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Application of Liposome: A Lipid Nanoparticle in Medicine and Drug Delivery

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ABSTRACT

Liposomes are well recognized small lipid particles which enhance the therapeutic activity of several drugs and plays important role as drug carriers. Liposomes can be used for a large number of applications and are especially effective in curing diseases which affect the phagocytes of the immune system because they accumulate in the phagocytes, which recognize them as foreign invaders.
For a drug to produce a specific pharmacological response, it must gain access to its specific "site of action". The last decade has seen the emergence of many approaches to the problem of controlled drug delivery, such as polymeric sustained release systems, liposomal drug carriers and antibody drug carriers. Drug targeting is one such pharmaceutical technology that makes a molecule a wonder drug. Drug targeting in simple words means reaching the drug to the site of its action and thus achieving the desired response without interactions at other sites.

Keywords: Liposome, Unilamellar and Multilamellar Vesicle; Amphipathic compounds, Phospholipid vesicles, Drug delivery

INTRODUCTION

Liposomes are carriers for targeted drug delivery. They are used in therapies for a range of biomedical applications by stabilizing therapeutic compounds. [1, 2, 3, 4] Alec D. Bangham first produced liposomes in England in 1961 when he was studying phospholipids and blood clotting.[5] One end of each liposome molecule is water soluble, while the opposite end is water insoluble hence they immediately form a sphere when comes in contact with water. These liposomes are also sometimes called "Bangosomes", after the name of the discoverer. A liposome is a tiny bubble (vesicle) made of phospholipids that have a head and a tail. The head is attracted to water, and the tail, which is made of oil (hydrocarbon), is repelled by water. When membrane phospholipids are disturbed, they can reassemble themselves into tiny spheres, which are smaller than a normal cell and either as bilayers or monolayers which are liposomes. These are amphipathic in nature, i. e. part of their structure is water-soluble (hydrophilic or water-loving) and the other part is oil-like (hydrophobic or fat soluble). When added to water, the water-soluble part of the phospholipid is able to interact with the water, while the oil-like part of the molecule is unable to interact with the water. [6]

STRUCTURE OF LIPOSOMES:

The liposome's size varies between 30 nm and 10,000 nm, making it suitable for transporting both water-soluble and water-insoluble compounds. Liposomes consist of phospholipids or various mixtures of phospholipids, with the addition of cholesterol, fatty acids in the non-phospholipid layer, and lipid-soluble molecules like vitamin E. Liposomes possess the potential to be manipulated in a manner that allows them to discharge their

contents once they attain a specific temperature and pH level. By altering the lipids within the liposome or the target tissues, specific proteins, liposomes can effectively aim at particular tissues or cell types. Conversely, they can evade certain tissues or cells by affixing complex sugars onto their surface. They evenly distribute fat-soluble (oil-like) compounds such as certain vitamins, antioxidants; antibiotics, flavours, etc., which often cannot be mixed in water-based products including most food; fuse with cells, which is important in delivering DNA to a cell; serve as model cell membranes making it easier to study specific cellular processes and how certain molecules, such as drugs, interact with cells. Liposome protect compounds from acidic and enzymatic degradation in the stomach and intestine by using certain molecules to coat the liposome; enhance the intestinal absorption of compounds by coating with certain molecules, carry drugs across the nasal mucosa (nasal drug delivery) and deliver drugs directly to lung tissue by inhalation of the liposomes.[6,7]

Phospholipids:

Liposomes are composed of phospholipids with mixed lipid chains (like egg phosphatidylethanolamine, cholesterol, phosphotidylcholine, dipalmitoyl-phosphatidylcholine, diacetylphosphate, stearylamine, phosphatidic acid, phosphati-dylserine, cardiolipin, sphingomyelin, etc.), or pure surfactant components like dioleoyl-phosphatidylethanolamine. The glycerols, including phospholipids, are commonly used component of liposome formulation and represent greater than 50% of the weight of lipid in biological membranes. These are derivatives of phosphatidic acid. [6, 8]

Cholesterol:

