INTERNATIONAL JOURNAL IN PHARMACEUTICAL SCIENCES

Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

A Review On Liposomes As Drug Delivery System

Ayush S. Jaiswal*[1], Rekha Gaukande[2], Gajanan Sanap[3]

Department Of Pharmacy, Late Bhagirathi Yashwantrao Pathrikar College Of Pharmacy ,Pathri, Ch. Sambhajinagar, Maharashtra, India.

ARTICLE INFO

Received: 17 Dec 2023
Accepted: 21 Dec 2023
Published: 30 Dec 2023

Keywords:
Lipid, Drug, Phospholipid, Liposomes

DOI:
10.5281/zenodo.10442217

ABSTRACT

Liposomes are composed of phospholipids and lipids, forming spherical or multilayered vesicles with a lipid bilayer structure in aqueous solutions due to self-assembly of diacyl chain phospholipids. The number of bilayers and the size of vesicles influence the amount of drug encapsulation in liposomes, a crucial factor in determining their circulation half-life. This method involves coating a medication and a lipid onto a soluble carrier to create a pro-liposome, which is free-flowing and granular. When hydrated, it forms an isotonic liposomal solution. This pro-liposome approach serves as a motivation for large-scale production of liposomes containing lipophilic medications at a low cost. These systems have unique properties, including increased drug solubility (as seen with amphotericin B), protection of molecules like DNA and RNA, enhanced intracellular uptake (especially for anticancer drugs), acting as a drug depot, and enhancing drug stability. Liposomes have been successfully utilized for the delivery of various drug categories such as anti-viral, anti-cancer, anti-inflammatory, antibiotics, and anti-fungal agents. Additionally, there have been efforts in the development and characterization of liposomal drug delivery systems, for instance, liposomes containing brimonidine tartrate for ocular applications. These advancements signify the transition of liposomes from a clinically established drug delivery system to a versatile nanoparticle platform for theragnostic nanomedicine

INTRODUCTION

Liposomes are minute, spherical synthetic vesicles crafted from safe, natural phospholipids and cholesterol. These artificial structures possess both hydrophobic and hydrophilic characteristics, coupled with biocompatibility, rendering them highly suitable as carriers for drug delivery. The properties of liposomes, including lipid composition, surface charge, size, and manufacturing techniques, exhibit considerable variation. The 'rigidity' or 'fluidity' and charge of the bilayer depend on the specific components incorporated. For instance, unsaturated phosphatidylcholine species from natural sources

***Corresponding Author:** Ayush Jaiswal*
Address: *Department Of Pharmacy, Late Bhagirathi Yashwantrao Pathrikar College Of Pharmacy ,Pathri, Ch. Sambhajinagar, Maharashtra, India.*
Email : ayushaj05@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

like eggs or soybeans result in more permeable and unstable bilayers, whereas saturated phospholipids featuring long acyl chains, such as dipalmitoyl phosphatidylcholine, yield rigid and predominantly impermeable bilayer structures [1-3]. Research has shown that the hydration of phospholipids in aqueous solutions leads to the spontaneous formation of closed structures. These vesicles, characterized by one or more phospholipid bilayer membranes, have the capacity to transport either aqueous or lipid pharmaceuticals depending on the specific type of drug involved. In aqueous conditions, lipids exhibit amphipathic properties—both hydrophobic and hydrophilic. This dual nature influences the entropic packing of their hydrophobic segments into spherical bilayers, a process influenced by the thermodynamic phase properties and self-assembling characteristics of lipids. These layers are referred to as lamellae [4]. Liposomes typically initiate as spherical vesicles with particle sizes ranging from 30 nm to several micrometers. These structures consist of aqueous compartments enclosed by one or more lipid bilayers, where the polar head groups are oriented towards the interior and outer aqueous phases. It is noteworthy that polar lipids have the ability to self-assemble into various colloidal particles beyond the conventional bilayer forms. The specific structure adopted depends on factors such as molecule shape, temperature, and the environmental and preparation conditions [5].

