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A Comprehensive Review on Liposomes: A Novel Drug Delivery System

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ABSTRACT
In modern field of nanotechnology, the development of anticancer drug loaded nanomedicine reach in a goal for emerging strategy of novel drug delivery devices. These types of nanodevices are more beneficial for passive as well as active targeting for malignant cells which can be effective for chemotherapy during treatment of cancer. Major advantages of these nanodevices reducing the cytotoxicity simultaneously enhance the therapeutic efficacy of active pharmaceutical ingredient(s). Several nanodevices are nowadays applied for treatment of cancer in the modern field of oncology such as liposomes, nanoparticles, nanogels, carbon nanotubes, quantum dots etc. Among them liposomes have drawn a lot of interest due to their passive targeting by the property showing enhanced permeability and retention effect and they also revealed optimum bioavailability, better biocompatibility, biocompatibility and rapid endocytosis compare to other nanodevices. Due to nanosize in structure they could easily entrapped by the malignant cells via leaky vasculature of the basement membrane of neoplastic cells, known as passive targeting. Targeting ligand molecules can be tagged at the surface of the outer surface of nanaolipid vesicles such as liposomes for reorganization of neoplastic cells, known as active targeting. According to the pathophysiology of the tumour cells of and site of the targeting action different liposomal formulations have been invented by the researchers. Stealth liposomes, antibody or aptamer tagged liposomes, angigenetic inhibitor linked liposome and genetic material linked with the liposomes are nowadays widely used for treatment in cancer chemotherapy.

Keywords: liposome, tumour, passive and active targeting, bioavailibity, biocompatibility.

I. INTRODUCTION:

Liposomes are concentric vesicles with a spherical form, derived from the Greek word soma, which means body, and lipos, which means fat [1]. Phosphatidyl choline was inadvertently dispersed throughout water by Bangham et al., who later observed that the molecule was creating a closed bilayer structure with an aqueous phase confined by a lipid bilayer [2]. This resulted in the first identification of liposomes in 1961. Liposomes are very useful since they may function as a carrier for a wide range of drugs and have additional or potential therapeutic uses. The sizes of liposomes, which are colloidal carriers, range from 0.01 to 5.0 µm. Because the medication needs to be released from the liposome before it can be metabolised and excreted, long-term therapeutic. These are small, man-made, spherical vesicles that may be formed from cholesterol and naturally levels. Different liposomal formulation are manufactured by the use of phospholipids, cholesterol for increase the structural rigidity [3]. Liposomes are appealing drug delivery vehicles due to their size, hydrophobic and hydrophilic properties, and biocompatibility [4]. Liposomes are attractive drug delivery vehicles for both hydrophilic and hydrophobic drugs because of their unique ability to encapsulate pharmaceuticals in both the lipid and aqueous phases [5]. The goal of the novel drug delivery technique known as liposomes is to deliver the medication directly to the site of action. They could be able to bind both hydrophilic and lipophilic molecules, which would stop the drug from breaking down and let the active ingredients release gradually [6]. Given that glycerol is known to be a molecule's backbone, it has been demonstrated that phospholipids containing it are essential for liposomal formation; these phospholipids make up 505 of the lipid weight [7].

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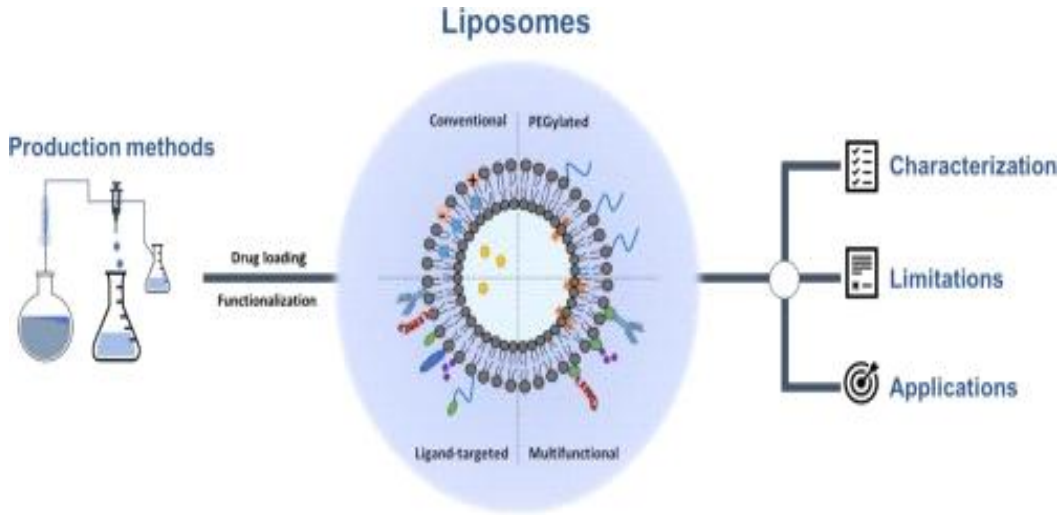

