World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 4.223

A COMPLETE REVIEW ON LIPOSOME IN TARGETING DRUG DELIVERY

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Article Received on 09/02/2017 **Article Revised on 02/03/2017** **Article Accepted on 23/03/2017**

ABSTRACT

Liposomes are acceptable, efficient and superior carriers and have ability to encapsulate hydrophilic and lipophilic drugs, vaccines, diagnostic agents and other bioactive agents have led to a rapid advancement in the liposomal drug delivery system. Liposomes are microparticulate lipoidal vesicles which are under extensive investigation as drug carriers for improving the delivery of therapeutic agents. This article is intended to provide an overview of liposomal drug delivery system. It has focused on the factors affecting the behavior of the liposomes in the biological environment. Structural components, Various aspects related to mechanism of liposome formation, transportations, methods of preparations characterization and stability of the liposomal drug product were also discussed in the article. Liposomes can be used as a therapeutic tool in the fields like tumor targeting, genetic transfer, immunomodulation, skin and topical therapy.

KEYWORDS: Lipoidal vesicles, Structural components, mechanism of liposome formation.

INTRODUCTION

Liposome's are colloidal, vesicular structures composed of one or more lipid bilayers surrounding an equal numbers of aqueous compartments.[1] The sphere like shell encapsulated a liquid interior which contain substances such as peptides and protein, hormones, enzymes, antibiotic, anti-fungal and anticancer agents. The name liposome is derived from two Greek words: 'Lipos' meaning fat and 'Soma' meaning body. Structurally, liposomes are concentricbleedervesicles in which an aqueous volumeis entirely enclosed by a membraneous lipid bilayer. Membranes are usually made of phospholipids, which are molecules that have a hydrophilic head group and a hydrophobic tail group. The head is attracted to water, and the tail, which is made of a long hydrocarbon chain, is repelled by water.[2]

In nature, phospholipids are found in stable membranes composed of two layers (a bilayer). In the presence of water, the heads are attracted to water and line up to form a surface facing the water. The tails are repelled by water, and line up to form a surface away from the water. In a cell, one layer of heads faces outside of the cell, attracted to the water in the environment, and another layer of heads faces inside the cell, attracted by the water inside the cell. The hydrocarbon tails of one layer face the hydrocarbon tails of the other layer, and the combined structure forms a bilayer.

Liposomal drug delivery is gaining interest due to its contribution to varied areas like drug delivery, cosmetics, and structure of biological membrane.[3] Liposomes can act as a carrier for a variety of drugs, having a potential therapeutic action. Liposomes are colloidal carriers, having a size range of 0.01 – 5.0 µm in diameter. Indeed these are bilayered vesicles that are formed when phospholipids are hydrated in excess of aqueous medium.[4-5] Liposomes have got a potential advantage of encapsulating hydrophilic as well as hydrophobic drugs and targeting them to the required diseased site in the body.[3] Fig. 1 depicts the structure of a liposome (bilayered vesicle) and phospholipid.

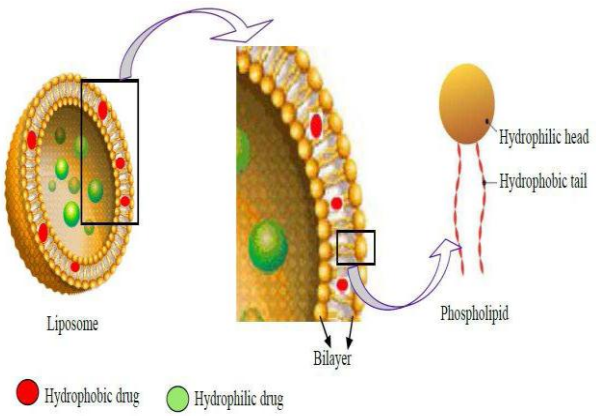

Figure 1: Structure of liposome and phospholipid.