Desirable Characteristics of Liposomes in Drug Delivery [6,7]

Liposomes enable precise drug or gene delivery to target sites, supporting cell growth within porous structures or adjacent tissues. An ideal liposomal drug delivery system should possess the following attributes:

- Exhibits low toxicity and high biocompatibility.
- Elicits no adverse immunological or inflammatory responses.
- Yields non-harmful degradation products.
- Protects active components from mechanical stress.
- Adapts to the intended site of use.
- Maintains stability within a physiological environment.
- Ensures long-term stability.
- Sustains normal bodily functions.
- Prevents unintended dose release.
- Accommodates a high payload.
- Facilitates straightforward processing.
- Adaptable for shaping to desired forms.
- Enables the production of sterile products

Composition of Liposomes:

Liposomes consist of phospholipids and lipids, forming spherical or multilayered vesicles with a lipid bilayer structure when diacyl chain phospholipids self-assemble in aqueous solutions [8]. These phospholipids have both a hydrophobic tail and a hydrophilic head, resulting in an amphiphilic structure [9, 10] (see Figure No. 1). Liposomes can be created using both natural and synthetic phospholipids [11]. The lipid content significantly influences various properties of liposomes, including particle size, stiffness, fluidity, stability, and electrical charge [12, 13]. For example, liposomes made from naturally occurring unsaturated phosphatidylcholine, found in sources like eggs or soybeans, exhibit high permeability and low stability. In contrast, liposomes composed of saturated phospholipids, such as dipalmitoyl phosphatidylcholine, form rigid and nearly impermeable bilayer structures [9].

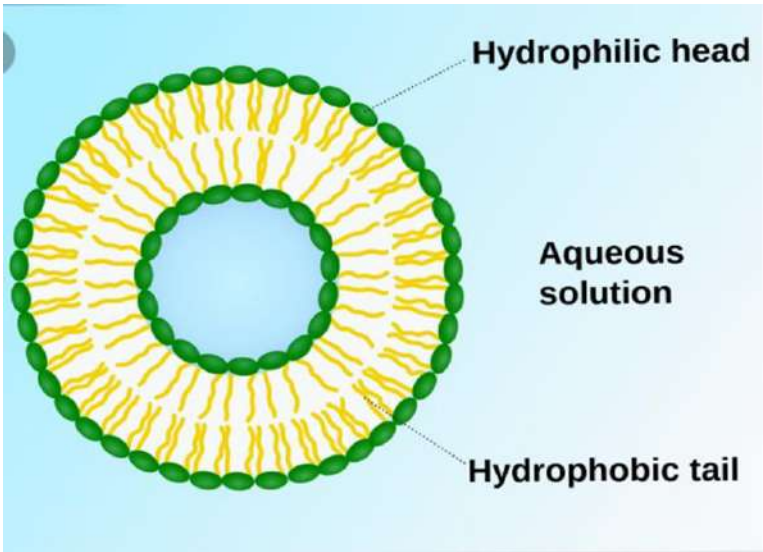

Figure 1. Schematic Representation of Liposomes.

Advantages of Liposomes:

- Effective solubilization capabilities
- Ability to encapsulate both hydrophilic and lipophilic drug compounds
- Demonstrates robust chemical, biological, and colloidal stability
- Reduces macrophage uptake
- Enhances the therapeutic efficacy of encapsulated medications
- Maintains a consistent therapeutic drug concentration in the bloodstream
- Shields drugs from environmental factors
- Facilitates the intracellular delivery of drug molecules

Challenges Associated with Liposomes:

- Phospholipid oxidation
- Phospholipid hydrolysis
- Limited solubility
- Short lifespan
- Reduced stability
- Elevated production expenses
- Leakage and fusion issues
- Rapid uptake by the reticuloendothelial system (RES)
- Potential allergic responses
- Challenges in drug targeting
- Requirement for specialized equipment
- Time-intensive process
- Increased costs attributed to expensive phospholipids [14-18]

Mechanism of Liposomes:

Liposomes are created by hydrating thin lipid films or lipid cakes, causing the liquid crystalline bilayers to swell and become fluid. Large multi-lamellar vesicles are produced when the hydrated lipid sheets self-seal after being agitated (LMV). The self-sealing shape prevents water from interacting with the hydrocarbon core of the bilayer at the edges. The shape and morphology of the resulting vesicles can be altered through the application of mechanical and sonic energy input (see Figure No. 2) [19-21].

