

A REVIEW ON “LIPOSOMAL DRUG DELIVERY SYSTEM”

Ketul Patel¹, Krishna Kalsara², Dr. Umesh Updhayay³

¹Student, ²Asst.Professor, ³Principal

Sigma Institute of Pharmacy, Bakrol Vadodara, 390019, Gujarat, India.

Corresponding Author's Email ID: ketulpatel308@gmail.com

Abstract

Self-forming encapsulated lipid bilayers that formed upon hydration led to the discovery of liposomes or lipid vesicles, and liposome drug delivery methods have been crucial in the development of powerful medications that have improved treatments. In recent years, liposome formulations have been developed with the specific goals of lowering toxicity and raising accumulation at the target region. Inhibiting the rapid clearance of liposomes by regulating particle size, charge, and surface hydration is one of a number of novel liposome manufacturing techniques based on lipid drug interaction and liposome disposition mechanism. The majority of therapeutic uses of liposomal drug delivery target tissue, either with or without target recognition molecules expressed on lipid membrane. Regarding physical, chemical, and biological properties, the liposomes are characterised. Liposome size is another important factor to consider.

Introduction:

The vesicular system known as a liposome is created when phospholipids are disseminated in water and spontaneously form a closed structure with an interior aqueous environment enclosed by phospholipid bilayer membranes. Liposomes are the small, spherical vesicles that can be made from membrane proteins, sphingolipids, glycolipids, long-chain fatty acids, cholesterol, and non-toxic surfactants. Liposomes are a type of drug delivery system that may carry a wide range of materials, including plasmids, proteins, nucleotides, and tiny drug molecules.

A.D. Bangham made the discovery of liposomes over 40 years ago, and they have since evolved into a useful tool in biology, biochemistry, and medicine. In its aqueous compartment, liposomes have been utilised as carriers to transport a wide range of chemicals since the 1960s. Size, content, charge, and lamellarity of liposomes can be modified during formulation and processing. Anti-tumor medications and antifungal medicines have both been commercialised in liposomal form to far.

The clinical promise of liposomes as a delivery system for replacement therapy in cases with lysosomal enzyme hereditary deficits was originally shown in the 1970s. Longer liposome circulation periods following intravenous administration as a result of significant advancements in liposome stability during the 1970s and 1980s improved liposome bio-distribution. To increase the therapeutic index, the significant anti-tumor medication doxorubicin was developed as a liposome in the 1980s.

There are several mechanisms by which liposomes act within and outside the body which are as follows:

- 1- The content of the liposome is released into the cell when it adheres to the cellular membrane and seems to merge with it.
- 2- Sometimes the cell absorbs them, incorporating their phospholipids into the cell membrane to release the medication that was trapped inside.
- 3- The lysosomes, which are organelles, interact with the phospholipid walls of the liposomes in the phagocyte cell, releasing the active medicinal ingredients. [1]

When used as drug carriers in different drug delivery systems, liposomes are small sealed vesicular structures that can encapsulate both hydrophilic and hydrophobic molecules.

By shielding a drug from the biological environment and limiting the drug's impact to the target cells, liposomes boost a medicine's therapeutic activity. These serve as delivery systems for pharmaceutical medications and nutrition.

The Greek words lipo and soma are the origin of the word liposome. Soma and lipo both refer to the body. The discovery of liposomes was made by Alec Douglas Bangham and colleagues. When phosphatidyl choline molecules were scattered in water, Bangham discovered that closed bilayer structures were produced. Weismann gave these entities the name "Liposomes".

A solution of lipids in an organic solvent is dried onto the wall of a flask or tube in the simplest method for creating drug-containing liposomes. The lipid is then hydrated and dispersed by adding buffer and vortexing. If the drug is water soluble, it can be added to the buffer; if it is hydrophobic, it can be added to the organic solvent. [2]

