Saudi Journal of Medical and Pharmaceutical Sciences **ISSN 2413-4929 (Print)**
Scholars Middle East Publishers **ISSN 2413-4910 (Online)**
Dubai, United Arab Emirates
Website: http://scholarsmepub.com/

Applications of Niosome and Targeting Strategies in the Field of Phyto-Pharmaceuticals: A Review

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Review Article

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Article History
Received: 10.04.2018
Accepted: 22.04.2018
Published: 30.04.2018

DOI:
10.21276/sjmps.2018.4.4.12

Abstract: Medication carrier systems are delineated as definitions intended to exchange a medication to the desirable territory of activity inside the body. Principle part of medication carrier is a proper bearer which shields the medication from fast degradation or clearance and along these lines improves concentration of drugs in the targeted tissues. In light of their biodegradable, biocompatible, and non-immunogenic properties, niosomes are promising nanoscale carriers that are formed by self-aggregation of non-ionic surfactants and cholesterol in a watery stage. As of late, various researches have been accounted for the capability of niosomes to fill in as a bearer for the conveyance of various kinds of medications. Niosomes make better substance and strength conditions other than lipid vesicles. Niosomes have been generally assessed for controlled discharge and focused on conveyance for the treatment of malignancy, viral contaminations and other microbial sicknesses. In this sense, the present work means to audit the principle niosomal approaches utilized for relationship of various medications and the fundamental accomplishments from utilizing this innovation.

Keywords: Medication carrier, lipid vesicles, controlled release.

INTRODUCTION

Rapid advancement of nanotechnology in medicinal field has allowed the evaluation of nanoparticles that, serving as drug carriers made of metals, polymers, hydrogel, ceramic, and lipid based carriers such as liposomes and niosomes, etc [1, 2].

Nanocarriers provide a huge access in drug delivery with some bright features such as targeted delivery of drug at site of action, secure drug from degradation and segmentation. Generally nanomaterials having size range between 0.1 to 100 nm, minimization of size offer many advantages such as: better pharmacokinetics and bioavailability of therapeutic agents due to higher ratio of surface area to volume, reduce toxicity, help in intracellular delivery and extend retention time resulting higher therapeutic potential of drugs, and exhibit better stability [3].

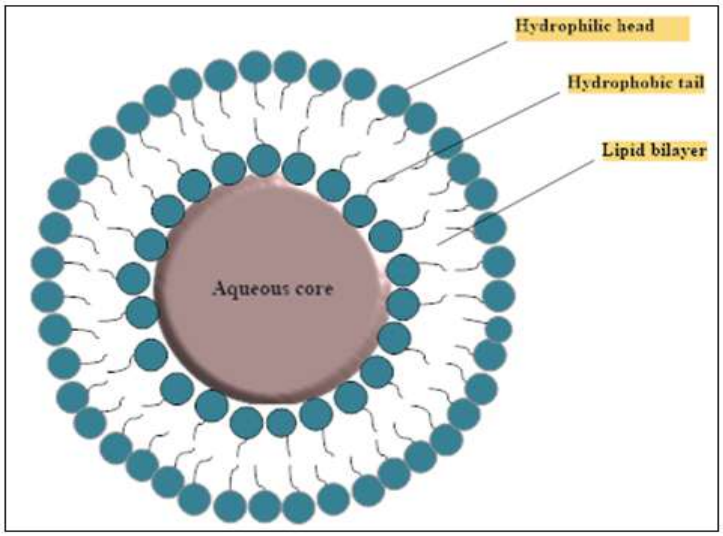

Fig-1: Basic structure of niosome

Niosomes are one of the hopeful nanocarriers having unique characteristics. Main properties of niosomes are biodegradable, biocompatible, and non-immunogenic. Basically niosomes are vesicles mainly consist of non-ionic surfactant and sometimes cholesterol and its derivatives. Because of unique bilayer structure of noisome, it can capsulize both hydrophilic and lipophilic substances (drugs, proteins, genes, vaccines). Niosomes are used as nanomedicines having sustained release property which also inflect absorption through skin and assure drug release in specific amount. By entrapping hydrophilic substances in vesicular aqueous core or assimilate on the bilayer surface and by capsulizing the lipophilic substances into the arena of the bilayers, the unique structure of niosomes can be attained. Depending on type of surfactants used, niosomes can be classified as non-ionic, anionic, cationic and zwitterionic. Application of niosome first started from cosmetic industry and then potentiality of noisome was explored in drug delivery [2]. Niosomes are notable vesicles for potential delivery of drug substances through different routes of administration. As niosomes are having very less disfavors with numerous application.

