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(Review Article)

Niosomes: A New Approach to Targeted Drug Delivery

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ABSTRACT

Targeted drug delivery, sometimes called smart drug delivery, is a method of delivering medication to a patient in a manner that increases the concentration of the medication in some parts of the body relative to others. The goal of a targeted drug delivery system is to prolong, localize, target and have a protected drug interaction with the diseased tissue. A niosome is a non-ionic surfactant-based liposome. They are structurally similar to liposomes in having a bilayer, however, the materials used to prepare niosomes make them more stable and thus niosomes offer many more advantages over liposomes. Various type of drug deliveries can be possible using niosomes like targeting, ophthalmic, topical, parentral etc.

Key words: Liposomes, Niosomes, Targeted drug delivery, Surfactants

INTRODUCTION

Smart drug delievery have been developed to optimize regenerative techniques[1]. The system is based on a method that delivers a certain amount of a therapeutic agent for a prolonged period of time to a targeted diseased area within the body. This helps maintain the required plasma and tissue drug levels in the body. Therefore, avoiding any damage to the healthy tissue via the drug. The drug delivery system is highly integrated and requires various disciplines, such as chemists, biologist and engineers, to join forces to optimize this system[2].

A niosome is a non-ionic surfactant-based liposome. Niosomes are formed mostly by cholesterol incorporation as an excipient. Other excipients can also be used. Niosomes have more penetrating capability than the previous preparations of emulsions.[1] They are structurally similar to liposomes in having a bilayer, however, the materials used to prepare niosomes make them more stable and thus niosomes offer many more advantages over liposomes.

Structure of Niosomes

Niosomes are lamellar structures that are microscopic in size. They constitute of non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol with subsequent hydration in aqueous media. The surfactant molecules tend to orient themselves in such a way that the hydrophilic ends of the non-ionic surfactant point outwards, while the hydrophobic ends face each other to form the bilayer as we can see in fig.1. This figure gives a better idea of the lamellar orientation of the surfactant molecules.

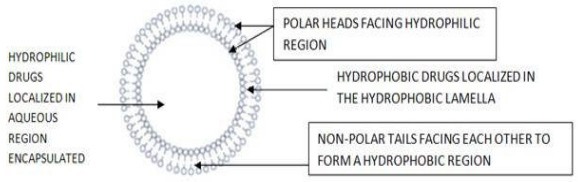

Fig.1: Diagrammatic representation of a niosomes[3]

The non-ionic surfactants form a closed bilayer vesicle in aqueous media based on its amphiphilic nature using some energy for instance heat, physical agitation to form this structure. In the bilayer structure, hydrophobic parts are oriented away from the aqueous solvent, whereas the hydrophilic heads remain in contact with the aqueous solvent. The properties of the vesicles can be changed by varying the composition of the vesicles, size, lamellarity, tapped volume, surface charge and concentration. Various forces act inside the vesicle like Vander Waals forces among surfactant molecules, repulsive forces emerging from the electrostatic interactions among charged groups of surfactant molecules, entropic repulsive forces of the head groups of surfactants, short-acting repulsive forces etc. These forces are responsible for maintaining the vesicular structure of niosomes. But, the stability of niosomes are affected by type of surfactant, nature of encapsulated drug, storage temperature, detergents, use of membrane spanning lipids, the interfacial polymerization of surfactant monomers *in situ*, inclusion of charged molecule[3].

Niosomes may act as a depot, releasing the drug in a controlled manner.The therapeutic performance of the drug

molecules can also be improved by delayed clearance from the circulation, protecting the drug from biological environment and restricting effects to target cells[4]. It can also be used as vehicle for poorly absorbable drugs to design the novel drug delivery system. It enhances the bioavailability by crossing the anatomical barrier of gastrointestinal tract via transcytosis of M cells of Peyer's patches in the intestinal lymphatic tissues[5].

The niosomal vesicles are taken up by reticulo-endothelial system. Such localized drug accumulation is used in treatment of diseases, such as leishmaniasis, in which parasites invade cells of liver and spleen[6,7]. Some non-reticulo-endothelial systems like immunoglobulins also recognize lipid surface of this delivery system[3,4,6-12].Encapsulation of various anti-neoplastic agents in this carrier vesicle has minimized drug-induced toxic side effects while maintaining, or in some instances, increasing the anti-tumour efficacy[13]. Many drugs are administered through niosomes via transdermal route to improve the therapeutic efficacy.