Figure 1: Design of liposome [7]

The elements of the structure are:

- **Phospholipids**

The main structural elements of a liposome are phospholipids. Phosphatidylcholine is the most often utilised phospholipid in liposomal preparation (PC) [8]. An amphiphatic molecule, phosphatidylcholine is made up of:

- Phosphocholine is a hydrophilic polar head group.
- An glycerol bridge
- Two hydrophobic chains of acyl hydrocarbon

The makeup of naturally occurring glycerol moiety of phosphatidylcholine is joined to two acyl chains, which could be unsaturated or saturated. The arrangement of the lipid molecules' hydrocarbon chains determines the stability of the liposome membrane [9]. Bilayer characteristics including elasticity and phase behaviour are determined by the kind of fatty acid in the lipid molecule, including the quantity of double bonds in the chain [10]. Liposomes are made from phospholipids, which are found in large quantities in nature and include choline.

A few instances of phospholipids are:
Lecithin (Phosphatidyl Choline) PC
Cephalin (Phosphatidyl Ethanoamine)-PE
Phosphatidyl serine (PS)
Glycerol Phosphatidyl (PG)

Cholestro

Another crucial liposome structural element is cholesterol. This sterol is often utilised. The function of stiffness and stability is modulated by the presence of steroids. It is unable to construct a bilayer structure on its own [11]. It is integrated into phospholipids at very high concentrations, up to a molar ratio of 1:1 or 2:1 between phosphatidyl choline and cholesterol. The lipid bilayer becomes more stable and forms a hard, highly organised structure when cholesterol is present [12].

Cholesterol increases the fluidity and durability of cellular membranes while decreasing the permeability of molecules that are soluble in water. Cholesterol [13] inhibited the liposomes from interacting and destabilising.

Liposomes

Liposomes are categorised into four groups depending on the size and quantity of bilayers in their structures: multilamellar vesicles (MLV), multivesicular vesicles (MVV), larunilamellar vesicles (LUV), and small unilamellar vesicles (SUV). In a multilamellar structure, liposomes resemble onions, but in a unilamellar structure, they feature a monophospholipid bilayer. When several unilamellar vesicles are formed within bigger liposomes, MVV forms a multilamellar configuration with concentric phospholipid spheres [14]. For hydrophilic substances exclusively, liposome encapsulation effectiveness falls with the number of bilayers and rises with liposome size [15]. One major aspect influencing the liposomes' half-life in circulation is their size. The quantity of the medicine enclosed is influenced by the size and quantity of bilayers. The ideal vesicles, when liposomes are used for drug delivery, typically measure between 50 and 150 nm. Several ideas explain how liposomes interact with the cell membrane, including phagocytosis [18], absorption

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into the membrane [19], local fusion (adhesion) [17], and selective (modified by receptor-mediated) or nonspecific endocytosis [16]. Numerous parameters, including as composition [20], liposome diameters [22], surface charge [21], targeting ligand on the liposome surface, and biological environment [22], affect liposome-cell interactions.