Main purpose of this review to furnish an overall description to the following prospects: factors to be considered during noisome preparation, chemical compositions, methods of preparations, characterizations, applications with several advantages, some recent applications. Ultimately this review will endeavour to help acquiring niosomes as drug delivery system.

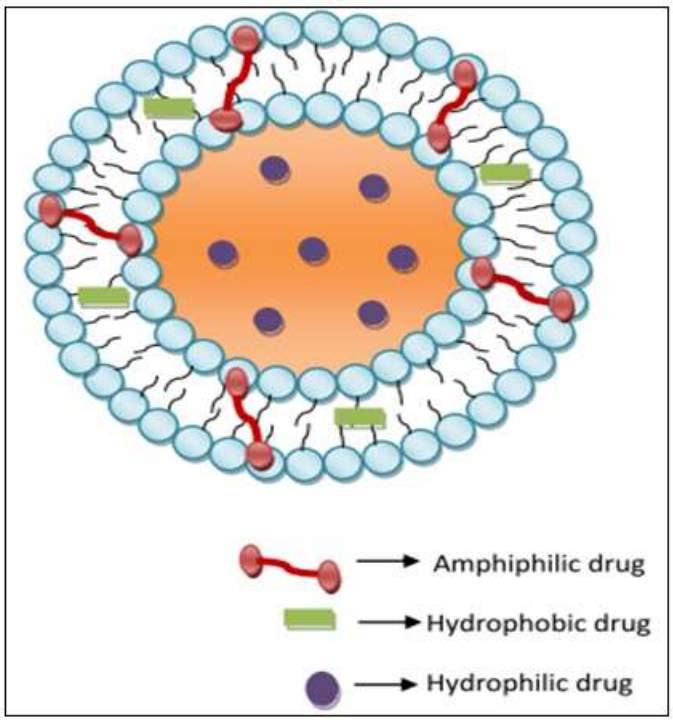

Fig-2: Area for encapsulation of different types of drug.

PREPARATION PROSPECTS

These are most crucial parameters that have impact on the characteristics of niosomes. The main components of noisome preparation are non-ionic surfactants, lipids, and charged molecules. The self-fabrication of non-ionic surfactants results in bilayer structures because of high interfacial stress. Sometimes mechanical energy or heat is applied to form a closed bilayer structure.

Non-ionic surfactants

Surfactants are amphiphilic molecules with two different regions having different solubilities, a hydrophilic head and a hydrophobic tail. Non-ionic surfactants are the surfactants, which have no charged groups in their hydrophilic heads. Hydrophilic head group involve sulfonates, phosphonates, carboxylates and ammonium derivatives and hydrophobic tail involve chains made up of alkanes, fluorocarbons, aromatic or other non-polar groups. For anionic surfactant head charge is negative. Cationic surfactant has positive charge and zwitterionic surfactant contains two oppositely charged head group. Non-ionic surfactants are more stable and less toxic compared to anionic, cationic, and amphoteric surfactants. Selection of surfactant depends upon the hydrophilic-lipophilic balance (HLB) and critical packing parameter (CPP) which are illustrated below [3].

Hydrophilic-lipophilic balance (HLB)

HLB is a dimensionless parameter which plays an important role for surfactant selection in controlling

drug entrapment efficiency [4]. HLB indicate the solubility of surfactant molecule and also describe the balance between hydrophilic head and lipophilic tail part. In case of non-ionic surfactants HLB value range from 0 – 20. Lower HLB value [<9] denotes lipophilic surfactant and higher HLB value denotes [>11] hydrophilic surfactant. Surfactants having HLB value 3 to 8 are suitable to form bilayer surfaces, known as W/O emulsifier and O/W emulsifier shows HLB value 8 to 18. Surfactant having HLB value 14 to 17 are not suitable to form bilayer surface because they are extremely water soluble [5].

