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OVERVIEW : NIOSOMES

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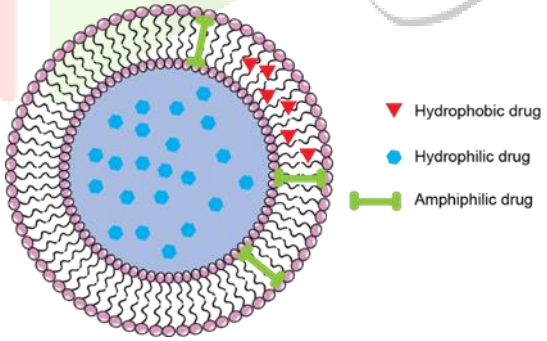
Abstract: Over decades treatment of various diseases and immunization undergone a revolutionary shift of biotechnology ,genetic engineering, not only a large number of disease-specific biological have been developed, emphasis has been made to effectively deliver these biologicals. Niosomes are vesicles composed of non-ionic surfactants, which are biodegradable, relatively nontoxic, more stable and inexpensive, an alternative to liposomes. This article reviews the current deepening and widening of interest of niosomes in many scientific disciplines and, particularly its application in medicine. And how niosomes are usefule in pharmaceutics with history, structure , types , method of preparation, materials used, niosomes as drug delivery system and its application with future aspects

I. INTRODUCTION

Novel Drug delivery System (NDDS) refers to the approaches, formulations, technologies, and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effects.

Niosomes are a novel drug delivery system, in which the medication is encapsulated in a vesicle. The vesicle is composed of a bilayer of non-ionic surface active agents and hence the name niosomes. The niosomes are very small, and microscopic in size. Their size lies in the nanometric scale. Although structurally similar to liposomes, they offer several advantages over them. Niosomes have recently been shown to greatly increase transdermal drug delivery and also can be used in targeted drug delivery, and thus increased study in these structures can provide new methods for drug delivery.

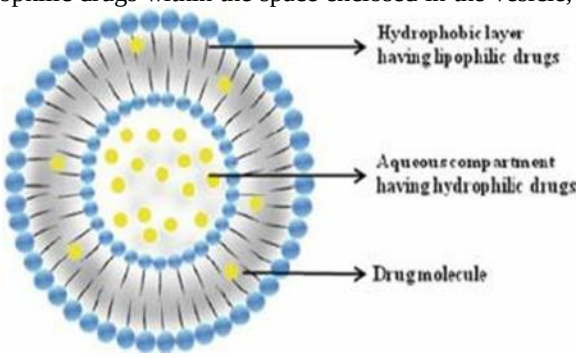


II. HISTORY

They were originally developed as an alternative controlled drug delivery system to liposomes, in order to overcome the problems associated with sterilization, large-scale production and stability (Azmin et al., 1985, 1986; El Maghraby & Williams, 2009). The hydration of a film, comprising a mixture of a single or double-alkyl chain and cholesterol, leads to the formation of vesicular dispersion. These dispersions were termed niosomes (Baillie et al., 1985). Basically, these vesicles do not form spontaneously. Thermodynamically stable vesicles form only in the presence of proper mixtures of surfactants and a membrane stabilizing agent (cholesterol), at a temperature above the gel/liquid transition of the main lipid forming vesicles (Azmin et al., 1985, 1986; Sahin, 2007). The first niosome formulations were developed and patented by L'Oreal in 1975 (Sahin, 2007). Niosomes were first utilized in drug delivery for anticancer drugs (Azmin et al., 1985, 1986). The developed niosome formulations were capable of altering the pharmacokinetic profile, organ distribution and metabolism of methotrexate in mice (Azmin et al., 1985, 1986). Niosomes are versatile in structure, morphology and size; they can entrap hydrophilic drugs in aqueous compartments or lipophilic drugs by partitioning of these molecules into bilayer domains (Figure 1). Furthermore, they can be formulated as unilamellar, oligolamellar or multilamellar vesicles (Figure 2). Niosomes also possess good physical stability, are cost-effective, and are relatively straight forward for routine and large-scale production (Baillie et al., 1985; Uchegbu & Florence, 1995; Uchegbu & Vyas, 1998)

