Comprehensive review on Vesicular drug delivery system: A promising approach.

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ABSTRACT

A unique drug delivery method is one that disperses the medication at a predetermined rate dictated by the need, pharmacological characteristics, drug profile, physiological state of the body, etc. There isn't a single unique drug delivery method that now exists that performs these high goals with fewer side effects. A vesicular drug delivery system (VDDS) bridges the gap between the ideal and the currently available innovative drug delivery systems by encapsulating active moieties in vesicular structures. Different vesicular drug delivery systems, such as liposomes, niosomes, archeosomes, and transferosomes, were created. Since then, improvements have been made to the vesicular drug delivery system. The goal of this paper is to provide an overview of the innovative vesicular drug delivery technology.

Keyword: Vesicular drug delivery system(vdds), Concept of targeting, carrier, liposomes, niosomes.

❖ INTRODUCTION:

The term "novel drug delivery system" (NDDS) refers to a set of techniques, technologies, and systems for safely delivering pharmaceutical compounds into the body at the appropriate times. The safest new medicine delivery method is considerably superior to the traditional dose type. Novel drug delivery system should full fill the following requirements:

 First off, it disperses a certain dosage of medication during the course of therapy at a rate determined by the body's demands.

 Second, it transports the drug's active moiety to the intended site of action.

Basic modes of novel drug delivery system are:

1. Targeted drug delivery system.
2. Controlled drug delivery system.
3. Modulated drug delivery system.

Vesicular drug delivery systems:

Vesicular drug delivery is now one of the most cutting-edge new drug delivery systems. Bingham documented the biological origins of the vesicles for the first time in 1965, leading to the moniker "Bingham bodies". Vesicles have been the preferred method of administration for new drugs in recent years. In genetic engineering, immunological, membrane, biological, and diagnostic procedures, vesicular drug delivery is extremely valuable . Vesicular drug transport is essential for membrane modelling, active principle administration, and targeting. Drug carriers are substances that are utilised in the delivery of drugs and they aid to increase the drugs' efficacy, safety, and/or selectivity.

Medication transporters carefully distribute the drug into the bloodstream. This can be accomplished in one of two ways: either by releasing the drug slowly over an extended period of time, or by activating the release of the drug at the drug target using stimuli such pH changes, the application of heat, or light activation. Drug carriers are used to enhance the pharmacokinetics and bioavailability of medicines, particularly those with low water solubility and/or membrane permeability.

Phospholipids, either organic or synthetic, make up liposomes. They are made up of hydrophilic, lipophilic, and amphiphilic components that aid in accommodating pharmacological molecules with a variety of solubilities. By adjusting the vesicle's shape, size, lamellarity, tapped density, surface charge, and concentration, one may change the vesicles' changeable and controlled characteristics as well as their qualities. It may serve as a repository and release drugs gradually.

Pharmaceutical delivery systems are divided into cellular, macromolecular, polymeric, and particle types. Low density lipoproteins and high density lipoproteins are examples of the colloidal carriers that are classified as particulate kinds and comprise lipid particles. There are many different drug carriers being researched, and each one has its own advantages and drawbacks. Niosomes, liposomes, polymeric micelles, microspheres, and nanoparticles are the most common types of drug carriers. Adsorption, encapsulation, and covalent bonding are some of the several processes used to bind the medicine to the carrier. Different drug carriers employ various attachment techniques. [1]

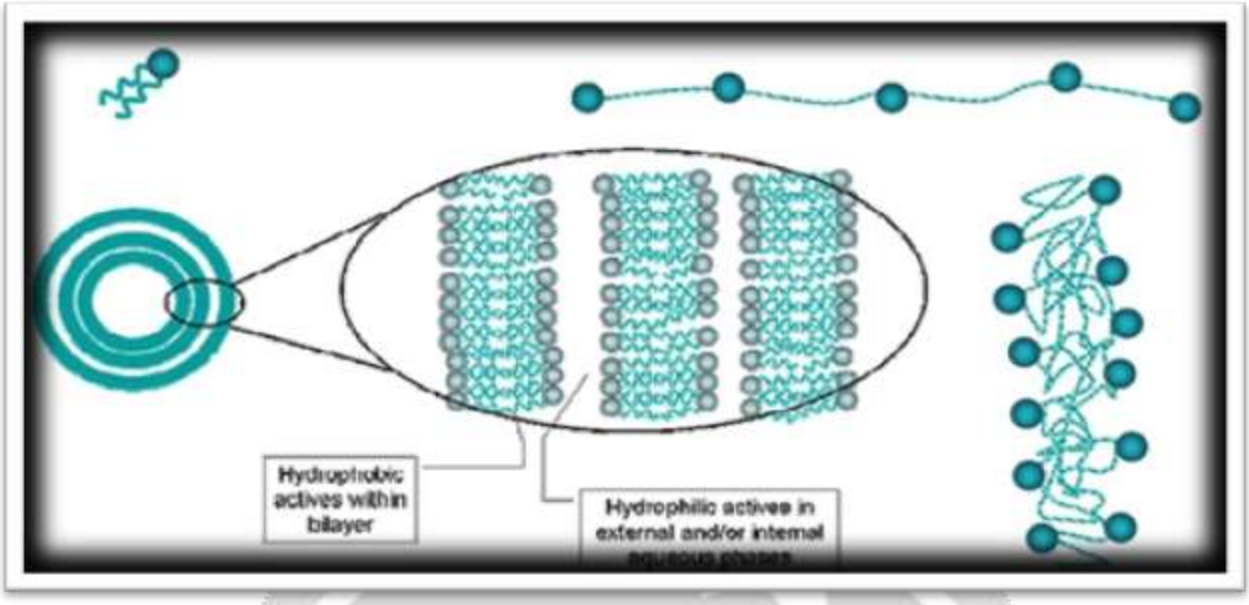


Fig 1. Vesicular Drug Delivery System

Definition :

"Vesicular Medication Delivery System" is the preferred method of drug delivery that uses vesicles.", e.g. liposomes, Niosomes, Pharmacosomes .

Why VDDS ?

Due to the limited medication penetration into cells, conventional chemotherapy is ineffective for treating intracellular infections. To eliminate adverse side effects of traditional & controlled release drug delivery methods, solve the issue of drug degradation &/or loss, and increase bioavailability at the site of illnesses.

Advantages of vesicular drug delivery system

- They increase the amount of the medicine in the bloodstream.
- Drug distribution using vesicles is an effective technique for minimising drug toxicity and directing medication to the site of action.
- This technique enhances bioavailability, especially for medicines that are poorly soluble in water.
- Both hydrophilic and lipophilic medications are incorporated in these systems.
- By extending the time of elimination since the medications are quickly metabolizable, it keeps the release of the pharmaceuticals going.
- They resolve issues with the drug's stability, solubility, and degradation.
- By functioning as a drug reservoir, conventional dosage forms' drawbacks can be overcome by encapsulating the medication.
- Due to their similarity in structure and function to biomolecular molecules, the carriers used in the vesicular drug delivery systemare both biocompatible and biodegradable.[2]

Disadvantages:

VDDS provides a lot of benefits, but they also have some significant drawbacks that limit its application. These are what they are: drugs passively, which might result in ineffective drug loading and drug leakage during in vivo preparation, preservation, and transport. Intense sonication is required, which causes medication leakages while being stored.[3]

Types of VDDS:

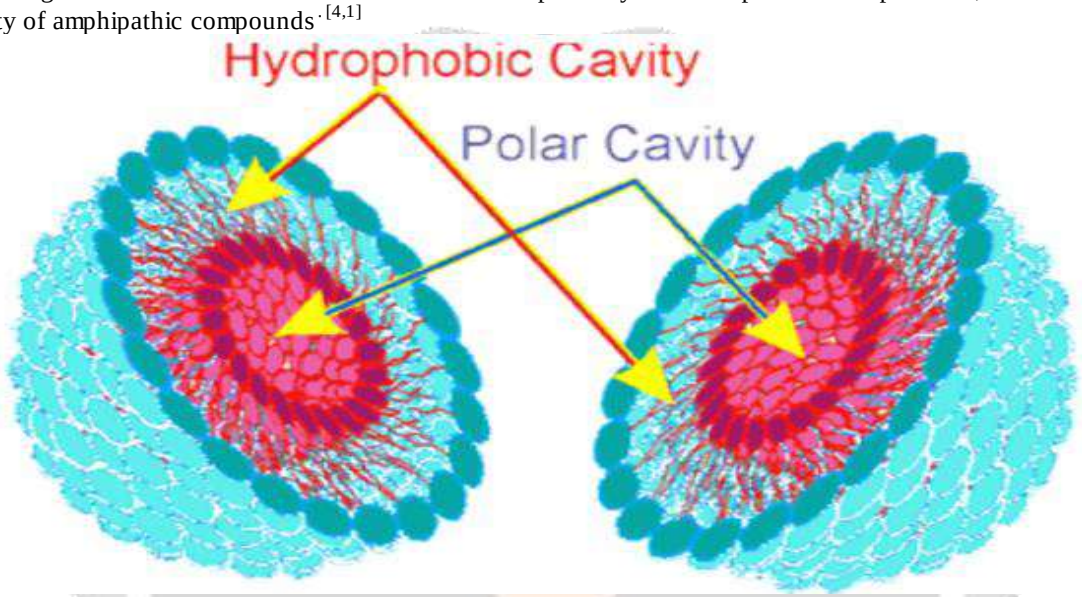
1. Liposomes
2. Niosomes
3. Ethosomes
4. Transferosomes
5. Pharmacosomes
6. Colloidosomes
7. Herbosomes
8. Sphinosomes
9. Layerosomes