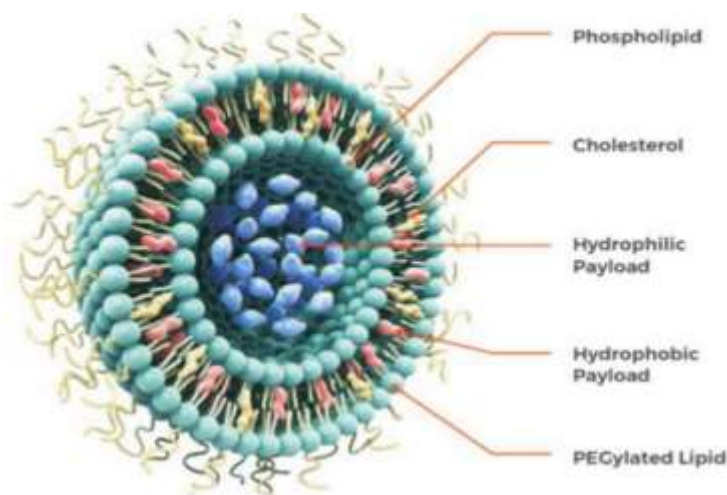


Figure: 1 structure of liposome [2]

As a new drug delivery system (NDDS), liposomes are bilayer-filled vesicular structures that form when phospholipids are disseminated in water. They are microscopic vesicles that completely surround an aqueous volume with a membrane made of lipid bilayers. The goal of NDDS is to give the medication at a pace determined by the body's demands during the course of treatment and to target the site of action. Liposomes, also known as vesicles, are colloidal spheres made of cholesterol, non-toxic surfactants, sphingolipids, glycolipids, long-chain fatty acids, even membrane proteins, and medicinal molecules. Size, composition, and charge are different. And drug carrier loaded with a range of substances, including proteins, nucleotides, plasmids, tiny drug molecules, etc. To increase their therapeutic index, only a small number of medicines are created as liposomes. As a result, several vesicular drug delivery systems, including liposomes, niosomes, transfersomes, and pharmacosomes, are being developed.

The first description of swollen phospholipid systems was published in 1965 by certain researchers. A variety of enclosed Phospholipid bilayer structures made up of single bilayers, initially known as "bangosomes" and then "liposomes," were described within a short period of time. The idea that liposomes can entrap pharmaceuticals and be employed as drug delivery devices was first discovered by early pioneers such as Gregoriadis and Perrie. The anti-cancer medication cytosine arabinoside was first used to demonstrate in vivo activity of liposome-entrapped medicines in animal models by showing measurable increases in the life periods of mice with L1210 leukaemia. Since then, it has been used frequently as a "model system" to examine how various liposome properties affect therapeutic results. [3]

Properties:

- Drug loading and control of drug release rate
- Overcoming the rapid clearance of liposomes
- Intracellular delivery of drugs
- Receptor-mediated endocytosis of ligand-targeted liposomes
- Triggered release
- Delivery of nucleic acids and DNA

Mechanism of liposome formation:

Phospholipids create liposomes (amphiphilic molecules Having a hydrophilic head and hydrophobic tail). The hydrophobic portion is made up of two fatty acid chains with 10–24 carbon atoms and 0–6 double bonds in each chain, whereas the hydrophilic portion is primarily phosphoric acid coupled to a water-soluble molecule. When they are spread in aqueous medium, they position themselves so that the polar head group faces outwardly the aqueous region and the fatty acid groups face each other, forming spherical, vesicle-like structures known as liposomes. This causes them to create lamellar sheets. Along with the non-polar portion's shielding, the polar fraction continues to be in contact with the aqueous layer. When energy is added, such as through sonication, shaking, heating, homogenization, etc., phospholipids are hydrated in water. To reach a thermodynamic equilibrium in the aqueous phase, bilayered vesicles are formed as a result of the hydrophilic/hydrophobic interactions between lipid-lipid and lipid-water molecules. As the primary constituents of the cell membrane, phospholipids have great biocompatibility and amphiphilic characteristics. Its amphiphilicity gives it the ability to self-assemble and has emulsifying and wetting properties. When phospholipids are introduced to an aqueous environment, they self-assemble, creating a variety of forms with unique properties depending on the environment. For instance, phospholipids naturally have a propensity to form liposomes, which are useful as drug targeting molecules. Additionally, they have effective emulsifying properties that stabilise emulsions. This can be utilised as a coating for medications to give hydrophobic pharmaceuticals hydrophilicity in addition to their wetting properties. These three characteristics are used in different medication designs. Various

phospholipids can be found due to variations in aliphatic chains and alcohols. Additionally, various phospholipid sources enhance various phospholipid varieties. [4]

The reason for bilayer formation includes:

- Folding into tight concentric vesicles can limit the undesirable interactions between the hydrophilic and hydrophobic phases.
- The development of massive vesicles reduces the significant free energy difference between a hydrophilic and a hydrophobic environment. Because of their highest stability and lowest surface tension, spherical structures. Hence there is formed by vesicles, which has the highest degree of self-assembly stability.

