e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:06/Issue:11/November-2024 Impact Factor- 8.187 www.irjmets.com

LIPOSOMES

Prerana Panage[*1], Tanaya Wakchaure[*2]

[*1,2]Department Of Pharmacy, Vidyaniketan Institute Of Pharmacy & Research Center, Bota, Maharashtra, India.

ABSTRACT

Liposomes, sphere-shaped vesicles consisting of one or more phospholipid bilayers. A number of clinical studies have now demonstrated the superiority of liposomal drug formulations over conventional delivery systems. Liposomes Characterize an advanced technology to deliver active molecules to the site of action, and at present, several formulations are in clinical use. Liposomes, as versatile lipid-based nanoparticles, have emerged as promising drug delivery systems in recent years. This comprehensive review aims to provide an in-depth analysis of the advancements, challenges, and potential applications of liposomes in drug delivery. the last few years, many techniques have been utilized to enhance the pharmacological activity of any Active Pharmaceutical Drug [API] resulting in better bioavailability and lesser side effects. Liposomes are a drug delivery system that is adaptable and optimistic. The benefits of liposomes over other drug delivery systems include site-targeting, prolonged or controlled release, protection of drugs from degradation and clearance, higher therapeutic effects, and fewer toxic adverse effects. As effective drug carriers in pre- clinical and clinical studies, liposomes provide a wide range of benefits and uses.

Keywords: Liposomes, Phospholipid, Liposomal Drug Delivery, API, Lipid Bilayers.

I. INTRODUCTION

Liposomes are colloidal, vesicular structures composed of one or more lipid bilayers surrounding an equal number of aqueous compartments. The sphere like shell encapsulated a liquid interior which contain substances such as peptides and protein, hormones, enzymes, antibiotic, antifungal and anticancer agents.A free drug injected in blood stream typically achieves therapeutic level for short duration due to metabolism and excretion. [1].

The Greek words 'Lipos' which means fat and 'Soma' that means body, was combined to form spherical concentric vesicles called liposomes. Liposomes are round sac phospholipid molecules. It encloses a water droplet especially as form artificially to carry drug into tissue membrane. Liposome is a nanoparticle (size-100 nm).[1].

Liposome is small artificial vesicles of spherical shape that can create cholesterol and naturally non-toxic phospholipids. They are depending upon size, hydrophobic and hydrophilic characteristics. Liposome is a spherical vesicles having at least one lipid bilayer.

It is use as vehicle for administration of nutrients as well as pharmaceutical drugs. It shows both characteristics:

1. **Hydrophilic head**
2. **Lipophilic tail. [3].**

The lipids in the plasma membrane are chiefly phospholipids like phosphatidylethanolamine and phosphatidylcholine. Phospholipids are amphiphilic with the hydrocarbon tail of the molecule being hydrophobic; its polar head hydrophilic.

Plasma membrane faces watery solutions on both sides, its phospholipids accommodate this by forming a phospholipid bilayer with the hydrophobic tails facing each other. Liposomes can be composed of naturally-derived phospholipids with mixed lipid chains (like egg phosphatidylethanolamine), or of pure surfactant components like DOPE (dioleoyl phosphatidyl-ethanolamine). Liposomes, usually but not by definition, contain a core of aqueous solution; lipid spheres that contain no aqueous material are called micelles, however, reverse micelles can be made to encompass an aqueous environment. [2].

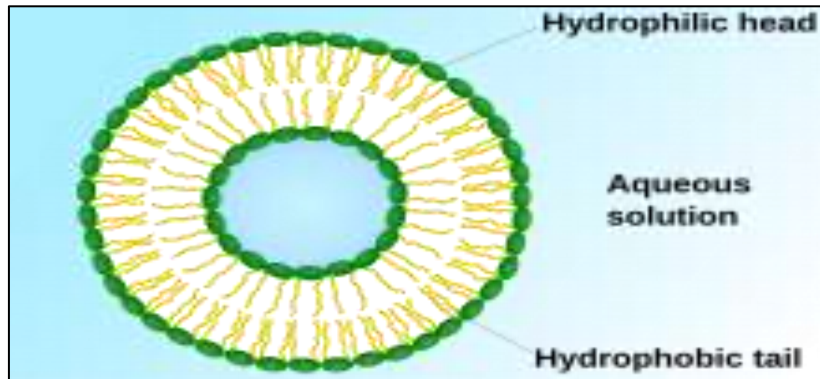

Fig 1: Structure of liposomes

Advantages:

