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Review Article

Liposomes in Modern Medicine: The Future of Life, Healthcare

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ABSTRACT

The word liposome is a combination of the Greek words "Lipos," which means fat, and "Soma," which means body. Liposomes are spherical-shaped vesicles made up of cholesterol and phospholipids that are being studied extensively as medication carriers to increase the delivery and bioavailability of medicinal substances. Many liposome-based drug delivery systems are presently undergoing clinical trials as a result of creative advancements in liposome technology, and some of them have recently been granted approval for clinical usage. Their hydrophobic and lipophilic properties, along with their size, make them emerging drug delivery methods. The goal of this innovative drug delivery method is to deliver the medication straight to the site of action. Liposomes are stable and biocompatible. Their ability to trap both hydrophilic and lipophilic drugs (due to their amphipathic nature) in their compartment makes them special.

INTRODUCTION

By maximizing the drug concentration, extending the drug's residence duration in target cells, and reducing side effects, drug delivery systems (DDSs) have the potential to improve the therapeutic index of pharmaceuticals. By enhancing drug pharmacokinetics and biodistribution, as well as serving as drug reservoirs, DDSs aim to improve the pharmacological qualities of free medicines and mask their undesired aspects by delivering the potentially active drug to the site of action via a nano-vehicle. Depending on their intended use, these nanoparticles (NPs) typically have sizes ranging from a few nanometres to several hundred nanometres. NPs are made from a variety of natural, organic, and inorganic materials, such as metals, polymers, ceramics, and lipids that form micelles and liposomes.

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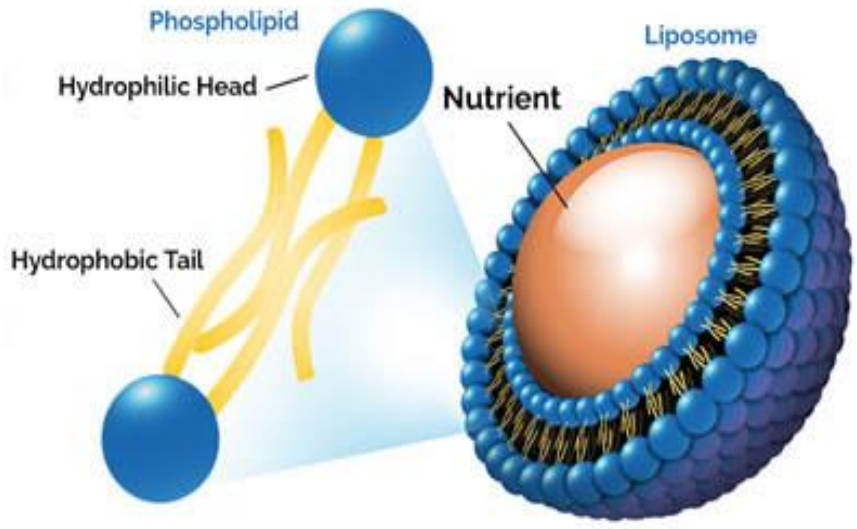

Fig. Design of Liposomes

The key physical interactions that allow therapeutic medicines to be integrated into NPs are entrapment, surface attachment, and encapsulation The distinct qualities and variances among various NPs may be leveraged to enhance the features of conventional treatments. Creating innovative therapeutic choices at the nanoscale range to offer a range of active biomedical ingredients for the diagnosis, treatment, and prevention of numerous diseases is made easier by nanomedicine. Even with the rapid advancements in this area, the majority of drug delivery systems based on nanoparticles exhibit inadequate loading capacity and insufficient specificity against their intended targets. Designing high and regulated capacity nanocarriers functionalized by recognition ligands that selectively target unique or overexpressed biomarkers is therefore necessary for the potential advancements in drug delivery systems. When it comes to targeted medication delivery systems, liposomes are the most studied nanocarrier. As a consequence of emulsifying natural or synthetic lipids in an aqueous media, liposomes—which typically have a diameter of 50–500 nm—are spherical lipid vesicles made up of one or more lipid bilayers. After Bengham made the first discovery of liposomes in the 1960s, they went on to become one of the most widely used drug delivery methods Furthermore, liposomes can be administered via a variety of methods, including ophthalmic, oral, pulmonary, transdermal, and parenteral, for both diagnostic and therapeutic purposes. Phospholipids like soybean phosphatidylcholine or synthetic dialkyl or trialkyl lipids [30] are the main ingredients used to make liposomes. Since cholesterol alters fluidity, enhances stability, and modifies membrane permeability in the presence of biological fluids like blood and plasma, it is imperative that cholesterol be incorporated into liposomes. In order to increase the efficiency of the encapsulated medication, prolong their circulation half-life, and optimize the biodistribution profile, liposomal formulations may additionally comprise polymers and even membrane protein. Furthermore, it has been demonstrated that Stealth stabilized liposomes, which incorporate polyethylene glycol (PEG) coupled to phospholipids into the liposomes' infrastructure, are a

Liposomes

Based on their size and lipid bilayer, liposomes can be divided into four primary categories: multivesicle vesicles (MV), small unilamellar

vesicles (SUV), large unilamellar vesicles (LUV), and multilamellar vesicles (MLV). MLVs have several concentric bilayers that resemble an onion structure, whereas SUVs have a phospholipid bilayer. Large liposomes containing several unilamellar vesicles produce a complicated multilamellar configuration within MVVs. Liposome entrapment efficiency for hydrophilic substances generally increases with liposome size and decreases with bilayer number. The vesicle size plays a crucial role in defining the blood circulation half-life. For drug delivery applications, liposomes typically have a diameter of 50–150 nm. Numerous mechanisms, including as receptor-mediated endocytosis, local fusion, phagocytosis, and direct entrance into the cell membrane, can be used to explain how liposomes interact with cell membranes. The biological milieu, targeted ligand presence, and liposome composition and surface charge are some of the variables influencing these interactions.

Makeup of liposomes

1.Liposome-producing lipids and phospholipids

Liposomes are a type of vesicle that can be spherical or multilamellar, which are created when diacyl-linked phospholipids in an aqueous solution self-assemble. Lipid bilayers with hydrophilic head groups and hydrophobic tailed phospholipids forming an amphiphilic arrangement are what define this structure. Phospholipids, both synthetic and natural, can be used to create liposomes. The lipid makeup of liposomes influences their stability, stiffness, fluidity, cost, and particle size. For instance, liposomes derived from phosphatidylcholine that occurs naturally and is unsaturated, like egg or liquid phosphatidylcholine, typically exhibit permeability and instability. On the other hand, the bilayer structure of liposomes derived from saturated phospholipids, like dipalmitoylphosphatidylcholine, is less permeable and more rigid.

Electrostatic repulsion can impact the stability of the liposomes through the hydrophilic component of the lipids, which can be negatively, positively, or zwitterionic charged. The lipids also differ in terms of length, symmetry, and saturation level of their hydrophobic tails.