III. STRUCTURE OF NIOSOMES

Structurally, niosomes are similar to liposomes, in that they are also made up of a bilayer. However, the bilayer in the case of niosomes is made up of non-ionic surface active agents rather than phospholipids as seen in the case of liposomes. Most surface active agents when immersed in water yield micellar structures however some surfactants can yield bilayer vesicles which are niosomes. Niosomes may be unilamellaror multilamellar depending on the method used to prepare them.The niosome is made of a surfactant bilayer with its hydrophilic ends exposed on the outside and inside of the vesicle, while the hydrophobic chains face each other within the bilayer. Hence, the vesicle holds hydrophilic drugs within the space enclosed in the vesicle, while hydrophobic drugs are embedded within the

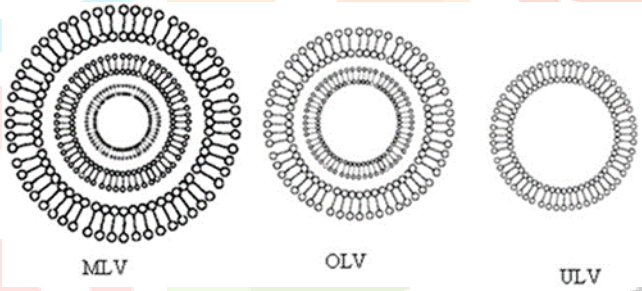


A typical niosome vesicle would consist of a vesicle forming ampiphile i.e. a non-ionic surfactant such as Span60, which is usually stabilized by the addition of cholesterol and a small amount of non ionic surfactant such as diacetyl phosphate, which also helps in stabilizing the vesicle

1. TYPES OF NIOSOMES

The niosomes are classified as a function of the number of bilayer (e.g. MLV, SUV) or as a function of size. (e.g. LUV, SUV) or as a function of the method of preparation (e.g.REV, DRV). The various types of niosomes are described below:

i) Multi lamellar vesicles (MLV),
ii) Large unilamellar vesicles (LUV),
iii) Small unilam ellar vesicles (SUV)



i) Multilamellar vesicles (mlv):
It consists of a number of bilayer surrounding the aqueous lipid compartment separately. The approximate size of these vesicles is 0.5-10 µm diameter. Multilamellar vesicles are the most widely used niosomes. It is simple to make and are mechanically stable upon storage for long periods. These vesicles are highly suited as drug carrier for lipophilic compounds.

ii) Large unilamellar vesicles (luv):
Niosomes of this type have a high aqueous/lipid compartment ratio, so that larger volumes of bio-active materials can be entrapped with a very economical use of membrane lipids.

ii)Small unilamellar vesicles (suv):
These small unilamellar vesicles are mostly prepared from multilamellar vesicles by sonication method, French press extrusion electrostatic stabilization is the inclusion of dicetyl phosphate in 5(6)-carboxyfluorescein (CF) loaded Span 60 based niosomes.

IV. THE PRINCIPLE OF GEOMETRICAL OR PACKING PROPERTIES

The role of molecular geometry or ‘‘packing’’ of amphiphiles(surfactants) was first described by (Israelachvili et al., 1976).Accordingly, an optimal polar head group area ao, optimalvolume of the hydrocarbon chains v and a maximum effective length that the hydrocarbon chains can assume (critical chain ength) lc will determine the self-assembly of the amphiphiles into organized aggregates The value of the dimensionless ‘‘packing parameter’’ v/ao lc will determine whether a certain amphiphile or will form spherical micelles (v/ao lc51/3); non-spherical micelles (1/35v/ao lc51/2); bilayers (1/25v/ao lc51); an inverted micellar structure (v/ao lc41); or even precipitate out of solution (e.g. cholesterol), since cholesterol molecules possess a head-group too small to pack into organized structures (Israelachvili & Mitchell, 1975; Israelachvili et al., 1976; Israelachvili et al., 1980). A summary of how surfactant’s geometrical packing parameter affects their aggregation in aqueous medium Apart from the selection of amphiphiles with proper geometrical properties, the formation of niosomes involvesinput of energy (physical agitation and heat), as closed vesicles do not form spontaneously (Baillie et al., 1985;Sahin, 2006). In pharmaceutical research, the hydrophilic-lipophilic balance (HLB) system, which is a measure of the relative contributions of the hydrophilic and lipophilic regions of the