The liposomes are more stable at the lamellar phase when the electrostatic interaction between the fatty acid carboxyl ions and repulsion is better at neutral pH. Fatty acid carboxyl groups are protonated at acidic pH, which causes the HII phase to develop. This results in unstable liposomes that are simple to cluster, fuse, and release their contents from. Thus, pH Sensitive liposomes are created for various medication delivery applications.

The temperature at which liposomes shift from their gel phase to their liquid crystalline phase is known as their "transition temperature" (TC).

At the crystalline phase, the enclosed carpets are released. Only at temperatures above the transition temperature can liposomes develop. The transition temperature of a liposome made of pure lipid is 41.4 °C, however lipids derived from natural sources, like lecithin, have a wider transition temperature range. The Krafft point of lecithin, which is 58°C, is the top limit of temperature for liposome formation, hence a temperature range between 41.4°C and 58°C is optimum for the production of thermosensitive liposomes. While the phospholipid content affects the size of the liposome vesicles.

The degree of fatty acid saturation plays a significant effect in determining how permeable lipid bilayers are to particular compounds (selective permeability). Because C-H bonds have more energy than C=C bonds, saturated fats have higher chemical energies than unsaturated fats. Other molecules can fit through the gaps created by the double bonds in its densely packed tails. As a result, lipid bilayers with a high proportion of unsaturated fatty acids have more gaps and permeability than bilayers with a lower proportion of unsaturated fatty acids. Typically, natural phospholipids contain unsaturated fatty acids. The gel liquid crystalline phase is influenced by the lipid chain's length and degree of unsaturation (transition temperature). Longer tailed phospholipids likely to form liposomes, while shorter, more compact tailed phospholipids tend to form micelles. By stabilising phosphatidylethanolamine into a bilayer using antibody derivatives of fatty acids like palmitic acid, liposomes that are targeted to certain tissues can be created. The concentration of immunoglobulin molecules at the contact point causes bilayers to become unstable after attaching to the target's cell surface. Finally, this site releases liposomal content. Targeting specific sub-cellular locations is currently experimental and in the in vitro research stage. For instance, the polymer (Rh123)-PEG-DOPE (Rhodamine 123-Polyethylene glycol-1,2-dioleoyl-sn-glycero-3-phosphoethanolamine), which contains the mitochondriotropic dye rhodamine, can be used to target mitochondria. Using rhodamine-123-conjugated polymer to modify the liposomal surface improves mitochondrial targeting. [5]

Classification of Liposomes:

Size and the number of bilayers in a liposome can be used to classify them. They are divided into three different categories: multilamellar vesicles (MLV), large unilamellar vesicles (LUV), and small unilamellar vesicles (SUV). They are divided into five categories based on their chemical makeup: conventional liposomes (CL), pH-sensitive liposomes, cationic liposomes, long-circulating liposomes (LCL), and immuno-liposomes. Reverse phase evaporation vesicles (REV), French press vesicles (FPV), and ether injection vesicles are the three types of preparations that they fall under (EIV).

Stability of Liposomes:

The Stability of the liposomes, which includes production processes, storage facilities, and delivery methods, controls the therapeutic efficacy of the drug molecule. During the course of development and storage, a stable dosage form preserves the active molecule's chemical and physical integrity. Evaluation of the product's physical, chemical, and microbiological parameters is part of the stability research with designing, along with the assurance of the product's integrity throughout storage.

Physical stability:

The vesicles produced by the processes of liposomal production have various sizes. Vesicles have a tendency to group together and become larger during storage in order to reach a thermodynamically advantageous condition. Leakage of the medication from the vesicles during storage can result in its fusion and breakdown. The liposomal medicinal product's physical stability is compromised as a result. As a result, the vesicle architecture and size distribution are crucial factors in determining the physical stability. Light scattering and electron microscopy are just two of the techniques used to determine the vesicle's size and form from the outside. Although cholesterol strengthens the lipid barrier, its concentration in the liposome structure cannot exceed

50%. It is essential for the preservation and stabilisation of the bioactive molecule at the liposome's centre. By preventing excessive unsaturation in the phospholipids during simple peroxidation and by controlling the pH levels, physical stability can be preserved. They must be kept in a 4°C environment without freezing or exposure to light.