2.Organic Fats

Glycerophospholipids make up the whole bilayer membrane of a typical cell. Two fatty acid chains and a phosphate group are joined to a glycerol backbone to form these phospholipids. Choline and other small, significant compounds can also have phosphate groups linked to them. Soybeans and egg yolks are natural providers of phospholipids. Based on their polar head groups, such as Acid (PA) or Serine (PS), Phospholipids are classified as phospholipids, phospholipid ethanolamine (PE), phospholipid glycerol (PG), phospholipid inositol (PI), and phospholipids. Since unsaturated fatty acid chains are present in natural phospholipids, they seem to be less stable than manufactured phospholipids in liposomal formulations. ... unsaturated fatty acids found in egg lecithin, such as oleic acid (9Z-octadecanoic acid) and heptadecanoic acid (heptadecanoic acid). Palmitic acid (C16:0), stearic acid (C18:0), oleic acid (C18:1), linoleic acid (C18:2), and arachidonic acid (C20:4) make up the phospholipids generated from eggs. Together, these fatty acids make up roughly 92% of all fatty acids. For instance, 1-palmitoyl-2-oleoylphosphatidylcholine makes up about 40% of egg PC. Whereas palmitic acid prevails among other phospholipids, stearic acid is the primary saturated fatty acid for phosphatidylethanolamine (PE) and phosphatidylserine (PS). Additionally high in oleic acid (C18:1), stearic acid (C18:0), palmitic acid (C16:0), linoleic acid (C18:2), and

linoleic acid (C18:3) is soy lecithin. Fatty acids comprise over half of unsaturated fatty acids. These unsaturated fatty acids are often located in phospholipids in the α- and β-positions of the glycerol moiety.

3. Artificial Fats

The polar and nonpolar portions of natural phospholipids are chemically modified to create synthetic phospholipids, which has led to the isolation and definition of numerous distinct phospholipids [56]. Large saturated synthetic phospholipids are often made of palmitic or stearic fatty acids. A range of commercially available synthetic and phospholipids frequently utilized in liposome formulations are depicted in Figures 3 and 4 [53]. Furthermore, unsaturated fatty acids, which can be in both hydrocarbon chains or only one directed chain, can be mixed with synthetic phospholipids or a fatty acid chain [52].

4.Anabolic

Tetracyclic hydrophobic lipids are known as steroids. The many functional groups that are affixed to these rings account for the variations in steroids. When making liposomes, cholesterol is frequently utilized and typically makes up less than 30% of the total lipid content. Its presence makes the liposome lipid bilayer more stable and stiffer. Studies that compare the effects of cholesterol and β-sitosterol on liposome membrane properties have revealed that both steroids alter the phase transition temperature (Tm) and enthalpy of DPPC, decrease membrane fluidity, increase zeta potential, and change size.

Kinds of Liposomes

Based on its makeup and intended applications, liposomes can be classified into several categories, including charged liposomes, stealth liposomes, active targeting liposomes, stimuli-responsive liposomes, and bubble liposomes. Every kind has special qualities and applications of its own.

1. Standard Liposomes

As an early lipid delivery technique, liposomes can be created from synthetic or natural phospholipids, with or without cholesterol [75]. By changing the bilayer's stability and rigidity, cholesterol can be added to liposomes to increase their fluidity [31, 32]. Wu et al. skin irritation by adding cholesterol to liposomes made of DSPE-PEG2000 and hydrogenated soybean lecithin (HSPC). Improved immune system performance and tumor penetration are linked to this alteration [76]. Kadar and colleagues investigated the impact of varying cholesterol concentrations on the permeability and fluidity of DPPC liposome membranes. More cholesterol, they discovered, causes liposomes to enlarge and transform from nanoscale spherical vesicles to nanoscale spherical vesicles. Furthermore, elevated cholesterol levels influence the release of hydrophilic molecules from lipid vesicles and decrease bilayer fluidity [77]. Giovanovi et al. have demonstrated that elevated cholesterol reduces fluidity and increases the absorption of liposomes. According to their findings, 50 mol% of cholesterol is the ideal concentration to provide the best membrane fluidity and stability [78]. crucial part. However, the composition of the encapsulated medication and the ratio of cholesterol to phospholipids influence these characteristics. Because the mononuclear phagocyte system (MPS) can readily eliminate normal liposomes and they quickly accumulate in the liver and spleen, they typically only stay in the blood for a brief period of time [79].

2. Ionized Liposomes

To create anionic and cationic liposomes, respectively, oleic acid and N-[1(2,3-dioleoyloxy)

propyl]-N, N, N-trimethylammonium chloride (DOTAP) are frequently utilized. Because comparable particles have repulsive interactions that lessen the likelihood for aggregation, charged liposomes will be more stable during storage. Because cationic liposomes may encapsulate nucleic acids through electrostatic interactions, they are especially helpful in gene therapy. Glycosides' size and valence prevent cells from absorbing them. Furthermore, angiogenic endothelial cells in malignancies can be specifically targeted by cationic liposomes. Due to their ability to cross the blood-brain barrier (BBB) by either receptor-mediated or uptake-mediated transcytosis, they also show potential for delivering treatments to the brain. On the other hand, the advantageous position could influence blood circulation, leading to buildup and perhaps influencing therapy.

3. Liposomal Stealth Stabilization

Enhanced target dispersion and aggregation at targeted areas are achieved by adding synthetic components, glycoproteins, glycans, or particular receptor ligands to the surface of second-generation liposomes. Liposomes can be efficiently protected by the application of valorinic acid, polyvinyl alcohol (PVA), and polyethylene glycol (PEG). Stealth liposomes, also known as pgylated liposomes, are long-acting liposomes that maintain their protective properties for the immune system. The first PEGylated liposome-based product to be successful was Doxil®. Comparing these stealth liposomes to conventional liposome models, their duration of action is greater, which increases their accumulation at target areas.

4.Intensely Focused Liposomes

Third-party liposomes, a recent development in liposome technology, serve the purpose of liposomes. These liposomes use a functional target to improve how well they interact with particular organisms. This is accomplished by combining ligands that bind to particular cellular receptors in order to cause receptor-mediated liposome endocytosis, which delivers the liposomes' therapeutic payload to the target cells. Enhanced permeability and retention (EPR) effects on tumor cells have been the basis for passive targeting in many liposomal nanocarriers historically. Antitumor medications can be delivered to tissues using this technique, however it is nonspecific and unable to discriminate between cancerous and healthy cells. Researchers have created disease-specific liposomes that can enhance the transport of antibodies straight to the illness in order to get around this restriction. Formulating a proactive objective These components include simple peptides, carbohydrates, nucleic acids, proteins (including antibodies and their fragments), and vitamins. Reducing adverse effects while improving medicine delivery efficiency is the goal. In spite of untargeted liposomes' effectiveness in the therapeutic context, ligand-targeted liposomes have seen tremendous development as well. The application of polyunsaturated fatty acids, folic acid, hyaluronic acid, or oligopeptides as target moieties is the main focus of new drug delivery strategies. Nevertheless, these ligands frequently have poor effectiveness, poor selectivity, and blood-level degradation. Due of their high affinity and specificity in drug administration, aptamers and aptamer-functionalized nanoparticles have garnered attention in recent years. Complete or surface binding, whether covalent or non-covalent, occurs on the nanocarrier.

5. Liposomes That React to Stimulants

Advanced drug delivery systems known as stimulus-responsive liposomes are made to release their medications in reaction to particular stimuli.

Many physicochemical or biological stimuli, including variations in pH, temperature, redox conditions, the presence of enzymes, ultrasound, and exposure to magnetic or electric fields, can cause these liposomes. Compounds that change the permeability and stability of the lipid bilayer are required for stimulus-responsive liposomes. The two primary forms of stimulation are local stimulation and distant stimulation. While local stimulation involves characteristics specific to the target tissue, such as pH, redox potential, and specific enzymes, remote stimulation involves additional elements like heat, magnetic field, light, electric field, and ultrasound.

