



An Overview Of : Liposomes

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ABSTRACT :

Liposomes are small rounded shaped vesicles which are made up of phospholipids & cholesterol. They have diameter of 50 — 150 nm for drug delivery applications. Now a days they become an important drug carrier. This review basically focus on liposome , its structure, advantages, disadvantages, components, types, method of preparation, evaluation & application. There are many uses of liposome such as a drug carrier, cosmetic , enzymatic immobilization bio reactor technology & also used in various therapies like Gene Therapy & Tumour Therapy.

LITERATURE OF REVIEW :

1. Gordon L Amidon : This study proposes a biopharmaceutic drug classification system (BCS) based on the correlation between in vitro drug dissolution and in vivo bioavailability. The BCS categorizes drugs into four classes based on their solubility and permeability. Class I drugs have high solubility and permeability, Class II drugs have low solubility and high permeability, Class III drugs have high solubility and low permeability, and Class IV drugs have low solubility and permeability. This classification system provides a framework for predicting the in vivo performance of oral drugs and guiding the development of new formulations.
2. Senthil Prabhu: The purpose of this study was to develop novel lipid-based formulations to enhance the dissolution and permeability of piroxicam, a poorly water-soluble model drug. Various formulations, including self-emulsifying drug delivery systems (SEDDS), microemulsions, and liposomes, were prepared and evaluated. Results showed that SEDDS formulations significantly improved piroxicam's dissolution rate and permeability across Caco-2 cell monolayers. These findings suggest that lipid-based formulations can be an effective strategy for enhancing the bioavailability of poorly water-soluble drugs like piroxicam.
3. Ann-Christine : This review discusses the potential of synthetic polymers as drugs, focusing on their therapeutic applications. The authors highlight the importance of polymer structure, molecular weight, and functional groups in determining their biological activity. Various examples of bioactive synthetic polymers are presented, including anticoagulants, antitumor agents, and immunomodulators. The challenges and opportunities in developing synthetic polymers as pharmaceuticals are also addressed.
4. Gregory Gregoriadis: This book provides a comprehensive overview of drug carriers, highlighting their potential in biology and medicine. Gregoriadis, a pioneer in liposome research, explores various drug carrier systems, including:
 1. Liposome
 2. Microspheres
 3. Nanoparticle

Cells and cellular components The book discusses:

1. Carrier preparation and characterization
2. Drug entrapment and releas
3. Targeting and specificity
4. Biological interactions and applications

"Drug Carriers in Biology and Medicine" is a seminal work, laying the foundation for the development of targeted drug delivery systems.

1. Martin Jay Ostro : This book provides a comprehensive overview of liposomes, covering their biophysical properties, preparation methods, and therapeutic applications. Ostro, a renowned expert in liposome research, explores:
 1. Liposome structure and composition
 2. Liposome preparation and characterization
 3. Liposome-cell interactions and targeting
 4. Liposome-mediated drug delivery and gene therapy

The book discusses the potential of liposomes as:

1. Drug carriers for cancer therapy
2. Vaccines and immunoadjuvants
3. Gene delivery systems

"Liposomes: From Biophysics to Therapeutics" is a seminal work, providing a thorough understanding of liposomes and their applications in biomedicine.

INTRODUCTION :

The identification of several medicinal compounds has been made possible by the availability of sophisticated techniques in drug development and research. However, because of the weak association between in vitro and in vivo results, the majority of them fail during the embryonic phase [1, 2]. In general, targeted or site-specific administration is necessary for powerful medications with a narrow therapeutic index. Liposomes, microparticles, nanoparticles, and other carrier-mediated drug delivery systems can be used to do this [3–7]. Because of their well-established qualities that aid in drug administration, liposomes have become a very important drug carrier [8]. Liposomes are phospholipid-based closed, concentrated vesicles with a colloidal size range of 0.01–5.0 μm . Amphiphilic compounds, phospholipids have both hydrophilic and hydrophobic.