10. Ufosomes

Liposomes Name Greek terms "Lipos" (which means fat) and "soma" (which means body) are the origin of the word "liposome." Vesicles formed of a lipid bilayer make up liposomes, which are manufactured. Drugs can be placed inside of liposomes and delivered to treat cancer and other disorders. Few drug carriers from a variety of carriers have advanced in clinical trials to the point where phospholipid vesicles (liposomes) have the ability to transfer drugs to the site of action efficiently. Natural phospholipids with mixed lipid chains or additional surfactants can make up liposomes. Although there are a few non-medical applications of liposome, such as in bioreactors, catalysts, cosmetics, and ecology. They can now be employed as therapeutic tools in areas like tumour targeting, gene and antisense treatment, etc. because of their dominance in drug transport and targeting.

At Cambridge's Babraham Institute, British haematologist Dr. Alec D. Bangham first identified liposomes in 1961 (published in 1964). When Bangham and R. W. Horne tested the institute's new electron microscope by adding negative stain to dry phospholipids, they made the discovery.

"Liposome is a small microscopic vesicle in which a membrane made of lipid molecules completely encloses an aqueous volume." Drug molecules can either be intercalated into a lipid bilayer or encapsulated in liposomes, which are made up of a variety of amphipathic compounds.[4,1]



Advantages : It offers selective passive targeting to tumour tissue (liposomal doxorubicin), increased drug efficacy and therapeutic index (Actinomycin-D), stability through encapsulation, biocompatibility, complete biodegradability, non-toxicity, flexibility, and lack of immunogenicity for systemic and non-systemic administrations, reduced toxicity of the encapsulated agent (Amphotericin B, Taxol), exposure of sensitive tissues to toxic drugs, site avoidance effect, and flexibility in pairing with ligands that target a particular location to accomplish active targeting. [1]

Disadvantages of liposomes

- High production costs.
- Drug or molecular leakage and fusion that has been encapsulated.
- Phospholipid occasionally experiences processes like oxidation and hydrolysis.
- Minimal half-life.
- Limited solubility
- Less stalls.

CLASSIFICATION

Liposome may be produced by variety of methods. Their nomenclature also depends upon the method of preparation, structural parameters or special functions assigned to them (table 1)1.Classification according to size:

Table 1: Classification of Liposomes according to size

TYPE	SPECIFICATIONS
MLV	Maltilamellar large vesicles-0.5 um
OLV	Oligolamellar vesicles -0.1um
UV	Unilamellar vesicles (all size ranges)
SUV	Small Unilamellar vesicles -20-100um
MUV	Medium sized unilamellar vesicles
LUV	Large uninamellar vesicles->100
GUV	Giant unilamellar vesicles ->1um

Classifications according to method of preparations

I) Extraction method: VET (Vesicles prepared by Extraction Technique)
II) French Pressure Cell method
III) Fusion method
IV) Reverse Phase Evaporation method: SUVs, MLVs & OLVs are made by reverse phase evaporation (REV) Method
V) Frozen & Thawed Multilayered Vesicles:
VI) Dehydration & Rehydration method: DRV
VII) Stable Plurilamella air Vesicles Method: SPLV

Based on In-Vivo applications

I. Conventional Liposomes

II. Long circulatory Liposomes

These can be characterised as liposomes that are typically made only of neutral or negatively charged phospholipids and/or cholesterol. This kind of liposome was used in the majority of early research on liposomes as a drug-carrier system. A type of vesicular structures called conventional liposomes is built on lipid bilayers enclosing water compartments. Due to the MPS system's quick absorption, conventional liposomes have a relatively short blood circulation period. They can be used as a local depot, to target macrophages, and for immunisation purposes. Application for the treatment of a wide range of disorders involving other tissues has been severely hampered by the quick and effective removal from the circulation by liver and spleen macrophages.

At the end of the 1980s, interest in liposomal delivery systems was revived by the development of new liposome formulations that can stay in the bloodstream for extended periods of time. In fact, the efficient MPS absorption of conventional liposomes made a wide range of new therapeutic options unfeasible until the advent of long-circulating liposomes. The ability of lengthy circulating liposomes to extravagate at body regions where the permeability of the vascular wall is elevated may be their most significant critical characteristic.

Fortunately, problematic areas like solid tumours and locations of infection and inflammation are characterised by enhanced capillary permeability. The fact that just two liposomal anticancer medicines have been licenced for use in humans is indicative of how crucial the long-circulation notion is for the tumor-selective delivery of antitumor medications (Doxil, DaunoXome). At the moment, covalently attaching the hydrophilic polymer polyethylene glycol (PEG) to the outer surface of liposomes is the most common method for producing long-circulating liposomes.

III. Immunoliposomes

To improve target site binding, immunooliposomes feature certain antibodies or antibody fragments (such Fab9 or single chain-antibodies) on their surface. They are helpful for targeting specific websites. [1]

Fig 2. Immunoliposomes

Structural Components of Liposome: There are number of the structural and nonstructural components of liposomes, major structural components of liposomes are:

a. Phospholipids Immunooliposomes have specific antibodies or antibody fragments (such as Fab9 or single chain-antibodies) on their surface to enhance target site binding. They are useful for focusing on particular websites. [1]

The most often employed component of liposome formulation, phospholipids including glycerol account for more than 50% of the weight of lipid in biological membranes. Phosphatidic acid is used to make these. Several phospholipids include: Lecithin (Phosphatidyl Choline) - PC 2. Phosphatidyl ethanolamine, also known as cephalin, or PE Phosphatidyl serine 3. (PS) 4. Phosphoinositide (PI) 5. Phosphodiesterol (PG)

b. Cholesterol : Although cholesterol does not naturally form a bilayer structure, it can be added to phospholipid membranes at very high concentrations—up to a 1:1 or even 2:1 molar ratio of cholesterol to phosphatidylcholine. With its hydroxyl group towards the aqueous surface and its aliphatic chain running parallel to the acyl chains in the bilayer's middle, cholesterol enters the membrane in this manner. Although both hydrophobic and particular headgroup interation have been suggested as the causes of the high solubility of cholesterol in phospholipid liposomes, the organisation of cholesterol in the bilayer has not been conclusively demonstrated[5].

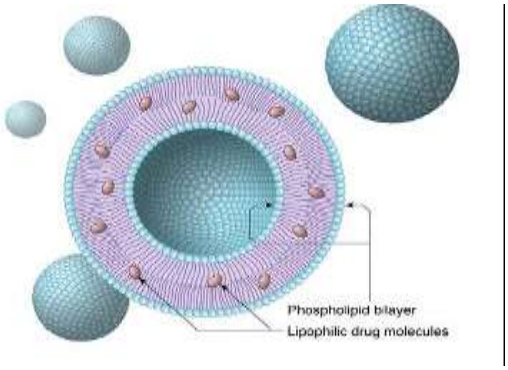
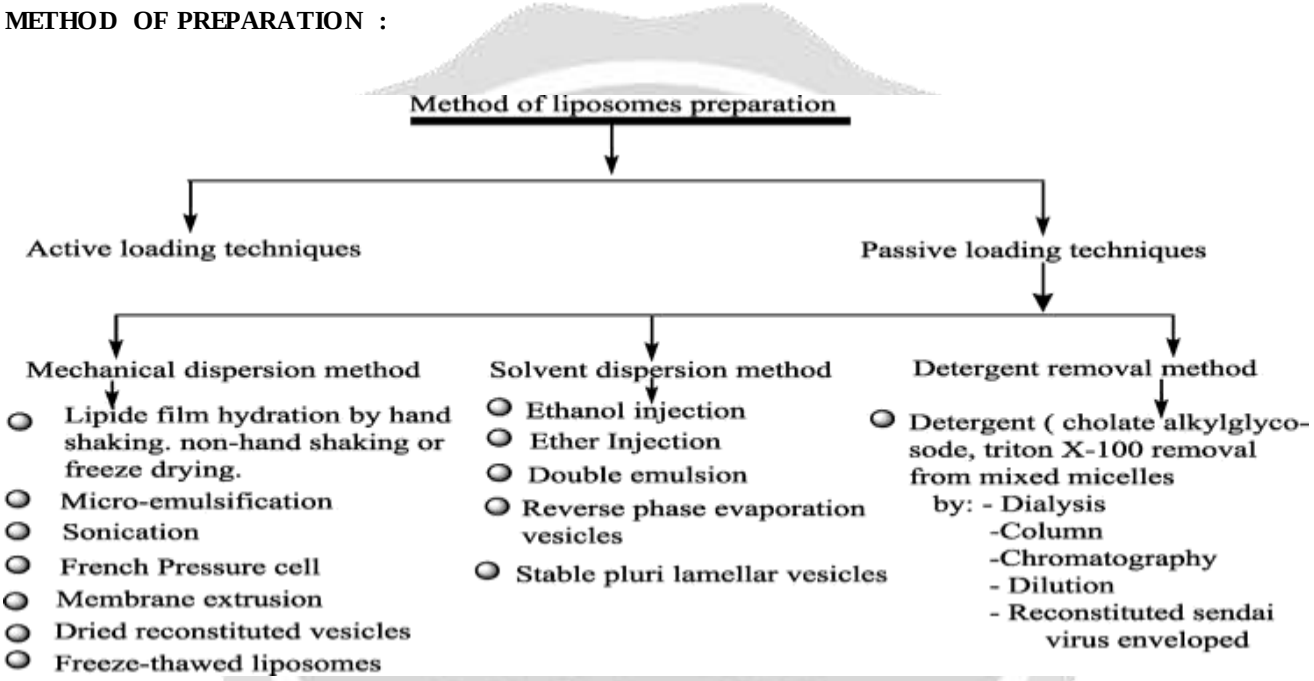


