International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2019): 7.583

Liposomes a Camouflaged Carrier: For Controlled Drug Delivery

Sumit Khutale*, Kavita Nangare

Department of Pharamceutics Vasantidevi Patil Institute of Pharmacy Kodoli, Tal- Panhala, Dist- Kolhapur (MH) 416114, India

Corresponding Author Email Address: skhutale12[at]gmail.com

Abstract: ***Controlled drug delivery is that type of system that dispenses the drugs in the dosage form at a prescribed local dose or systematically for a specified period of time. The liposome is a circular fabric made up of one or more phospholipid circles, which closely resembles the cell membrane. The ability of liposomes to incorporate hydrophilic or lipophilic compounds has allowed these vesicles to become efficient delivery systems. The liposome is a tiny bubble (vesicle), made of the same material as the cell membrane. Liposomes can be filled with drugs, and used to deliver cancer drugs and other diseases. Ribs are usually made of phospholipids, molecules with a group of head and tail.***

Keywords: Liposomes, Controlled Drug Delivery, vesicle

1. Introduction

Liposomes were first produced in England in 1961 by Alec D. Bangham, who studied phospholipids and blood clotting [6] In all novel drug delivery systems, liposomes are considered the most useful, researched and comprehensive. The circular vesicle formed by the spinal cord enclosed in phospholipid molecules is commonly known as the liposome [5]. The word liposome is derived from two Greek words: 'Lipos' meaning' fat 'and' Soma 'meaning' body. [7] A few successes since the discovery of banned liposomes in microscale to nanoscale as well as a surface-based polymer working with peptide, protein, and antibody. Although liposomes have been widely studied as promising carriers of therapeutic chemicals, some of the major drawbacks of liposomes used in pharmacology are rapid deterioration due to reticulo endothelial system (RES) and failure to deliver long-term drug delivery [1]Alec Bangham first explained that membrane molecules, e.g. phospholipids, combine with water to form different structures now labeled as liposomes4 and found that phospholipids combined with water form a direct base because one side of each molecule dissolves in water, and the opposite side is insoluble. Water-soluble drugs have been added to the water trap within the integration of hydrophobic limits; fat-soluble drugs are placed in layers of phospholipids. [7] To enter the market, Liposome must remain consistent and uninterrupted during and after the arrival of the intended destination to produce a therapeutic action. However, due to physiological and chemical instability, liposomes are an unstable colloidal system [5]. There are two types of liposome identification: synthetic and functional5. Negative identification uses the natural tendency of other cells namely Kupffer cells in the liver and macrophages of the mononuclear phagocyte (MPS) system to foreign microparticles such as liposomes5. The result of this phagocytosis is the inactivation of the drug trapped in the desirable part5. Effective administration requires the formation of immune liposomes before their direct contact with target tissues. Although the presence of poorly charged lipids in liposomes including phosphatidic acid (PA), phosphatidylserine (PS) and phosphatidylglycerol (PG) leads to rapid absorption by the mononuclear phagocyte system (MPS), the relationship between the presence of lipids charged and life cycle cycle is very complex. The longer a liposome can circulate to prevent liver transplantation, the greater the chance that it will leave the vascular system in areas where the blood vessels are full. Summary drugs can be released in a variety of ways such as: fusion, difference in pH and temperature. The rate of excretion in liposomal formation depends on the drug. Therapeutic benefits will be obtained if the drug is stored in liposomes a few hours after administration. Major instability of liposomes is associated with their hydrolysis potential, as well as peroxidation reactions and the ability to synthesize. The chemical instability of liposomes can be caused by the hydrolysis of the ester bond and / or the peroxidation of acyl chains unlit in lipids through a large free radical reaction. Peroxidation reactions can be avoided by choosing lipids with only full bonds, subconscious, and the inclusion of antioxidants such as α-tocopherol, quercetin and coenzyme Q (CoQ) and chelating agents. A day of literature shows that by using grape seed extracts to prepare chitosan-liposomes chemical stability against lipid oxidation is enhanced The kinetic hydrolysis of phospholipids depends on temperature, pH and bilayer rigidity. The choice of the appropriate liposome type depends on the physicochemical properties of the substance to be absorbed, its active concentration, strong toxicity and internal volume. The effectiveness of encapsulation depends largely on the liposomal content, lipid concentration, method of preparation and the drug used. The different ways in which liposomes are prepared lead to the formation of liposomes of various sizes and characteristics. An important part of the liposome is produced by phospholipids, which are amphiphilic particles (with a hydrophilic head and a hydrophobic tail). The hydrophilic component is usually phosphoric acid bound to a water-soluble molecule, whereas the hydrophobic component consists of two chains containing 10 - 24 carbon atoms and 0 - 6 bonds in each chain. When these phospholipids are dispersed in a wet environment, they form lamellar sheets by arrangement in such a way that, the polar head group faces out in the wet region while the fatty groups face. The polar part is always in contact with the watery region and the

non-polar part of the shield (facing the corner of the membrane surface) [4]

