Review Article

Liposomes – A Unique Transdermal Drug Delivery System

Musavad Sunny[1]*, Prashar Bharat[1], Passi Deepti[2] ,Thakur Varun[1] and Patil Vishal[1]

[1]Department of Pharmaceutics, Manav Bharti University, Solan, Himachal Pradesh, India.
[2]Department of Pharmacology, Manav Bharti University, Solan, Himachal Pradesh, India.

INTRODUCTION

Liposomes are the leading in transdermal drug delivery systems for the systemic (intravenous) administration of drugs. liposomal formulations of conventional drugs that have received clinical approval and many others in clinical trials that bring benefits of reduced toxicity and improved efficacy for the treatment of cancer and other life-threatening diseases. The mechanisms giving rise to the therapeutic advantages of liposome's, such as the ability of long-circulating liposome's to preferentially accumulate at disease sites such as tumours, sites of infection and sites of inflammation are increasingly well understood. These liposomes are of two types Multilamellar Liposomes (MLV) and) Small Unilamellar Liposomes (SUV). Further, liposome-based formulations of drugs such as Doxorubicin ciprofloxacin fluconazole terbinafine clotrimazole miconazole and plasmids for gene therapy that have clear potential for systemic utility are increasingly available. This work reviews the liposomal drug delivery field, summarizes the success of liposomes for the delivery of small molecules and indicates how this success is being built on to design effective carriers for genetic drugs. Liposome used in Respiratory Drug Delivery System, Nucleic Acid Therapy, Eye Disorders ,Vaccine Adjuvant, Brain Targeting.

CLASSIFICATION

➢ **Based Upon Conventional Liposome**

- Stabilize natural lecithin (PC) mixtures
- Synthetic identical, chain phospholipids
- Glycolipids containing liposome

➢ **Based Upon Speciality Liposome**

- Bipolar fatty acid
- Antibody directed liposome.
- Methyl/ Methylene x- linked liposome.
- Lipoprotein coated liposome.
- 5- Carbohydrate coated liposome.
- 6- Multiple encapsulated liposome.

PREPARATION OF LIPOSOMES[1]

An important parameter to be considered when preparing the liposome is the rigidity of bi-layers. There are several groups of phospholipids that can be used for the liposome preparation which are as follows:

1. Phospholipids from natural source
2. Phospholipids modified from natural source
3. Semi synthetic phospholipids
4. Fully synthetic phospholipids and
5. Phospholipids with natural head groups

Dilauryl phosphotidyl choline (DLPC), Dimyristoyl phosphatidyl choline (DMPC), Dipalmitoyl phosphotidyl choline (DPPC), Distearoyl phosphotidyl choline (DSPC), Dioleolyl phosphatidyl choline (DOPC), Dilauryl phosphotidyl ethanolamine (DLPE), Dimyristoyl phosphotidyl ethanolamine (DMPE), Distearoyl phosphatidyl ethanolamine (DSPE), Dioleoyl phosphotidyl ethanolamine (DOPE), Dilauryl phosphotidyl glycerol (DLPG), Distearoyl phosphotidyl serine (DSPS) are the commonly used phospholipids for liposome preparation . Cholesterol can be added to

the bilayers mixture for the following purposes:

1. Act as a fluidity buffer
2. Act as intercalator with phospholipids molecules Alters the freedom of formation of carbon molecule in the acyl chain
3. Restrict the transformation of Trans to gauche conformation[1]