Various therapeutic agents like anticancer drugs, vaccines, antimicrobials, genetic materials, proteins and macromolecules can been capsulated within the bilayered vesicles.[6] Liposomal technology was used for the successful encapsulation of various drug molecules like paclitaxel,[7] acyclovir,[8] tropicamaide,[9] arteether,[10] chloroquine diphosphate,[11] cyclosporine[12] and dithranol.[13] Table 1 indicates the list of few liposomal products that have been approved for human use.[14]

Advantages of Liposome

- Liposome are increased efficacy and therapeutic index of drug (Actinomycin-D).
- Liposome is increased stability via encapsulation.
- Liposomes are biocompatible, completely biodegradable, non-toxic, flexible and nonimmunogenic for systemic and non-systemica dministrations.
- Liposome are reduction in toxicity of the encapsulated agent (Amphotericin B, Taxol).
- Liposomes help to reduce exposure of sensitive tissues to toxic drugs.
- Site avoidance effect.
- Flexibility to couple with site-specific ligands to achieve active targeting.

Disadvantages of Liposome

- Production cost is high.
- Leakage and fusion of encapsulated drug /molecules.
- Sometimes phospholipid undergoes oxidation and hydrolysis like reaction.
- Short half-life.
- Low solubility.
- Fewer stables.

Structural Components of Liposome

a. Phospholipids

Phospholipids are the major structural component of biological membranes, where two type of phospholipids exit Phosphodiglycerides and Sphingolipids. The most common phospholipid is phosphatidylcholine (PC) molecule. Molecule of phosphatidylcholine are not soluble in water and in aqueous media they align themselves closely in plannar bilayer sheets in order to minimize the unfavorable action between the bulk aqueous phase and long hydrocarbon fatty chain. The Glycerol containing phospholipids are most common used component of liposome formulation and represent greater than 50% of weight of lipid in biological membranes. These are derived from Phosphatidic acid.

Examples of phospholipids are:

- Phosphatidyl choline (Lecithin) – PC
- Phosphatidyl ethanolamine (cephalin) – PE
- Phosphatidyl serine (PS)
- Phosphatidyl inositol (PI)
- Phosphatidyl Glycerol (PG)

b. Cholesterol

Cholesterol dose not by itself form bilayer structure, but can be incorporated into phospholipid membranes in very high concentration upto 1:1 or even 2:1 molar ration of cholesterol to phosphatidylcholine. Cholesterol inserts into the membrane with its hydroxyl group oriented towards the aqueous surface and aliphatic chain aligent parallel to the acyl chains in the center of the bilayer. The high solubility of cholesterol in phospholipid liposome has been attributed to both hydrophobic and specific headgroup interation, but there is no unequivocal evidence for the arrangement of cholesterol in the bilayer.[15-16]

Mechanism of Liposome Formation

The basic part of liposome is formed by phospholipids, which are amphiphilic molecules (having a hydrophilic head and hydrophobictail). The hydrophilic part is mainly phosphoric acid bound to a water soluble molecule, whereas, the hydrophobic part consists of two fatty acid chains with 10 – 24 carbon atoms and 0 – 6 double bonds in each chain.[17] When these phospholipids are dispersed in aqueous medium, they form lamellar sheets by organizing in such a way that, the polar head.group faces outwards to the aqueous region while the fatty acid groups face each other and finally form spherical/ vesicle like structures called as liposomes. The polar portion remains in contact with aqueous region along with shielding of the non-polar part (which is oriented at an angle to the membrane surface).[18] When phospholipids are hydrated in water, along with the input of energy like sonication, shaking, heating, homogenization, etc. it is the hydrophilic/ hydrophobic interactions between lipid – lipid, lipid – water molecules that lead to the formation of bilayered vesicles in order to achieve a thermodynamic equilibrium in the aqueous phase.[19] The reasons for bilayered formation include:

- The unfavorable interactions created between hydrophilic and hydrophobic phase can be minimized by folding into closed concentric vesicles.
- Large bilayered vesicle formation promotes the reduction of large free energy difference present between the hydrophilic and hydrophobic environment.
- Maximum stability to supramolecular self assembled structure can be attained by forming into vesicles.

Classification of Liposomes

Various classes of liposomes have been reported in literature. They are classified based on their size, number of bilayers, composition and method of preparation. Based on the size and number of bilayers, liposomes are classified as multilamellarvesicles (MLV), large unilamellar vesicles (LUV) and small unilamellar vesicles (SUV) as depicted in Fig. 2. Based on composition, they are classified as conventional liposomes (CL), pH-sensitive liposomes, cationic liposomes, long circulating liposomes (LCL) and

immuno-liposomes. Based on the method of preparation, they are classified as reverse phase evaporation vesicles (REV), French press vesicles (FPV) and ether injection vesicles (EIV). In this context, the classification based on size and number of bilayers is discussed below.