Types of Internal Signs [1-6]

Liposomes are classified on the basis of

A) Support Called Support:

1. Unilamellar Fabrics:

- Unilamellar small vesicles (SUV): distances range from 20-40 40 nm
- Unilamellar medium vesicles (MUV}: distance ranges from 40-80 nm.
- Large unilamellar vesicles (LUV): sizes range from 100 nm to 1, 000 nm

2. Oligolamellar vesicles (OLV): These are made up of 2-10 bubbles of lipids around a large internal volume
3. Multilamellar vesicles (MLV): They have several bilayers. They can separate the liquid volume by unlimited means. They differ in the way they are arranged. Arrangements can be onions like arrangements for round bilayers LUV / MLV including a large number of SUVs etc.

B) Based On the Liposome Preparation Process

1. REV: Single or oligolamellar fabrics made by the Revers- Phase Evaporation Method.
2. MLV-REV: Multilamellar vesicles produced by Reverse-Phase Evaporation Method.
3. SPLV: Stable Plurilamellar Vesicles
4. FATMLV: MLV Frozen and Thawed.
5. VET: Vesicles prepared for the extrusion process
6. DRV: A method of dehydration.

C) Your Construction and Use

1. Conventiuonal Liposomes (CL): Phospholipids that are neutral or poorly charged with Cholesterol.
2. Fusogenic Liposomes (RSVE): Regenerated Sendai virus envelopes
3. Sensitive pH Liposomes: Phospholipids such as PE or DOPE with CHEMS or OA
4. Cationic Liposomes: Cationic lipids containing DOPE
5. Long Circulatory (Stealth) Liposomes (LCL): They contain ingredients of polyethylene glycol (PEG) attached to their surface to reduce their loss through the phagocyte system (reticuloendothelial system; RES). The attachment of PEG to liposomes reduces the removal of blood from the blood and increases the time it takes for the circulation of liposomes in the body. PEG attachment is also known as pegylation.
6. Immuno-Liposomes: CL or LCL with anti-monoclonal antibody or recognition sequence.

2. Structural Components

1. Phospholipids

Glycerol-containing phospholipids are widely used in liposome formation and represent more than 50% of lipid weight in organic components. These are found in Phosphatidic acid. The back bone of the molecule is the glycerol moiety. In the C3 OH group it is separated from phosphoric acid. OH in C1 & C2 is secured with a long chain. Fatty acids create a lipidic state. One of the remaining OH groups of phosphoric acid can also be confirmed in a wide range of alcohols including glycerol, choline, ethanolamine, serine and inositol. The parent compound of the series is therefore a phosphoric ester of glycerol.

Examples of phospholipids are;

- Phosphatidyl choline (Lecithin) - PC
- Phosphatidyl ethanolamine (cephalin) - PE

Phosphatidyl serine (PS)
Phosphatidyl inositol (PI)
Phosphatidyl Glycerol (PG)

For stable liposomes, saturated acids are used. Unused fatty acids are not commonly used.

2) Sphingolipids

The backbone is sphingosine or a related base. These are vital components of plant and animal cells. This contains 3 building blocks;

- F.A mol
- Sphingosine mol
- The main group that can vary from simple alcohols such as choline to more complex carbohydrates.

The most common Sphingolipids - Sphingomyelin. Glycosphingo lipids.

Gangliosides - found in gray matter, are used as a small part of liposome production.

This molecule contains complex saccharides that contain one or more residues of Sialicacid in their primary polar group and thus have one or more negative effects on neutral pH. These are embedded in the liposomes to give a layer of the most charged group.

3) Sterols: Cholesterol and its ingredients are often absorbed into the liposomes of

- To reduce the liquid or small part of the state
- Reduce membrane penetration into water-soluble molecules
- Stabilizing membranes in the presence of organic fluids such as plasma. (This result is used to createi.v. liposomes)

Cholesterol-free liposomes are known for their rapid interaction with plasma proteins such as albumin, transferrin, and macroglobulin. These proteins tend to release large amounts of phospholipids into liposomes, which by eliminating the external monolayer of vesicles

lead to instability. Cholesterol seems to greatly reduce this type of contact. Cholesterol has been called the mud of bilayers, because because of its cellular structure and dissolve, it fills the empty spaces between Phospholipid molecules, attaching them firmly to the structure. The OH group in position 3 gives a small polar head group and the hydrocarbon chain in C17 becomes a non-polar end of these molecules, cholesterol enters the bilayers.