Earlier prepared liposome from egg lecithin by modified ether injection technique using stearylamine added dicetylphosphate as the charge inducing agent. The charged liposomes were larger in the size and showed better drug entrapment efficiency and were found more entrapped in the organs of the reticuloendothelial system than neutral liposome. It was also shown that cholesterol decreased the permeability coefficients of negative, neutral as well as positively charged membranes to Na+, K+, Cl- and glucose. Cholesterol also stabilized the membranes against temperature changes, leading to lower permeability at elevated temperatures[2]. Cholesterol is essential for lowering membrane permeability, and imparting better stability. Cholesterol also modulates membrane-protein interactions. The polymorphic phase behavior of lipids is modulated by a variety of factors including hydration, temperature and divalent cations, degree of unsaturation of the acyl chains and the presence of other lipids such as sterols[3, 4]. tried active trapping of amphipathic weak bases inside liposomes by using pH induced transmembrane potential establishment[5]. Doxorubicin was used as a model drug. Triton X-100 has been observed to affect the physical properties of liposomes[6]. Solubilizing effect of Triton X-100 on the membranes composed of different phospholipids and cholesterol has been evaluated[7]. The measured changes indicated a drastic structure transformation into entities of fairly high dipolar moment leading to solubilization of phospholipids membranes. The three different strategies for the preparation of liposomes are as follows:

Multilamellar Liposomes (MLV)

(i) Lipid Hydration Method

(a) This is the most widely used method for the preparation of MLV. The method involves drying a solution of lipids so that a thin film is formed at the bottom of round bottom flask and then hydrating the film by adding aqueous buffer and vortexing the dispersion for some time. The hydration step is done at a temperature above the gel-liquid crystalline transition temperature Tc of the lipid or above the Tc of the highest melting component in the lipid mixture. The compounds to be encapsulated are added either to aqueous buffer or to organic solvent containing lipids depending upon their solubilities. MLV are simple to prepare by this method and a variety of substances can be encapsulated in these liposomes. The drawbacks of the method are low internal volume, low encapsulation efficiency and the size distribution is heterogeneous[8].

(b) MLVs with high encapsulation efficiency can be prepared by hydrating the lipids in the presence of an immiscible organic solvent (petroleum ether, diethyl ether). The contents are emulsified by vigorous vortexing or sonication. The organic solvent is removed by passing a stream of nitrogen gas over the mixture. MLVs are formed immediately in the aqueous phase after the removal of organic solvent[9]. The main drawback of this method is the exposure of the materials to be encapsulated to organic solvent and to sonication.

(ii) Solvent Spherule Method

A method for the preparation of MLVs of homogeneous size distribution was proposed by Kim[10]. The process involved dispersing in aqueous solution the small spherules of volatile hydrophobic solvent in which lipids had been dissolved. MLVs were formed when controlled evaporation of organic solvent occurred in a water bath.

B) Small Unilamellar Liposomes (SUV)

(i) Sanitation Method

Here MLVs are sonicated either with a bath type sonicator or a probe sonicator under an inert atmosphere. The main drawbacks of this method are very low internal volume/encapsulation efficiency, possibly degradation of phospholipids and compounds to be encapsulated, exclusion of large molecules, metal contamination from probe tip and presence of MLV along with SUV[11]. Recently, prepared a polymer coated liposomes by this method[12].

(ii) French Pressure Cell Method

The method involves the extrusion of MLV at 20,000 psi at 4°C through a small orifice. The method has several advantages over sonication method. The method is simple rapid, reproducible and involves gentle handling of unstable materials[13]. The resulting liposomes are somewhat larger than sonicated SUVs. The drawbacks of the method are that the temperature is difficult to achieve and the working volumes are relatively small (about 50 mL maximum).

(iii) A new method for the preparation of SUV[14].

They deposited egg phosphatidylcholinc mixed with 1.5 %w/v of cetyl tetramethylammonium bromide (a detergent) in CHCI3/CH3OH on various supports for example silica gel powder, zeolite X, zeolite ZSM5. After the removal of organic phase, the system was resuspended by shaking or stirring in distilled water or 5 mM NaCl. There was some loss of phospholipid (about 10-20%) due to adsorption on the supports. The loss was 70% and 95% in the case of silica gel and zeolite ZSMS respectively. An homogenous population of vesicle with average diameter of 21.5 nm was obtained when zeolite X (particle size of 0.4 mm) was used as a support.

