Vesicles of Non-ionic Surfactants (Niosomes) and Drug Delivery Potential

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ABSTRACT: Vesicles prepared from self-assembly of hydrated non-ionic surfactants molecules are called niosomes. These types of vesicles were first reported in the cosmetic industries. Niosomes exhibit more chemical stability than liposomes (a phospholipids vesicle) as non-ionic surfactants are more stable than phospholipids. Non-ionic surfactants used in formation of niosomes are polyglyceryl alkyl ether, glucosyl dialky ether, crown ether, polyoxyethylenealkyl ether, ester-linked surfactants, and steroid-linked surfactants and a spans, and tweens series. Niosomes preparation is affected by processes variables, nature of surfactants, and presence of membrane additives and nature of drug to be encapsulated. This review article presents an overview of theoretical concept of factors affecting niosome formation, techniques of noisome preparation, characterization of niosome, applications, limitations and market status of such delivery system.

KEY WORDS: Niosomes; Liposomes; Anticancer; Surfactant; Proniosomes; Cholesterol.

Introduction

In the era of novel drug delivery system (NDDS) emphasis is given on spatial placement of drug for chronic conditions. Targeted delivery of anticancer and anti-infective drugs appears to be a challenging but achievable task with the use of novel drug delivery systems. Different novel approaches used for delivering these drugs include liposomes, microspheres, nanotechnology, microemulsions, antibody-loaded drug delivery, magnetic microcapsules, implantable pumps and niosomes. Niosomes are formations of vesicles by hydrating mixture of cholesterol and nonionic surfactants (Handjani-vila RM et al., 1979). These nonionic surfactants vesicles are called niosomes. These are formed by self-assembly of non-ionic surfactants in aqueous media as spherical, unilamellar, multilamellar system and polyhedral structures in addition to inverse structures which appear only in non-aqueous solvent (Sternberg B et al., 1995; Uchegbu IF and Florence AT, 1995; Murdan S et al., 1998). The process vesicle formulation by self-assembly of nonionic surfactants is rarely spontaneous and usually requires some input of energy through physical agitation, extrusion or heat (Lasic DD, 1990).

Niosomes and liposomes are equiactive in drug delivery potential and both increase drug efficacy as compared with that of free drug. Niosomes are preferred over liposomes because the former exhibit high chemical stability and economy (Hunter CA et al., 1988). Niosomes also exhibit special characteristics such as easy handling and storage. Surfactant forming niosomes are biodegradable, non-immunogenic and biocompatible. Incorporating them into niosomes enhances the efficacy of drug, such as nimesulide; flurbiprofen, piroxicam, ketoconazole and bleomycin exhibit more bioavailability than the free drug (Shahiwala A and Misra AJ, 2002; Reddy DN and Udupa N, 1993; Satturwar PM et al., 2002; Naressh RAR et al., 1996).

Factors affecting formation of niosomes

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 steroideal group (Uchegbu F et al., 1998). The ester type surfactants with single chain alkyl as hydrophobic tail is more toxic than corresponding dialkylether chain (Hunter CA et al., 1988). 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 (Hunter CA et al., 1988). The surfactants with alkyl chain length from C_{12}-C_{18} are suitable for preparation of niosome (Ozer AY et al., 1991; Nasseri B and Florence AT, 2003). Surfactants such as C_{18}EO_{5} (poly-oxyethylene cetyl ether) or C_{18}EO_{5} (polyoxyethylene steryl ether) are used for preparation of polyhedral vesicles (Nasseri B and Florence AT, 2003). Span series surfactants having HLB number of between 4 and 8 can form vesicles (Yoshioka T et al., 1994).

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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 can predicate geometry of vesicle to be formed. Critical packing parameters can be defined using following equation,

\[ \text{CPP (Critical Packing Parameters)} = \frac{v}{lc \times a_0}, \]

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 micellar structure formed can be ascertained as given below,
- If CPP < \( \frac{1}{2} \) then formation of spherical micelles,
- If \( \frac{1}{2} < \text{CPP} < 1 \) formation of bilayer micelles,
- If CPP > 1 formation inverted micelles.

