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LIPOSOME : A Novel Drug Delivery System

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Abstract: *As synthetic vesicles, liposomes have emerged as crucial instruments for enhancing the delivery of a vast numerous medications, including peptide hormones, enzymes, antimicrobial agents, cancer medications, antifungal medications, genetic materials and vaccinations. Owing to variations in lipid compositions and preparation techniques, The lamellarity, size, charge, and application of liposomes can all be used to categorize them. The adaptability of their Behavior can be used to deliver drugs via a variety of administration methods, regardless of their solubility characteristics. Drug encapsulation in liposomes has made it possible to improve the therapeutic indices of numerous medications, primarily by modifying their biodistribution, directing the medication to certain tissues. The regulated delivery of drugs is the function of liposomes as a drug delivery system. Decreasing unfavorable side effects, increasing its activity both in vitro and in vivo, and lowering the toxicity of the medication and improving the encapsulated medicine's effectiveness. This article offers a summary of techniques for Liposome preparation and analysis techniques to regulate physical, chemical, and biological parameters for several kinds of medications.*

Keywords: Liposomes, Drug delivery system, Phospholipids, Components of liposome

I. INTRODUCTION

A liposome is a synthetic spherical vesicle made of a lipid bilayer in the lamellar phase.

Pharmaceutical medications and nutrients can be administered via liposomes (Torchillin, 2006) [1]. The Greek terms lipo ("fat") and soma ("body") are the origin of the word liposome, which gets its name from the fact that phospholipid makes up the majority of its makeup[2]. When phospholipids are dispersed in water, they spontaneously Form closed structure with internal aqueous environment bounded By phospholipid bilayer membranes, this vesicular system is called As liposome[3]. Today, liposomes have become a versatile tool in the fields of biology, biochemistry, and medicine. Since the 1960s, they have been used as carriers for delivering a wide range of compounds within their aqueous compartments. Liposomes can be designed and processed to vary in size, composition, surface charge, and lamellarity. Currently, several liposomal formulations of anti-tumor and antifungal drugs have been successfully commercialized [4]. The clinical potential of liposomes as carriers for replacement therapy in genetic disorders caused by lysosomal enzyme deficiencies was first demonstrated in the 1970s .Significant advancements were achieved during the 1970s and 1980s in enhancing liposome stability, resulting in prolonged circulation time after intravenous administration and improved bio-distribution.In the 1980s, the important anti-tumor drug doxorubicin was formulated in liposomal form to enhance its therapeutic index.Liposomes function through several mechanisms both within and outside the body, which are summarized as follows [5].

1. Liposomes attach to the cell membrane and may fuse with it, thereby releasing their contents directly into the cell.
2. Sometimes, liposomes are internalized by the cell, and their phospholipids become part of the cell membrane, leading to the release of the encapsulated drug.

A fluid liposomal drug formulation was designed to enhance the bactericidal activity of antibiotics by facilitating effective interaction between the liposomes and bacteria[6]. .Liposomes encapsulating fluoroquinolones and aminoglycosides showed a decreased minimum inhibitory concentration (MIC) compared to the free drugs against both Gram-positive and Gram-negative bacteria (Puglisi et al., 1995; Furneri et al., 2000)[7]. Unlike normal tissues, which possess tight intercellular junctions (2–6 nm) between endothelial cells [8]. Abnormal tissues, such as solid tumors or

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inflammatory sites, exhibit highly porous structures[9]. Liposomes can traverse the discontinuous neovasculature and become passively accumulated and retained within abnormal tissues—a phenomenon known as the enhanced permeability and retention (EPR) effect. Active targeting, on the other hand, involves specific interactions between ligands on the liposome surface and receptors expressed on tumor cells. Tumor cells often overexpress receptors such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), folic acid (FA), integrin, CD44 (a cell surface glycoprotein), CD13, and prostate-specific membrane antigen [10]. Based on these receptors, various specific ligands have been proposed for liposomal surface modification, including antibodies [11], nucleic acids proteins , peptides small molecules and carbohydrates that target macrophages.A major advantage of systemic liposomes as drug formulations lies in their high biocompatibility, low immunogenicity, biodegradability, enhanced therapeutic efficiency, prolonged drug half-life, targeted delivery, reduced systemic toxicity, and protection of sensitive molecules, resulting in improved pharmacokinetics. One of the most notable benefits of systemic liposomes is their ability to encapsulate and release two different substances with varying solubilities simultaneously [12]. Various studies have reported that liposomes can be classified based on the number of bilayers, particle size, and lipid composition, which are briefly discussed in the following sections.Several publications have focused on different aspects of liposome research, including conventional preparation methods [13], biomedical applications [14], and recent advancements in liposomal technologies [15]. Apart from their use with specific drugs, liposomes represent an outstanding platform for drug delivery. However, only 14 liposomal products are currently available on the market, indicating that their full potential has yet to be realized. Therefore, this review summarizes existing knowledge on commercial liposomal products 8approved by the FDA and EMA, focusing on their composition and manufacturing technologies. Additionally, it discusses the critical quality attributes (CQAs) of liposomes, the current regulatory landscape, and future prospects. The aim of this review is to provide valuable reference information to support and accelerate the advancement of liposomal drug development.