a. Can carry both water and lipid soluble drugs.
b. Non-ionic in nature.
c. Liposome is biocompatible, completely biodegradable, non-toxic, and non-Immunogenic.
d. Suitable for delivery of hydrophobic, amphipathic and hydrophilic drug.
e. Protect encapsulated drug from the external environment.
f. Liposome reduces toxicity and increase stability via encapsulation.
g. They are increase activity of chemotherapeutic drug.

Disadvantages:

a. Leakage and fusion of encapsulated.
b. Short half-life.
c. Stability problems.
d. Allergic reaction may occur to liposome constituents.
e. Problem to targeting to various tissues due to their large size.
f. Phospholipid undergoes oxidation, hydrolysis. [2, 17].

Classification of liposomes:

1. Classification of liposome depending upon size and shape

a) Multilamellar vesicles (MLV)
b) Large unilamellar vesicles (LUV)
c) Small unilamellar vesicles(SUV)

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
c) Lipid hydration by hand shaking or freeze dryin
d) Micro emulsification
e) Sonication
f) French pressure cell
g) Solvent dispersion method

- Ethanol injection
- Ether injection
- Double emulsion vesicle
- Reverse phase evaporation

h) Detergent removal method

- Dialysis
- Detergent removal of mixed micellar
- Dilution

i) Active loading technique. [3,18].

1. Classification of liposome depending upon size and shape

a. Multilamellar vesicles:

MLV have a size greater than 0.1µm and consists of two or more bilayer. Their method of formulation is simple and very easy to carry which includes thin– film hydration method or hydration of lipids in excess of organic solvent. They are mechanically stable on long storage. Due to the large size, they are cleared early or rapidly by the reticuloendothelial system (RES) cells and hence can be beneficial for various targeting the organs of RES. MLV have a moderate trapped volume, i.e., amount of aqueous volume to lipid ratio.

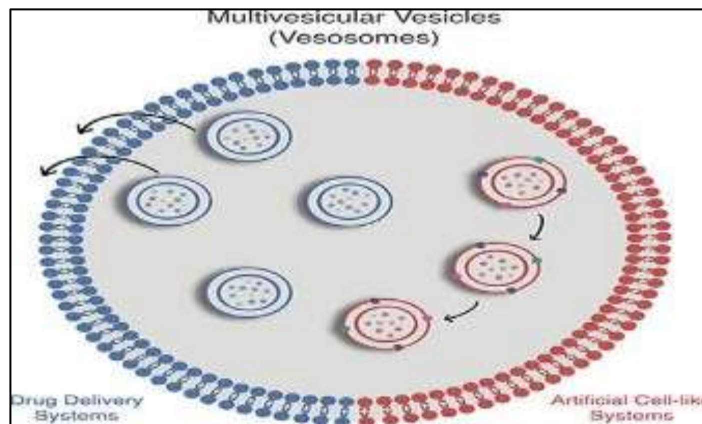

Fig 2: Multilamellar vesicles

b. Large unilamellar vesicles:

The large unilamellar vesicles of liposome consist of a single bilayer or single lamella. LUV size is ' > 0.1 micrometer and can reach size up to 1000 nm). They have mainly high efficiency of encapsulation, since ability to hold large volume of solutions in their cavity. They are similar to multilamellar vesicle. Large unilamellar vesicles are prepared from various methods like ether injection, reverse phase evaporation technique and detergent dialysis.[3,9,19,20).