6. Liposomes In Bubble Form

In gene and medication delivery systems, bubble liposomes—also called gas-encapsulated liposomes—have become an innovative technique. The efficiency of drug delivery can be increased by using liposomes to encapsulate bioactive gasses and/or pharmaceuticals and offer controlled release of ultrasound, as evidenced by recent advancements. For instance, since they stop NO from dislodging hemoglobin—a issue that occurs when NO is absent—nitric oxide (NO) bubble liposomes have a particular therapeutic effect on NO. Furthermore, oxygen bubble liposomes (OBL) are made to deliver large amounts of oxygen and sustain elevated pO2 levels in the lungs. This establishes OBL as an oxygen delivery system and sets it apart from other oxygen delivery systems like hemoglobin-based and fluorocarbon-based systems.

An Analysis of Liposomes

1. Outward Look

The appearance of liposome suspensions can range from translucent to milky, depending on their size and composition. Small particle sizes are indicated by a blue hue in the turbidity, but the presence of non-liposomal dispersions, such as scattered inverted hexagonal phases or crystallites, is typically indicated by a gray hue. Using phase-contrast light microscopy, one may detect bigger particles and liposomes exceeding 0.3 μm in size.

2. Calculating the Size of the Liposomal

Liposome sizes are frequently determined using dynamic light scattering, particularly when there is little variation in them. A straightforward technique for figuring out the real hydrodynamic radius of liposomes is gel exclusion chromatography. Liposomes ranging in size from 30 to 300 nm can be separated using Sephacryl-S100. Furthermore, it is possible to differentiate between micelles and small unilamellar vesicles (SUVs) using Sepharose-4B and Sepharose-2B columns.

3. The Lamellarity Calculus

Liposomal lamellar structure is frequently evaluated by means of electron microscopy or other spectroscopic techniques. Liposome spectroscopy in nuclear magnetic resonance (NMR) spectroscopy can be recorded with or without paramagnetic materials. The signal from the liposome's outer surface core can be changed or diminished by this substance. The presence of hydrophilic indicators in liposomes is examined and their encapsulation ability is evaluated.

4. The Stability of Liposomes

Liposomes need to be stable in terms of their structure, chemistry, and biology. Maintaining lipid equilibrium for therapeutic drugs and consistent liposome size are examples of physical stability. In order to stop oxidative and hydrolytic breakdown, chemical stability is crucial. In phospholipids, oxidation mostly affects unsaturated fatty acid chains, and the process still

happens even in the absence of particular oxidizing agents. Liposomes should be kept in a low-temperature environment and shielded from light and air to reduce oxidation. Controlling the agent's size and lipid content is crucial for its stability within the body. Once sterilised, cationic liposomes remain stable at 4°C for extended periods

5. Confined Tone

You can utilize data for each of the liposomes' fluids to estimate the liposome population's influence (measured in μL/mg phospholipids). This approach makes the assumption that, once the entrapped fluid is isolated from the unencapsulated material, the fluid within the liposome is homogenous. Phospholipids can be measured in μL/mg to determine the impact of each liposomal fluid on the total population. After the liposomes are separated from the unencapsulated material, this approach assumes that the fluid inside the liposomes is homogeneous.

To determine encapsulation efficiency, use the formula below:

Encapsulation efficiency = (Total drug added (mg) / Amount of drug encapsulated (mg)) × 100

Here, the amount of drug processed into the formula is measured, its amount is compared to the overall amount of drug added, and the result is multiplied by 100 to display the percentage.

6. Elevated Surface

Since lipids that provide, a charge is typically used to make liposomes, it is critical to determine the charge of the vesicles. Zeta potential measurement and free-flow electrophoresis are the two techniques that are typically employed for this purpose. The mobility of liposome dispersions in suitable buffers can be used to calculate the number of vesicles.

Procedures For Getting Ready

There are several ways to produce liposomes, and the final liposomes' characteristics can be influenced by the phospholipids that are employed. Many categories can be used to group this production technology.

1. Bangham Method, Or Thin Film Hydration Method

All lipids and hydrophobic materials are dissolved in an appropriate organic solvent within a glass substrate during this procedure. To create a thin film, the organic weight is then gradually evaporated under lower pressure. After that, the film is hydrated with an aqueous solution at a temperature that is higher than the lipid's transition temperature (Tm). Add any hydrophilic materials needed to make liposomes to the hydration solution. The rate of hydration has an impact on the effectiveness of drug encapsulation. In general, increased encapsulation efficiency results from slower hydration. The suspension can be exposed to bath or probe sonication, or it can be extruded through a polycarbonate membrane with a specified pore size to control the size, lamellarity, and particle distribution of the liposomes. Comparatively speaking, sonication is less effective in stabilizing liposomes than the extrusion procedure. Experimental sonication has the ability to introduce metal particles into liposome solution while also producing small unilamellar vesicles (SUVs) and perhaps causing the hydrolysis or destruction of medicines contained in lipids.

2. The Reverse-Phase Method of Evaporation

Reverse evaporation offers an additional pathway for membrane hydration and can be used to produce water-in-oil emulsions. Lipids are dissolved in organic solvents during this procedure and combined with hydrophilic water. By

employing an evaporator to evaporate the organic solvent at low pressure and submerge it in the aqueous phase, lipid vesicles are created. Larger and more numerous vesicles can be made via extrusion. Though useful for high molecular weight products, this approach may not be appropriate for purifying peptides due to the potential for denaturation caused by organic solvents and ultrasonic treatments.

3. Methods of Injecting Solvents

The distribution of injection techniques is contingent upon the kind of organic solvent employed [151]. This procedure involves incorporating active hydrophobic compounds and lipid-solving organic solvents into the aqueous phase. For instance, when agitated at temperatures higher than its boiling point, diethyl ether permits the solvent to evaporate directly [152]. Nevertheless, ethanol used for injection must be diluted ten to twenty times with the aqueous solution. Using methods like filtering, dialysis, or rotary evaporation, the ethanol can be eliminated in vacuo. Liposome formulations with a higher polydispersity index (PDI) are typically produced by this method [153]. Furthermore, the stability of drugs and lipids may be impacted by extended exposure to high temperatures and organic solvents [154].

4. Method For Removing Detergents

Using a round-bottom flask and an appropriate organic solvent, lipids and surfactants with high critical micelle concentrations (CMC) are dissolved in this procedure. A thin layer forms at the flask's bottom as the solvent gradually evaporates. To create a micellar mixture, an aqueous solution containing drug molecules is hydrated onto the lipid membrane. After that, the surfactant is eliminated using techniques like dilution, size chromatography, hydrophobic bead adsorption, and dialysis. The solution is concentrated in the last phase to create large unilamellar vesicles, or LUV liposomes. The possibility of losing a large number of hydrophilic molecules during surfactant removal is a significant drawback of this strategy.

5. Method Of Dehydration and Rehydration

Lipids were directly dispersed in an aqueous solution containing drug molecules under sonication in order to create large unilamellar vesicles (LUVs) without the need of chemical solvents. Water first turns into nitrogen by evaporation, forming a multilayer sheet that traps molecules of chemicals. Subsequently, the medication is encapsulated in huge vesicles formed by hydration. Despite being straightforward, this approach frequently produces variations in liposome size.

6. Technique Of Heating

Lipids are directly hydrated with aqueous solutions in this solvent-free organic process. In order to complete this process, the temperature must be raised to a level above the phospholipid's melting point (Tm) for at least an hour. A humectant, such as propylene glycol or glycerin, is added at a concentration of 3-5% during this procedure. One option is to heat the suspension to 100 °C before adding cholesterol to the sample. Water-based compounds provide isotonicity, stabilize the nanoparticles, and inhibit coagulation and sedimentation. The respiratory powder liposomes are formed more efficiently by the heating procedure thanks to the cryopreservation provided by these reagents.