Cholesterol can be added into phospholipid membranes in very high concentrations of up to 1:1 or even 2:1 molar ratio of cholesterol to phosphatidylcholine. The hydroxyl group of cholesterol is oriented towards the aqueous surface and the aliphatic chain aligned parallel to the acyl chains in the centre of the bilayer. Cholesterol is highly soluble in the phospholipid liposome and has been attributed to both hydrophobic and definite head group interaction, but there is no clear arrangement of cholesterol in the bilayer. [7]

CLASSIFICATION OF LIPOSOME

Liposomes contain a series of concentric bilayers alternating with aqueous compartments. According to number of layers and size of the liposome, they are classified as SUV (small unilamellar vesele), LUV (large unilamellar vesicle), MLV (multilamellar vesicle) and MVV (multivesicular vesicle). The most common preparation is the MLV (multilamellar vesselel), an "onion-like" structure of concentric aqueous and lipid layers. These structures are heterogeneous in size, but range up to several microns in diameter. Sonication can reduce MLVs to SUVs (small unilamellar vesicles), which are single walled vesicles of 200 to 500 A diameter. It is also possible by various means to construct LUVs (large unilamellar vesicles), where a single large aqueous compartment is bounded by a single bimolecular lipid membrane which is usually about 1 µ in diameter. These vesicles are synthesized by reverse phase evaporation. Typically, the thickness of a lipid bilayer membrane is about 50 A. [6, 7]

Small Unilamellar Vesicles: Small unilamellar vesicles (SUV) consist of a single lipid bilayer having a diameter of 25nm. They may be prepared by exhaustive sonication (solvent dilution technique) of MLVs using a probe or bath type sonicator. Any contaminated MLV can be removed by ultracentrifugation or column chromatography. An alternative method for SUV production involves use of a fine hypodermic needle for infection of an ethanolic solution of lipid into an aqueous. These SUVs are very inefficient in trapping water-soluble compounds. [6, 7]

Large Unilamellar Vesicles: Large unilamellar vesicles (LUVs) are reformed using acid phos- pholipids. The preparation requires formation of SUV by sonication and their further fusion into large sheets by the insertion of calcium ions. Treatment with EDTA opens out the sheets and LUVs are formed. The vesicles demonstrate high efficiency in capturing water-soluble drugs (achieving up to 40-60% entrapment), although they exhibit lower stability compared to other vesicle varieties. [6, 7]

Multilamellar Vesicles: A solution of lipid is dried in an organic solvent. The lipid is then hydrated and dispersed by adding a buffer. Aqueous soluble materials are combined to the aqueous phase, while lipid-soluble materials are combined to the lipid phase. The free and liposome bound drug can then be separated by gel filtration chromatography. The liposomes formed in this manner are heterogeneous in size (about 0.1-3u) and have several concentric layers of membranes. These are called multilamellar vesicles (MLVs). [6, 7]

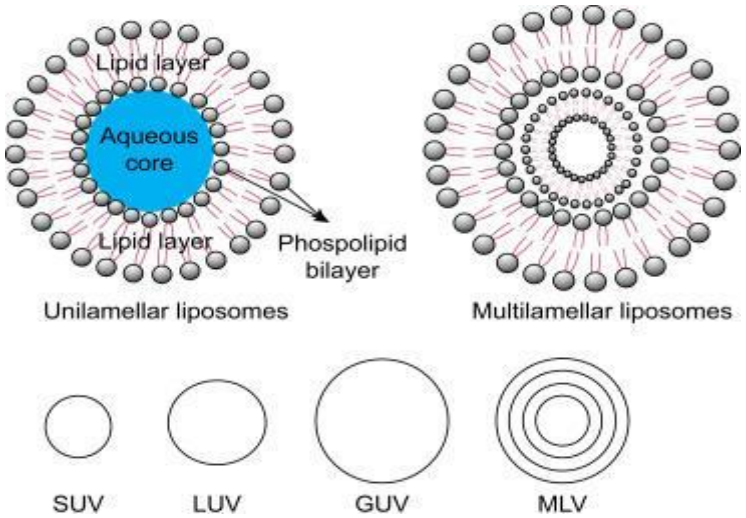

FIGURE 1: STRUCTURE AND TYPES OF LIPOSOME
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Table 1: SIZES OF LIPOSOMES [6]

Structure	SUV	MLV	REV(LUV)
Size(nm)	20-50	400-3500	200-1000
Capture Volume (ii/mg)	0.5	4.1	13.7
Encapsulation	0.5-1.0	5-11	35-65