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 \( C_{16}G_2 \), the shape of these polyhedral niosome remains unaffected by adding low amount of solulan \( C_{24} \) (cholesteryl poly-24-oxyethylene ether), which prevents aggregation due to development of steric hindrance (Arunothayanun P et al., 2000). In contrast spherical niosomes are formed by \( C_{16}G_2: \) cholesterol:solulan \( (49:49:2) \) (Arunothayanun P et al., 2000). The mean size of niosomes is influenced by membrane composition such as polyhedral niosomes formed by \( C_{16}G_2: \text{solulan C}_{24} \) in ratio \( 91:9 \) having bigger size \( (8.0 \pm 0.03) \mu m \) than spherical/tubular niosomes formed by \( C_{16}G_2: \text{cholesterol: solulan C}_{24} \) in ratio \( 49:49:2 \) \( (6.6\pm0.2) \mu m \) (Arunothayanun P et al., 2000). Addition of cholesterol molecule to niosomal system provides rigidity to the membrane and reduces the leakage of drug from niosome (Rogerson A et al., 1987).

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 (Stafford S et al., 1988). The aggregation of vesicles is prevented due to the charge development on bilayer.

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 (Uchegbu F et al., 1998; Arunothayanun P et al., 2000). Arunothayanun et al. reported that a polyhedral vesicle formed by \( C_{16}G_2: \text{solulan C}_{24} \) \( (91:9) \) at \( 25^\circ C \) which on heating transformed into spherical vesicle at \( 48^\circ C \), but on cooling from \( 55^\circ C \), the vesicle produced a cluster of smaller spherical niosomes at \( 49^\circ C \) before changing to the polyhedral structures at \( 35^\circ C \) (Arunothayanun P et al., 2000). In contrast vesicle formed by \( C_{16}G_2: \) cholesterol: solulan \( C_{24} \) \( (49:49:2) \) shows no shape transformation on heating or cooling (Arunothayanun P et al., 2000).

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.

Characterization of niosome
Size
Shape of niosome vesicles assumed to be spherical, their mean diameter can be determined by using laser light scattering method (Almira I et al., 2001). Also, diameter can be determined by using electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy and optical microscopy (Kreuter J, 1966; Azmin MN et al., 1985).

Bilayer formation
Assembly of non-ionic surfactants to form bilayer vesicle is characterized by X-cross formation under light polarization microscopy (Manosroi A et al., 2003).

Number of lamellae
It is determined by using NMR spectroscopy, small angle X-ray scattering and electron microscopy (Kreuter J, 1966).

Membrane rigidity
Membrane rigidity can be measured by means of mobility of fluorescence probe as function of temperature (Manosroi A et al., 2003).

Entrapment efficiency (EE)
The entrapment efficiency (EE) is expressed as

\[ \text{EE} = \frac{\text{amount entrapped}}{\text{total amount added}} \times 100. \]
It is determined after separation of unentrapped drug, on complete vesicle disruption by using about 1ml of 2.5% sodium lauryl sulfate, briefly homogenized and centrifuged and supernatant assayed for drug after suitable dilution (Balasubramanian A et al., 2002). Entrapment efficiency is affected by following factors.

**Surfactants**
The chain length and hydrophilic head of non-ionic surfactants affect entrapment efficiency, such as stearyl chain C_{18} non-ionic surfactant vesicles show higher entrapment efficiency than lauryl chain C_{12} non-ionic surfactant vesicles (Manosroi A et al., 2003). The tween series surfactants bearing a long alkyl chain and a large hydrophilic moiety in the combination with cholesterol at 1:1 ratio have highest entrapment efficiency for water-soluble drugs (Manosroi A et al., 2003). HLB value of surfactants affects entrapment efficiency, such as HLB value of 14 to 17 is not suitable for niosomes but HLB value of 8.6 has highest entrapment efficiency and entrapment efficiency decreases with decrease in HLB value from 8.6 to 1.7 (Shahiwala A and Misra AJ, 2002). The entrapment efficiency is affected by phase transition temperature of surfactants, i.e. span 60 exhibits highest entrapment efficiency in series having highest transition temperature (Tc) (Yoshida Hetal., 1992).