surfactant molecules, is more commonly used as an indicator on potential niosomes formation Surfactants possessing HLB values of 4 to 8 have been found to be favorable for the formation of niosomes (Girigoswami et al., 2006). On the other hand, surfactants of high HLB values (9.6–16.7) such as
polysorbates (Tween) tend to form micelles or open lamellar structures (Manosroi et al., 2003). Some surfactants such as sorbitan monooleate (Span 80, HLB of 4.3) cannot assemble into niosomes (on their own) due to their inadequate geometry, hence packing properties. The oleate moiety of this surfactant molecule has a double bond (with relatively high electron density) at the C9 which repels adjacent hydrocarbon chains resulting in the characteristic ‘‘kink’’ in the structure p (Yoshioka & Florence, 1994; Abdelkader et al., 2010).

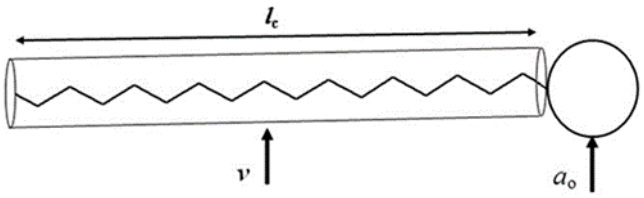


FIG. Schematic of a single-chain surfactant, ao ¼ hydrophilic head group area, v ¼ hydrophobic chain volume, lc ¼ hydrophobic chain length.

V. METHOD OF PREPARATION OF NIOSOMES

1. Ether Injection Method

In this method, a solution of the surfactant is made by dissolving it in diethyl ether. This solution is then introduced using an injection (14 gauge needle) into warm water or aqueous media containing the drug maintained at 60°C. Vaporization of the ether leads to the formation of single layered vesicles. The particle size of the niosomes formed depend on the conditions used, and can range anywhere between 50-1000 µm.

2. Hand Shaking Method (Thin Film Hydration Technique)

In this method a mixture of the vesicle forming agents such as the surfactant and cholesterol are dissolved in a volatile organic solvent such as diethyl ether or chloroform in a round bottom flask. The organic solvent is removed at room temperature using a rotary evaporator, which leaves a thin film of solid mixture deposited on the walls of the flask. This dried surfactant film can then be rehydrated with the aqueous phase, with gentle agitation to yield multilamellar niosomes.

3. Reverse Phase Evaporation Technique (REV)

This method involves the creation of a solution of cholesterol and surfactant (1:1 ratio) in a mixture of ether and chloroform. An aqueous phase containing the drug to be loaded is added to this, and the resulting two phases are sonicated at 4-5°C. A clear gel is formed which is further sonicated after the addition of phosphate buffered saline (PBS). After this the temperature is raised to 40°C and pressure is reduced to remove the organic phase. This results in a viscous niosome suspension which can be diluted with PBS and heated on a water bath at 60°C for 10 mins to yield niosomes.

4. Transmembrane pH gradient Drug Uptake Process (Remote Loading)

In this method, a solution of surfactant and cholesterol is made in chloroform. The solvent is then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask, similar to the hand shaking method. This film is then hydrated using citric acid solution by vortex mixing. The resulting multilamellar vesicles are then treated to three freeze thaw cycles and sonicated. To the niosomal suspension, aqueous solution containing 10mg/ml of drug is added and vortexed. The pH of the sample is then raised to 7.0-7.2 using 1M disodium phosphate and mixture is later heated at 60°C for 10 minutes to give niosomes

5. The “Bubble” Method

It is a technique which has only recently been developed and which allows the preparation of niosomes without the use of organic solvents. The bubbling unit consists of a round bottom flask with three necks, and this is positioned in a water bath to control the temperature. Water-cooled reflux and thermometer is positioned in the first and second neck, while the third neck is used to supply nitrogen. Cholesterol and surfactant are dispersed together in a buffer (pH 7.4) at 70°C. This dispersion is mixed for a period of 15 seconds with high shear homogenizer and immediately afterwards, it is bubbled at 70°C using the nitrogen gas to yield niosomes.