Critical packing parameters (CPP)

Besides HLB value another important dimensionless parameter is CPP. CPP of surfactant determines geometry of vesicles, chemical structure. CPP can be represent as below.

$$\mathrm{CPP} = \frac{\mathrm{v}}{l_c a_o}$$

Where, v = Hydrophobic part volume,
l_c = Hydrophobic group length,
a_o = Hydrophobic head group area,

CPP value of surfactant can predict the type of vesicle. If (CPP < 1/3), it indicate that the surfactant is able to form spherical micelles, if (1/3 < CPP > ½), indicate surfactant's ability to form non-spherical micelles and (CPP > 1) indicate bilayer vesicles or inverted micelles.

Gel liquid transition temperature (Tc)

Gel liquid transition temperature is directly related to entrapment efficiency. Higher the T_C, greater the entrapment efficiency, for example span 60 [6].

Cholesterol

Various additives can be used for niosomal drug delivery, among these cholesterol is most important. Cholesterol forms hydrogen bond with the hydrophilic head of surfactant in the bilayer structure [7]. Cholesterol influences some important vesicular properties, such as - entrapment efficiency, increase stability, release of payload [8]. Cholesterol promotes stability to the bilayer surface by influencing the gel liquid transition temperature. In case of surfactants having HLB > 6, cholesterol is essential to form bilayer vesicles and for lower HLB value, stability is improved by adding cholesterol. Cholesterol content also alters drug loading capacity, which is an important factor for niosomal preparation. Agarwal *et al*. has been demonstrated that with increasing cholesterol content, stability of enoxacin is improved. Another study has shown that cholesterol have less effect on the flurbiprofen entrapment into niosome prepared from span 20 and span 80. But entrapment efficiency is improved when 10% of cholesterol was added into noisome prepared from span 40 and span 60, further increase in cholesterol content leads to decrease in entrapment efficiency. It has also been proved that in case of more hydrophobic surfactants, addition of cholesterol helps in inhibiting the chances of aggregation and promotes vesicles formation [9].

Charged molecule

Charged molecules are mainly added to increase stability of the vesicles and to prevent aggregation by providing charged groups to the bilayer surface. Dicetyl phosphate is mostly used charged molecules which impart a negative charge on the bilayer surface. Generally, charged molecule is added in an amount of 2.5 – 5 mol%. Even so increasing amount of charged molecules can suppress niosome formulation [10].

Table-1: Components used for niosome preparation

Components	Example
1. Surfactants	
a. Non-ionic	
I. Fatty alcohol	Cetyl alcohol, Steryl alcohol, Cetosteryl alcohol, Oleyl alcohol
II. Ethers	Brij, Decyl glucoside, Lauryl glucoside, Triton X-100
III. Esters	Glyceryl laurate, Polysorbates, Spans
IV. Block polymers	Poloxomers
b. Anionic	Stearate, Soap
c. Cationic	Lauryl amine, Trimethyl dodecyl ammonium
d. Zwitterionic	Dodecyl betaine, Lauramidopropyl betaine
2. Lipidic components	Cholesterol, 1-α-soya phosphotidylcholine
3. Charged molecules	
a. Negative charge	Dicetyl phosphate, Phosphatidic acid, Stearylamine
b. Positive charge	

TYPES OF NIOSOME

Depending upon vesicle size, niosomes can be categorized into three groups. These are small unilamellar vesicles (SUV_S, size= 10-100 nm), multilamellar vesicles [MLV_S], and large unilamellar vesicles [LUV_S, size= 100-3000 nm] [11].

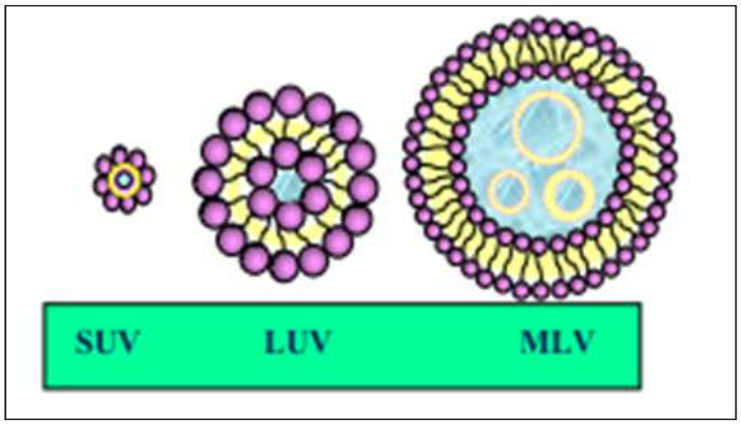

Fig-3: Types of niosomes

METHOD OF PREPARATION

Thin film hydration method [TFH]