METHODS OF LIPOSOME SYNTHESIS;

Liposomes are prepared by following methods

Sonication:

Bengham in 1965 described this method and is usually used for the synthesis of multilamellar vesicles. Phospholipids are solubilized in a blend of chloroform and methanol, with a volumetric ratio of 2:1. The solvent blend is subsequently evaporated to make a lipid film, which is later dispersed in water at a temperature exceeding the lipid's transition point (Tc) or the Tc of the most high melting component in the blend. The size of the structure can be further reduced by disrupting the lamellar structure by sonication. Sonication for a brief time gives rise to both multilamellar as well as unilamellar structures, but prolonged sonication converts the former into the later. Unilamellar liposomes could be easily separated from MLVs by ultracentrifugation or column chromatography on sepharose 2B

or Sepharose 4B. The disadvantage of this process is that encapsulation efficiency is very low (usually 4-7%), but can be increased by gentle shaking and lengthening the hydration time. [6, 7, 9]

Ethanol Injection:
This method involves the injection of a solution of lipid in ethanol, into a buffer. Nearly all vesicles obtained by this process are unilamellar. The primary drawbacks include the dilution of the lipid dispersion and the low efficiency of encapsulation. [6, 7, 9]

Ether Infusion:
Phospholipids can be dissolved in a diethyl ether-methanol mixture at temperatures ranging from 55-65°C or under reduced pressure at 0°C. These dissolved phospholipids can then be added into an aqueous solution containing the desired material to be trapped. The solvent is then removed by evaporation and vesicles of a size between 1500-2500 A are formed. The method is suitable for large unilamellar macromolecules. The drawbacks are unnecessary exposure of materials to high temperature and organic solvents, low encapsulation efficiency and production of heterogeneous population of liposomes. [6, 7, 10]

Reverse Phase Evaporation:
In this approach, the aqueous substance is added to a blend of phospholipids and organic solvent, and subsequently eliminated under decreased pressure, which results in the formation of large unilamellar vesicles (LUV) and oligolamellar liposomes. The encapsulation efficiency is very high (up to 65%). The method cannot be applied for entrapment of proteins that get denatured on exposure to organic solvent. [6, 11]

Rehydration-Dehydration:
This method was developed by Kirby and Gregoriadis in 1984 and is used for industrial preparation of liposomes which has very high entrapment efficiency. Initially the liposomes are made by dissolving lipids in organic solvent, removing the solvent under reduced pressure and then dispersing into aqueous phase. The prepared liposome is then freeze-dried and can be stored frozen without any major leakage of entrapped material for more than a year. Whenever desired, the dried lipid can be regenerated into liposomes by adding water. The encapsulation efficiency is achieved when the lipid is fully dehydrated as a SUV prior to freeze-drying. One advantage of this process is the extended shelf life of the lipid powder, making it ideal for diagnostic applications. Additionally, it could be easily prepared whenever needed. [6]

French Press:
Initially MLVs are made by suspending lipids in aqueous buffers as described in sonication method. Instead of sonication, the dispersion of MLVs is reduced in size by extrusion at high pressure through a French press. When extrusion is done at 20,000 lbs/ in one pass, vesicles with a size range 250-500 A are formed. Further extrusions may yield more homogeneous preparations of MLV. The technique offers numerous benefits in contrast to sonication. The liposomes exhibit a larger size when compared to sonicated SUVs.This method works at high temperatures which is difficult to maintain. [6, 7,9,12,13]

Detergent Dialysis:
Detergent removal method involves the solubilisation of unsolicited lipid dispersion with a detergent such as sodium deoxycholate or sodium cholate followed by its removal by gel filtration or dialysis. The liposomes formed by this method are homogeneous and of the SUV category. However, the complete removal of detergent may not always be possible. The ratio of lipids to detergents is crucial in determining the size of SUVs. [6, 7,14]

PROPERTIES OF LIPOSOME

Liposomes exhibit varying physical properties based on factors such as their chemical composition, temperature, pH, ionic strength, and the presence of divalent cations. Changes in temperature can cause bilayer membranes to transition from a rigid "gel" state to a more fluid state, impacting stability, permeability, and overall behaviour. This phase transition is most noticeable in liposomes with uniform phospholipids, with cholesterol playing a role in modulating the transition behaviour. [6]