7. Using The Ph Leaping Technique

The pH jump approach is another solvent-free way to manufacture liposomes. The procedure entails quickly raising the pH of an aqueous solution

containing phosphatidic acid and phosphatidylcholine—typically by four times. QuickpH shifts cause multicellular vesicles (MLVs) to break down and encourage the growth of tiny unilamellar vesicles (SUVs). The ratio of SUVs to large unilamellar vesicles (LUVs) generated in the combination depends on the ratio of phosphatidic acid to phosphatidylcholine.

8. The Microfluidic Channel Approach

A novel technique for liposome preparation is microfluidic channel technology. The water flow is managed by the technology through tiny channels. Lipids are initially dissolved in isopropyl alcohol or ethanol in this procedure. Next, either in parallel or countercurrent to the aqueous medium flow, this lipid solution is introduced into the microchannel. Liposome production is facilitated by the mixing of aqueous and organic solutions in this line. Liposomes are stabilized with the use of surfactants to avoid issues like aggregation and separation. By precisely controlling the two phases' mixing, the microfluidic channel approach guarantees that the final liposomes will have the same size, shape, polydispersity, and layering.

9. The Supercritical Fluidic Approach

Lipids are dissolved using the technique, which substitutes supercritical carbon dioxide (CO2) for organic solvents. The supercritical lipid solution is contained in a pool to which the aqueous phase is continually supplied by a high-pressure pump. The transfer of phospholipids that have dissolved is facilitated by this arrangement. Liposomes occur when the pressure is lowered and the CO2 is eliminated entirely. Compared to conventional approaches, this approach is five times more efficient at encapsulating. However, because of its high cost, low efficiency, and requirement for specialized infrastructure, the use of carbon dioxide is restricted even if it is economical and environmentally good**.**

After-Preparation Management

1.Initial Freeze-Thaw Periods

This process is frequently applied to liposome synthesis in order to improve lamellarity and encapsulation efficiency. It includes freezing and thawing the liposome and then swapping it in liquid nitrogen at a temperature below the phospholipids' transition point, which can be as low as -196°C.

2.Lyophilization, Or Freeze-Drying

To increase the shelf life and preserve the quality of liposomal products, freeze drying is frequently utilized. The liposome suspension is thoroughly mixed before being combined with a cryoprotectant (such as 5%–10% sucrose or trehalose). Sublimation is then used to turn the liquid into a powder combination at a low temperature and low pressure. Lyophilization is especially crucial for liposomes that contain biomolecules that are heat sensitive.

Production Procedure

Numerous techniques have been created to create liposomes, and publications and patent documents have detailed a range of production options. The methods include double emulsification, ethanol injection, and thin film hydration. Broadly speaking, the production process consists of:
1.MLV or ULV Preparation: Depending on the method selected, create multilamellar vesicles (MLV) or unilamellar vesicles (ULV).
2.Important Note: If needed, the vesicles' size can be decreased.
3. Drug Loading: This is injecting the drug solution into the vein once it has been prepared.

When it comes to passive chemical loading, step 1 and this step are integrated.

4.Predictability and Focus: Although they can be changed as needed, bubbles are not interchangeable.

5.Aseptic Processing or Sterile Filtration: Guarantees the sterility of the product.

6.Packaging And Drying: The product is packaged after being freeze-dried if needed.

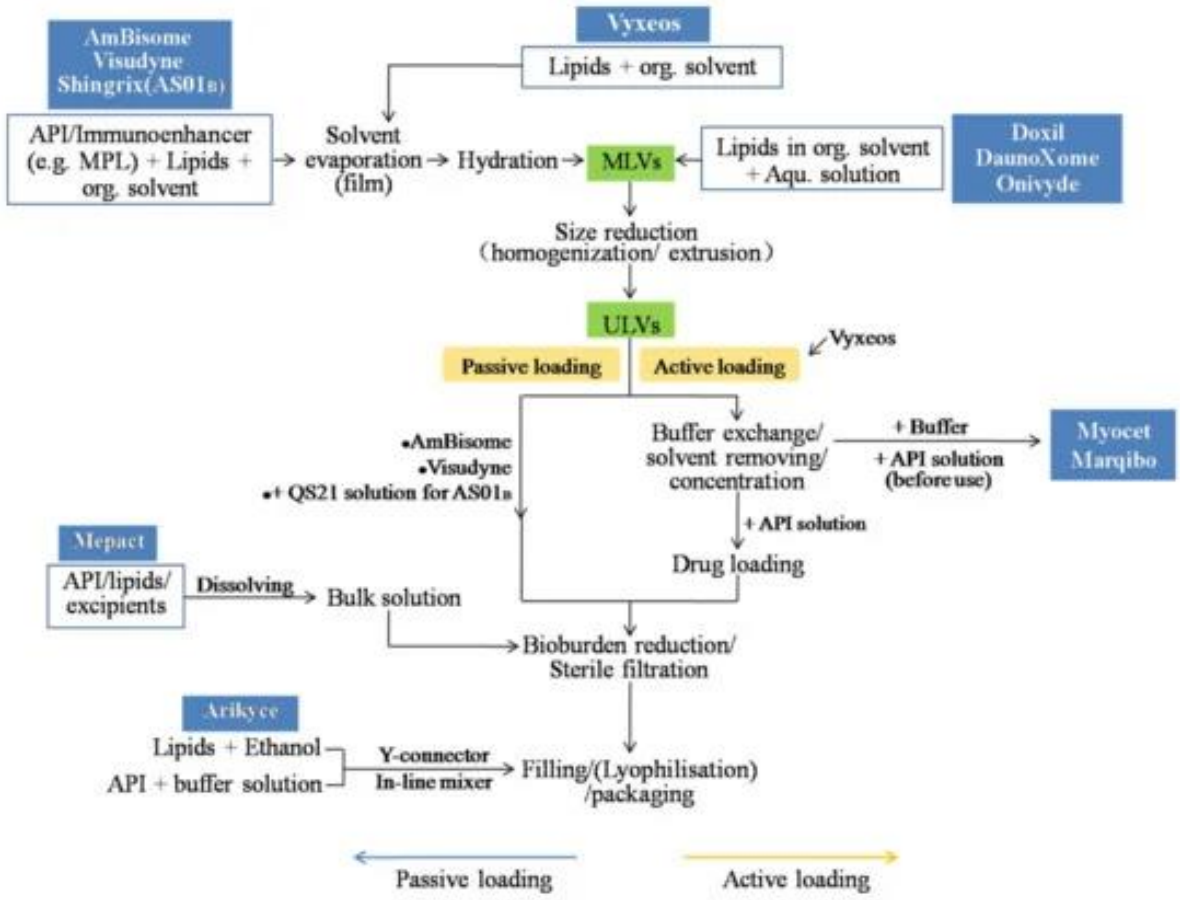

Fig: 2 Publications and Patents Suggest the Following Possible Liposomal Product Manufacturing Processes:

Methods of Reducing Size

Liposome size and shape frequently have an impact on safety and effectiveness. Different techniques, including homogenization, French pressing, extrusion, and (ultra) sonication (with a bath or probe), can be applied to decrease liposome size. Furthermore, employed are technologies like freeze-thaw ultrasonic treatment, high-pressure homogenization and extrusion, and freeze-thaw extrusion. Two especially sophisticated and often used pharmaceutical production procedures are extrusion and high-pressure homogenization (HPH).