Thin film hydration method is a very common and well known noisome preparation method. In this method, the surfactants, cholesterol and charged molecules are dissolved in an organic solvent in a round bottomed flask. Then the organic solvent is removed by using rotary vacuum evaporator and thus the thin film is obtained on the inside wall of the round bottomed flask. An aqueous solution such as water or phosphate buffer containing the drug is added and the dry film is hydrated above the gel liquid transition temperature and continuous shaking is done. By this method MLV_S are prepared. TFH method has been used for preparation of noisome of various drugs such as- minoxidil, insulin, nimesulide, doxorubicin, etc [12].

Hand shaking method (HSM)

Hand shaking method is similar to TFH method. MLV_S are also prepared by using this method. In this method, the surfactants, cholesterol are dissolved in an organic solvent in a round bottomed flask. Then the organic phase is removed by using rotary vacuum evaporator thus a thin film is obtained on the inside wall of the flask. Then the dried film is hydrated using aqueous solution containing drug. Gentle mechanical shaking is done for 1 hr, thus milky niosomal dispersion is appeared. This method has been used for preparation of noisome of various drugs such as- diclofenac sodium, flurbiprofen, etc [13].

Ether injection method [EIM]

In ether injection method the surfactants and other additives are dissolved in an organic solvent like diethyl ether. Then the organic solution is injected into an aqueous solution containing drug through a needle, temperature is maintained at about 60ºC. The organic solvent is evaporated by using rotary vacuum evaporator. During vaporization single layered vesicles are formed. This method has been used for the noisome preparation of drugs like fluconazole, adriamycin, diclofenac sodium [14-16].

The 'bubble' method

This technique is used for noisome preparation without addition of organic solvents. In this method surfactants, other additives, and phosphate buffer [pH - 7.4] were taken into a glass flask with three necks. A thermometer is kept in the first neck, second neck is used to supply nitrogen and water-cooled reflux in the third neck. At 70ºC noisome components are dispersed for 15s with high shear homogenizer and right away followed by the bubbling of nitrogen gas at 70ºC [17].

Microfluidization method

Microfluidization method offers unilamellar vesicles, smaller size, better reproducibility and greater uniformity. This method is based upon submerged jet principle, in which two fluidized streams [drug, surfactant] interact at ultrahigh velocities, in precisely defined micro channels within the interaction chamber. The high speed impact and the energy supplied leads to formation of noisome [18, 19].

Reverse phase evaporation

In this method, surfactants, additives are dissolved in an organic solvent, then aqueous phase containing drug is added to the organic phase. The mixture is then sonicated to form an emulsion and by using rotary evaporator the organic phase is removed at about 40-60ºC. LUV_S are prepared through this method [20, 21].

Sonication method

In this method, buffer solution of drug is added to the surfactant and cholesterol mixture. Then at 60ºC the mixture is sonicated with a titanium probe for 3 min. this method has been used for niosome preparation of diallyl disulfide [22].

Heating method [HM]

In this method, surfactant and cholesterol are separately hydrated in phosphate buffer [p^H=7.4] under nitrogen atmosphere for 1 hour, then, after about 15-20 min, the solution is heated at about 120ºC on a hot plate, stirring is done to dissolve cholesterol. The temp

is then cooled down to 60ºC. Then the surfactant and other additives are added to the buffer solution of cholesterol with continuous stirring for another 15 min. Niosomes are obtained and kept at room temp for 30 min then again kept at 4-5ºC under nitrogen atmosphere upto use [23].

Freeze and thaw method [FAT]

In this method MLV_S are prepared. At first niosomal suspension are prepared by TFH method then the suspension is frozen in liquid nitrogen for 1 min and thawed for another 1 min in a water bath at 60ºC [24] .