DRUG LOADING IN LIPOSOMES

Hydrophilic drugs are predominantly located within the internal aqueous compartments of liposomes, although there is also a possibility of some degree of binding to the bilayer. On the other hand, lipophilic or amphipathic drugs can be inserted into the liposome membrane, but the polar molecule is rapidly and completely released when the liposome membrane is disrupted by sonication, while the lipophilic drug remains associated with the liposome membrane. The maximum incorporation of lipophilic drug into liposomes depends on the amount of lipid and the solubility of the drug in the lipid. Typically, drug/lipid molar ratios of 1:10 can be easily achieved without affecting the bilayer structure. The entrapment of polar drugs depends on their solubility in water and the amount of water enclosed per unit mass of lipid. This characteristic can differ greatly among various liposome types. As a result, the ratios of encapsulation can vary from around 0.5-1/mol for small unilamellar vesicles (SUVs) to more than 15-1/mol for large unilamellar vesicles (LUVs). While selecting a liposome type and composition for a particular application, it is crucial to consider encapsulation efficiency. However, stability, lack of toxicity, and unique biochemical attributes are also important factors to take into consideration. Liposomes have the ability to easily incorporate a wide variety of drugs, but challenges arise when formulating liposome drugs on a large scale commercially and preventing potential leakage of amphipathic drugs from the vesicles. Achieving high drug lipid ratios, minimizing size heterogeneity, and maintaining chemical stability during extended storage may present several obstacles. However the stable incorporation and storage of polar drugs, which reside in the entrapped aqueous compartment, maybe difficult while stable incorporation of lipophilic drugs is not a problem. [6, 15]

MECHANISM OF TRANSPORTATION THROUGH LIPOSOME

Liposomes have the ability to engage with cells through four fundamental mechanisms: adherence to the cell surface, endocytosis, fusion, and lipid exchange. Recent findings indicate that absorption or endocytosis is the primary mechanism of liposome-cell interaction for the majority of vesicle compositions and cell types. In contrast, solid vesicles in a gel state have a tendency to strongly adsorb to the cell surface, whereas fluid vesicles do not exhibit the same behaviour. Cells, which are "professional" phagocytes, such as neutrophils and macrophages have a tendency to engulf and internalize vesicles by an active, energy dependent, actinomycin related phagocytic process. Cells such as fibroblasts have a tendency to internalize vesicles (particularly SUVs) by using the coated pit endocytosis mechanism. The inclusion of protein or carbohydrate ligands on the surface of liposomes, have ability to specifically interact with certain cellular receptors (such as the Fe-receptor on macrophages) and can significantly enhance the efficiency and magnitude of liposome uptake by cells. [6]

DRUG DELIVERY BY LIPOSOME

Drugs delivered by liposomes have many advantages. The drug remains concentrated in the liposomes instead of diffusing throughout the body due to which lower doses can be administered. Since many

drugs used in the cure of diseases such as cancer have toxic side effects on the healthy cells and the diseased ones, the lower dose means less side effects for the patient and lower cost for treatment. Secondly, the liposomes can sometimes be targeted to a tumour or site of disease. Just as biological membranes in a normal cell contain proteins and a variety of other materials, synthetic liposomes can also be manufactured to contain small proteins or carbohydrates that will "lock on" to a specific target molecule when they come in contact with it. Inflammation sites and certain tumours frequently exhibit distinct molecules on their surfaces that can be targeted, such as liposome-bound molecules that enhance drug delivery to the intended body area while reducing absorption by non-target cells. Lastly, the release of the drug at the site is prolonged as the drug slowly releases from the liposome. Since the liposome is composed of lipids like the membrane itself, it can fuse to the membrane and deliver the drug directly inside the cell (Figure 2). The effectiveness of the drug is increased by direct delivery and prolonged exposure. An attractive but elusive approach in the liposomal drug delivery area has been the notion of coupling antibodies to vesicles so as to target drugs to specific cell populations. [6, 8, 16]