4) Synthetic phospholipids

Eg .: Of full phospholipids

- Dipalmitoyl phosphatidyl choline (DPPC)

Distearoyl phosphatidyl choline (DSPC)

- Dipalmitoyl phosphatidyl ethanolamine (DPPE)
- Dipalmitoyl phosphatidyl serine (DPPS)
- Dipalmitoyl phosphatidic acid (DPPA)
- Dipalmitoyl phosphatidyl glycerol (DPPG) Eg .: For non-saturated phospholipids
- Dioleoyl phosphatidyl choline (DOPC)
- Dioleoyl phosphatidyl glycerol (DOPG)

5) Polymeric materials

Synthetic phospholipids and the diactylenic group in the hydrocarbon chain polymerize when exposed to UV, leading to the formation of polymer liposomes with very high barriers to the binding of trapped drugs. Eg. For other immovable lipids - lipids containing diene compound, Methacrylate etc.

6) Polymer that carries lipids

The stability of the abnormal contact with macromolecules is largely determined by the abnormal electrostatic energy. This depression can be caused by wearing a liposome that contains charged polymers.

Ionic and water-soluble polymers such as polyethylene oxide, polyvinyl alcohol, and Polyoxazolidines provide high solubility. However the advertising of such copolymers containing hydrophilic components with a hydrophobic part leads to liposome leakage, so good results can be obtained by attaching polymers to phospholipids. E.g..: Diacyl Phosphatidyl ethanolamine and PEG polymer bonded with carbon at or succinate bond.

7) Cationic lipids

E.g.: DODAB / C - Dioctadecyl dimethyl ammonium bromide or chloride;

DOTAP - Dioleoyl propyl trimethyl ammonium chloride - this is an analogue of DOTAP and various others including various DOTMA analogues and cationic derivatives of cholesterol.

8) Other Items

- A variety of other lipids and surfactants used to form liposomes
- Many chain surfactants can form liposomes in combination with cholesterol
- ionic lipids
- A variety of Polyglycerol and Polyethoxylated mono and dialkyl amphiphiles are widely used in cosmetic preparations
- Lipids in single and double chains with fluoro carbon fibers can form very stable liposomes
- Sterylamine and Dicetyl phosphate
- Incorporated into liposomes to convey negative or positive charges on these properties.

Lipid is dissolved in organic solvent. The solvent evaporates leaving a thin film of lipids on the wall of the vessel. Water-based solution is added. In the first process the mixture is stirred to produce multi lamellar vesicles and then sonicated to obtain SUVs. In the second process the mixture is made sonicated and the solvent evaporates to form LUVs. After extrusion SUVs are built. The drug can be added to an aqueous solution or buffer if dissolved in water or added to an organic solvent if hydrophobic. Free drugs and liposomes can be separated by gel chromatography.

B) Special Methods: These are classified as 3 types depending on the distribution methods. That's right

1. Methods of physical disintegration
2. Solvent dispersion methods
3. Abdominal solutions

1) Body Distribution Techniques: In these methods the volume of water embedded within the lipid membrane is approximately 5–10%, which is a very small fraction of the total volume used for preparation. Therefore a large amount of water dissolved in water is consumed during the preparation. But a lipid-soluble drug can be added to a higher percentage. In these methods, MLVs are formed and further treatment is required in the preparation of Unilamellar vesicles

Motivated Hand Method:

This is a simple and widely used method. The lipid and compound mixture is dissolved in a mixture of chloroform and methanol (a ratio of 2: 1) and the mixture is placed in a 250 ml circular flask. The bottle is attached to a rotating evaporator connected to a vacuum pump and rotated at 60 rpm. Natural solvents evaporate at about 30 degrees. There remains a dry residue on the walls of the bottle and the rotation continues 15 minutes after the appearance of the dry residue. The evaporator is disconnected from the respirator pump and nitrogen is added to it. The flask is removed from the evaporator and then fixed to the lypholizer to remove the solid solvent. After that the bottle is again coated with nitrogen and 5 ml of phosphate buffer is added. The bottle is attached to the evaporator and is also rotated at about 60 rpm for 30 minutes or until all the lipid has been removed from the bottle wall. Eventually a

white milk-form suspension was formed. The suspension was allowed to stand for two hours to complete the inflammatory process to give MLVs.