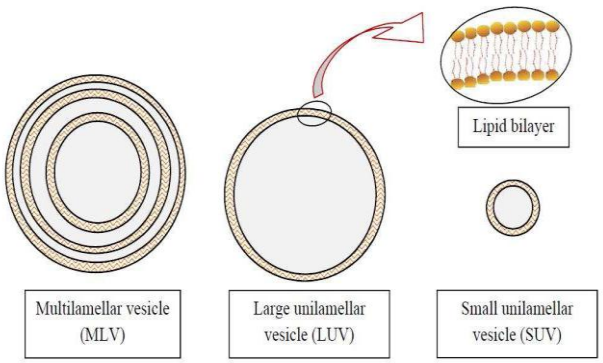

Fig. 2: Classification of liposomes based on size and number of bilayers.

Liposomal drug delivery

Multilamellar vesicles (MLV)

MLV have a size greater than 0.1 µm and consist of two or more bilayers. Their method of preparation is simple, which includes thin – film hydration method or hydration of lipids in excess of organic solvent. They are mechanically stable on long storage. Due to the large size, they are cleared rapidly by the reticulo-endithelial system (RES) cells and hence can be useful for targeting the organs of RES.[14] MLV have a moderate trapped volume, i.e., amount of aqueous volume to lipid ratio. The drug entrapment into the vesicles can be enhanced by slower rate of hydration and gentle mixing.[20] Hydrating thin films of dry lipids can also enhance encapsulation efficiency.[21] Subsequent lyophilization and rehydration after mixing with the aqueous phase (containing the drug) can yield MLV with 40% encapsulation efficiency.[22-23]

Large unilamellar vesicles (LUV)

This class of liposomes consists of a single bilayer and has a size greater than 0.1 µm. They have higher encapsulation efficiency, since they can hold a large volume of solution in their cavity.[24] They have high trapped volume and can be useful for encapsulating hydrophilic drugs. Advantage of LUV is that less amount of lipid is required for encapsulating large quantity of drug. Similar to MLV, they are rapidly cleared by RES cells, due to their larger size.[14,25] LUV can be prepared by various methods like ether injection, detergent dialysis and reverse phase evaporation techniques. Apart from these methods, freezethawing of liposomes,[26-27] dehydration/ rehydration of SUV[28] and slow swelling of lipids in non-electrolyte solution[29] can also be used to prepare LUV.

Small unilamellar vesicles (SUV)

SUV are smaller in size (less than 0.1 µm) when compared to MLV and LUV, and have a single bilayer. They have a low entrapped aqueous volume to lipid ratio and characterized by having long circulation half-life. SUV can be prepared by using solvent injection method[30] (ethanol or ether injection methods) or alternatively by reducing the size of MLV or LUV using sonication or extrusion process under an inert atmosphere like nitrogen or Argon. The sonication can be performed using either a bath or probe type sonicator. SUV can also be achieved by passing MLV through a narrow orifice under high pressure. These SUV are susceptible to aggregation and fusion at lower or negligible/ no charge.[31]

METHODS OF LIPOSOME PREPARATION

Method of liposome preparation and drug loading

The following methods are used for the preparation of liposome:

- Passive loading techniques
- Active loading technique.

Passive loading techniques include three different methods

- Mechanical dispersion method
- Solvent dispersion method.
- Detergent removal method (removal of nonencapsulated material).

Mechanical dispersion method

The following are types of mechanical dispersion methods:

- Sonication.
- French pressure cell: extrusion.
- Freeze-thawed liposome's.
- Lipid film hydration by hand shaking, non-hand shaking or freeze drying.
- Micro-emulsification.
- Membrane extrusion.
- Dried reconstituted vesicles.

Sonication

Sonication is perhaps the most extensively used method for the preparation of SUV. Here, MLVs are sonicated either with a bath type sonicator or a probe sonicator under a passive atmosphere.[32] The main disadvantages of this method are very low internal volume/encapsulation efficacy, possible degradation of phospholipids and compounds to be encapsulated, elimination of large molecules, metal pollution from probe tip, and presence of MLV along with SUV.