Structures of Liposomes

Depending on the lamellarity and compartment structure, liposomes can be categorized as unilamellar vesicles (ULVs), oligolamellar vesicles (OLVs), multilamellar vesicles (MLVs), and multivesicular liposomes (MVLs)[16] . MLVs and OLVs have an anonion-like structure, but they have more than five concentric lipid bilayers and two to five, respectively. In contrast to MLVs, MVLs have a structure resembling a honeycomb and contain hundreds of non-concentric aqueous chambers surrounded by a single bilayer lipid membrane[17]. Small unilamellarvesicles (GUVs, >1000 nm) are other classifications of ULVs based on particle size[18]. There have been reports of ULVs with varying sizes, such as SUVs smaller than 200 nm and LUVs larger than 200–500 nm. [19].

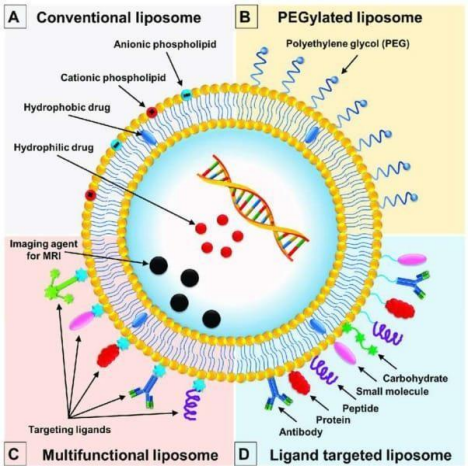

Fig 1:- Structure of liposomes

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Advantages of liposomes: -[20].

1) Capable of transporting lipid-soluble and water-soluble medications.
2) Naturally non-ionic.
3) Liposomes are non-toxic, fully biodegradable, immunogenic, and biocompatible.
4) Adequate for the administration of hydrophilic, amphipathic, and hydrophobic medications.
5)Keep the medicine that is enclosed safe from the outside world.
6) Through encapsulation, liposomes lower toxicity and boost stability.
7) They are making the chemotherapy medication more aactive .
8) Biodegradable medications can be prevented from oxidizing.
9)Limit hazardous drug exposure to delicate tissues.
10) Boost the stability of proteins.
11) Maintain proper hydrated.
12) Offer a prolonged release.
13) Site-specific or targeted medication delivery.
14) It can be administered in a number of ways.

Disadvantages of liposome [21]. :-

1) The cost of production is expensive.
2) Encapsulated leakage and fusing.
3) short half-life.
4) issues with stability.
5) The components of liposomes may cause an allergic reaction.
6) Due to their size, it is difficult to target different tissues.
7) Phospholipids go through hydrolysis and oxidation.

II. LITRATURE RIVIEW

A.D.; Standish Bangham, M.M.; Watkens,

To simulate biological membranes, the authors employed aqueous suspensions of phospholipids organized as concentric bimolecular lamellae, which we now call liposome-type structures. They discovered that these systems exhibited several characteristics similar to those of cell membranes, including selective permeability to water, some tiny nonelectrolytes, and specific ions. Specifically, in the conditions examined, the model membranes were successfully impermeable to sugars and cations (positively charged ions). This study is one of the first to show how phospholipid lamellar structures, or liposomes, can be used as a model for membrane permeability.

Sessa, G.; Weismann.

The scientists looked into the integration of lysozyme, a model enzyme, into synthetic phospholipid vesicles, or liposomes. To simulate biological compartments, they employed liposomes made from phospholipid spherules (smectic mesophase). Lysozyme's enzymatic activity becomes "latent" when it is "captured" inside these liposomes, meaning that very little or no lysozyme activity can be detected against its substrate (Micrococcus lysodeikticus) when it is trapped. This latency points to a structural-linked effect: the bilayer structure of the liposomal environment limits substrate availability to the enzyme, which lowers reported activity. According to the authors, this system can be used as a model for "structure-linked latency" of enzymes, which is the idea that physical limitations rather than chemical inhibition could control enzyme activity by encapsulation (or compartmentalization) in membrane-bound structures.