C) Large Unilamellar Liposomes (LUV)

They have high internal volume/encapsulation efficiency and are now a days being used for the encapsulation of drugs and macromolecules.

(i) Solvent Injection Methods

(a) Ether Infusion Method

A solution of lipids dissolved in diethyl ether or ether/methanol mixture is slowly injected to an aqueous solution of the material to be encapsulated at 55-65°C or under reduced pressure. The subsequent removal of ether under vacuum leads to the formation of liposomes. The main drawbacks of the method are that the population is heterogeneous (70-190 nm) and the exposure of compounds to be encapsulated to organic solvents or high temperature[15]

(b) Ethanol Injection Method

A lipid solution of ethanol is rapidly injected to a vast excess of buffer. The MLVs are immediately formed. The drawbacks of the method are that the population is heterogeneous (30-110 nm), liposomes are very dilute, it is difficult to remove all ethanol because it forms azeotrope with water and the possibility of various biologically active macromolecules to inactivation in the presence of even low amounts of ethanol[16]. 70 Liposomes preparation methods

(ii) Detergent Removal Methods

The detergents at their critical micelles concentrations have been used to solubilize lipids. As the detergent is removed the micelles become progressively richer in phospholipid and finally combine to form LUVs. The detergents were removed by dialysis[17]. The advantages of detergent dialysis method are excellent reproducibility and production of liposome populations which are homogenous in size. The main drawback of the method is the retention of traces of detergent(s) within the liposomes. A commercial device called LIPOPREP[18] which is a version of dialysis system is available for the removal of detergents. Other techniques have been used for the removal of detergents: (a) by using Gel Chromatography involving a column of Sephadex G-25, (b) by adsorption or binding of Triton X-100 (a detergent) to Bio-

Beads SM-2[19]. (c) by binding of octyl glucoside (a detergent) to Amberlite XAD-2 beads[20].

(iii) Reserves Phase Evaporation Method

First water in oil emulsion is formed by brief sonication of a two phase system containing phospholipids in organic solvent (diethylether or isopropylether or mixture of isopropyl ether and chloroform) and aqueous buffer. The organic solvents are removed under reduced pressure, resulting in the formation of a viscous gel. The liposomes are formed when residual solvent is removed by 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 for example 0.01 M NaCl. The method has been used to encapsulate small, large and macromolecules. The main disadvantage of the method is the exposure of the materials to be encapsulated to organic solvents and to brief periods of sonication. These conditions may possibly result in the denaturation of some proteins or breakage of DNA strands[21]. We get a heterogeneous sized dispersion of vesicles by this method. Modified Reverse Phase Evaporation[22] and the main advantage of the method is that the liposomes had high encapsulation efficiency (about 80%).

(iv) Calcium-Induced Fusion Method

This method is used to prepare LUV from acidic phospholipids. The procedure is based on the observation that calcium addition to SUV induces fusion and results in the formation of multilamellar structures in spiral configuration (Cochleate cylinders). The addition of EDTA to these preparations results in the formation of LUVs[23]. The main advantage of this method is that macromolecules can he encapsulated under gentle conditions. The resulting liposomes are largely unilamellar, although of a heterogeneous size range. The chief disadvantage of this method is that LUVs can only be obtained from acidic phospholipids[12].

(v) Microfluldization Method

Mayhew[24] suggested a technique of microfluidization/microemulsification/ homogenization for the large scale manufacture of liposomes. The reduction in the size range can be achieved by recycling of the sample. The process is reproducible and yields liposomes with good aqueous phase encapsulation. liposomes consisting of egg yolk, cholesterol and brain phosphatidylserin diasodium salt (57:33:10) by this method[25]. First MLV were prepared by these were passed through a Microluidizer (Microlluidics Corporation, Newton, MA, USA) at 40 psi inlet air pressure. The size range was 150-160 nm after 25 recylces. In the Microluidizer, the interaction of fluid streams takes place at high velocities (pressures) in a precisely definedmicrochannels which are present in an interaction chamber. In the chamber pressure reaches up to 10,000 psi this can be cause partial degradation of lipids.