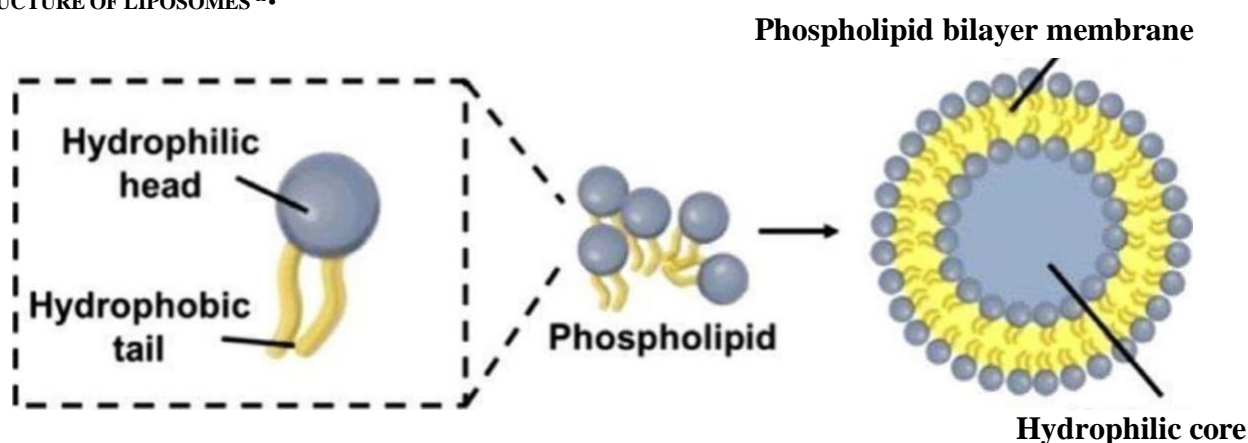
A. D. Bangham initially described liposomes in the early 1960s after researching how phospholipids can form spherical shapes encounter water. This finding has resulted in the encapsulation of numerous medication types in phospholipid bilayers for enhancing medicinal Performance [9]. Drugs in water can become stuck. In

aqueous space, while medications that are poorly soluble can be accommodated inside the bilayers of phospholipids[10]

DEFINITION :

One or more concentric lipid bilayers that encapsulate an interior aqueous volume or volumes make up liposomes. Liposomes are typically unilamellar and have a diameter of 50–150 nm for drug delivery applications. Greater liposome size is quickly taken out of the bloodstream. Liposomes are distinct in their capacity to accept medications, which vary extensively in physicochemical characteristics like charge and polarity and dimensions. Locations of these medications in liposomes include the liposome bilayer, which has a broad polar surface that can be neutral or hydrophobic, and a hydrocarbon chain core. Charged, as well as the aqueous interior. The term "drug" is utilized as a general word to describe traditional medications like the anticancer medication doxorubicin and the antifungal agent AmpB, in addition to genetics.

STRUCTURE OF LIPOSOMES II•



ADVANTAGE 1121

1. Liposomes improve the medication's therapeutic index and efficacy (Actinomycin-D).
2. Encapsulation increases the stability of liposomes.
3. For both systemic and non-systemic delivery, liposomes are biocompatible, fully biodegradable, non-toxic, flexible, and nonimmunogenic.
4. The encapsulated agent's toxicity is decreased by liposomes (Amphotericin B, Taxol).
5. Liposomes lessen the amount of hazardous medications that are exposed to delicate tissues.
6. The effect of site avoidance.
7. The ability to combine with ligands unique to a spot to accomplish active targeting

DISADVANTAGES 1121

1. The expense of production is substantial.
2. Drug or molecule fusion and leakage from encapsulation
3. brief half-life
4. Reduced stables

COMPONENTS 1121

Despite having a number of structural and nonstructural components, liposomes' primary structural pillars are:

1. Phospholipids
2. Cholesterol

1. Phospholipids

Phospholipids are the major structural element of biological membranes, where two types of phospholipids exist: phosphoglycerides and sphingolipids. The most common phospholipid is

phosphatidylcholine (PC). Phosphatidylcholines are not answerable in water and in waterless media they align themselves nearly in a planar bilayer to minimize the inimical action between the bulk waterless phase and long hydrocarbon adipose chain. (Fig. 4) The Glycerol

containing the most often utilized component of liposome expression, phospholipids make up less than 50% of weight of lipid in natural membranes. These are deduced from phosphatidic acid.

