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A REVIEW ARTICLE ON A NOVEL AND TARGETED DRUG DELIVERY SYSTEM IN FORM OF LIPOSOMES

Satendra Kumar[1]* and Anil Kumar[2]

[1]Department of Pharmaceutics, L.N Pharmacy College, Baitalpur, Deoria, U.P.

[2]Departments of Pharmacognoscy, Pharmacy College, Itaura, Chandeshwar, Azamgarh, U.P

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***Corresponding Author**
Dr. Satendra Kumar
Department of Pharmaceutics, L.N Pharmacy College, Baitalpur, Deoria, U.P.

ABSTRACT

In this review article, we discussed about liposome, these are one amongst the various drug delivery system used to target the drug to particular tissue. Because of structure similarity between lipid bilayers & cell membrane Liposome is a spherical sac Phospho lipid molecule. Liposomes are a novel drug delivery system (NDDS), The term liposome means lipid body. It has been derived on the basis of name of sub cellular particles, ribosome. Liposomes were first made by A.D Bangham in early 1960s. Their size ranges from 25 to 500nm.It encloses a water droplet especially as form artificially to carry drug into tissue membrane. It is spherical sac vesicle it consists at least one lipid bilayers. The process of sonication(extrusion) is required to obtain small size and narrow size distribution of liposome. They are simple microscopic vesicles in which an aqueous volume is entirely enclosed by a membrane composed of lipid bilayers. Novel drug delivery system aims to deliver the drug at a rate directed by the needs of the body during the period of treatment, and channel the active entity to the site of action. Liposomes are colloidal spheres of cholesterol non-toxic surfactants, sphingolipids, glycolipids, long chain fatty acids and even membrane proteins and drug molecules It is differ in size, composition and charge. Consequently a number of vesicular drug delivery systems such as liposomes, niosomes, transfer some, and Pharma cosmos were developed. It is a drug carrier loaded with great variety of molecules such as small drug molecules, proteins, nucleotides and even plasmids. Few drugs are also formulated as liposomes to improve their therapeutic index. The main significant role in formulating of potent drug, improve therapeutic effect.

KEYWORD: Drug delivery system using components of liposomes, Method of preparation of liposomes Structural components of liposomes, Vesicles, Colloidal spheres.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body, to achieve promptly and then maintain the desired drug concentration.

Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment only when taken several times a day. This results in a significant fluctuation in drug level. The concept of designing specified delivery system to achieve selective drug targeting has been originated from the perception of Paul Ehrlich, who proposed drug delivery to be as a "magic bullet".

Liposomes were first described by Bangham in 1965 while studying cell membranes. He found that liposomes are vesicular structures consisting of hydrated bilayers which form spontaneously when phospholipids are dispersed in water. Since this, further studies into liposomes and their application in various fields such as medicine and research have been explored.[1]

Liposomes have reached the clinical only recently, but they are not a new invention Alec D. Bangham of the Agricultural Research Council's institute of Animal physiology in Cambridge, England, inadvertently produced the first liposome in 1961, while evaluating the effect of phospholipids on blood clotting. When Bangham put water in a flask containing a phospholipids film, the water molecules to arrange themselves in to what he discovered. He found vesicles composed of a bilayers phospholipids membrane surrounding water entrapped from the environment.

Phospholipids form closed, fluid-filled spheres when they are mixed with water in part because the molecules are amphipathic; they have a hydrophobic "tail" and a hydrophilic or polar "head". Two fatty acid chains, each composed of 10 to 24 carbon atoms, make up the hydrophobic tail of most naturally occurring phospholipidsmolecules. Phosphoric acid bound to any of several water soluble molecules composes the hydrophilic head. When a high enough concentration of phospholipids is mixed with water, the hydrophobic tails spontaneously herd together to exclude water, whereas the hydrophilic heads bind to water.

The result is bilayers in which the fatty acid tails in to the membrane's interior and the polar

head groups point outward the polar groups at one surface of themembrane point toward the liposome's interior and those at the other surface point toward the external environment. It is this remarkable reactivity of phospholipids to water that enables workers to load medications in to liposomes.

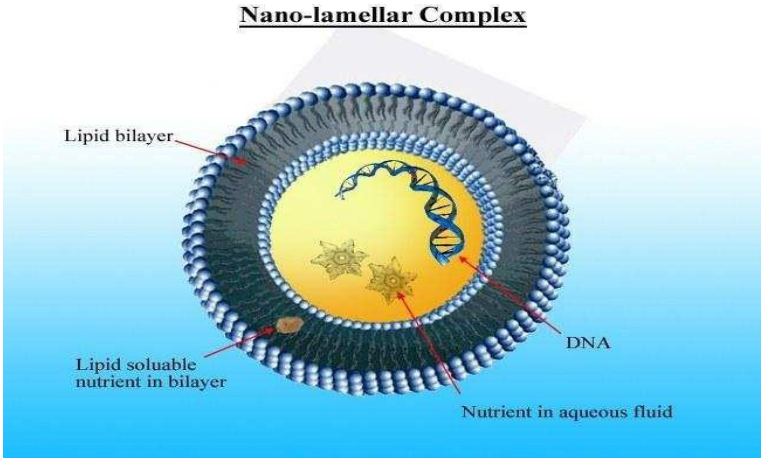
In a liposome form, any water soluble molecules that have been added to the water are incorporated in to the aqueous spaces in the interior of the spheres, whereas any lipid soluble molecules added to the solvent during vesicle formation are incorporated in to the lipid layer. Liposomes employed for drug delivery typically range in diameter from 250 angstrom units to several micrometers and are usually suspended in a solution.