Proniosome technology

In this method, water soluble carrier such as sorbitol and mannitol are coated with surfactant. This process results in the formulation of dry 'proniosomes' which need to be hydrated before use. This method leads to production of more physically stable niosomes than conventional niosomes [25].

Dehydration rehydration method [DRM]

This method involves niosome preparation by TFH method, then niosomes are frozen in liquid nitrogen followed by freeze drying overnight. Niosome powders are hydrated using phosphate buffer (pH=7.4) at 60ºC [26].

CHARACTERIZATION

The characterization of niosome is very crucial for clinical applications. Hence the parameters such as size and size distribution, morphology, polydispersity index (PdI), zeta potential, bilayer formation, number of lamellae, membrane rigidity, entrapment efficiency, stability study, *in vivo* studies and *in vitro* release must be evaluated.

Size and morphology

Niosomes are presumed to be spherical in shape and vesicle size can range from 20-50 µm. Size and morphology of niosomes are studied using light microscopy, coulter counter, dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), photon correlation spectroscopy, freeze fracture replication-electron microscopy (FF-TEM), zetasizer and mastersizer. Also size distribution and polydispersity index can be determined by using dynamic light scattering particle size analyzer [27-30].

Zeta potential

Zeta potential of niosome plays a vital function for vesicle stability. Generally, charged vesicles show better stability against accumulation and fusion compared to uncharged niosome vesicles. Surface zeta potential is determined by zetasizer and DLS instrument, microelectrophoresis, pH sensitive fluorophores. A study has been shown that negative zeta potential values ranging from - 41.7 to - 58.4 mV are sufficiently high for electrostatic stabilization [31].

Bilayer formation

Bilayer characterization is important for determination of drug entrapment efficiency. Non-ionic surfactants form a self-assembly in order to make bilayer surface. Bilayer characterization is done by an X-cross formation using light polarization microscopy [32-34].

Number of lamellae

This can be measured by using nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering and electron microscopy.

Membrane rigidity

This can be determined by way of mobility of fluorescence probe as a function of temperature [35].

Entrapment efficiency (EE%)

Entrapment efficiency is referred as fraction of drug capsulized by the niosome vesicles. It is a significant parameter for drug application. Uncapsulated drug can be taken out from the preparation by centrifugation, filtration, dialysis and gel chromatography. Vesicles are ruptured to obtain drug concentration in the niosomal preparation by addition of 0.1% Triton X-100 or 50% propane to the preparation with 1 hr incubation period. Amount of total drug in µg/ml can be determined by HPLC, ELISA, or spectrophotometer [36].

Entrapment efficiency can be represented as,

$(WT-WF)/WT \times 100\%$ or

$EE\% = WL/WT \times 100\%$

Where,

WT = Amount of total drug in preparation.
WF = Amount of free drug.
WL = Amount of loaded drug.

Stability study

Stability study is carried out to investigate vesicle size, size distribution, encapsulation efficiency during storage period. Stability study is done over several months, during this period samples are taken at regular time intervals. Amount of drug present into the niosomes are determined by UV spectroscopy or HPLC methods [37, 38].

***In vitro* release**

In Vitro Release study is often done by using dialysis bag. A dialysis bag is washed and then soaked in distilled water. Niosomal preparation containing drug is kept into the dialysis bag and sealed. Then the bag is immersed in buffer solution, continuous stirring is done and temperature is maintained at 25ºC or 37ºC. Samples are withdrawn at specific time interval and drug content is analyzed by suitable assay method [39].

***In vivo* release**

Tsuyoshi shimamura *et al*., perform the antifungal studies of topical gel using Specific-pathogen-free Hartley guinea pigs, as an animal model.

The animals are acclimatized to laboratory conditions for more than 7 days, including quarantine period, and are used when 6 weeks old. They are housed in a colony room with a 12:12 h light, dark cycle at 21 ± 2ºC and handled according to standard laboratory protocol. These animals are divided into four groups: control, standard drug, test and blank formulation, each containing 5 animals. Prior to the study, hairs are clipped from the dorsal region of 20 animals. Pre-treatment is done by shaving and tape-stripping. The infection is developed in guinea pigs by topical application of 50 µl *T. mentagrophytes* suspension. After inducing infection, antifungal treatment is initiated on the third day after inoculation on shaved and non-occluded areas. These animals are treated with standard as well as prepared gel formulation, except control group. The standard group treated with a marketed gel formulation of a standard antifungal drug, while the formulation treated groups from each set are treated with prepared phyto-niosome gel formulation. The animals are observed for 30 days to check the efficacy of prepared phyto-niosomal gel formulation against tinea corporis [40].