By pushing bigger liposomes through an asymmetric ceramic filter or a polycarbonate membrane with hole diameters ranging from 50 nm to 5 µm, extrusion technology—which was first utilized in 1971—manufactures small liposomes. A number of commercial nanoliposome products, including Onivyde, Vyxeos, and Marqibo, are made using this technique. Simple, dependable, and requiring little setup time are its main selling points. Several vesicles (MLVs), which fragment as they cross the membrane and reassemble to create tiny liposomes, are the basis for this approach. A number of extrusion cycles, pressure, flow rate,

and membrane pore size are factors that influence liposome structure and size during the extrusion process. When extrusion technology was first launched in 1971, it was used to create small liposomes by pushing bigger liposomes through polycarbonate membranes or asymmetric ceramic filters with hole diameters ranging from 50 nm to 5 µm. Onivyde, Vyxeos, and Marqibo are just a few of the commercial nanoliposome products that have been made using this technique. Its benefits include little setup, simplicity, and dependability. In the course of extrusion, multilamellar vesicles (MLVs) push through the membrane, cause the membrane to rupture, and then reconstitute into tiny liposomes. Pressure, flow rate, number of extrusion cycles, and membrane pore size are only a few of the variables that affect the liposomes' final size and shape. When extrusion technology was first launched in 1971, it was used to create small liposomes by pushing bigger liposomes through polycarbonate membranes or asymmetric ceramic filters with hole diameters ranging from 50 nm to 5 µm. Onivyde, Vyxeos, and Marqibo are just a few of the commercial nanoliposome products that have been made using this technique. Its benefits include little setup, simplicity, and dependability. In the course of extrusion, multilamellar vesicles (MLVs) push through the membrane, cause the membrane to rupture, and then reconstitute into tiny liposomes. Pressure, flow rate, number of extrusion cycles, and membrane pore size are only a few of the variables that affect the liposomes' final size and shape.

Techniques for Drug-Loading

High drug loading is beneficial because it lowers the dose, speeds up drug administration, and minimizes the amount of additional medication needed to meet therapeutic objectives. Drug-lipid drug conjugates, passive and active methods, and additional tactics including a mix of passive and active encapsulation are examples of drug loading technologies. During the creation of the lipid bilayer, hydrophilic medications are integrated into the aqueous core of liposomes through a process known as passive loading. Conversely, hydrophobic drugs are incorporated into the hydrophobic area of the lipid bilayer. However, there are drawbacks to passive loading as well, including rapid drug release, high drug-to-lipid ratio, and bilayer instability. The cyclodextrin complexation method has been employed to address these issues by making hydrophobic medications more soluble in water. By using this method, the medication is incorporated into the liposomes' aqueous core by forming it inside the cyclodextrin. Technologies for active or distal loading have been developed to improve the effectiveness of key chemotherapeutic medicines' encapsulation. Ionic or pH gradients across the liposome bilayer membrane can be used to induce distal loading into produced liposomes. Two main aspects affect the effectiveness of loading into liposomes: (i) the drug's water solubility and (ii) the existence of ionizable functional groups in the drug's chemical structure. It has been designed to drive the dissolution of liposome bilayers by pH gradients or ions. This method permits the hydrophobic medication to stay within the liposome core following vesicle formation. This approach's primary benefit is its ability to load drugs regardless of the liposome preparation circumstances. A large number of practical compounds are weak bases that respond to pH changes by facilitating transport thanks to primary, secondary, or tertiary amine groups. To improve encapsulation and storage in liposomes, medications with weak bases or non-ionizable functional groups can be transformed into weak materials or bundled with amino-modified carriers like cyclodextrin.

Refinement of Liposomes

Typically, methods including centrifugation, dialysis, gel filtration, and column chromatography are used to purify liposomes. Because Sephadex G-50 is so good at separating liposomes, it is often employed in gel filtration. This method has a drawback, though, in that lipid loss may result from interactions between the liposome membrane and the Sephadex beads. The loss of lipids causes the liposome membrane to become unstable, which increases permeability and causes the encapsulated substance to leak out. It is advised to collect samples both before and after filling the line in order to minimize this issue and prevent the production of extremely tiny liposomes. Centrifugation is typically used to separate small unilamellar vesicles (SUVs) and is carried out at 200,000 g for 10 to 20 hours. Comparatively, multilamellar vesicles (MLVs) are separated using centrifugation, which takes less than an hour at 100,000 g.

Liposomes' Pharmacokinetic Properties

- Liposomal medications can be either topically or delivered intravenously (IV), although both methods are frequently used. Liposomes have a number of ways to interact with cells once they are in the circulation or surrounding environment.
- Cells take in and internalize other chemicals through a process known as endocytosis. Within the reticuloendothelial system (R.E.S.) of phagocytes, such as neutrophils and macrophages, this process entails the cell membrane producing vesicles around particles, such as pathogens or dead cells. The vesicle, known as a phagosome, then joins forces with a lysosome to break down its contents, enabling the cell to eliminate or neutralize toxic chemicals. Immunity and tissue homeostasis maintenance depend on this process.
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- Many mechanisms, such as weak water contacts, electrostatic forces, or specialized binding to cell components, can lead to adsorption to a cell surface.
- The lipid bilayer of liposomes is integrated with the cell membrane to guarantee fusion of liposomes with plasma cell membranes. The liposomes' contents are discharged into the cytoplasm during this procedure.
- Transfer of liposomal lipids to cellular or subcellular membranes and vice versa can occur irrespective of changes in the composition of liposomes.
- Finding the machine that is operating can be challenging, especially since multiple units might be operating simultaneously.

Liposome-encapsulated drugs' pharmacodynamics

Liposomes are one technique used to deliver medications to particular parts of the body. The medication will be gradually released from these liposomes after they are directly applied to the desired location. Furthermore, liposomes can interact with cells without dispensing medication right away. This tactic seeks to lower overall

toxicity while raising the drug's concentration at the targeted site.

The Liposomes' Stability

The stability of liposomes has a major impact on the therapeutic effect of medicinal compounds. The stable structure guarantees the physical and chemical integrity of the active components during development and storage. Security can be separated into two primary categories:

1.Stability in Physical Form: The form, size, and fusion of liposomes are just a few of the numerous physical processes that might shorten their shelf life. Leakage of encapsulated pharmaceuticals is a significant issue that occurs. Size distribution and morphology are crucial for evaluating stability. The negative effects of phospholipids will be lessened by keeping the body balanced. Liposomes need to be kept at 4°C, not frozen, and kept out of direct sunlight.

2.Chemical Resistance: Unsaturated fatty acids that are readily hydrolyzed and impact the stability of drugs are known as phospholipids. To stop liposomes from degrading oxidatively, antioxidants like butylated hydroxyanisole can be added. But during storage, liposomes frequently encounter stability issues.

In order to produce stable liposomal products, a number of crucial considerations need to be made.To guarantee the solvents' and lipids' quality: During processing, avoid overheating or cutting too high. anti-oxidant pH-neutral formulation to stabilize the final product.

Benefits of Liposome Technology:

Amphiphilic compounds can interact differently with chemicals that are soluble or insoluble in water. They can collect or contain a wide range of compounds thanks to this feature, regardless of how soluble they are.