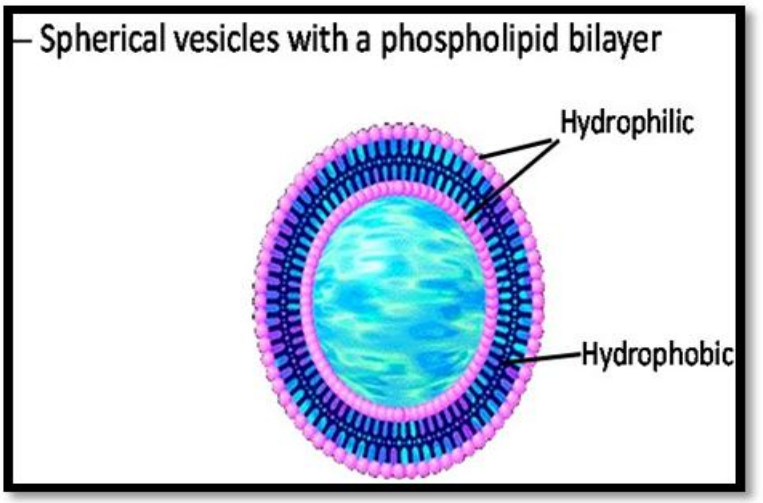
Paul Ehrlich in 1906 initiated the era of development for targeted delivery when he envisaged a drug delivery mechanism that would target drug directly to diseased cells, what he called as magic bullets.[2,3]Liposome is a spherical sac phospholipids molecule enclosing a water droplet, especially are formed artificially to carry drug into the tissue.[4] "Liposomes are colloidal, vesicular structures composed of one or more lipid bilayers surrounding an equal numbers of aqueous compartments". The sphere like shell encapsulated a liquid interior which contain substances such as peptides and protein, hormones, enzymes, antibiotic, antifungal & anticancer agents. A free drug injected in blood stream typically achieves therapeutic level for short duration due to metabolism & excretion. Drug encapsulated by liposomes achieve therapeutic level for long duration as drug must first be release from liposome before metabolism & excretion.[5]

Liposome are also defined as artificial microscopic vesicles consisting of aqueous compartment and surrounded by one or more concentric layer of phospholipids. The sphere like encapsulated a liquid interior contain more substance like peptides, protein, hormones, enzymes, antibiotic, antifungal and anticancer agents. Liposome is small artificial vesicles of spherical shape that can create cholesterol and naturally non-toxic phospholipids. They are depending upon size, hydrophobic and hydrophilic characteristic. Liposome is a spherical vesicle having at least one lipid bilayers. The key common feature that bilayers-forming compounds share is their ampiphilicity i.e., they have defined polar and non polar regions. This is the reason the non-polar regions orientate themselves towards the interior away from the aqueous phase, the polar regions being in contact with it. Liposomes were discovered about 40 years ago by A.D. Bangham which has become the versatile tool in biology, biochemistry and medicine today. In 1960s, liposome has been used as a carrier to transport a

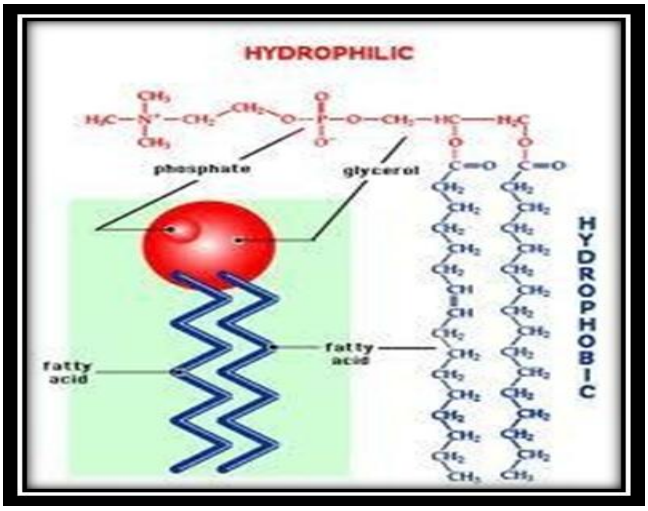
wide variety of compounds in its aqueous compartment. Liposome can be formulated and processed to differ in size, composition, charge and lamellarity. To date liposomal formulations of anti-tumor drugs and antifungal agents have been commercialized.[6,7]