Fig 3. Structure and component of liposomes

METHOD OF PREPARATION :



DETAILING OF LIPOSOMES:

General advances associated with the arrangements of Liposomes different general advances that are developed in the arrangements of liposomes are:

1.Preparation of Lipids for Hydration
2.Hydration of lipid film/cake
3.Sizing of lipid suspension
i.Sonication
ii.Extraction

Techniques for Liposomes Preparations[6]

All the technique for getting ready liposomes includes four essential stages:

1.Drying down lipids from organic solvent.
2.Dispersion of lipid in aqueous media.
3.Purification of resultant liposome.
4.Analysis of end result.

ACTIVE LOADING TECHNIQUE:

Specific sorts of medications with ionisable gatherings and those with both lipid and water dissolvability can be brought into liposomes after the development of the unblemished vesicles. Drug is stacked into the preformed liposomes utilizing pH angle and likely distinction across liposomal film.

Approach for active loading:

Vesicles are ready in low pH arrangement, hence creating low pH inside liposome inside followed by expansion of the base to outside vehicle of liposomes. Essential mixtures with amino gathering are generally lipophilic at high pH and hydrophilic at low pH. Unprotonated type of essential medication can diffuse through the bilayer. At the low pH side, the particles are overwhelmingly protonated, which bring down the convergence of the medication in the unprotonated structure.

PASSIVE LOADING TECHNIQUE:

Stacking of captured specialists previously or during the assembling system. Utilized for drugs which are watery dissolvable yet lipid insoluble. It is additionally partitioned into

1.Mechanical scattering Technique:

Lipid hydration technique:

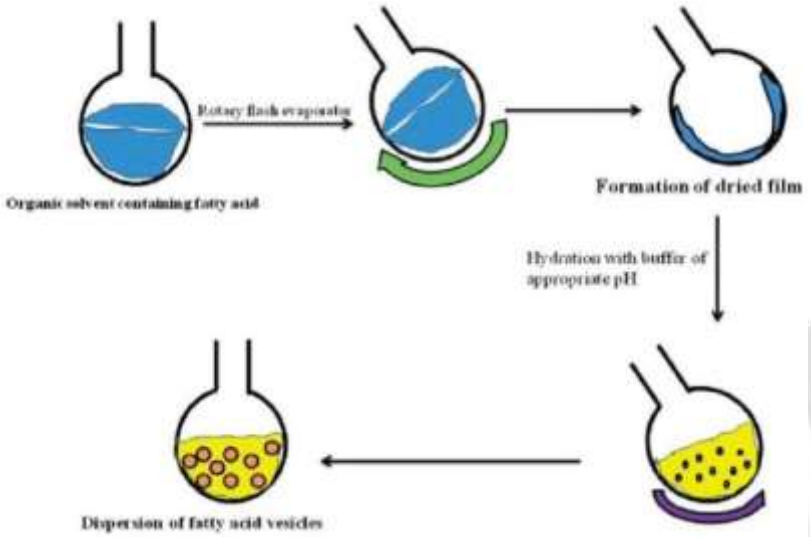


Fig.4: Multilamelar Vesicles (MLVs) formed either Handshaking technique or Rotatory flash Evaporator.

In this strategy, lipid blends are broken up in dissolvable combination of chloroform: methanol (2:1) in revolving evaporator carafe and dried slight film of lipid is made utilizing rotating evaporator under decreased pressure (60 rpm, 30ºC, and around 15 min). Cup is flushed with nitrogen and Hydration lipid is finished by adding 5ml of saline phosphate cradle containing drug/solute to be epitomized and again utilization of rotational evaporator for making homogeneous smooth white suspension. It is permitted to represent 2 hr at RT/above Tc for complete expanding process. This will give MLVs.

Microfludization/Miniature emulsification technique:

In this strategy, Miniature fluidizer siphons the liquid at exceptionally high tension through a 5µm screen. Then, at that point, it is constrained along characterized miniature channels which direct two floods of liquid to impact together at right points at an exceptionally high speed, in this way influencing an extremely effective exchange of energy. The lipid can be brought into the fluidizer, either as a suspension of huge MLVs, or as slurry of anhydrate lipid in a natural medium. The liquid gathered can be reused through the siphon and association chamber until vesicles of the circular aspect are gotten.

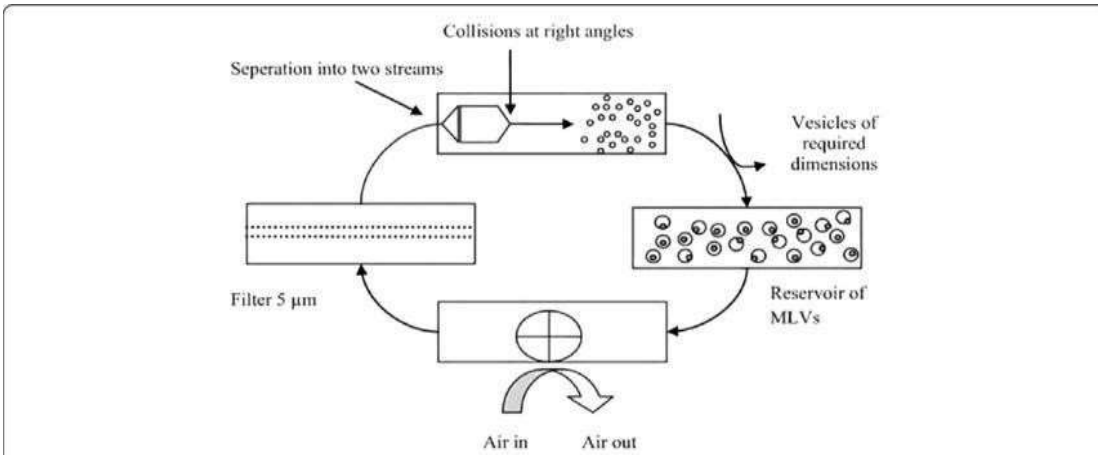


Fig.5: Representation of use of micro-fluidizer to prepare Small Unilamellar Vesicles (SUVs) from MLVs.

Benefits:

- Great size decrease up to 0.2mm.
- High pace of creation.
- for embodiment of water dissolvable materials because of high extent of lipid.

Sonication:

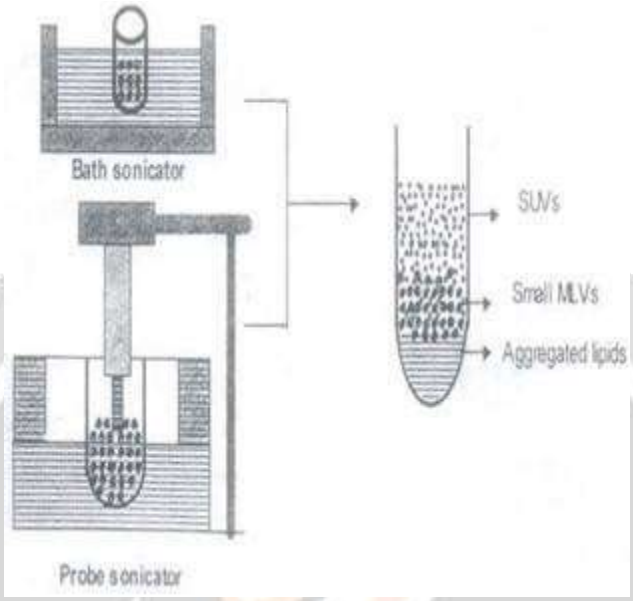


Fig.6: Preparations of Small Unilemilar Vesicles (SUVs) by Bath/Probe Sonication Process from MLVs.