Non-invasive method: This is similar to a non-invasive method unless care is taken through the inflammatory process. A lipid solution in chloroform and a mixture of methanol is distributed under a circular layer. The solution is heated to room temperature by the flow of nitrogen in a bottle without interfering with the solution. After dehydration the complete nitrogen is transported in a bottle until the light of the dry film ends. After hydration, the lipid is swollen by immersion in a lot of fluids. The bottle is tilted to one side, 10 to 20 ml of 0.2M sucrose in distilled water is introduced to the bottom and side of the bottle and the bottle is returned to the correct position. The solution is allowed to work well over the lipid layer under the bottle. The bottle is coated with closed nitrogen and allowed to stand for 2 hours at 37 degrees for swelling. After that the mixed vesicles secrete a milk suspension. The suspension is centered at 1200 per minute for ten minutes. A layer of floating MLV floors is removed. From the remaining liquid, LUVs are produced.

Freeze Drying: Another method of dispersing lipid in a finely separated manner before the addition of liquid media is to intensify the drying of lipid dissolved in a suitable natural solvent. The most commonly used solvent is high butanol.

Advantages of Liposomes

Liposome's offer a degree of protection to the DNA from degradative processes
Liposomes are biocompatible compleely biodegradable
Protect for delivery of hydrophobic drug
Liposome's can be targeted to specific cells or tissues
Protect he encapsulated drug from the external environment

Disadvantages of Liposome

Liposome encapsulated drug require high Production cost
Leakage and fusion of encapsulate d drug molecule
Liposome have a Shorter half life
Liposome have lower solubility

Sometimes phospholipid undergoes oxidation and hydrolysis like reaction

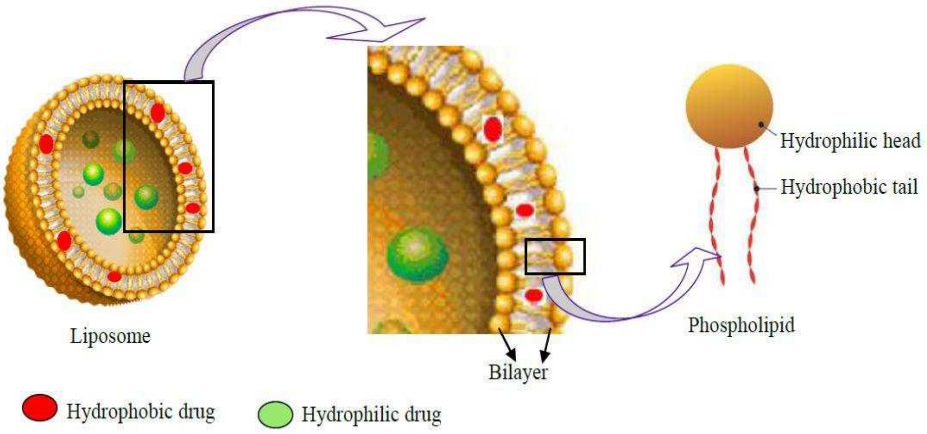

Figure 1: Structure of liposome and phospholipid

Liposome-Based Technology

The liposome is a thin layer with an aqueous core bound within one or more of the natural phospholipids that form closed bilayered structures (Figure 2) [24]. Liposomes have been widely used as potential delivery mechanisms of various compounds mainly due to their high degree of consistency and wide variation in structure and structure. The lipid components of liposomes are mainly the phosphatidylcholine found in eggs or soy lecithins. [25]

Liposomes are a feature of biphasica that enables them to act as carriers of both lipophilic and hydrophilic drugs. It has been observed that drug molecules are found separately in the liposomal region and depending on their signs of dissolving and dissociation, exhibiting different binding and liberating properties. Lipophilic drugs are usually bound almost entirely to lipid bilayers of liposomes and as they do not dissolve well in water, problems such as loss of the drug trapped in the cell are rarely encountered.

