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A review on Drug Delivery System: Liposome

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❖ **ABSTRACT:**

The liposome is firstly described in 1961 at Babraham institute by Alec D Bangham. The liposomal drug delivery system is an efficient drug delivery system. It is both hydrophilic and lipophilic groups hence it is most convenient to bypass gastric degradation. They are spherical lipid bilayers that consist of an aqueous core. They have a cell membrane-like structure i.e., phospholipid bilayer. Hence, they can easily fuse with cell membranes and enter the cell by endocytosis. In this way, liposome releases their drug in cells. There are various liposomal types according to their uses i.e., immune liposomes, cationic liposomes, long-circulating liposomes, and pH-sensitive liposomes. The cationic liposomes are used to carry DNA. The immune liposomes contain immunological adjuvant which enhances immunological response. pH-sensitive liposomes are used to avoid degradation in lysosomes. Long circulating liposomes are having more molecular weight groups to extend their life. They are widely used in fungal infection, cancer therapy, as DNA vaccine, respiratory diseases, viral diseases, and other diseases. They are recently mostly used in mRNA vaccines and liposomal amphotericin B antifungal drugs. The mRNA vaccine is consisting of lipid nanoparticles, which are made by Pfizer and Moderna companies. The liposomal preparation of amphotericin B reduces nephrotoxicity and amphotericin B is the first line treatment for fungal infections like mucormycosis, systemic fungal infections via intravenously or intrathecally including systemic candida, cryptococcus, blastomycosis, and histoplasmosis[17]. They are also used in dietary and nutritional supplements recently. They are easy to target specific tissues by passive or active targeting of liposomes. In passive liposomes, there are simple liposomes that are taken up by the liver. Inactive targeting of liposomes, they are targeted in such a way there is the interaction like a drug with receptors (a plug with socket).

❖ **KEYWORDS:** Liposome, structural components of liposomes, Method of preparation of liposomes, Targeting of liposomes.

❖ INTRODUCTION:

A liposome has at least one lipid bilayer and it has a globular shape. The term liposome is made from two words: 'Lipos' and 'Soma' Greek words meaning fat and body respectively. It can be utilised to administer medicinal medications and nutrients, similar to how lipid nanoparticles are used in DNA and mRNA vaccines. Liposomes can be created by disturbing cellular membranes (much like sonication). Liposomes are microscopic bubbles (vesicles) formed of the same materials as cell membranes. Medications can be loaded into liposomes, and they are utilised to deliver anticancer drugs. Liposome membranes are typically composed

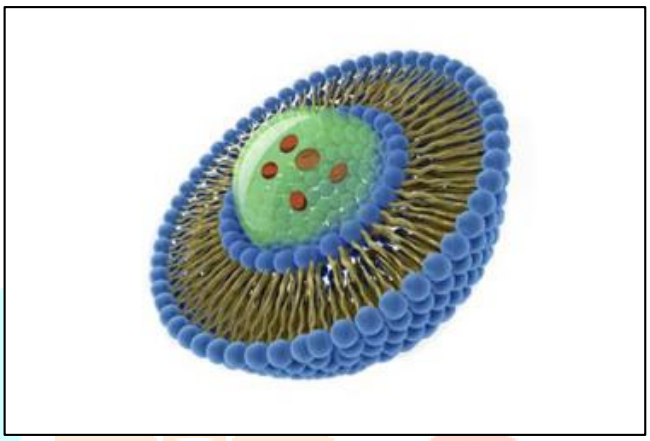

Figure No. 1 Liposome

of phospholipids with a head group and a tail group. The head is pull towards aqueous like water because it is made up of phosphate group (hydrophilic group), and the tail, which is made of a long hydrocarbon chain (hydrophobic group), is attracted towards non-ionic groups.

Liposomes are consisting of phospholipids, phosphatidylcholine, but may also include other lipids as egg phosphatidylethanolamine. A liposome design can be used for surface ligands for binding to unhealthy tissue.

▪ Advantages Of Liposomes:

- Liposomes are biocompatible, fully biodegradable, non-toxic, and immune-immunogenic.
- Effective in the delivery of both hydrophobic and hydrophilic medicines.
- Keep the enclosed core medicine safe from the elements.
- Improved therapeutic action of chemotherapeutic drugs due to liposome encapsulation, which reduces toxic characteristics and increases stability.Liposome are biocompatible, completely biodegradable, non-toxic and non-immunogenic
- This minimises the risk of side effects that occur at concentrations that are similar to or lower than those required for maximum therapeutic action.
- Reduce the chance of hazardous medications reaching delicate tissues by limiting their exposure.

▪ Disadvantages of Liposomes:

- It has high production high.
- Fusion and leakage of encapsulated drug/molecules.
- It has less half-life

❖ History-

At the Babraham Institute in Cambridge, British haematologist Alec D Bangham initially described liposomes in 1961 (published 1964). They were discovered by applying negative stain to dry phospholipids Bangham and R. W. Horne were putting the institute's new electron microscope through its paces at the time. The cell membrane (also known as the plasma membrane (PM) or cytoplasmic membrane, and previously known as the plasmalemma) is a biological membrane that separates the interior of all cells from the extracellular space, protecting the cell from its surroundings. The similarities to the plasmalemma were striking, and the microscope images provided the first proof that the cell membrane had a bilayer lipid structure. Bangham, Standish, and Weissmann confirmed their integrity as a closed, bilayer structure that might release its contents after detergent treatment (structure-linked latency) the next year. Weissmann termed the formations "liposomes" after the lysosome, which his research had been studying: a basic organelle whose structure-linked latency could be broken by detergents and streptolysins, during a Cambridge pub debate with Bangham. Negative staining transmission electron microscopy can easily identify liposomes from micelles and hexagonal lipid phases.