Exemplifications of phospholipids are:

1. Phosphatidyl choline (Lecithin) — PC
2. Phosphatidyl ethanolamine (cephalin)-PE
3. Phosphatidyl serine (PS)
4. Phosphatidyl inositol (PI)
5. Phosphatidyl Glycerol (PG)

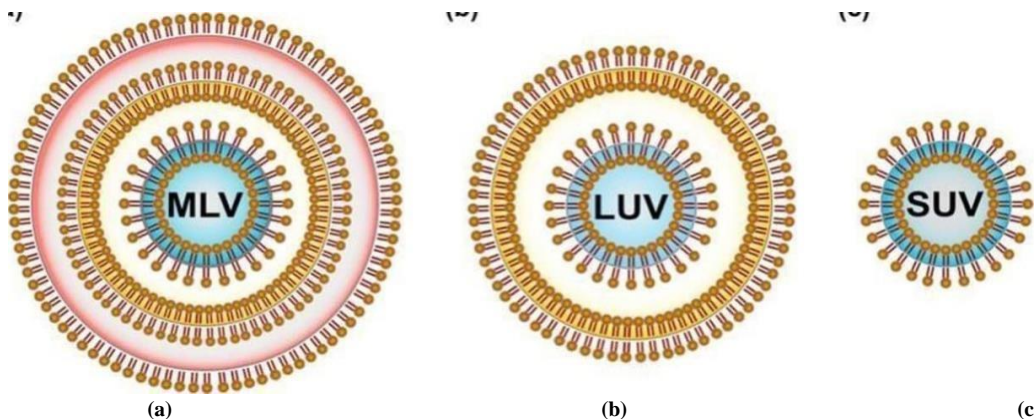
2. CHOLESTEROL:

In phospholipid membranes, cholesterol can be present in very high concentrations, up to a 1:1 or even 2:1 molar ratio of cholesterol to phosphatidylcholine, but it does not by itself create a bilayer structure. With its hydroxyl group facing the aqueous surface and its aliphatic chain aligned parallel to the acyl chains in the middle of the bilayer, cholesterol enters the membrane. Both hydrophobic and particular head group interactions have been implicated in the high solubility of cholesterol in phospholipid liposomes; however, the organization of cholesterol in the bilayer has not been conclusively demonstrated. [13, 14].

TYPES OF LIPOSOMES 115,161 :

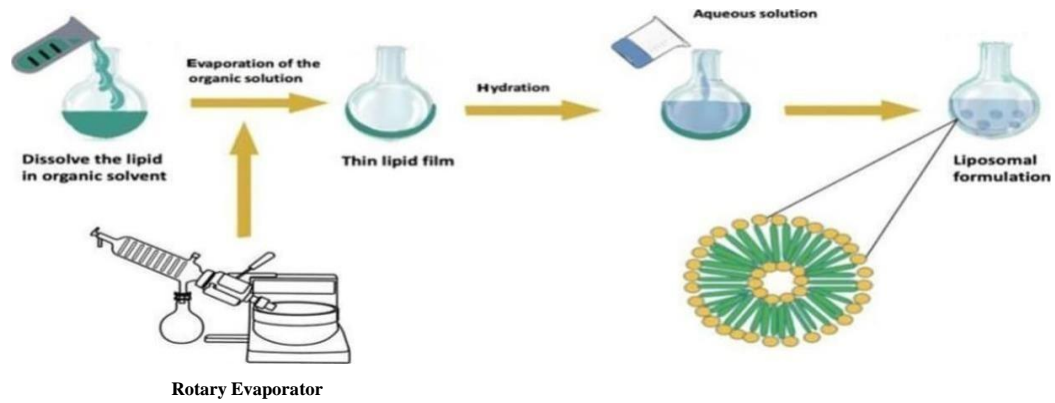
Liposomes are typically categorized based on their size and lamellarity. The primary liposome types are displayed in the following categories.