Shah, S., Dhawan, V., Holm.

A variety of medications, including subsequent generic versions, have been approved using liposomes, which are widely acknowledged as efficient drug delivery methods. Liposomes are currently made using complicated multi-batch production techniques. Furthermore, the development and uptake of new liposomal systems may be delayed because

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laboratory-based liposome synthesis techniques are difficult to translate to large-scale production. This analysis examines the variety of liposome production techniques accessible, from laboratory scale and scale-up to large-scale manufacture, and assesses their benefits and drawbacks in order to foster innovation and progress in liposome manufacturing methods. Additionally covered are the regulatory issues related to the production of liposomes. Self-assembling liposome systems and microfluidic production are two new developments that offer leaner scalable solutions for liposome fabrication.

Grubber, S.M.

This chapter examines the basic biophysical characteristics of liposomes and connects these characteristics to possible medical applications. It outlines how to prepare unilamellar and multilamellar vesicles and explains how membrane curvature, lamellarity, and bilayer phase behavior are influenced by temperature, ionic environment, and lipid composition. The book explores molecular-scale events that affect membrane permeability, fusion, and drug-release profiles, such as lateral phase separation, transitions between lamellar and non-lamellar phases, and lipid packing. X-ray scattering, electron microscopy, calorimetry, and permeability tests are among the analytical and experimental methods used to examine liposome structure. Lastly, the chapter outlines methods to modify circulation lifespan and enhance therapeutic index by relating biophysical discoveries to practical issues in drug encapsulation, stability, and targeted delivery.

Shashi K., Satinder K., Bharat P.

Liposomes, a significant class of drug delivery devices, are lipid-based vesicular structures made of phospholipid bilayers. The basic characteristics of liposomes, such as their structure, kinds (based on lamellarity, size, and charge), and the ways in which they encapsulate both hydrophilic and lipophilic medicines, are covered by the authors in this review. The article describes several liposome preparation techniques (such as thin-film hydration, reverse-phase evaporation, etc.) and emphasizes evaluation metrics including size, stability, release properties, and entrapment efficiency.

III. CLASSIFICATION OF LIPOSOME

1) Liposome classification based on size and shape .
a) Large unilamellar vesicles (LUV),
b) small unilamellar vesicles (SUV), and
c) multilamellar vesicles (MLV)
2) Classification of liposome according to Composition
a) Conventional liposome
b) PH- sensitive liposome
c) Cationic liposome
d) Long circulating liposome
e) Immuno- liposome
3) Classification of liposome depending Upon production method
a) Passive loading technique
b) Mechanical dispersion method
i) Lipid hydration by hand shaking Or freeze drying ii) Micro emulsification iii) Sonication
iv) French pressure cell
c) Solvent dispersion method
i) Ethanol injection ii) Ether injection iii) Double emulsion vesicle iv) Reverse phase evaporation
d) Detergent removal method
i) Dialysis ii) Detergent removal of mixed micellar iii) Dilution
e) Active loading technique

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1) Depending upon size and shape:-

a. Large unilamellar vesicle (LUV) :-

A single bilayer or single lamella makes up the enormous unilamellar vesicles of liposomes. LUVs are larger than 0.1 micrometers and have a maximum size of 1000 nm. Due to their capacity to contain a sizable volume of solutions in their cavity, they have a high encapsulation efficiency. They resemble multilamellar vesicles. Many techniques, including detergent dialysis, reverse phase evaporation, and ether injection, are used to create large unilamellar vesicles[22]. b. Small unilamellar vesicle (SUV):-

Compared to multilamellar and large unilamellar vesicles, small unilamellar vesicles are typically smaller (less than 0.1 micrometers). A single bilayer is seen in tiny unilamellar vesicles. The solvent injection method (ethanol and ether injection) is used to prepare SUV.

c. Multilamellar vesicle (MLV):-

Multilamellar vesicles typically have two or more bilayers and range in size from 100 to 1000 nm. The thin-film hydration approach, which involves hydrating lipids in excess of organic solvent, is a very straightforward way for creating multilamellar vesicles. Because they are mechanically stable, they can be stored for a very long time. The "Reticulo Endothelium System" (RES) cell quickly eliminates it.