- **Liposomes Evolution:**

1965- Closed lipid bilayer vesicles are described for the first time.

1967- The term "liposome" was coined to characterise closed lipid bilayer vesicles.

1972- Liposomes were first employed as medicine delivery methods.

1974- Liposomes were administered into the first patients.

1979- Liposomes were first employed to transfer nucleic acids to cells.

1980- Immunoliposomes were the first monoclonal antibodies that target liposomes.

1987-Synthetic cationic liposomes were the first to carry genes to cells.

1987- The first system of sterically stabilised long circulating liposomes was developed.

1992-The first clinical trial of a liposome-based nonviral vector gene therapy in cystic fibrosis patients.

1993- The first hepatitis A vaccine based on liposomes has been released.

1995- Long immunoliposomes were the first to circulate.

1995- The anticancer drugs doxorubicin and daunorubicin were encapsulated in liposomes that were licenced for human usage.

1997-The first DNA vaccination based on liposomes.

❖ Structural components of liposome[1]:

Liposomes are spherical lipid bilayers with diameters ranging from 50 to 1000 nanometres that serve as effective delivery vehicles for therapeutically active substances. The use of topical liposomes in the

administration of dermatological and anticancer treatments offers a lot of potential in terms of reducing medication toxicity, increasing drug effectiveness, and increasing circulation time. Liposomes could be used to target specific cells by attaching amino acid fragments, such as suitable fragments, proteins, or antibodies, to receptor sites that are specific to those cells. Liposomes will be used to improve the efficiency of gene therapy in the future. Currently, DNA and mRNA vaccination are the most used methods.

The major structural components liposomes are:

- **Phospholipids[1]:**

Phospholipids are the major structural component of living cells, and two classes of phospholipids exist - Sphingolipids and Phosphodiglycerides. The phosphatidylcholine (PC) molecule is the most common phospholipid. Phosphatidylcholine particles are not soluble in aqueous mediums such as water, thus they arrange themselves in planar bilayer sheets to reduce the interaction between the bulk aqueous phase and the long hydrocarbon fatty series. Phospholipids are the most prevalent component of liposome composition, accounting for more than half of the lipid weight in biological membranes.

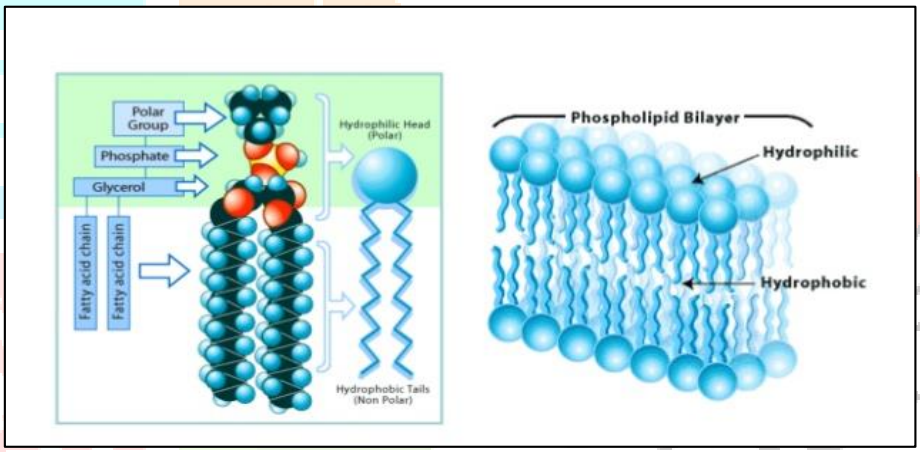

Figure No. 2 Structure of liposomes: Phospholipids

Examples of phospholipids are:

PE- Phosphatidyl ethanolamine-cephalin.

PC- Phosphatidyl Choline-Lecithin.

(PS) - Phosphatidyl serine.

(PG)-Phosphatidyl Glycerol.

❖ Cholesterol[1]:

Cholesterol not role in formations of bilayer, but it is incorporated into phospholipid membranes in high concentrations as equal or half concentration of phosphatidylcholine. Cholesterol having hydroxyl group oriented towards aqueous surface and the aliphatic chain oriented in between bilayers. Because of both hydrophilic and lipophilic part, it shows high solubility in phospholipid, but there is no clear arrangement of cholesterol in the bilayer **(**Antoaneta V., et al.)

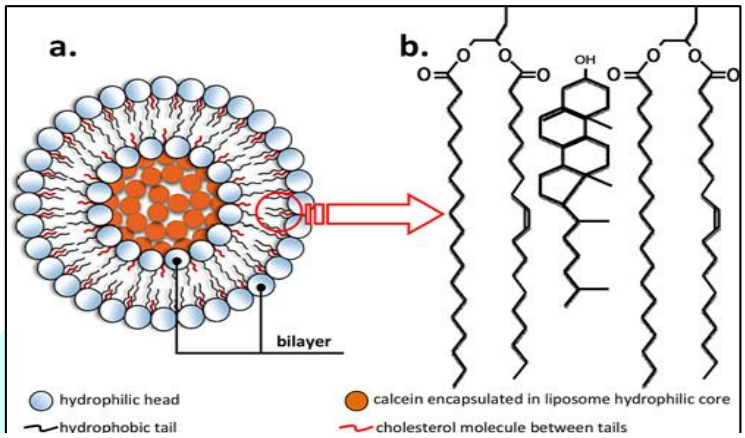

Figure No. 3 Structure of Cholesterol

❖ Mechanism of Action of Liposomes[11]:

A liposome consists of aqueous or lipophilic core inside the bilayers. While the drug's extent of distribution will be determined by its physiochemical properties and lipid makeup. The lipid bilayers fuse with the bilayers of the cell membrane to release the drug content for delivery to the therapeutic location.

