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A REVIEW ON NIOSOMES AS TARGETED DRUG DELIVERY SYSTEM

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Abstract:

The advanced technique is a targeted drug delivery in which drugs deliver to the patients in a targeted sequences that increases the absorption of delivered drug to the targeted body part only (organs, tissues, cells) which in turn improves efficacy of treatment by reducing side effects of drug administration. Principally targeted drug delivery is to help the drug molecule to reach first to the desired site. The inherent benefit of this technique leads to administration of necessary drug with its reduced dose and reduced its side effect. This important benefit of targeted drug delivery system is under high consideration of research and development in clinical and pharmaceutical fields as backbone of therapeutics & diagnostics as well. Various drug carriers which can be used in this advanced delivery system are soluble polymers, biodegradable microsphere polymers (synthetic and natural), niosomes, liposomes, micelles and immune micelle etc. The purpose of a targeted drug delivery system is to target, localize, prolong and have a protected drug interaction with the diseased tissue. This review exhibits the significance of vesicular drug delivery (niosomes, liposomes) as one of the future targeted delivery system. Furthermore it depicts the advantages, disadvantages, preparation methods and characterization of niosomes.

Keywords: *Targeted drug delivery, Niosomes, Method of preparation of niosomes, Characterization of niosomes.*

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INTRODUCTION:

Targeted drug delivery is a kind of smart drug delivery system which is fewer doses in delivering the drug to a patient. This conventional drug delivery system is done by the absorption of the drug across a biological membrane where as the targeted release system is that drug is released in a dosage form [1-3].

Targeted drug delivery system is based on a method that delivers a certain amount of a therapeutic agent for a prolonged period of time to a targeted diseased area within the body. This helps maintain the required plasma and tissue drug levels in the body therefore avoiding any damage to the healthy tissue by means of the drug. The drug delivery system is highly integrated and requires various disciplines such as chemists, biologist and engineers, to join forces to optimize this system. When implementing a targeted release system, the following design criteria for the system need to take into account:

Properties of drugs

Route taken for the delivery of the drug

Side effects of the drugs,

Targeted site and the disease [1,2,4]

Drug Targeting is defined as the ability of a drug molecule to gather in the target cell or organ or tissue therefore concentration of the drug at the disease site is high and concentration in Non target cells, organs and tissues is less helps to prevent any toxic effect. Thus drug targeting can overcome the non-specific toxic effect of conventional drug delivery. This may also reduce the frequency of dose. The drug can be targeted on the level of a whole organ, on the level of certain cells specific for a given organ or even on the sub-cellular level of specific tissue. The idea of drug targeting was primary mentioned by Paul Ehrlich when he suggested the imaginary "magic bullet" as an entity consisting of two components the first one should identify and bind the target while the second should give a therapeutic action in this target. Currently, the concept of 'magic bullet' includes a corresponding behavior of three components 1.drug, 2.targeting moiety and 3.pharmaceutical carrie [5,6].

DRUG TARGETING METHODS:

Drug targeting to an area of interest within the body increases the therapeutic effectiveness as well as it reduces the toxicity that may arise otherwise. There are mainly two methods used for drug targeting to the preferred organ/tissue [7].

I. Passive targeting: In this targeting method the accumulation of drug at areas around the site of interest such as in case of tumor tissues. This is called Enhanced Permeability Retention (EPR) effect. Such a types of targeting occurs with almost all types of drug delivery carriers. Passive targeting is actually a misnomer because it cannot really be described as a form of selective targeting. Although the EPR effect applies for nanoparticle administered, the bulk (>95%) of these nanoparticles tend to gather in organs other than those of interest such as liver, lungs and spleen. Thus, it is the supply of drug by blood circulation. Examples take in the use of anti-malarial drugs being targeted for the treatment of microbial infections such as candidiasis, and brucellosis, leishmaniosis [7,8].

Active targeting

The use of ligand-receptor interactions, active targeting describes the drug targeting interactions. Though, interactions between a ligand and a receptor are possible only when the two are in close propinquity (i.e. less than about 0.5mm) . The presently available drug delivery systems are able to reach the target by the virtue of blood circulation and extravasation. Therefore we can conclude that active receptor targeting truly means ligand-receptor interaction but that takes place only after blood circulation and extravasation.[8] Active targeting can additionally be divided into three different targeting levels:

1. First order targeting: In this the distribution of drug to capillary beds of target sites, organ or tissue, for example in case of lymphatic tissue, peritoneal cavity, pleural cavity, cerebral ventricles, eyes, joints, etc.