Chemical stability:

Chemically, phospholipids are unsaturated fatty acids that are vulnerable to oxidation and hydrolysis, which could change how stable a medicinal product is. A liposomal formulation is also significantly influenced by pH, ionic strength, solvent system, and buffered species. Oxidation As a result of the production of free radicals during the oxidation process, degradation entails the synthesis of cyclic peroxides and hydroxyperoxidases. By shielding them from light, adding anti-oxidants like A-tocopherol or butylated hydroxyl toluene (BHT), manufacturing the product in an inert environment (the presence of nitrogen or argon), or adding EDTA to eliminate trace heavy metals, liposomes can be protected from oxidative deterioration. The glycerol moiety of phospholipids' ester bond at the C-4 position undergoes hydrolysis. results in the lyso-phosphatidylcholine being produced (lysoPC). The liposomal contents' permeability will be improved as a result. Controlling the lysoPC limit within the drug's lysosomal product is therefore crucial. It can be done by combining phosphatidylcholine and lysoPC free liposomes. [6]

Mechanism of Action of Liposomes:

An area of aqueous solution enclosed in a hydrophobic membrane makes up a liposome. Due to the ease with which hydrophobic substances can be dissolved into the lipid membranes, liposomes are capable of transporting both hydrophilic and hydrophobic molecules. While the drug's physiochemical properties and lipid makeup will determine its location and spread. The lipid bilayers combine with other bilayers of the cell (cell membrane) to release the liposomal content, which then transports the required drug molecules to the site of action. [7]

Steps involved in liposome action of drug delivery:

- 1. Adsorption:** Liposomes come into touch with cell membranes through a process known as adsorption.
- 2. Endocytosis:** Liposomes adhere to the cell surface membrane, are engulfed by the cell, and are then internalised by the liposomes.
- 3. Fusion:** Direct transport of liposomal contents into the cytoplasm is achieved via lateral diffusion and lipid intermixing of the lipid bilayers of liposomes with the lipoidal cell membrane.
- 4. Lipid exchange:** Lipid transfer proteins in the cell membrane are able to recognise liposomes and initiate lipid exchange because the lipid membrane of liposomes and the phospholipids that make up cell membranes are comparable. [8]

For example, when it comes to cancer cells, which need to ingest a lot of fat to meet their demand for quick development, they see the anti-cancer drug-loaded liposomes as a potential source of nutrition. They are absorbed when a liposome targets them. Cancer cells are killed by the anti-cancer medications as soon as they are released from the liposome and reach the location. [9]

Therapeutic Applications of Liposomes:

In comparison to current formulations, liposomes offer greater therapeutic efficacy and safety. The following are some of the main therapeutic uses for liposomes in medication delivery:

Site-avoidance delivery:

The limited therapeutic index of anti-cancer medications is what causes their cytotoxicity to normal tissues (TI). In these situations, reducing the amount of medicine delivered to normal cells by encapsulating the drug in liposomes can enhance the TI. Doxorubicin, for instance, has a serious side effect known as cardiac toxicity; however, when it was developed as liposomes, the toxicity was decreased without affecting the therapeutic activity. [10]

Site specific targeting:

Site-specific targeting can increase drug delivery to the desired (diseased) Site while minimising drug exposure to healthy tissues. Long circulating Immunoliposomes have a stronger ability to recognise and bind to target cells after systemic delivery. When Muramyl peptide derivatives were made into liposomes and given systemically, for instance, there was an increased tumoricidal activity of monocytes in patients with recurrent osteosarcoma. [11]

Intracellular drug delivery:

LDDS can be used to increase the delivery of prospective medications to the cytosol (where drug receptors are located). Normal cell uptake of N-(phosphonacetyl)-L-aspartate (PALA) is subpar. In comparison to free medicines, these substances demonstrated increased action against ovarian carcinoma cell lines when encapsulated within liposomes. [12]

Sustained release drug delivery:

Liposomes offer sustained release of target pharmaceuticals since the best therapeutic efficacy requires a prolonged plasma concentration at therapeutic levels. For prolonged release and optimised medication release rate in vivo, drugs like cytosine arabinoside can be encapsulated in liposomes. [13]