Steps involved in medication delivery using liposomes:

1. Adsorption: In this stage there is only attachment to the cell membrane.

2. Endocytosis: It means the engulfment of liposomes in the cell membrane.

3. Fusion: Fusion of lipid bilayers of liposomes done by lateral diffusion and ther is direct liposomal drug delivered by mingling together with cell membrane

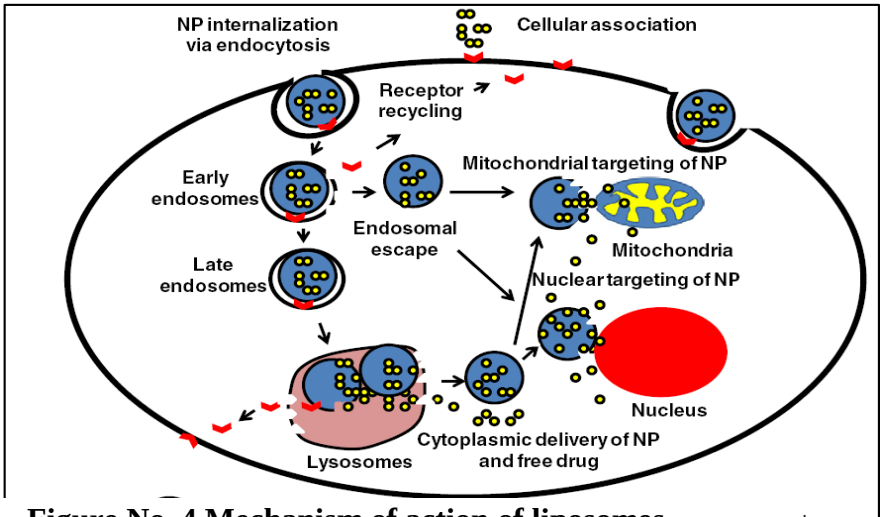

Figure No. 4 Mechanism of action of liposomes

4. Lipid exchange: Liposomal lipid membranes are analogous to phospholipids in cell membranes, causing lipid transfer proteins to form in the cell membrane.

For example, in the case of anticancer drugs the liposomes are loaded with nutrients which are required for cancer cell growth hence liposomes are easily targeted towards cancer cells and releases anticancer drugs. When the anti-cancer drugs enter the cancer cells then cells will be killed. The transformation of DNA into host cell with use of liposomes is known as lipofection. Liposomes can be used as carriers for the delivery of nutritional supplements to foods, and cosmetics to the skin, pesticides to plants and dyes to textiles.

❖ Dietary and nutritional supplements:

The applications of liposomes were primarily limited to drug delivery only, but the recent developments extend its uses for oral delivery of certain nutritional and dietary supplements. These developments were possible because of low bioavailability and absorption rates of oral dietary and capsules and nutritional tablets. These are clinically well documented. Hence, an effective method to efficiently deliver the encapsulated nutrients to tissues and cells by avoiding degradation of drugs by elements of gastric system such as gastric juices, acids and alkalis, would be the encapsulation of hydrophilic and lipophilic nutrients within liposomes.

❖ Types of Liposomes[1]:

Based on Structural Parameters:

1. Uni-lamellar vesicles: These are made up of only one lipid bilayer.

Types	Small Uni-lamellar vesicles (SUV)	Medium Uni-lamellar vesicles (MUV)	Large Uni-lamellar vesicles (LUV)
Size range (nm)	20-40	40-80	100 nm-1,000

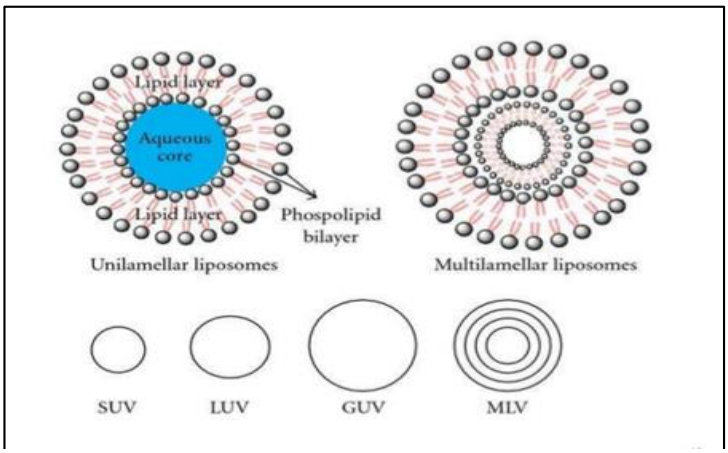

Figure No. 5 Different types of liposomes according to structural basis

2. Oligolamellar vesicles (OLV): This type of vesicles consists of 2-10 lipids bilayers with a large internal volume around.

3. Multilamellar vesicles (MLV): These vesicles consist several bilayers and can store the aqueous volume in myriad ways. The have concentric spherical bilayers of LUV/MLV containing huge number of vesicles like in onion.