2. Second order targeting: The targeting of drugs to specific sites such as the tumor cells for example to kupffer cells in liver.

3. Third order targeting: Type of drug targeting where in the drug is intracellularly localized at the target site via through receptor-based ligand mediated entry or endocytosis [7-9].

COMPONENTS OF TARGETED DRUG DELIVERY

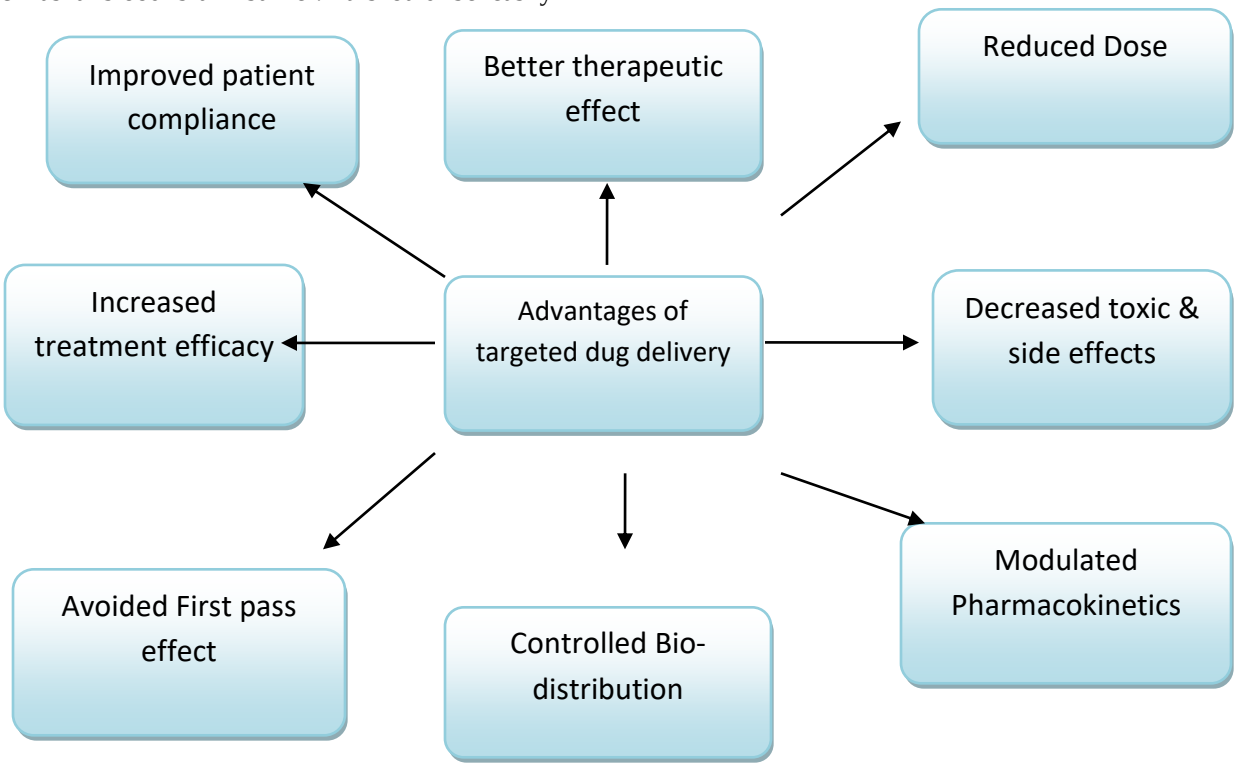
There are mainly three Components of drug carrier are Target, Drug carrier, Delivery of drug vehicles.

Target: Means an organ or a tissue or a cell, which is in need of treatment.

Drug Carrier or Marker: delivery of drug is possible only by means of a carrier system. Carriers are molecules or any other. Systems responsible for the

successful transportation of a drug to the site of interest. Carriers are vectors specifically engineered for the purpose of holding a drug inside them. This is possible by means of encapsulation.

Delivery of drug vehicles: Transport the drug either within or in the locality of target. Ideal drug delivery vehicle is supposed to cross even immovable sites such as a blood brain barrier. It should be easily recognized by the target cells and the drug-ligand complex hence formed should be stable. These need to be non-toxic, biodegradable as well. The biodegradable nature of drug carrier enables them to be simply cleared away from body and physiological mechanism and thus avoids any chance of their accumulation within cells that may lead to cytotoxicity [10].