1.permits the administration of drugs in a targeted manner.
2.Extends the drug's therapeutic range and efficacy.
3. Natural and non-ionic.
4.The amount of hazardous medication that reaches delicate tissues is reduced by liposomes.
5.Makes it easier to target tumor tissues passively and specifically.
6.Stops the oxidation of the medication.
7.It is biodegradable for liposomes.
8.Biocompatible.
9.Imparts more stability to the medication.
10.Steers clear of undesirable drug action locations.
11.Enables better protein stability.
12.Permits a prolonged release of medication.
13.Enables direct communication between the medicine and the cell.
14.Diminishes effects that are off target.

The Drawbacks of Liposomes:

1.Inadequate solubility
2. Short duration of effect
3.Danger of drug fusion and leakage from encapsulated substances
4. Potential oxidation of phospholipids - Potential impacts on liposome constituents Reactions to antibiotics
5. Decreased steadiness

Critical Quality Attribution

The delivery of therapeutic molecules packaged in liposomes to tumor cells following systemic administration (e.g., intravenous injection) is more complicated and primarily involves the following stages in contrast to the standard drug dosage form (e.g., injectable solution for small molecules): (a) Extravasation from the intravascular space into the tissue interstitium: liposomes diffuse and/or convectively penetrate the discontinuous

endothelial junctions (100 nm–2 µm) of the tumor vascular wall to enter the interstitium surrounding the tumor. In the meantime, MPS removes some liposomes from the bloodstream, particularly those that are big (>200 nm), hydrophobic, and have a charged particle surface (positive or negative charge). (b) Diffusion and convectional interstitial transfer to the individual tumor cells. Active targeted surface modification of liposomes will overcome the extracellular matrix's (ECM) physical resistance to particle diffusion because of the increased affinity that the particles' targeted ligands generate for the tumor cells' surface receptors. Use either specific or non-specific binding to adhere to the cell membrane. Infiltrate the cell by diffusion, membrane fusion, or endocytosis. Particle size determines the endocytosis pathways: clathrin- and caveolae-mediated endocytosis occurs with particles between 200 and 500 nm in size, while macropinocytosis occurs with particles up to 5 µm in size. Drug release and intracellular transport. Because the circulating liposome particles cannot penetrate the continuous endothelial junctions of the heart, Doxil significantly lessens the cardiac toxicity when compared to the administration of traditional doxorubicin. connections between the heart's blood vessels. DaunoXome offers prolonged release in vivo and enhances daunorubicin tumor delivery by roughly ten times compared to traditional medication.

Surface Modification

An essential tool for liposome modification (explained in Section 3.2) is liposomes covered with extremely flexible PEG chains to form a hydration layer. This technique lowers MPS clearance, increases circulation lifespan, and keeps liposomes from aggregating. Using ligands for active targeting on liposome surfaces is another typical surface modification. According to FDA rules, the thickness of the coating on nanomaterials should be reported in the dossier , as the layer's thickness and covering density influence cellular uptake and regulate the passage of nanoparticles across biological matrices . The effects of surface coatings, whether covalently or non-covalently bound, on product stability, pharmacokinetics, biodistribution, bimolecular interaction, and receptor-mediated cellular contact should be taken into account, according to the EMA reflection paper. Furthermore, every aspect of the coating material needs to be thoroughly understood and managed, including its homogeneity and repeatability, surface coverage heterogeneity, ligand orientation and conformational state, physico-chemical stability, premature detachment and/or coating degradation, etc.

Phase Transition Temperature

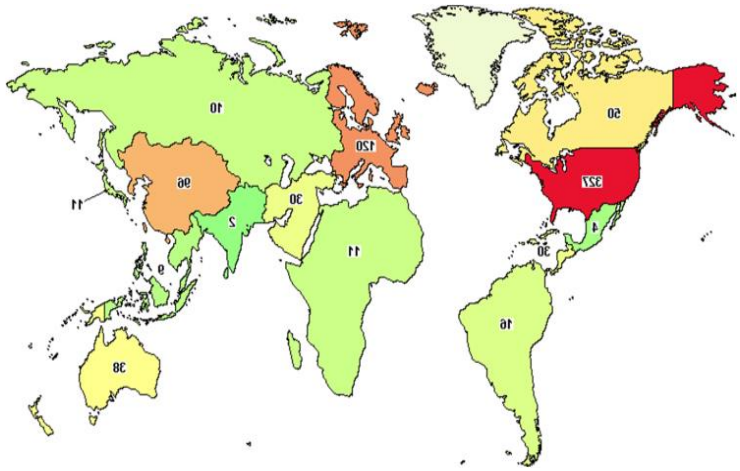
Bilayer membrane phase transition temperature is an essential factor in liposome formation, stability during storage, and in vivo drug release. Numerous studies pertaining to the phase transition have been finished. Figure 5 illustrates the three lamellar forms of hydrated lipid bilayers: a liquid-crystal phase (Lα), a "solid" gel phase (Lβ: hexagonal lattice unnamed chain or Lβ’: quasi hexagonal array with titled chain), and a crystal phase (LC). The acyl chains are preferentially aligned in an all-trans configuration during the lamellar gel phase, and lateral diffusion proceeds very slowly. The lamellar transitions from a gel phase to an LC phase upon cooling below the transition temperature of Tc. Another name for LC is the subgel phase, in which the hydrocarbon chains are in an all-trans, completely stretched shape, with the polar head groups largely stationary. The metastable precursor SGII phase, often referred to as sub-subgel or LR1 phase, may occur between the gel phase and LC. When the temperature is raised above the melting transition temperature (Tm), the hydrocarbon chains exhibit rapid trans-gauche fluctuations and the membrane

transitions from an orderly state (gel state) to a relatively disordered state (Lα). This increases the permeability of the membrane and makes it easier for drug molecules to pass through.

Regulatory Consideration

48 nanomedicines are currently undergoing clinical trials in the European Union, whereas about 100 and 11 nanomedicines, respectively, have been approved by the FDA and EMA during the past few decades. The FDA, EMA, Ministry of Health, Labour and Welfare—Japan (MHLW), and Chinese National Medical Products Administration (NMPA) have released several guidelines regarding nanomaterials and nanoproducts in light of the growing number of applications for nanomedicine and the sharing of regulatory network experience in the scientific evaluation of nanomedicines. These guidelines cover a variety of nano-dosage forms, including as liposomes, block copolymer micelles, iron-based nano-colloidal products, and nanoproducts loaded with SIRNA. The liposome guidance was developed by all four regulatory bodies among these guidelines, which may be explained by the relatively common dose form and the comparatively high number authorized in clinical trials and the market.

Therapeutic Use



From the 83316 active clinical trials registered, 511 liposomal clinical trials investigating liposomal products which are distributed worldwide as shown in figure . The drugs being examined belong to anticancer drugs, analgesics, immune-modulators, anti-fungal, etc. Among these drugs, 121 of the 511 are in phase III testing, 236 are in phase II, 120 are in phase I, and 6 in early phase I.

Clinical Application

Numerous liposomal-based formulations have been effectively used as analgesics, antifungal medications, and tumor treatments in clinical settings . In the USA, Doxil® was the first clinical anticancer liposome medication to be licensed (1995). By inventing the pH gradient active loading and using PEGylation for stealth liposomes, it paved the road for numerous new liposomal formulations to enter the clinical application sectors. When circulation half-life is not the main objective, conventional liposomes without PEGylation may be appealing. The primary purpose of Depo Foam TM is to release drugs gradually, ensuring a steady supply of medication for an extended period of time.