At high energy level, performed MLVs are sonicated using either probe or bath ultrasonic disintegrator.
Using bath: Utilized for suspensions which require high energy in a little volume. What's more, defilement of planning with metal can prompt debasement of lipid.
Using Probe: Utilized for huge volume of weaken lipids where may not important to arrive at the vesicle size limit. At long last, they are filtered into the SUVs by ultracentrifugation and gathered from supernant of rotator tube. Size of liposome is affected by temperature, sythesis, and fixation, sonication time and power, volume of item.

French Pressure Cell:

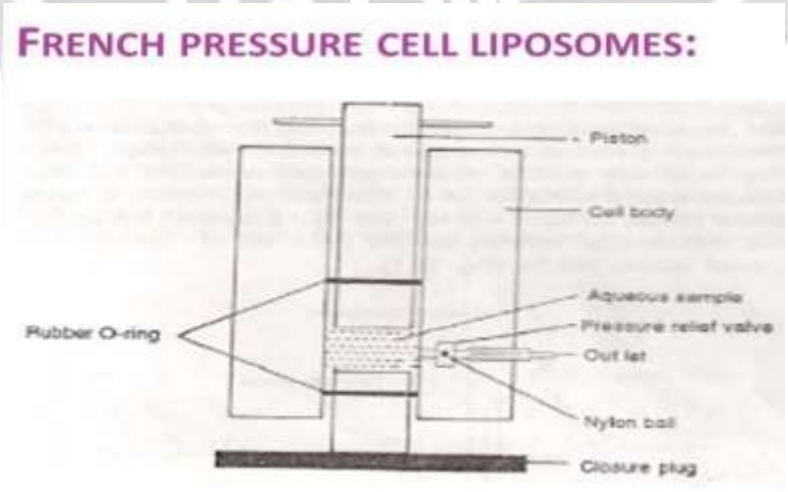


Fig. 7: French pressure cell & parts used for pre-parations of Uni or oligo Lamellar Vesicles

In this method, liquid sample of preformed MLVs are introduced into the sample cavity, then the position of piston and pressure is set up to fill sample up to the outlet hole. Then power is switched on. At high pressure (2000 psi) and at 40°C, MLVs are extruded through small orifice, which is collected in suitable container. This technique yields uni- or oligo lamellar liposome of intermediate size. More stable than they obtained by sonication method and also leakage of the content from the liposomes are lesser.

Drawback:
High cost of the pressure cell.

Membrane Extraction Method:
Size of prepared liposomes is reduced by gently passing them through membrane filter of defined pore size and this can be achieved at much lower pressure.In this process, the vesicles content are extruded with the dispersion medium during breaking and resealing of phospholipids as they pass through the polycarbonate membrane in order to achieve high entrapment. The liposomes produced by this method have been termed as LUVETs and 30% encapsulation can be obtained using high lipid concentration.

Dried Reconstituted Vesicles:
It begins with freeze drying of a scattering of void SUVs and rehydrating it with the watery liquid containing the materials to be captured. This prompts scattering of strong lipids in finely partitioned structure. Freeze drying is utilized to freeze and lyophilize the preformed SUVs scattering instead of to dry the lipids from a natural arrangement. This prompts coordinated film structure which on expansion of water can rehydrate, intertwine and reseal to frame vesicle with high catch limit. It is utilized for assembling of uni - or olio lamellar of the request for 1.0µm or less in distance across.

Advantages:High capture of water solvent substance and utilization of gentle condition for arrangement and stacking of bioactive.

Freeze Thawed Sonication:
This strategy depends on freezing of unilamellar scattering and defrosting (liquefying) by remaining at RT for 15 min. lastly exposed to a sonication cycle. This cycle breaks and declines SUVs during which the solute equilibrates among inside and outside, and liposomes themselves meld and uniquely expansion in size. The second step of the sonication extensively decreases the porousness of the liposome film, by speeding up the rate at which the pressing imperfections are wiped out. For creating monster vesicles of width having 10 - 50 µm, the sonication step is supplanted by the dialysis against hypo-osmolar cushion. For this situation, SUVs are blended in with salt arrangement followed by freeze defrosting. During this dialysis, the enormous vesicles shaped by freeze defrosting swell and crack because of the osmotic lysis, where the wire and get ready as monster vesicles.
Drawback:

- -Lesser embodiment proficiency,
- -Presence of charge molecule for the arrangement of ice gem to help with the burst or combination process, so unbiased liposomes can't be come about.

Advantage:

- Basic
- Fast
- Bring about extent of enormous unilamellar vesicles development.

2.Solvent scattering strategy:

Ethanol Injection technique:
Ethanol is utilized to break up the lipids and arrangement is quickly infused through a fine needle into an overabundance of cushion arrangement. SUVs structure suddenly. Strategy is confined to the creation of moderately weaken SUVs suspension. Expulsion of lingering ethanol is likewise present an issue. This should be possible by ultrafiltration or vacuum refining

Ether Injection Strategy:
In this strategy, arrangement of lipids in diethyl ether or ether: methanol combination is gradually infused to fluid arrangement of materials to be typified at 55 - 65ºC. Ensuing expulsion of ether under vacuum prompts the arrangement of liposomes.
Drawbacks: Heterogeneous size (70 - 190µm), openness of mixtures to natural solvents or high temperature.

Double Emulsion Vesicles:
At the point when natural arrangement which as of now contain water bead, is brought into overabundance fluid stage followed by mechanical scattering, multi compartment vesicles are acquired. The arranged scattering so got is alluring as a w/o/w framework. The vesicles with fluid center are suspended in watery medium. So two fluid compartments being isolated from one another by sets of phospholipids monolayer whose hydrophobic surface face each other across a dainty film of natural dissolvable. Evacuation of this dissolvable obviously brings about moderate measured unilamellar vesicle. The hypothetical ensnarement might reach up to 90%.

Reversed-phase Evaporation of Vesicles:
The fundamental component of this strategy is the expulsion of dissolvable from emulsion by vanishing. In this

technique, lipids broke up in natural solvents are sonicated by shower sonication which structures emulsion (w/o) and afterward emulsion is dried down to a semi strong gel utilizing revolving evaporator under diminished pressure. The following stage is to Bing about the breakdown of a specific extent of water beads by enthusiastic mechanical shaking with a vortex blender. This will give LUVs. Epitome rate: up to half.

Stable plurilamellar vesicles:

In this strategy, w/o scattering is ready as portrayed in Fire up Technique with abundance lipid, yet drying process is joined by proceeded with shower sonication with a flood of nitrogen. The rearrangement and equilibration of watery dissolvable and solute happen during this in the middle of between the different bilayers in each plurilamellar vesicle. Capture rate: 30%.

3. Detergent removal method:

In this strategy, the phospholipids are carried into private contact with the fluid stage by means of the delegate of cleansers, which partner with phospholipid particles and screen the hydrophobic bits of the atom from water. Cleanser consumption is accomplished by four following methodologies:

Dialysis:

The dialysis can be acted in dialysis sacks drenched in enormous cleanser free cushions (balance dialysis) or by utilizing consistent stream cells, diafiltration and cross filtration.

Gel filtration:

In this technique the cleanser is drained by size select chromatography. Sephadex G-50, Sephadex G-100, Sepharose 2B-6B and Sephacryl S200-S1000 can be utilized for gel filtration. The liposomes don't enter into the pores of the dabs pressed in a segment.

Adsorption utilizing bio beads:

Cleanser adsorption is accomplished by shaking of blended micelle arrangement in with beaded natural polystyrene safeguards, for example, XAD-2 dabs and Bio-dots SM2. The incredible benefit of the utilizing cleanser safeguards is that they can eliminate cleansers with an exceptionally low basic micelle fixation (CMC) which are not totally drained by dialysis or gel filtration techniques.

Dilution:

Endless supply of watery blended micellar arrangement of cleanser and phospholipids with cushion the micellar size and the polydispersity increments decisively, and, as the framework is weakened past the blended micellar stage limit, an unconstrained change from polydisperse micelles to monodisperse vesicles happens.

Evaluation Tests of Liposomes:

1. Size and size distribution
2. Surface charge
3. Lameliarity
4. Encapsulation Capacity
5. Entraped volume
6. Drug release
7. Chemical Characterization:

Determination of Phospholipids:The phospholipids are measured by :-

- *Bartlett assay*
- Stewart assay
- Phospholipid Hydrolysis
- *Phospholipid Oxidation*
- *Cholesterol analysis*

Therapeutic Application of Liposome [7]

1. Liposomes as protein and medication delivery systems, controlled drug release over time, Changes in pharmacokinetics and biodistribution, increased drug solubilization Enzyme replacement therapy and lysosomal storage diseases, as well as biodistribution.

