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NANO-NIOSOMES AS PROMISING DRUG DELIVERY SYSTEM: RECENT REVIEW

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ABSTRACT

The pasture of nanochemistry research has shown an immense development in the embryonic of novel nanocarriers as prospective drug delivery systems. Niosome is used as a colloidal vesicular carrier in drug delivery and is a class of molecular cluster formed by self-association of non-ionic surfactants in an aqueous phase. The unique structure of niosome presents an effective novel drug delivery system (NDDS) with ability of loading both hydrophilic and lipophillic drugs. Development trends in nanotechnology in health and medicine are expected to provide solution to many of modern medicines unsolved problems. Nanotechnology offers potential developments in therapeutics, diagnosis, cancer treatment, implantable materials, and tissue regeneration and made up of non-ionic surfactant vesicles which are biodegradable and safe. These are cost effective and stable compared with other colloid carriers. It has applications in oral, topical, parental and novel drug delivery as controlled and targeted delivery. This review article focuses on niosome structure, composition, advantages, types of niosomes, methods of preparation, characterization and its application.

KEYWORDS

Nanotechnology, Nano-niosomes, Surfactants, Method of preparations, Reviews of literature and Applications.

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INTRODUCTION

Rapid development in the function of nanotechnology for treatment and diagnosis has made a new meadow called “nanomedicine”. This review introduces nanometre scale materials named nano-niosomes, being part of nanochemistry, as well as nanomedicine fields. This review introduces nanometre scale materials named nano-niosomes, being part of nanochemistry, as well as nanomedicine fields[1]. Niosomes structurally consist

of a non-ionic surfactant bilayer with its hydrophilic ends exposed on the outside and inside of the vesicle to the aqueous phase, while hydrophobic chains face each other within the bilayer[2].

Vesicular systems are a novel means of drug delivery that can enhance bioavailability of encapsulated drug and provide therapeutic activity in a controlled manner for a prolonged period of time. Non-ionic surfactants offer a few reward over the phospholipids since they are more inexpensive and are chemically more stable as they are not easily hydrolysed or oxidised during storage. The vesicular composition can be customized to afford sustained or controlled drug delivery thus ornamental efficacy of system for prolonged periods[3].

Reducing the size into nanoscale in drug carriers offer many advantages such as: declining toxicity by their privileged build up at the target site, recuperating pharmacokinetics and bio distribution of therapeutic agents due to superior ratio of surface area to volume; facilitating intracellular delivery and prolonging their maintenance time either inside the cell which improves therapeutic potential of drugs or in blood circulation[1].

Definition

A niosome is a non-ionic surfactant-based liposome and these are formed mostly by incorporation of cholesterol asexcipients, other excipients can also be used. They are having a bilayer which is structurally similar to liposomes, however, the resources used to prepare niosomes formulate them more stable and thus niosomes propose a lot of compensation over liposomes. The sizes of niosomes are microscopic and lie in nanometric scale. The particle size of nano-niosomes ranges from 10nm-100nm[5,21].

Structure

A typical niosome vesicle would consist of a vesicle forming ampiphillic i.e. a non-ionic surfactant such as Span60, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as dicetyl phosphate, which also helps in stabilizing the vesicle[5,22].

TYPES OF NIOSOMES

Niosomes are classified based on number of bilayer, size and method of preparation.

Multilamellar- 0.5μm to 10μm in diameter.

Larger unilamellar- 0.1μm to 1μm in diameter.

Small unilamellar - 25-500nm in diameter[6].

Multilamellar vesicles (MLV)

It consists of a number of bilayer neighbouring the aqueous lipid compartment separately. The approximate size of these vesicles is 0.5-10μm diameter; these are the most extensively used niosomes. It is simple to make and are mechanically stable upon storage for long periods. These vesicles are extremely suited as drug carrier for lipophillic compounds.

Large unilamellar vesicles (LUV)

Niosomes of this type have a high aqueous/lipid compartment ratio, so that larger volume of bio-active materials can be entrapped with a very inexpensive use of membrane lipids.

Small unilamellar vesicles (SUV)

These small unilamellar vesicles are mostly prepared from multilamellar vesicles by sonication method[5].

Compostition of niosome

Niosomes are composed of.

Cholestrol

It gives proper shape and rigidity to the niosomes.

Non-ionic surfacant

The non-ionic surfactant contains hydrophobic tail and hydrophilic head. For the most part of non-ionic surfactants used are Span (60, 40, and 80), Tween (20, 40, and 80), Brij (52, 58, 35, and 30), Alkyl Amides, Sorbitan ester, Ester linked surfactants[6].

Cholesterol

Cholesterol is a waxy steroid metabolite originates in the cell membranes. Cholesterol and its derivatives are the most common additives found in niosomal systems and this is added usually to the non-ionic surfactants to give rigidity and orientational order to the niosomal bilayer. Cholesterol enables the configuration of vesicles, reduces aggregation and provides better permanence and is also known to eradicate gel to

liquid phase transition of niosomal systems consequential in niosomes that are less leaky[3].

Cholesterol is used to complete the hydrophobic moiety of high HLB single alkyl chain non-ionic surfactant for vesicle configuration. In general, it has been initiates that a molar ratio of 1:1 between cholesterol and non-ionic surfactant is an optimal ratio for the formulation of physically stable niosomal vesicles. Some information denotes the development of monohydrate or anhydrous cholesterol crystals among the surfactant/cholesterol bilayer. The minimum amount of cholesterol required to appearance vesicles with no evoking surfactant aggregates or other irregular structures depended on the type of surfactant and it's HLB.