***Ex vivo* study**

Ex vivo skin permeation study is carried out by using Franz diffusion cell taking Phosphate buffer (pH 7.4) is used as medium.

NIOSOME MODIFICATION

Several modification agents and techniques are adopted to alter wet ability and side effects of niosomes; among these PEG is most significant.

Polyethylene glycol coating helps niosomes able to circulate in the blood stream for longer period of time because body immune system cannot recognize. Thus niosomes can avoid engulfment by reticulo-endothelial-system [41].

APPLICATIONS OF NIOSOMES AS NANOCARRIERS

Anticancer agents

Modern cancer treatment is based on chemotherapy, chemotherapeutic agents are having poor penetration and massive side effects. Several efforts have been made by using niosomes as a nanocarrier to defeat these problems.

Dwivedi *et al*., encapsulized artemisone in niosome prepared by TFH method. This preparation showed massive selective cytotoxicity against the melanoma cells and very less toxic effect against healthy cells [42]. Cosco *et al.*, tested 5-FU-loaded polyethylene glycol coated and uncoated bola-niosomes on breast cancer cell lines. Both formulations showed increased cytotoxic effect with respect to the free drug [43].

Uchegbu *et al.*, formulated doxorubicin loaded niosomes and checked activity in hexadecyl diglycerol ether and Span 60 against human ovarian cell line. Result was obtained that a little decrease in the IC50 against the resistant cell line in case of Span 60 encapsulated drug, compared to the free drug [44].

Dalia *et al.*, evaluated tamoxifane Citrate niosomes for localized cancer therapy through in-vitro breast cancer cytotoxicity and in-vivo solid anti-tumor efficacy. Niosomes were prepared using different formula and characterized. The resulted niosomes prepared using span 60 and cholesterol in 1:1 molar ratio, showed prolonged release in TMC, enhanced cellular uptake and higher entrapment efficiency [45].

Targeted delivery

Cell targeting specificity and efficiency can be improved by attaching a ligand coupled to the niosome surface for tumor therapy. Cell specific targeting niosomes can be prepared by using micro and macromolecules to the surface.

Bragagni *et al*., formulated brain targeted doxorubicin containing niosome. *In Vivo* study in rats showed that IV administration of a single dose of the formulated niosome compared to commercial preparation was able to reduce heart accumulation significantly and also circulation time period was longer with higher doxorubicin concentration in brain [46].

Dufes *et al.*, formulated epidermoid carcinoma targeted doxorubicin encapsulated niosome prepared by sonication method using Span 60, cholesterol, solulan C24, N-palmitoyl glucosamine for anticancer therapy. The formulation had superior *in vivo* safety profile compared to the free drug [47].

Co-drug delivery

Niosomes are promising drug carriers suitable for co-delivery of multiple drugs in combination. Thus therapeutic efficacy of drug is enhanced with greater efficacy and decreased dose.

Sharma *et al.*, recently investigated niosome by dual encapsulation with hydrophobic curcumin and hydrophilic doxorubicin as multiple drug delivery against cancer. Result obtained that compared to free drug, dual encapsulated niosome had greater cytotoxicity on HeLa cells [48].

Antibiotics

Delivery of antibiotics and anti-inflammatory agents through niosome has been reported to enhance skin penetration and skin retention of drugs.

Begum *et al.,* formulated rifampicin loaded niosomes and evaluated activity of the formulation *In Vitro* conditions. Study proved that rifampicin loaded niosomes provide uniform and sustained release of drug [49]. Akbari *et al.,* Prepared ciprofloxacin loaded niosomes by film hydration method using various non-ionic surfactants and cholesterol in various concentration. Drug release and antibacterial activity were studied. Result indicated that cholesterol content and phase transition temperature of the surfactants greatly influenced niosome performance and moreover all formulations showed more antibacterial property than free ciprofloxacin [50].

Anti-inflammatory drugs

NSAIDS loaded niosomes cause mucosal irritation as adverse effect. Drug penetration is enhanced when applied topically.