2.Liposomal medicines, Liposomal biological response modifiers, and liposomes in antibacterial, antifungal, and antiviral therapy.

3. Liposomes as a vehicle for tiny cytotoxic compounds in the treatment of tumours Genes or cytokines are macromolecules' vehicles.

4. Gene and antisense therapy, genetic (DNA) vaccination, and liposome in gene delivery.

5. Immunology uses for liposomes include immunoadjuvant immunomodulation and immunodiagnostics.

6. Liposomes as substitutes for synthetic blood.
7. Liposomes as carriers for radiopharmaceuticals and radiodiagnostics.
8. Liposomes in dermatology and cosmetics.
9. The use of liposomes in bioreactor and enzyme immobilisation technologies.

NIOSOME

A nonionic surfactant-based liposome is known as a niosome. cholesterol is primarily used as an excipient in the formation of niosomes. excipients can also be used in other ways. niosomes are more capable of penetrating than earlier emulsion formulations. although they share a bilayer with liposomes architecturally, niosomes are more stable due to the materials employed in their preparation, and as a result, they have many additional benefits over liposomes [8,9]. niosome sizes are minuscule and fall into the nanometric range. the range of particle sizes is 10nm–8100nm.

STRUCTURE OF NIOSOME

A typical niosome vesicle would be made up of a vesicle-forming amphiphile, such as Span860, which is a non-ionic surfactant that is typically stabilised by the addition of cholesterol and a little amount of dicetyl phosphate, an anionic surfactant that also aids in stabilising the vesicle.[10,11]

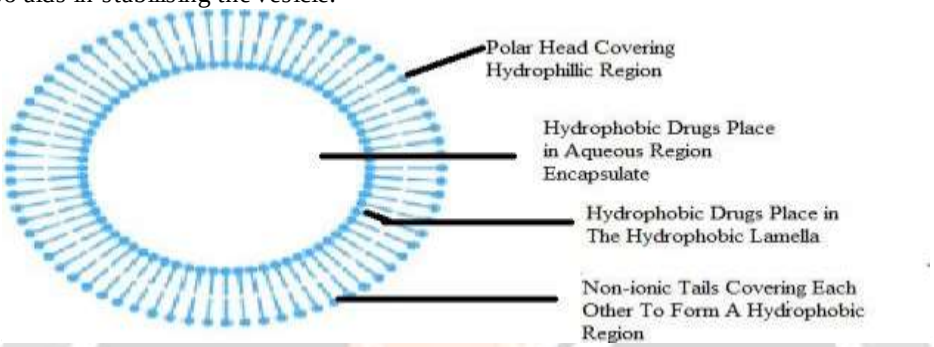


Figure:8 Structure of Niosome

ADVANTAGES

1. Drug moieties that are hydrophilic, lipophilic, or ampiphilic can all fit inside a niosome.
2. By modifying the composition of the vesicle, size lamellarity, surface charge, tapping volume, and concentration, vesicle properties can be changed.
3. The medicine can release in a regulated and sustained manner.
4. There are no unique requirements for handling and storing surfactants.
5. The depot formulation permits a regulated release of the medication.
6. Oral bioavailability of medicines that are poorly soluble has enhanced.
7. Surfactants have the following properties: biodegradability, biocompatibility, non-toxicity, and immunogenicity.
8. They can stop biological circulation from reaching the active moiety.
9. Drug defence against enzyme metabolism.
10. Increase the drug's stability when entrapped.
11. They can make it easier for medications to penetrate the skin.
12. Due to the medication molecules' prolonged clearance from the bloodstream, they enhance the therapeutic profile of the molecules. [12,13]

DISADVANTAGES [14]

1. Aggrigation
2. Long-lasting
3. Stability in the body

COMPOSITIONS OF NIOSOMES: [15-17]

The two major components used for the preparation of niosomes are,

1. Cholesterol
2. Nonionic surfactants

1. Cholesterol

Cholesterol is utilised to give niosome preparations stiffness, correct shape, and conformation.

2. Nonionic surfactants

Surfactants have a significant impact on how niosomes are formed. The manufacture of niosomes typically uses the following non-ionic surfactants.

E.g.

- Spans (span 60, 40, 20, 85, 80)
- Tweens (tween 20, 40, 60, 80) and
- Brijs (brij 30, 35, 52, 58, 72, 76).
- A hydrophilic head and an ahydrophobic tail are features of the non-ionic surfactants. (18)

Other surfactants that are reported to form niosomes are as follows(19)

1. Ether linked surfactant
2. Di-alkyl chain surfactant
3. Ester linked
4. Sorbitan Esters
5. Poly-sorbates

FACTORS AFFECTING VESICLES SIZE, ENTRAPMENT EFFICIENCY AND RELEASE CHARACTERISTICS:

Drug:

Vesicle size increases when a drug is trapped in niosomes, most likely due to an increase in the charge and mutual repulsion of the surfactant bilayers or an interaction between the solute and the head groups of the surfactant. However, certain drugs are caught in the lengthy PEG chains. The propensity to grow shrinks in vesicles covered with polyoxyethylene glycol (PEG). The drug's hydrophilic lipophilic balance influences the level of entrapment.(20)

Amount and type of surfactant:

The mean size of niosomes increases proportionally when the hydrophilic-lipophilic balance (HLB) of surfactants increases, from Span 85 (HLB 1.8) to Span 20 (HLB 8.6). This is because as surfactant hydrophobicity increases, surface free energy reduces.

The bilayers of the vesicles can be in either the so-called liquid state or the so-called gel state depending on the temperature, the kind of lipid or surfactant, and the presence of additional elements like cholesterol. When the bilayers are disordered, they are in a liquid state, and when they are well organised with alkyl chains, they are in a gel state.

The phase transition temperature of surfactants has an impact on entrapment effectiveness as well. For instance, Span 60, which has a greater phase transition temperature, offers better entrapment.(21)

Cholesterol content and charge:

Both the chain order of gel state bilayers and the chain order of liquid state bilayers are altered by cholesterol. At a high cholesterol concentration, the gel state changes to a liquid-ordered phase. The bilayers' stiffness increased with increasing cholesterol content because it reduced the rate at which material was released from its encapsulation. The presence of charge tends to increase the interlamellar distance between succeeding bilayers in multilamellar vesicles, which results in a bigger overall volume entrapped.(22)

CHARACTERISATION OF NIOSOMES:

Size: Niosomal vesicles are thought to be spherical in shape, and a number of methods, including the laser light scattering method, electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy and optical microscopy, and freeze fracture electron microscopy, can be used to determine their mean diameter [23,24,25].

Bilayer formation, Membrane rigidity and Number of lamellae:

Bilayer vesicle assembly including non-ionic surfactants is characterised by the production of X-crosses under light polarisation microscopy, and the mobility of a fluorescence probe in relation to temperature can be used to quantify membrane stiffness. The number of lamellae is counted using NMR spectroscopy, small angle X-ray scattering, and electron microscopy[26,27].

Entrapment efficiency: According to the procedure outlined above, after creating the niosomal dispersion, the unentrapped drug is separated by dialysis, centrifugation, gel filtration, and/or complete vesicle disruption using 50% n-propanol or 0.1% Triton X-100. The solution is then subjected to the appropriate assay method for the drug before being analysed. Where, according to [11]'s definition of entrapment efficiency (EF):

Entrapment efficiency (EF) = (Amountentrapped/ total amount) x100.

***In vitro* Release StudyDialysis:** Dialysis tubing can be used to conduct an in vitro release rate research. A dialysis bag has been cleaned and put in distilled water to soak. The vesicle suspension was pipetted into a bag made of tubing, which was then sealed. It was then placed in a 250 ml beaker containing 200 ml of buffer solution, which was constantly shaken at either 25°C or 37°C. Using an appropriate assay method, the buffer was examined for the presence of drugs at various time periods.(28)

Reverse dialysis:
This method involves putting niosomes in a number of tiny dialysis tubes with 1 mL of dissolution liquid, and then displacing the niosomes from the dissolution medium.[29]

Franz diffusion cell:
The cellophane membrane serves as the dialysis membrane in a Franz diffusion cell. At room temperature, the niosomes are dialyzed through a cellophane membrane in opposition to an appropriate dissolving liquid. The samples are removed at appropriate intervals and their drug content is examined .[30]

***In vivo* Release Study:**
Niosomal suspension was administered intravenously (via the tail vein) to the albino rats for the in vivo investigation using the proper disposal syringe. There were 35 groups created from these rats.

APPLICATIONS OF NIOSOMES [31-34]
Niosome technology has a wide range of applications and can be utilised to treat many different ailments. The usage of niosomes listed below have either been established or are still being studied.

