glucose solution<sup>20</sup>.

**(ii) Gel Filtration**

The untrapped drug is removed by gel filtration of niosomal dispersion through a Sephadex-G-50 column and elution with phosphate buffered saline or normal saline<sup>24,25</sup>.

**(iii) Centrifugation**

The niosomal suspension is centrifuged and the supernatant is separated. The pellet is washed and then resuspended to obtain a niosomal suspension free from untrapped drug<sup>26,27</sup>.

**CHARACTERIZATION OF NIOSOMES****(i) Size**

Shape of niosomal vesicles is assumed to be spherical, and their mean diameter can be determined by using laser light scattering method<sup>28</sup>. Also, diameter of these vesicles can be determined by using electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy, optical microscopy and freeze fracture electron microscopy<sup>29,30</sup>. Freeze thawing (keeping vesicles suspension at -20°C for 24 hrs and then heating to ambient temperature) of Niosomes increases the vesicle diameter, which might be attributed to fusion of vesicles during the cycle<sup>14</sup>.

**(ii) Bilayer Formation**

Assembly of non-ionic surfactants to form a bilayer vesicle is characterized by an X-cross formation under light polarization microscopy<sup>31</sup>.

**(iii) Number of Lamellae**

This is determined by using nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering and electron microscopy<sup>30</sup>.

**(iv) Membrane Rigidity**

Membrane rigidity can be measured by means of mobility of fluorescence probe as a function of temperature<sup>31</sup>.

**(v) Entrapment Efficiency**

After preparing niosomal dispersion, untrapped drug is separated by dialysis, centrifugation, or gel filtration as described above and the drug remained entrapped in Niosomes is determined by complete vesicle disruption using 50% n-propanol or 0.1% Triton X-100 and analyzing the resultant solution by appropriate assay method for the drug<sup>32</sup>.

Entrapment efficiency = (Amount entrapped / total amount) x 100

**In Vitro Release Study**

A method of *in vitro* release rate study has been reported with the help of dialysis tubing<sup>24</sup>. A dialysis sac is washed and soaked in distilled water. The vesicle suspension is pipetted into a bag made up of the tubing and sealed. The bag containing the vesicles is then placed in 200 ml buffer solution in a 250 ml beaker with constant shaking at 25°C or 37°C. At various time intervals, the buffer is analyzed for the drug content by an appropriate assay method. In another method, isoniazid-encapsulated niosomes are separated by gel filtration on Sephadex G-50 powder kept in double distilled water for 48 h for swelling<sup>33</sup>. At first, 1 ml of prepared niosome suspension is placed on the top

of the column and elution is carried out using normal saline. Niosomes encapsulated isoniazid elutes out first as a slightly dense, white opalescent suspension followed by free drug. Separated niosomes are filled in a dialysis tube to which a sigma dialysis sac is attached to one end. The dialysis tube is suspended in phosphate buffer of pH (7.4), stirred with a magnetic stirrer, and samples are withdrawn at specific time intervals and analyzed using high-performance liquid chromatography (HPLC) method.

**In Vivo Release Study**

Albino rats are used for this study. These rats are subdivided with groups. Niosomal suspension used for *in vivo* study is injected intravenously (through tail vein) using appropriate disposal syringe.

**Factors Affecting Physico-chemical Properties of Niosomes**

Various factors that affect the physico-chemical properties of niosomes are discussed further.

**(i) Nature of Surfactants**

A surfactant used for preparation of niosomes 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<sup>19</sup>. The ether type surfactants with single chain alkyl as hydrophobic tail is more toxic than corresponding dialkyl ether chain<sup>34</sup>. The ester type surfactants are chemically less stable than ether type surfactants and the former is less toxic than the latter due to ester-linked surfactant degraded by esterase's to triglycerides and fatty acid *in vivo*<sup>34</sup>. The surfactants with alkyl chain length from C12-C18 are suitable for preparation of niosomes<sup>35,36</sup>. Surfactants such as C16EO5 (poly-oxyethylene cetyl ether) or C18EO5 (polyoxyethylene steryl ether) are used for preparation of polyhedral vesicles<sup>37</sup>. Span series surfactants having HLB number of between 4 and 8 can form vesicles<sup>24</sup>.

**Table 2:** Different Types of Non-Ionic Surfactant<sup>24</sup>

| Type of Non-ionic surfactant | Examples                                                                            |
|------------------------------|-------------------------------------------------------------------------------------|
| Fatty alcohol                | Cetyl alcohol, Steryl alcohol, Cetosteryl alcohol, oleyl alcohol                    |
| Ethers                       | Brij, Decyl glucoside, Lauryl glucoside, Octyl glucoside, Triton X-100, Nonoxynol-9 |
| Esters                       | Glyceryl laurate, Polysorbates, Spans                                               |
| Block copolymers             | Poloxamers                                                                          |

**(ii) Structure of Surfactants**

The geometry of vesicle to be formed from surfactants is affected by its structure, which is related to critical packing parameters. On the basis of critical packing parameters of surfactants, we can predicate geometry of vesicle to be formed. Critical packing parameters can be defined using following equation,

CPP (Critical Packing Parameters) =  $v/lc \times a_0$



Where  $v$  = hydrophobic group volume,  $l_c$  = the critical hydrophobic group length,  $a_0$  = the area of hydrophilic head group.