There are two sonication techniques

Probe sonication

The tip of a sonicator is directly engrossed into the liposome dispersion. The energy input into lipid dispersion is very high in this method. The coupling of energy at the tip results in local hotness; therefore, the vessel must be engrossed into a water/ice bath.

Throughout the sonication up to 1 h, more than 5% of the lipids can be de-esterified. Also, with the probe sonicator, titanium will slough off and pollute the solution.

Bath sonication

The liposome dispersion in a cylinder is placed into a bath sonicator. Controlling the temperature of the lipid dispersion is usually easier in this method, in contrast to sonication by dispersal directly using the tip. The material being sonicated can be protected in a sterile vessel, dissimilar the probe units, or under an inert atmosphere.

French pressure cell: extrusion

French pressure cell involves the extrusion of MLV through a small orifice. An important feature of the French press vesicle method is that the proteins do not seem to be significantly pretentious during the procedure as they are in sonication. An interesting comment is that French press vesicle appears to recall entrapped solutes significantly longer than SUVs do, produced by sonication or detergent removal. The method involves gentle handling of unstable materials. The method has several advantages over sonication method. The resulting liposomes are rather larger than sonicated SUVs. The drawbacks of the method are that the high temperature is difficult to attain, and the working volumes are comparatively small (about 50 mL as the maximum).

Freeze-thawed liposomes

SUVs are rapidly frozen and thawed slowly. The short-lived sonication disperses aggregated materials to LUV. The creation of unilamellar vesicles is as a result of the fusion of SUV throughout the processes of freezing and thawing. This type of synthesis is strongly inhibited by increasing the phospholipid concentration and by increasing the ionic strength of the medium. The encapsulation efficacies from 20% to 30% were obtained.

Solvent Dispersion Method

Ether injection (solvent vaporization)

A solution of lipids dissolved in diethyl ether or ether-methanol mixture is gradually injected to an aqueous solution of the material to be encapsulated at 55°C to 65°C or under reduced pressure.[33] The consequent removal of ether under vacuum leads to the creation of liposomes. The main disadvantages of the technique are that the population is heterogeneous (70 to 200 nm) and the exposure of compounds to be encapsulated to organic solvents at high temperature.

Ethanol injection

A lipid solution of ethanol is rapidly injected to a huge excess of buffer. The MLVs are at once formed. The disadvantages of the method are that the population is heterogeneous (30 to 110 nm), liposome's are very dilute, the removal all ethanol is difficult because it forms into azeotrope with water, and the probability of the various biologically active macromolecules to inactivate in the presence of even low amounts of ethanol is high.

Reverse phase evaporation method

This method provided a progress in liposome technology, since it allowed for the first time the preparation of liposomes with a high aqueous space-to-lipid ratio and a capability to entrap a large percentage of the aqueous material presented. Reverse-phase evaporation is based on the creation of inverted micelles. These inverted micelles are shaped upon sonication of a mixture of a buffered aqueous phase, which contains the water-soluble molecules to be encapsulated into the liposomes and an organic phase in which the amphiphilic molecules are solubilized. The slow elimination of the organic solvent leads to the conversion of these inverted micelles into viscous state and gel form. At a critical point in this process, the gel state collapses, and some of the inverted micelles were disturbed. The excess of phospholipids in the environment donates to the formation of a complete bilayer around the residual micelles, which results in the creation of liposomes. Liposomes made by reverse phase evaporation method can be made from numerous lipid formulations and have aqueous volume-to-lipid ratios that are four times higher than hand-shaken liposomes or multilamellar liposomes. Briefly, first, the water-in-oil emulsion is shaped by sonication of a two-phase system, containing phospholipids in organic solvent such as isopropylmether or diethyl ether or a mixture of isopropyl ether and chloroform with aqueous buffer. The organic solvents are detached under reduced pressure, resulting in the creation of a viscous gel. The liposomes are shaped when residual solvent is detached during continued rotary evaporation under reduced pressure. With this method, high encapsulation efficiency up to 65% can be obtained in a medium of low ionic strength e.g 0.01 M NaCl. The method has been used to encapsulate small, large, and macromolecules. The main drawback of the technique is the contact of the materials to be encapsulated to organic solvents and to brief periods of sonication. These conditions may possibly result in the breakage of DNA strands or the denaturation of some proteins. Modified reverse phase evaporation method was presented by Handa et al., and the main benefit of the method is that the liposomes had high encapsulation efficiency (about80%).