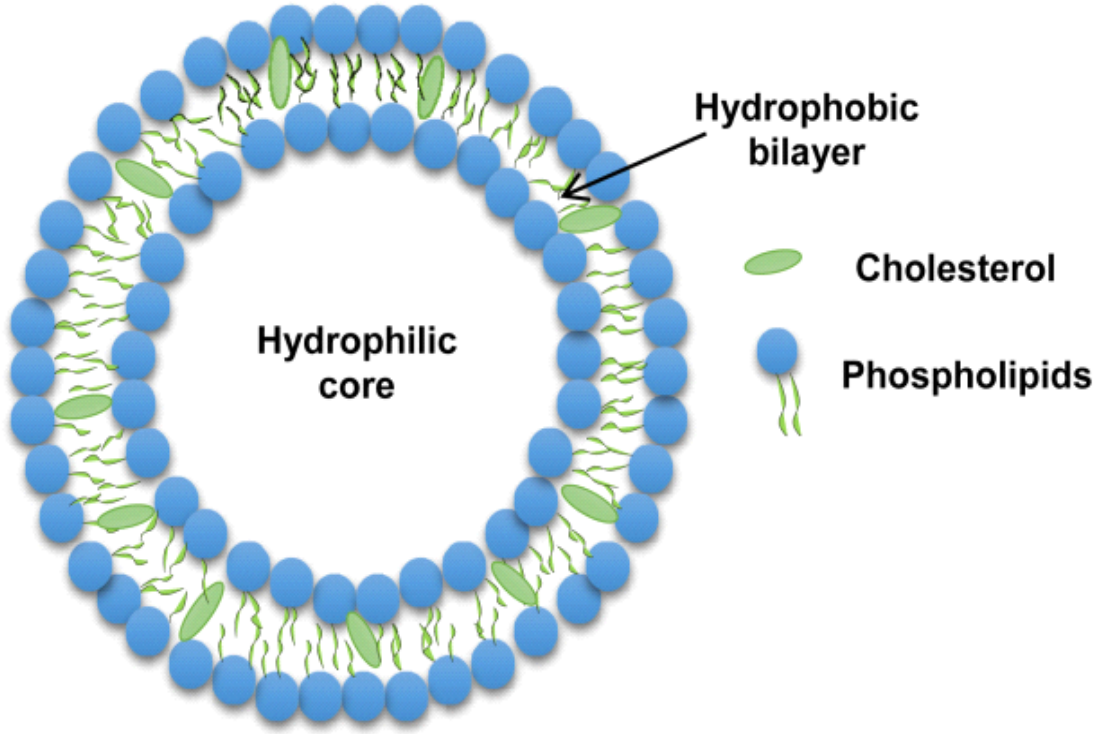

Figure -2 Liposome [22]

Composition of liposomes

Phospholipids, of which liposomes are mostly made up of, fall into two primary categories: glycerophospholipids and sphingomyelins. Glycerophospholipids, of which glycerol is regarded as the foundation, make up the majority of the phospholipids in eukaryotic cells backbone. Glycerophospholipids have a hydrophilic head group and a hydrophobic side chain making a single bilayer membrane or many. Variations in the head group result in the production of various glycerophospholipids. such as phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), phosphatidic acid (PA), phosphatidylglycerol (PG), and cardiolipin (CL) [27,28]. Moreover, other glycerophospholipids, such as dimyristoyl, dipalmitoyl, or distearoyl PC, are produced by the length change of the nonpolar moieties. Furthermore, distinct glycerophospholipids are produced depending on the kind of bonding (ether or ester) that exists between both aliphatic chains and glycerol.An essential membrane component of animal cells is sphingomyelins (SMs) [25,26].The foundation of SM is sphingosine; on average, each molecule of SM has cis-double bonds in acyl chains connected by amides. Natural SMs are regarded as asymmetric compounds since their normal acyl lengths are typically longer than sphingosine paraffin residues. Both intramolecular and intermolecular hydrogen bonds may be formed by SMs. When compared to DSPC liposomes, SMs in the liposomal formulation demonstrated improved serum stability, quick release profile, and high entrapment efficiency [27]. According to a different study, a spherically shaped vesicle with small particle size was successfully created from sphingomyelin solution using the ultrasonic–supercritical CO2 technique; however, as the operating temperature was raised, aggregation caused the vesicles' size distribution to increase [28].

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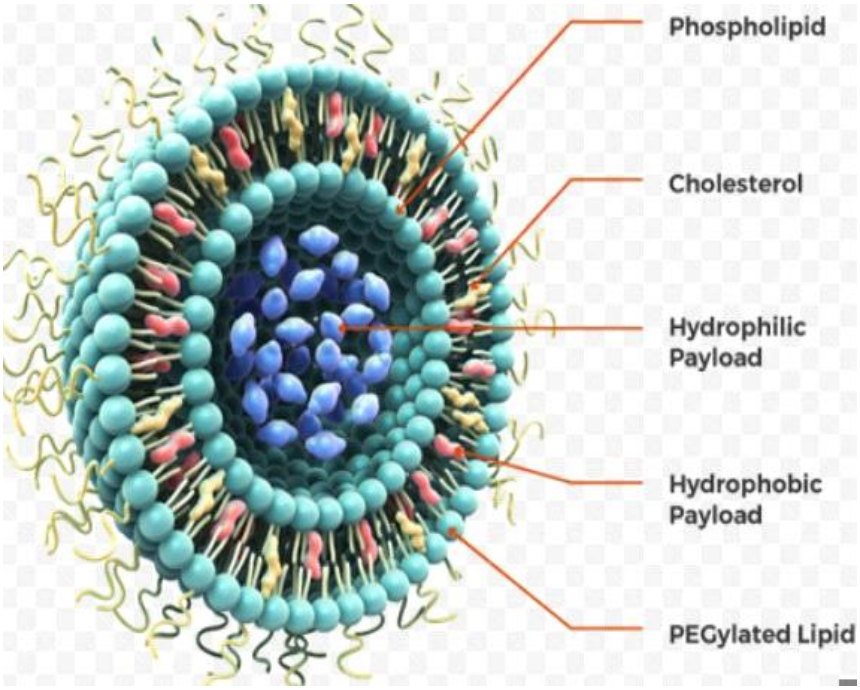