**Cholesterol contents**
The incorporation of cholesterol into bilayer composition of niosome induces membrane-stabilizing activity and decreases the leakiness of membrane (Rogerson A et al., 1988). Hence, incorporation of cholesterol into bilayer increases entrapment efficiency. The permeability of vesicle bilayer to 5, 6-carboxy flourescein (CF) is reduced by 10 times due to incorporation of cholesterol (Baillie AJ et al., 1985).

**Techniques for preparation of niosome**
By using following general steps niosomes can be prepared:
- Hydration of mixture of the surfactants/lipids at elevated temperature,
- Sizing of niosomes,
- Removal of the unentrapped material from the vesicles by different methods.

**Hydration stage**
Hydration of mixture of the surfactants / lipids at elevated temperature can be done by using following method.

**Hand shaking/lipid layer hydration**
Solution of surfactants/lipids is prepared by dissolving both in organic solvent (chloroform). The organic solvent is removed by rotary flask evaporation/under reduced pressure leads formation of drug surfactant/lipid film. The surfactant/lipid film is then hydrated with aqueous solution of drug at temperature slightly above the phase transition temperature of surfactants used, for specified period of time (time of hydration) with constant mild shaking (Naresh RAR et al., 1996; Nasseri B and Florence AT, 2003; Azmin MN et al., 1985 and Baillie AJ et al., 1985).

**Reverse phase evaporation**
The surfactants/lipids and cholesterol dissolve in a mixture of ether and chloroform, followed by addition of aqueous phase containing drug. The resulting two-phase system is then homogenized using homogenizer (Balasubramanian A et al., 2002). The organic phase is removed under reduced pressure to form niosomes dispersed in aqueous phase. In some cases suspensions results a must be further hydrated or homogenized to yield niosomes (Balassubramanian A et al., 2002; Parthsarathi G et al., 1994).

**Ether injection**
In this method, surfactant or surfactant-cholesterol or surfactant cholesterol-diacetyl phosphate or surfactant-cholesterol-drug solution mixture dissolves in diethyl ether then it is injected slowly into aqueous solution of drug or aqueous phase which is heated above the boiling point of the organic solvent.

**Bubbling of inert gas nitrogen**
Niosomes are prepared by bubbling of nitrogen gas through the homogenized mixture of surfactant/lipid (Talsma H et al., 1999). Uchegbu et al. reported that niosomes may also be formed from a mixed micellar solution by enzymatic process (Uchegbu F et al., 1998).

**Sizing of niosomes**
The size ranges of niosomes have a major effect on their fate in-vivo and in-vitro. Hence, size reduction stage of niosome is essential after hydration stage. The more commonly used methods for niosome size reduction found in literature are given below:

**Probe sonication**
Niosomes prepared by reverse phase evaporation and hand-shaking method are usually in micron size range (1.15 and 2.75mm) (Naresh RAR et al., 1996; Azmin MN et al., 1985). By using probe sonication size of C_{16}G_{3} niosomes formed by hand shaking method are reduced to 100-140 nm (Bhaskaran S and Panigrahi L, 2002).

**Nucleopore filters extrusion**
Size of niosome reduces to nano range (140 nm) by extrusion of niosome through nucleopore filters of pore size 100 nm (Stafford S et al. 1988).
Laser diffraction
This method is used to reduce niosomes size up to nano range. Apart from the above-stated methods that the other methods are used for size reduction are microfluidization and high pressure homogenization (Arunothayanun P et al., 2000).

Removal of unentrapped materials
Lipophilic drugs are fully associated with niosomes due to their high affinity to the lipid bilayer. But other drugs exhibit less attachment tendency to lipid bilayer hence have entrapment efficiency less than 100%. Small fraction of unentrapped drugs can cause unacceptable side effects (anti-cancer drugs). The methods that have been used for the removal of unentrapped material identified in literature are listed below.

Separation by gel chromatography
The unentrapped drugs remove by eluting the product through sephadex-50 using phosphate buffer saline of pH 7.4 as eluting fluid (Naresh RAR et al., 1996; Balasubramanian A et al., 2002 and Bhaskaran S and Panigrahi L, 2002). Other methods used for separation of unentrapped drugs are exhaustive dialysis, ultracentrifugation (200,000 g at 40°C for 45min) and centrifugation (2750 g for 30 min) (Hunter CA et al., 1988; Satturwar PM et al., 2002; Baillie AJ et al., 1985; Nasseri B and Florence AT, 2003; Arunothayanun P et al., 2000 and Arunothayanun P et al., 1999).