Surface pressure measurements on monolayer of non-ionic surfactant/cholesterol mixture demonstrated a condensing effect of cholesterol as evidenced by the decreases in the effectual area per molecule as the cholesterol content of the monolayer increased. This effect may be attributed to the accommodation of cholesterol in the molecular cavities created by surfactant monomers assembled into vesicles and is responsible for the observed decreased permeability of cholesterol containing membranes compared to cholesterol free membranes[7,8].

Non-ionic surfactant

Surfactants form a unique class of chemical compounds. Surfactants are ampiphillic molecules with two distinct regions that have very different solubilities, a hydrophilic (water-soluble) end and a lipophillic (organic-soluble) end that is highly hydrophobic, for example, phospholipids (phosphatidyl choline) which are the foundation of biological cell membranes. The lipophillic region is chains made up of alkanes, fluorocarbons, aromatic or other non-polar groups. The head group involves highly solvated hydrophilic functionalities, such as sulfonate, carboxylates, phosphonates and ammonium derivatives. Surfactants can be classified to anionic, cationic, amphoteric and non-ionic; according to their hydrophilic functionality head group; being sulfonate, quaternary ammonium salts zwitterionic butanes and fatty acids, respectively.

Non-ionic surfactants are a category of surfactants which have no charge groups in their hydrophilic heads. Therefore in solutions, non-ionic surfactants can form structure in which hydrophilic heads are contradictory to aqueous solutions and hydrophilic tails are contradictory to organic solutions. Because of this property of the non-ionic surfactants, niosomes are formed by the self-assembly of non-ionic surfactants in aqueous dispersions.

Non-ionic surfactants are enormously one of the most excellent polymeric nanocarriers with awide role in controlled, sustained, targeted and incessant drug delivery. Commonly, surfactants are classified according to their polar head group. A non-ionic surfactant has no charge groups in its head. The head of an ionic surfactant has a net charge and is called an anionic surfactant. Examples of such surfactants include: fatty acid salts ("soaps"), sulphates, ether sulphates and phosphate esters. If the head charge is positive, it is called a cationic surfactant. If a surfactant contains a head with two oppositely charged groups, it is termed as a zwitterionic (amphoteric) surfactant. Cationic surfactants are also recurrently irritant and sometimes even toxic; therefore their relevance in drug delivery is narrower than the three other classes of surfactants. Non-ionic amphiphiles used in niosomes are classified in four categories: Alkyl esters, Alkyl amides, Alkyl ethers and esters of fatty acids. Surfactant assortment depends on the hydrophilic-lipophillic balance (HLB) and critical packing parameter (CPP) values[1].

OTHER ADDITIVES

Charged molecules

The electrostatic stability of vesicle is enhanced by incorporation of charged molecules into vesicular formulation, to amplify the encapsulation or adsorption of charged molecules, to enlarge the Transdermal iontophoretic transport of active materials and to familiarize the vesicles for enhanced specific interface with target cells. Dicetyl

phosphate is the largely used charged molecule introducing a negative charge in bilayer.

Polyethoxylated molecules

Solulan C24, a poyethoxylated derivative of cholesterol has also been as surface amendment material which contains PEG moiety with molecular weight of approximately 1000Da. It has a steric stabilizing consequence on the non-ionic surfactant vesicles. Solulan C24 also increases the elasticity of some vesicle bilayer[7].

Preparation methods of niosomes[1,5]

The preparation methods should be chosen according to the use of the niosomes, since the preparation methods influence the number of bilayer, size, size distribution, and entrapment efficiency of the aqueous phase and the membrane permeability of the vesicles.

Thin film hydration method

Exactly weighed quantity of cholesterol and surfactant were dissolved in chloroform - methanol mixture (1:1 v/v) in 100 ml round bottom flask. The weighed amount of drug is added to the solvent mixture. The solvent mixture was separated from liquid phase by flash evaporation at 60^0C to get a thin film on the wall of the flask at a rotation speed of 150 rpm. The complete elimination of remaining solvent can be ensured by applying vaccum. The dry lipid film was hydrated with 5 ml phosphate buffer saline of pH 7.4 at a temperature of 60^0C for a period of 1hour until the formation of niosomes[6,11].

Sonication method

The aqueous phase phosphate buffer solution pH 7.4 containing drug (100 mg) was added to the chloroform containing mixture of span 60 and cholesterol at 1:1 ratio in a scintillation vial and was subjected to bath sonication, keep up the temperature at 60^oC for 3 minutes to make small and uniform size niosomes[6].

Ether injection method

In this method the lipid layer cholesterol and the non-ionic surfactants are dissolved in the organic solvent like diethyl ether. This solution was injected little by little through a 14 gauge needle into an aqueous solution (drug solution) which was preheated to 60°C. The ether solution was evaporated using rotary evaporator, after evaporation of the organic solvent it form single layered vesicles. The size of the vesicles produced ranges from 50-1000nm[6].