Considerable progress was made during 1970s and 1980s in the field of liposome stability leading to long circulation times of liposomes after intravenous administration resulting in the improvement in bio-distribution of liposome. The important anti- tumor drug doxorubicin had been formulated as liposome in 1980s to improve the therapeutic index. There are several mechanisms by which liposomes act within and outside the body which is as follows Liposome attaches to cellular membrane and appears to fuse with them, releasing their content into the cell. Sometimes they are taken up by the cell and their phospholipids are incorporated into the cell membrane by which the drug trapped inside is released.[8]





[Structure of liposome]



[Shape of phospho lipids molecule]

Advantages of liposomes

a) Provide controlled drug delivery
b) Non ionic
c) Biodegradable, biocompatible, flexible
d) Can carry both water and lipid soluble drugs
e) Improve protein stabilization
f) Drugs can be stabilized from oxidation
g) Provide sustained release
h) Controlled hydration
i) Stabilization of entrapped drug from hostile environment
j) Targeted drug delivery or site specific drug delivery
k) Can be administered through various routes
l) Alter pharmacokinetics and pharmacodynamics of drugs
m) Act as reservoir of drugs
n) Can incorporate micro and macro molecules
o) Site avoidance therapy
p) Therapeutic index of drugs is increased
q) Can modulate the distribution of drug

Disadvantages of liposome

[1] Production cost is high.
[2] Leakage and fusion of encapsulated.
[3] Short half-life.

[4] Stability problems.

[5] Allergic reaction may occur to liposomeconstituents.

[6] Problem to targeting to various tissuesdue to their large size.

[7] Phospho lipid undergoes oxidation,hydrolysis.[9]

Ideal properties of liposomes

- Liposomes are biocompatible.
- Liposome-incorporated pharmaceuticals are protected from the inactivating effect of external conditions; yet do not cause undesirable side reactions.
- Liposomes can entrap water-soluble (hydrophilic) pharmaceutical agents in their internal water compartment and water-insoluble (hydrophobic) pharmaceuticals into the membrane
- Size, charge and surface properties of liposomes can be easily changed simply by adding new ingredients to the lipid mixture before liposome preparation and/or by variation of preparation method.
- Liposomes provide a unique opportunity to deliver pharmaceuticals into cells or even inside individual cellular compartments

Classification of liposomes

(1) Based on Composition and Mode of drug delivery

- **Conventional liposomes**

Composed of neutral or negatively charge phospholipids and cholesterol. To increase circulation time, liposome surface coated with a hydrophilic polymer, repulsive forces of liposome and serum-components Subject to coated pit endocytosis, contents ultimately delivered to Lysosome if they do not fuse with the endosomes, useful for E.E.S targeting; rapid and saturable uptake by R.E.S; short circulation half life, dose dependent pharmacokinetics.

- **Cationic liposomes**

Composed of cationic lipids Fuse with cell or endosome membranes; suitable for delivery of negatively charged macromolecules (DNA, RNA); ease of formation, structurally unstable; toxic at high dose, mainly restricted to local administration.

- **pH sensitive liposomes**

Subjected to coated pit endocytosis at low pH, fuse with cell or endosomes membrane and

release their contents in cytoplasm; suitable for intra cellular delivery of weak base and macromolecules. Bio-distribution and pharmacokinetics are similar to conventional liposomes.

❖ **Long circulating**

Hydrophilic surface coating, low opsonisation and thus low rate of uptake by RES long circulating half life (40 hrs); Dose independent Pharmacokinetics.

❖ **Magnetic liposomes**

These are liposomes that indigenously contain binding sites for attaching other molecules like antibodies on their exterior surface. Can be made use by an external vibrating magnetic field on their deliberate, on site, rapture and immediate release of their components.

❖ **Immune liposomes**

Stealth liposomes with attached Antibody or Recognition Sequence subject to receptor mediated endocytosis, cell specific binding (targeting); can release contents extra cellular near the target tissue and drugs diffuse through plasma membrane to produce their effects.

❖ **Temperature (or) heat sensitive liposomes**

These are vesicles showed maximum release at 41o, the phase transition temperature of Dipalmitoyl P.C. Liposomes release the entrapped content at the target cell surface upon a brief heating.

(2) Based on Size and Number of lamellae

❖ **Large Unilamellar Vesicles (L.U.V)**

(Size 0.1 - 10 micro meters)Have single bilayers, high aqueous volume to lipid ratio (7: 1 mole lipid), useful for hydrophilic drugs, high capture of macromolecules; rapidly cleared by R.E.S. Prepared by detergent dialysis, ether injection, reverse phase evaporation or active loading methods.