Figure 3 Liposome [28]

Advantages of liposomes:

- Due to their amphiphatic structure, they may ensnab both water-soluble and insoluble pharmaceuticals.
- Enhanced medication effectiveness and therapeutic index [29]
- Not ionic
- Liposomes aid in lowering the amount of harmful medication exposure to delicate tissues.
- Provides selective passive targeting to tumor tissues.
- Stop the oxidation of medication.
- It is biodegradable for liposomes.[30]
- biocompatible
- Drug stability is increased by liposomes [31].
- Effect of site avoidance.
- Boost the stabilisation of proteins [32].
- Give a prolonged release.
- The drug's direct contact with the cell.
- Effect of site avoidance.

Disadvantages of liposome [33-34]

- short half-life
- Insufficient solubility
- Leakage and fusion of drugs or compounds within capsules
- High production costs
- Reduced stable numbers0
- Phospholipids can occasionally experience an oxidation and hydrolysis-like process.

Classification of liposomes

Liposomes can range in size from tiny vesicles (0.025 μm) to big ones (2.5 μm). Furthermore, the membranes of liposomes might be single or bilayer. The amount of medicine encapsulated in the liposomes is influenced by the size and number of bilayers, and vesicle size is an important determinant in determining the circulation half-life of liposomes. Liposomes can also be divided into two groups based on the size and quantity of their bilayers: (1) multilamellar vesicles (MLV) and (2) unilamellar vesicles. Additionally, unilamellar vesicles may be divided into two groups: small unilamellar vesicles (SUV) and large unilamellar vesicles (LUV) [35]. The aqueous solution is encased in a single phospholipid bilayer sphere on the vesicle of unilamellar liposomes. Vesicles in multilamellar liposomes have an onion-like shape.

Methods of preparation of liposomes [36]

There are different methods involved in the preparation of liposomes

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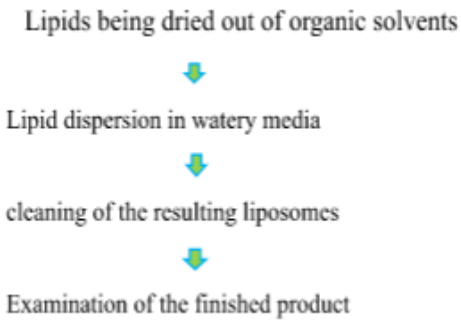
General method of preparation – It involves four steps for the preparation of liposomes



Handling of Liposomes

Volatile solvents like chloroform that are utilised in the manufacture of liposomes have a tendency to evaporate from the container; also, the lipids used in this process are unsaturated and consequently oxidation-prone. Liposomes must thus be kept in glass containers with a tight-fitting lid, in the dark, and in an inert nitrogen environment.

General Method of Preparation and Drug Loading

Most methods for creating liposomes include entrapping water-soluble (hydrophilic) components either by adding a drug or drug solution at a certain point in the liposome-making process, or by employing an aqueous solution of these materials as hydrating fluid. The constituent lipid's organic solution solubilizes the lipid-soluble (lipophilic) components, which then evaporate to form a dry medication with a lipid film before being hydrated. With these techniques, the ensnared agents are loaded either before to or throughout the production process (passive loading). Nonetheless, when complete vesicles form, specific kinds of molecules with ionizable groups and those that exhibit both lipid and water solubility can be added to the liposomes (remote loading).

Mechanism of action of liposomes

Liposomes use four distinct mechanisms to carry out their functions. They are listed in the following order:

1. Endoytosis: This process is carried out by phagocytic reticuloendothelial system cells, such as neutrophils.20.

2. Adsorption: Adsorption to the cell surface is caused by interactions with components of the cell surface or by non-specific electrostatic forces. Lipid exchange is the transfer of liposomal lipids to the cellular membrane without the association of liposomal content.

3. Fusion: Fusion is the insertion of liposomal bilayer into the plasma membrane with continuous release of liposomal content into the cytoplasm.

4. Lipid exchange: In this process, liposomal lipids are transferred to the cellular membrane independently of liposomal content.

Mechanical dispersion method

The following are types of mechanical dispersion methods:

- Sonification.
- Extrusion is the French pressure cell.
- frozen-thawed liposomes
- Micro-emulsification
- extrusion of membranes.
- preserved and rebuilt vesicles [36,37].