Use of Niosome instead of Liposomes: Reasons behind the use of niosomes instead of liposomes are one of the most significant problems associated with the use of liposomes as adjuvant is the susceptibility of phospholipids to oxidative degradation in air. This requires that purified phospholipids and liposomes have to be stored and handled in an inert (e.g. nitrogen) atmosphere. Phospholipid raw materials are naturally occurring substances and as such require extensive purification thus making them costly. Alternatively phospholipids can be synthesised de novo, however this approach tends to be even more costly than using naturally occurring lipids. Because of liposomes above mentionioned drawbacks, alternative nonionic surfactants i.e niosomes have been investigated.

NIOSOMES:

Niosomes are a novel drug delivery system in which the medication is encapsulated in a vesicle.Drug targeting can be defined as the ability to direct a therapeutic agent specifically to desired site of action with little or no interaction with non-target tissues or organ [12].

Niosomes or non-ionic surfactant vesicles are microscopic lamellar structures formed on admixture of non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol with subsequent hydration in aqueous media [13]. In Niosomes the vesicles forming amphiphilic is a non-ionic surfactant such as Span-60 which is usually stabilized by addition of cholesterol and small amount of anionic surfactant such as dicetyl phosphate [14]. Niosomes are one of the best among these carriers. Structurally, niosomes are similar to liposomes and also are equiactive in drug delivery potential but high chemical stability and economy makes niosomes superior than liposomes. Both consist of bilayer, which is made up of non-ionic

surfactant in the case of niosomes and phospholipids in case of liposomes. Niosomes are microscopic lamellar structures of size range between 10 to1000 nm and consists of biodegradable, non-immunogenic and biocompatible surfactsnts [15].

Niosomes have recently been shown to greatly increase transdermal drug delivery and also can be used in targeted drug delivery and thus increased study in these structures can provide new methods for drug delivery.

Ideal properties: The property of Niosome depends upon both on composition of the bilayer & on method of their production.

- Biocompatible, Biodegradable, non-toxic, non-immunogenic & non carcinogenic.
- Niosomes can be characterized by their size distribution studies.
- High resistance to hydrolytic degradation.
- The ability of nonionic surfactant to form bilayer vesicles is dependent on HLB value of the surfactant, the chemical structure of the components and the critical packing parameter.

Advantages of Niosomes

- Osmotically active and increase the stability of the entrapped drug.
- Handling and storage of surfactants do not require any special conditions.
- Can increase the oral bioavailability of drugs.
- Can enhance the skin penetration of drugs.
- The surfactants are biodegradable, biocompatible and non- immunogenic.
- Improve the therapeutic performance of drug by protecting it form the biological environment and restricting effects to target cells.
- At times the maintenance of the constant drug concentration whithin the biophase is not desired.
- Useful to diagnose various diseases.
- Extremely versatile as a drug carrier, niosomes can entrap drugs a wide range of drugs. In niosomes preparation drugs are entrapped like as hydrophilic, amphiphilic and lipophilic moieties.
- Manufacturing of niosomes can be easily done and requirements are easily available for the formulation of niosomes.
- They improve oral bioavailability of poorly absorbed drugs.
- Can protect the drug from enzyme metabolism.
- Can release the drug in sustained/controlled manner.

Disadvantages of Niosomes

- Aqueous suspension of niosome may exhibit fusion, aggregation leaching or hydrolysis of entrapped drug, thus limiting the shelf life of niosome dispersion.
- Required specialized equipment.
- Insufficient drug loading.
- Niosomes are physically unstable.
- In niosomes preparation chances of entrapped drug leaking.

COMPONENTS OF NIOSOMES:

There are mainly three types of components are used for the preparation of niosomes:

1. Cholesterol, 2.Non-ionic surfactants, 3.Charged molecules

1. Cholesterol: Most important components of niosomes is cholesterol. It forms hydrogen bond with the hydrophilic head of surfactant in the bilayer structure. Cholesterol influences some significant vesicular properties such as entrapment efficiency, increase stability. 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. Its content also alters drug loading capacity which is an important factor for niosomal preparation. 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.[16-18]

2. Non-ionic surfactants: Surfactants play an important role in the preparation of niosomes the following non-ionic surfactants are generally used for the preparation of niosomes.

Spans (span 60, 40, 20, 85, 80) Tweens (tween 20, 40, 60, 80) and Brijs (brij 30, 35, 52, 58, 72, 76) 15, 19 etc.

3. Charged molecule: 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 added in an amount of 2.5 – 5 mol%. Even so increasing amount of charged molecules can suppress niosome formulation. Examples: Dicetyl phosphate (DCP)-Negative charge, Stearyl amine (SA) - positive charge.[19]

Basis for site specific drug delivery:

1) Reducing the drug dose and side effects.