(vi) Extrusion under nitrogen through polycarboriate filters

LUV can be prepared by passing MLV under nitrogen through polycarbonate membrane filters[26]. The vesicles produced by this method has narrow size distribution. The extrusion is done under moderate pressures (100-250 psi). A special filter holder is required. Such devices are available commercially under the trade names such as LUVET and EXTRUDER and are equipped with a recirculation mechanism that permits multiple extrusions with little difficulty. Small quantities of liposome preparations (about 10 mL) can be easily prepared by the help of a commercial extruder. Riaz and Weiner prepared liposomes by this technique. The liposomes contained phosphatidylcholine from egg yolk and crude phosphoinositide sodium salt in the ratio of 4:1 and the lipid concentration was 12.5 /mole/ml. MLVs were passed through Extruder Lipex Membrane Inc., Vancouver, Canada) ten times through a stalk of two 100 nm polycarbonate filters employing nitrogen pressures upto 250 psi. Freeze fracture electron microscopy and

p31-FT NMR revealed that the liposomes were unilamellar. Photon Correlation Spectroscopy revealed that the size range was 99-135 nm.

(vii) method for the instant formation of a rather homogeneous preparation of LUV by a simple technique[14]. The formation of multilammelar liposomes is prevented by inducing a surface charge (+ ve) on the bilayer while the size of the vesicles is controlled by the topography of the wafer support surface on which phospholipid film was formed. They deposited 0.5-1.0 mg egg yolk lecithin doped with 3 ml of CHCl3/CH3OH on a specially etched 2 inch silicon wafer. This wafer was put in place of the original bottom of an Erlenmeyer flask that is bottom of the flask is replaced by wafer. After having dried overnight at 102 tore (about 1 Pa), the film was resuspended by gentle shaking in 1-2 ml water. Liposomes were formed instantly. The contamination of liposomes with large structures such as MLVs, giant vesicles and phospholipid particles was ruled out by video enhanced phase contrast microscopy. 72 Liposomes preparation methods

(viii) Freeze-Thaw Method

SUVs are rapidly frozen and followed by slow thawing. The brief sonication disperses aggregated materials to LUV. The formation of unilamellar vesicles is due to the fusion of SUV during the processes of freezing and or thawing[27]. This type of fusion is strongly inhibited by increasing the ionic strength of the medium and by increasing the phospholipid concentration.The encapsulation efficiencies from 20 to 30% were obtained[27].

MECHANISM OF LIPOSOMAL ACTION

Although the use of liposomal drug formulations for topical application has been steadily increasing, few studies have been undertaken in order to explain the mech anism of liposomal action on drug transfer into the skin and ultimately, its improved therapeutic effect. Most in-vitro transport studies, which typically concern themselves with permeation of drug through the skin, do not focus on the extent of drug accumulation in the various skin strata. In order to evaluate formulation effects on the treatment of dermatological diseases by topical application, knowledge of such tissue levels is crucial, since it is expected that for a formulation to be most effective it should facilitate increased drug levels in the epidermis. The stratum corneum of humans, mice and pigs have shown to be devoid of phospholipids. The lipid composition is rather non-polar in nature and consists primarily of ceramides (~40%), cholesterol (~-25%), fatty acids (~25%) and cholesteryl sulfate (~10%). Such lipid compositions have been referred to as 'skin lipids' and they are arranged in bilayer sheet structures that fill the intercellular space in the stratum corneum. The pathway for the transport of water and other drugs is believed to reside mainly in these bilayer structures. Removal of these bilayer sheets either by solvent treatment or by successive tape stripping[28] increases the permeability of water, suggesting a decreased barrier function. The ability of the stratum corneum to act as a reservoir for drug transport through the skin[29]. Who reported that the absorption of a variety of drugs through the skin was proportional to the amount of drug recovered in the stratum corneum following 30 min topical application. It is therefore important to examine the extent of drug accumulation in the various strata of the skin in addition to estimating percutaneous absorption profiles.