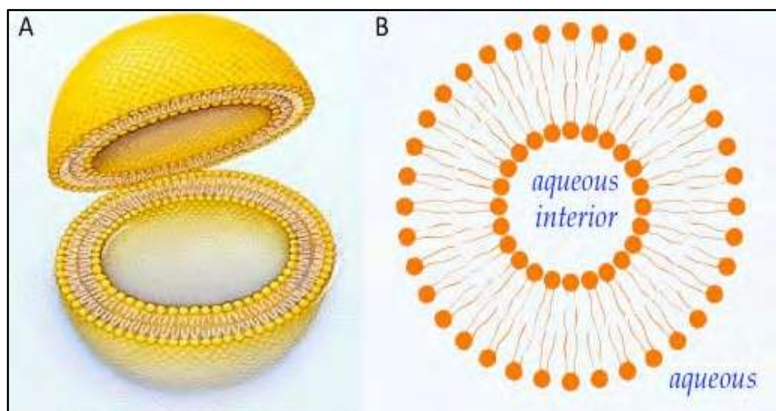

Fig 3: Large unilamellar vesicles

e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:06/Issue:11/November-2024 Impact Factor- 8.187 www.irjmets.com

c. Small unilamellar vesicles

SUV are smaller in size (less than 0.1 μm) when compared to MLV and LUV, and have a single bilayer. They have a low entrapped aqueous volume to lipid ratio and characterized by having long circulation half-life.

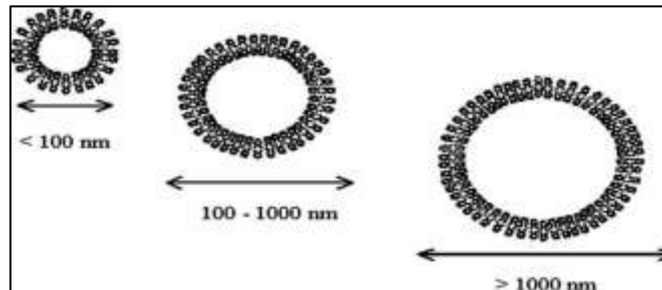

Fig 4: Small unilamellar vesicles

2. Classification of liposome according to composition:

a. Conventional Liposomes (CL): Made up of neutral and negatively charged cholesterol and phospholipids[15].

Conventional liposome- based technology is first generation of liposome to be used in pharmaceutical applications. Several attempts to overcome their challenges have been made, specifically manipulation of the lipid membrane.[25, 26,27].

b. pH sensitive Liposomes: Phospholipids such as DOPE with either

c. Cationic liposomes: Cationic lipid with DOPE .

d. Long Circulatory (Stealth) Liposomes (LCL):

Liposomes that persist for prolong period of time in the blood stream. LCL contains PEG (polyethylene glycol) which is termed pegylation.Pegylation increases circulation of liposomes in the body by reducing its body clearance [16].

e. Immuno liposome:

Enhance target site binding. Immuno-liposome (ILs) is generated Immuno-liposome (ILs) is generated by coupling antibodies either directly to liposome lipid bilayer in the presence of PEG chains (type l liposome) or to the distal end of PEG chains (type ll liposome).Coupling antibodies to the lipid bilayer of PEGylated. Liposome can result in reduced antigen binding depending on amount of PEG and length of the PEG chains.[34, 35].

3. Classification of liposome depending upon production method:

b. Passive loading Technique :

Passive loading is a technique used to load a system, circuit, or signal without actively controlling or modifying its behavior.

c. Mechanical dispersion methods:

lipid to organic solvent, drug to be entrapped is solubilised in aqueous solvent. the lipid phase is hydrated at high speed stirring & due to affinity of aqueous phase. to polar head it is entrapped in - lipid vesicles.

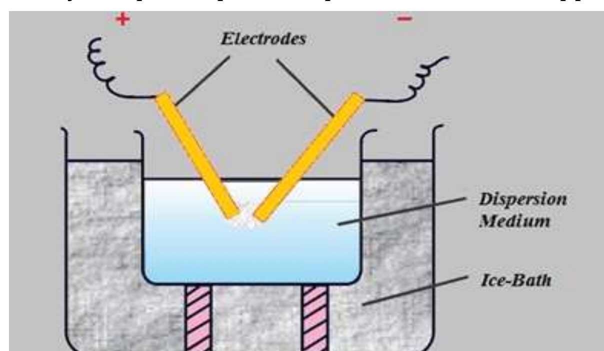

Fig 5: Mechanical dispersion method

e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:06/Issue:11/November-2024 Impact Factor- 8.187 www.irjmets.com

1. Lipid hydration by hand shaking or freeze drying:

The most typical and widely used method for MLV preparation is the hydration method. The method involves vortexing the dispersion and adding fluid buffer before hydrating the thin layer by dehydrating the lipid arrangement. The hydration phase is complete. Depending upon their solubilities substances that are to be enclosed are included either in a watery buffer or organic solvent containing lipids. The reduced application efficacy can be solved by hydrating the lipids adjacent to characteristic solvents that are immiscible, such as petroleum ether and diethyl ether. Then, sonication is used to emulsify it. By passing nitrogen, MLVs are formed by releasing a natural layer.