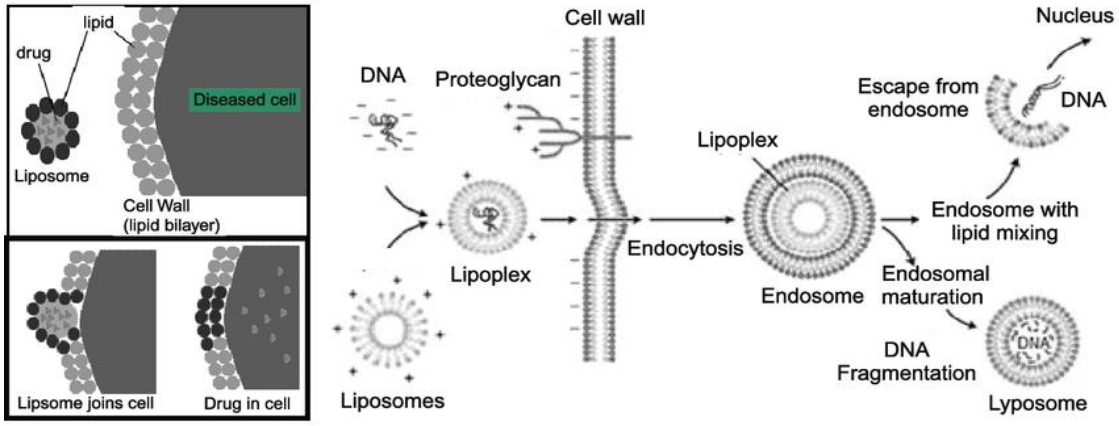

FIGURE 2: A Lipoplex mediated Transfection B Endocytosis

MODE OF ACTION

The primary sites of liposome uptake are the liver and spleen which are suitable for the clearance of circulating particles since they contain abundance of phagocytic reticuloendothelial cells and their capillary endothelium is fenestrated the by permitting the egress of comparatively large particles. [6]

Several researches have investigated the function of reticuloendothelial (RE) cells in eliminating vesicles from the bloodstream. In vivo performance of liposomes can be significantly influenced by modifying their physical attributes like size, surface charge, and stability. Initial studies on the elimination rate of lipid vesicles revealed that larger vesicles were removed more rapidly than smaller ones. Moreover, among vesicle populations of similar sizes, negatively charged liposomes were eliminated much faster compared to neutral or positively charged ones. Thus, liposomes seem ideally suitable as means to deliver drugs to macrophages of the RE system. [6]

Some prospects for promoting specific liposome-cell association are by simply coating the liposome with antibodies or lectins, by coupling of monoclonal antibodies or affinity purified fab fragments to vesicles, by incorporation of glycolipid determinants into the liposome membrane so as to promote specific association with lectin-like receptors on cell surfaces and by using vesicles coated with an antigen (e.g., myelin basic protein) to specifically

manipulate certain aspects of immune function. This model may provide an exciting approach for the specific suppression of a variety of autoimmune or allergic processes by "Targeting" vesicles to specific lymphocyte populations. [6]

APPLICATIONS OF LIPOSOME TECHNOLOGY

Liposome technology has many applications such as gene therapy, cancer therapy, clinical pathogenesis, enzyme replacement therapy, chelation therapy, imnunomodulation, thermal transitions of phospholipids, neurobiological applications, leucoyte phagocytosis, botanical research, drug interactions with membranes, bacterial cell wall synthesis, lectin receptor interactions, microvillus formation in cells and many more. Some of the important applications of liposome technology are discussed below. [6]