Detergent removal method (removal of nonencapsulated material)

The detergents at their critical micelle concentrations (CMC) have been used to solubilize lipids. As the detergent is detached, the micelles become increasingly better-off in phospholipid and lastly combine to form LUVs. The detergents were removed by dialysis. A commercial device called LipoPrep (Diachema AG, Switzerland), which is a version of dialysis system, is obtainable for the elimination of detergents. The dialysis

can be performed in dialysis bags engrossed in large detergent free buffers (equilibrium dialysis).

Detergent (cholate, alkyl glycoside, Triton X-100) removal of mixed micelles (absorption)

Detergent absorption is attained by shaking mixed micelle solution with beaded organic polystyrene adsorbers such as XAD-2 beads (SERVA Electrophoresis GmbH, Heidelberg, Germany) and Bio-beads SM2 (Bio-RadLaboratories, Inc., Hercules, USA). The great benefit of using detergent adsorbers is that they can eliminate detergents with a very low CMC, which are not entirely depleted.

Gel-permeation chromatography

In this method, the detergent is depleted by size special chromatography. The liposomes do not penetrate into the pores of the beads packed in a column. They percolate through the inter-bead spaces. At slow flow rates, the separation of liposomes from detergent monomers is very good. The swollen polysaccharide beads adsorb substantial amounts of amphiphilic lipids; therefore, pre-treatment is necessary. The pre-treatment is done by pre-saturation of the gel filtration column by lipids using empty liposome suspensions.[34]

Dilution

Upon dilution of aqueous mixed micellar solution of detergent and phospholipids with buffer, the micellar size and the polydispersity increase fundamentally, and as the system is diluted beyond the mixed micellar phase boundary, a spontaneous transition from polydispersed micelles to vesicles occurs.

Drug loading in liposomes

Drug loading can be attained either passively (i.e., the drug is encapsulated during liposome formation) or actively (i.e., after liposome formation). Hydrophobic drugs, for example amphotericin B taxol or annamycin, can be directly combined into liposomes during vesicle formation, and the amount of uptake and retention is governed by drug-lipid interactions. Trapping effectiveness of 100% is often achievable, but this is dependent on the solubility of the drug in the liposome membrane. Passive encapsulation of water-soluble drugs depends on the ability of liposomes to trap aqueous buffer containing a dissolved drug during vesicle formation. Trapping effectiveness (generally <30%) is limited by the trapped volume delimited in the liposomes and drug solubility. On the other hand, water-soluble drugs that have protonizable amine functions can be actively entrapped by employing pH gradients, which can result in trapping effectiveness approaching 100%.

Freeze-protectant for liposomes (lyophilization)

Natural excerpts are usually degraded because of oxidation and other chemical reactions before they are delivered to the target site. Freeze-drying has been a standard practice employed to the production of many pharmaceutical products. The overwhelming majority of these products are lyophilized from simple aqueous solutions. Water is the only solvent that must be detached from the solution using the freeze-drying process. Freeze-drying (lyophilization) involves the removal of water from products in the frozen state at tremendously low pressures. The process is normally used to dry products that are thermo-labile and would be demolished by heat-drying. The technique has too much potential as a method to solve long-term stability difficulties with admiration to liposomal stability. Studies showed that leakage of entrapped materials may take place during the process of freeze-drying and on reconstitution. Newly, it was shown that liposomes when freeze-dried in the presence of adequate amounts of trehalose (a carbohydrate commonly found at high concentrations in organism) retained as much as 100% of their original substances. It shows that trehalose is an excellent cryoprotectant (freeze-protectant) for liposome.

Purification of liposome

Liposomes are generally purified by gel filtration chromatography,[35] Dialysis and centrifugation. In chromatographic separation, Sephadex-50 is most widely used. In dialysis method hollow fibre dialysis cartridge maybe used. In centrifugation method, SUVs in normal saline may be separated by centrifuging at 200000 g, for 10-20hours. MLVs are separated by centrifuging at 100000g for less than one hour.