- **The classification of Liposomes is based on their mechanism and work of intracellular delivery into five types as[1]:**

A. Conventional liposomes
B. pH sensitive liposomes
C. Cationic liposomes
D. Immune liposomes
E. Long circulating liposomes

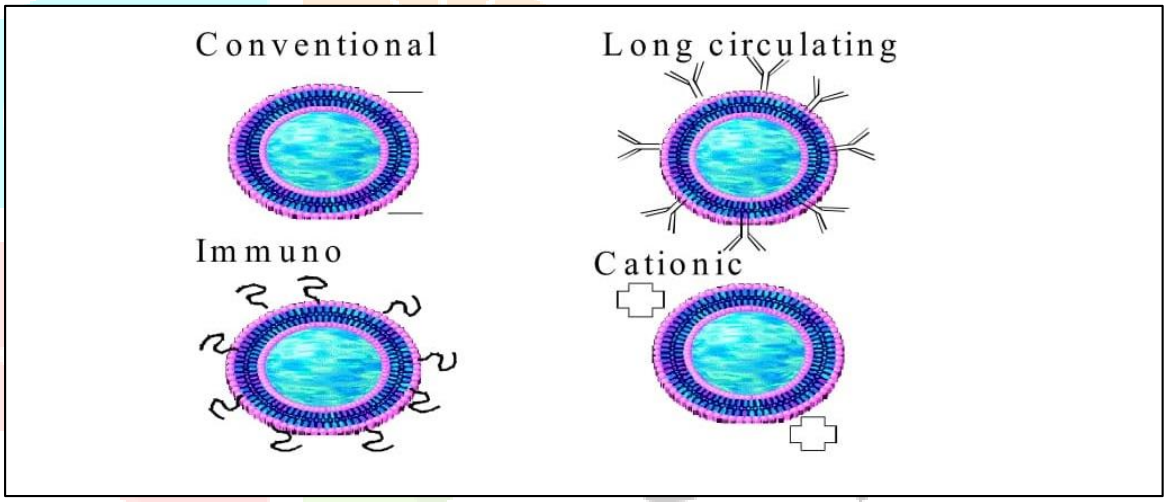

Figure No. 6 Classes of liposomes

A. Conventional liposomes:

The conventional liposome is first type which are used in pharmaceutical applications. They are mainly made up of natural phospholipids or lipids such as egg phosphatidylcholine, 1, 2-distearoryl-sn-glycero- 3-phosphatidyl choline (DSPC) and sphingomyelin.

B. pH-sensitive liposomes:

These are used to deliver content to cytosol not to lysosomes. Because lysosomes degrade the drug and decreases drug concentration. hence pH sensitive liposomes are used for cytosol targeting. Liposomes of varied compositions can bind to cell surface in large quantities. For pH-sensitive liposomes, dioleoyl phosphatidylethanolamine (DOPE) is by far the efficient lipid for in vitro gene transfection.

pH-sensitive liposomes were inspired by viruses that merge with endosomal membranes and before reaching the lysosomes they deliver their genetic material to the cytosol. Liposomes and their contents are transported to lysosomes and dyed using standard, pH-insensitive liposomes.

C. Cationic liposomes:

Generally, there is mixing of lipids with DNA. Feigner et al. were the first to synthesise and describe the cationic lipid DOTMA (1987). The ionic interactions between the negatively charged phosphate groups of DNA and the positively charged head group of DOTMA generate complex formation. The entrapment of DNA molecules in lamellae in clusters of aggregated multilamellar structures may be owing to an excess of lipids in terms of charge, according to cryo TEM study.

D. Immune liposomes:

By acting as immunological adjuvant there is wide applications in generating immune response. The incorporation of antigens into liposomal membranes or in the aqueous core causes increase immune response by antibody production, macrophage activation subsequent antitumor activity and effective induction of cytotoxic cell. Liposomes have several advantages as immunological adjuvants, including low toxicity, low antigenicity, biodegradability, and the ability to target specific cells in vivo. Liposomes are effective adjuvants for increasing immunogenicity to proteins, pathogenic viral antigens, glycolipids (gangliosides), and other antigens.

E. Long circulating liposomes:

The insertion of ganglioside GM1 or phosphatidylinositol at 5–10 mol percent into the bilayer resulted in the first significant improvements in blood circulation times. Long-acting liposomes are incorporated into the mononuclear phagocytic system through intrahepatic absorption. Long circulation periods were accomplished by covalently adding polyethylene glycol to the phospholipid. The molecular mass should be between 1500 and 5000 Da.

❖ PREPARATION OF LIPOSOMES[1]:

A. Active Loading Techniques

B. Passive Loading Techniques

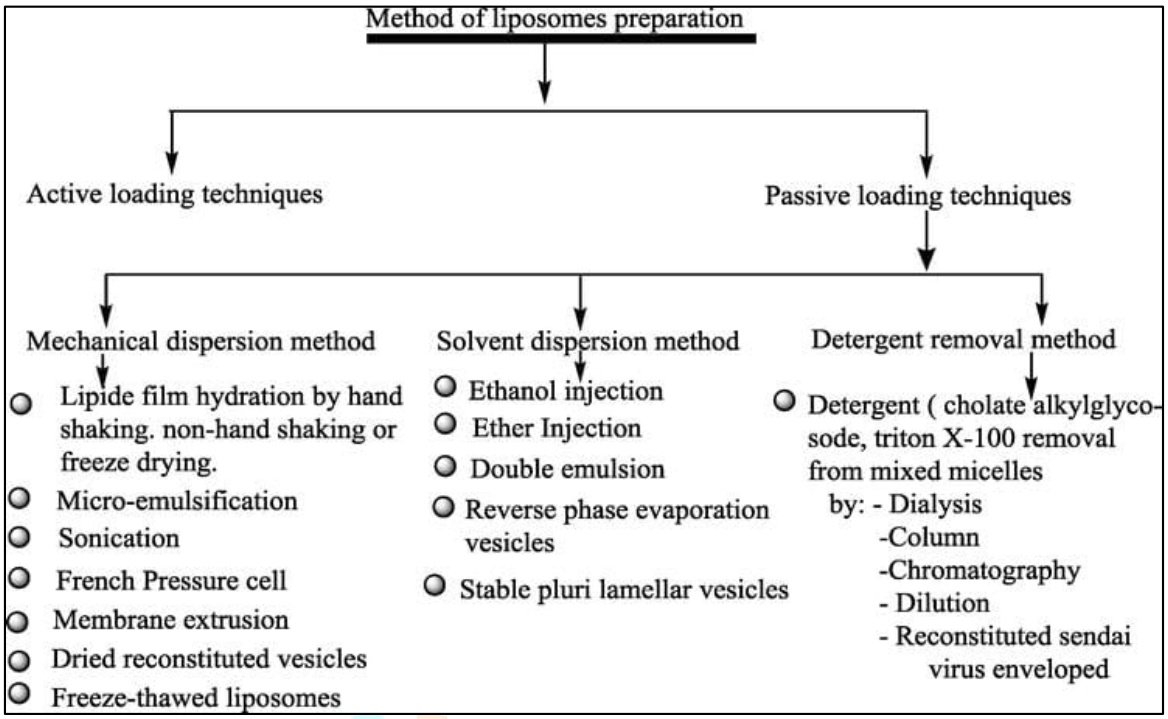

Figure No. 7. Methods of liposomal preparation

A) Active Loading Techniques: In an organic solvent, the lipid is dissolved. The solvent evaporates, leaving a thin lipid layer on the container's wall. A medication aqueous solution is introduced. The mixture is agitated to create multi lamellar vesicles, and then sonicated to obtain SUVs in the first procedure. To obtain LUVs, the mixture is sonicated and the solvent is evaporated in the second procedure. SUVs are produced after extrusion. If the drug is water soluble, it can be integrated into an aqueous solution or buffer, or it can be dissolved in an organic solvent if it is hydrophobic. Gel chromatography can separate free medicines from liposomes.

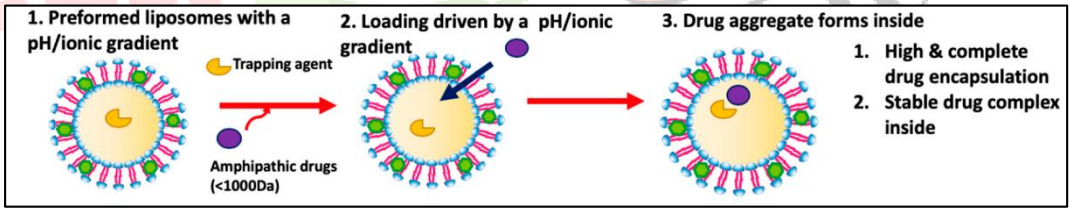

Figure No. 8 Active loading

B) Passive Loading Techniques: Based on the ways of dispersion, these are divided into three categories. Diagram[11]

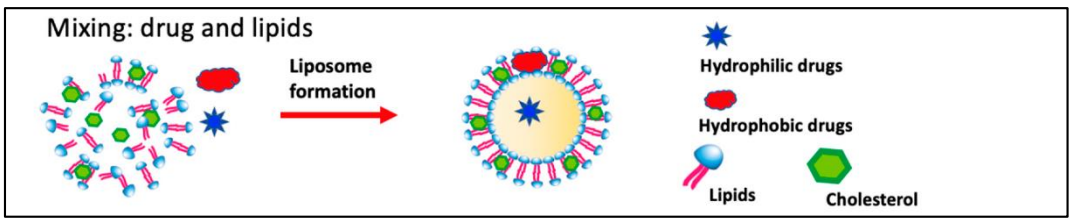

Figure No. 9 Passive loading

There are three methods Passive loading Techniques:

i. Mechanical Dispersion Methods

ii. Solvent Dispersion Methods

iii. Detergent Solubilization Technique

i) Mechanical Dispersion Methods: The aqueous quantities enclosed by lipid membranes in these procedures are around 5- 10% of the total volume used for preparation, which is a very tiny proportion of the total volume used. During preparation, a considerable proportion of water-soluble medication is squandered. A lipid soluble medication, on the other hand, can be encapsulated to a high proportion. MLVs are generated in these procedures, and further treatment is required to prepare Unilamellar vesicles.

The following are some of the methods that can be used.

a. Hand Shaken Method
b. Non-Shaking Method
c. Freeze Drying
d. Micro-emulsification of liposomes
e. Sonication
f. Membrane Extrusion Liposome
g. Freeze and Thaw Sonication

ii) Solvent Dispersion Methods: Lipids are first dissolved in an organic solution, then brought into contact with an aqueous phase containing components to be entrapped within liposomes in these procedures. The phospholipids align themselves at the interface between the organic and aqueous phases to create a monolayer, which is a critical step in the formation of the liposome bilayer.

There are two methods

a. Ethanol injection method
b. Ether injection

iii) Detergent Solubilization Technique: Phospholipids are brought into intimate contact with the aqueous phase in this procedure using detergents that bind to phospholipid molecules. Micelles are the structures that emerge as a result of this interaction. They are made up of a large number of individual molecules. CMC is the concentration of detergent in water at which micelles begin to form. The detergent molecule exists in free solution below CMC. Micelles occur in significant quantities when the detergent molecule is dissolved in water at concentrations higher than the CMC. The amount of detergent integrated into the bilayer increases as the concentration of detergent applied increases, until a point is reached where the bilayer converts from lamellar to spherical micellar form. The size of the micelles decreases as the detergent concentration is raised.