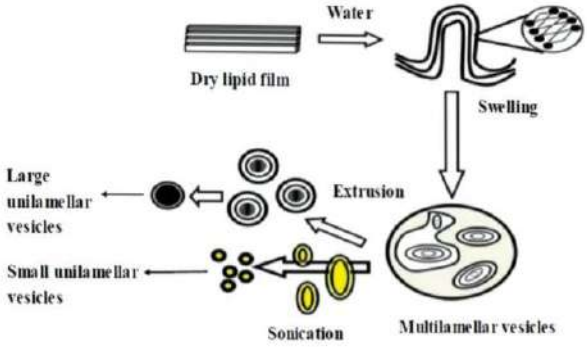

Figure 2: - Mechanism of Liposomes Formation.

Classification of Liposomes:

Liposomes exhibit a range of sizes, from very small (0.025 μm) to relatively large (2.5 μm), and their membranes can be either single or bilayer. The number of bilayers and the vesicle size significantly affect the capacity for drug encapsulation within liposomes, a critical determinant of their circulation half-life. Based on their size and bilayer composition, liposomes can be classified into two main categories:

1. **Multilamellar Vesicles (MLV) :**

These liposomes consist of multiple bilayers, creating an onion-like structure.

2. **Unilamellar Vesicles:**

Unilamellar liposomes, in turn, can be further classified into two subtypes:

- **Small Unilamellar Vesicles (SUV):**

These liposomes are characterized by a single phospholipid bilayer encapsulating the aqueous solution.

- **Large Unilamellar Vesicles (LUV):**

Similar to SUVs but larger in size**.**

This classification system is based on the size and bilayer structure of liposomes, with variations in bilayers and size influencing their drug encapsulation capacity and pharmacokinetics. [22]

Research Methodology

The preparation of liposomes typically involves four fundamental steps:

I. Lipid Drying from Organic Solvent:

This step entails removing the solvent from lipids, leaving a dry lipid film.

II. Lipid Dispersion in Aqueous Media:

The dried lipids are dispersed in an aqueous medium to initiate the formation of liposomes.

III. Purification of Liposomes

The resulting liposomes undergo a purification process to remove impurities.

IV. Examination of Final Products:

The final liposome products are subject to examination and analysis.

There are three distinct methods for liposome preparation:

A. Passive Loading Technique:

This technique includes several sub methods:

A. Mechanical Dispersion:

a. Lipid film hydration method (with or without hand-shaking)
b. Micro emulsification
c. Sonication
d. French pressure cell
e. Membrane extrusion
f. Dried reconstituted vesicles
g. Freeze-thawed liposomes

B. Solvent Dispersion:

a. Ethanol injection method
b. Ether injection method
c. Double emulsion
d. Reverse-Phase evaporation

C. Detergent Removal:

a. Removal of detergent from mixed micelles vesicles via dialysis dilution

B. Active Loading Technique: This technique includes:

i. Proliposome Lyophilization

This research methodology outlines the key steps and techniques used in the preparation of liposomes for various applications [23-25].

1. Technique of passive loading

a. Mechanical dispersion:

- **Lipid Hydration Method:**

The most well-known method for creating Multilamellar Vesicles (MLVs) involves using a flask with a circular bottom. In this method, the dispersion is thoroughly mixed, and the lipophilic mixture is dehydrated to form a thin coating. Then, the membrane is hydrated by adding an aqueous buffer. This hydration process occurs at a temperature just above the maximal melting point of the lipid mixture or slightly above the gel-liquid-crystalline (L-L) transition temperatures of the lipid. Medications are introduced either into an aqueous buffer or an organic solvent containing

lipid solvents, depending on their compatibility. One drawback of this method is the variation in size, low internal volume, and inefficient encapsulation. To overcome lipid's weak encapsulation capacity, lipids are hydrated in the presence of non-miscible organic solvents, such as petroleum ether or diethyl ether. The mixture is then emulsified using sonication. Finally, nitrogen flow is applied over the organic layer to remove it, resulting in the formation of MLVs.[26]