2) Classification of liposome depending Upon composition :-

The natural components of living cell membranes often make up the liposome membrane, however similar components can also be found in synthetic materials.

• Conventional liposome:-

Natural phospholipids or lipids like sphingomyelin, egg phosphatidylcholine, 1-2disteroryl-snglycero-3-phosphatidyl choline (DSPC), and monosialonganglioside make up conventional liposomes. It has been noted that liposomes with both positive and negative charges have shorter half-lives, are poisonous, and are quickly removed from the bloodstream[23]. The "Reticulo-endothelial system" (RES) is the primary target of these liposomes. Because it shortens the liposome's circulation times, conventional liposomes are used more frequently than other varieties[24]. The hydrophilic polymer-coated liposome surface and the repulsive interactions between the liposome and serum components are used to extend the circulation period[25].

• pH- sensitive liposome:-

Oleic acid (OA), phosphatidyl ethanolamine (PE), and cholesterol hemisuccinate (CHEMS) make up PH-sensitive liposomes[26]. Lipid compositions known as pH-sensitive liposomes are susceptible to destabilization when the external pH shifts, often from neutral or slightly alkaline to acidic. In cell culture, pH-sensitive liposomes can enhance the cytoplasmic transport of proteins, fluorescent markers, cytotoxic substances, RNA, and DNA[22].

• Cationic liposome:-

Dimethyl-dioctaatidecyl ammonium bromide (DDAB), dioctadecyldimethyl ammonium chloride (DOGS), and 2,3-dioleoyloxy-N- (2(spermine carboxamido)-ethyl are the components of cationic liposomes. -N, N-dimethyl-l-propanaminiu fluoracetate (DOSPA) 1,2 dioleoyloxy-3- (trimethylammonio)propane (DOTAP), 1,2 di mrystyloxypropyl-3-dimethyl-hydroxethyl ammonium bromide (DORIE), and dioleoylphosphatidyl ethanolamine (DOPE). Due to their extreme toxicity and short longevity, these liposomes can only be administered locally. They are mostly used to transport negatively charged macromolecules[27]. DNA can be transported across the plasma membrane by fusion between cationic vesicles and cell surfaces. This procedure avoids the endosomal-lysoma pathway, which causes the anionic liposome formulation to degrade[28].

• Long circulating liposome:-

To create long-circulating liposomes, a hydrophilic layer of oligosaccharides, glycoproteins, and synthetic polymers can be applied to the liposome surface. Mononuclear phagocyte system scavenger cells[29].

• Immuno-liposome (ILs):-

Immuno-liposomes (ILs) are produced by attaching antibodies to the distal end of PEG chains (type ll liposome) or directly to the liposome lipid bilayer when PEG chains are present (type l liposome). Attaching antibodies to the

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PEGylated lipid bilayer. Depending on the quantity and length of PEG chains, liposomes can decrease antigen binding. By attaching the antibody to the PEG chain's terminus, ILs antigen binding can be reinstated[30].

3) Classification of liposome depending Upon production method:-

1. Passive loading technique:-

Drug loading and liposome formation happen simultaneously in passive loading. When working with water-soluble pharmaceuticals, hydrophobic drugs are retained inside the lipid bilayer of the liposome because hydrophilic chemicals are uniformly dispersed in the aqueous phase (both inside and outside the liposomes). To create a drug-containing thin film, the drug is first dissolved with lipid in an organic solvent. This is followed by the solvent evaporation procedure. To create a liposome, prepare a thin film that has been hydrated with an aqueous phase. The lipid film is distributed in a drug-containing aqueous phase during the loading of water-soluble medications[31].

2. Mechanical dispersion method:-

This approach encloses aqueous volume (5–10%), which is a minor percentage of the overall volume required for swelling. Consequently, a significant amount of water-soluble material is lost during swelling, although lipid-soluble compounds can be encapsulated with 100% effectiveness.

As long as their amounts don't exceed the membrane's structural component[32].

• Sonication:- One technique for converting MLVs into small unit lamellar vesicles (SUVs) is sonication. MLVs are transformed into SUVs using ultrasonic radiation Two methods are employed: , The probe sonication method , The bath sonication technique[33].

d. Solvent dispersion method:-The lipid and other components of the liposome membrane can be dissolved in another solution using these methods. The resultant solution is supplemented with the aqueous phase. This aqueous phase contains the substance that will be trapped. Ether injection, ethanol injection, and reverse phase evaporation are methods used in the solvent dispersion process[34].