Intraperitoneal administration:

The medicine can be injected into the intra-peritoneal cavity (ip cavity) to treat tumours that form there. However, the quick removal of the medications from the ip cavity minimises their presence at the sick spot. However, liposomal encapsulated medications can deliver the maximal amount of medication to the target site for an extended period of time and have a lower clearance rate than free medications. [14]

Immunological adjuvants in vaccines:

By encasing adjuvants, liposomes can be employed to improve the immune response. Depending on the lipophilicity of the antigens, the liposome can either incorporate the antigens within the bilayers or accommodate them in the aqueous cavity. Initially utilised as immunological adjuvants, liposomes were used to boost the immune response to diphtheria toxoid.

In addition to PED coating, stealth liposomes contain a small number of biological species as a ligand to enable binding with tailored expression on the drug delivery site (targeted site). These targeting ligands may be monoclonal antibodies, particular antigens, or vitamins (creating an immuno-liposome), but they must be readily available. Drugs that are naturally toxic may be less hazardous overall if they are administered to the affected tissues or locations. [15]

Maleylated bovine serum albumin (MBSA) and O-steroyl amylopectin are two ligands that are utilised to target the lungs in the treatment of tuberculosis. Transfersomes, a subclass of liposomes utilised for transdermal substance distribution, are extremely malleable vesicles (non-invasive method). Liposomes can be used to provide the anticancer medications doxorubicin (Doxil) and dunorubicin. Since cancer cells contain excessively expressed folate and transferrin receptors, liposomes are utilised in cancer therapy, making transferrin and folic acid appropriate ligands. Peptides and antibodies that target VEGF, VCAM, matrix metalloproteases (MMPs), Integrins, etc. are additional ligands utilised in cancer therapy. Recent Phase I/II research assessing the efficacy and safety of a novel neoadjuvant combination therapy combining hyperthermia, pegylated liposomal doxorubicin, and paclitaxel to treat locally advanced breast cancer. a phase II clinical research using carboplatin and pegylated liposomal doxorubicin in Japanese patients with platinum-sensitive primary peritoneal, fallopian tube, or recurrent ovarian cancer. Treatment for people with platinum-sensitive recurrent ovarian cancer involves its combination chemotherapy. Phase II/III human clinical trials are currently being conducted on the thermosensitive liposomal formulation ThermoDox® (Celsion Corporation, Lawrenceville, NJ), which contains lysophosphatidylcholine and is used to treat a number of cancers, including primary liver cancer, recurrent chest wall breast cancer, colorectal, pancreatic, and metastatic liver cancer. In order to treat cancer, lipoplatin was recently produced using cisplatin as a carrier. High cytotoxic T lymphocyte (CTL) responses have been seen when escheriosomes (a type of liposome) made from polar lipids derived from *Escherichia coli* are used to transfer their encapsulated molecules directly into the cytoplasm of APCs (Antigen Presenting Cells). [16]

Advantages of liposomes as a drug delivery system for antimicrobials are:[17]

- Improvement and control over pharmacokinetics and Pharmacodynamics
- Decreased toxicity
- Enhanced drug activity against intracellular pathogens
- Liposomes used as target selective
- Enhanced activity against extracellular pathogens

Improvement of pharmacokinetics and pharmacodynamics:

When administered without a drug delivery system, many medications call for regular doses. While liposomes can be designed to circulate for a long time in the body, maintaining the drug's consistent level for a longer period of time. The fluidity of the membrane, the size of the liposomes (smaller liposomes circulate longer), and the charge on the liposomes are all factors that affect the duration of circulation (neutral liposomes have a long circulation time). Some medications are shielded by liposomes from immune system and chemical attack as well as from the effects of enzymes. Because of the sustained drug levels provided by liposomes, especially when so-called "stealth" liposomes are utilised, toxicity is reduced and dose is reduced. [18]

Liposomes used as target selective:

The composition and structure of cell membranes play a significant role in how cells react. This can be used to target drugs by getting particular cells to respond to and take up the liposomes. To target a particular medicine, the membrane surface structure can be altered. This can be done by altering the membrane's charge or by including particular proteins, antibodies, or immunoglobulins. It raises liposomes' affinity for particular cells. Creating liposomes that release a medicine only when exposed to a certain pH or temperature is one way to experiment with liposomes. Liposomes can be designed to only interact with a certain type of creature. Site avoidance therapy, also known as liposome site avoidance, aims to reduce toxicity by making liposomes avoid specific regions. [19]