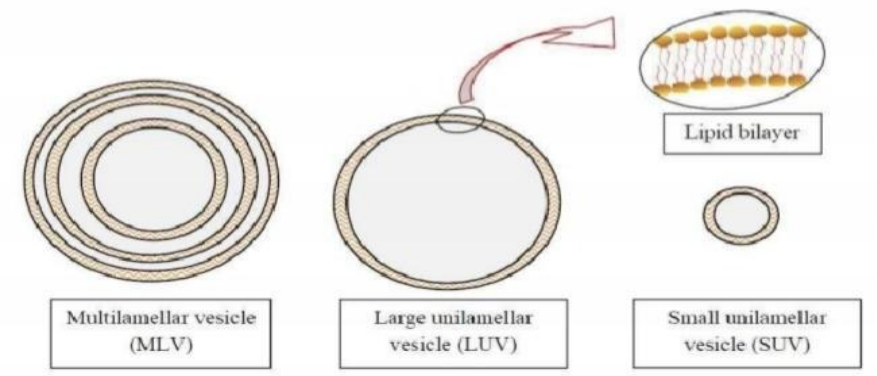
❖ **Small Unilamellar Vesicles (S.U.V)**

(Size 0.1 micro meters) Single bilayers, homogeneous in size, thermodynamically unstable, susceptible to aggregation and fusion at low or no charge, limited capture of macro molecules, low aqueous volume to lipid ratio (0.2 : 1.5 : 1 mole lipid) prepared by reducing the size of M.L.V or L.U.V using probe sonicator or gas extruder or by active loading or solvent injection technique.

❖ **Multi lamellar vesicles (M.L.V)**

(Size 0.1 - 0.3 micro meters) Have more than one bilayers; moderate aqueous volume to lipid ratio 4: 1 mole lipid. Greater encapsulation of lipophilic drug, mechanically stable upon long term storage, rapidly cleared by R.E.S, useful for targeting the cells of R.E.S, simplest to prepare by thin film hydration of lipids in presence of an organic solvent.

- Paucilamellar vesicles – Intermediate between L.U.V & MLV.
- Multi vesicular liposomes – Separate compartments are present in a single M.L.V.
- Stable Pluri lamellar vesicles – Have unique physical and biological properties due to osmotic compression.



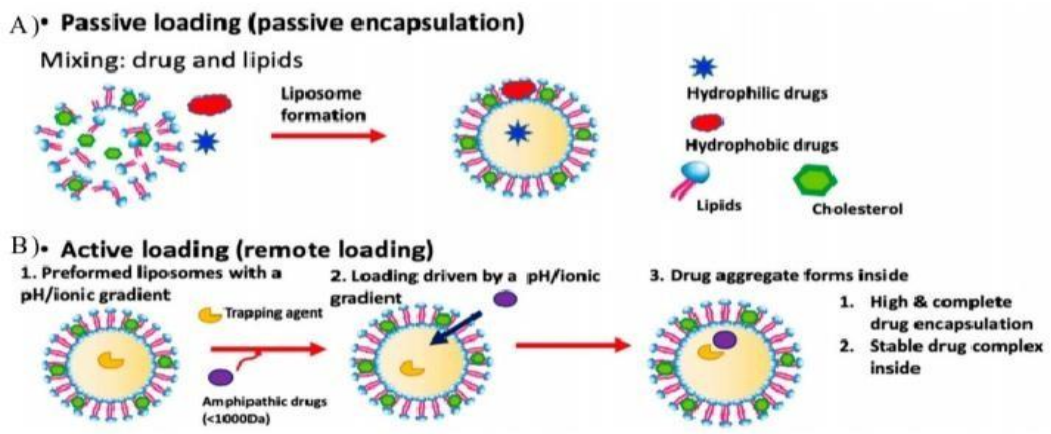
[Liposome based on size and number of bilayers]

(3) Classification of liposome based on size and number of bilayers

Liposome are classified depending upon the production method

(A) Passive loading technique

In this method that hydrophilic compound are distributed homogeneous in the aqueous phase (both inside and outside the liposomes), hydrophobic drugs are retaining inside the lipid bilayers of liposome, when working with water soluble drugs. The drug is firstly dissolved with lipid in organic solvent, followed by solvent evaporation method to prepare drug containing thin film. After prepare thin film hydrated with on aqueous phase to prepare liposome.[10]



[Formation of Passive and Active loading liposome]

(a) Mechanical dispersion method

Aqueous volume (5-10%) enclosed using this method, which is small proportion of total volume used for swelling.

❖ **Lipid hydration by hand shaking**

To prepared firstly lipid mixture of different phospholipids and charge components in chloroform: methanol (2:1 v/v) solvent mixture. Then introduce into a round bottom flask a ground glass neck. This flask is attached to rotary evaporator (rotated at 60 rpm). The organic solvent is evaporated at about 30° C or about transition temperature of lipid. The evaporator is isolated from the vacuum source by close the tip. The nitrogen is introduced into the evaporator and thepressure of cylinder is gradually raised up tono difference between inside and outside theflask. Remove the flask from the evaporator and fixed on lyophilizer to remove residual solvents.