Sonification

- By using this technique, the vesicles get smaller in size and shapes while the lipid mixture gains energy. By exposing it to ultrasonic pulses, the MLV might be forced to perform this function. Sonication may be done in two ways: (1) with a bath sonicator and (2) with a probe sonicator. The probe sonicator is commonly used to make suspensions that need a lot of energy in a compact container. [37–39]. For large volumes of diluted lipids, the bath sonicator is employed. The primary disadvantages of this strategy include poor internal encapsulation efficacy, phospholipid breakdown, removal of particularly big molecules, metal . contaminants from the probe tip and MLV and SUV coexisting. [40]

Extrusion is the French pressure cell

MLV is extruded during the procedure at 4°C at 20,000 pressure through a small hole. There are several benefits to this technology over sonication procedures. Although the method is easy to use, rapid, and repeatable, it requires careful handling of dangerous ingredients. As a result, liposomes generated are larger than those generated by SUVs that have been sonicated. Among the disadvantages are the challenges associated with achieving the desired temperature and the relatively low working volumes (A maximum of 50 mL) [42].

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Frozen-thawed liposomes

SUVs are quickly frozen during this process, and then progressively thawed. Sonication is used to disperse aggregated chemicals to LUV. SUV17 causes unilamellar vesicles to develop during the freezing and thawing processes. The fusion process is significantly impeded when the ionic strength and phospholipid content of the medium are increased. About 20 to 30 percent entrapment efficiency was attained using this method.

Micro-emulsification

With this method, small lipid vesicles are produced on a commercial scale. Small vesicles manufactured partially from concentrated lipid solution are created using a device called a micro fluidizer. Large MLV lipid suspensions have to be added to the fluidizer. This device applies a very high pressure to the fluid as it pumps it into a 5µm panel [43]. Subsequently, a long microchannel is pushed, which results in the collision of two fluid streams at high speed and angle. One may modify the rotation speeds between 20 and 200 to produce a micro emulsion for biological applications. [44]

Extrusion of membranes

Processing a heterogeneous liposomal solution involves the use of a polymer filter with a web-like structure. This results in the formation of a tortuous-path capillary pore, a network of linked capillaries with a membrane at least 100 microns thick. The modified liposomes have a narrow size range and a particular mean size of less than 0.4 microns [45]. This method may be applied to MLVs as well as LUVs.

Reconstituted desiccated spheres

Using this technique, lyophilized protein is combined with liposomes or placed in an aqueous solution containing medications before being dried.

Freeze-Thaw Method

SUVs are quickly frozen during this process, then progressively thawed. Sonication is used to disperse aggregated chemicals to LUV. SUV17 causes unilamellar vesicles to develop during the freezing and thawing processes. The fusion process is significantly impeded when the ionic strength and phospholipid content of the medium are increased. About 20 to 30 percent entrapment efficiency was attained using this method.

Sizing of Liposome

It appears that a liposome's destiny or potential uses are greatly influenced by its size. For liposomes to be used therapeutically, the phospholipid bilayer must be uniform and functionally viable. As a result, the liposome processing method must have a particle size distribution that fits within a specific size range and be dependable and consistent. For liposome sizing, sonification, gel chromatography, and sequential extrusion are the usual methods [46-48].

Characterization of Liposomes

The liposome must first be produced and then characterised in order to be employed in immunoassays. The physical, chemical, and biological techniques are the three main categories that may be utilised to organise the assessment. For the physical techniques, different criteria are required, including size, shape, surface features, lamellarity phase behaviours, and drug release profile. "Chemical characterization" describes studies that show the specific liposomal components' potency and accuracy. The evaluation of a formulation's viability and efficacy for in vivo pharmacological intervention is aided by biological characterisation [49-54].

1. Visual Appearance

Depending on the size and makeup of the particles, the liposomal suspension might have a clear or milky appearance. The samples are homogenous if the turbidity has a bluish tint; non-liposomal dispersion is characterised by a flat, grey colour and is typically comprised of scattered microcrystallites or a distributed inverse hexagonal phase. Liposomes bigger than 0.3 µm can be detected with an optical microscope, in addition to contamination from larger particles.

2. Determination of Liposomal Size

When liposomes are meant to be administered parenterally or by inhalation, the size distribution is crucial because it controls the destiny of the liposomes and the therapeutic molecules they contain in vivo. The standard method for measuring liposomes is dynamic light scattering. Liposomes with a rather uniform size distribution work well for this technique. A straightforward method for identifying a fully hydrodynamic radius is gel exclusion chromatography. Liposomes may be separated using Sephacryl-S100 in the 30-300 nm size range.