Reverse phase technique

The cholesterol and surfactant of equivalent ratio is been dissolved in a mixture of organic solvent (ether and chloroform). An aqueous phase which contain drug is added to the above phase it form a mixture of two phases. The phase is sonicated at 4-5°C and it forms a clear gel, it is further sonicated by adding little quantity of PBS (phosphate buffer solution). The organic phase is separated by means of rotary vacuum evaporator at 40-60°C. The consequential viscous noisome suspension is diluted with PBS solution in a water bath at 60°C for 10mins to yield niosomes[6].

Bubble method

It is a single step preparation method for the niosomes. In this method organic solvents are not used. The bubbling unit contains round bottom flask with 3 necks positioned in the water bath. Water-cooled reflex is in the first neck, the thermometer is in the second neck to the check the temperature and the third neck for the nitrogen supply. The cholesterol and surfactant is dispersed in the buffer (7.4) at 70°C. The dispersed mixture is mixed for 15sec with high shear homogenizer and immediately afterwards bubbled at 70°C using nitrogen gas[6,10].

Hand shaking method (HSM)

Hand shaking method is one of the methods for synthesis of multilamellar vesicles which is similar to thin film hydration method and sometimes both these methods have been put in one category. In this method, the surfactants and a few additives such as cholesterol are dissolved in an organic solvent in a round-bottom flask. The organic solvent was separated using a rotary evaporator to form a thin film on the inside wall of the flask. The absolutely dried film was directly hydrated with aqueous solution [containing drug] for about 1 h with moderate mechanical shaking to form niosomal dispersion with a milky appearance and this method

has been used for preparation of niosome entrapped more in hydrate (MH), diclofenac sodium (DCS), luteinizing hormone releasing[1].

Micro fluidization method

Better uniformity, smaller size, unilamellar vesicles and superior reproducibility of niosomes could be achieved by using micro fluidization technique. In this method, the flooded jet principle in which two fluidized streams act together at ultra high velocities, in specifically defined micro channels inside the interaction compartment is used. The impingement of a thin liquid sheet along a general front is arranged in such a way that the energy abounding to the system remnants within the area of niosome formation[1].

Heating method (HM)

Surfactants and a number of additives such as cholesterol were separately hydrated in PBS (pH = 7.4) for one hour under nitrogen atmosphere at room temperature. Then, after about 15-20 min, on a hot-plate stirrer the solution is heated (about 120°C) to dissolve cholesterol. The temperature is decreased to 60°C and the other components, surfactants and other additives, are then added to the buffer in which cholesterol is dissolved while continues stirring for another 15 min. At this stage niosomes obtained are left at room temperature for 30min and then reserved at 4–5°C under nitrogen atmosphere until use[1].

Freeze method

Frozen and thawed multilamellar vesicles (FAT-MLVs) are produce by this method. Niosomal suspensions, prepared using thin film hydration method, were frozen in liquid nitrogen for 1 min and thawed in a water bath at 60°C for another 1 min[1,13].

Dehydration rehydration method (DRM)

The method was first described by Kirby and Gregoriadis in 1984. The dehydration rehydration vesicles (DRVs), prepared by thin film hydration, are frozen in liquid nitrogen and then followed by freeze drying overnight and then niosome powders are hydrated with PBS (pH = 7.4) at 60 °C[1,14].

Proniosome technology (PT)

The use of Proniosomes technology for preparation of niosomes was started about two decades ago. Proniosome technique has been used for the preparation of niosomes entrapped vinpocetine, valsartan, 17β-estradiol, tenoxicam, etc. Usually, small unicellular vesicles are prepared by converting of multi lamellar vesicle dispersions into small unicellular vesicles by either sonication (a bath or a probe sonicator) or by high pressure homogenization (a micro fluidizer) or by extrusion under high pressure (using French pressure cell). During application of energy, the multi lamellar vesicle structure is broken down and small unicellular vesicles with a high radius of curvature are formed[1].

SALIENT FEATURES OF NIOSOME

- Niosomes acquire infra structure consisting of hydrophilic and hydrophobic predominantly together and so accommodate the drug molecules with a wide range of solubility.
- Niosomes are osmotically active and more stable.
- Niosomes surfactants are biodegradable, biocompatible and non-immunogenic.
- The bilayer of the niosomes protects the covered active pharmaceutical ingredient from the heterogeneous factors present both inside and outside the body. So niosomes can be used for the delivery of labile and perceptive drugs.
- Niosomes exhibit flexibility in their structural characteristics and can be premeditated according to the desired situation.
- Better availability at the particular site, just by protecting the drug from biological environment.
- The formulation is in the form of aqueous vehicle based suspension having greater patient compliance when compared to oily dosage forms.

- Niosomal dispersion being aqueous can be emulsified in anon aqueous phase to regulate the drug release rate and to administer the vesicles in non-aqueous phase[9,12].

ADVANTAGES OF NIOSOMES

- The vesicle suspension being water-based vehicle offers high patient compliance when compared to oily dosage forms.
- Wide range of drug solubilities can be accommodated in the niosomes provided by the infrastructure consisting of hydrophilic, lipophillic and ampiphillic moieties.
- By altering the composition of vesicle, size lamellarity, surface charge, tapped volume and concentration vesicle characteristics can be controlled.
- They can release the drug in sustained/controlled manner.
- Storage and handling of surfactants oblige no special conditions like low temperature and inert atmosphere.
- They can act as a depot formulation, thus allowing the drug release in a controlled manner.
- They augment the oral bioavailability of scantily soluble drugs.
- They possess stable structure even in emulsion form.
- Surfactants are biodegradable, biocompatible, non-toxic and non-immunogenic.
- They are economical for large scale production.
- They can protect the drug from enzyme metabolism.
- They are not only osmotically stable and active but also improve the stability of entrapped drug.
- They can increase the penetration of drugs through skin.
- Therapeutic performance of the drug molecules can be improved by delayed clearance from circulation.
- They can protect the active moiety from biological circulation.
- They can confine the drug delivery rate as aqueous phase niosomal dispersion can be emulsified in the non-aqueous phase and thus common vesicle can be administered in an external non-aqueous phase[9,15].