Hydrophilic drugs may be trapped inside the strong particles of liposomes or found in the outer water phase. It is noteworthy that the percentage of encapsulation of hydrophilic compounds by liposomes depends on the formation of a bilayer repair process [26, 27]

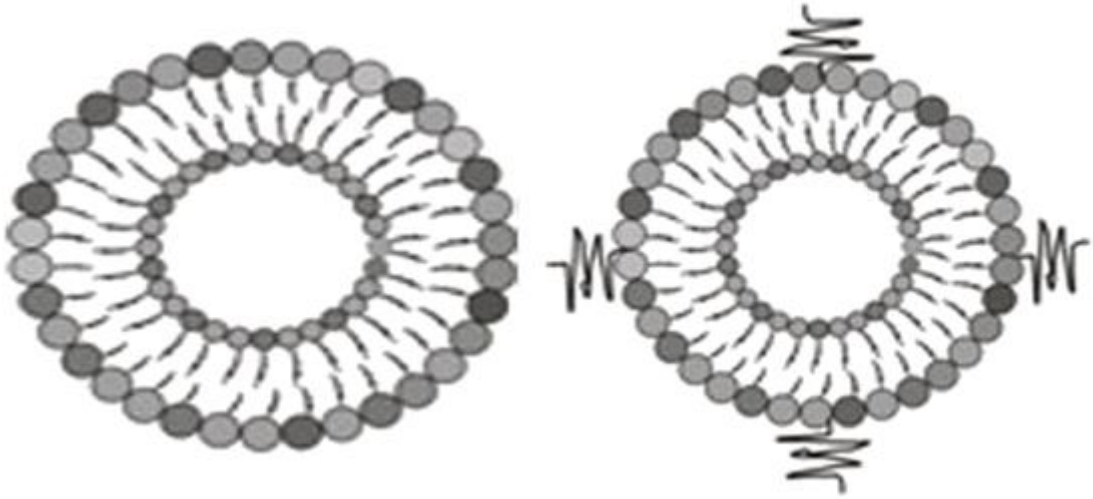

Figure 2: Schematic representation of liposome-based systems. (a) Conventional liposomes. (b) Stealth liposome coated with a polymeric conjugate such as PEG

Conventional Liposomes **/Normal Liposomes**. A common liposome-based technology is the first generation of liposome to be used in drug applications [28]. The most common liposome formation is mainly natural phospholipids or lipids such as 1, 2-distearoryl-sn-glycero-3-phosphatidyl choline (DSPC), sphingomyelin, egg phosphatidylcholine, and monosialoganglioside. Since these structures are composed of only phospholipids, the liposomal structure has met with many challenges; another major factor is plasma instability, which leads to shorter blood circulation half-life. Liposomes that are badly charged or fined are reported to be short-lived, toxic, and quickly removed from distribution. Several other efforts have been made to overcome these challenges, especially in the use of lipid membranes. One of the efforts focused on the use of cholesterol. The addition of cholesterol to normal formulation reduces the rapid release of plasma bioactive compounds. In addition, studies by Tran and colleagues have shown liposome stability after the introduction of lead-based lipids such as cholesterol and 1, 2-dioleoyl-snglycero-3-phosphoethanolamine (DOPE). Harashimaandco staff have shown that phagocytosis of liposomes is caused by the size of the liposome formation. Large or multilamellar liposomes with a size range of 500-5000 nm were the first to be released in the system distribution .Nanosised liposomes or small uni lamellar vesicles with an assist range of 20-50 nm were developed only later. The following drugs: Ambisone, Myocet, Daunoxome, and Daunorubicin have received clinical approval using standard liposome technology. Although it is reported that small unilamilar liposomes have the potential to reduce microphage acquisition, adequate drug interventions remain a major problem. On the basis of this study, the success of cholesterol and other phospholipids did not completely overcome the major challenges.

Stealth Liposomes. Stealth liposome technology is one of the most widely used liposome-based systems for the delivery of active molecules. This strategy is designed to overcome many of the challenges posed by the integration of all iposome technologies such as inability to avoid antibodies, toxins due to charged tubes, low blood circulation half-life, and strong Stealth liposome stability was easily achieved by altering liposome membranes engineering hydrophilic polymer conjugates.

Liposomes Building Activities

Lipids that are capable of forming liposomes show the dual chemical nature. Their hydrophilic head groups and their hydrophobic acyl chains.It is estimated that each of the Zwitter ionic head groups of Phosphatidyl choline has an order of 15 water molecules that are loosely attached to it, which means they end up liking the water phase. Hydrocarbon fatty acid chains on the other hand are more selective for each company than H2O. This can be understood by considering CMC for PC. CMC's Dipalmitoyl PC was found to be 10 M in water, which is a small number indicating the thermal selectivity of this molecule in a hydrophobic environment such as that found in a micelle or bilayer component. Free transfer power from water In micelle is 15.3K cal / mol for Dipalmitoyl PC and 13.0K cal / mol for Dimyristoyl PC These results clearly indicate the thermodynamic basis of the bilayer assembly called hydrophobic effect. The free energy transfer between the water and the hydrophobic environment means a warm selection of the lipids that normally combine in the two states, including water as much as possible from the hydrophobic core to achieve the lowest energy, hence the highest stability of the composite structure.