1. **Multilamellar vesicles (MLVs):** This population has a broad range of size distribution that occurs in a range of 100-1000 nm. The lamellarity of these MLVs may be influenced by their lipid composition. On the other hand, the lamellarity usually ranges from 5 to 20 concentric lamellae.
2. **Large unilamellar vesicles (LUVs):** These vesicles are typically up to 1000 nm in size and have a single lamellae structure.
3. **Small unilamellar vesicles (SUVs):** These structures typically have a diameter of less than 100 nm and are composed of a single lamellae.



METHOD OF PREPARATION:

L) Film Method¹⁸: The most straightforward technique for creating liposomes is still the original Bangham et al. Method [17], however it has several drawbacks due to its poor encapsulation effectiveness. This method creates liposomes by hydrating a thin layer of lipids in an organic solvent, which is subsequently eliminated through vacuum-assisted film deposition. Once all of the solvent has been removed, the solid lipid combination is hydrated using an aqueous buffer. Lipids hydrate and swell on their own to produce liposomes. A diverse population of MLVs larger than one micrometer in diameter is produced by this technique.



2) Ultrasonic Method¹⁹ : SUVs with a diameter of 15 to 25 meters are prepared using this technique. Two types of sonicators—probe sonicators and bath sonicators—are used to ultrasonically sonicate an aqueous dispersion of phospholipids. While bath sonicators are used for big volumes, probe sonicators are utilized for small volumes that demand a lot of energy[20].

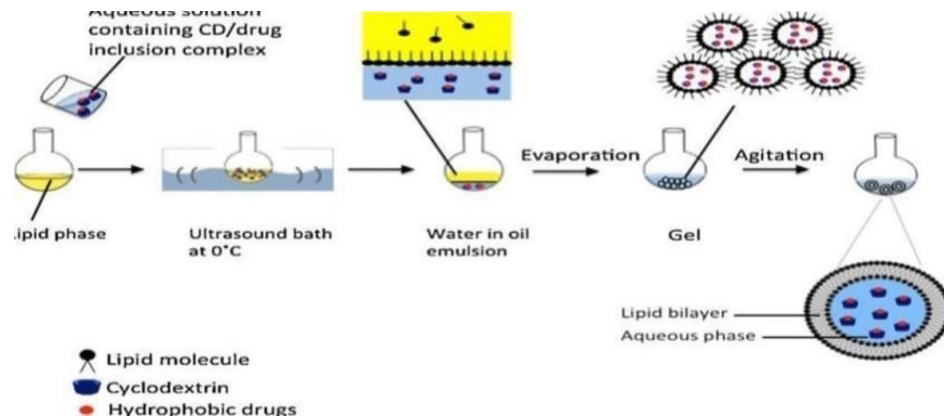
Preparatiorm via Rev-verse



Reverse Phase Evaporation²¹ :

3)

After adding the lipid mixture to a round-bottom flask, a rotary evaporator removes the solvent at a lower pressure. The reverse phase vesicle formed when nitrogen is added to the system, causing the lipids to breakdown again in the organic phase. Generally, the recommended solvents are isopropyl and diethyl ether. Typically, diethyl and isopropyl ether are the preferred solvents. Once the lipids have been redissolved, an emulsion is produced. The solvent is then extracted from the emulsion by evaporating it into a semisolid gel at a lower pressure. Material that is not enclosed is then eliminated. Huge macromolecules can be encapsulated using this technique, which is used to prepare huge uni-lamellar and oligo-lamellar vesicles.[22,23]