6. 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 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 noisome are formed.

7. 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 polycarbonate membranes solution and the resultant suspension extruded through which are placed in series for up to 8 passages. It is a good method for controlling niosome size.

8. Sonication

A typical method of production of the vesicles is by sonication of solution. 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.

VI. MATERIALS USED IN MANUFACTURING OD NIOSOMES

Niosome forming amphiphiles Unlike naturally occurring phospholipids (the principal liposome-
forming lipids) which have double alkyl chains, most widely used niosome forming amphiphiles are single chain, synthetic, non-ionic surfactants (Florence & Baillie, 1989; Uchegbu & Florence, 1995). Alkyl ethers, alkyl esters and alkyl amides, as well as fatty acid and amino acid compounds,
can form vesicles (Uchegbu & Florence, 1995). Recently, niosomes comprising Pluronic L64 and P105 (copolymers of ethylene oxide and propylene oxides) have been prepared and used as a transdermal delivery system for sulfadiazine sodium (a model hydrophilic drug) (Muzzalupo et al., 2011). However, both alkyl ethers and alkyl esters have a wider application as niosomes drug delivery carriers, due to their commercial availability and low toxicity.

Alkyl ethers

Alkyl ethers can be divided broadly into two subclasses, based on their hydrophilic head group: alkyl ethers possessing head groups of glycerol subunits or larger sugar molecules, and alkyl ethers whose hydrophilic head groups consist of repeated ethylene oxide subunits (Uchegbu & Florence, 1995;Rajera et al., 2011). Alkyl glycerol ethers, most notably hexadecyl diglycerolether ($C_{16}G_2$), have been reported as niosome-forming surfactants and have been used in many drug delivery applications such as experimental cancer chemotherapy (Baillie et al., 1985; Uchegbu & Florence, 1995). These surfactants were used to alter the pharmacokinetics of methotrexate (Azmin et al., 1985) and doxorubicin (Uchegbu et al., 1996). Alkyl glycerol ethers were also usedto encapsulate sodium stibogluconate to control leishmaniasis (Baillie et al., 1986). The second group of alkyl ether surfactnats, in which the hydrophilic region consists of repeated oxyethylene units (Brij_), was used to encapsulate insulin for oral delivery, in order to prevent the inactivation of insulin by the gastric juice (Pardakhty et al., 2007). However, Brij 72- and Brij 52-based niosomes have been reported to show physical instability and technical problems due to rapid creaming and floating of ggregated vesicles rather than sedimentation during ultracentrifugation, respectively (Abdelkader et al., 2010;
Abdelkader, 2012).

Alkyl esters

Alkyl esters, such as sorbitan fatty acid esters (Span) and polyoxyethylene sorbitan fatty acid esters (Tween), are widely used in cosmetics and foodstuffs, as well as oral, parenteral and topical pharmaceutical formulations. They are regarded as non-toxic and non-irritant materials (Lawrence, 2003). These surfactants have been utilized in manufacturing niosomes as a drug delivery system, including oral (Varshosaz et al., 2003), trandermal (Ibrahim et al., 2005; Balakrishnana et al., 2009; Muzzalupo et al., 2011) and ocular delivery (Aggarwal et al., 2004; Kaur et al., 2008; Abdelbary & El- gendy, 2008). Cell culture toxicity studies have shown thatniosomes composed of ester-type surfactants are less toxic than ether-type ones. This could be attributed to the possible enzymatic degradation of ester bonds (Hofland et al., 1992)

Cholesterol (bilayer membrane stabilizer)