Enhanced drug activity against intracellular pathogens:

For many years, different liposome formulations have been investigated against a wide range of intracellular parasites and other infections. As the macrophages that are infected with *Leishmania* actively eliminate them in

vivo, it has been utilised to treat leishmaniasis with considerable effectiveness. In the treatment of Leishmania in hamsters, the modified encapsulated medication is 700 times more effective than the free drug. [20]

Other investigations that were conducted after this one in order to corroborate these results with regard to leishmaniasis. Anti-tuberculosis medications including clarithromycin, isoniazid, and rifampicin have all shown much higher efficacy when compared to the free version of the medication in tests. Other investigations revealed decreased tissue toxicity. With medications that are already quite toxic, such as those used to treat *Trypanosoma brucei* and *Trypanosoma cruzi*, this reduced toxicity is crucial. The liposomes did have a protective effect against the toxicity of the medications used in some situations, even though the in Vivo impact against the parasite is not noticeably better than the free Drug. [21]

Anti-malarial medications are mostly enclosed in liposomes to reduce side effects, provide sustained release, and safeguard the medication against degradation. In a study, encapsulating liposomes boosted the maximum plasma concentration more quickly. [22] It takes less time for the medication concentration to rise to its highest point. In a significant experiment, the bioavailability of arteether in liposomes was close to 98%, while that of arteether in suspension was only about 32%. Chloroquine and Primaquine are two antimalarials that have been utilised in the past and employed for trapping in liposomes. [23] It is evident that liposomes can be a valuable tool in the fight against malaria. Liposomes can, in some circumstances, defeat bacterial resistance, as has been demonstrated. According to other research, the dosage needed to effectively cure *Pseudomonas* can even be reduced by 4–16 times.

Disadvantages of Liposomes:

The expense of making lipid-based drug delivery systems is considerable, which drives up production costs. The price is high because producing more fatty excipients requires expensive machinery and raw materials, both of which are expensive. [24]

Sterilization

Since liposomes are susceptible to high temperatures and specific types of radiation, sterilising them is a tricky dilemma. Chemical sterilisation is not an option either because it can compromise the liposomes' stability. There is just one way of filtration through a 0.22 m membrane filter for the manufacture of sterile liposomes. Because it doesn't get rid of viruses and is ineffective with liposomes larger than 0.2 m in diameter, this approach is not recommended[42]. Before beginning production, another option is to filter the initial solutions with 0.45 m regenerated Cellulose filters and glass fibre filters. After that, the entire production process must be carried out in an aseptic environment.

Short shelf life and stability:

A pharmaceutical product needs to stay stable in some capacity for at least one and a half to two years in order to be commercially successful. If the liposomes are in suspension, it is quite challenging to accomplish this. Using freeze drying after manufacture will extend the liposomes' shelf life. The stability of liposomes is greatly influenced by two factors: chemical and physical degradation. They deteriorate chemically by hydrolysis and oxidation. Only fresh, brand-new, and high-quality chemicals are used, high temperatures are avoided, inert atmosphere is used to store liposomes, aqueous solutions are deoxygenated, and all manufacturing is done in an oxygen-free environment to reduce oxidation and hydrolysis. Finally, an antioxidant such -tocopherol may be included. The variation in lipid packing density in the bilayer structure is frequently blamed for physical deterioration. By keeping the Liposomes at a temperature around the phase transition temperature until the lipid arrangement equalises, this can be corrected. Liposomes frequently fuse together, which is what causes the instability of this structure. Cholesterol is added to the lipid mixture to boost the transition temperature, which reduces instability. When the membrane's composition changes, different types of liposomes have various problems. The development of thermosensitive liposomes makes use of this phenomena. As soon as the temperature is high enough, the medication is released from the liposomes. When the produced formulations are freeze-dried, physical deterioration is a significant problem. Cryoprotector is added during the manufacturing of freeze-dried items to ensure its stability during reconstitution. [25]

Encapsulation efficacy:

The optimal drug carrier is a liposome, which must contain the drug in a therapeutic dose. Liposomes could become harmful if they contain too many lipids or other components. The technique of trapping is therefore crucial. Since liposomes only entrap a little amount of the drug, procedures like active loading are utilised to improve entrapment when it is low. With this technique, a medication that can easily penetrate the lipid bilayer in its uncharged form transforms into a charged species once it enters the liposome (the drug is unable to escape the interior of the liposome in the charged form). By trapping a low pH environment inside the liposome and suspending the vesicles in a neutral pH environment that also includes the medicine, the desired effect can be achieved.