From the critical packing parameter value type of micellar structure formed can be ascertained as given below,

If  $CPP < \frac{1}{2}$ , then formation of spherical micelles,

If  $\frac{1}{2} < CPP < 1$ , then formation of bilayer micelles,

If  $CPP > 1$ , then formation inverted micelles.

### (iii) Amount and type of surfactant

The mean size of niosomes increases proportionally with increase in the HLB of 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<sup>24</sup>.

The bilayers of the vesicles are either in the so-called liquid state or in gel state, depending on the temperature, the type of lipid or surfactant and the presence of other components such as cholesterol. In the gel state, alkyl chains are present in a well-ordered structure, and 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)<sup>38</sup>. Phase transition temperature (TC) of surfactant also affects entrapment efficiency i.e. Span 60 having higher TC, provides better entrapment.

### (iv) Membrane Composition

The stable niosomes can be prepared with addition of different additives along with surfactants and drugs. Niosomes formed have a number of morphologies and their permeability and stability properties can be altered by manipulating membrane characteristics by different additives. In case of polyhedral niosomes formed from C16G2, the shape of these polyhedral niosome remains unaffected by adding low amount of solulan C24 (cholesteryl poly-24-oxyethylene ether), which prevents

aggregation due to development of steric hindrance<sup>39</sup>. The mean size of niosomes is influenced by membrane composition such as Polyhedral niosomes formed by C16G2: solulan C24 in ratio (91:9) having bigger size ( $8.0 \pm 0.03\text{mm}$ ) than spherical/tubular niosomes formed by C16G2: cholesterol: solulan C24 in ratio (49:49:2) ( $6.6 \pm 0.2\text{mm}$ )<sup>39</sup>. Addition of cholesterol molecule to niosomal system provides rigidity to the membrane and reduces the leakage of drug from niosome<sup>40</sup>.

Inclusion of cholesterol in niosomes increases its hydrodynamic diameter and entrapment efficiency<sup>24</sup>. In general, the action of cholesterol is two folds; on one hand, cholesterol increases the chain order of liquid-state bilayers and on the other, cholesterol decreases the chain order of gel state bilayers. At a high cholesterol concentration, the gel state is transformed to a liquid-ordered phase<sup>27</sup>.

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<sup>27,41</sup>. Presence of charge tends to increase the interlamellar distance between successive bilayers in multilamellar vesicle structure and leads to greater overall entrapped volume.

### (v) Nature of Encapsulated Drug

The physico-chemical properties of encapsulated drug influence charge and rigidity of the niosome bilayer. The drug interacts with surfactant head groups and develops the charge that creates mutual repulsion between surfactant bilayers and hence increases vesicle size<sup>42</sup>. The aggregation of vesicles is prevented due to the charge development on bilayer. In polyoxyethylene glycol (PEG) coated vesicles, some drug is entrapped in the long PEG chains, thus reducing the tendency to increase the size<sup>26</sup>. The hydrophilic lipophilic balance of the drug affects degree of entrapment.

**Table 3:** Effect of the nature of drug on the formation of niosomes<sup>26</sup>

| Nature of the drug | Leakage from the vesicles | Stability | Other properties                                          |
|--------------------|---------------------------|-----------|-----------------------------------------------------------|
| Hydrophobic drug   | Decreased                 | Increased | Improved transdermal delivery                             |
| Hydrophobic drug   | Increased                 | Decreased | -                                                         |
| Amphiphilic drug   | Decreased                 | -         | Increased encapsulation, Altered electrophoretic mobility |
| Macromolecules     | Decreased                 | Increased | -                                                         |

### (vi) Temperature of Hydration

Hydration temperature influences the shape and size of the niosome. For ideal condition it should be above the gel to liquid phase transition temperature of system. Temperature change of niosomal system affects assembly of surfactants into vesicles and also induces vesicle shape transformation<sup>19,39</sup>. Arunothayanun *et al.* reported that a polyhedral vesicle formed by C16G2: solulan C24 (91:9) at 25°C which on heating transformed into spherical vesicle at 48°C, but on cooling from 55°C, the vesicle produced a

cluster of smaller spherical niosomes at 49°C before changing to the polyhedral structures at 35°C. In contrast vesicle formed by C16G2: cholesterol: solulan C24 (49:49:2) shows no shape transformation on heating or cooling<sup>39,43</sup>. Along with the above mentioned factors, volume of hydration medium and time of hydration of niosomes are also critical factors. Improper selection of these factors may result in formation of fragile niosomes or creation of drug leakage problems.