Niosomes provides better drug concentration at the site of action administered by oral, parenteral and topical routes. The evolution of niosomal drug delivery technology is still at the stage of infancy, but this type of drug delivery system has shown promise in cancer chemotherapy and anti-leishmanial therapy.

Advantages

- They help accommodate hydrophilic, lipophilic as well as ampiphilic drug moieties, they can be used for a variety of drugs.
- These are flexible in their nature so can be easily modulated.
- They improve the therapeutic performance of the drug by protecting it from the biological environment and restricting effects to target cells, thereby reducing the clearance of the drug.
- Niosomes offer a controlled release of drug.
- They can increase the oral bioavailability of drugs.
- They are osmotically active and stable.
- They increase the stability of the entrapped drug.
- They can enhance the 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
- Handling and storage of surfactants very easy. The vesicle suspension being water based comply patients need.

COMPARISON OF NIOSOME WITH LIPOSOME

a)Niosomes are now widely studied as an alternative to liposomes, 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 is variable.

b) Differences in characteristics exist between liposomes and niosomes, especially since niosomes are prepared from uncharged single-chain surfactant and cholesterol whereas liposomes are prepared from double-chain phospholipids (neutral or charged)[5]. Handjani-Vila *et al* [6] 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 liposomes, prolonging the circulation of entrapped drug and altering its organ distribution and metabolic stability[7]. 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-tumor efficacy [8]. Such vesicular drug carrier systems alter the plasma clearance kinetics, tissue distribution, metabolism and cellular interaction of the drug[7,9]. They can be expected to target the drug to its desired site of action and/or to control its release [10].

d) As with liposomes, the properties of niosomes depends both on the composition of the bilayer and on method of their production[11]. It was observed by Baillie *et al* [10] 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. Chandraprakash *et al* 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[12].

METHOD OF PREPARATION

A. Ether Injection Method

This method provides a means of making niosomes by slowly introducing a solution of surfactant dissolved in diethyl ether into warm water maintained at 60°C. The surfactant mixture in ether is injected through 14-gauge needle into an aqueous solution of material. Vaporization of ether leads to formation of single layered vesicles. Depending upon the conditions used, the diameter of the vesicle range from 50 to 1000 nm.

B. Hand Shaking Method (Thin Film Hydration Technique)

The mixture of vesicles forming ingredients like surfactant and cholesterol are dissolved in a volatile organic solvent (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 can be rehydrated with aqueous phase at 0-60°C with gentle agitation. This process forms typical multilamellar niosomes[14].

Thermosensitive niosomes were prepared by Raja Naresh et al by evaporating the organic solvent at 60°C and leaving a thin film of lipid on the wall of rotary flash evaporator. The aqueous phase containing drug was added slowly with intermitten t shaking of flask at room temperature followed by sonication[15].

C. Sonication
In this method an aliquot of drug solution in buffer is added to the surfactant/cholesterol mixture in a 10-ml glass vial. The mixture is probe sonicated at 60°C for 3 minutes using a sonicator with a titanium probe to yield niosomes[14].

D. Micro fluidization
Micro fluidization is a recent technique used 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 she*et al*ong 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[16].

E. Multiple membrane extrusion method
Mixture of surfactant, cholesterol and dicetyl 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 series for upto 8 passages. It is a good method for controlling niosome size[16].

F. Reverse Phase Evaporation Technique (REV)
Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform. An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. The clear gel formed is further sonicated after the addition of a small amount of phosphate buffered saline (PBS). The organic phase is removed at 40°C under low pressure. The resulting viscous niosome suspension is diluted with PBS and heated on a water bath at 60°C for 10 min to yield niosomes.
Raja Naresh *et al* have reported the preparation of Diclofenac Sodium niosomes using Tween 85 by this method[15].

G. Trans membrane pH gradient (inside acidic) Drug Uptake Process (remote Loading)
Surfactant and cholesterol are dissolved in chloroform. The solvent is then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask. The film is hydrated with 300 mM citric acid (pH 4.0) by vortex mixing. The multilamellar vesicles are frozen and thawed 3 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 give niosomes[17].

H. The "Bubble" Method
It is novel technique for the one step preparation of liposomes 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[18].

I. 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 > Tm and brief agitation.

T = Temperature.
Tm = mean phase transition temperature.