A common procedure for the determination of drug levels in the skin strata involves stripping of treated skin with adhesive tape. With the use of appropriately radio labeled drugs and liposomal lipids, it has been possible to obtain both drug and liposomal lipid distributions in the various strata of the skin. The experimental procedure adopted in our in-vitro studies[30, 31] with full thickness hairless mouse and guinea pig skin was as follows. Briefly, the skin was mounted on a Franz diffusion cell with a nominal surface area of 2 cm 2 and a receiver compartment with a 7 ml capacity (Crown Glass,

Somerville, NJ). The epidermal side of the skin was exposed to ambient conditions while the dermal side was bathed by a 0.05 M isotonic HEPES buffer (pH=7.4). The receiver solution was stirred continuously using a small Teflon-covered magnet. Care was exercised to remove any air bubbles between the underside of the skin and solution in the receiver compartment. The temperature of the receiver was maintained at 37°C. Following mounting of the section of skin, 200p, l of the test formulation was applied to the epidermal surface. A smaller amount of formulation was found to be insufficient to ensure uniform spreading across the entire exposed surface of the skin in the cell. A minimum of three cells was used for each formulation and duplicate experiments were carried out using sections of skin from different skin specimens for each formulation. All experiments were carried out with non occluded donor compartments. At predetermined time periods the experiments were stopped and the diffusion set-up was dismantled for assay of radio labeled drug and lipids. Upon dismantling the donor compartment of the cell was rinsed carefully 5 times with 0.5 ml HEPES buffer (pH 7.4). The skin was then removed and it too was rinsed twice with 3 ml of the same buffer. The washing procedure was found to be sufficient to remove more than 99% of the formulation when determined at time zero. All washings were collected and assayed for radiolabel. Following, the rinsing procedure, the skin patch was mounted on a board and a piece of adhesive tape (Scotch Magic Tape, 810, 3M Commercial Office Supply Division, St. Paul, MN), 1.9 cm wide and about 6 cm long, was used to strip the skin. The tape was of sufficient size to cover the area of skin that was in contact with the formulation. Nine strippings were carried out for each specimen and each strip was analyzed separately for radio labeled drug and lipid. The amount adhering to the stratum corneum surface is determined by analysis of the first two strippings and the amount in the deeper stratum corneum is determined by analysis of the remaining strips. The amount of drug and lipid penetrating the deeper skin strata is determined by analysis of the remainder of the stripped full thickness skin. A mass balance of more than 95% was achieved after the donor compartment, and the skin rinses were taken into account. Assay of the donor and skin rinses and receiver solutions were carried out after addition of about 15 ml of Ecolite scintillation cocktail to each System. The tape strippings and the skin remaining after stripping were assayed as follows. Each sample was placed in a combustion cone and burnt in a tissue oxidizer (Model 306 Packard oxidizer, Packard Instrument, Downers Grove IL). The separated radionuclides were then assayed using a scintillation counter. A variety of liposomal formulations were examined in both an in vivo and an in-vitro study. These included phospholipid-based Liposomes and Liposomes prepared from mixtures similar in composition to the stratum corneum lipids, termed 'skin lipids'. The formulation of stable Liposomes from mixtures of 'skin lipid' has been documented by us and others[30]. The first to report that 'skin lipid' liposomes are effective drug delivery systems. They demonstrated that topical application of or-interferon entrapped in 'skin lipid' liposomes showed a greater reduction of lesion scores than interferon entrapped in liposomes prepared from phospholipid mixtures, when tested in a HSV-1 guinea pig model . The method of preparation affected the efficacy of interferon action[30]. In an effort to understand effects of liposomal composition and method of preparation on the deposition of interferon into the stratum corneum and deeper strata of the skin the topical delivery of several interferon formulations was evaluated[31] using in-vitro diffusion experiments. It was found that application of liposomes prepared from 'skin lipids' resulted in almost twice the amount of interferon deposited in the deeper skin layers than application of iiposomes prepared from phospholipids.