2. Micro- emulsification:

High pressure homogenizer is used for this method. This method is used to prepare SLVS. By using high shear stress lipid composition is micro emulsified.

3. Sonication:

Sonication is perhaps the most extensively used method for the preparation of SUV. Here, MLVs are sonicated either with a bath type sonicator or a probe sonicator under a passive atmosphere. [11].

4. French pressure cell:

This method is based on mechanism of high pressure. This method used to preparation of 1-40 ml of homogeneous unilamellar liposomes of intermediate size (30-80 nm).[43].

C. Solvent dispersion method:

1. Ethanol injection:

A lipid solution of ethanol is rapidly injected to a vast excess of buffer. The MLVs are immediately formed. The drawbacks of the method are that the population is heterogeneous (30-110 nm), liposomes are very dilute, it is difficult to remove all ethanol because it forms azeotrope with water and the possibility of various biologically active macromolecules to inactivation in the presence of even low amounts of ethanol.

2. Ether injection:

A solution of lipids dissolved in diethyl ether or ether/methanol mixture is slowly injected to an aqueous solution of the material to be encapsulated at 55-65°C or under reduced pressure. The subsequent removal of ether under vacuum leads to the formation of liposomes. The main drawbacks of the method are population is heterogeneous (70-190 nm) and the exposure of compounds to be encapsulated to organic solvents or high temperature. [7]

3. Double emulsion vesicles:

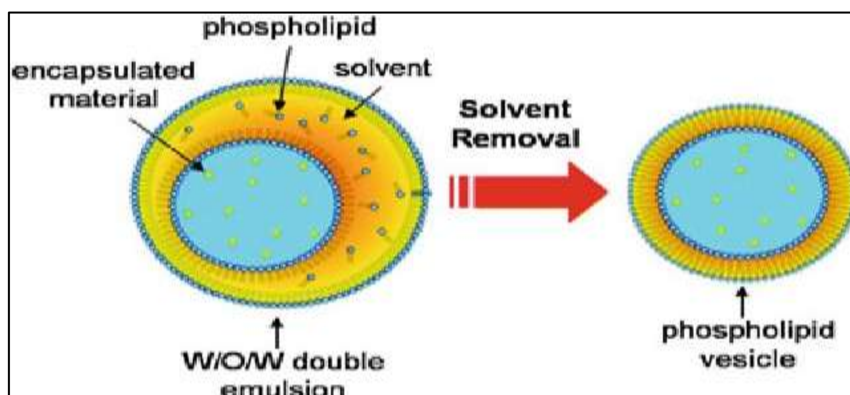

Fig 6: Double emulsion vesicles

4. Reverse phase Evaporation:

This method is used for preparing liposomes with high encapsulation efficiency.

Steps:

a. Dissolve lipids in an organic solvent along with an aqueous solution containing the substance to be encapsulated.

e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:06/Issue:11/November-2024 Impact Factor- 8.187 www.irjmets.com

b. Evaporate the organic solvent under reduced pressure to form a water-in-oil emulsion.

c. Remove the organic phase, leaving behind liposomes containing the encapsulated substance.[30, 31].

D. Detergent removal method:

This method is used for preparing liposomes encapsulating hydrophobic substances.

Steps:

a. Dissolve lipids and the hydrophobic substance in a detergent solution.

b. Remove the detergent using techniques like dialysis or chromatography to obtain liposomes with the encapsulated substance.[35, 36].

1. Dialysis:

The detergent at their critical Michelle concentration (CMC) is used to solubilize lipids. The detergent is detached, the micelles in phospholipid and last combine to form LUVs. The detergent can be removed by dialysis. [2,50,51].