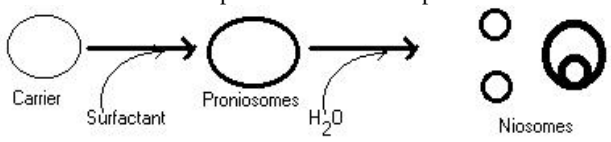

Fig .2: Niosomes from maltodextrin based proniosomes

Blazek-Walsh A.I. *et al* [19] have reported the formulation of niosomes from maltodextrin based proniosomes as shown in fig.2. This provides rapid reconstitution of niosomes with minimal residual carrier. Slurry of maltodextrin and surfactant was dried to form a free flowing powder, which could be rehydrated by addition of warm water[13,14].

Table 1: shows in brief example of some drugs incorporated into niosomes using different methods.

Table 1: Drugs incorporated into niosomes by various methods

Method of preparation	Drug incorporated
Ether Injection	Sodium stibogluconate [14,20] Doxorubicin[21]
Hand Shaking	Methotrexate[12] Doxorubicin[21]
Sonication	9-desglycinamide 8-arginine Vasopressin Oestradiol[5,19]

Separation of Unentrapped Drug
The removal of unentrapped solute from the vesicles can be accomplished by various techniques, which include: -
1. Dialysis [18]
The aqueous niosomal dispersion is dialyzed in a dialysis tubing against phosphate buffer or normal saline or glucose solution.

2. Gel Filtration[22,23]
The unentrapped drug is removed by gel filtration of niosomal dispersion through a Sephadex-G-50 column and elution with phosphate buffered saline or normal saline.

3. Centrifugation[24,25-28]
The niosomal suspension is centrifuged and the supernatant is separated. The pellet is washed and then resuspended to obtain a niosomal suspension free from unentrapped drug.

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[29]. 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[10,30].

(ii) Bilayer Formation

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

(iii) Number of Lamellae

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

(iv) Membrane Rigidity

Membrane rigidity can be measured by means of mobility of fluorescence probe as a function of temperature[31].

(v) Entrapment Efficiency

After preparing niosomal dispersion, unentrapped 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[32].

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

***In Vitro*Release Study**

A method of *in vitro* release rate study was reported with the help of dialysis tubing[26]. A dialysis sac was washed and soaked in distilled water. The vesicle suspension was pipetted into a bag made up of the tubing and sealed. The bag containing the vesicles was 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 was analyzed for the drug content by an appropriate assay method. In another method, isoniazid-encapsulated niosomes were separated by gel filtration on Sephadex G-50 powder kept in double distilled water for 48h for swelling[33]. At first, 1 ml of prepared niosome suspension was placed on the top of the column and elution was carried out using normal saline. Niosomes encapsulated isoniazid elutes out first as a slightly dense, white opalescent suspension followed by free drug. Separated niosomes were filled in a dialysis tube to which a sigma dialysis sac was attached to one end. The dialysis tube was suspended in phosphate buffer of pH (7.4), stirred with a magnetic stirrer, and samples were withdrawn at specific time intervals and analyzed using high-performance liquid chromatography (HPLC) method.

***In Vivo* Release study**

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

FACTORS AFFECTING PHYSIO 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[22]. The ether type surfactants with single chain alkyl as hydrophobic tail is more toxic than corresponding dialkyl ether chain[13].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 esterases to triglycerides and fatty acid *in vivo*[13].The surfactants with alkyl chain length from C12-C18 are suitable for preparation of niosomes[34,35].Surfactants such as C16EO5 (poly-oxyethylene cetyl ether) or C18EO5 (polyoxyethylene steryl ether) are used for preparation of polyhedral vesicles[36].Span series surfactants having HLB number of between 4 and 8 can form vesicles[26].

Table 2: Different Types of Non-Ionic Surfactant

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, lc = the critical hydrophobic group length, a_0= the area of hydrophilic head group.

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

If CPP < ½, then formation of spherical micelles,

If ½ < 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[26]. 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). Phase transition temperature (TC) of surfactant also effects 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[37]. 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 ± 0.03mm) than spherical/tubular niosomes formed by C16G2: cholesterol: solulan C24 in ratio (49:49:2) (6.6±0.2mm)[37].Addition of cholesterol molecule to niosomal system provides rigidity to the membrane and reduces the leakage of drug from niosome[38].