❖ **Hydration of lipid layer**

After removal from lyophilizer, the flask flushed with nitrogen; 5ml saline phosphate buffer is added. The flask is again attached to evaporator and flushed with dinitrogen (N2). The evaporator are rotated at room temperature and pressure at same speed (for below 60 rpm). The flask is stop rotate after 30 minute or until all lipid has been removed from the wall of the flask andhas given homogeneous milky suspension. The suspension is allowed to stand for 2hours at room temperature or at atemperature above transition temperature of the lipid in order to complete the swelling process to give MLVs (Multilamellar vesicle).[11]

Sonication

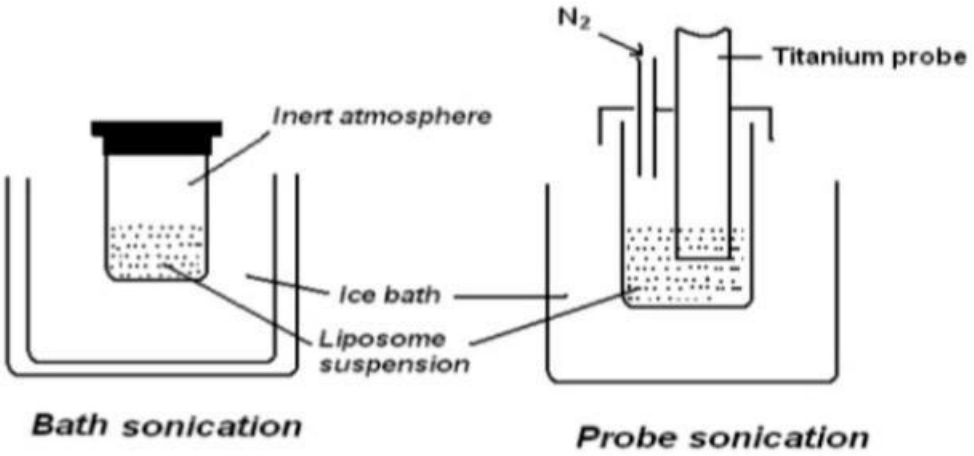
Sonication is a process in which sound waves are used to agitate particle in solution. Such disruption can be used to mix solutions, speed the dissolution of a solid into a liquid and

remove dissolved gas from liquid. [12]

The ultrasonic irradiation is provided to convert MLVs to SUVs. There are two method use. 1-Probe sonication method. 2-Bath sonication method.

- **Probe sonication method**

The probe sonicator is used for high energy in small volume (e.g. high concentration of lipid or viscous aqueous phase). The tip of sonicator is directly immersed into the liposome dispersion is very high in this method.



[Sonication apparatus]

Then vessel must be immersed into an ice bath. Throughout, the sonication up to 1 hour more than 5% of the lipids can is de- esterifying. Also, with the probe sonicator, titanium will slough off and contaminate thesolution.

- **Bath sonication method**

The bath sonicator is used for large volume of dilute lipids. The dispersion of liposome in a tube is placed into a bath sonicator. This method is easier to sonication the dispersion directly using tip. Material being sonicated and place into sterile container, under an inert atmosphere. Then lipid bilayers of the liposomes can fuse with other bilayers, thus delivering the liposome contents. By making liposomes in a solution of DNA or drug they can be deliver lipid bilayers.[13,14]

- **French pressure method**

This method is based on mechanism of high pressure. This method used topreparation of 1-40 ml of homogeneous unilamellar liposomes of intermediate size (30-80 nm). This liposome

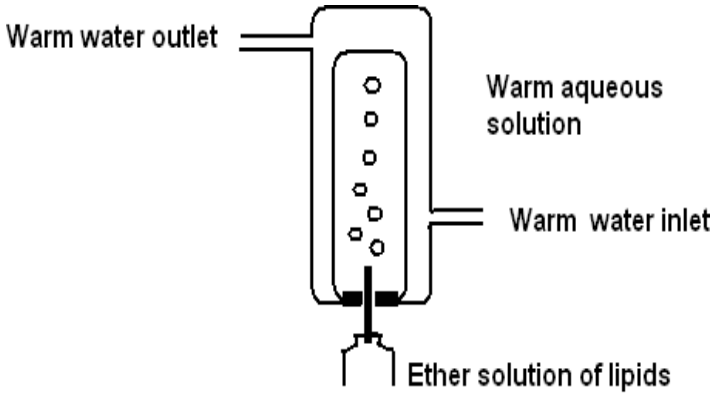
is more stablecompared to the sonicated liposomes. This method is some drawbacks are that initial high cost for the pressure cell. Liposome prepared by this method having less structural defects compared to sonicatedliposome.