2. Detergent removal of mixed micellar:

Mixed micelles are complexes formed by surfactants (detergents) and lipids (fats) during cleaning processes. Removing these micelles is crucial in various industries, such as:

1. Biotechnology (protein purification)
2. Pharmaceutical (drug development)
3. Food processing (cleaning and sanitation)
4. Textile manufacturing (detergent removal)

II. METHODS FOR REMOVING MIXED MICELLAR DETERGENT

1. Dialysis: Using semi-permeable membranes to separate micelles from solutions.

2. Ultrafiltration: Applying pressure to force micelles through membranes.

3. Gel filtration chromatography: Separating micelles based on size and molecular weight.

4. Centrifugation: Sedimenting micelles using high-speed centrifuges.

5. Precipitation: Adding agents to precipitate micelles out of solution.

6. Adsorption: Using materials like activated carbon or silica to capture micelles.

7. Ion exchange chromatography: Separating micelles based on ionic interactions.

3. Dilution:

Dilution is the process of reducing the concentration of a substance by adding more solvent or diluent.

Types of Dilution:

1. **Simple Dilution:** Mixing a solution with a solvent.
2. **Serial Dilution:** Gradual dilution through multiple steps.
3. **Stock Dilution:** Creating a less concentrated solution from a stock solution.

E. Active loading technique:

Active loading is a technique that uses active components (e.g., amplifiers, transistors) to control and modify the behavior of a system, circuit, or signal.

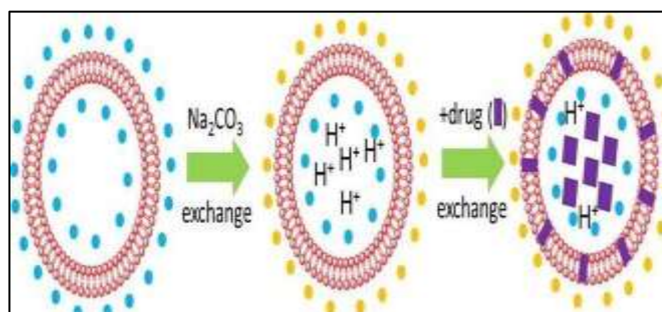

Fig 7: Active loading technique

Components of liposomes:

The most common components are A.Phospholipids.

B. Cholesterol.

Liposomes are composed lipidbilayer size: - 50-1000nm in diameter that serve as targeted delivery vehicle that contain active biological compound. Liposome most often composed of phospholipid and cholesterol[.1, 5].

A. Phospholipids:

It is major structural component of liposome. It has the characteristic of excellent biocompatibility and amphiphilic in nature [4].

It is the major component of the biological membrane.The most common natural phospholipid is Phosphatidylcholine or lecithin which is an amphipathic molecule & is obtained from animal & vegetable.

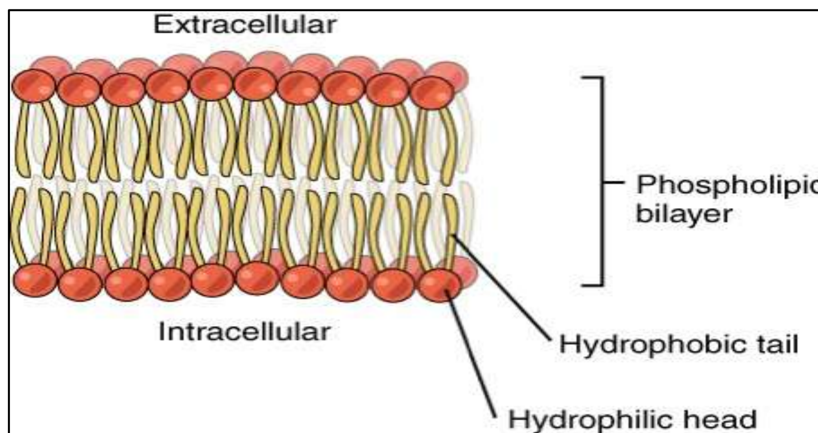

Fig 8: Phospholipid

B. Cholesterol:

Incorporation of sterols in liposome bilayer Can bring about major changes in the Preparation of these membranes. It inserts inte membrane with hydroxyl group oriented towards agreaus Surface area & aliphatic chain aligned Paralled to acyl chains in the centre of bilayer.