Purification of Liposomes

Liposomes are usually purified by gel filtration chromatography, Dialysis and centrifugation. In chromatographic classification, Sephadex-50 is widely used. With dialysis the empty fiber dialysis shell can be used. By centrifugation, SUVs with standard salt can be separated by centrifuging at 200000 g, 10-20 hours. MLVs were separated by centrifuging at 100000 g for less than one hour.

Evaluation of Liposomes [19-23]

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, phase behaviour and drug release profile.
- **Chemical characterization** includes those studies which establish the purity and potency of various lipophillic constituents
- **Biological characterization** parameters are helpful in establishing the safety and suitability of formulation for therapeutic application.

Some of parameters are:

Vesicle Condition and Lamellarity: Vesicle Condition can be assessed using Electron Microscopic Techniques. Lamellarity of vesicles eg the number of particles extracted from liposomes is determined using Freeze-Fracture Electron Microscopy and P-31 Nuclear Magnetic Resosance Analysis.

Vesicle size and size distribution: Various techniques are described in the literature by determining size and size distribution. These include Light Microscopy, Fluorescent Microscopy, Electron Microscopy (specifically Transmission Electron Microscopy), Laser light scaterring Photon correlation Spectroscopy, Field Flow fractionation, Gel permeation and Gel Exclusion. The most direct way to determine the size of a liposome is Electron Microscopy because it allows one to look at each liposome and get direct information about the profile of liposome people throughout the range of sizes. Unfortunately, it takes a lot of time and requires equipment that may not always be available to supply it. In contrast, the laser light distribution method is very simple and quick to perform but has the problem of balancing the properties between the mass of liposomes. All of these methods require expensive equipment. If only a limited sense of size is required when chromatography techniques for gel extraction are recommended, because the only costs incurred are those for buffers and gel materials. Another newly developed process known as atomic force microscopy has been used to study liposome morphology, size and toughness. Most of the methods used for size, shape and distribution of analysis can be grouped into various categories namely microscopic, diffraction, scattering, and hydrodynamic techniques.

Small strategies

Negative Stain TEM: Electron Microscopic methods used to test liposome formation and size are mainly TEM bad spots and Electron Microscopy Scan. This last process is less preferred. Negative Stain Electron Microscopy detects bright spots behind a dark background (hence the name bad spot). The negative stains used in TEM analysis were ammonium molybdate or Phosphotungstic acid (PTA) or uranyl acetate. Both PTA and ammonium molybdate are anionic by nature while uranyl acetate is naturally cationic.

Diversity and distribution skills: Laser Light Distribution: Photon correlation spectroscopy (PCS) is a time-dependent analysis of the intensity of laser light intensity dispersed due to the movement of Brown particles in solution / suspension. Since smaller particles disperse much faster than larger particles, the degree of diffusion of light differs accordingly. Therefore, the amount of translation separation (D) can be measured, which can also be used to determine the hydrodynamic radius (Rh) ratio of particles using the Stoke-Einstein figure. By using this method one can measure the particles at a distance of about 3nm.

Hydrodynamic Strategies: This process includes Gel Permeation and Ultracentrifuge. Chromatography extraction in large pure gels was introduced to distinguish SUVs from radial MLVs. However, large vesicles of 1-3μm in size often fail to penetrate the gel and are stored over the column. A small chromatography program using agarose beads has been introduced as a modest, quick process to detect a disproportionate amount of liposome correction size. However, it has not been reported whether this procedure was effective in blocking the pores of agarose gel as is the case with most standard chromatography.

Effectiveness of Encapsulation and Captured Volume: This determines the amount and rate of dissolving of soluble solvents in an area with liquid liposomes.

Efficiency of Encapsulation: defines the percentage of aqueous phase which is why the percentage of soluble water that is trapped during liposomes is usually expressed as% entrapment / mg lipid. The effectiveness of Encapsulation has been tested using 2 techniques including the minicolumn centrifugation method and the Protamine synthesis method Minicolumn centrifugation is usually used both for the purpose of purification and separation of liposomes on a small scale. With a small centrifugation column, the hydrated gel is filled into a 1ml syringe without the plunger connected with a filter whatman GF / B. This barrel rests in a centrifuge tube. The tube was spun at 2000 rpm for 3 minutes. to remove excess saline solution from the gel. After centrifugation the gel column should be dried and removed from the side of the barrel. The elute salt is then removed from the collection tube. Liposome suspension (0.2ml) is used to lower the top of the gel bed, and the column is spun at 2000 rpm for 3 minutes. extracting an empty volume containing liposomes into a centrifugation tube. The elute is removed and set aside for testing. The Protamine synthesis method can be used for neutral and poorly charged liposomes.