Removal from circulation by the reticulo-endothelial system (RES):

The fast clearance of liposome drug delivery systems from the bloodstream by phagocytic cells of the RES or mononuclear phagocyte system (MPS) is one of their main challenges. The size and charge of the liposomes, as

larger ones are cleared from circulation more quickly than smaller ones, are two parameters that affect how quickly absorption occurs. Due to the rich blood supply and the large number of accumulating macrophages in the liver and spleen, liposomes tend to build up there. Some methods for extending circulation time have been discovered, such as the creation of LCLs, or long circulating liposomes. Different methods are used to create these liposomes, with the most prominent one being the coating of pre-existing liposomes with polyethylene glycol (PEG). Stealth liposomes are the name given to these kinds of liposomes. To boost the TC of the formulation, adding cholesterol and sphingomyelin (SM) is an additional option. It decreases RES uptake while increasing plasma stability. [26]

Conclusion:

Since its discovery in 1964, liposomes have a broader range of applications. Liposomes are made up of a huge variety of various lipids, both synthetic and naturally occurring, each with their own functions, benefits, and drawbacks. Because it is neutral and quite inexpensive, phosphatidylcholine is the most commonly used lipid component. Size, shape, composition, and production process are all used to classify liposomes. Benefits of using liposomes as a drug delivery vehicle include greater therapeutic efficacy against infections, improved drug-target selectivity, and improved pharmacokinetics and pharmacodynamics. The drawbacks, on the other hand, include issues with encapsulation efficacy, problems with short shelf-life and stability, and issues with some lipids, particularly charged lipids, being poisonous at larger quantities. The way liposomes interact with cells affects how well drugs are delivered. A few commercially available formulations of liposomes have been used as drug delivery devices in recent years; these formulations exhibit better efficacy. Future medication delivery methods based on liposomes hold out a lot of potential.

Reference:

1. Samad A, Sultana Y, Aqil M. Liposomal Drug Delivery Systems: An Update Review. *Curr Drug Deliv*. 2007;4(4):297–305.
2. II . Characterization of Liposomal Preparations Liposomal preparations can be adequately characterized by three main para-. 1986;40:89–107.
3. Buckner CA, Lafrenie RM, Dénonnée JA, Caswell JM, Want DA, Gan GG, et al. We are IntechOpen , the world ' s leading publisher of Open Access books Built by scientists , for scientists TOP 1 % . Intech [Internet]. 2016;11(tourism):13. Available from: <https://www.intechopen.com/books/advanced-biometric-technologies/liveness-detection-in-biometrics>
4. Taylor KMG, Morris RM. Thermal analysis of phase transition behaviour in liposomes. *Thermochim Acta*. 1995;248(C):289–301.
5. Access O. We are IntechOpen , the world ' s leading publisher of Open Access books Built by scientists , for scientists TOP 1 % for Therapeutic and Diagnostic Applications : Part I : Lipids and Fabrication Techniques.
6. Alyane M, Barratt G, Lahouel M. Remote loading of doxorubicin into liposomes by transmembrane pH gradient to reduce toxicity toward H9c2 cells. *Saudi Pharm J* [Internet]. 2016;24(2):165–75. Available from: <http://dx.doi.org/10.1016/j.jsps.2015.02.014>
7. Grit M, Crommelin DJA. Chemical-stability-of-liposomes-implications-for-their-physical-stability_1993_Chemistry-and-Physics-of-Lipids. *Chem Phys Lipids*. 1993;64:3–18.
8. Cruz-Leal Y, Machado Y, López-Requena A, Canet L, Laborde R, Alvares AM, et al. Role of B-1 cells in the immune response against an antigen encapsulated into phosphatidylcholine-containing liposomes. *Int Immunol*. 2014;26(8):427–37.
9. Akbarzadeh A, Rezaei-sadabady R, Davaran S, Joo SW, Zarghami N. Liposome : classification , prepNew aspects of liposomesaration , and applications. *Nanoscale Res Lett* [Internet]. 2013;8(102):1–9. Available from: <http://www.nanoscalereslett.com/content/8/1/102>
10. Torchilin VP. Immunoliposomes. *Drug Deliv Oncol From Basic Res to Cancer Ther*. 2011;2:951–87.
11. Krieger ML, Eckstein N, Schneider V, Koch M, Royer HD, Jaehde U, et al. Overcoming cisplatin resistance of ovarian cancer cells by targeted liposomes in vitro. *Int J Pharm* [Internet]. 2010;389(1–2):10–7. Available from: <http://dx.doi.org/10.1016/j.ijpharm.2009.12.061>
12. Loira-Pastoriza C, Todoroff J, Vanbever R. Delivery strategies for sustained drug release in the lungs. *Adv Drug Deliv Rev* [Internet]. 2014;75:81–91. Available from: <http://dx.doi.org/10.1016/j.addr.2014.05.017>