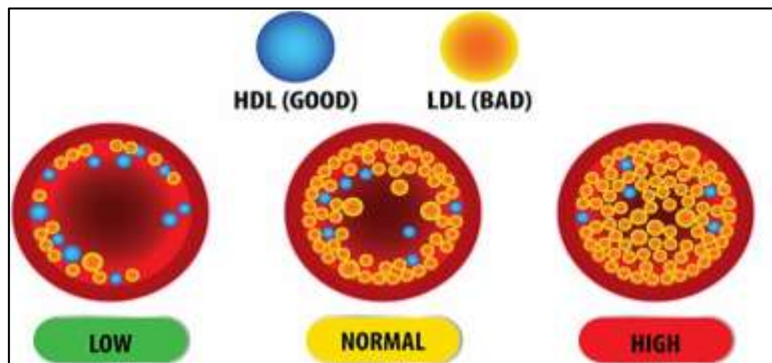

Fig 9: Cholesterol

- **Evaluation of liposomes:**

1. **Physical characterization Parameter:** This parameter evaluates size, shape, surface Features, lamellarily, Phase behaviour f drug release profile.
2. **Chemical characterization Parameter:** This parameter evaluates the purity & potency of Various liposomal constituents.
3. **Biological characterization parameter:** safety, & suitability of the formulations for in vivo use or therapeutic application.

- **Application:**

1. They are used as drug / protein delivery vehicles.

2. They are used in antimicrobial, antifungal & antiviral therapy.
3. They are used in tumour therapy.
4. They are used in gene delivery.
5. They are used in immunology.
6. They are used as radiopharmaceutical &radio-diagnostic carrier
7. They are used in cosmetic & dermatology.
8. liposome for pulmonary deliver.

III. CONCLUSION

Traditional pharmaceutical dosage forms often face limitations that can be addressed by using liposomal drug delivery systems. Nanocarrier systems, such as liposomes, have been developed as promising tools for drug delivery, enabling targeted delivery to specific sites, tissues, or organs. Many anti-cancer drugs are now available in liposomal formulations to enhance therapeutic outcomes. When liposomal formulations are designed effectively, they can improve bioavailability and reduce side effects. Overall, liposomes stand out as an excellent choice among nanocarriers for drug delivery, particularly for site-specific and organ- or receptor-targeted therapies.

IV. REFERENCE

[1] Torchilin V. Multifunctional nanocarriers, Advanced Drug Delivery Reviews, 58(14), 2006, 1532-55

[2] Sawant GS, Sutar KV, Kanekar AS. Liposome: A Novel Drug Delivery System. International Journal of Research and Review. 2021; 8(4): 252-268.

[3] Rajiv Kumar A., Vivek Kumar, Rishi pal, etal. Liposome: A novel approach as a carrier. World Journal of Pharmaceutical Research. 2018; 7(3): 323-342.

[4] Vyas S.P. & Khar R.K. “Targeted & controlled drug delivery : Novel carrier system”. CBS publishers and distributors, 2007.

[5] Abolfazl A., Soodabeh D., Younes H., et al.Liposome: Classification, Preparation, and Application. Nanoscale Research Letters. 2013; 8: 102.

[6] Shashi K., Satinder K., Bharat P., et al. A Complete Review on Liposome. International Research Journal of Pharmacy. 2012; 3(7): 10-16.

[7] Ramkrishna S., Sunit K. S., SoumyaranjanS. Liposome as drug delivery system: A brief review. International Journal of Research in Pharmaceutical Science. 2014;5(4): 309-321.

[8] Mansoori M. A., Agraval S., Jawade S., etal. A Review on Liposome. InternationalJournal of Advance Research in Pharmaceutical and Bio Science. 2012; 2(4):453-464.

[9] Kalepu S., K.T. Sunilkumar, Sudheer Betha,et al. Liposomal drug delivery system- A Comprehensive Review. Dept of Pharmaceutical Technology. 2013; 5(4): 62-75.

[10] Shailesh S., Sandeep K., Neelam S., et al.Liposome: A review. Journal of Pharmacy Research. 2009; 2(7): 1163-1167.