DISADVANTAGES OF NIOSOMES

- Physical instability
- Aggregation
- Fusion
- Leaking of entrapped drug
- Hydrolysis of encapsulated drugs which limiting the shelf-life of the dispersion[9].

Nano-niosomes in drug delivery

Nano-niosomes are currently used as adaptable drug delivery systems with a lot of pharmaceutical applications, including for oral, pulmonary, transdermal, parenteral, vaginal, nasal and ophthalmic route of administration

Intramuscular (IM)

After intramuscular injection of the drugs, a moderate drug penetration from tissues to capillaries has been observed.

Intravenous (IV)

Intravenous admin of drugs can directly place the drugs into the circulation system and drug loaded niosomes compared to free drugs can improve stability of the drugs and prolong the circulation time. Loaded drug can be released into the blood stream or into target tissue under certain condition or into the targeted cells.

Transdermal

The exact characteristic of transdermal route is slow penetration of the drug through the skin[1,16].

Oral

The oral route is the mainly chosen route for delivering a therapeutically active substance. But acids and digestive enzymes in the stomach and small intestine can degrade the some active substance. However, niosomes have been reported as feasible vesicles to deliver drug molecules to the required mucous membrane or skin layers[1,18].

Subcutaneous (SC)

After subcutaneous injection, drugs transfer to capillaries and this route of administration is used for quite a lot of drugs such as insulin, hydroxycamptothecin and so on however, IV, IM and subcutaneous injections are more persistent routes than others which generally are not an ideal method for the administration of drugs[1,17].

Pulmonary

Pulmonary administration, through inhalation of drugs, is one of suitable routes used for glucocorticoids such as beclometasone dipropionate (BDP) for Patients with asthma. Pulmonary delivery of BDP through polysorbate 20 niosomes offers the advantages of sustained delivery, an enhanced mucus permeation, targeted drug delivery and amplified beneficial effect.

A number of other routes of administration of niosomal drugs have been reported such as intraperitoneal route, brain and vaginal deliveries where niosomes improved brain uptake. Also, it has been reported that niosomes may be a good carrier for vaginal delivery of protein drugs

Ocular

Topical ocular drug delivery is one of the frequently used and chosen routes for treating circumstances that influence the anterior segment of the eye. However, there are numerous anatomical and physiological barriers such as exclusive fixed junctions of corneal epithelium and precorneal tear film that prevent absorption of the administered particles from residing on the eye surface for deeper sites. Therefore, the bioavailability of drugs administrate by ocular route from simple solutions is typically less than 5% and often less than 1%[1,19].

Routes of administration. Schematic illustration of the whole process of intravenous, ocular, and transversal, oral, pulmonary and intramuscular drug delivery *in vivo*, involving stages of systemic penetration, circulation time, tissue and intracellular targeting. Drug releasing can be achieved in per step of process, depending on the route of administration and asked releasing site, size, charge, stability, sensitivity and niosome coating can be altered (panels a, b, c have been adapted from and d ; respectively)[1].

REVIEW OF LITERATURE

Monavari S. Hamid Reza *et al.* investigated Acyclovir loaded nano-niosomes prepared by thin film hydration method. The results of this study revealed Acyclovir loaded nano niosomes have a higher antiviral activity compared with free drug, and could be a suitable carrier for delivery of Acyclovir in the treatment of Herpes simplex virus - 1 infections. We found that niosomes containing acyclovir had 3 times greater antiviral activity than acyclovir. Therefore the niosomal formulation could be a promising drug delivery system capable of increasing the antiviral activity of acyclovir[23].

Anand kumar Y *et al.*, developed and characterized Aceclofenac niosomes by modified ether injection method using non-ionic surfactant (span 60, 20) and cholesterol in different ratios. They have reported that the prepared formulation shows improved bioavailability[24].

M. U. Sakthi *et al.,* have reviewed that infections are caused by several microorganisms, which are mostly affecting the mucosal surfaces such as gastrointestinal tract, respiratory tract, vaginal tract *etc*., These microorganisms are treated with anti-infective drugs based on their severity of action in the individuals. They also discussed that conventional anti-infective short residence time at the site of application and poor bioavailability, which leads to incomplete elimination of organisms causing reoccurrence and tolerance. This paper focus on various vesicular systems such as liposomes, niosomes, ethosomes, which have gained attraction because of its improved therapeutic efficacy and stability. The vesicular delivery systems give many advantages such as increasing bioavailability, targeting and better stability in delivering drugs. Since, it has many advantages over the conventional medicine, vesicular mode of delivery can be used for efficient administration of anti-infective drugs in near future[25].