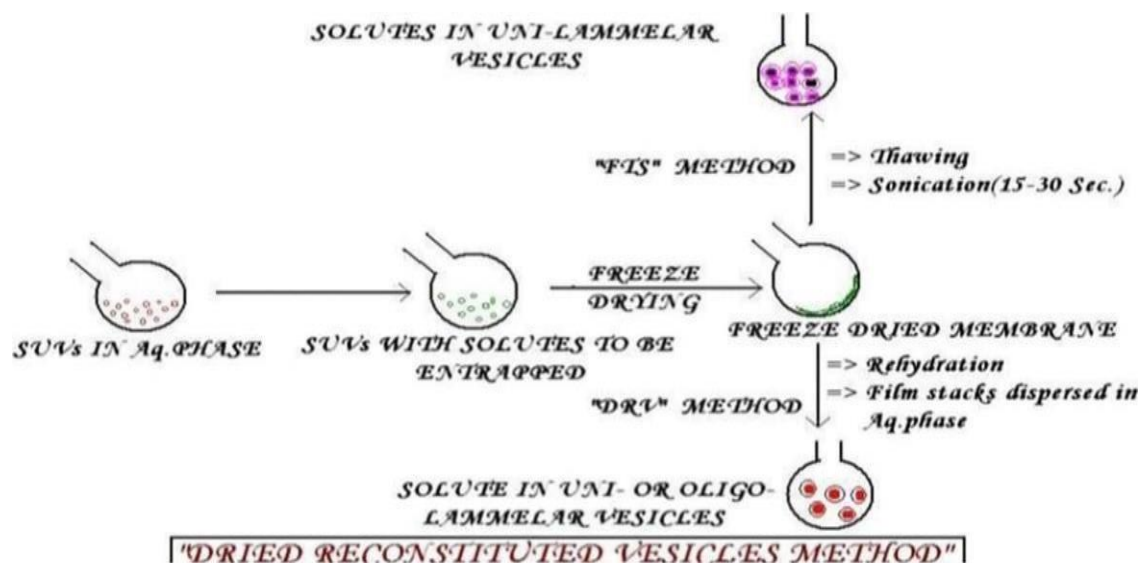
AqHuyedoruosphoolbuiticidornugs containing CO/drug inclusion

Ether Vaporization Method: Depending on the solvent being utilized, there are two methods:

1. The infusion of ethanol.
2. Injection of ether

The ethanol injection method involves rapidly injecting the lipid with a tiny needle into an excess of saline or similar aqueous medium. The ether injection method involves slowly injecting the lipid into an excess of saline or another aqueous media using a tiny needle.

Freeze Thaw Extrusion Method ²⁵ : An extension of the traditional DRV method is the freeze-thaw technique. After the entrapped solute has been vortexed with the film-formed liposomes, the entire film is suspended. After that, the resultant MLVs are vortexed again after being frozen in lukewarm water. Following two cycles of freezing, thawing, and vortexing, the sample undergoes three extrusions. Eight extrusions and six freeze-thaw cycles are then included. In the procedure, SUVs are ruptured and defused, the solute equilibrates between the interior and exterior, and the liposomes fuse and enlarge to create huge Uni lamellar vesicles using the extrusion technique (LUVET). [24].



CHARACTERIZATIONS (26.27.28):

It is necessary to characterize liposomes made using one of the previously mentioned methods. Visual appearance is one of the most crucial aspects of liposome characterisation. Concentration, lamellarity, turbidity, size distribution, Composition, existence of products of degradation, and stability.