Some water-soluble surfactants, such as Tween 20 and Tween61, can not form vesicles under normal conditions; thesesurfactants prefer to form micelles, in a manner identical tolyolecithin (Florence & Baillie, 1989; Manosroi et al., 2003). These surfactants might form vesicles when mixed with cholesterol. Cholesterol molecules operate cooperatively to
form bilayer vesicles. Cholesterol is considered as lipid, but it is a comparatively rigid molecule and lacks the accommodating ability of an acyl-chained lipid. In particular, cholesterol does not form bilayers and its shape can be represented as an inverted cone (Figure 4) (Israelachvili et al., 1980). However, cholesterol has been called the ‘‘mortar’’ of bilayers because, by virtue of its molecular shape and solubility properties, it fills in empty spaces among the amphiphiles, thereby anchoring them more strongly into the bilayer structure. Cholesterol in niosomes is reported to increase membrane stability, decrease the fluidity of the membrane and alter membrane permeability (Uchegbu & Florence, 1995; Uchegbu & Vyas, 1998; Abdelkader et al., 2010). Other excipients, such as dicetyl phosphate and stearyl amine, were used in niosomes formulation to impart negative and positive charges, respectively (Yoshioka & Florence, 1994; Abdelbary & El-gendy, 2008).

Bilayer membrane additives

Bilayer membrane additives can be defined as lipid excipientswhich are unable to form surfactant vesicles (liposomes andniosomes) by their own but can be accommodated by the bilayer domains (Figure 5). Membrane additives have been found in surfactant vesicles basically for two reasons; either to alter the bio-distribution, or to improve the physical properties. Non-ionic surfactants can form niosomes in absence of other membrane additives under specified conditions. However, such niosomes have been found to be highly permeable and leaky to the solutes. Cholesterol is the most common membrane additive found in surfactant vesicles; it can significantly alter membrane permeability, fluidity, vesicle stability, entrapment efficiency and niosomes size and is widely known as a membrane stabilizer. Other membrane additives can be broadly classified into charge inducers and water-soluble surfactants. Table 2 outlines structure and some physical properties for commonly used membrane additives used in niosome formulations (Abdelkader, 2012).

Charge inducers

Stearyl amine and dicetyl phosphate are positive and negativecharge inducers respectively, and are frequently incorporatedin the bilayer membranes. These charge inducers have beenmainly utilized to improve the physical stability of thevesicular dispersions against aggregation

VII. NIOSOMES AS DRUG DELIVERY SYSTEMS

Over the past three decades, niosomes have been successfully utilized as a drug delivery system to solve some major biopharmaceutical problems. Poor bioavailability of slightly soluble drugs can be improved, as niosomes can accommodate hydrophobic molecules in their bilayer domains (Waraporn et al., 2006; Nasr et al., 2008). Niosomes can also minimize the side effects of some potent drugs by localizing the pharmacological effects to the target tissues (Baillie et al., 1985; Baillie et al., 1986; Vyas et al., 1998; Guinedi et al., 2005). Niosomes can serve as a non-toxic penetration enhancer for transdermal drug delivery (Schreier & Bouwstra, 1994; Solanki et al., 2010; Ammar et al., 2011). Moreover, niosomes can improve the chemical stability of photosensitive drugs by entrapping drug molecules in the aqueous internal milieu (Manconi et al., 2003, Abdelkaderet al., 2012b). Below are discussed the most common

CHARACTERIZATION OF NIOSOMES

1. Size, Shape and Morphology

Structure of surfactant based vesicles has been visualized and established using freeze fracture microscopy while photon correlation spectroscopy used to determine mean diameter of the vesicles. Electron microscopy used for morphological studies of vesicles while laser beam is generally used to determine size distribution, mean surface diameter and mass distribution of niosomes.

2. 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 analysing the resultant solution by appropriate assay method for the drug. Where, % Entrapment efficiency (% EF) = (Amount of drug entrapped/ total amount of drug) x 100

3. Vesicle diameter

Niosomes diameter can be determined using light microscopy, photon correlation microscopy and freeze fracture electron microscopy. 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.

4. In-vitro release

A method of in-vitro release rate study includes the use of dialysis tubing. 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 placed in 200 ml of 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.