❖ TARGETING OF LIPOSOMES:

There are two types of targeting namely:

1. Passive targeting- Such commonly supplied liposomes have been proven to be rapidly removed from the bloodstream and taken up by the RES in the liver and spleen as a passive targeting method. When liposomes are addressed to macrophages, this potential of macrophages can be taken advantage of. Successful delivery of liposomal antimicrobial drugs to macrophages has proved this. Successful delivery of liposomal antimicrobial drugs to macrophages has proved this. As an initial stage in the development of immunity, liposomes have been utilised to target antigens to macrophages. For example, in rats, i.v. treatment of liposomal antigen induced a spleen phagocyte mediated antibody response, but non-liposome related antigen elicited no antibody response.

2. Active targeting – The targeting agents must be positioned on the liposomal surface in such a way that the interaction with the target, i.e., the receptor, can be tabulated, similar to a plug and socket mechanism. The liposome has been physically manufactured in such a way that the lipophilic section of the connection is fixed into the membrane during membrane formation. The hydrophilic portion of the liposome's surface to which the targeting agent should be maintained in a sterically proper location to connect to the cell's receptor.

i. Immuno liposomes: Antibodies or other recognition sequences [e.g. carbohydrate determinants like glycoprotein] are linked to these conventional or stealth liposomes. The antibody binds to the liposome and directs it to certain antigenic receptors on a cell. Glycoproteins and glycolipids are cell surface components that aid in cell-cell recognition and adhesion.

ii. Magnetic liposomes: Magnetic iron oxide is present. An external oscillating magnetic field in the delivery sites can steer these liposomes.

iii. Temperature or heat sensitive liposomes: They're made to have a transition temperature that's just over body temperature. After arriving at the spot, the medication was released by heating it from the outside.

❖ Other applications:

1.Liposomes in anticancer therapy:

There are very adverse effects of anticancer drugs but in liposome formulation it decreases (Weiner et al. 1989). Liposomal preparation has high selectivity towards cancer cells by targeting to the tumour vasculature/microenvironment has several advantages compared to cell surface receptors. Destruction of the vasculature inhibit or diminishes the metastasis and growth of the tumour. There is enhanced retention and permeation to cancer cells. In this way liposomes are attached for long time to accumulate in tumour cells. Then in the tumour cells liposomes delivers the drug inside the cancer cells. This reduces toxicity to normal tissues. Various differently liposome formulation shows mixed results in diverse stages of clinical trials (Bakker-Woudenberg et al. 1994).

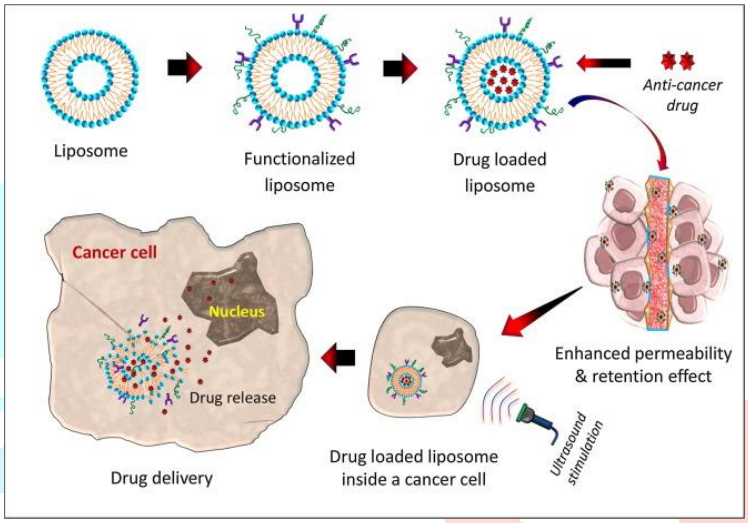

Figure No.10 Mechanism of acion of anticancer drugs

2. Liposomes as a delivery method for respiratory drugs:

In respiratory diseases liposomes are widely used. Liposomal aerosol has a number of benefits over regular aerosol. (Fendler and Romero 1977):

3.Liposomal Amphotericin B – Mucormycosis (zygomycosis):

Mucormycosis is becoming more common in Covid-19 patients, owing to growing use of steroids like dexamethasone, particularly among diabetics. Even if a patient is not at risk for the black fungus disease, uncontrolled and unsupervised use of steroid therapy can typically make things worse.

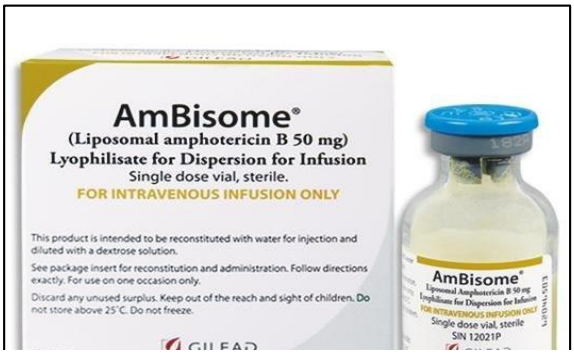

Figure No. 11 Amphotericin B liposomal preparation

Mucormycosis is a difficult-to-treat, often lethal infection that affects both immunocompromised and immunocompetent patients. Early diagnosis and treatment with an antifungal medication, as well as surgical intervention, have been found to be crucial for a positive result of the disease. There are only a few antifungal medicines available for treatment. For many years, amphotericin B (AmB) deoxycholate has been the treatment of choice, and it is typically administered at high daily doses that can cause kidney damage. Rather than conventional AmB, lipid formulations of AmB (liposomal AmB (L-AmB), AmB lipid complex (ABLC), and AmB colloidal dispersion (ABCD) have become the usual therapy. The use of lipid formulations is justified since they reduce the nephrotoxicity associated with long-term Amphotericine B use. Despite a growing consensus that large dosages of lipid formulations of AmB are the antifungal medication of choice for all Mucormycosis patients.