IV. COMPONENTS OF LIPOSOMES

The major constituents of liposome includes:-

• Phospholipids
• Cholesterol
• Phospholipid :-

One of the main structural elements of liposomes is phospholipid. It is amphiphilic in nature and possesses exceptional biocompatibility[35]. Liposomes are typically spherical sac vesicles with a distinct form and particle sizes ranging from 30 nm to several micrometers. It displays traits related to biocompatibility. Lamellae are referred to in this stratum.[36]. The pharmaceutical and cosmetic industries make extensive use of liposomes. [37]. The "liposome encapsulation" delivery technique is widely used in the food agricultural industry. It can employ trapped unstable substances, such as tastes, antimicrobials, and antioxidants. There are two types of phospholipids: phosphodiglycerides and sphingolipids. The phosphatidylcholine (PC) molecule is the most prevalent phospholipid. Both water-soluble and lipid-soluble drugs are transported to the target location via phospholipid.

Phospholipid examples include:

1) Phosphatidyl choline (PC), often known as lecithin
2) Cephalin, or phosphatidyl ethanolamine, or PE
3) PS, or phosphatidyl serine
4) PI, or phosphatidyl inositol
5) Glycerol phosphatidyl (PG)[38].

• Cholesterol:-

One of the other substances found in liposomes is cholesterol. Although cholesterol does not form bilayers, it can be incorporated into phospholipid membranes at concentrations of 1:1 or even 2:1 molar ratios of cholesterol to phosphatidyl choline. The liposome's particle size is influenced by the cholesterol content.[39].

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4. Method of preparation:-

Liposomes can be prepared by physical, mechanical, solvent-based, or detergent-based techniques.

Below are the standard and widely accepted methods.

A. Film-Hydration Method

a) Double-Emulsification Method

b) Solvent Injection Techniques

B. Combination Method

A. Film-Hydration Method :-

Step 1 : Dissolve lipids in organic solvent Weigh phospholipids + cholesterol.

Dissolve in chloroform or chloroform:methanol mixture.

Gives a clear lipid solution.

Step 2: Formation of a thin lipid film

Transfer the lipid solution to a round-bottom flask.

Rotate under reduced pressure in a rotary evaporator at 40–60°C.

Step 3: Removal of residual solvent

Dry further under vacuum or with nitrogen for 1–2 hours.

Ensures complete solvent removal.

The solvent evaporates → a thin, uniform lipid film forms on the flask wall.

Step 4: Hydration of lipid film

Add aqueous buffer preheated to above lipid phase transition temperature.

Rotate or shake vigorously.

Lipid layers peel off and form multilamellar vesicles (MLVs)

Step 5: Size reduction (optional) To obtain smaller vesicles:

Sonication → Small Unilamellar Vesicles (SUVs)

Extrusion → Large Unilamellar Vesicles (LUVs)

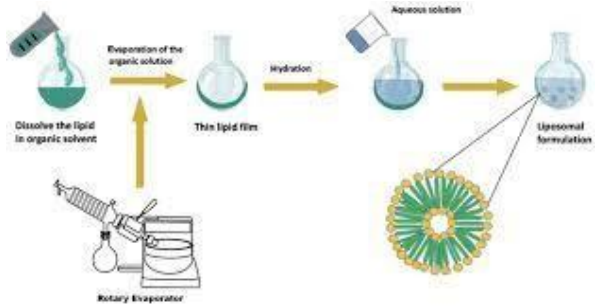

Fig 2:-Film-Hydration method

a) Double-Emulsification Method:-

A — Prepare lipid solution (organic phase)

1.Weigh lipids: Total lipids = 100 mg (e.g., PC:Cholesterol = 7:3 molar ratio). Optionally add 5 mol% PEG-DSPE if stealth behavior desired.

2.issolve lipids in 5 mL chloroform : methanol (2:1 v/v) in a glass vial or round-bottom flask.

B — Inner aqueous phase (W_1)

1.Prepare 1.0 mL of aqueous drug solution (e.g., drug at desired concentration in PBS). Keep cold if drug unstable.

C — Primary emulsion (W_1/O)

1.Add the 1.0 mL W_1 dropwise into the lipid/organic solution while stirring (magnetic stirrer).

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2.Emulsify with probe sonicator (pulse mode) for 15–60 s total (e.g., 3 × 10 s pulses with 30 s cooling) at moderate amplitude to produce a fine W_1/O emulsion. Avoid overheating.

D — Secondary emulsion (W_1/O into W_2 → $W_1/O/W_2$)

1.Prepare 20 mL W_2 = 1% (w/v) PVA in water (warmed to dissolve, then cooled). Keep stirring gently.