Marianecci *et al*., prepared ammonium glycorrhizate loaded niosomes with various surfactant and cholesterol by altering concentration and tested in mice. Prepared niosomes showed no toxicity, improved anti-inflammatory activity and better skin tolerability [51].

Manosroi *et al.,* developed a novel elastic bilayer vesicle encapsulating diclofenac diethyl ammonium for topical use by chloroform film method using Tween 61 or Span 60 and cholesterol in different concentration. The result has demonstrated enhancement of transdermal absorption through rat skin and also in vivo anti-inflammatory effect of DCFD when entrapped in the developed novel elastic Tween 61 niosomes [52].

Antiviral drugs

Niosomes has been used as also potential carrier for various antiviral drugs. Ruckmani *et al*., formulated niosomes by combining tween, span, cholesterol, and encapsulating zidovudine, which is the first approved anti HIV compound for clinical use, they also analyzed entrapment efficiency and sustainability of release. Result was obtained that niosomes containing tween 80 encapsulated maximum amount of zidovudine and addition of dicetyl phosphate influenced drug release for long time [53].

Monavari *et al*., prepared and characterized acyclovir loaded nano-niosomes. The vesicles were prepared by thin film hydration method consist of cholesterol and Span 60 in various molar ratio. Result showed significant increase in entrapment efficiency and also exhibited retarded release compared with the free drug [54].

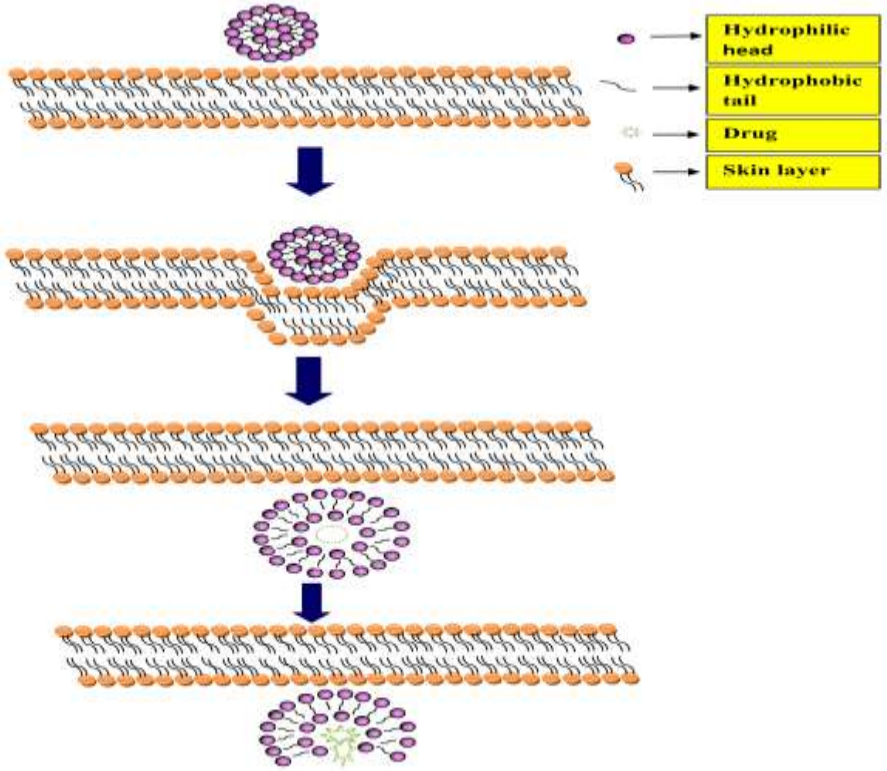

Fig-4: Drug release mechanism from niosome.