Liposomes as carrier of drugs for curing diseases

Various drugs, including antitumor drugs, polygene antibiotics, antibacterial drugs, and chelation therapy drugs, have been effectively incorporated into liposomes. Some agents utilized for treating fungal or parasitic infections can be highly toxic, and in certain cases, these infections may not respond well to traditional drug treatments. Exploration of liposomes in these situations seems a sound prospect. The first highly successful use of a liposomal carrier system in infectious disease occurred in connection with leishmaniasis (kalaazar), a protozoan disease which is endemic in many tropical areas and also prevalent in India such as in Assam, Bihar, Orissa and Bengal. This parasite has a rather unusual life cycle, which makes it particularly susceptible to liposome drug therapy. The organism enters and colonizes macrophages, managing to live within endocytotic vacuoles without being destroyed. Liposomes are convenient means of "targeting" drug directly to the site of parasitic infestation. Fungal infections like aspergillosis, candidiasis, and others are frequently seen in immunosuppressed individuals with diseases such as AIDS, tuberculosis, cancer, and more. Such infections can be severe and life threatening to them. Fungizon, a commercial preparation of amphotericin-B (Amp-B) in deoxycholate, is the only accepted therapy to treat fungal infections. Amphotericin, an antifungal medication, induces severe adverse reactions including fever, anaphylaxis, nephrotoxicity, and pulmonary function abnormalities thus restricting the high dosages required for curative effect. The drug being a polyene antibiotic interacts with ergosterol of fungal cell membrane and forms a transmembrane channel leading to the release of vital metabolites, thus causing fungal death and similarly lysis of RBCs simultaneously. Amphotericin is also effective for the cure of kalaazar. The other application of the liposomal delivery approach in infectious diseases involves the therapy of systemic fungal infections with polyene antibiotics incorporated into the vesicles. Another very promising example of therapy of an intracellular parasite with liposomal drugs involves the use of liposomal aminoglycosides to treat brucellosis. [6, 7]

Cancer Chemotherapy

Many drugs used in cancer chemotherapy are toxic to normal tissues, particularly bone marrow, kidney, heart and the rapidly dividing cells of the gut lining. Liposomes have the ability to target cancer cells. Hence, liposomally carried anti-cancer drugs were hailed as a major new approach to the chemotherapy of cancer. The concept driving this excitement was the possibility of directing liposomes and their cytotoxic drug contents towards cancer cells by altering the physical or immunological properties of the liposomes introduced into the bloodstream. These liposomes would need to traverse the endothelial barrier, basement membrane barrier, and ultimately be efficiently absorbed by cancerous cells within the tumour. The tight junctions between endothelial cells form a protective

barrier along the endothelial walls of human blood vessels. This barrier prevents the escape of large particles from the bloodstream. Tumour vessels are diagnostically leaky; they do not contain the same level of seal between cells and are known as the Enhanced Permeability and Retention (EPR) effect. Liposomes smaller than 400 nm can efficiently penetrate tumour sites from the bloodstream, while being retained in the blood vessels of healthy tissues by the endothelial wall. Doxorubicin (Doxil) and Daunorubicin (Daunoxome) are examples of anti-cancer drugs which are being marked in liposomal delivery systems. The first objective of Inex's research program is to use a lipid-based drug delivery system, called the Transmembrane Carrier System (TCS) to deliver anticancer drugs more effectively to tumours. Inex is using the anti-cancer drug, vincristine, in liposomes to treat non-Hodgkin's lymphoma and other cancers. Additionally, they are exploring alternative anticancer medications to determine whether their efficacy could be enhanced through the use of liposomal encapsulation for improved targeting and delivery. [6]