2.Add the primary W_1/O emulsion slowly into W_2 while sonicating or homogenizing. Use probe sonication in pulse mode for 30–120 s or use a high-speed homogenizer. This creates the $W_1/O/W_2$ double emulsion. Maintain temperature above lipid Tm (e.g., 40–50 °C if lipids have Tm near room temp).

E — Remove organic solvent and form liposomes

1.Transfer the $W_1/O/W_2$ emulsion to a rotary evaporator and remove the organic solvent under reduced pressure at gentle heat (e.g., 30–40 °C) until solvent is gone. Alternatively, evaporate under a gentle N_2 stream with stirring. As solvent is removed, lipids self-assemble around the inner aqueous droplets producing liposomes.

2.Continue until no organic solvent smell remains (careful to avoid overheating).

F — Size control & purification

1.Size reduction / homogenization: Sonicate briefly (bath or probe) or pass the suspension through polycarbonate membranes by extrusion (e.g., 400 nm → 200 nm → 100 nm) to obtain uniform vesicles.

2.Remove stabilizer and free drug: Purify by dialysis (against large volume of buffer), gel filtration (Sephadex G-50/G-100), or repeated centrifugation/resuspension (for larger liposomes). If PVA was used, gel filtration or prolonged dialysis helps remove it.

3.Sterile filtration: If needed and vesicle size permits (<200 nm), filter through 0.22 µm filter (note: may remove/rupture larger vesicles).

4.Characterize: measure particle size & PDI (DLS), zeta potential, encapsulation efficiency (by separating free drug and quantifying — e.g., UV/fluorimetry, HPLC), and morphology (TEM/AFM).

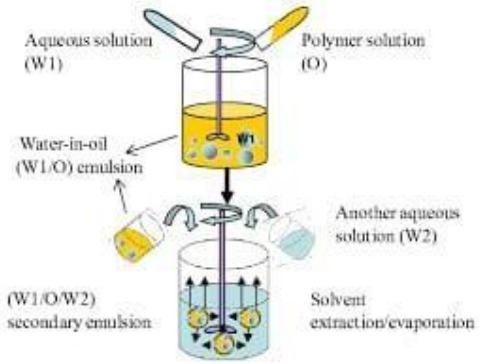

Fig 3:-Double-Emulsification Method

b) .Solvent Injection Technique

1.Prepare lipid solution (organic phase):

Dissolve lipids in absolute ethanol to desired concentration (example: 10–20 mg/mL). Ensure complete dissolution.

2.Prepare aqueous phase:

Warm buffer (e.g., PBS) to room temperature or slightly above lipid Tm (e.g., 25–45 °C depending on lipids). Stir gently.

3.Injection:

Using a syringe (or syringe pump), inject the lipid/ethanol solution rapidly into the aqueous phase under vigorous stirring. Typical injection ratio: 1:10 to 1:20 (organic:aqueous v/v).

Alternative: inject aqueous into organic (less common for ethanol method).

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4.Mixing & self-assembly:
As ethanol disperses into the aqueous phase, lipids self-assemble into vesicles. Continue stirring for several minutes.
5.Remove / dilute solvent:
Final ethanol concentration should be reduced (either by dilution or evaporation) to acceptable levels for the intended use. If necessary, remove residual ethanol by dialysis or rotary evaporation under reduced pressure (keep temperature controlled).
6.Size control & purification (optional):
Extrude through polycarbonate membranes (100–400 nm) or sonicate to narrow size distribution.Remove free drug or solvent by dialysis, gel filtration, or ultracentrifugation.