2) To reach previously inaccessible domains e.g. intracellular site, bacteria, viruses, Parasites etc.

3) Special drug delivery to the specific cells or diseased site.

4) To control the rate and frequency of drug delivery

at the pharmacological receptor.
5) To protect the drug and the body from one another until it reaches at the desired site of action [20].

TYPES OF NIOSOMES: Niosomes can be divided into three groups depends on their vesicles size: 1) Multi lamellar vesicles (MLV) 2) Large unilamellar vesicles (LUV), 3) Small unilamellar vesicles (SUV).

1. Multilamellar vesicles (mlv): It consists of a number of bilayer surrounding the aqueous lipid compartment and size of these vesicles is 0.5-10 µm diameter. Multilamellar vesicles are the most widely used niosomes. They are mechanically stable upon storage for long periods of time. Mlv vesicles are highly suited as drug carrier for lipophilic compounds.

2. Large unilamellar vesicles (luv): These types of niosomes have a high aqueous/lipid compartment ratio so that larger volumes of bio-active materials can be entrapped with a very economical use of membrane lipids.

3. Small unilamellar vesicles (suv): These are mostly prepared from multilamellar vesicles by sonication method French press extrusion electrostatic stabilization is the inclusion of dicetyl phosphate in 5(6)-carboxyfluorescein (CF) loaded Span 60 based niosomes 20].

STRUCTURE OF NOISOME
A typical Niosomes vesicle would consist of a vesicle forming amphiphilic i.e. a non-ionic surfactant such as Span-60 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. Niosomes are microscopic lamellar structures which are formed on the admixture of non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol with subsequent hydration in aqueous media [21].

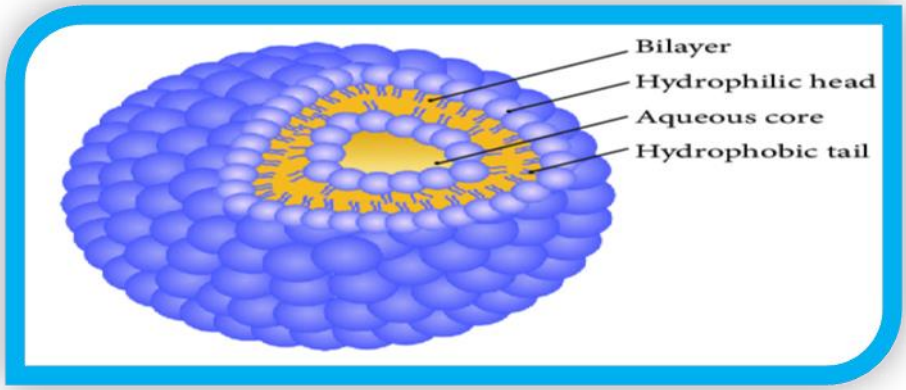
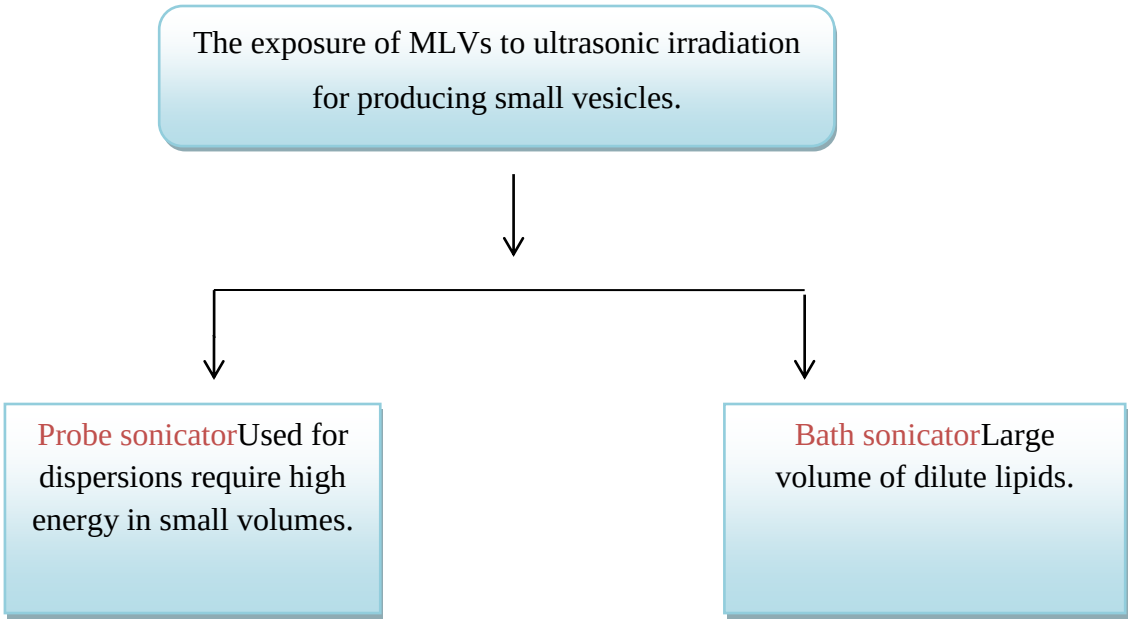