5. Vesicle charge

The vesicle surface charge can play an important role in the behavior of niosomes in vivo and in vivo. In general, charged niosomes are more stable against aggregation and fusion than uncharged vesicles. In order to obtain an estimate of the surface potential, the zeta potential of individual **niosomes can be** measured by microelectrophoresis. An alternative approach is the use of pH sensitive fluorophores. More recently, dynamic light scattering have been used to measure the zeta potential of niosomes**.**

6 .Bilayer Rigidity and Homogeneity

The biodistribution and biodegradation of niosomes are influenced by rigidity of the bilayer. In omogeneity can occur both within niosome structures themselves and between niosomes in dispersion and could be identified via. NMR, differential scanning calorimetry (DSC) and fourier

Niosomal drug loading and encapsulation efficiency To determine drug loading and encapsulation efficiency, the niosomal aqueous suspension was ultracentrifuged, supernatant was removed and sediment was washed twice with distilled water in order to remove the adsorbed drug.

The niosomal recovery was calculated as:

$$\text{Niosome recovery (\%)} = \frac{\text{Amount of niosomes recovered}}{\text{Amount of polymer + Drug + Excipient}} \times 100$$

The entrapment efficiency (EE) was then calculated using formula:

$$\text{Entrapment efficiency (\%)} = \frac{\text{Amount of drug in niosomes}}{\text{Amount of Drug used}} \times 100$$

The drug loading was calculated as:

$$\text{Drug loading (\%)} = \frac{\text{Amount of drug in niosomes}}{\text{Amount of niosomes recovered}} \times 100$$

VIII. APPLICATIONS OF NIOSOMES AS DRUG DELIVERY SYSTEMS.

Anticancer delivery

Methotrexate-loaded niosomes were first utilized as a morestable and economic alternative drug delivery system toliposomes, in order to improve the therapeutic index of the anticancer drug by localizing the cytotoxic effects to target cells (Baillie et al., 1985). The anti-tumor activity of vincristine also increased in S-180 sarcoma and Ehrlich-ascites-bearing
mice when encapsulated in niosomes (Parthasarathi et al., 1994). Moreover, Span 60 bleomycin niosomes increased the anti-tumor action of bleomycin in the abovementioned two tumor models (Naresh & Udupa, 1996). Cytotoxic side effects of doxorubicin decreased when encapsulated in C16G2 niosomes. Doxorubicin copolymer-loaded niosomes were not hemolytic in vitro at the doses selected for in vivo use. C16G2 niosomes also showed localized and sustained effects on liver and spleen (Uchegbu& Duncan, 1997). Furthermore, Span 40- and Span 60-based niosomal delivery systems for 5-flurouracil showed a sustained and higher local concentration of the drug in the liver and kidney of the rats, compared with the injectable drug solution (Namdeo & Jain, 1999). Recently, niosomes for the magnetic targeting of doxorubicin to a specific organ have successfully controlled drug release with no additional toxicity

Anti-infective delivery

Sodium stibogluconate is a drug used in the treatment ofvisceral leshmniasis (a protozoan infection of the reticuloendothelialsystem). The drug's pharmacokinetics was equallyaltered by encapsulation into liposomes and niosomes (Hunteret al., 1988). It was found that niosomal sodium stibogluconate was significantly more active in reducing parasite burden than the free drug; the effect observed after multiple dosing suggested that niosomal formulations act as a depot within the liver.Rifampicin, an anti-tuberculosis drug, encapsulated in Span 85 niosomes was found to accumulate in the lungs of mice (Jain & Vyas, 1995). Therefore, it can offer the possibility of improving anti-tuberculosis therapy (Jain & Vyas, 1995). Moreover, niosomes composed of Span 60: cholesterol: dicetyl phosphate at 4:2:1 molar ratio successfully encapsulated ribavirin (an antiviral agent used for treatment of hepatitis C). The concentration of ribavirin in the rat liver obtained from the ribavirin niosomes was 6-fold higher than that obtained from the ribavirin solution after an intraperitoneal injection of a single dose equivalent to 30 mg/kg of the drug. This demonstrates effective liver targeting properties for niosomes (Hashim et al., 2010). Vaccine and macromolecule delivery Span 60 niosomes loaded with tetanus toxoid (TT) were prepared by the REV method. The prepared niosomes were coated with a modified polysaccharide O-palmitoyl mannan (OPM), in order to protect the niosomes from enzymatic degradation in the gastrointestinal tract and to enhance their affinity towards the antigen presenting cells of Peyer's patches. The results were compared with alum-adsorbed TT following oral and intramuscular administration, and it was observed that OPM-coated niosomes produced higher IgG levels compared with plain uncoated niosomes and alumadsorbed TT upon oral administration. Oral niosomes also elicited a significant mucosal immune response (sIgA levels in mucosal secretions). The developed niosomes also elicited a combined serum IgG2a/IgG1 response suggesting that they were capable of eliciting both humoral and cellular response. The proposed system was simple, stable, and cost-effective and may be clinically acceptable. The study emphasized the potential of OPM-coated niosomes as an oral vaccine delivery carrier (Jain & Vyas, 2006).