Manivannan Rangasamy *et al*., prepared Acyclovir entrapped niosomes by hand shaking and ether injection process with different ratios of cholesterol and span. They have reported that the *in-vitro* release of drug was significantly extended a period of 1 day and 16 hrs for release and shows prolonged activity with simultaneously reduces the side effect[26].

Vijay S Jatav *et al*. prepared the niosomes containing Rifampicin by hand shaking method using surfactant (span 20, 85) and cholesterol. They reported that the cumulative percent Rifampicin released is maximum for span 20 based niosomes and minimum for span 85 based niosomes. The niosomes were observed as spherical vesicles with smooth surface. The vesicles were discrete and separate with no aggregation or agglomeration. The size of the vesicles was uniform and independent of surfactant, as vesicles of all the surfactants were sonicated to same size[27].

Punitha Sundaresan *et al*. prepared Aceclofenac niosomes by different techniques namely ether injection method, ethanol injection method, sonication method, thin film hydration and reverse phase evaporation techniques using 1:1:1 ratio of drug, cholesterol and surfactant (span 60). Among the 5 techniques thin film hydration and reverse phase evaporation formulation were reported to sustain the drug release rate for more than 24 hrs[28].

Pavala Rani N *et al*. prepared Rifampicin and Gatifloxacin niosomes by lipid hydration technique using rotary flash evaporator. The prepared Rifampicin and Gatifloxacin niosomes were reported as vesicle size in the range of 100-300nm, the entrapment efficiency are 73% and 70% respectively. The *in-vitro* release study shows that 98.98% and 97.74% release of Rifampicin and Gatifloxacin niosome respectively. The study showed that the drugs loaded in niosome vesicles exhibited improved bactericidal activity against the tubercle bacilli. The diffusion study of the Rifampicin niosome and gatifloxacin niosomes gave extended release of the drug, which suffices to decreased dose, lesser days of treatment and more patient compliance[29].

APPLICATIONS OF NIOSOMES[4]

Leishmaniasis therapy

Is a one of the disease caused by parasite genus Leishmaniasis which invades the cells of the liver and spleen. Most regularly prescribed drugs for the treatment are the derivatives of antimony - which, in higher concentrations - can cause liver, cardiac and kidney damage. Use of niosomes as a drug carrier showed that it is feasible to administer the drug at high levels without the triggering the side effects, and thus showed greater efficacy in treatment.

Niosomes as drug carriers

Topical niosomes may serve as solubilization matrix, as a local depot for sustained release of dermally active compounds, as penetration enhancers, or as rate-limiting membrane barrier for the modulation of systemic absorption of drugs. Niosomes have been used as carriers for iobitridol, a diagnostic agent used for X-ray imaging.

Drug targeting

Capability to target drugs is one of the most useful aspects of niosomes. Niosomes can be used to target drugs to the reticuloendothelial system. The reticulo-endothelial system (RES) preferentially takes up niosome vesicles. Opsonise called as circulating serum factors which is controlled the uptake of niosomes. These opsonise mark the niosome for clearance. Such localization of drugs is utilized to treat tumours 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 reticulo-endothelial system. A carrier system can be attached to niosomes to target them to specific organs.

Anti-neoplastic treatment

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

Use in studying immune response

Niosomes are being used to study the nature of the immune response provoked by antigens due to their immunological selectivity, low toxicity and greater stability. Non-ionic surfactant vesicles have obviously established their ability to function as adjuvant following parenteral administration with a numeral of different antigens and peptides.

Delivery of peptide drugs

Oral peptide drug delivery has long been faced with a challenge of bypassing the enzymes which would break down the peptide. Make use of niosomes to successfully protect the peptides from gastrointestinal peptide break down 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 considerably enlarged the firmness of the peptide.

Niosomes as carriers for haemoglobin

Within the blood niosomes can be used as carriers for haemoglobin. The niosomal vesicle is permeable to oxygen and for this reason can act as a carrier for haemoglobin in anaemic patients.

Other applications

Sustained release

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

Localized drug action

To achieve localized drug action drug delivery through niosomes is one of the approaches, since their size and low penetrability through epithelium and connective tissue keeps the drug localized at the site of administration.

Table No.1: Method for evaluation of niosomes[5]

S.No	Evaluation parameter	Method
1	Morphology	SEM, TEM, freeze fracture technique
2	Size distribution,	Dynamic light scattering particle
3	polydispersity index	size analyzer
4	Viscosity	Ostwald viscometer
5	Membrane thickness	X-ray scattering analysis
6	Thermal analysis	DSC
7	Turbidity	UV-Visible diode array spectrophotometer
8	Entrapment efficacy	Centrifugation, dialysis, gel chromatography
9	In-vitro release study	Dialysis membrane
10	Permeation study	Franz diffusion cell

Table No.2: Drugs used in niosomal delivery with different routes of administrarion[6,20]

S.No	Routes of administration	Examples of drug
1	Intravenous route	Doxorubicin, Methotrexate, Sodiumstibogluconate, Iopromide, Vincristin, Diclofenac Sodium, Flurbiprofen, Centchroman, Indomethacin, Colchicine, Rifampicin, Tretinoin, Transferrin and glucose ligand, Zidovudin, Insulin, Cisplatin, Amarogentin, 5-fluorouracil, Daunorubicin, Amphotericin B, Camptothecin, Adriamycin, Cytarabine hydrochloride.
2	Peroral route	DNA vaccines, Proteins, Peptides, Ergot alkaloid, Ciprofloxacin, Norfloxacin, Insulin
3	Transdermal route	Flurbiprofen, Piroxicam, Estradiol, Levonorgestrol, Nimesulide, Dithranol, Ketoconazole, Enoxacin, Ketorolac
4	Ocular route	Timolol maleate, Cyclopentolate
5	Nasal route	Sumatriptan, Influenza viral vaccine