At therapeutically effective concentrations, AmBisome® has a lengthy blood residence time, with an elimination half-life of roughly 32 hours in humans. However, significantly greater doses of AmBisome® are common, and these higher levels result in increased antifungal effectiveness. Basic investigations in immune cooperation on the mechanism of action of AmBisome® in animals reveal that intact AmBisome® is effective in a rigorous infection. Direct interaction between AmBisome® and the fungal cell may occur at the site of infection, or AMB may be released from AmBisome® in the area of the fungus. Our group created sterically stabilised AMB-containing liposomes to achieve extended circulation of AMB liposomes without the need for a substantial lipid dose.

4.Next generation liposomes- Lipid nanoparticles in COVID-19 vaccines

Liposomes and lipid nanoparticles differ in those liposomes have a phospholipid bilayer while lipid nanoparticles have a micelle-like structure. The new Pfizer/BioNTech and Moderna mRNA COVID-19 vaccines contain lipid nanoparticles, which serve an important role in preserving and moving the mRNA to the correct location in cells. They are liposomes of the next generation. They are nanotechnology-enabled next-generation liposomes that are highly adapted to the steady and efficient delivery of a variety of medicines. Despite the fact that mRNA vaccines have attracted a lot of attention since they are a new form of medicine, lipid nanoparticles have been a staple of drug delivery systems (DDS) since the discovery of liposomes in the 1960s.

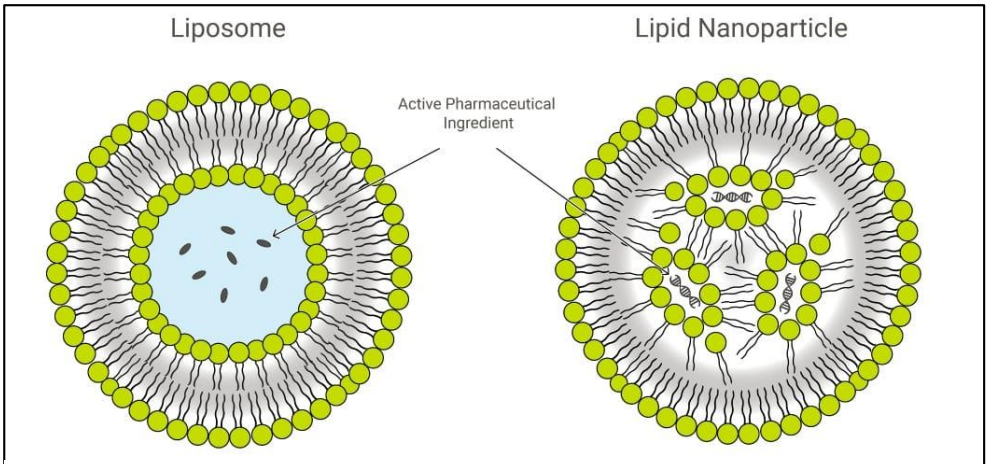

Figure No. 12 Liposome and lipid nanoparticle

Despite their obvious benefits for medication administration, lipid nanoparticles have one unfavourable side effect: they have the potential to cause an allergic reaction, especially in people who have severe allergies. However, anaphylaxis is uncommon, with researchers estimating a rate of one occurrence per million first doses of the Pfizer/BioNTech COVID-19 vaccine.

The lipid nanoparticles in both vaccines (Pfizer/BioNTech and Moderna) contain an ionizable cationic lipid, a PEGylated lipid, cholesterol, and a helper lipid, distearoylphosphatidylcholine (DSPC). The risk of sensitization appears to be higher with formulations having higher-molecular-weight PEG, such as PEG3350–PEG5000, leading scientists to conclude that these reactions are linked to the vaccine's PEG-lipid component. It's worth noting that only MW PEG2000 is used in mRNA vaccinations.

mRNA editing for optimal stability and translation capacity in vivo[14]

In pH ranges 5-7 often used for parenteral, mRNA is a polyanionic macromolecule due to the negative charges on its phosphate groups (Lipfert et al., 2014). A first challenge for mRNA vaccines is that naked mRNA is quickly destroyed by ribonucleases (RNase), which are abundant in the extracellular environment. Second, intracellular RNA sensors such as endosomal Toll-like receptors (TLR) and cytoplasmic nucleic acid sensors detect mRNA internalisation. Innate immune pathways are activated when mRNA binds to these host defence receptors, resulting in the activation of hundreds of genes. On the one hand, this might act as an adjuvant, increasing the vaccine's potency. On the one hand, this could serve as an adjuvant, boosting the vaccine's effectiveness. On the other hand, it causes cells to enter an antiviral state, reducing intracellular stability and mRNA translation (Pepini et al., 2017). In order for the encoded protein to be produced, mRNA strands must be recruited into ribosomes after internalisation. The rate of protein synthesis and the functional half-life of mRNA can both be greatly improved through mRNA editing. The typical elements of an mRNA strand for inclusion in an mRNA vaccine are schematically depicted in Fig. 1.