Drug Targetting

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

Anti-neoplastic Treatment

Most antineoplastic drugs cause severe side effects. Niosomes can alter the metabolism; prolong circulation and half life of the drug, thus decreasing the side effects of the drugs. Niosomes, is decreased rate of proliferation of tumor and higher plasma levels accompanied by slower elimination.

Leishmaniasis

Leishmaniasis is a disease in which a parasite of the genus Leishmania invades the cells of the liver and spleen. Use of niosomes in tests conducted showed that it was possible to administer higher levels of the drug without the triggering of the side effects, and thus allowed greater efficacy in treatment.

Delivery of Peptide Drugs

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

Use in Studying Immune Response

Due to their immunological selectivity, low toxicity and greater stability; niosomes are being used to study the nature of the immune response provoked by antigens. Nonionic surfactant vesicles have clearly demonstrated their ability to function as adjuvant following parenteral administration with a number of different antigens and peptides.

Niosomes as Carriers for Haemoglobin Niosomes can be used as carriers for haemoglobin within the blood. The niosomal vesicle is permeable to oxygen

IX. LIMITATIONS AND FUTURE DIRECTION ;

The physical stability and sterilization of niosomes are the two major obstacles that hinder its utilization as potential drug delivery systems. There are two approaches to improve the physical stability of lipid vesicles at ambient conditions. Dispersing liposomes in a viscous gel has been used either to reduce the rapid leakage of the encapsulated drug from liposomes (Meisnera & Mezeib, 1995) or to minimize the burst release effect observed with liposomes (Mehanna et al., 2009, 2010). This approach may be extrapolated to improve the physical stability of ocular niosomes. However, the drug release from such a system is likely to be complex, as the drug molecules have to release from the bilayer membranes and diffuse through the viscous gel. Furthermore, the improvement in the physical stability of the niosomes can be offset by reducing the ocular bioavailability of the administered drug. Additionally, a topical application of a viscous gel is less convenient than eye drops in terms of ocular administration and the adjustment of the dose. In addition to the previous approach, converting the final liposomal/niosomal liquid dispersion to a powder form by lyophilization (freeze-drying) or spray-drying not only enhances the physical stability of the vesicles (Ingvarsson et al., 2011), but can also dramatically reduce the oxidative instability of oxidizable drug molecules, by minimising the formation of hydroxyl free radicals (Uchegbu & Vyas, 1998;Waterman et al., 2002).

X. CONCLUSION

Recent advancements in the field of scientific research have resulted in the endorsement of small molecules such as proteins and vaccines as a major class of therapeutic agents. These, however, pose numerous drug-associated challenges such as poor bioavailability, suitable route of drug delivery, physical and chemical instability and potentially serious side effects. Opinions of the usefulness of niosomes in the delivery of proteins and biologicals can be unsubstantiated with a wide scope in encapsulating toxic drugs such as anti-AIDS drugs, anti-cancer drugs, and anti-viral drugs. It provides a promising carrier system in comparison with ionic drug carriers, which are relatively toxic and unsuitable. However, the technology utilised in niosomes is still in its infancy. Hence, researches are going on to develop a suitable technology for large production because it is a promising targeted drug delivery system.

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