- **Micro emulsification:**

In commercial-scale production, small lipid vesicles are generated using a method involving a device known as a microfluidizer. First, concentrated lipid suspension containing large Multilamellar Vesicles (MLVs) is prepared. This suspension is then pumped into the microfluidizer. High-pressure fluid is forced through a 5-meter panel in this equipment. [27] Through a long microchannel, two fluid streams are made to collide at a straight angle and at very high speeds. By adjusting rotation speeds ranging from 20 to 200, microemulsions suitable for biological purposes can be created using this technique.[28]

- **Sonication:**

Sonication is a process that imparts energy to a lipid mixture while simultaneously decreasing the size of vesicles. The application of ultrasonic waves to irradiate Multilamellar Vesicles (MLV) facilitates this reduction in size. Two common techniques for sonication include: (1) utilizing a bath sonicator and (2) using a probe sonicator. The probe sonicator is often preferred when dealing with suspensions that require a substantial amount of energy in a confined space [29,30,31]. The bath sonicator is employed for processing large quantities of diluted lipids, but it comes with several notable drawbacks. These include the coexistence of Multilamellar Vesicles (MLV) and Small Unilamellar Vesicles (SUV), low internal encapsulation efficacy, potential phospholipid disintegration, removal of particularly large molecules, introduction of metal contaminants from the probe tip, and suboptimal phospholipid breakdown. [32,33]

- **French Pressure Cell Method**

In this extrusion method, Multilamellar Vesicles (MLV) are forced through a small hole under high pressure (20,000) and at a low temperature (4°C). This technique offers several advantages over sonication methods, including its speed, ease of duplication, but it necessitates careful handling of hazardous substances. However, the liposomes produced through this method tend to be larger than those created by sonicated Small Unilamellar Vesicles (SUVs). Some challenges associated with this method include maintaining precise temperature control and the limitation of working volumes, typically up to a maximum of 50 mL. [34]

- **Membrane extrusion**

In this method, a polymer sieve with a web-like structure is employed to treat a heterogeneous liposomal suspension. This sieve creates tortuous-path capillary pores and an interconnected network with a membrane thickness of at least 100 microns. By employing this technique, liposomes in the suspension can be effectively treated, resulting in liposomes with a narrow size distribution and a specified mean size of less than 0.4 microns. [35] Notably, this method can be applied to both Large Unilamellar Vesicles (LUVs) and Multilamellar Vesicles (MLVs).

- **Dried reconstituted vesicles**

In this approach, either lyophilized protein or an aqueous solution containing a medication is introduced into pre-existing liposomes. Subsequently, these liposomes are dehydrated, leading to the incorporation of the protein or medication within the liposomal structure. [36]

- **Freeze-Thaw Method**

During this technique, the vehicles are rapidly frozen and then slowly thawed. Sonication is employed to disperse aggregated chemicals into

Large Unilamellar Vesicles (LUV). Small Unilamellar Vesicles (SUV) with a size of 17 nm are formed through the freezing and thawing processes. It's noteworthy that increasing the ionic strength and phospholipid content of the medium significantly hampers this fusion process. With this method, an entrapment efficiency of 20% to 30% was attained. [37]

b. Solvent dispersion

- **Ethanol Injection Method**

In this method, an excess of saline or another aqueous medium is rapidly mixed with an ethanol lipid solution through a thin needle. [38] Ethanol dissolves in water, and phospholipid molecules are evenly dispersed throughout the liquid. However, this method has drawbacks, including the potential for heterogeneous particle sizes (ranging from 30 to 110 nm). Additionally, it is challenging to completely eliminate all ethanol, which could lead to the creation of an azeotrope with water. [32]

- **Double emulsification**

In this method, therapeutics are first combined in an aqueous phase (w1) to create a primary emulsion. This initial w1/o emulsion is further emulsified in an organic polymer solvent. The first emulsion is then mixed with an emulsifier-containing aqueous solution to form the w1/o/w2 double emulsion (w2)[33]. As the solvent is withdrawn from the aqueous continuous stage, microspheres are left behind and further separated through centrifugation or filtering.