Mechanism of Transportation through Liposome

The limitations and benefits of liposome drug carriers lie critically on the interaction of liposomes with cells and their destiny *in vivo* after administration. *In vivo* and *in vitro* studies of the contacts with cells have shown that the main interaction of liposomes with cells is either simple adsorption (by specific interactions with cellsurface components, electrostatic forces, or by nonspecific weak hydrophobic) or following endocytosis (by phagocyte cells of the reticuloendothelial system, for example macrophages and neutrophils). Fusion with the plasma cell membrane by insertion of the lipid bilayer of the liposome into the plasma membrane, with simultaneous release of liposomal content into the cytoplasm, is much rare. The fourth possible interaction is the exchange of bilayer components, for instance cholesterol, lipids, and membrane-bound molecules with componentsof cell membrane.

Targeting of Liposomes[36-41]

Passive targeting

As a mean of passive targeting, such usually administered liposomes have been shown to be rapidly cleared from the blood stream and taken up by the RES in liver spleen. Thus capacity of the macrophages can be exploited when liposomes are to be targeted to the macrophages. This has been demonstrated by successful delivery of liposomal antimicrobial agents to macrophages. Liposomes have now been used for targeting of antigens to macrophages as a first step in the index of immunity. For e.g. in rats the i.v administration

of liposomal antigen elicited spleen phagocyte mediated antibody response where as the non liposome associated antigen failed to elicit antibody response.

Active targeting

A pre-requisite for targeting is the targeting agents are positioned on the liposomal surface such that the interaction with the target i.e., the receptor is tabulated such as a plug and socket device. The liposome physically prepared such that the lipophilic part of the connector is anchored into the membrane during the formation of the membrane. The hydrophilic part on the surface of the liposome, to which the targeting agent should be held in a stericaly correct position to bond to the receptor on the cell surface. The active targeting can be brought about the using.

Immuno liposomes

These are conventional or stealth liposomes with attached Antibodies or other recognition sequence [e.g. Carbohydrate determinants like glycoprotein] The antibody bound, direct the liposome to specific antigenic receptors located on a particular cell. Glycoprotein or Glycolipid cell surface component that play a role in cell-cell recognition and adhesion.

Magnetic liposomes

Contain magnetic iron oxide. These liposomes can be directed by an external vibrating magnetic field in their delivery sites.

Temperature or heat sensitive liposomes

Made in such a way that their transition temperature is just above body temperature. After reaching the site, externally heated the site to release the drug.

Characterization of Liposomes[42-43]

Liposome prepared by one of the preceding method must be characterized. The most important parameters of liposome characterization include visual appearance, turbidity, size distribution, lamellarity, concentration, composition, presence of degradation products, and stability.

Visual Appearance

Liposome suspension can range from translucent to milky, depending on the composition and particle size. If the turbidity has a bluish shade this means that particles in the sample are homogeneous; a flat, gray color indicates that presence of a nonliposomal dispersion and is most likely a disperse inverse hexagonal phase or dispersed microcrystallites. An optical microscope (phase contrast) can detect liposome> 0.3 μm and contamination with larger particles.

Determination of Liposomal Size Distribution

Size distribution is normally measured by dynamic light scattering. This method is reliable for liposomes with relatively homogeneous size distribution. A simple but powerful method is gel exclusion chromatography, in which a truly hydrodynamic radius can be detected. Sephacryl-S100 can separate liposome in size range of 30-300nm. Sepharose -4B and -2B columns can separate SUV from micelles.

Determination of Lamillarity

The lamellarity of liposomes is measured by electron microscopy or by spectroscopic techniques. Most frequently the nuclear magnetic resonance spectrum of liposome is recorded with and without the addition of a paramagnetic agent that shifts or bleaches the signal of the observed nuclei on the outer surface of liposome. Encapsulation efficiency is measured by encapsulating a hydrophilic marker.

Liposome Stability

Liposome stability is a complex issue, and consists of physical, chemical, and biological stability. In the pharmaceutical industry and in drug delivery, shelf life stability is also important. Physical stability indicates mostly the constancy of the size and the ratio of lipid to active agent. The cationic liposomes can be stable at 4°C for a long period of time, if properly sterilized.