Table-2: Various drugs administered and their preparation method

Routes of administration	Loaded drug	Compositions used	Preparation method	Reference
Intravenous	Morin hydrate	Span-60,80	HSM	[55]
Intramuscular	Anti-HBsAg	Span-85,	REV	[56]
Transdermal	Vinpocetine	Sugar ester, sucrose palmitate, sucrose myristate	PT	[57]
	Tenoxicam	Span-60,80 Tween-20,60,80	PT	[58]
	Ellagic acid	Span-60, Tween-60	REV	[59]
	Sulfadiazine	Pluronic L64, P105	TFH	[60]
	Gallidermin	Tween-61	FDEL	[61]
Oral	Valsartan	Span-60	PT	[62]
	Insulin	Brij-52,72,76,92,97	TFH	[63]
	Antioxidants(gallic acid, ascorbic acid)	Tween-60	TFH	[64]
	Hydroxychloroquine	Tween-20	RXV, Sonication, HSM, EIM	[65]
Ocular	Naltrexone	Span-60	REV	[66, 24]
	pCMSEGFP	Combination of cationic lipid, Tween-80	REV	[67]
Pulmonary	Glucocorticoid	Polysorbate 20	TFH	[68]
	Beclometasone dipropionate	Span-60	PT	[69]

Table-3: Recent studies carried out on niosomes using various drugs

Type of drug	Name of drug	Composition	Study	Reference
Angiotensin receptor blockers	Candesartan cilexetil	Span 60, cholesterol, dicetyl phosphate, maltodextrin.	*In* vitro and *in vivo* evaluations of *in situ* niosome of maltodextrin.	[70]
Anti-inflammatory	Naproxen	Tween 80, Tween 20, cholesterol.	Formulation, optimization and characterization of naproxen niosome.	[71]
	Dexamethasone	Span 60, cholesterol.	Effect of formulation and processing variables and release study of dexamethasone entrapped niosomes.	[72]
	Ammonium glycyrrhizinate	Tween 85, span 20, cholesterol.	Anti-inflammatory activity of ammonium glycyrrhizinate containing niosomes in human and murine models.	[51]
Antibacterial	Moxifloxacin	Tween 60, cholesterol.	Efficiency of Chitosan gel-embedded moxifloxacin niosomes: for treatment of burn infection.	[73]
	Cefixime	C-Glycoside derivative surfactant, cholesterol.	Glycoside-based niosomes for better *in-vivo* performance of cefixime.	[74]
Anticancer	Doxorubicin	Span 60, cholesterol, dicetyl phosphate, N-lauryl glucosamine.	Glucosamine anchored niosomal drug delivery system of doxorubicin for cancer targeting.	[75]
	Paclitaxel	Span 40, cholesterol, dicetyl phosphate.	Pharmacokinetics and tissue distribution in rats of paclitaxel loaded niosomes.	[76]
	Hydroxycamptothecin	Span 60, cholesterol	Transferrin modified hydroxycamptothecin loaded PEGylated niosomes for tumor targeting.	[77]
	Methotrexate	Alkyl glucopyranoside, cholesterol	Evaluation of physic-chemical and biological properties of alkyl glucopyranoside-based niosome containing methotrexate.	[78]
Antiviral	Nevirapine	Tyloxapol, cholesterol	Prospective drug delivery module for antiretroviral drug nevirapine.	[79]
H2 receptor antagonist	Famotidine	Span 60, cholesterol	*In vitro* and *ex vivo* study of famotidine proniosomes.	[80]
Opioid peptide	Dynorphin-B	Span 60, cholesterol, solulan C24, N-palmitoyl glucosamine	Development and characterization of dynorphin-B niosomes for brain targeting.	[46]
Peptide hormone	Vasoactive intestinal peptide	Span 60, cholesterol, solulan C24, N-palmitoyl glucosamine	Glucose-targeted niosomes for delivery of vasoactive intestinal peptide (VIP) to the brain.	[47]
Antioxidant, anti-inflammatory, antitumor	Resveratrol	G64, stabilizer(OA or LA), absolute ethanol	Formulation of resveratrol encapsuled niosomes for topical use.	[81]
Anti-leishmanial	Itraconazole	Span 40, span 60, cholesterol	*In vitro* susceptibility and anti-leishmanial effect of itraconazole niosome.	[82]

CONCLUSION

The concept of drug encapsulation into vesicular system like liposome and niosome has been widely adopted by researchers in the recent years. Potential of niosome is far better than liposome in terms of targeted delivery. Niosomes offer more effective, convenient and prolonged drug delivery at site of action, as well as it can capsulize both hydrophilic and lipophilic drugs at a same time. Hence, further study and researches are needed to construct a better technology to serve as a promising carrier system compared to ionic drug carriers.

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