1. **Visual Appearance**: Depending on the particle size and composition, liposome suspension can have a range of colors from milky to transparent. If the turbidity seems bluish, it indicates that the sample's particles are uniform; a flat, gray, shows that a nonliposomal is present. dispersion and is probably an inverse of dispersion. Either scattered microcrystallites or a hexagonal phase. An Phase contrast in an optical microscope can identify $>0.3 \mu\text{m}$ liposome and contamination with bigger fragments.
2. **Entrapped Volume**: It is frequently possible to infer the entrapped volume of a liposome population (in $\mu\text{L}/\text{mg}$ phospholipid) from measurements of the total amount of solute entrapped. Within liposomes, guaranteeing that the amount of Within liposomes, the solute in the aqueous media is the same after being separated from the untrapped substance. For instance, in the two-phase preparation procedure, water Can be eliminated from the internal space throughout the removing organic solvent by drying down.
3. **Surface Charge**: Because liposomes are typically made with lipids that impart charge, it is instructive to examine the charge on the vesicle surface. Generally speaking, two Methods like as zeta potential testing and freeflow electrophoresis are employed to evaluate the charge Based on the liposomal dispersion's mobility in a appropriate buffer, the vesicle surface charge.
4. **Determination of Liposomal Size Distribution** : Dynamic light scattering is typically used to measure size distribution. For liposomes with a rather uniform size distribution, this technique is dependable. A gel exclusion chromatography is a straightforward but effective technique that uses a really hydrodynamic Radius is detectable. Sephacryl-S100 is capable of separating liposomes between 30 and 300 nm in size. Sepharose -4B And -2B columns are capable of separating micelles from SUV.
5. **Liposome Stability** : Physical, chemical, and biological stability are all components of liposome stability, which is a complicated topic. Stability of shelf life is equally crucial for drug delivery and the pharmaceutical business. Stability of body mostly shows the size and ratio's consistency. Lipid to the active ingredient. The liposomes that are cationic can be Stable for an extended length of time at 4°C , if appropriately Sterilized

APPLICATIONS29:

1. Liposomes are used as medicine delivery vehicles.
2. Liposomes are used in antimicrobial, antifungal, antiviral remedy.
3. Liposomes are used in tumour remedy
4. Liposomes are used in Gene Therapy.
5. Liposomes are used in enzyme immobilization & memoir reactor technology.
6. Liposomes are used in cosmetics & dermatology.
7. Liposomes are also used in immunology.

CONCLUSION:

The use of liposomes in drug delivery has been studied for 25 years. Liposomes represent a novel medication delivery technology that may find application in directing and managing the supply of drugs. Liposomes are administered topically, parenterally, and orally. As used to hair and cosmetic technology, maintained compositions for release, diagnostic purposes, and as excellent carriers in the administration of different medications using liposomal Systems for delivery have been authorized. These days liposomes serve as flexible delivery systems for specific drug delivery.

REFERENCE :