Fig2: Structure of Niosome

METHODS OF PREPARATION OF NIOSOMES:
1. Sonication
2. Ether injection method
3. Micro fluidization
4. Thin film hydration method
5. The Bubble Method
6. Reverse Phase Evaporation Technique (REV)
7. Preparation of Niosomes from Proniosomes
8. Tran membrane pH gradient (inside acidic) drug uptake process

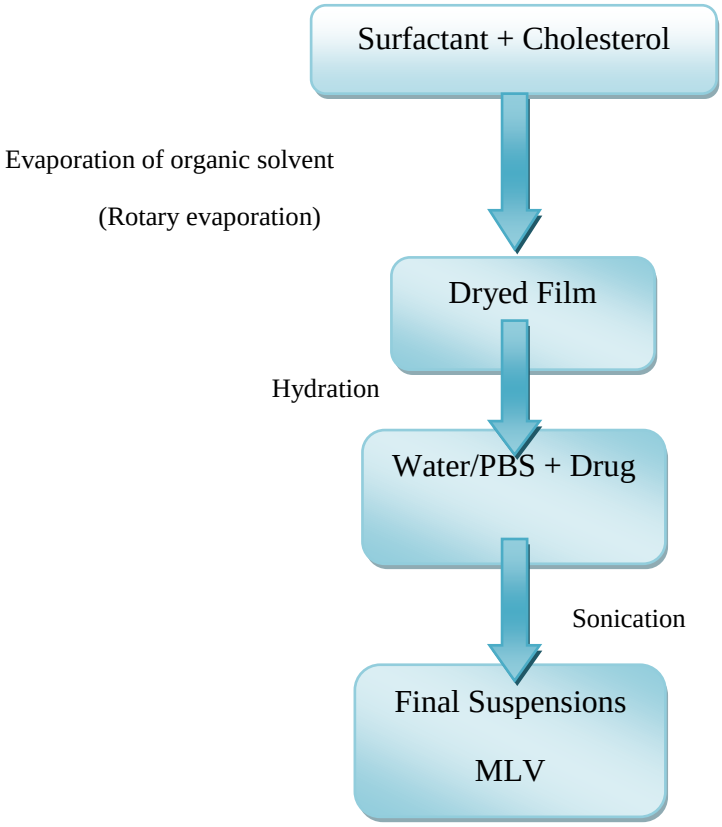
1. Sonication: The aqueous phase containing drug is added to the mixture of surfactant and cholesterol in a scintillation vial [22]. The mixture is probe sonicated at 60°C for 3 minutes to produce small and uniform in size niosomes. Two types of sonicator:1.Probe sonicator
2. Bath sonicator



2. Ether injection method: This method provides a means of making Niosomes by slowly introducing a solution of surfactant dissolved in diethyl ether into warm water maintained at 60°C. The surfactant mixture in ether is injected through 14-gauge needle into an aqueous solution of material. Evaporation of ether leads to formation of single layered vesicles. Depending upon the conditions used the diameter of the vesicle range from 50 to 1000 nm [23,24].

3. Micro fluidization: Micro fluidization is a recent technique to prepare unilamellar vesicles of defined size distribution. This method is based on submerged jet principle in which two fluidized streams interact at ultra high velocities in precisely defined micro channels within the interactionchamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation. The result is a greater uniformity, smaller size and better reproducibility of niosomes formed [25].

4. Thin film hydration method: The mixture of vesicles forming ingredients like surfactant and cholesterol are dissolved in a volatile organic solvent (diethyl either, chloroform or methanol) in a round bottom flask. The organic solvent is removed at room temperature (20°C) using rotary evaporator leaving a thin layer of solid mixture deposited on the wall of the flask. The dried surfactant film can be rehydrated with aqueous phase at 0-60°C with gentle agitation. This process forms typical multilamellar niosomes.