**(vii) Methods of Preparation**

Hand shaking method forms vesicles with greater diameter (0.35-13 nm) compared to the ether injection method (50-1000 nm)<sup>14</sup>. Small sized niosomes can be produced by Reverse Phase Evaporation method<sup>16,44</sup>. Micro fluidization method gives greater uniformity and small size vesicles<sup>14</sup>. Niosomes obtained by Trans membrane pH gradient (inside acidic) drug uptake process showed greater entrapment efficiency and better retention of drug<sup>44</sup>.

**(viii) Resistance to Osmotic Stress**

Addition of a hypertonic salt solution to a suspension of niosomes brings about reduction in diameter. In hypotonic salt solution, there is initial slow release with slight swelling of vesicles probably due to inhibition of eluting fluid from vesicles, followed by faster release, which may be due to mechanical loosening of vesicles structure under osmotic stress<sup>45,46</sup>.

**Therapeutic Applications of Niosomes**

Niosomal drug delivery is potentially applicable to many pharmacological agents for their action against various diseases. Some of their therapeutic applications are discussed below.

**(i) Targeting of Bioactive Agents****(a) To reticulo-endothelial system (RES)**

The cells of RES preferentially take up the vesicles. The uptake of niosomes by the cells is also by circulating serum factors known as opsonins, which mark them for clearance. Such localized drug accumulation has, however, been exploited in treatment of animal tumours known to metastasize to the liver and spleen and in parasitic infestation of liver<sup>45</sup>.

**(b) To organs other than RES**

It has been suggested that carrier system can be directed to specific sites in the body by use of antibodies<sup>47</sup>. Immunoglobulins seem to bind quite readily to the lipid surface, thus offering a convenient means for targeting of drug carrier<sup>43</sup>. Many cells possess the intrinsic ability to recognize and bind particular carbohydrate determinants and this can be exploited to direct carriers system to particular cells.

**(ii) Neoplasia**

Doxorubicin, the anthracyclic antibiotic with broad spectrum anti tumour activity, shows a dose dependant irreversible cardio toxic effect. Niosomal delivery of this drug to mice bearing S-180 tumour increased their life span and decreased the rate of proliferation of sarcoma<sup>48</sup>. Niosomal entrapment increased the half-life of the drug, prolonged its circulation and altered its metabolism. Intravenous administration of Methotrexate entrapped in niosomes to S-180 tumour bearing mice resulted in total regression of tumour and also higher plasma level and slower elimination<sup>49,50</sup>.

**(iii) Leishmaniasis**

Niosomes can be used for targeting of drug in the treatment of diseases in which the infecting organism resides in the organ of reticulo-endothelial system. Leishmaniasis is such a disease in which parasite invades cells of liver and spleen. The commonly prescribed drugs are antimonials, which are related to arsenic, and at high concentration they damage the heart, liver and kidney.

The study of antimony distribution in mice, performed by Hunter *et al* showed high liver level after intravenous administration of the carrier's forms of the drug<sup>34</sup>.

**(iv) Delivery of Peptide Drugs**

Yoshida *et al* investigated oral delivery of 9-desglycinamide, 8-arginine vasopressin entrapped in niosomes in an *in-vitro* intestinal loop model and reported that stability of peptide increased significantly<sup>41</sup>.

**(v) Immunological Application of Niosomes**

Niosomes have been used for studying the nature of the immune response provoked by antigens. Brewer and Alexander have reported niosomes as potent adjuvant in terms of immunological selectivity, low toxicity and stability<sup>51</sup>.

**(vi) Niosomes as a Carrier for Haemoglobin**

Niosomes can be used as a carrier for haemoglobin<sup>52,38</sup>.

**(vii) Transdermal Delivery of Drugs by Niosomes**

Slow penetration of drug 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.

**(viii) Other Applications****a) Sustained Release**

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

**b) 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.

Localized drug action results in enhancement of efficacy of potency of the drug and at the same time reduces its systemic toxic effects e.g. Antimonials encapsulated within niosomes are taken up by mononuclear cells resulting in localization of drug, increase in potency and hence decrease both in dose and toxicity<sup>34</sup>.

**CONCLUSION – FUTURE PROSPECTS**

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. 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. Vesicular drug carriers like niosomes can be transported by macrophages which are known to infiltrate tumour cells. It may be possible to take advantage of these activated macrophage system in delivering the anti-tumour agents within vesicles more quantitatively to tumour sites. So far only animal experimentation of this targeted drug delivery system is reported but further clinical investigations in human volunteers, pharmacological and toxicological investigations in animals and human volunteers may help to exploit niosomes as prosperous drug carriers for targeting drugs more efficiently, for treating cancer, infection and AIDS etc.

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