Incorporating drugs

To understand the performance characteristics of liposomal systems, it is important to understand the mechanisms of introducing drugs into liposomes. That process is achieved using one of three primary mechanisms: encapsulation, partitioning, and reverse loading.

A. Encapsulation. Useful for water-soluble drugs, the encapsulation is simple hydration of a lipid with an aqueous solution of drug. The formation of liposomes passively entraps dissolved drug in the interlamellar spaces, essentially encapsulating a small (captured) volume.

B. Partitioning. A drug substance that is soluble in organic solvents will go through partitioning. It is dissolved along with phospholipid(s) in a suitable organic solvent.That combination either is dried first or added directly to the aqueous phase,and residual solvent is removed under vacuum. The acyl chains of the phospholipids provide a solubilizing environment for the drug molecule, which will be located in the intrabilayer space.

C. Reverse loading. The reverse-loading mechanism uses the fact that certain drugs (such as weak acids) may exist in both charged and uncharged forms depending on the pH of their environment. Such drug molecules can be added to an aqueous phase in the uncharged state to permeate into liposomes through their lipid bilayers. Then the internal pH of the liposomes is adjusted to create a charge on the drug molecule. Once charged, the drug substance no longer is lipophilic enough to pass through the lipid bilayer and return to the external medium. Use of liposomes to carry peptide and protein drugs and DNA vaccines involves simple, easily scaled technology that is capable of high-yield vaccine entrapment. A dehydration–rehydration technique applied for entrapping particulate antigens freeze-dries giant vesicles (4–5 μm in diameter) in the presence of spores. On rehydration and sucrose-gradient fractionation of the resultant suspension, 30% or more of the spores used will be associated with generated giant liposomes of similar mean size.

CHARACTERIZATION

In addition to concentrations of the drug and lipids in the vesicles, measurements of captured volume, size distribution, and *lamellarity* (the number of layers making up the shell of the bubble or vesicle) characterize lipid vesicles. The size of liposomes is considered an important factor in measuring liposome–complement interactions. In a study by Yamada et al., the release of carboxyfluorescein (CF) from liposomes was measured for three different diameters (800, 400, and 200 nm) by changing the liposome concentration from 1 to 1,000 nmol/ mL. At a low liposome concentration range (1–10 nmol/mL), small liposomes (200 nm) released CF to a similar extent (about 35%) as medium (400 nm) and large (800 nm) liposomes. The affinity (Km) and capacity (max) of a complement system to release liposomal encapsulated CF were estimated by kinetic analysis of the liposome–complement interaction. Surprisingly, no remarkable size dependency was found in the Km or max by liposome number, although parameters depended on the lipid concentrations. Those results indicate the possibility that the complement system does not discriminate according to liposome size. The study indicated that placental uptake and the transfer rate of liposomal CF were dependent on liposome size.

Mean vesicle size and size distribution

These essential parameters describe the quality of liposome suspensions. They are important parameters for the physical properties and biological fate of liposomes and their entrapped substances in vivo. (Part II of this article will discuss those further.) A number of methods are used to determine size and size distribution, but one of the most commonly used methods is light-scattering analysis. A number of

techniques are available to size liposomes based on that methodology. Light scattering is popular because of the ease of operation and the speed by which Scientists can obtain data. Newer instruments are based on laser light scattering. If the liposomes to be analyzed are monodisperse, light-scattering analysis is the method of choice; unfortunately, most liposomal preparations are heterogeneous, and they require an accurate estimate of their size–frequency distributions. Light scattering methods rely on algorithms to determine particle-size distributions, and the results obtained can be misleading. Some complex algorithms have been developed as an attempt to address that problem. However, such methods cannot distinguish between a large particle and a flocculated mass of smaller particles. Most important, it may be necessary to remove any micron-sized particles that are present in such masses before analysis.