5. The Bubble Method: It is novel technique for the one step preparation of liposomes and niosomes without the use of organic solvents. The bubbling unit consists of round-bottomed flask with three necks positioned in water bath to control the temperature. Water-cooled reflux and thermometer is positioned in the first and second neck and nitrogen supply through the third neck. Cholesterol and surfactant are dispersed together in this buffer (pH 7.4) at70°C, the dispersion mixed for 15 seconds with high shear homogenizer and immediately afterwards "bubbled" at 70°C using nitrogen gas [26].

6. Reverse Phase Evaporation Technique (REV): Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform. An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. The clear gel formed is further sonicated after the addition of a small amount of phosphate buffered saline (PBS). The organic phase is removed at 40°C under low pressure. The resulting viscous noisome suspension is diluted with PBS and heated on a water bath at60°C for 10 min to yield Niosomes [27].

7. Preparation of Niosomes from Proniosomes: To produce niosomes the final step is to coat the carrier which is soluble in water for example glucitol with surface acting agents. The dry formulation is obtained by this technique. Where each paticle which is soluble in water is coated with a surfactant which is thin film and dry. This formulation is called as "Proniosomes". [28]E.g.Nateglinidemaltodextrin complex [29].

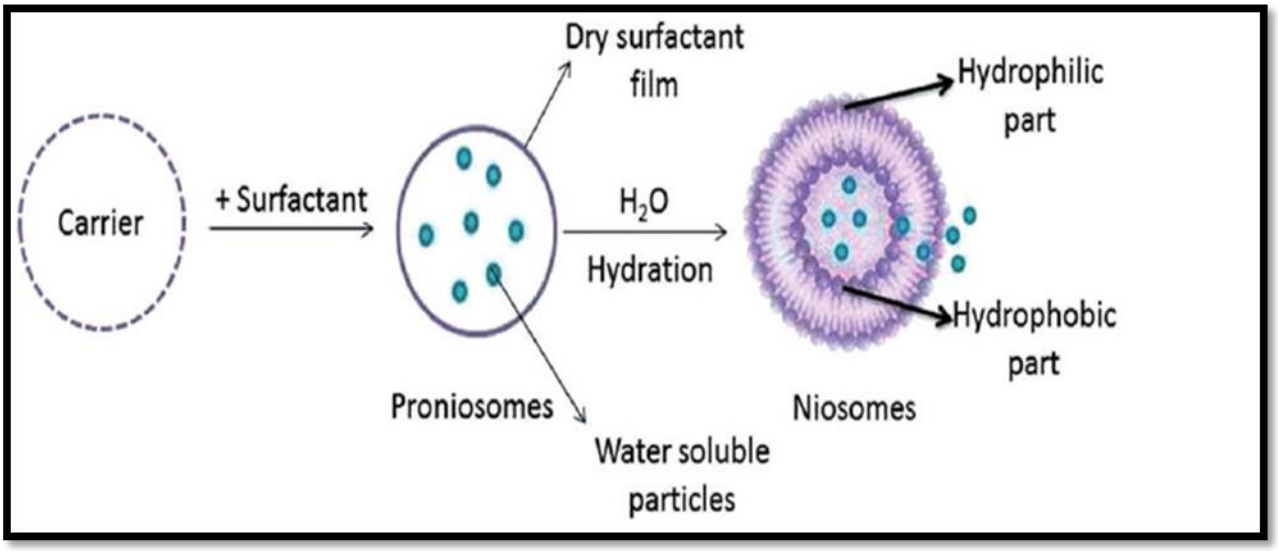


Fig3: Formation of Niosomes from Proniosomes

8. Tran membrane pH gradient (inside acidic) drug uptake process: This method is done by dissolving cholesterol and surfactant in chloroform. The organic solvent is reordered to obtain a thin film of surfactant cholesterol mixture on RBF wall the solvent in which the mixture is dissolved is evaporated under low pressure. The MLV's formed are freeze thawed for three times which are then subjected to sonication. The aqueous solution of the drug of concentration 10mg/ ml is added to suspension of niosomes and vortexed. Using disodium phosphate solution of 1M the products pH is made to somewhat neutral. To yield niosomes the obtained mixture is further heated at temperature of 600 C [30].

Evaluation of niosomes [31]:

a. Scanning electron microscopy Particle size of niosomes is very important characteristic. The surface morphology (roundness, smoothness, and formation of aggregates) and the size distribution of niosomes were studied by Scanning Electron Microscopy (SEM). Niosomes were sprinkled on to the double- sided tape that was affixed on aluminum stubs.