Marketed clinical liposomes

1.Therapy For Cancer

Doxil® (sometimes called Caelyx®) is a polyethylene glycol (PEG)-coated liposomal version of doxorubicin (DOX) that was first commercialized in 1995 by Sequus Pharmaceuticals. The main reason this formulation was created was to treat Kaposi sarcoma. Sun Pharma produces LipoDox®, a pegylated liposomal variant of DOX that is comparable in formulation and was approved by the FDA in 2012. Another anthracycline included in DaunoXome® is daunorubicin, which is liposome-encapsulated and prescribed only for the treatment of acute myeloid leukemia (AML). The short half-life and diminished cardiovascular effects of Myocet®, a non-PEGylated liposomal version of DOX, are well-known. The cytotoxic medication cytarabine is formulated as Depocyt® and is released every two weeks thanks to the DepoFoamTM multivesicular technology. Mepact® is a popular liposomal formulation that is authorized for the treatment of osteosarcoma globally. Via gradual drug release, vincristine is present in Marqibo®'s sphingomyelin/cholesterol-based liposomes, which lengthens the time of circulation and benefits tissues. Rinotecan has anticancer action and is present in Onivyde® pegylated liposomes. Utilizing a 5:1 ratio in liposomes, Vyxeos® (sometimes referred to as CPX-351) boosts effectiveness while lowering negative effects. Paclitaxel is also incorporated into liposomes by Lipusu® in order to cure cancer and lessen adverse effects.

2. Treatment With Fungus

Ambisome® and Fungisome® are two recognized liposomal preparations of the antibiotic amphotericin B. These preparations are superior than those made by the white people. Amphotericin B is more stable in saline when encapsulated in liposomes, which also increases its bioavailability and decreases toxicity and adverse effects.

3. Photodynamic Intervention

For the treatment of age-related macular degeneration, Visudyne® is the only liposomal medication that has been approved. It functions by preventing the development of new blood vessels in the eye.

4. Pain Relief

Using DepoFoamTM technology, the morphine formulation DepoDurTM has a delayed release and longer-lasting therapeutic effects [206]. Similarly, to extend pain relief, Exparel® releases bupivacaine gradually using the same Depo Foam TM technology [197].

Applications of Liposome

Liposomes have great pharmaceutical applications in oral and transdermal drug delivery systems. This drug delivery system achieves a reduction in the toxic effect and enhancement of the effectiveness of drugs. The targeting of liposome to the site of the action takes place by the attachment of amino acid fragments that target specific receptors cells. Several modes of drug delivery application have been proposed for the liposomal drug delivery system, a few of them are as follows:

1. Enhancement of Solubilisation (Amphotericin-B, Paclitaxel)
2. Protection of sensitive drug molecules (Cytosine arabinose, DNA, RNA, Ribozymes)
3. Enhancement of intracellular uptake (Anticancer, antiviral and antimicrobial drugs)
4. Alteration in pharmacokinetics and biodistribution (prolonged or SR drugs with short circulatory half-life)

Several recent applications of liposomal drug delivery system are as follows:

A. Liposome for Respiratory Drug Delivery System:

Liposome is widely used in several types of respiratory disorders. Liposomal aerosols can be formulated to achieve sustained release, prevent local irritation, reduced toxicity, and improved stability. Whilst preparing liposomes for lung delivery, composition, size, charge, Drug/lipid ratio and drug delivery method should be considered. The liquid or dry form is taken for inhalation during nebulization. Drug powder liposome is produced by milling or by spray drying.

B. Liposomes in Ophthalmic Disorders:

Dry eyes, keratitis, corneal transplant rejection, uveitis, endophthalmitis, and proliferative vitro retinopathy are the examples of eye disorders against which liposomes have been found to possess beneficial effects. The drug verteporfin that is found to be effective against eye disorders has been recently approved as liposomal formulation.

C. Liposome as Vaccine Adjuvant:

Liposome has been established firmly as an immune adjuvant that is potentiating both cells mediated and noncell mediated immunity. Liposomal immuno-adjuvant acts by slow release of encapsulated antigen on intramuscular injection and also by passive accumulation within the regional lymph node. Depending on the lipophilicity of antigens, the liposome can accommodate antigens in the aqueous cavity or incorporate them within the bilayers. The targeting of liposome does the accumulation of liposome to lymphoid with the help of phosphotidyl serine. The liposomal vaccine can be prepared by inoculating microbes, soluble antigens and cytokinesis of deoxyribonucleic acid with the liposomes .

D. Liposomes for Brain Targeting:

The biocompatible and biodegradable character of liposomes makes it's used in brain drug delivery system. Liposomes with a small diameter (100 nm) and large diameter undergo free diffusion through the BBB. However small unilamellar vesicles (SUVs) coupled to brain drug transport vectors may be transported by Receptor-mediated or absorptive mediated transcytosis through the BBB. Cationic liposomes undergo absorptive mediated endocytosis into cells whereas the same undergoing absorptive mediated transcytosis through the BBB has not yet been determined. Liposomes coated with the mannose reach brain and assist the transport of loaded drug through BBB. The neuropeptides, leuenkephaline and mefenkephalin kyoforphin normally do not cross BBB when given systemically. The anti-depressant amitriptyline normally penetrates the BBB, due to the versatility of this method.

E. Liposomes in Cosmetics:

They are used in cosmetics because their physiology is similar to the cell membrane, and they release materials to the cells.

F. Liposomes in Sustained Release Drug Delivery:

Sustained release systems are required to achieve and then to maintain the concentration of drug administered within the therapeutically effective range needed for medication, it is often necessary to take this type of drug delivery systems several times a day. This results in a fluctuated drug level and consequently undesirable toxicity and poor efficiency to minimize this fluctuation, novel drug delivery systems have been developed, which include niosomes, liposomes.

G. Liposomes in Gene Therapy:

Liposomes have been used widely in the analytical sciences as well as for drug and gene delivery. Several systemic diseases are caused by a lack of enzymes or factors which are due to missing or defective genes. In recent years, several attempts have been made to restore gene expression by delivery of the relevant exogenous DNA or genes to cells. Because of the polyanionic nature of DNA, cationic (and neutral) lipids are typically used for gene delivery, while the use of anionic liposomes has been fairly restricted to the delivery of other therapeutic macromolecules. Some of the widely used cationic liposome formulations are lipofectin, cytofectin, lipofectamine, transfectace.

Applications of Liposomes in multidisciplines

1. Mathematics Topology of 2-Dimensional surfaces in 3-Dimensional space governed only by bilayer elasticity
2. Physics Aggregation behaviour, fractals, soft and high-strength material
3. Biophysics Permeability, Phase transition in 2-Dimension, Photophysics
4. Physical chemistry Colloid behaviour in a system of well-defined physical characteristics, inter-and intraaggregate forces, DLVO
5. Chemistry Photochemistry, artificial photosynthesis, catalysis, micro compartmentalization
6. Biochemistry Reconstitution of membranes, cell function, fusion, recognition studies of drug action
7. Biology Model biological membranes, Cell function, fusion, recognition
8. Pharmaceutics Studies of drug action
9. Medicine Drug delivery and medical diagnostics, gene therapy

Protein corona fingerprints of liposomes

There have been attempts to offset anti-inflammatory medication effects with liposomes. However, a lack of knowledge about liposome activity in vivo has hampered their clinical usefulness. The plasma-coated lipid vesicles in vivo form the protein corona (PrC), a biomolecular layer. According to recent research, PrC can improve liposome attachment to cancerous cells, which in turn improves the internalization and localization of particles. Research has demonstrated that liposomal formulations supplemented with PrCF have a high transport capacity and enhance cellular absorption in pancreatic cancer cells. For instance, liposomes with higher PrCF abundance demonstrated superior absorption over Onivyde®, which is FDA-approved. Furthermore, novel methods have been developed, such as the use of liposomes to extract protein biomarkers from human blood, which will help with personalized treatment by finding new biomarkers.