COMPLICATIONS

The difficulty in interpreting data about particle size can be demonstrated with a simple example of a dispersion composed of 97% SUV with a radius of 15 nm and 3% MLV with a radius three times greater (45 nm). Table I lists the results. Thus, 3% of the particles constitute almost one-half the volume of the liposomes present. Similar problems of data analysis occur with other dispersion systems such as emulsions and suspensions. Single values for particle size in dispersion systems such as emulsions and suspensions reported in the literature are usually the average mean diameter. Each dispersion system has its own size distribution. Typically that size distribution is close to an average mean diameter. A single value often is reported in the literature for mean diameter values that are different from the expected center of distribution. an average mean diameter for a suspension in which the particle size distribution ranges from 0.05 μm to 0.5 μm, with a mean diameter 0.140 μm. Fewer than 4% of the particles are 0.05 μm, and particles 0.45 μm are more than 0.4% of each lot reported. The specification set for both the lower and upper range is 10%. Set specifications indicate a wider spread than does the actual data, which shows a much tighter distribution in the middle and less than a few percent on the lower and upper ends. So the mean diameter of 0.140 μm is far below the center of distribution, indicating that the particle-size distribution does not follow a normal distribution around the mean.

APPLICATION OF LIPOSOME

The field of liposome research has expanded considerably over last 30 years. It is now possible to engineer a wide range of liposome of varying size, phospholipids composition, cholesterol composition, surface morphology suitable for wide range of application. Liposomes interact with cells in many ways to cause liposomal components to be associated with target cells. The liposome carrier can be targeted to liver and spleen and distinction can be made between normal and tumors tissue using tomography. In case of transdermal drug delivery system, liposome has a great application. Liposomal DNA delivery vectors and further enhancement in the form of LPDI -I and LPD-II are some of the safest and potential most versatile transfer vectors which are used to date. DNA vaccination and improved efficiency of gene therapy are just a few of the recent application of liposome. Several modes of drug delivery application have been purposed for the liposomal drug delivery system, few of them are as follows:

1. Enhance intracellular uptake (Anticancer, anti viral and antimicrobial drugs).
2. Protection of sensitive drug molecules (Cytosine arabinosa, DNA, RNA, Anti-sense oligo-nucleotides, Ribozymes).
3. Enhance drug solublisation (Amphotericin-B, Minoxidil, Paclitaxels, and Cyclosporins).
4. Altered pharmacokinetics and bio-distribution (prolonged or sustained

released drugs with short circulatory half life)

A. Liposome for Respiratory Drug Delivery System
B. Liposome in Nucleic Acid Therapy
C. Liposome in Eye Disorders
D. Liposome as Vaccine Adjuvant
E. Liposomes for Brain Targeting
F. Liposome as Anti-Infective Agents

CONCLUSION

Many factors contribute to their success as drug delivery vehicles. Liposomes solubilise lipophillic drug candidates that would otherwise be difficult to administer intravenously. The encapsulated drug is inaccessible to metabolizing enzyme; conversely, body component such as erythrocyte and tissue injection site are not directly exposed to full dose of the drug. Liposome can prolong the drug action by slowly releasing the drug in the body. Targeting option change the distribution of the drug in the body. They can also be used as adjuvant in vaccine formulation. Liposome are prepared by various methods in which the most common method applied for research purpose are film method and dehydration rehydration method and many more. Stabilization of liposomes has been an area of concern for optimum shelf life of the liposomal formulation.The concept of incorporating the drug into liposomes for a better targeting of the drug at appropriate tissue destination is widely accepted by researchers and academicians

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