The aluminum stub was placed in the vacuum chamber of a scanning electron microscope (XL 30 ESEM with EDAX, Philips, Netherlands).

b. Optical Microscopy: The niosomes were mounted on glass slides and viewed under a microscope (Medilux-207RII, Kyowa-Getner, Ambala, India) with a magnification of 1200X for morphological observation after suitable dilution. The photomicrograph of the preparation also obtained from the microscope by using a digital SLR camera.

c. Measurement of vesicle size: Vesicle dispersions were diluted about 100 times in the same medium used for their preparation. Vesicle size was measured on a particle size analyzer (Laser diffraction particle size analyzer, Sympatec, Germany). The apparatus consists of a He-Ne laser beam of 632.8 nm focused with a minimum power of 5 mW using a Fourier lens [R-5] to a point at the center of multielement detector and a small volume sample holding cell (Su cell). The sample was stirred using a stirrer before determining the vesicle size. Hu C. and Rhodes 7 in 1999 reported that the average particle size of niosomes derived niosomes is approximately 6µm while that of conventional niosomes is about 14µm.

d. Entrapment efficiency: Entrapment efficiency of the niosomal dispersion in can be done by separating the unentrapped drug by dialysis centrifugation or gel filtration as described above and the drug remained entrapped in niosomes is determined by complete vesicle disruption using 50% n-propanol or 0.1% Triton X-100 and analyzing the resultant solution by appropriate assay method for the drug.

e. Osmotic shock: The change in the vesicle size can be determined by osmotic studies. Niosomes formulations are incubated with hypotonic, isotonic, hypertonic solutions for 3 hours. Then the changes in the size of vesicles in the formulations are viewed under optical microscopy.

f. Stability studies: To determine the stability of niosomes the optimized batch was stored in air tight sealed vials at different temperatures. Surface characteristics and percentage drug retained in niosomes and niosomes derived from proniosomes were selected as parameters for evaluation of the stability, since instability of the formulation would reflect in drug leakage and a decrease. In the percentage drug retained. The niosomes were sample at regular intervals of time (0,1,2,and 3months),observed for color change, surface characteristics

and tested for the percentage drug retained after being hydrated to form niosomes and analyzed by suitable analytical methods(UV spectroscopy, HPLC methods etc).

g. Zeta potential analysis: Zeta potential analysis is done for determining the colloidal properties of the prepared formulations. The suitably diluted niosomes derived from pronoisome dispersion was determined using zeta potential analyzer based on electrophoretic light scattering and laser Doppler velocimetry method (Zeta plus™, Brookhaven Instrument Corporation, New York, USA). The temperature was set at 25°C. Charge on vesicles and their mean zeta potential values with standard deviation of measurements were obtained directly from the measurement.

h. Permeation study: The in vitro diffusion studies can be performed by using Franz diffusion cell. Proniosomes is placed in the donor chamber of a Franz diffusion cell fitted with a cellophane membrane. The proniosomes is then dialyzed against a suitable dissolution medium at room temperature; the samples are withdrawn from the medium at suitable intervals, and analyzed for drug content using suitable method (U.V spectroscopy, HPLC, etc) . The maintenance of sink condition is essential.

APPLICATIONS OF NIOSOMES [32]