Remote loading
It means enhancement of drug loading by use of pH gradients. The lower pH value inside niosome develops pH differential across the niosome membrane. The added basic drug in an unionized state passes the membrane barrier of the niosome. After entering the drug into niosome inner chamber, it becomes ionized at lower pH and unable to leave the niosome. The acid pH within the niosome interior thus acts as an intravesicular trap. Parathasarathi et al. have been employed remote loading method in the formulation of vincristine sulphate niosome Parthasarathi G et al., 1994).

Stability of niosomes
Stable niosome suspension must exhibit a constant particle size and constant concentration of entrapped drug. Stability of niosomes is influenced by entrapped drug, its concentration and type of surfactant used along with cholesterol content. Sonicated niosomes exhibit different stability at room temperature on basis of formulation ingredients(Arunothayanun P et al., 2000). Cholesterol-rich spherical/tabular C6,G2 niosomes are at room temperature, where as sonicated polyhedral niosomes are stable above phase transition temperature but not at room temperature (Arunothayanun P et al., 2000).

Toxicity studies
Hofland et. al. studied the toxicity of CxEOy surfactants using cilio toxicity model on nasal mucosa reported that an increase in alkyl chain length of surfactant decreases its toxicity while an increase in the polyoxyethylene chain length causes an increase ciliotoxicity (Hofland HEJ et al., 1992). An increase in alkyl chain length of surfactant favour its gel state, whereas an increase in polyoxyethylene chain length favors its liquid state. From study it is indicated that liquid state of niosomes are more toxic than its gel state(Hofland HEJ et al., 1992). Hofland et al., also reported while studying on cell proliferation of human keratocytes, that ester-linked surfactants exhibits less toxic effect than ether-linked surfactants (Hoflaand HEJ et al., 1992). Parathasarathi et al., reported that niosomal encapsulated vincristine exhibits less toxic effect than free drug of vincristine(Parthasarathi G et al., 1994).

Specialized systems
Aspasomes (Ascorbyl palmitate vesicles)
Rambhau et al., reported that ascorbyl palmitate in combination with cholesterol and negatively charged lipid diacetyl phosphate forms vesicles called aspasome. The film hydration method was used for preparation of aspasomes, followed by sonication. The aqueous solution of azidothymidine was entrapped in aqueous region of bilayers. The cholesterol content in aspasomes exhibits very less effect for vesicle size and percent entrapment that affect release rate of azidothymidine. Aspasome with 45% of cholesterol shows maximum retardation in release rate than other composition. Aspasomes have inherent anti-oxidant properties that have potential applications toward disorder caused by reactive oxygen species. Transdermal permeation of aspasomal drug is much higher than aqueous dispersion and aqueous solution of drug (Gopinath D et al., 2004).

Niosomes in carbopol gel
Niosomes prepared from nimesulide, span and cholesterol and incorporated in carbopol-934 gel (1%W/W) base contain propylene glycol (10%W/W) and glycerin (30%W/W). In vitro diffusion studies of such niosomal gel, plain drug gel and marketed gel were carried out in diffusion cell using human cadaver skin. The mean flux value and diffusion co-efficient were found to be 5 to 7 times lower for niosomal gel as compared to plain drug gels. Skin retention of drug was maximum (58.19%) in niosomal gel formulation after 24 hours of diffusion studies. This formulation also evaluated for inhibition of edema using carrageenan-induced rat paw edema method. It was found that the percent of inhibition of edema in niosomal gel i.e.66.68±5.19% is high as compared to plain gel (Shahiwala A and Misra AJ, 2002).
**Polyhedral niosomes**

Polyhedral niosomes can be obtained from mixture of C_{16}EO_5 and solulan-C_{24} in low concentration of cholesterol (Nasseri B and Florence AT, 2003). A.T.Florence et al., worked on extrusion of polyhedral niosomes by capillary and studied some properties of extruded polyhedral niosomes(Nasseri B and Florence AT, 2003). When polyhedral niosomes extruded under certain condition into aqueous media fuse to produce long continuous stable tubules by controlling factor such pressure need to extrude niosomes and composition of vesicles(Nassseri B and Florence AT, 2003). The applied shear stress on vesicle affects its release pattern such as increasing sheer stress by narrowing size of micropipette aperture increases higher release pattern of entrapped materials(Arunothayanum P et al., 1998).