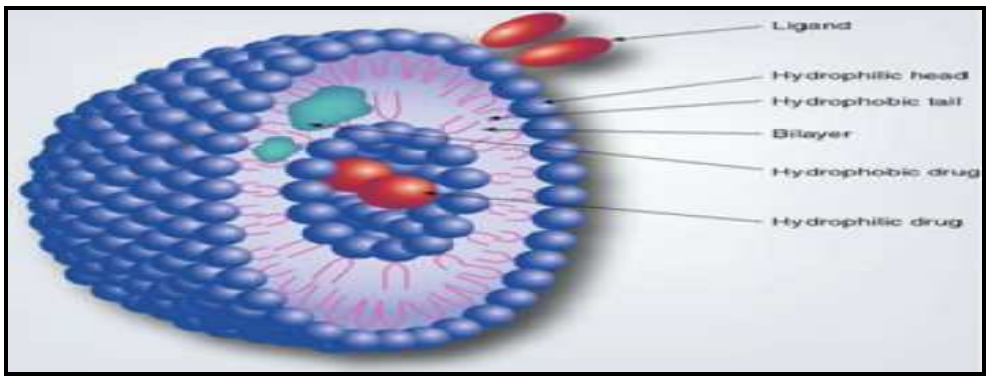

Figure No.1: Structure of niosomes

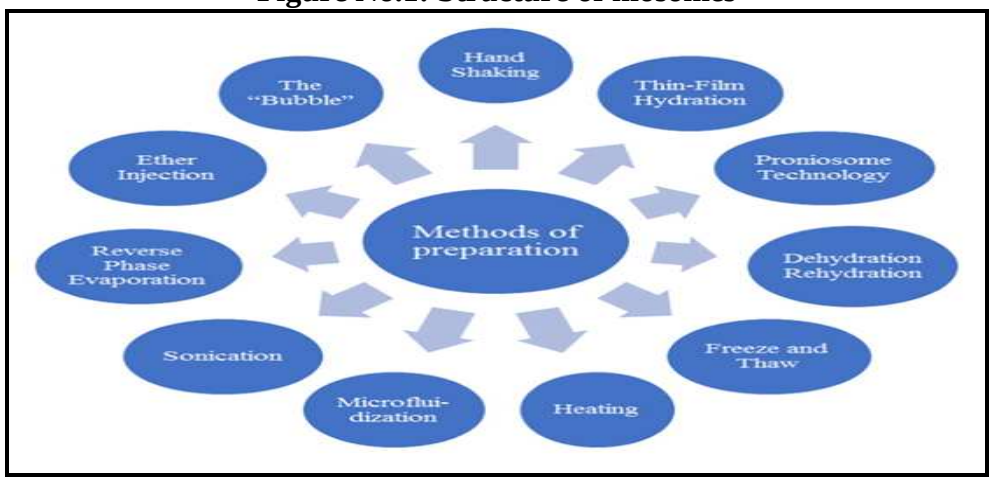

Figure No.2: Method of preparation

Figure No.3: Rotary evaporator

Figure No.4: Sonicator

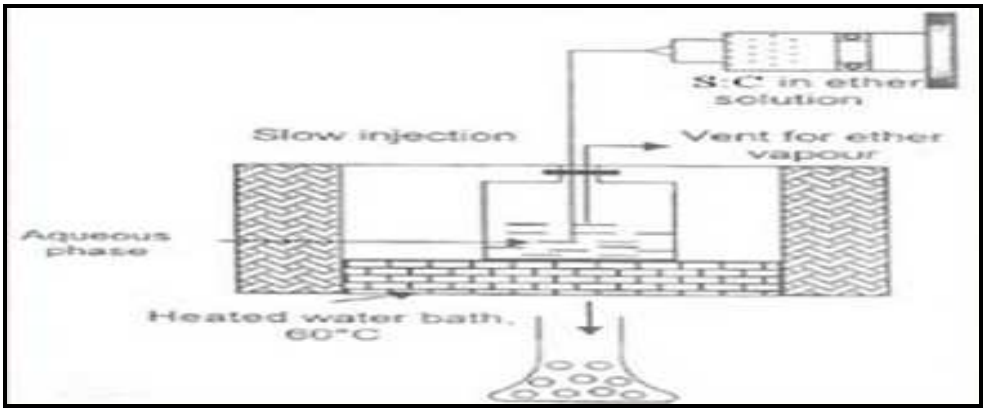

Figure No.5: Ether injection method

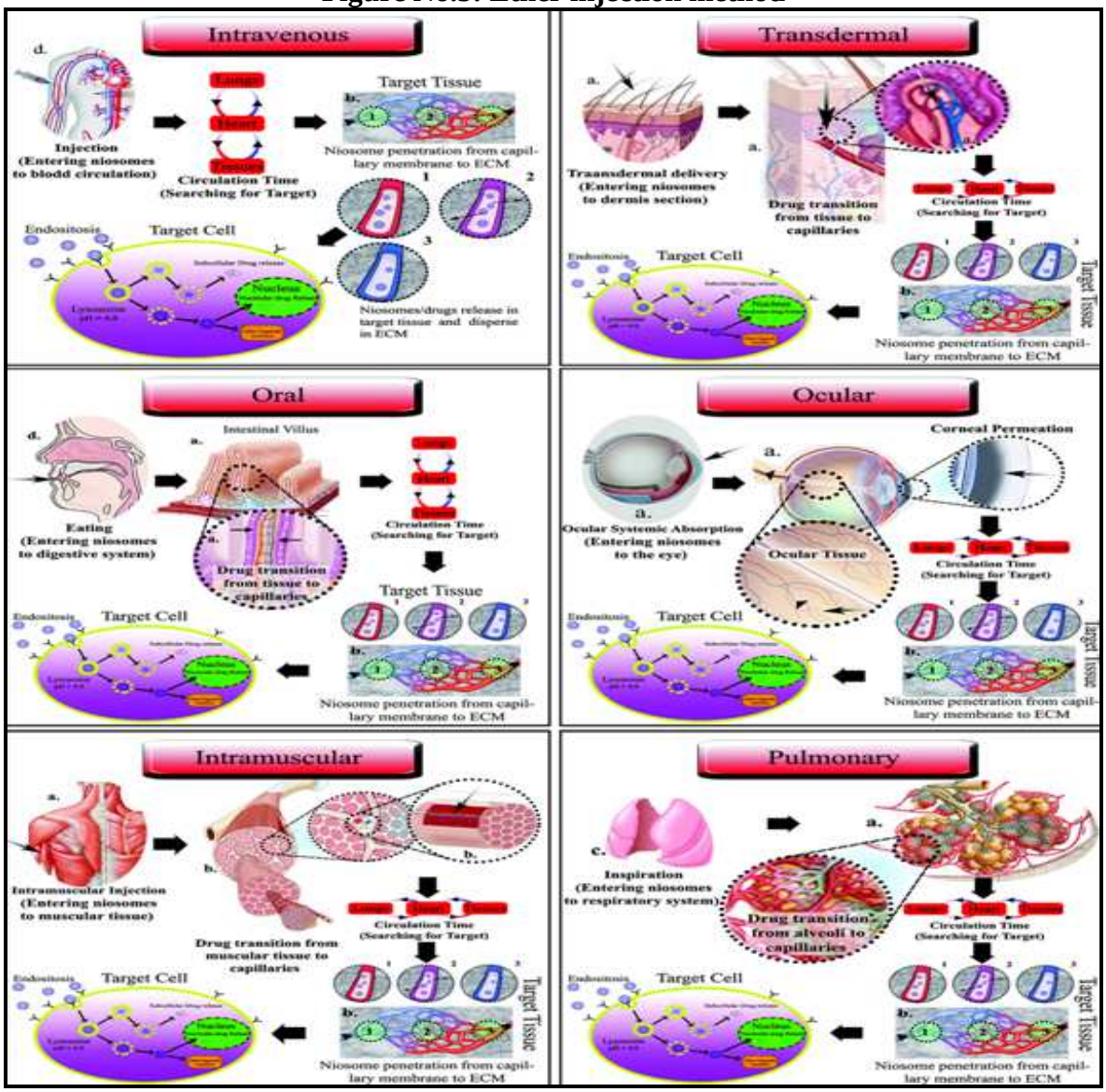

Figure No.6: Route of Administration

CONCLUSION

In the recent years, attentions have been attracted toward vesicular drug delivery systems such as liposomes and niosomes. It is palpable that niosome appears to be a well chosen drug delivery system over liposome. Niosomes present a convenient, prolonged, targeted and effective drug delivery system with the capability of loading both hydrophilic and lipophillic drugs. The potential of niosome can be enhanced by using novel preparations, loading and modification methods. Thus, these areas need further investigation and research so as to bring out commercially available niosomal preparations.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Saeid Moghassemi, Afra Hadjizadeh, Nano-niosomes as nanoscale drug delivery systems: An illustrated review, *Journal of Controlled Release*, 185(1), 2014, 22-36.
2. Ali Bagheri, Boon-Seang Chu and Harisun Yaakob. Niosomal Drug Delivery Systems: Formulation, Preparation and Applications, *World Applied Sciences Journal*, 32(8), 2014, 1671-1685.
3. Ali Nasir, Harikumar S L, Kaur Amanpreet. Niosomes: An excellent tool for drug delivery, *International Journal of Research in Pharmacy and chemistry*, 2(2), 2012, 479-487.
4. Pola V, Chand, Arunachalam A, Jeganath S, Yamini K, Tharangini K G, Chaitanya. Niosomes: A Novel Drug Delivery System, *International Journal of Novel Trends in Pharmaceutical Sciences*, 2(1), 2012, 25-31.