1) **Pulmonary delivery:** Inhalation therapy is commonly used in asthmatic patients but is limited by poor permeation of drug through hydrophilic mucus. To overcome by developing polysorbate 20 niosomes containing beclomethasone dipropionate for pulmonary delivery to patients with COPD (chronic obstructive pulmonary disease). Theyimproved mucus permeation and better therapeutic effect and also provided sustained and targeted delivery.
2) **Carrier for hemoglobin:** Niosomes can be used as a carrier for hemoglobin. Vesicles were permeable to oxygen and could be modified to produce a hemoglobin dissociation curve similar to that of non-encapsulated hemoglobin. In addition, a niosomal suspension showed a visible spectrum super imposable onto that of free hemoglobin.
3) **Treatment of HIV-AIDS:** Zidovudine is commonly used to treat patients with AIDS but is limited by its toxicity and low potency. A noisome formulation that may overcome these drawbacks**.**They concluded that Zidovudine loaded niosomes would provide sustained delivery of drug and a more effective AIDS therapy.
4) **Protein and peptide delivery:** 1. proteins delivery to the systemic circulation after their oral administration is slowed down by numerous barriers including proteolytic enzymes, pH gradients and low epithelial permeability. The oral administration of recombinant human insulin in a niosomal formulation was established in a study involving niosomes based on polyoxyethylene alkyl ethers. Entrapment of insulin in the bilayer structure of niosomes was shown to protect it against proteolytic activity of a-chymotrypsin, trypsin and pepsin in vitro.and it increase therapeutic activity of insulin. 2. Even higher protection was provided by Brij 92/cholesterol niosomes in which only about 26% of entrapped insulin was released over 24 h in simulated intestinal fluid.[35]The kinetics of drug release was described by the Baker and Lonsdale equation indicating a diffusion based delivery mechanism. These results hint that niosomes can be developed as sustained release oral dosage forms for delivery of peptides and proteins.
5) **Vasoactive intestinal peptide (VIP)** has diverse therapeutic applications because of its anti-inflammatory and immunomodulatory effects and its ability to regulate cell growth and differentiation and participate in the development of neural tissue. VIP has been tested in the treatment of Alzheimer's disease but, like most endogenous peptides, its therapeutic effect is limited by its failure to cross the blood–brain barrier (BBB) and by its rapid elimination after intravenous administration. This can be overcome glucose-bearing niosomes encapsulating VIP for delivery to specific brain areas. They concluded that glucose-bearing vesicles represent a novel tool to deliver drugs across the BBB.
6) **Cancer chemotherapy:** Niosomes are an effective means of targeting delivery of anticancer drugs to tumors. To developed niosomes containing 5-fluorouracil to treat skin cancer. They reported enhanced drug penetration compared to an aqueous solution of drug and to a suspension of empty bola-niosomes in an aqueous solution of drug. Niosomes of doxorubicin prepared from C16 monoalkyl glycerol ether with and without cholesterol. Compared to simple drug solution, methotrexate loaded niosomes produced increased antitumor activity against tumors in serum and lung but not in liver and spleen.
7) **Vaccine and antigen delivery:** A number of surfactants have immunostimulatory properties41 and have been used as vaccine

adjuvants. The adjuvanticity of niosomes prepared from 1-monopalmitoyl glycerol: cholesterol: dicetyl phosphate (5:4:1) was demonstrated in mice administered a subcutaneous injection of ovalbumin or a synthetic peptide containing a known T-cell epitope and bovine serum albumin. Intraperitoneal administration of the same niosome formulation was also shown to act as a vaccine adjuvant in immune reconstituted SCID-human mice.

8) **Transdermal delivery:** Transdermal delivery of NSAIDs is the best way to avoid gastric disturbances. Transferosomes and elastic niosomes are novel types of vesicles for transdermal delivery with the latter having the advantage of low cost of manufacturing. reported novel elastic niosomes containing diclofenac diethylammonium for topical use They concluded that the niosomal gel was superior to a conventional gel formulation because of the ability of niosomes to penetrate into the deeper layers of the skin. However, for transdermal delivery of other drugs, penetration of niosomes into the deeper layers of the skin remains a problem. Hopefully, the design of elastic noisome formulations will extend the application of this route of drug delivery.

9) **Leishmaniasis therapy:** Leishmaniasis is a disease caused by parasite genus Leishmania which invades the cells of the liver and spleen. Most Commonly 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 possible to administer the drug at high levels without the triggering the side effects, and thus showed greater efficacy in treatment.

10) **Antibiotics:** The feasibility of using non-ionic surfactant vesicles (niosomes) as carriers for the ophthalmic controlled delivery of a water soluble local antibiotic, gentamicin sulphate was investigated and the results demonstrated niosomes to be promising ophthalmic Carriers for the topical application of gentamicin sulphate. Preparation and evaluation of Cefpodoxime proxetil niosomes showed controlled release of 65.25% for 24 hours with zero order kinetics, thus reducing the chances of dose dumping during usage. The bioavailability of Cefuroxime axetil which is just 25% was improved by preparing niosomes. The prepared niosomes showed good entrapment efficiency and in vitro release and also were stable in bile salts.

11) **Ophthalmic drug delivery:** From ocular dosage form like ophthalmic solution, suspension and ointment it is difficult to achieve excellent bioavailability of drug due to the tear production, impermeability of corneal epithelium, nonproductive absorption and transient residence time. But niosomal and liposomal delivery systems can be used to achieve good bioavailability of drug. Bioadhesive-coated niosomal formulation of acetazolamide prepared from span 60, cholesterolstearylamine or dicetyl phosphate exhibits more tendencies for reduction of intraocular pressure.

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