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SUVs and micelles may be separated using sepharose columns -4B and -2B.

3. Determination of lamellarity

The lamellarity needs to be established in order to specify the liposome structure and its in vivo efficiency. Both the encapsulation efficiency and the drug release kinetics are significantly influenced by the quantity of lipid bilayers in the liposome. Lamellarity affects liposome absorption and intercellular destiny. The choice of lipid and the industrial processes have a significant impact on the liposomal lamellarity. Using techniques like electron microscopy or spectroscopy, one may ascertain the lamellarity of liposomes. The most common way to display the NMR liposome spectrum is with and without a paramagnetic material added which alters or bleaches the signal of the detected nuclei on the liposome surface.

4. Liposome Stability

Taking stability into account is crucial when employing liposomal drug delivery methods. An effect on a drug molecule's chemical purity and physical stability is the storage conditions and processing system. The therapeutic effect of the drug molecules is controlled by their liposomal stability. The physical integrity of liposomes is connected to factors such as size, size distribution, composition, and drug retention, whereas chemical equilibrium faces challenges related to drug degradation and phospholipid oxidation and hydrolysis. A safe liposomal medication has the necessary microbiological, chemical, and physical stability to ensure the product's integrity throughout storage. Because of this, a specified stability research procedure highlights the need of using well-established techniques for product development, characterisation, efficacy, and stability testing in order to determine the physical and chemical integrity of the product.

5. Entrapped Volume

This is a crucial factor that controls the shape of the vesicles. To ensure that the concentration of solute within liposomes in the aqueous medium remains constant after isolation from the untrapped material, measurements of the cumulative amount of solute trapped within liposomes can also be used to calculate the entrapped liposome volume (in µL/mg phospholipids). Water from the inner compartment may be lost in two stages of preparation to get rid of the organic solvent during the drying down process.

This can be calculated by a given formula

$$\%\text{Entrapment Efficiency} = \frac{\text{Entrapped Drug X 100}}{\text{Total Drug}}$$

6. Surface Charge

The kind and concentration of charge present on the liposome surface will control how the lipid and cell interact. Since charge-imparting/constituting lipids are commonly used to make liposomes, the charge on the vesicle's surface is investigated. To evaluate the charge, two methods are often used: zeta potential testing and free flow electrophoresis.

STABILIZATION OF LIPOSOME

Liposome safety should be comparable to that of conventional drug formulations. The durability of a pharmaceutical product is its ability to stay, in the suggested formulation, within defined or predefined limits for a predetermined period of time. Chemical stabilisation of phospholipid bilayers necessitates ester bond hydrolysis prevention and oxidation of unsaturated lipid chain sites. Through physical instability or drug leakage from encapsulated bilayers, chemical instability leads to vesicle aggregation. [55] Techniques like lyophilization and efficient formulation can be utilised to improve liposomal stability. Liposomes frequently have the tendency to pose problems with stability when being kept. In order to successfully produce a stable liposomal therapeutic component, a few factors often need to be taken into account: [56, 57]

I. Using newly purified solvents and lipids during processing
II. Avoiding high temperatures and applying too much shear force
III. It is necessary to maintain low oxygen demand (nitrogen purging).
IV. Using metal chelators or antioxidants
V. Creating a pH-neutral formula
VI. Lyo-protectant use during freeze-drying

Application of Liposome

Over the past 30 years, there has been a significant advancement in the study of liposomes. It is now possible to create a wide range of liposomes with different surface morphologies,

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phospholipid and cholesterol compositions, and sizes that are appropriate for a number of uses[58].

The liposome carrier may be directed towards the liver and spleen, and tomography makes it simple to distinguish between cancerous and non-cancerous tissue. When it comes to transdermal medication distribution, liposomes are particularly useful. The liposomal drug delivery technique helps to reduce the toxic effect and boost medicinal effectiveness while treating tumour cells. Liposomes link a segment of amino acid to specific cell receptors in the region of operation to target it. [59]

A few of the most recent uses for liposomal treatments include DNA vaccination and improved gene therapy outcomes. For liposomal drug delivery, several drug administration strategies have been proposed; a few of these are listed below:

I. Improve the solubility of medications (paclitaxel, amphotericin-B, minoxidil, and cyclosporins).

II. Sensitive drug molecules (RN, ribozymes, DNA, antisense oligonucleotides, and cystosine arabinosa) are shielded

III. Promote intracellular absorption of antiviral, antitumor, and antimicrobial medications

IV. Changes to pharmacokinetics and biodistribution (long- or sustained-release medications with brief half-lives in the circulation)

A. Respiratory Drug Delivery System Using Liposomes [60]

Liposomes are commonly employed in treating various respiratory ailments. Liposomal aerosols can be designed to have a delayed release, prevent localised inflammation, reduce adverse effects, and enhance stability over the whole aqueous core.