(b) Solvent dispersion method

In these method can be dissolvingthe lipid and other constituents of theliposome membrane in other solution. The aqueous phase is added to resulting solution. In this aqueous phase contain material which is to be entrapped. Solvent dispersion method involving ether injection method, ethanol injection method, and reverse phase evaporation method.[15]

❖ **Ether injection method[16]**

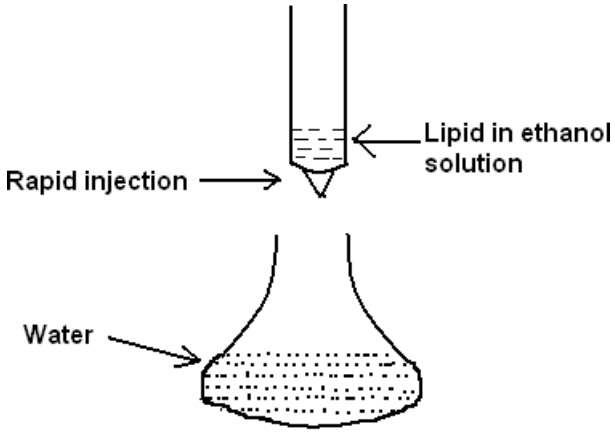
Ether injection, solution of lipid is dissolve into ether or diethyl ether ormethanol mixture. These mixtures slowly injected into aqueous solution of the material to be encapsulation at 55-65°C or under reduce pressure. Then ether is removed with the help of vacuum leads to formation of liposome. This is simple method.



ETHER INJECTION TECHNIQUE

❖ **Ethanol injection method**

In this method an ethanol solution of the lipid is directly injected rapidly to an excess of saline through a fine needle. The solution of ethanol is diluted in water and Phospho lipid molecules. They are dispersed evenly through the medium. This procedure yields a high proportion of

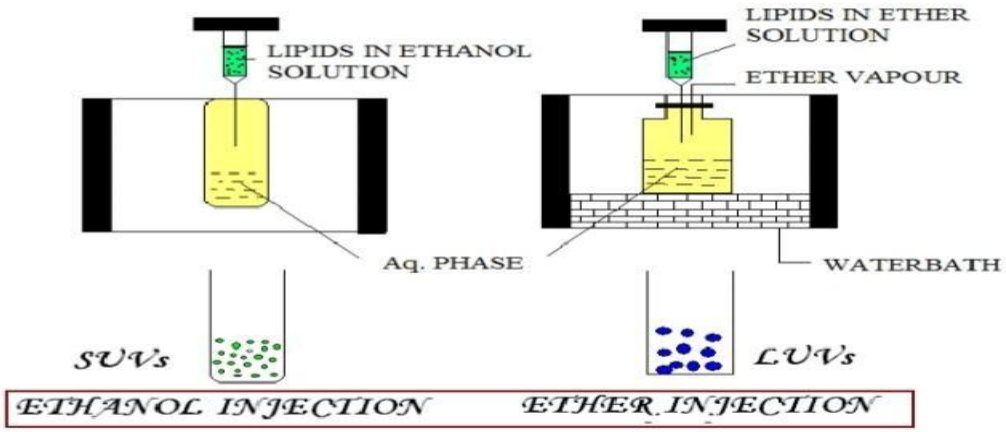


ETHANOL INJECTION TECHNIQUE

SUVs (about 25 nmdiameter)

❖ **Reverse phase evaporation method**

The water in oil emulsion is formed by sonication of two phase system. It contains Phospho lipid in organic solvent diethyl ether) and aqueous buffer. This mixture of lipid is added to round bottom flask. The organic solvent is removingunder pressure by a rotary evaporation. The system is purge with nitrogen and lipids are re-dissolved in the organic phase. Diethyl ether and isopropyl ether are the solvent of choice after the lipids are re-dissolved the emulsion are obtaining and then the solventsare evaporated by evaporation of semi solid gel under reduce pressure, at 20-25°C rotating at approximately 200 rpm. A viscous gel forms and an aqueous suspension appears. Add excess water or buffer and evaporate the suspension for an addition 15 minute at 20°C to remove traces of solvent. Dialyze the preparation, and passthrough 4B column or centrifuge. Resulting liposome are called 'reverse phaseevaporation vesicle' (REV



(B) Active loading technique

In active loading, liposomes are first generated containing a Tran's membrane gradient, i.e. aqueous phase inside and outside the liposomes are different. Subsequently, an amphipathic drug is dissolved in exterior aqueous phase can permeate the phospholipids bilayers. In 1976, Deamer and Nicols demonstrate that a pH gradient could be utilized to load catecholamine intoliposomes, resulting stable drug retention invitro.