[11] Rumiana S., Wurm, Frederik R., et al.Liposome and Polymersomes: A comparative review towards cell mimicking. Chemical Society Reviews. 2018; 47(23):8572-8610.

[12] Zaquiyya Naaz*, Dr. Kapil Kumar and Deepak Teotia. A Comprehensive Review on Liposomes. International Journal of Modern Pharmaceutical Research. 2020, 4(5), 70-74.

[13] Ugochukwu AE, Nnedimkpa OJ, Rita NO. Preparation and characterization of Tolterodine tartrate proniosomes, Universal Journal of Pharmaceutical Research. 2017; 2(2): 1-3.publishers. 2019; p.53-100.

[14] M. L. Immordino, F. Dosio, and L. Cattle.Stealth liposome: review of the basic science, rational, and clinical applications, existing and potential. International Journal of Nanomedicine. 2006; 1(3): 297-315.

[15] R. M. Abra, R. B. Bankert, F. Chen, et al. The next generation of liposome delivery systems: recent experience with tumor targeted, sterically-stabilized immunoliposomes and active-loading gradients.

Journal of Liposome Research. 2002; 12(1-2): 1-3.

[16] Muhammad K. R., Muhammad A. R., Xuez., et al. Surface functionalization and targeting strategies of liposomes in solid tumor therapy: A review. International Journal of Molecular Sciences. 2018; 19(1):195.

[17] Park JW, Hong K., Carten P., et al.Development of anti-p185HER2 Immunoliposome for cancer therapy. PreNatl Acad Science USA. 1995; 92(5):1327-1331.

[18] Bendas G., Krause A., Bakowsky U., et al.Targetability of novel immunoliposomes prepared by a new antibody conjugation technique. International Journal of Pharm.1999; 181(1): 79-93.

[19] Deamer D. and Bangham A.D. Biochim. Biophys. Acta.; 1976; 443: 629.

[20] Shehata T, Ogawara K, Higaki K, Kimura T: Prolongation of residence time of liposome by surfacemodification with mixture of hydrophilic polymers. Int J Pharm 2008, 359:272–279.

[21] Robert L. Hamilton, Luke S. S. Guo, Jon G., et al. Unilamellar liposomes made with the French pressure cell: a simple preparative and semi quantitative technique. Journal of lipid Research. 1980; 21: 981-992.

[22] Godbole MD, Mathur VB. Selection of phospholipid and method of formulation for optimum entrapment and release of lamivudine from liposome. Journal of Drug Delivery and Therapeutics. 2018; 8(5-s):175-183.

[23] Kaur D, Kumar S. Niosomes: present scenario and future aspects. Journal of Drug Delivery and Therapeutics. 2018; 8(5) 35-43.

[24] Riaz Mohammad. Review Liposomes Preparation Method Pakistan Journal of Pharmaceutical Sciences.1996; 19(1): 65-77.

[25] Dwivedi. C, Yadav. R Tiwari. S.P, Liposome: a Powerful Approach for Vesicular Drug Delivery System, Elixir Pharmacy 81 (2015) 31461-31474.

[26] Daeme T., Hofstede G., Ten Kate MT, et al. Liposomal doxorubicin induced toxicity: dipletion and impairment of phagocytic activity of liver macrophages. Int Cancer. 1995; 61: 721-761.

[27] Alpes H., Allmann K., Plattner H., et al. Formation of large unilamellar vesicles using alkyl maltoside detergents. Biochim Biophy. Acta 1986; 862: 294.

[28] Hadis D., Ali E., Mohammad K., et al. Application of Liposome in Medicine and Drug delivery. An International Journal of Artificial Cells, Nanomedicine, and Biotechnology. 2016; 44(1): 381-391.

[29] Li-Ping T., Hong-Jen L., Yi-You H., et al.Liposome incorporated with cholesterol for drug release triggered by Magnetic field. Journal of Medical and Biological Engineering. 2007; 27(1): 29-34.

[30] Jing L., Xulin W., Ting Z., et al. A Review on phospholipids and their main application in drug delivery system. Asian Journal of Pharmaceutical Science. September 2015;10: 81-98.