- It serves as a drug targeting method.
- It is used to treat cancer by preventing the growth of new tumours.
- It is used to treat leishmaniasis, which includes skin and mucous membrane infections, such as sodium stibogluconate.
- It serves as a means of delivering peptide medications.
- It's employed in the study of immunological response.
- Niosomes as Hemoglobin Carriers.
- Niosome-based transdermal drug delivery systems.
- It is employed in the delivery of Opthalmic drugs.
- Other Application; Niosomes can also be used for localised drug action and sustained drug release, considerably enhancing the safety and effectiveness of many medications. Niosomal encapsulation might make it possible to safely distribute toxic medications that require greater concentrations.

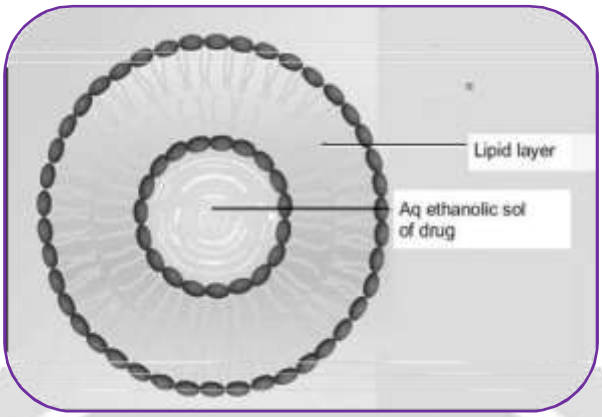
TABLE : Route of application of niosomes drugs.

Routes of drug administration	Examples of Drugs
Intravenous route	Doxorubicin, methotrexate, sodium stibogluconate, iopromide, vincristine, diclofenac sodium, flurbiprofen, centchroman, indomethacin, colchicine, rifampicin, tretinoin, transferrin and glucose ligands, zidovudine, insulin, cisplatin, amarogentin, daunorubicin, amphotericin B, 5-fluorouracil, camptothecin, adriamycin, cytarabine hydrochloride
Peroral route	DNA vaccines, proteins, peptides, ergot alkaloids, ciprofloxacin, norfloxacin, insulin
Transdermal route	Flurbiprofen, piroxicam, estradiol, levonorgestrol, nimesulide, dithranol, ketoconazole, enoxacin, ketorolac
Ocular route	Timolol maleate, cyclopentolate
Nasal route	Sumatriptan, influenza viral vaccine
Inhalation	All-trans retinoic acids

ETHOSOMES
Ethosomes: Alcohol (ethanol and isopropyl alcohol) and water are all present in quite high concentrations in lipid vesicles called ethosomes.[35] Soft vesicles known as ethanolosomes are composed of phospholipids, ethanol (in higher

concentrations), and water. Ethosomes can range in size from tens of nanometers to microns. Compared to traditional liposomes, ethosomes have a much higher transdermal flow and penetrate the skin layers more quickly [36,37].

Figure illustrates how ethosomes are visualised. However, the precise process by which ethosomes better penetrate deeper epidermal layers is still unknown. Deeper distribution and penetration in the lipid bi-layers of the skin are thought to be caused by the synergistic interactions between phospholipids and high concentrations of ethanol in vesicular formulations.



ADVANTAGES [38, 39, 40, 41]

- Improved transdermal drug administration by the skin penetration of the drug.
- Its formulation includes non-toxic row material.
- The components of ethosomes are harmless and can be used in pharmaceutical and cosmetic products.
- Lunge molecules (peptides and protein molecules) may be delivered.
- A less complicated drug delivery method than phonophoresis, iontophoresis, and other complicated methods.
- The ethosome system may be immediately commercialised and is passive and non-invasive.
- High patient adherence The semisolid form (gel or cream) in which the ethosomal medication is administered results in great patient compliance.
- Ethosomal drug delivery systems are widely applicable in the pharmaceutical, veterinary, and cosmetic industries.

DISADVANTAGES [39, 42, 43]

- Only powerful molecules, those requiring a daily dose of 10 mg or less, can be administered; drugs requiring high blood levels cannot.
- Ethosomal administration is often intended to provide steady, sustained medication delivery, not quick bolus type drug input.
- Sufficient solubility of the medication in aqueous and lipophilic conditions to reach dermis.
- reach the systemic circulation through the microcirculation.
- The drug's molecular size needs to be appropriate for percutaneous absorption.
- Some types of skin may not respond well to adhesive.
- A discomfort to wear.
- Might not be cost-effective. bad yield
- Dermatitis or skin irritation brought on by excipients and enhancers used in medication delivery systems.
- The ethosomes may agglomerate if shell locking is inadequate and disintegrate upon passage into water.
- Product loss during the transition from organic to aqueous media.
- The improved drug penetration of ethosomes over liposomes is their principal benefit.

COMPOSITION OF ETHOSOMES [44-51]

Ethosomes display a lipid bilayer similar to that of liposomes, although they are different from liposomes in terms of their composition (high content of ethanol). The hydroalcoholic or hydro/glycolicphospholipids that make up the ethosomes contain a sizable amount of alcohol. Phospholipids of different chemical structures, such as phosphatidylcholine, may be present in ethosomes.

Alcohol (ethanol or isopropyl alcohol), water, phosphatidicacid, phosphatidylserine, phosphatidyl ethanolamine, phosphatidyl glycerol, and phosphatidyl inositol (or other glycols). Phospholipon 90 is one of the chosen phospholipids (PL-90). It is typically used between 0.5 and 10% W/W. Cholesterol may be included in the preparation at amounts

ranging from 0.1% to 0.10%. Propylene glycol and Transcutol are typically employed among glycols, with their percentages in the final product ranging from 20 to 50%. Alcohol, such as ethanol and isopropyl alcohol. The phospholipids can be mixed with non-ionic surfactants (PEG-alkyl ethers) and cationic lipids (cocoamide, POE alkyl amines, dodecylamine, cetrimide, etc.) in the formulations. The alcohol and glycol mixture's non-aqueous phase content can range from 22 to 70%.

Mechanism of Drug Penetration [52]: The improved drug penetration of ethosomes over liposomes is their principal benefit. There is no known mechanism for how drugs are absorbed from ethosomes. The following two steps are likely involved in medication absorption. [53,54] (Figure: 9)

1. **Ethanol Effect;** Through the skin, ethanol enhances permeation. Its penetration-enhancing effect has a well-known mechanism. Ethanol permeates intercellular lipids, increasing their fluidity and decreasing the density of the cell membrane's lipid multilayer.

2. **Ethosomal Effect:** The ethanol of ethosomes causes an increase in cell membrane lipid, which increases skin permeability. As a result, the ethosomes easily penetrate the deep layers of the skin, where they fuse with the lipids and release the medicines.

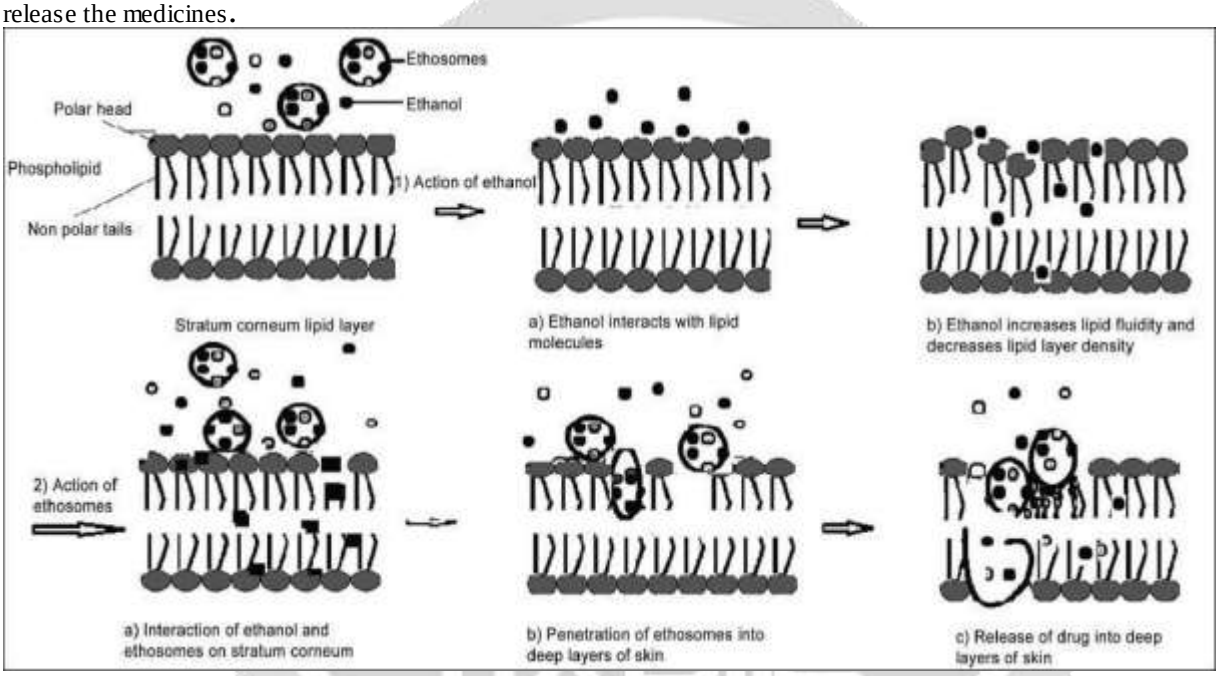


FIGURE 9: DIAGRAMMATICALLY REPRESENTATION OF MECHANISM OF ACTION OF ETHOSOMES

Therapeutic applications

Ethosomes, which contain a lot of ethanol and may pass through the skin's deeper layers, seem to be the best vesicles for transdermal drug delivery of hydrophilic and impermeable substances via the skin.