Evaluation of liposomes[17,18]

Liposomal formulation and processing for specified purpose are characterized to ensure their predictable in vitro and in vivo performance. The characterization parameters for purpose of evaluation could be classified into three broad categories which include physical, chemical and biological parameters.

- Physical characterization evaluates various parameters including size, shape, surface features, lamellarty and phase behavior and drug release profile.
- Chemical characterization includes those studies which establish the purity and potency of various lipophilic constituents
- Biological characterization parameters are helpful in establishing the safety and suitability of formulation for therapeutic application.

Evaluation parameter

(A) Vesicle Shape and Lamellarity: Vesicle shape can be assessed using Electron Microscopic Techniques. Lamellarity of vesicles i.e. number of bilayers presents in liposomes is determined using Freeze-Fracture Electron Microscopy and P-31 Nuclear Magnetic Resonance Analysis.

(B) Vesicle Size and Size distribution: Various techniques are described in literature for determination of size and sizedistribution.

The most precise method of determine size of liposome is Electron Microscopy since it permit one to view each individual liposome and to obtainexact information about profile of liposome population over the whole range of sizes. Unfortunately, it is very time consuming and require equipments that may not always beimmediately to hand.

In contrast, laser light scattering method is very simple and rapid to perform but having disadvantage of measuring an average property of bulk of liposomes. All these methods require costly equipments. If only approximate idea of size range is required then gel

exclusion chromatography techniques are recommended, since only expense incurred is that of buffers and gel material.

Another more recently developed microscopic technique known as atomic force microscopy has been utilized to study liposome morphology, size, and stability. Most of methods used in size, shape and distribution analysis can be grouped into various categories namely microscopic, diffraction, scattering, and hydrodynamic techniques.

(a) Microscopic techniques

I. **Negative- Stain TEM:** Electron Microscopic Techniques used to assess liposome shape and size are mainly negative- stain TEM and Scanning Electron Microscopy. The latter technique is less preferred. Negative Stain Electron Microscopy visualizes bright areas against dark background (hence termed as negative stain) the negative stains used in TEM analysis are ammonium molybdate or Phosphotungstic acid (PTA) or uranyl acetate. Both PTA and ammonium molybdate are anionic in nature while uranyl acetate are cationic in nature.

II. **Optical Microscopy:** The microscopic method includes use of Bright-Field, Phase Contrast Microscope and Fluorescent Microscope and is useful in evaluating vesicle size of large vesicle.

III. **Transmission Electron Microscopy Techniques (TEM):** This technique has been used to elucidate the surface morphology and size of vesicles.

(b) Diffraction and Scattering techniques

(1) Hydrodynamic techniques: This technique includes Gel Permeation and Ultracentrifuge. Exclusion chromatography on large pure gels was introduced to separate SUVs from radial MLVs. However, large vesicles of 1-3μm diameter usually fail to enter the gel and are retained on top of column. A thin layer chromatography system using agarose beads has been introduced as a convent, fast technique for obtaining a rough estimation of size distribution of liposome preparation. However, it was not reported if this procedure was sensitive to a physical blockage of pores of the agarose gel as is the more conventional column chromatography.

(C) Encapsulation Efficiency and Trapped Volume: These determine amount and rate of entrapment of water soluble agents in aqueous compartment of liposomes.

Encapsulation efficiency: it describes the percent of the aqueous phase and hence percent of

water soluble drug that become ultimately entrapped during preparation of liposomes and is usually expressed as % entrapment/mg lipid. Encapsulation efficiency is assessed using 2 techniques including minicolumn centrifugation method and Protamine aggregation method. Minicolumn centrifugation is generally used both as a mean of purification and separation of liposomes on small scale.

In mini column centrifugation method, the hydrated gel is filled in a barrel of 1ml syringe without plunger which is plugged with whatman GF/B filter pad. This barrel is rested in a centrifuge tube. This tube is spun at 2000 rpm for 3 min. to remove excess saline solution from gel. After centrifugation the gel column should be dried and have come away from side of barrel. Then eluted saline is removed from collection tube. Liposome suspension (0.2ml) is applied drop wise to top of gel bed, and the column is spun at 2000 rpm for 3 min. to expel the void volume containing the liposomes into centrifugation tube. The elute is then removed and set aside for assay. Protamine aggregation method may be used for neutral and negatively charged liposomes.

Trapped volume

It is an important parameter that governs morphology of vesicles. The trapped or internal volume is aqueous entrapped volume per unit quantity of lipids. This can vary from 0.5 to 30 micro liter/micro mol. various materials including spectroscopically inert fluid, radioactive markers and fluorescent markers are used to determine trapped/internal volume.

The best way to measure internal volume is to measure quantity of water directly, by replacing external medium (water) with spectroscopically inert fluid (deuterium oxide) and then measuring water signal using NMR.

Trapped volume is also determined experimentally by dispersing lipid in an aqueous medium containing non- permeable radioactive solute. The proportion of solute trapped is determined by removing external radioactivity by centrifugation and subsequently residual activity per lipid is determined.