Inclusion of cholesterol in niosomes increases its hydrodynamic diameter and entrapment efficiency[26]. 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[28].

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[28,46]. 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 influencecharge and rigidity of the niosome bilayer. The drug interacts withsurfactant head groups and develops the charge that creates mutualrepulsion between surfactant bilayers and hence increases vesiclesize[39].The aggregation of vesicles is prevented due to the chargedevelopment 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[39]. The hydrophilic lipophilic balance of the drug affects degree of entrapment.

Table 3: Effect of the nature of drug on the formation of niosomes

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 elecrophoretic mobility
Macromolecules	Decreased	Increased	-

(vi) Methods of Preparation

Hand shaking method forms vesicles with greater diameter (0.35-13 nm) compared to the ether injection method (50-1000 nm) [17]. Small sized niosomes can be produced by Reverse Phase Evaporation method[19,40]. Micro fluidization method gives greater uniformity and small size vesicles[17]. Niosomes obtained by trans membrane pH gradient (inside acidic) drug uptake process showed greater entrapment efficiency and better retention of drug[40].

(vii) 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[2,41].

(viii) 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 transitiontemperature of system. Temperature change of niosomal systemaffects assembly of surfactants into vesicles and also induces vesicleshape transformation[22,37]. Arunothayanun et al. reported that a polyhedralvesicle formed by C16G2: solulan C24 (91:9) at 25°C which onheating transformed into spherical vesicle at 48°C, but on coolingfrom 55°C, the vesicle produced a cluster of smaller spherical niosomesat 49°C before changing to the polyhedral structures at 35°C**.** In contrastvesicle formed by C16G2: cholesterol: solulanC24 (49:49:2) showsno shape transformation on heating or cooling[42]. Along with theabove mentioned factors, volume of hydration medium and time ofhydration of niosomes are also critical factors. Improper selection ofthese factors may result in formation of fragile niosomes or creationof drug leakage problems.

APPLICATIONS

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

1) 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 tumors known to metastasize to the liver and spleen and in parasitic infestation of liver[3].

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[36]. Immunoglobulins seem to bind quite readily to the lipid surface, thus offering a convenient means for targeting of drug carrier[37]. 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.

2) Neoplasia

Doxorubicin, the anthracyclic antibiotic with broad spectrum anti tumor activity, shows a dose dependant irreversible cardio toxic effect. Niosomal delivery of this drug to mice bearing S-180 tumor increased their life span and decreased the rate of proliferation of sarcoma[38]. 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 tumor bearing mice resulted in total regression of tumor and also higher plasma level and slower elimination[31,39].

3) 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* [40] showed high liver level after intravenous administration of the carriers forms of the drug.

ulation and that the effect of two doses given on successive days was additive.

4) Delivery of Peptide Drugs

Yoshida *et al*[28] 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.

5) Immunological Application of Niosomes

Niosomes have been used for studying the nature of the immune response provoked by antigens. Brewer and Alexander [41] have reported niosomes as potent adjuvant in terms of immunological selectivity, low toxicity and stability.

6) Niosomes as Carriers for Hemoglobin.

Niosomes can be used as a carrier for hemoglobin. Niosomal suspension shows a visible spectrum superimposable onto that of free hemoglobin. Vesicles are permeable to oxygen and hemoglobin dissociation curve can be modified similarly to non-encapsulated hemoglobin[42,43].

7) 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. Jayraman *et al* [(44)] has studied the topical delivery of erythromycin from various formulations including niosomes or hairless mouse. From the studies, and confocal microscopy, it was seen that non-ionic vesicles could be formulated to target pilosebaceous glands.

8) Other Applications

a) Sustained Release Action

Azmin *et al* [7] suggested the role of liver as a depot for methotrexate after niosomes are taken up by the liver cells. 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[(18,40)].

The evolution of niosomal drug delivery technology is still at an infancy stage, but this type of drug delivery system has shown promise in cancer chemotherapy and anti-leishmanial therapy.

CONCLUSION

The concept of incorporating the drug into liposomes or niosomes for a better targeting of the drug at appropriate tissue destination is widely accepted by researchers and academicians. Niosomes represent a promising drug delivery module. They presents 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. Niosomes are thoughts to be better candidates drug delivery as compared to liposomes due to various factors like cost, stability etc. Various type of drug deliveries can be possible using niosomes like targeting, ophthalmic, topical, parentral, etc.

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