Captured volume: It is an important parameter that controls the morphology of vesicles. Captured or internal volume blocked fluid volume by the quantity of each unit of lipids. This can vary from 0.5 to 30 microlitre / micro mol. A variety of materials including clear liquid, markers that use markers and fluorescent markers are used to determine the stuck / internal volume.

Phase Response and Temporary Behavior: liposomes and lipid bilayers exhibit various physiological mutations

that are studied for their role in drug synthesis or in reactivating the composite liposomal component with target cell. The understanding of phase transition and phase transition and the phospholipids particles are important both in the synthesis and exploitation of liposomes since liposomal cell membrane behavior determines structures such as durability, fusion, fusion, and protein binding. Phase transfer was assessed using electron microscopy intensity. They are confirmed by a high degree of understanding by colorimeter scanning (DSC) scans.

Drug Dissociation: The mechanism of drug extraction in liposomes can be tested using vitro diffusion cell activation. Liposome-based formulations can be assisted by using in vitro tests to predict pharmacokinetics and drug availability before using costly and time-consuming costs in vivo studies. Dissolved drug extraction in buffer and plasma was established as a predictor of pharmacokinetic activity of liposomal formation and another trial that determined intracellular drug release caused by liposome damage in the presence of mouse-liver lysosome lysate was used to test the findings.

Setting Public Signs 15-20

Two types of identification

1. Direction for inactivity: For the purpose of random identification, such liposomes are often shown to be quickly removed from the bloodstream and taken up by the RES in the liver spleen. Macrophage energy can therefore be used when liposomes are targeted at macrophages. This was demonstrated by the successful delivery of liposomal antimicrobial agents to macrophages. Liposomes are now used to target antigens in macrophages as a first step in the immune response. Eg. In mice iv administration of liposomal antigen elevated the phagocyte response mediated response when anti-liposome associated antigen failed to detect antibody response.

2. Effective direction: The first requirement for identifying targeting agents located in the liposomal field such as communication with the target is, the receptor is set as a plug and socket device. The liposome is physically designed so that part of the lipophilic component is attached to the membrane during the formation of the membrane. The hydrophilic component on the surface of the liposome, where the targeting agent must be held in the appropriate place to bind to the receptor on the surface of the cell. Effective guidance can be provided through use.

Immuno liposomes: These are regular or stealth liposomes with attached Antibodies or other recognition sequences [e.g. Carbohydrate breakers such as glycoprotein] A binding antibody, directs the liposome to specific antigens found in a particular cell. Glycoprotein or Glycolipid cell surface component plays a role in cell acceptance and adhesion.

Magnetic liposomes: Contains magnetic iron oxide. These liposomes can be directed by an external magnetic field that vibrates at their delivery points.

Temperature or heat-sensitive liposomes: They are designed in such a way that their temperature changes just above body temperature. After accessing the site, the burning area without removing the tree.

3. Applications

- Cancer chemotherapy
- 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

4. Conclusion

This review addresses the use of Liposomes as biological carriers of therapeutic agents, such as drugs, enzymes, and peptides, as well as mainly used drug loading methods for formulations, and further potential applications of the carrier system. The use of liposomes helps in a safe and effective delivery of various drugs for passive and active targeting. The same concept also can be extended to the delivery of biopharmaceuticals. In near future, liposomes based delivery system with their ability to provide controlled and site specific drug delivery will revolutionize disease management. For the present, it is concluded that liposomes carriers are “golden eggs in novel drug delivery systems” considering their tremendous potential.

References

[1] Bangham AD, Liposomes, (Ed. I), Marcel Dekker, New York, 1983, pp 1-26.
[2] Hiremath PS, Soppimath KS, Betageri GV (2009) Proliposomes of exemestane for improved oral delivery: formulation and in vitro evaluation using PAMPA, Caco-2 and rat intestine. Int J pharm 380: 96-104.
[3] V. P. Torchilin, “Recent advances with liposomes as pharmaceutical carriers,” *Nature Reviews Drug Discovery*, vol. 4, no.2, pp. 145–160, 2005.
[4] AD and Horne RW. Negative staining of phospholipids and their structural modification by surface-active agents as observed in the electron microscope. J Mol Biol (1964) 12: 660-668.
[5] Yadav A, Murthy MS, Shete AS, Sakhare S (2011) Stability aspects of liposomes. Ind J Pha Edu 45: 402-413
[6] Chanda H, Das P, et al “Development and evaluation of liposomes of fluconazole” *JPBMS*, 2011, 5 (27): 1-9.
[7] Vyas, S.P., Khar, R.K. In Vyas, S.P., Khar, R.K. (Eds.), Targeted and controlled drug delivery: Novel carrier systems. CBS publishers. 2002; 173-248.
[8] Lasic, D.D. The mechanism of vesicle formation. Biochem J. 1988; 256: 1-11.