There are now a number of injectable liposome-based medications on the market, such as Myocet, Fungisome, and Ambisome. The drug-to-lipid ratio, size, charge, lipid composition, and delivery methods all affect how well liposomal medications are delivered to the lungs. The use of liposomes for DNA transmission to the lungs is becoming more common, which suggests that understanding of their application in the inhalation of macromolecules is improving. All of this new knowledge may be applied to enhance protein compositions based on liposomes. For liposome inhalation, the dry or liquid form is used, and during nebulization, the medication is released. Drug powder liposomes have been created using milling or spray drying.

B. Liposome in Eye Disorders [61]

Liposomes have been utilised to treat the anterior and posterior segments of the eye for a very long period. Dryness, keratitis, endopthelmitis, proliferative vitreoretinopathy, and rejection of corneal transplants are examples of ocular diseases. In developing nations, retinal defects are the main cause of blindness. Using liposomes as a vector and carrier for genetic transfection with monoclonal antibodies. Treatments for specific tumours and neovascular artery blockage include angiography, retinal and choroidal blood vessel stasis, and more contemporary therapeutic techniques like the use of heat-activated liposomes in concentrated laser beams and the release of liposomal medications and colours for targeted delivery when heated. Two patent medications have been issued for liposomal medical compositions thus far, and numerous more are being studied scientifically. A liposomal medication called "verteporfin" is commercially advised for ocular

C. Liposome as Vaccine Adjuvant [62]

An immune adjuvant that is well-known for boosting both cell-mediated and non-cell-mediated immunity is liposomes.

After intramuscular injection, liposomal immune adjuvants function by releasing encapsulated antigen into the localised lymph node gradually and passively. Phosphatidyl serine is used to target liposomes in order to accumulate them into lymphoid tissue. By immunising bacteria, soluble antigen, and deoxyribonucleic acid cytokinesis with liposomes, a liposomal vaccine can be made. On the other hand, it triggers an immune response to the production of antigenic proteins. Antigens will further form a covalent bond with the liposomal membrane.

Liposomal vaccinations can be stored in a refrigerator for up to a year. [63]

D. Liposomes for Brain Targeting

The use of liposomes as a brain medication delivery method has grown recently because of their biocompatibility and biodegradability. [64] Liposomes with sizes as tiny as 100 nm or more can effortlessly pass through the blood-brain barrier (BBB). Conversely, SUVs associated with cognitive drug carriers have the ability to pass the blood-brain barrier through either receptor- or absorptive-mediated transcytosis. It has not yet been established that absorptive driven transcytosis takes place across the BBB, despite the

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fact that absorptive mediated endocytosis of cationic liposomes happens in cells.Mannose-coated liposomes pass the blood-brain barrier and aid in the transportation of drugs into the brain. Leu-enkephalin, mefenkephalin, oxyforphin, and neutropeptides do not usually cross the blood-brain barrier when given systemically.

This strategy is so versatile that the antidepressant amitriptyline often crosses the blood-brain barrier. Several stabilisers have been used to create nanoparticles (NP). When amitriptyline was adsorbed to the NP and wrapped or the particle stayed stable with polyoxyethylene 20 sorbitan trioleate, it was found that the amount of the medication in the brain was significantly increased. [65]

E. Liposome as Anti-Infective Agents

Liposomes can be used as a transport mechanism to deliver therapeutic compounds to the liver and spleen, which are organs that are home to intracellular pathogens like bacteria, fungus, and protozoa.[66] By integrating and targeting the drug with the liposomal carrier, disorders including leishmaniasis, histoplasmosis, candidiasis, erythrococosis, aspergelosis, gerardiasis, TB, and malaria can be treated. Using the polyene antibiotic amphotericin B to treat a systemic fungal infection has been linked to serious kidney damage. Amphotericin B works by attaching itself to sterol in the membranes of fungi that are sensitive, increasing the permeability of such membranes. This chemical is dangerous due to its non-specificity and affinity for cholesterol in mammalian cells. Recently, Amphotericin B's first liposome formulation was tested in all clinical settings and is now available for purchase to treat a variety of fungal infections, including aspergillosis, blastomycosis, candidasis, coccidioidomycosis, and cryptococcosis.By passively targeting the liver and spleen, liposomal amphotericin B reduces both renal and general toxicity at the recommended dosage. However, renal toxicity often occurs when a medication is administered at a high dose because of liver and spleen macrophage saturation. Liposomes that are preferentially directed towards the lungs may also be made by covering the vesicle with either monosialogangliocyte liposomes, polyoxyl ethylene, or ostearoyl amylopectin. Isoniazid and rifampicin are two examples of anti-tuberculous drugs whose encapsulation in lung-targeted liposomes reduces their toxicity and boosts their efficacy.