Transferosomes:

For the efficient transdermal distribution of a variety of low and high molecular weight medications, transferosomes were developed. Transfersomes can spontaneously pass through the intact stratum corneum along two intracellular lipid pathways with different bilayer characteristics [55]. Due to its great deformability and combination of hydrophilic and hydrophobic qualities, intact vesicles can be penetrated more effectively [56]. Since they are several orders of magnitude more elastic than regular liposomes, these vesicular transfersomes are well suited for skin penetration. Transfersomes overcome the barrier to skin penetration by squeezing along the stratum corneum's intracellular sealing lipid. Owing to the high vesicle deformability, which allows the entry due to the mechanical stress of the environment in a self-adapting way, there is provision for this The appropriate surface-active components are combined in the proper ratios to create the flexible membrane of transfersomes. Formulations of lidocaine and tetracaine based on transferosomes showed penetration similar to subcutaneous injections. Anti-cancer drugs like methotrexate were investigated for transdermal delivery using transferosome technology. This provided a novel approach to treating cancer, especially skin cancer. [57]

Advantage:

- Transferosomes can accommodate medicinal molecules with a wide spectrum of solubilities because its infrastructure combines hydrophobic and hydrophilic moieties.

- Transferosomes can deform and pass through small openings (by a factor of 5 to 10 less noticeable loss than their own diameter).
- poses a high entrapment efficiency, close to 90% in the case of a lipophilic drug.
- both systemic and topical applications delivery of drug.

Limitation:

- Transferosomes are prone to oxidative destruction, which makes them chemically unstable.
- Another factor that works against the use of transfersomes as drug delivery systems is the purity of natural phospholipids.
- Formulations for transferosomes are pricey.

[58]

Pharmacosomes:

Pharmacosomes are phospholipid-drug complexed amphiphilic lipid vesicular systems. Pharmacosomes are drug carriers because Pharmacon denotes drugs and Soma denotes a carrier. System created by connecting the medicine and the carrier. Drugs that are colloidally dispersed have a covalent connection to lipids. Because it is made up of amphiphilic prodrugs, it is simple to obtain high drug loading and very low drug leakages. increases contact area and finely enhances bioavailability by raising interfacial tensions.

Advantages:targeted drugs, regulated release, high effectiveness of trapping, There is no requirement to remove trapping medicines from formulations as there is with liposomes. purely soluble medicines' bioavailability is improved. lowers the price of therapy[59]

Disadvantages:Covalent bonds are necessary to prevent medication leaks, and compounds are synthesised due to their amphiphilic character. Fusion, aggressiveness, and chemical hydrolysis occur on storages. [60]

COLLOIDOSOME:

During the interphase of emulsion droplets, coagulated or fused particles form hollow shell microcapsules. Application flexibility is made possible through size control. Colloidosome membrane has enormous potential for regulating the permeability of spices that are trapped in it. allows for timed and selective release.

Colloidosomes are the coagulated or fused particle-filled hollow shell microcapsules seen at the interface of emulsion droplets. Exciting potential uses for colloidalosomes include the controlled release of medications, proteins, and vitamins, as well as the production of cosmetics and dietary supplements.

With extensive control over size, permeability, mechanical strength, and compatibility, colloidosomes have a high encapsulation efficiency. Colloidosomes are a brand-new kind of microcapsules that form at the interface of emulsion droplets from colloid particles that have coagulated or fused.

In order to create colloidosomes with the least amount of total interfacial energy, the particles self-assemble on the surface of droplets. These structures were created for the first time by applying latex particles to the surface of octanolin-water emulsion drops, fusing the monolayers, and then removing the oil.

Similar structures have also been produced by layer-by-layer assembly of multilayer shells made of alternately positively and negatively charged nanoparticles or polyelectrolytes, as well as by template solid nanoparticles on the surface of solid sacrificial microparticles based on electrostatic attraction.

Removal of the core, sacrificial colloidal particles yields the final hollow shells. Colloidosomes combine polymer latex colloidal particles into shells around drops of a water-in-oil emulsion, followed by partial fusing of the shell and centrifugal transfer into water to produce stable capsules, the permeability of which can be altered by varying the partial fusion conditions. Using innovative colloidosome capsules with an aqueous gel core and shells made of polymeric micro rods, hairy colloidosomes with micro rod particles make their appearance. Templating water-in-oil emulsions supported by rod-like particles, gelling the aqueous phase, dissolving the oil phase in ethanol, and redispersing the resulting colloidosome microcapsules in water were used to achieve this.

Advantages:

Colloidosome membranes have considerable potential in managing the permeability of the entrapped species and allow the selective and temporal release, and control of the size allows flexibility in applications and choice of encapsulated materials. The yield stress can be regulated by mechanical strength control to resist a range of mechanical loads and to enable release at specific shear rates[61].

HERBOSOMES:

Herbo implies a plant, and some means resembling a cell. Numerous botanical items' chemical and biological make-ups, biological functions, and health-promoting qualities have been demonstrated during the past century by phytochemical and phytopharmacological studies. The majority of a plant's biologically active components are polar or water soluble compounds. However, water-soluble phytoconstituents (such as flavonoids, tannins, glycosidic aglycones, etc.) are poorly absorbed either because of their large molecular size, which prevents passive diffusion, or because of their poor lipid solubility, which severely restricts their ability to cross the lipid-rich biological membranes, leading to poor

bioavailability. Since ancient times, complex chemical concoctions made from plants, or phytomedicines, have been utilised to maintain health. However, many phytomedicines' efficiency is constrained due to their poor oral absorption. Phytosomes are another name for herbosomes. Compared to standard herbal extracts, herbosomes have a better pharmacokinetic and pharmacodynamic profile. The proteins insert into a continuous matrix that is provided by a molecular layer made of PC and other phospholipids.

Advantages

It improves the bioavailability of lipid-insoluble polar phytoconstituents when applied topically and orally, leading to a much larger therapeutic value. Improved absorption of the active component(s) results in a lower dose required, Herbosomes permeate the non-lipophilic botanical extract to be better absorbed in intestinal lumen because phosphatidylcholine, which is used in their synthesis in addition to serving as a carrier, also has hepatoprotective properties. Herbosomes exhibit superior stability profiles than liposomes because phosphatidylcholine molecules and phytoconstituents create chemical connections.

SPHINOSOMES:

Naturally, liposome stability issues are more serious, making liposomal stability improvement a top priority. When liposomes are kept in aqueous suspension, their phospholipids may clump, fuse, or leak their contents as a result of chemical degradation such as oxidation and hydrolysis. At pH values near to neutral, the hydrolysis of ester linkages will stall. By using lipids with ether or amide linkages rather than ester linkages (such as those present in sphingolipid) or phospholipid derivatives with the 2-ester linkage substituted by carbomoyloxy activity, the hydrolysis can be completely avoided. As a result, sphingolipid is now employed to create stable liposomes known as sphingosomes.

According to one definition, a sphingosome is a "concentric, bilayer vesicle in which an aqueous volume is completely surrounded by a membranous lipid bilayer primarily formed of natural or synthesised sphingolipid. There are several ways to give sphingosomes, including intravenous, intramuscular, subcutaneous, and intra-arterial parenteral routes. It is mostly given intravenously, however occasionally it is inhaled. To deliver a highly concentrated solution into large volume and flow channels, it is frequently injected into a major central vein, such as the inferior or superior vena cava. Sphingosomes can be used topically or orally. Sphingosomes are just liposomes made of sphingolipid, to put it simply.

ADVANTAGES:

select tumour tissue for passive targeting, Increase stability through encapsulation, Increase therapeutic index and efficacy. decrease in the encapsulating agent's toxicity, increase in pharmacokinetic impact (increase circulation time), ability to combine with ligands that are unique to a given location in order to achieve active targeting. [61]

LAYEROSOMES:

In order to stabilise their structures, layerosomes are regular liposomes coated with one or more layers of biocompatible polyelectrolytes. One of the methods for preparing or stabilising nanosystems is the layer-by-layer coating concept[62]. The layersomes are regular liposomes that have had their structure stabilised by coating them with one or more layers of biocompatible polyelectrolytes. The formulation strategy is based on a different coating method using initially charged tiny unilamellar liposomes and positive poly (lysine) (pLL) and negative poly (glutamic acid) (PGA) polypeptides. Liposomes' primary flaw, which is connected to surface characteristics, is their instability during storage or in biological media. The liposomes' structure was stabilised as a result of the surface change, creating stable drug delivery systems. either oral administration One of the potential areas of use is inclusion in biomaterials [63]. Thus, the stable nanosystem has been developed thanks to the layerosome concept.