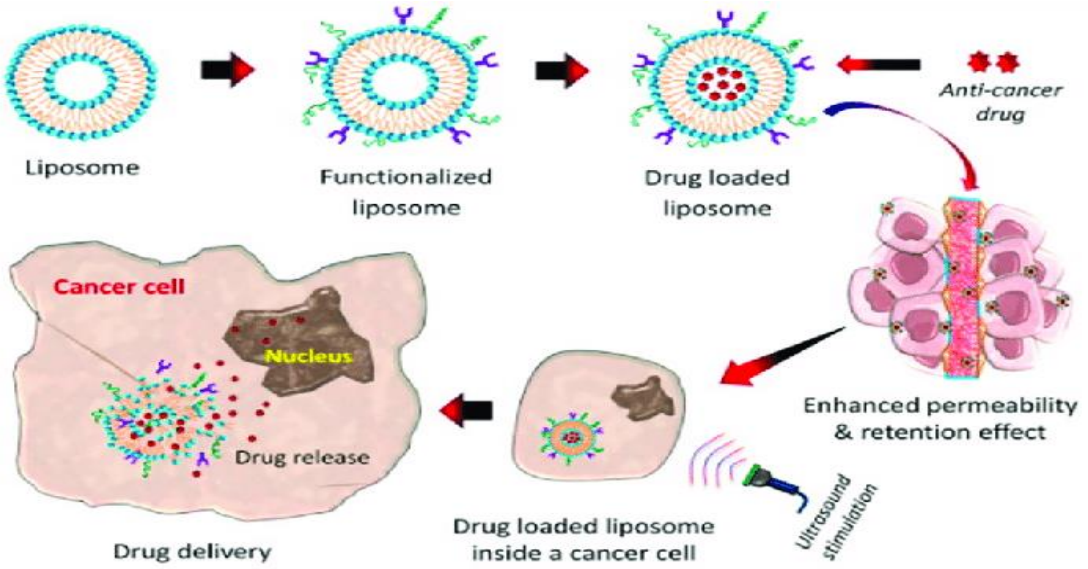

FIGURE 3: Liposome based drug delivery
Source: under cc

Table 2: Liposome as carrier of drugs [6]

Carrier	Drug	Comments
Liposomes	Anticancer	Poor tumour accessibility without targeting
Liposomes	Anti-infectious	Excellent penetration to parasites residing in reticuloendothelial system
Liposomes	Immunomodulators	Exciting possibility of enhancing immune response by encapsulating macrophages activating factor 9MAF0.Targetting using antibodies and other ligands to specific cell structure receptors.
Liposomes	Chelating agents	Limited accessibility of parenchyma tissue, site of iron storage
Liposomes	Gold products	Potential treatment of rheumatoid arthritis
Liposomes	Amphotericin B	Liposomes generally diminish the generalized cytotoxicity of the antifungal agent
Liposomes	Enzymes	Immunoglobulin mediated targeting
Liposomes	Interferon	Altered Pharmacological properties
Liposomes	Genetic Material	Useful for the development of gene delivery both in vivo and in vitro
Liposomes	Radionucleotide	Diagnostic Imaging
Liposomes	Polymerized Vesicles	Stabilized time released carriers

GENE THERAPY

By gene therapy the quality of life can be enhanced through the correction of genetic disorders by the use of genes to mitigate disease symptoms. Nevertheless, a significant challenge lies in effectively targeting the affected cells while preserving the integrity of unaffected cells. Liposomes have the ability to merge with protoplasts through the use of tools like PEG, making them valuable for gene transfer. This method presents numerous benefits including shielding DNA/RNA from nuclease breakdown, minimal cell toxicity, durability, and preservation of nucleic acids by enclosing them in liposomes. Moreover, it is adaptable to various cell types. The use of liposomes in both in vitro and in vivo settings, along with their resulting high level of cell integration and gene expression, aids in comprehending the precise role of a specific gene. [6, 7]

Inex's Oligo Vax system for targeted immunotherapy uses liposomes containing specific disease markers called antigens, along with an immunostimulatory DNA molecule. An antigen is derived from a specific virus, tumour or bacteria. It triggers the generation of immune cells capable of targeting, destroying, or rendering harmless any foreign substance that bears the same antigen. For instance, introducing an antigen from a cancerous cell will lead to the creation of T cells that can eliminate any abnormal cell exhibiting the same identifier on its surface, whether in a primary tumour or a secondary growth. In the same vein, the inclusion of a virus antigen within a liposome will elicit the production of immune T cells and antibodies. These immune components will be able to identify intact virus particles within the body and the cells infected with the virus. These cells will present fragments of viral antigens on their surface that can be inspected by T cells by incorporating an antigen into the liposome. Inex aims to direct the immune system towards specifically targeting the desired target. Additionally, the liposome contains a short segment of DNA called an oligonucleotide or "oligo". Oligo can stimulate the immune system through various mechanisms. One commonly used method is the inclusion of Immunostimulatory Sequences (ISS) or CpG sequences. These are DNA sequences with a high frequency of repeated CG bases. In vertebrates such as humans, these sequences are rare and are furthermore, modified by the addition of a methyl residue. However, in bacteria, these sequences are more common and are less likely to be methylated. In nature, when a bacterium invades a vertebrate and tries to infect it, one of the ways in which the vertebrate's immune system recognises the bacteria as an invader is by unmethylated GG motifs in bacterial DNA. The bacterial DNA itself causes an inmune response leading to the generation of killer T cells that can recognize and kill the bacteria. By including such sequences from bacteria in the liposomes, Inex hopes to boost the immune response and direct it against the antigen that was also included in the liposome. Having these two inmune stimulators delivered together by liposome may result in better tumour recognition and killing. The OligoVax targeted immunotherapy method is being evaluated with an antigen from a protein called tyrosine-related protein-2 (TRP-2) found in melanoma cells. Using an antigen from cancerous melanoma cells in liposomes with immunostimulatory DNA may generate enough killer T cells to eliminate the melanoma from the body. [6]