5. Sudhamani T, Priyadarisini N, Radhakrishnan M. Proniosomes - A Promising Drug Carrier, *International Journal of Pharm Tech Research*, 2(2), 2010, 1446-1454.
6. Sharma R, Mahatma R, Goyal A. Niosomes - As potential drug delivery system, *International journal of drug research and technology*, 2(6), 2012, 422-429.
7. Arul Jothy M, Shanmuganathan S, Nagalakshmi. An Overview on Niosome As Carrier In Dermal Drug Delivery, *Journal of Pharmaceutical Sciences and Research*, 7(11), 2015, 923-927.
8. Abbas Pardakhty, Esmaeil Moazeni. Nano-niosomes in drug, vaccine and gene delivery: a rapid overview, *Nanomedicine Journal*, 1(1), 2013, 1-12.
9. Vandana Arora, Sameer Rastogi, Abdul W, Siddique, Monish Gupta and Bhalla. Pharmaceutical Application of Nano-Niosomes in Drug, Vaccine, and Gene delivery, *International journal of Phamaceutical Sciences and Nanotechnology*, 7(4), 2014, 2603-2611.
10. Rajesh Mujoriya, Ramesh Babu Bodla, Kishor Dhamande, Devendra singh, Lokesh Patle. "Niosomal Drug Delivery System: The Magic Bullet", *Journal of Applied Pharmaceutical Science*, 1(9), 2011, 20-23.
11. Arijit Gandhi, Suma Oomen Sen, Abhijit Paul. "Current trends in Niosome as Vesicular Drug Delivery system", *Asian Journal of Pharmacy and Life Science*, 2(2), 2012, 123-135.
12. Abdelkader H, Ismail S, Kamal A, Alany R G. Design and evaluation of controlled release niosomes and discomes for naltrexone hydrochloride ocular delivery, *Jounal of pharmaceutical sciences*, 100(5), 2011, 1833-1846.
13. Hope M J, *et al*. Generation of multilamellar and unilamellar phospholipid vesicles, *Chem. Phys. Lipids*, 40(2-4), 1986, 89-107.
14. Mayur Gandhi, Sanket Parakar, Mahendra Sonule, Dhiraj Dabhade, Sagar Pagar. Niosomes; novel drug delivery system,