[67] Amphotericin formulations in various forms are currently available for purchase in several European nations after undergoing multiple clinical trials and receiving approval.[68]

F. Liposome in Tumor Cell Therapy

Long term use of anti-cancer medications can have very dangerous adverse effects. By minimising side effects, the liposomal therapy for tumour cell targeting has improved the field of tumour treatment. Though they can circulate for extended periods of time and vasate in tissues with higher vascular permeability, the small and stable liposomes are intended to be passively targeted to a variety of tumours. [69;70.] For almost two decades, liposome growth as a drug delivery system has been hindered by the liver and spleen ingesting liposome macrophages. Nowadays, a lot of herbal anticancer drugs have been added to liposomes to offer better targeting and higher bioavailability.[71]

Advancements In Liposomes

Ethosomes: They work well to penetrate the skin with 30% ethanol and soy phosphatidylcholine.

Immuno liposomes: Antibodies were used to alter them.

Niosomes: These are tiny unilamellar vesicles made of non-ionic surfactants.[72]

Stealth liposomes: These novel liposome varieties are intended to improve stability and lengthen their half-lives in circulation. To manufacture these liposomes, polyethylene glycol (PEG) should be used for coating.[73]

Liposome's in biomedical research applications: An Experiment

Liposomes have the potential to be used in medicine to treat a wide range of pathological conditions with novel and powerful treatments. Lipid-based therapeutic carrier research seems to be significantly increasing at the trial in vitro and in vivo phases. Therapeutic compounds, bioactive agents, and gene therapy are just a few of the many therapeutic and diagnostic components that are being transported by liposomes.To improve efficacy, lower RES clearance, and minimise toxicity, changes in lipid content, charge, and the addition of surface coatings and ligands are all being investigated[74,75].

Active targeting techniques, which include conjugating targeting ligands to the liposome surface for a variety of biological applications, have been extensively investigated in the early

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stages of research, particularly after parenteral injection. [76–77]. Targeting ligands are used to further reduce non-target deposition while improving the selectivity of encapsulated cargo delivery to and retention of disordered cellular components. It is possible that adding targeting moieties enhances receptor-mediated absorption of drug-encapsulated liposomes into target cells, hence boosting therapeutic effectiveness, after the buildup of nano carriers in damaged tissues [78,79].

Although most preclinical studies have shown that ligand-targeted liposomes improve bio distribution and therapeutic outcomes, the benefits of these liposomes have not yet materialised in clinical trials.[80] It is still unknown how many targeting ligands should be placed on the surface of each liposome; this will probably depend on the characteristics of the molecular target. Our extensive testing is revealing additional information regarding the more pertinent clinical indications for ligand-targeted liposomal formulations. Additionally, there has been a lot of interest in the modification of the lipid bilayer through the use of charged lipids[81]. Delivery methods based on nucleic acids, membrane adhesives, and bioadhesives have all benefited from the integration of charged lipids into the liposomal bilayer.

Another strategy to improve the therapeutic efficacy of liposomal formulations is to use triggering mechanisms for site-specific release of medications from liposomes.

Understanding the achievements in liposomal innovation to date, together with the challenges now facing the field, will facilitate future investigations aimed at improving upon legacy systems and resolving current regulatory and translational constraints [82,83].

II. CONCLUSION

Over the past ten years, there has been a dramatic increase in the creation of different kinds of liposomes as a targeted drug delivery method for treating a wide range of illnesses. The present study examined liposomes as a targeted drug delivery technique, encompassing their present state, constraints, and potential future applications. Their behavior's adaptability might also be employed to give medications in any way and for any constituent, regardless of how soluble it is. Because liposomes are excellent therapeutic agents, several liposome-based formulations with higher drug concentrations have been developed. Many incredibly powerful medicines can have their toxic effects reduced and their pharmacokinetics and therapeutic efficacy increased by the application of liposomal device active and passive targeting approach. The liposomal delivery has been achieved in the modern field of nanotechnology as well as nanomedicines of a goal has the power to revolutionise traditional medicine for the treatment of a variety of serious diseases, including cancer. The use of liposomes in gene and pharmacological delivery is encouraging, and further research on this technology is sure to come soon. In the upcoming years, the development of liposomes as drug carriers will continue to be a top focus because to their increased potential for transfer into treatment.

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