**Vesicles in water and oil system (V/W/O)**

Yoshioka et al., reported that the emulsification of an aqueous niosomes into an oil phase form vesicle in water in oil emulsion (V/W/O)(Yoshioka T and Florence AT, 1994). On addition of niosomes suspension formed from mixture of sorbitol mono stearate, cholesterol and solulan C_{24} to oil phase at 60\(^\circ\)C(Murdan S et al., 1999). There is formation of vesicle in water in oil emulsion but cooling to room temperature forms vesicle in water oil gel (V/W/O gel)(Murdan S et al., 1999). The (V/W/O gel) can entrap protein and also protect it from enzymatic degradation after oral administration and controlled release. The release of entrap material is lowest in case of V/W/O gel as compared to W/O gel and niosomal suspension (Murdan S et al., 1999). Florence et al., studied on immugencity properties of V/W/O gel and (W/O) gel, reported that both exhibit immunoadjuvant tendency.

**Niosomes in hydroxypropyl methylcellulose**

Reddy et al., studied on anti-inflammatory effect of noisome after incorporating into hydroxypropyl methyl cellulose semi-solid base containing 10% glycerin (Reddy DN and Udupa N, 1993). The bio availability and reduction of carageenan induced higher rat paw edema in case of noisome formulated in hydroxypropyl methyl cellulose as compared to plain formulation of flurbiprofen (R Reddy DN and Udupa N, 1993).

**Therapeutic Application**

There are very less marketed niosomal formulations found in market. But some experimentally evaluated application of niosomal formulation identified in literature listed below.

**Anti-cancer drug**

**Daunorubicin HCl**

Niosomal daunorubicin hydrochloride exhibited an enhanced anti-tumor efficacy when compared to free drug. The niosomal formulation was able to destroy the Dalton’s ascitic lymphoma cells in the peritoneum within the third day of treatment, while free drug took around six days and the process was incomplete. The hematological studies also prove that the niosomal formulation was superior to free drug treatment. An enhanced mean survival time was achieved by the niosomal formulation that finally substantiates the overall efficacy of the niosomal formulation (Balasubramanian A et al., 2002).

**Doxorubicin**

Rogerson et al., studied distribution of niosomal doxorubicin prepared from C_{16}, monoalkyl glycerol ether with or without cholesterol. Niosomal formulation exhibited an increased level of doxorubicin in tumor cells, serum and lungs, but not in liver and spleen. Doxorubicin-loaded cholesterol-free niosomes decreased the rate of proliferation of tumor and increased life span of tumor-bearing mice. The cardio toxicity effect of doxorubicin was reduced by niosomal formulation. Niosomal formulation changes the general metabolic pathway of doxorubicin (Rogerson A et al., 1988).

**Methotrexate**

Aznim et al., quoted in their research article that niosomal formulation of methotrexate exhibits higher AUC as compared to methotrexate solution, administered either intravenously or orally. Tumoricidal activity of niosomally-formulated methotrexate is higher as compared to plain drug solution (Aznim MN et al., 1985).

**Bleomycin**

Niosomal formulation of bleomycin containing 47.5% cholesterol exhibits higher level drug in the liver, spleen and tumour as compared to plan drug solution in tumor-bearing mice (Naresh RAR et al., 1996). There is no significant difference in drug concentration with niosomal formulation in lung as compared to plan drug solution. Also, there is less accumulation of drug in gut and kidney in case of niosomal formulation (Naresh RAR et al., 1996).

**Vincristine**

Niosomal formulation of vincristine exhibits higher tumoricidal efficacy as compared to plain drug formulation (Parthasarathi G et al., 1994). Also, niosomal formulation of carboplatin exhibits higher tumoricidal efficacy in S-180 lung carcinoma-bearing mice as compared to plain drug solution and also less bone marrow toxic effect (Zhang JQ et al., 2001).