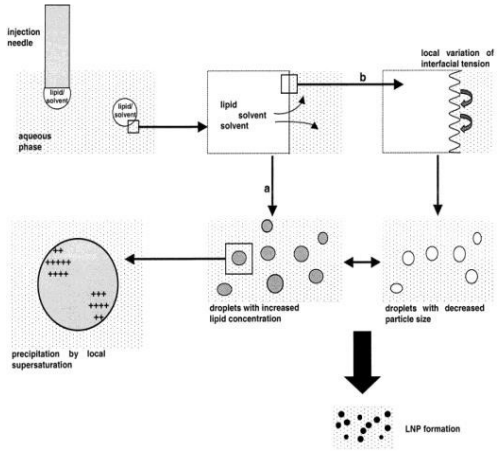

Fig 4:-Solvent Injection Technique

5.Evaluation of liposome:-
Liposomal processing and formulation for specific purposes are characterized to ensure consistent in vivo and in vitro performance. Characterization parameters for evaluation can be grouped into three groups.
1) Physical Characterization.
2) Chemical characterisation.
3) Biological characterisation.
1) Physical characterization:-
Physical characterization assesses aspects such as size, shape, surface features, release profile, and phase behavior.
1. Size
Liposomes range from 20 nm to several micrometers.
Classification by size:
a. Small Unilamellar Vesicles (SUVs): 20–100 nm
b. Large Unilamellar Vesicles (LUVs): 100–1000 nm
c. Multilamellar Vesicles (MLVs): >500 nm, multiple bilayers
d. Giant Unilamellar Vesicles (GUVs): >1 μm
2).Chemical characterization:-
Chemical characterization involves analyzing the composition, integrity, and stability of lipids and encapsulated drugs in liposomes. It ensures reproducibility, efficacy, and safety of liposomal formulations.
3).Biological characterization:-
Liposomes exhibit excellent biocompatibility, biodegradability and low immunogenicity because they are composed of natural phospholipids. They can encapsulate both hydrophilic and hydrophobic drugs and show controlled release behavior. Liposomes interact with biological membranes by fusion or endocytosis and their biodistribution is

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influenced by size, charge and PEGylation. They also exhibit passive and active targeting abilities, making them useful in drug delivery and diagnostics.

5. Marketed products:-

Marketed liposomal products are utilized in a variety of purposes, including medications, cosmetics, and food. Cancer therapies like Doxil and Marqibo, antifungal medications like

AmBisome, and pain relievers like Exparel and DepoDur are all examples of pharmaceuticals. Liposomes are used in cosmetics to deliver active chemicals, and in food to encapsulate tastes and vitamins.

Product Name	Active ingredient (API)	Approval Year /regional	Dosage form	Route of administrat ion	Indication
Doxil /Caelyx	Doxorubicin hydrochloride	(US), (EU)	Liposomal suspension	Intravenous	Ovarian cancer,Kaposi's sarcoma,myeloid melanoma
DaunoXome	Daunorubicin	1996 (US)	Liposomal suspension	Intravenous	Kaposi's sarcoma
Am Bisome	Amphotericin B	1997 (US)	Lyophilized liposome Intravenous	Intravenous	Systemic fungal infections
Myocet	Doxorubicin	2000 (EU marketing authorisati on July 13, 2000).	Sterile vial	Intravenous	Infusion Metastatic breast cancer (in combination regimens) — EU/Canada approvals.
Visudyne	Verteporfin	2000 (U.S. approval Apr 12, 2000).	Powder for reconstitution (injectable)	Intravenous	Photodynamic therapy for classic subfoveal CNV pathologic myopia, ocular histoplasmosis

Table No 1:- Marketed Products 7. Applications of Liposomes:-

7.1 In Ophthalmic Disorders:-

Different medications are used to treat conditions of the eyes, such as dry eyes, corneal transplant rejection and keratitis, which ought to be used topically as a suspension, solution, or ointment. Owing to several obstacles in the eye, these preparations show low ocular bioavailability. To get around this obstacle, Formulations of liposomes are employed. When treating dry eyes, the drugdelivering spray and liposome suspension are studied and developed into the conjunctival sac. The most popular eye drops that work against both gram +ve and gram −ve germs are ciprofloxacin/ciprocin. When ciprocin eye drops and ciprocin liposome preparations are compared in rabbits, the liposome preparations' area under the curve values are higher than those of ciprocin eye drops, resulting in improved ocular bioavailability, residence time, and low dose[40].

7.2 In Cancer Chemotherapy :-

The nature and activity of cancer cells differ greatly from those of normal cells, and thus have an elevated penetration rate effect. Due to the tumor's high permeability, both macromolecules and microorganisms can readily enter different tumor cells. Additionally, the tumor tissue is unique for targeted drug administration because cancer cells have particular biomarkers (integrins and amino peptidases). Many medications, including paclitaxel, docetaxel, and methotrexate, are prepared as liposomes. Two strategies are used to release anticancer drugs into the tumor site:

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pHresponsive (the pH difference between the blood (7.4) and the tumor cell (acidic pH)) and lysozyme-mediated polymer breakdown. Co-loading umbelliprenin and doxorubicin (a medication for breast cancer) into liposomes improves the uniform size and distribution of liposomes at the target site and boosts toxicity to the tested human breast cancer cell lines[41].