[9] Alving C.R. Macrophages, as targets for delivery of liposome encapsulated antimicrobial agents. Adv Drug Delivery Rev, (1998);2.
[10] C. J. Chapman Allison, A.C., Gregoriadis, G, 1974. Liposomes as immunological adjuvant. Nature 252, 252.
[11] Deamer, D. and Uster, P., Liposome preparation methods and monitoring liposome fusion. In: Baserga, R., Croce, C. and Royeza, G. (Eds.), Introduction of Macromolecules into viable Mammalian Cells, Alan R. Liss, New York, 1980, pp. 205220.
[12] de Marie, S., Janknegt, R., Bakker-Woudenberg, I.A.J.M., 1994. Clinical use of liposomal and lipid-complexed amphotericin B. J. Antimicrob. Chemother. 33, 907-916.
[13] D.J.A Crommelin. Liposomes, Lasic, D.D., Papahadjopoulos, D., 1995. Liposomesre visited. Science 267, 1275 1276.
[14] Emanuel, N., Kedar, E., Bolotin, E.M., Smorodinsky, N.I., Barenholz, Y., 1996. Preparation and characterization of doxorubicin-loaded sterically stabilized immunoliposomes. Pharm. Res. 13, 352-359.
[15] 1996. Preparation and characterization ofdoxorubicin-loaded sterically stabilized immunoliposomes. Pharm. Res. 13, 352-359.
[16] Felgner, J.H., Kumar, R., Sridhar, C.N., Wheeler, C.J., Tsai, Y.J., Border, R., Ramsey, P., Martin, M., Feigner, P.L., 1994. Enhanced gene delivery and mechanism studies witha novel series of cationic lipid formulations. J. Biol. Chem.269, 2550-2561.
[17] H.A.H Rongen, A. Bult and W.P van Bennekom. J. Immuno. Methods, (1997)204:105-133.
[18] New, R.R.C., Preparation of liposomes. In: New, R.R.C.(Ed.), Lipsomes: a practical approach, IRL Press, Oxford, 1990, pp. 33104.
[19] Jr. F. Szoka and D. Papahadjopoulos. Proc. Natl. Acad. Sci. USA, (1978) 60:4194-4198.
[20] Jain N.K. Controlled and Novel Drug Delivery. CBS Publisher, Page no. 304-326.
[21] Kersten, G.F.A., Crommelin, D.J.A., 1995. Liposomes and ISCOMS as vaccine formulations. Biochim. Biophys. Acta 1241, 117-138.
[22] K. Horton. Disertation for degree of Advanced Studies in Chemical Engineering, Universitat Rovira I Virgili, 2003.
[23] Remington. The Science and Practice of Pharmacy. Volume I, 21st Edition, B.I Publishers Pvt Ltd, Page no.314-316.
[24] A. D. Bangham, M. W. Hill, and G. A. Miller, “Preparation and use of liposomes as. models of biological membranes, ” in *Methods in Membrane Biology*, vol. 1, pp. 61–68, Plenum Press, New York, NY, USA, 1974.
[25] J. Y. Fang, T. L. Hwang, and Y. L. Huang, “Liposomes as vehicles for enhancing drug delivery via skin routes, ” *Current Nanoscience*, vol. 2, no. 1, pp. 55–70, 2006.
[26] M. Manconi, C. Sinico, D. Valenti, G. Loy, and A. M. Fadda, “Niosomes as carriers for tretinoin. I. Preparation and properties, ” *International Journal of Pharmaceutics*, vol. 234, 1-2, pp. 237–248, 2002.
[27] M. Johnsson and K. Edwards, “Liposomes, disks, and spherical micelles: aggregate structure in mixtures of gel phase phosphatidylcholines and poly (ethylene glycol)- phospholipids, ” *Biophysical Journal*, vol. 85, no. 6, pp. 3839– 3847, 2003.
[28] M. L. Immordino, F. Dosio, and L. Cattel, “Stealth liposomes: review of the basic science, rationale, and clinical applications, existing and potential, ” *International Journal of Nanomedicine*, vol. 1, no. 3, pp. 297–315, 2006