**Anti-infective agents**

Sodium stibogluconate is a choice drug for treatment of visceral leishmaniasis is a protozoan infection of
reticuloendothelial system. Niosomal or liposomal formulation of sodium stibogluconate exhibits higher levels of antimony as compared to free drug solution in liver (Ballie AJ et al., 1986). Antimony level is same in both formation i.e. niosome and liposome.

Niosomal formulation of rifampicin exhibits better anti-tubercular activity as compared to plain drug (Uchegbu F et al., 1998).

**Anti-inflammatory agents**

Niosomal formulation of diclofenac sodium with 70% cholesterol exhibits greater anti-inflammation activity as compared to free drug (Naresh AR et al., 1993). Niosomal formulation of nimesulide and flurbiprofen also exhibits greater anti-inflammation activity as compared to free drug (Shahiwala A and Misra AJ, 2002; Reddy DN et al., 1993).

**Diagnostic imaging with niosomes**

Niosomal system can be used as diagnostic agents. Conjugated niosomal formulation of gadobenate dimeglumine with [N-palmitoyl-glucosamine (NPG)], PEG 4400, and both PEG and NPG exhibit significantly improved tumor targeting of an encapsulated paramagnetic agent assessed with MR imaging (Luciani A et al., 2004).

**Ophthalmic drug delivery**

It is difficulty to achieve excellent bioavailability of drug from ocular dosage form like ophthalmic solution, suspension and ointment due to the tear production, impermeability of corneal epithelium, non-productive absorption and transient residence time. But to achieve good bioavailability of drug various vesicular systems are proposed to be use, in experimental level, like niosomes, liposomes.

Bioadhesive-coated niosomal formulation of acetazolamide prepared from span 60, cholesterol stearylamine or dicetyl phosphate exhibits more tendency for reduction of intraocular pressure as compared to marketed formulation (Dorzolamide) (Aggardwal D et al., 2004). The chitosan-coated niosomal formulation timolol maleate (0.25%) exhibits more effect for reduction intraocular pressure as compared to a marketed formulation with less chance of cardiovascular side effects (Aggarwal D et al., 2004).

**Transdermal drug delivery**

Administration of drugs by the transdermal route has advantages such as avoiding the first pass effect, but it has one important drawback, the slow penetration rate of drugs through the skin. Various approaches are made to overcome slow penetration rate, one approach for it is niosomal formulation. Alssarra et al., studied transdermal delivery pro-niosomal formulation of ketorolac prepared from span 60 exhibits a higher ketorolac flux across the skin than those proniosome prepared from tween20 (Alssarra AI et al., 2005). It is also identified in literature that the bioavailability and therapeutic efficacy of drug like diclofenac , flurbiprofen and nimesulide are increased with niosomal formulation (Naresh AR et al., 1993; Reddy DN and Udupa N, 1993; Shahiwala A and Misra AJ, 2002).

**Niosomes in oral drug delivery**

An oral administration of niosomal formulation of methotrexate exhibits higher concentration of drug in serum with more uptakes by the liver as compared to plain drug in mice (Azmin MN et al., 1985). So it concludes that gastrointestinal tract absorption of drug increases in niosomal formulation. Niosomal formulation of insulin prepared from span 20, 40, 60, 80 shows lower in-vitro release of insulin in simulated intestinal fluid from span 40 and 60 than span 20 and 80 (Varshosaz J et al., 2003). Niosomes prepared from span 60 exhibits highest protection of insulin against proteolytic enzymes and good stability in presence of sodium deoxycholate and storage temperature (Varshosaz J et al., 2003).

**Niosome formulation as a brain targeted delivery system for the vasoactive intestinal peptide (VIP)**

Radiolabelled (I^{125}) VIP-loaded glucose-bearing niosomes were injected intravenously to mice. Encapsulated VIP within glucose-bearing niosomes exhibits higher VIP brain uptake as compared to control (Dufes C et al., 2004).

**Conclusion**

It is obvious that niosome appears to be a well preferred drug delivery system over liposome as niosome being stable and economic. Also niosomes have great drug delivery potential for targeted delivery of anti-cancer, anti-infective agents.Drug delivery potential of niosome can enhance by using novel concepts like proniosomes, disosomes and aspasome.Niosomes also serve better aid in diagnostic imaging and as a vaccine adjuvant. Thus these areas need further exploration and research so as to bring out commercially available niosomal preparation.

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