Regulatory Consideration

Over the last few decades, approximately 100 nanomedicines and 11 nanomedicines have been approved by the FDA and EMA, respectively, while 48 nanomedicines are presently under clinical trials in the European Union [**109**]. Considering the increasing number of nanomedicine applications and sharing the experience of the regulatory network in the scientific evaluation of nanomedicines, several guidelines about nanomaterial and nanoproducts were released by the FDA, EMA, Ministry of Health, Labour and Welfare—Japan (MHLW), and Chinese National Medical Products Administration (NMPA). These guidelines involve different nano-dosage forms, including liposomes, iron-based nano-colloidal products, block copolymer micelles, and nucleic-acid (siRNA)-loaded nanoproducts (Table 3). Among these guidelines, all four regulatory agencies

worked out the guidance about liposomes, which might be attributed to the relatively common dosage form and the relatively large numbers approved in market and clinical trials. Because liposomal products are complex and diverse, it is essential to guarantee quality, safety, and performance across the whole product life cycle. Gaining a comprehensive awareness of the risks related to the manufacture, inspection, and maintenance of equipment is essential to achieving this goal. Early drug research and development can provide this information, which should be updated often in accordance with manufacturing procedures and control schemes. Linking in vivo symptoms to one another can lower risk. Excipients are also crucial for the quality of liposomal products, particularly lipids. Because fatty material can change a drug's pharmacokinetics or pharmacodynamics, even minute levels of it can have substantial negative effects. The FDA offers comprehensive lipid management information, with particular recommded. For the development of liposome formulations, in vivo monitoring of the carrier is as important as the cargo since cargo leakage from nanoparticles may happen faster than previously believed. In vivo transport vectors are frequently tracked using fluorescent labels, but it's critical to discern between free fluorescent molecules released by nanoparticles and negative vectors. To tackle this problem, aggregation-induced quenching (ACQ) works exceptionally well. When ACQ probes are in the carrier matrix, they glow in the near-infrared, but as soon as they are in an aqueous medium, α-β stacking causes them to instantly become quenchable. Thus, the presence of the completed carriage is indicated by the luminous display. The ACQ probe has been used to study a variety of nanoparticles, including micelles, polymeric nanoparticles, nanoemulsions, and nanocrystals, to examine their transport across various

Future Perspectives and Concluding Remarks

Between 1970 and 2020, the TITLE-ABS-KEY set included the terms "liposome", "(liposome and drug) or (liposome and drug)", "(nano and liposome and drug)" or ("Nano and Liposomes and Drugs"), and "(Nano and Drugs) OR (Nano and Drugs)". Positive outcomes are obtained. We can infer from Figure 6 that: (1) During the 1970s and 1990s, liposomes were first used as drug carriers in industries other than nanomedicine, such as food and cosmetics. Utilizing medication carriers Drug carriers in liposomes have been the subject of more publications throughout time; for instance, 50% in 2000, 70% in 2010, and 74% in 2020. (3) Despite the fact that advances in nanomedicine predate the usage of liposomes, the field has seen an exponential growth in publications over the yea From the first liposome product of Doxil approved in 1995, liposome techniques have been further developed for more than 20 years. We summarize the successful experience and pain points based on the abundance of publications and commercial products. Liposomes can be well-designed and display intended functions depending on human requirements and needs. On the one hand, there are major obstacles during the development and commercialized production, such as the individual differences in the EPR effect, accelerated blood clearance (ABC) phenomenon of PEGylated liposomes, scale-up, the reproducibility/consistency among different batches and manufacturing sites, and excipient control. Numerous cutting-edge liposome technologies, such as stimulus-responsive liposomes (like ThermoDox) and targeted liposomes (like anti-EGFR immunoliposomes, MBP-426) are being developed or tested in clinical settings. These systems respond to stimuli like temperature, pH, light, electromagnetic fields, enzymes, and hypoxia by releasing drugs based on the microenvironment at the infection site. Clinical

translation is complicated by issues including premature delivery, patient variability, and clinical variability, despite the encouraging outcomes. As an illustration, a Phase III trial for the treatment of hepatocellular cancer with the thermosensitive liposome Thermo Dox was unsuccessful. But in the future, these developments might enhance care and lessen adverse effects Recent debates have addressed advancements in the field of nanomedicine while focusing on the background and purpose of liposomes. Three liposome products—liposu (paclitaxel liposome), doxorubicin hydrochloride liposome, and amphotericin B liposome—have been approved by the NMPA in China. Nanomedicines, such as liposomes, nanocrystals, inorganic particles, and polymer micelles, are being developed in China by both established pharmaceutical corporations and up-and-coming businesses. The State Food and Drug Administration is putting a lot of effort into creating a set of basic guidelines for these novel treatments and has designated the safety and quality evaluation of nanomedicines as a priority research topic since 2019.

CONCLUSION

Since liposomes offer advantages including better drug stability and greater clinical results, they have emerged as a significant drug delivery technology. They are perfect for enhancing the pharmacokinetics and pharmacodynamics of poorly soluble, weakly bioavailable, or highly toxic medicines due to their biocompatibility, biodegradability, and low immunogenicity. Over the years, liposomal formulations have improved and overcome initial issues to produce a plethora of goods, including more than 500 formulations that are presently undergoing clinical studies. Liposomes still have a lot of problems with chemical and physical stability, despite their benefits. Their clinical results are impacted by this issue, which makes the creation of sustainable designs necessary. Predicting the composition and three-dimensional structural morphology of liposome formulations has been made possible through the use of computer simulations and computational investigations. It also has an affinity to keratin of horny layer of skin and can penetrate deeper into the skin and hence give better absorption. Applied on the skin, liposomes may act as a solubilizing matrix for poorly soluble drugs, penetration enhancers, and local depot at the same time diminishing the side effects of these drugs. These systems can be administered through oral, parenteral as well as topical routes. This wide range of selection of route of administration makes it flexible in designing the drug delivery system. Also, these systems provide as an effective carrier for cosmetic formulations also. The major problem in the formulation of liposome is their stability problem. These problems can be overcome by employing modification in the preparation method and using some specialized carriers. Nowadays, liposomes are used as a carrier for a wide variety of drugs. In spite of its few disadvantages, liposomes serve as versatile carriers for a wide range of drugs. The success of liposomes as drug carriers has been reflected in a number of liposome-based formulations, which are commercially available or are currently undergoing clinical trials. The mechanisms giving rise to the therapeutic advantages of liposomes, such as the ability of long-circulating liposomes to preferentially accumulate at disease sites such as tumours, sites of infection, and sites of inflammation, are increasingly well understood. The use of liposomes in the delivery of drugs and genes is promising and is sure to undergo further developments in the future. Because liposomes have a unique affinity for keratin found in the skin's outermost layer, they can enter the epidermis deeply and improve absorption. Liposomes can function as a solubilizing matrix when applied topically, improving permeability and facilitating

local drug delivery while minimizing negative effects for poorly soluble medications. A variety of delivery methods, such as topical, parenteral, and oral, offer versatility in the way drugs delivered. Cosmetics are another application for liposomes. But one of the main concerns with liposome compositions is safety. The plan can be changed, and specific vectors can be used to solve these issues. Liposomes are employed in numerous medical specialties and have spawned a wide range of medications that are either commercially available or undergoing clinical studies, despite certain drawbacks. The medicinal advantages of liposomes include

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