Entrapped Volume

The entrapped volume of a population of liposome (in μl/ mg phospholipid) can often be deduced from measurements of the total quantity of solute entrapped inside liposome assuring that the concentration of solute in the aqueous medium inside liposomes is the same after separation from unentrapped material. For example, in two phase method of preparation, water can be lost from the internal compartment during the drying down step to remove organic solvent.

Surface Charge

Liposome are usually prepared using charge imparting constituting lipids and hence it is imparting to study the charge on the vesicle surface. In general two method are used to assess the charge, namely free flow electrophoresis and zeta potential measurement. From the mobility of the liposomal dispersion in a suitable buffer, the surface charge on the vesicles.

Stability of Liposomes[44-45]

Physical stability

The stability of a pharmaceutical product usually is defined as the capacity of the delivery system to remain within defined or pre-established limits during the self life of the product. There is no established protocol for either accelerated or long–term stability studies for the liposomal formulation. Classical models from colloidal science can be used to describe liposome stability. Colloidal systems are stabilized electrostatically, sterically or electrosterically. In addition the self-assembling colloids can undergoes fusion or phase change after aggregation. Liposome exhibit both physical and chemical stability characteristics. Generally, the physical characteristic describes the preservation of liposome structure and the chemical characteristic refers

to molecular structure of liposomal components. (hydrolysis and oxidation of phospholipid) Physically stable formulations preserve both liposome size distribution and the amount of material encapsulated. The stability problem overcomes by using appropriate techniques likefreezing, lyophilization and osmification. It is also prevented by using fresh solvents and freshly purified lipid, using inert nitrogen gas, avoid high temperature and include anti-oxidants α,β,γ and δ tocopherol.

Plasma Stability

Although liposomes resemble biomembranes, they still are foreign objects for the host. Therefore, liposomes are recognized by the mononuclear phagocytic system (MPS) after interaction with plasma proteins. As a result, liposomes are cleared from the blood stream. These stability problems solve by using synthetic phospholipids, gangliosides, polymerization, coating liposomes with chitin derivatives, freeze drying, microencapsulation and particle coated with amphipathic polyethylene glycol.

Applications

- Gene therapy
- Liposomes as carriers for vaccines
- Liposomes as carrier of drug in oral treatment
- Liposomes for topical applications
- Liposomes for pulmonary delivery
- Against Leishmaniasis
- Lysosomal storage disease
- Cell biological application
- Metal storage disease
- Ophthalmic delivery of drugs.

Therapeutic Applications of Liposomes

Liposome as drug/protein delivery vehicle

Controlled and sustained drug release insitu. Enchaned drug solubilization, Altered pharmacokinetic and biodistribution. Enzyme replacement therapy and lysosomal disorders.

Liposome in antimicrobial, antifungal and antiviral therapy

Liposomal drugs
Liposomal biological response modifier

Liposomes in tumour therapy

Carrier of small cytotoxic molecule. Vehicle for macromolecule as cytokines or genes.

Liposome in gene therapy

Gene and antisence therapy, Genetic (DNA) vaccination

Liposome in immunology

Immunoadjuvant. Immunomodulator and Immunodiagnosis, Liposome as artificial blood surrogates, Lipososmes as radiopharmaceutical and radio-diagnostic carrier. Liposomes in cosmetics and dermatology. Liposomes in enzyme immobilization and bioreactor technology.

Limitation in Liposome Technology

- Stability
- Sterilization
- Encapsulation efficiency
- Active targeting
- Gene therapy
- Lysosomal degradation

CONCLUSIONS

Liposomes are extremely useful carrier systems for targeted drug delivery. 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. Drugs encapsulated in liposomes can have a significantly altered pharmacokinetics. The drugs are encapsulated within the phospholipid bilayers and are expected to diffuse out from the bilayer slowly. Various factors like drug concentration, drug to lipid ratio, encapsulation efficiency and in vivo drug release must be considered during the formulation of liposomal drug delivery systems. The development of deformable liposomes and ethosomes along with the administration of drug loaded liposomes through inhalation and ocular route are some of the advances in the technology. Thus liposomal approach can be successfully utilized to improve the pharmacokinetics and therapeutic efficacy, simultaneously reducing the toxicity of various highly potent drugs. The use of liposomes in the delivery of drugs and genes are promising and is sure to undergo further development in future

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