7.3 In Vaccines:-

In order to increase immunity and immunological responses, liposomes are utilized as adjuvants in vaccine delivery by altering their surface with various compounds, such as peptide antigens or virus antigens. For instance, the HIV antigen on the virion's surface, known as the membrane proximal external area, has low immunogenicity and boosts immune responses[42].

7.4 In Gene Delivery:-

As gene carriers, cationic liposomes are most frequently utilized. A commercial cationic liposome used for gene transfection is called Lofectamine 2000. Skin cancer is treated with curcumin-loaded STAT3 si-RNA liposomes made using the Bangham technique. In contrast to free STAT3 si-RNA and free curcumin, liposomes suppress the development of B16F10 melanoma cells. Additionally, liposomes carry the CRISPR or Cas9 gene to treat various malignancies and genetic problems[43].

7.5. Other Miscellaneous Applications:-

For diagnostic imaging, X-ray, magnetic resonance imaging (MRI), and near-IR fluorescence spectroscopy are frequently utilized. Super paramagnetic liposomes work incredibly well as MRI contrast agents. To improve their thermal structural durability, vitamins like tocopherol and C are encapsulated in liposomes. To prevent the natural pigment from deteriorating, carotene was encapsulated in pro-liposomes. Lemongrass oil, a compound that resembles bacteriocin, exhibits antibacterial action in liposomes, preventing cheese spoiling[44].

VIII. RECENT APPROACHES

For many years, liposomes have been researched and employed as drug delivery systems, and their prospects for the future are still bright. Liposomes are lipid-based vesicles that can contain a variety of medications, including both hydrophilic and hydrophobic substances. They continue to be relevant and have potential in the field of medication delivery since they provide a number of benefits as drug carriers[45]. Future opportunities for liposomes as innovative medication delivery systems include the following:

➢ Targeted Drug Delivery:- When it comes to treating diseases like cancer, where precise drug delivery is essential, liposomes can be engineered to target particular tissues or cells, increasing the therapeutic efficacy of medications while reducing adverse effects [54].

➢ Personalized medicine:-Customizable liposomes enable tailored treatment regimens by encapsulating various medicines and combinations. This could transform healthcare by personalizing pharmacological regimens to specific patients' requirements.

➢ Co-Delivery of Therapeutics:- Liposomes are appropriate for co-delivery of synergistic therapeutic agents since they can transport several medications at once. For a number of illnesses and ailments, this strategy can enhance therapy results.

➢ Controlled release :- By extending the therapeutic effect and lowering the frequency of dose, liposomes can be designed to release medications in a sustained and regulated manner. This is particularly helpful for long-term illnesses.

➢ Vaccine Delivery:-Liposomes have demonstrated potential as vaccine carriers. They may improve the immunogenicity and stability of antigens, which could result in the creation of more potent vaccines against infectious illnesses.

➢ Gene therapy: -Genetic material, such as CRISPR-Cas9 components or small interfering RNA (siRNA), can be delivered to target cells using liposomes. This has enormous promise for the treatment of hereditary illnesses.

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➢ Overcoming Biological Barriers:- Liposomes can be altered to get past biological barriers, like the blood-brain barrier, which makes it easier to transport medications to the central nervous system to treat neurological conditions.

➢ Combination Therapies:- For synergistic effects in the treatment of cancer, liposomes can be utilized to combine various therapeutic modalities, such as immunotherapy and chemotherapy.

➢ Formulation Improvements:-In order to increase the usefulness of liposomal formulations, ongoing research attempts to improve stability, lower toxicity, and increase drug-loading capacity.

➢ Regulatory Approvals: The use of liposome-based drug delivery systems in healthcare is expected to expand as more of them complete clinical trials and receive regulatory approvals.

X. CONCLUSION

Liposomes have become one of the most promising and adaptable drug delivery systems in contemporary medicine. Their distinctive capacity to encapsulate both hydrophilic and hydrophobic drugs, combined with their biocompatibility, potential for targeted delivery, and ability to mitigate toxicity, renders them effective carriers for a diverse array of therapeutic agents. Over the years, substantial progress in formulation techniques and surface modifications has enhanced their stability, circulation duration, and targeting efficiency, particularly in the realms of cancer therapy, vaccines, gene delivery, and diagnostics. Nevertheless, challenges such as scalability, regulatory complexities, and quality control persist as significant barriers to widespread clinical implementation. Ongoing innovation in manufacturing technologies and a deeper comprehension of liposomal behavior within biological systems will be crucial to fully exploit their therapeutic potential and expand their role in the pharmaceutical market.

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