13. Eloy JO, Claro de Souza M, Petrilli R, Barcellos JPA, Lee RJ, Marchetti JM. Liposomes as carriers of hydrophilic small molecule drugs: Strategies to enhance encapsulation and delivery. *Colloids Surfaces B Biointerfaces* [Internet]. 2014;123:345–63. Available from: <http://dx.doi.org/10.1016/j.colsurfb.2014.09.029>
14. Kaur CD, Nahar M, Jain NK. Lymphatic targeting of zidovudine using surface-engineered liposomes. *J Drug Target*. 2008;16(10):798–805.
15. Takemoto SK, Zeevi A, Feng S, Colvin RB, Jordan S, Kobeshigawa J, et al. National conference to assess antibody-mediated rejection in solid organ transplantation. *Am J Transplant*. 2004;4(7):1033–41.
16. Cabanes A, Reig F, Garcia-Anton JM, Arboix M. Evaluation of free and liposome-encapsulated gentamycin for intramuscular sustained release in rabbits. *Res Vet Sci*. 1998;64(3):213–7.
17. Zou Y, Lee HY, Seo YC, Ahn J. Enhanced Antimicrobial Activity of Nisin-Loaded Liposomal Nanoparticles against Foodborne Pathogens. *J Food Sci*. 2012;77(3).
18. Bremond N, Santanach-Carreras E, Chu LY, Bibette J. Formation of liquid-core capsules having a thin hydrogel membrane: Liquid pearls. *Soft Matter*. 2010;6(11):2484–8.
19. Biswas S, Dodwadkar NS, Sawant RR, Koshkaryev A, Torchilin VP. Surface modification of liposomes with rhodamine-123-conjugated polymer results in enhanced mitochondrial targeting. *J Drug Target*. 2011;19(7):552–61.
20. Rodrigues C, Gameiro P, Prieto M, De Castro B. Interaction of rifampicin and isoniazid with large unilamellar liposomes: Spectroscopic location studies. *Biochim Biophys Acta - Gen Subj*. 2003;1620(1–3):151–9.
21. Altaf S, Bhai M, M SAB, Yadav V, Mamatha Y, Prasanth V V. Journal of Pharmaceutical and Scientific Innovation LIPOSOMES : AN OVERVIEW. *J Pharm Sci Innov*. 2012;1(1):13–21.
22. Toh MR, Chiu GNC. Liposomes as sterile preparations and limitations of sterilisation techniques in liposomal manufacturing. *Asian J Pharm Sci* [Internet]. 2013;8(2):88–95. Available from: <http://dx.doi.org/10.1016/j.ajps.2013.07.011>
23. Gibis M, Rahn N, Weiss J. Physical and oxidative stability of uncoated and chitosan-coated liposomes containing grape seed extract. *Pharmaceutics*. 2013;5(3):421–33.
24. Lee DE, Lew MG, Woodbury DJ. Vesicle fusion to planar membranes is enhanced by cholesterol and low temperature. *Chem Phys Lipids* [Internet]. 2013;166(1):45–54. Available from: <http://dx.doi.org/10.1016/j.chemphyslip.2012.11.004>
25. Pattni BS, Chupin V V., Torchilin VP. New Developments in Liposomal Drug Delivery. *Chem Rev*. 2015;115(19):10938–66.
26. Ishida T, Harashima H, Kiwada H. Liposome clearance. *Biosci Rep*. 2002;22(2):197–224.