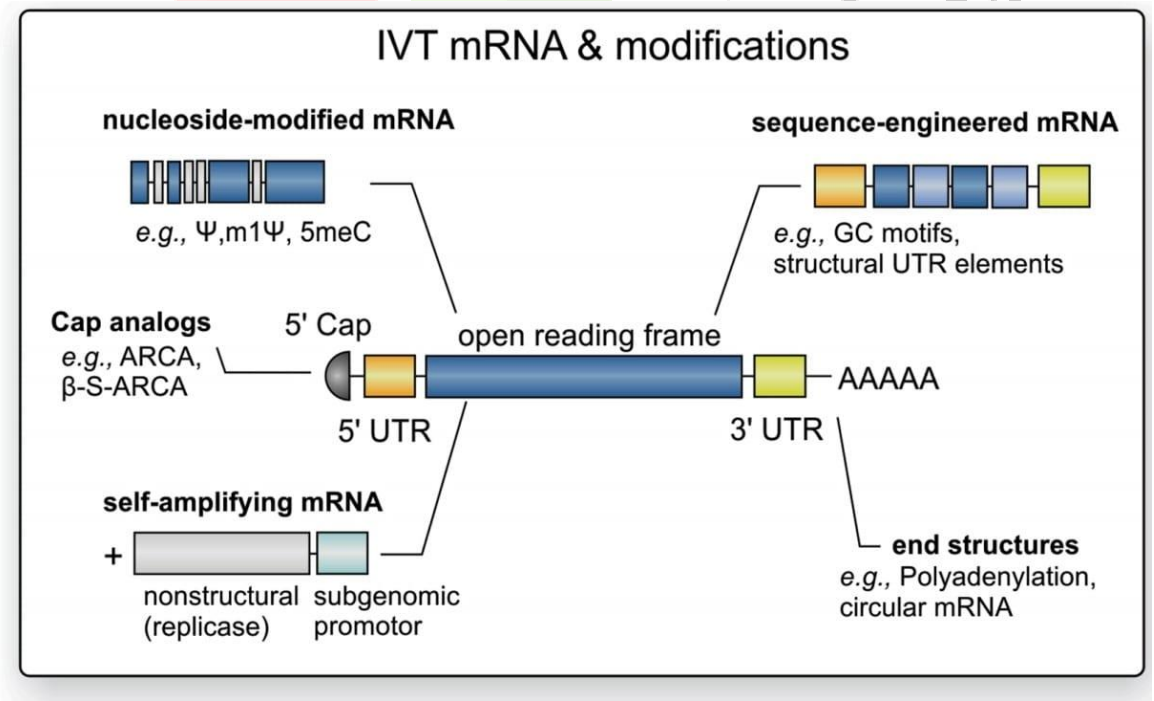

Figure No. 13 mRNA modification

Many attempts have been made to increase the stability and translation capability of the mRNA molecule in vivo while avoiding unwanted innate immune activation. One widely held belief is that this can be accomplished by optimising the 5′ cap, poly-A tail, and untranslated sections of the mRNA (UTRs). The UTRs are mRNA portions that border the coding region and influence the mRNA's stability and translation. Because its shortening and eventual removal leads to mRNA degradation, the poly-A tail also regulates stability. Protein synthesis and the recruitment of translation initiation components are both dependent on the

Therapeutic application	**Liposomal preparation (brand name)**	**Active compound**	**Type**
Cancer Therapy	Daunoxome®	Daunorubicin (Dspc and Ch)	Conventional Technology
	Depocyt®	CYTARABINE (DOPC, Triolein, DPPG and CH)	Depofoam Technology
	Evacettm	DOXORUBICIN	Conventional Technology
	Mepact®	MIFAMURTIDE	Non-Pegylated Liposome Technology
	Myocet®	DOXORUBICIN	Non-Pegylated Liposome Technology
	Onivydetm	IRINOTECAN	Stealth Liposome Technology
Fungal Infection	Abelcet®	Amphotericin B (Dmpc and Dmpg)	Non-Pegylated Liposome Technology
	Ambisome®	AMPHOTERICIN B (HSPC, CH And DSPG)	Conventional Technology
	Amphocil®	AMPHOTERICIN B (Sodium Cholesteryl Sulphate)	Non-Pegylated Liposome Technology
Analgetics	Depodurtm	MORPHINE SULFATE (DOPC, CH, DPPG, Tricaprylin, And Triolein)	Depofoam Technology
	Exparel®	BUPIVACAINE	Exparel®
Viral Vaccines	Epaxal®	Hepatitis A Vaccine (Dopc and Dope)	Detergent Removal Method
	Pfizer’s mRNA	Nucleoside-modified messenger RNA encoding viral spikes of SARS-Cov-2	Lipid Nanoparticles

5′ cap structure (Pardi et al., 2018). Furthermore, high-GC (guanine-cytosine) mRNA paired with codon optimization, i.e., the use of "frequent codons" in the coding region, leads to better stability and translation (Thess et al., 2015).

❖ Liposome-based products in clinical use, their active ingredients, therapeutic uses, lipid bilayer structure, and preparation method:

❖ CONCLUSION:

Liposomes are used in broad spectrum of pharmaceutical applications. And it is extensively used as targeted drug delivery system. Liposomes are promisingly a good drug delivery system to reduce all toxicities compared with other dosage forms. Their reduced toxicities due to their specific targeting tissues targeting by their passive and active loading. Currently it is very used in mRNA vaccine with lipid nanoparticles which liposome with single layer like micelle. The liposomal preparation of amphotericin B is first line treatment for mucormycosis which is developed from Covid patients due to excess of using steroids. From all data and recent wide applications, we can say it is probably most efficient drug delivery system in current DDS.

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