ENZYME REPLACEMENT THEORY

Numerous enzymes have the potential to be transported via liposomes to address genetically inherited storage diseases, offering significant therapeutic benefits by delivering the deficient enzyme to the affected tissue. An illustration of this is cystinosis, a type of lysosomal storage disease. Liposomes containing cysteamine have shown effectiveness in releasing stored cystine in fibroblasts. Studies have performed to find out the effects of

liposome-mediated adenomatous polyposis coli (APC) gene therapy on intestinal neoplasia in vivo.[16] The reduction of intestinal neoplasia by APC gene replacement suggests their role in intestinal tumorigenesis. Bis (guanidinium)-tren-cholesterol/dioleoylphosphatidylethanolamine (BGTC/DOPE) encapsulated liposomes can facilitate gene transfection into the fetal sheep airway epithelium for the cure of congenital lung diseases.[16] similarly, it was shown that 7-Dehydrocholesterol enhances ultraviolet A-induced oxidative stress in keratinocytes. In addition, immobilization of enzymes on the liposome significantly decreased entropy and enthalpy of activation of enzymes and made it functionally and thermodymamically more stable and reusable compared to soluble ones. Recently, liposome-bound cellulase has been used for the hydrolysis of insoluble cellulose. [(6, 17)]

CHELATION THERAPY

Chelating agents such as EDTA, DTPA and esferrioxamine are used intravenously and intraperitonially for treating metal poisoning. They are rapidly excreted from the body and do not cross cell membranes. Liposomes entrapped chelating agents are free of all these difficulties. Studies have shown the efficacy of liposome encapsulated triethylenetetramine hexaacetic acid (TTHA) drug against cadmium intoxication in mice pre-exposed to cadmium. Their results indicate that TTHA encapsulated in liposomes exhibited the highest efficacy in mobilizing cadmium from the body of pre-exposed mice. [(6)]

IMMUNOMODULATION WITH LIPOSOMAL DRUGS

Macrophages are versatile cells that are essential components of the host defence system. They serve as a key defence mechanism against the proliferation and spread of cancerous cells. By undergoing activation, macrophages can acquire cytotoxic properties against tumour cells. This activation is induced by various immunomodulating substances such as MAF, lipopolysaccharide, and synthetic compounds like muramyl dipeptide. Thus, liposomes selectively deliver immunomodulators to macrophages for the purpose of enhancing host defences against metastases. The other major immunological applications of liposomes are: as an immunological adjuvant, as a carrier for haptens, as a carrier of additional immunomodulator and as a tool in immunodiagnostics. [(6)]

The liposome immune lysis assay (LILA) appears to have a potential application in immunodiagnosis in future. This has been exploited to diagnose patients with systemic Lupas Erythematosus (SLE), hemolytic anemia, Behcet's disease and several other diseases. LILA has certain advantages over the existing assay systems like ELISA and RIA, such as, the assay system is a homogenous one, it does not require the separation of free antigen or antibody from the immune complex, it avoids the use of hazardous chemicals such as radioisotopes and the assay system is very sensitive, almost same to regular EIA or RIA and for detection of some antibodies. [(6)]

CONCLUSION

Liposomes technology serves as a model membrane system to study the functions of cell surface molecules, their transportation, and interactions with different ligands. Additionally, liposomes are carriers for delivering drugs and bio-molecules to specific locations within the body. The utilization of liposome technology has significantly increased in pharmaceutical applications and has been approved for enhancing drug delivery to targeted disease sites. This progress is especially vital in areas like cancer treatment, gene therapy, chelation therapy, bioengineering, and the agro-food industry. The FDA has given permission for more than a dozen drug delivery systems by liposome, with numerous others in various stages of development. However, the high production cost of liposomes and the potential

oxidation of phospholipids are challenges that need to be addressed.

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