UFOSOMES:

Unsaturated fatty acid liposomes, also known as ufosomes, are the forms of fatty acid vesicles. Colloidal suspensions of closed lipid bilayers made up of fatty acids and their ionised species are known as fatty acid vesicles (soap). They can be seen in a small area above the chain melting temperature (Tm) of the matching fatty acid-soap mixture in the ternary phase diagram for fatty acids, soap, and water[64]. Both the nonionized neutral form and the ionised form of amphiphiles are present in fatty acid vesicles (the negatively charged soap). The stability of the vesicle depends on the ratio of nonionized neutral form to ionised form. In reality, "fatty acid/soap vesicles" are fatty acid vesicles. Ufasome membranes are significantly more stable than liposomes[65].

STRATEGIES TO IMPROVE VDDS:

Pro-Vesicular Drug Delivery: The two basic strategies for improving VDDS are: Pro vesicular drug delivery, such as Proliposomes and Proniosomes, was created to address the stability issues with vesicular drug delivery systems made of dry goods or liquid crystalline gel that can be moistened right before usage. [66]

Characterization:

Size and size distribution, morphology, angle of repose, rate of hydration, entrapment effectiveness, degree of deformity, and permeability assessments, among other things.

Types of pro vesicular drug delivery systems:

- Proliposome
- Proniosomes

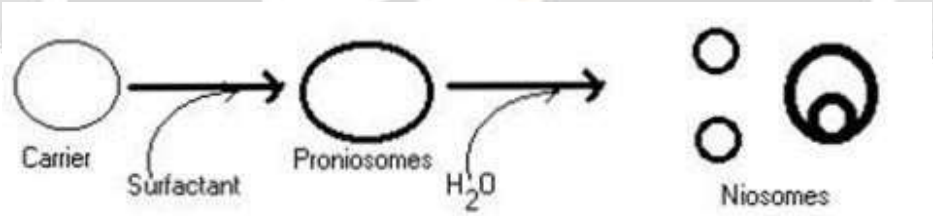
Proliposomes: In proliposomes, the medication and lipid are combined to create a free-flowing granular substance that, when hydrated, transforms into an isotonic liposomal suspension. The proliposome technique might make it possible to mass produce liposomes containing, in particular, lipophilic medicines, at a low cost. Proliposomes: Relatively good stability; fewer handling and storage requirements. higher drug encapsulation and release characteristics than liposomes. Proliposomes of the Dry Granular and Mixed Mecellar types are available.

Comparison between liposomes and proliposomes

Liposomes are spherical, unilamellar or multilamellar structures made of lipid molecules, typically phospholipids. They have enhanced solubility and regulated release. but are prone to hydrolysis or oxidation, and have a tendency to agglomerate or fuse.

Proliposomes-a substitute for the common liposomal formulation composed of pharmaceuticals that have been dissolved in an organic solvent, phospholipids, and a porous powder that is water soluble. A soluble carrier is coated with lipid and medication to create a free-flowing granular substance. Demonstrate regulated release, enhanced solubility, improved stability, and ease of handling.

Proniosomes: Easy transfer, distribution, storage, and high medication loading capacity, low side effects, high efficacy, versatile drug delivery system, Surfactant type and concentration have an impact on proniosome encapsulation effectiveness and medication release rate.



Method of Preparation of Proniosome: A water soluble carrier, such as sorbitol, is first coated with the surfactant in order to produce proniosomes.

To coat the sorbitol powder stored in a rotary evaporator, a solution containing the surfactant and cholesterol is prepared in a volatile organic solvent and sprayed onto the powder.

The sorbitol particles are left with a thin layer after the organic solvent evaporates. The finished coating is a dry formulation in which a thin layer of dry surfactant is applied to a water-soluble particle. The name of this preparation is proniosome. Other preparation techniques include:

- Slurry technique
- phase separation with co-acervation
- slow spraying technique
- The efficiency of encapsulation will increase with lipophilicity.

such as the proniosomal TDS of Losartan potassium, Alprenolol HCL,Valsartan proniosomes.

Improve permeability:

Physical means: **Iontophoresis:-** Effective medication delivery techniques, such as mitomycin C and bethanecol, can reach the deeper layer of the bladder. Electroporation (greater voltage than Ionotophoresis) (high voltage than

Ionotophoresis). increases the electric field's penetration through tissues. helpful for drug delivery during the treatment of bladder cancer. Low density ultrasonic waves used in electroporation-sonophoresis reduce tissue injury.

Chemical means: A perior DMSO injection improves the absorption of chemotherapy medications like Paclitaxal and Pirarubicin. Saponin intravenous injection prior to anticancer medication administration

Eg. 4-0-Tetrahydropyranaldoxorubicin, for instance (THP). boosts the levels of THP in bladder tissues. Chitosan and cyclodextrin applied topically perturb intracellular tight junction. makes paracellular transport more active.

FUTURE PROSPECTIVES IN VDDS:

Aquasomes*:*

Three-layered self-assembling compositions with a glassy cellobiose coating, a ceramic carbon nanocrystalline particle core, and molecular shielding [67]

Cryptosomes*:*

Lipid vesicles with a surface layer made of phosphotidyl ethanolamine and a suitable polyoxoyethylene derivative. able to target drugs through ligands.

Discomes*:*

Utilizing non-ionic surfactant solutions to solubilize niosomes (polyoxyethylene cetyl ether class). Display drug targeting mediated by ligands.

Emulsomes*:*

Parenteral administration of poorly water soluble medicines was carried out using nanosize lipid particles (bioadhesives nanoemulsion), which were composed of tiny lipid assembly with an apolar centre.

Enzymosomes*:*

Enzymes are covalently bound or linked to the surface of liposomal structures to create a micro bioenvironment. Delivery to tumour cells with precision.

Genosomes*:*

macromolecular assemblies made in the lab for effective gene transfer. Because of their great biodegradability and blood-stream stability, cationic lipids are ideal. gene transfer is cell-specific.

Photosomes:

Liposomes that include photolysase release the photo-activated charges that affect membrane permeability.

Virosomes*:*

Virus glycoprotein-infused liposomes that were inserted into the liposomal bilayers based on lipids produced from retroviruses.

Vesosomes*:*

Through the interdigested bilayer phase created by adding ethanol to a variety of saturated phospholipids, nested bilayer compartment can be achieved in vitro. The inner components of serum are better protected by the vesosomes' many compartments.

Proteosomes*:*

With respect to the assembly pattern of enzymes, high molecular weight multi-submit enzyme complexes with catalytic activity are produced. superior turnover of the catalytic activity compared to unrelated enzymes.

Emulsomes*:*

A liposome carrying Hb that has been artificially immobilised using polymerisable phospholipids.

Erythrosomes*:*

Human erythrocytes that have been chemically cross-linked serve as the basis for a lipid bilayer in a lyposomal system.

Enzymosomes*:*

On the surface of liposomes, enzymes are covalently immobilised or linked.

Archaeosome*:*

Over the past ten years, compounds generated from organic archaeal membrane lipids and/or synthetic lipid analogues have been thoroughly investigated for possible uses in the delivery of drugs and vaccines. Archaeal-type lipids are composed of the archaeol (diether) and/or caldarchaeol (tetraether) core structures, which are joined to the sn-2,3 carbons of the glycerol backbone by ether bonds to form regularly branched and typically fully saturated phytanyl chains (20–40 carbons in length). A new generation of liposomes known as archaeosomes exhibits remarkable stability to low or high temperatures, acidic or alkaline pH, oxidative circumstances, high pressure, phospholipase activity, bile salts, and serum proteins. . Nanotechnological applications in medication and gene delivery benefit from these qualities associated with a favourable safety profile. Additionally, in addition to boosting antigen-specific mucosal immune responses in the recipients of vaccinations, archaeosome formulations could be exploited as effective transporters of antigens and/or adjuvants. Strong memory responses are triggered by the immunological responses, and they are effectively sustained over time. The use of archaeosomes in nanodelivery-based immunizations could thus be a promising strategy for treating and preventing infections, allergies, and neoplastic or malignant illnesses. This review discusses the few recent US, international, and European patents that create archaeosomes for these biotechnological applications in health. [68]

CONCLUSION:

Liposome, niosome, and other outstanding examples of vesicular drug delivery systems have demonstrated themselves as novel approaches and very useful as drug delivery systems in current field, and have remarkable place in pharmaceutical dosage forms over and above the conventional drug delivery system. These examples have been used to utilise and solve critical issues of the pharmaceutics field.

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