International Journal of Pure and Applied Bioscience, 2(2), 2014, 267-274.

15. Mehta A K, Dubal A P, Mane P D, Recent trends in niosomes as nanocarriers, *unique journal of pharmaceutical and biological sciences,* 1(2), 2013, 12-17.
16. Sevukaranjann M. Niosomal drug delivery system-A review, *Indo American journal of pharmaceutical research,* 2(9), 2012, 1-10.
17. Lohumi A, Rawat S, Sarkar S. A novel drug delivery system: Niosomes review, *Journal of drug delivery and therapeutics,* 2(5), 2012, 129-135.
18. Tarekegn A, *et al*. Niosomes in targeted drug delivery: some recent advances, *International journal of Pharmaceutical Science and Research,* 1(9), 2010, 1-8.
19. Bendas E R, Abdullah H, El-komy M H M, Kassem M A A. Hydroxychloroquine niosomes: a new trend in topical management of oral lichen planus, *International Journal of Pharmacy,* 458(2), 2013, 287-295.
20. Minghuang Hong S Z, Yanyan Jiang, Guotao Tang, Yuanying Pei. Efficient tumor targeting of hydroxycamptothecin loaded PEGylated niosomes modified with transferrin, *J. Control. Release,* 133(2), 2009, 96-102.
21. Shilpa, Srinivasan B P, Chauhan M. Niosomes as vesicular carriers for delivery of proteins and biologicals, *International Journal of Drug Delivery,* 3(1), 2011, 14-24.
22. Mirzaei Parsa Mohamad Javad, Monavari S. Hamid Reza, Dadashzadeh Simin, Ebrahimi S, Ahmed, Bolouri Bahram, Haeri Azadeh. Preparation And Evaluation of The Antiviral Activity of Acyclovir Loaded Nano-Niosomes Against Herpes Simplex Virus Type 1, *Pharmacophore,* 5(4), 2014, 483-493.
23. Anandkumar Y, Srinivas S, Hemanth A, Anitha M. Preparation and evaluation of niosome containing Aceclofenac, *Dig J Nanomater Bios,* 5(1), 2010, 249-254.
24. Udaya Sakthi M, Ramya Devi D, Vedha Hari B N. Vesicular Mode of Drug Delivery: A Promising-Approach for Anti-Infective Therapy, *Int J Chem. Sci,* 12(3), 2014, 797-814.
25. Manivannan Rangasamy M, Balasubramanium A, Sandeep G, Sanaullan S. Formulation and *in vitro* evaluation of noisome encapsulated Acyclovir, *J Pharm Res,* 1(2), 2008, 163-168.
26. Vijay S Jatav, Santosh K Singh, Ashish K Sharma, Rambir Singh. Formulation and *in vitro* evaluation of Rifampicin loaded niosomes, *J Chem Pharm Res,* 3(2), 2011, 199-203.
27. Punitha Sundaresan, Sravanthi, Tananki Gowtham. Evaluation of Aceclofenac niosomes prepared by various techniques, *Int J Pharm Sci Rev Res,* 16(1), 2012, 75-78.
28. Pavala Rani N, Suriyaprakash T N K, Senthamarai R. Formulation and evaluation of Rifampicin and Gatifloxacin niosomes on logarithamic-phase cultures of mycobacterium tuberculosis, *Int J Pharma Bio Sci,* 1(4), 2010, 379-386.
29. Navneet Kumar Verma, Asha Roshan. Niosomes and Its Application- A Review, *International Journal of pharmacy and life science,* 2(1), 2014, 182-184.

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