- 1) Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutical drug classification: The correlation of in vitro drug product dissolution and in vivo bioavailability. *Pharmaceut Res* 1995; 12: 413-20.
- 2) Prabhu S, Ortega M, Ma C. Novel lipid-based Formulations enhancing the in vitro dissolution and Permeability characteristics of a poorly water-soluble Model drug, piroxicam. *Int J Pharmaceut* 2005; 301:209-16.
- 3) Albertsson AC, Donaruma L, Vogl O. Synthetic Polymers as Drugs. *Ann NY Acad Sci* 1985; 446: 105-15.
- 4) Tyrrell D, Heath T, Colley C, Ryman BE. New aspects of liposomes. *Biochimica et Biophysica Acta (BBA)-Rev Biomemb* 1976; 457: 259-302.
- 5) Tirrell DA, Takigawa DY, Seki K. pH Sensitization of Phospholipid Vesicles via Complexation with Synthetic Poly (carboxylic acid) sa, b. *Ann NY Acad Sci* 1985; 446: 237-48.
- 6) Gregoriadis G. Drug carriers in biology and medicine: Academic Press; 1979.
- 7) Abra R, Hunt CA. Liposome disposition in vivo: III. Dose and vesicle-size effects. *Biochimica et Biophysica Acta (BBA)-Lipids and Lipid Metabol* 1981; 666: 493-503.
- 8) Ostro MJ. Liposomes: From biophysics to Therapeutics: Courier Corporation; 1987.
- 9) Bangham A, Standish MM, Watkins J. Diffusion of univalent ions across the lamellae of swollen phospholipids. *J Mol Biol* 1965; 13: 238-1N27.
- 10) Massing U, Fuxius S. Liposomal formulations of anticancer drugs: selectivity and effectiveness. *Drug Resistance Updates* 2000; 3: 171-7
- 11) Liposome-based delivery of biological drugs — Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/The-basic-structure-of-a-liposome-fig1_354432545 [accessed 6 Nov 2024]
- 12) Sharma Vijay, Mishra D, Sharma A , Srivastava B. Liposomes: Present Prospective and Future Challenges, *International Journal of Current Pharmaceutical Review and Research*. I(2);August — October 2010:5-16
- 13) Pati1 S. G., Gattani S. G., Gaud R. S., Surana s.J., Dewani S. P.And Mahajan H. S (2005). *The Pharma Review*, 18(3):53-58
- 14) Patel S. S (2006). Liposome: A versatile platform for targeted Delivery of drugs. *Pharmainfo.net.*, 4;5: 1-5
- 15) Riaz M (1996). Liposome preparation method. *Pakistan Journal of Pharmaceutical Sciences*, I :6577.
- 16) Nanoparticle-Mediated Combination Therapy: Two-in-One Approach for Cancer - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Classification-of-liposomesbased-on-the-lamellarity-a-Multilamellar-vesicles-MLV_fig4_328418123 [accessed 6 Nov 2024]
- 17) Nov 2024] 17) Bangham, A.D.; Standish, M.M.; Watkens, J.C. *J. Mol. Biol.*, 1965,13, 238.
- 18) Microfluidics Technology for the Design and Formulation of Nanomedicines — Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Thin-film-hydrationmethodfor-empty-liposome-preparation-The-liposomes-produced-from-fig1_357159659 [accessed 7 Nov 2024]
- 19) Yao, X., Bunt, C., Cornish, J., Quek, S.-Y. and Wen, J. (2014): Preparation, Optimization and Characterization of Bovine Lactoferrin-loaded Liposomes and Solid Lipid Particles Modified by Hydrophilic Polymers Using Factorial Design. *Chemical Biology and Drug Design* 83, 2014. 560-575 Read more: <https://www.hielscher.com/liposomes-via-reverse-phaseevaporationmethod-using-sonication.htm>
- 20) Hwang, R.J.; Padki, M.M. •, Chow, D.D. *Biochim. Biophys. Acta*, 1987, 901, 88.
- 21) Liposomes incorporating cyclodextrin—drug inclusion complexes: Current state of knowledge — Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Reversephase-evaporation-method-fig6_276486730 [accessed 7 Nov 2024]
- 22) Papahadjopoulos, D.; Vali, W. J.; Jacobson, K.; Poste, G. *Biochim. Biophys. Acta*, 1975, 394, 483.
- 23) Pleumchitt, R.; Narong, S.; Korakot, C.; Krisana, K. *Drug Dev. Ind. Pharm.*, 2000, 29(1), 31
- 24) Mayer, L.D.; Hope, M.; Cullis, P.R. *Biochim. Biophys. Acta* 1985b, 817,

- 25) ROLE OF LIPOSOME IN NOVEL DRUG DELIVERY SYSTEM - Scientific Figure onResearchGate. Available from: https://www.researchgate.net/figure/Method-of-preparationofliposomes-by-freeze-thaw-sonication-PH-INDUCED-VESICULATION_fig2_326670097 [accessed 7 Nov 2024]
- 26) Gregoriadis G., ed. (1993) Liposome Technology, vols. 1, 2, 3, 2nd edit. CRC Press, Boca Roton, FL.
- 27) Lasic D. D and Paphadjopoulos D., eds. (1998) Medical Application of Liposomes. Elsevier, New York, NY
- 28) Senior J, Gregoriadis G and Mitopoulous K. A.(1983). Stability and clearance of small unilamellar liposome. Studies with normal and liipoprotein-deficient mice. Biochim. Biophys. Acta, 760:
- 29) Lasic D.D. Application of liposome, Liposome Technology, 1050 Hamilton Court, Menlo Park, California, USA Hand book of biological physics. Vol. 1st edited by R. Lipowsky and E.Sackmann:493-515.