(D) Phase Response and Transitional behavior liposome and lipid bilayers exhibit various phase transitions that are studied for their role in triggered drug release or stimulus mediated fusion of liposomal constituents with target cell. An understanding of phase transitions and fluidity of phase transitions and fluidity of phospholipids membranes is

important both in manufacture and exploitation of liposomes since phase behavior of liposomal membrane determine such properties such as permeability, fusion, aggregation, andprotein binding.

The phase transistion have been evaluated using freeze fracture electron microscopy. They are more comprehensively verified by differential scanning colorimeter(DSC) analysis.

(E) Drug release: The mechanism of drug release from liposomes can be assessed by use of well calibrated in vitro diffusion cell. The liposome based formulation can be assisted by employing in vitro assays to predict pharmacokinetics and bioavailability of drug before employing costly and time-consuming in vivo studies. The dilution-induced drug release in buffer and plasma was employed as predictor for pharmacokinetic performance of liposomal formulations and another assay which determined intracellular drug release induced by liposome degradation in presence of mouse-liver lysosome lysate was used to assess the bioavailability of drug.

List of marketed products [Liposomal][19]

Sr.no	Drug	Drug Product name	Manufacturer
1	HLB-B7 plasmid	Allovecti-711	Vical incorporation[USA]
2	Amphotericin B	Abelcet	The liposome company [USA]
3	Amphotericin B	3 Am Bisome	NeXatar pharmaceuticals[USA]
4	Doxorubicin	Doxilt	SEQUUS Pharmaceuticals[USA]
5	Amphotericin B	Amphocil	SEQUUS Pharmaceuticals[USA]
6	Doxorubicin	Doxosome	Indian Institute of chemical biology[India]

Applications

Liposomes as carriers for vaccines

Cancer chemotherapy

Gene therapy

Liposomes as carrier of drug in oral treatment

Liposomes for pulmonary delivery

Liposomes for topical applications

Liposomes against Leishmaniasis

Cell biological application

Lysosomal storage disease

Ophthalmic delivery of drugs

Metal storage disease.[20]

Use of liposomes

Drug	Composition	Process of Preparation	Result	Reference
Cyproterone acetate	phosphatidylcholine (PC): cholesterol	solvent evaporation and thin film formation technique	better penetration	[21]
Acetazolamide	Egg phosphotidyl choline, cholesterol (steryl amine and diacetyl phosphate as + or – charge inducers)	Reverse phase evaporation and thin film hydration	Increasing the stability and reducing the intra ocular pressure	[22]
N-Methyl-*N*-D-fructosyl amphotericin B methyl ester (MFAME)	dimyristoyl phosphatidylcholine cholesterol or ergosterol	chloroform film method	Reduction In toxicity of amphotericin	[23]
Ferrous sulphate	egg lecithin, 10% (mol/mol) Cholesterol and 10% (mol/mol) Tween 80. Ascorbic acid	thin-film hydration, thin-film sonication, reverse- phase evaporation and freeze-thawing,	Increased electrostatic and steric stability	[24]
Doxorubicin	Cholesterol Phosphatidylserhe, phosphatidylglycerol or cardiolipin Saturated or unsaturated Phospholipids acyl chains	Thin Film hydration method	Reduction I cardio toxicity and enhanced antitumor activity	[25]
TopotecanHCl	soyabean phosphatidylcholine or hydrogenated soybean phosphatidylcholine and cholesterol (PEG Ligated)	chloroform film method	Improved stability and enhanced efficacy by accumulation in tumor cells	[26]
Hydroxyzine	L-α-phosphatidylcholine 95%(PC), cholesterol	Ethanol injection method and lipid film hydration method	Increase in drug concentration in skin and enhanced efficacy	[27]
Paclitaxel	Soyabean phosphatidyl choline (S100PC) and 1,2- distearoyl-*sn*-glycero-3- phosphoethanolamine [methoxy (polyethylene glycol)-2000]Cholesterol (CH)4 .C for further experiments.	thin-film hydration method	Increased aqueous solubility	[28]

CONCLUSION

Liposomes have been realized as extremely useful carrier systems for targeted drug delivery. One of these successful technologies is the commercial formulation of topically applied liposomal formulations, particularly those prepared from lipid mixtures of a composition. This would be an effective delivery system for the treatment of skin disease. With the advancement of other technologies in medicine,the field of liposomes will be a more advanced and reliable platform for the development of more useful byproducts', especially in terms of medical diagnostics and public health areas. The liposomal drug delivery is very effective in the delivery of genes andvaccines due to their adjuvant property and tumor targeting ability.

The flexibility of their behavior can be exploited for the drug delivery through any route of administration and for any drug material irrespective of their solubility properties. The use of liposomes in the delivery of drugs and genes are promising and is sure to undergo further developments in future.

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