- **Reverse-phase evaporation**

The process involves placing the lipid mixture in an Erlenmeyer bulb, and the solvent is extracted from the mixture by reducing the pressure using a rotary evaporator. As the pressure decreases, the solvent evaporates. Once the nitrogen is removed from the system, the lipids break down in the organic phase [39]. In this phase, reverse phase vesicles are formed. Typically, isopropyl ether and diethyl ether are the solvents of choice. After the redistribution of lipids in this phase, the medication intended for encapsulation is introduced into an aqueous phase. All-aqueous systems undergo sonication until a clear, one-phase dispersion is achieved, and the system is consistently maintained under nitrogen pressure. Subsequently, the mixture is transferred to a rotary evaporator (arotovap), where the organic solvent is removed until a gel forms, and any non-encapsulated material is then eliminated [39,40]. The resulting liposomes from this process are referred to as reverse-phase evaporation vesicles. One of the notable advantages of this method is its exceptionally high encapsulation efficiency [41,42].

c. Detergent removal

In the detergent dialysis method, detergents solubilize lipids at optimal micellar concentrations. As the detergent is gradually removed through dialysis, the micelles become enriched in phospholipids and eventually fuse to form Large Unilamellar Vesicles (LUVs). [43] This method offers the advantages of producing homogeneous liposome populations and high repeatability. However, a significant drawback is the potential retention of detergent residues within the liposomes.[44]

2. Active loading technique

- **Proliposome**

In this method, the medication and lipid are coated onto a soluble carrier, creating a pro-liposome that is free-flowing and granular. When hydrated, it forms an isotonic liposomal solution.[45] This approach has the potential to drive mass production of liposomes containing lipophilic medications at a low cost.[46]

- **Lyophilization**

Cryodesiccation, or freeze drying, is a process that involves removing water from a material under extremely low pressure while the substance is frozen. It is commonly used for drying materials that are sensitive to heat and can be damaged by traditional drying methods. Cryodesiccation is

particularly important for ensuring the long-term stability of liposomes. During the freeze-drying and reconstitution process, trapped materials within liposomes may leak, and this method helps address such issues. [47,48]

LIPOSOME APPLICATIONS

Drug Delivery Using Liposomes

Various liposomal systems have been proposed for delivering drugs to treat opportunistic infections such as tuberculosis, salmonellosis, herpes simplex virus, leishmaniasis, cryptococcoses, and histoplasmosis. Liposomes offer several advantages, including increased drug solubility (especially for drugs like amphotericin B), protection of molecules like DNA and RNA, enhanced intracellular uptake for anti-cancer drugs, acting as a drug depot, and improving the stability of the drug. These properties have made liposomal systems successful for delivering a wide range of drugs, including antiviral, anticancer, anti-inflammatory, antibiotics, and antifungal medications.[49]

Delivering Genes using Liposomes

Indeed, various lipid complexes have been extensively studied for gene delivery due to their advantageous properties. These technologies have enabled the successful delivery of genetic materials such as DNA, RNA, plasmids, and siRNA to target organs. Liposomal systems, with their ability to protect genetic materials and enhance their intracellular delivery, have played a significant role in advancing gene therapy research and applications.[50]

Dermatology and Cosmetic Liposomes

Certainly, liposomes have gained attention in the fields of dermatology and cosmetics due to their similar lipid composition and structure to human skin. Researchers have been exploring the Transepidermal and Transfollicular pathways to target bioactive compounds encapsulated in liposomes. These investigations hold promise for the development of effective delivery systems for skin-related applications in both medical and cosmetic contexts.[51]

Diagnose Using Liposomes

Liposomes produced through this process can incorporate various markers and diagnostic agents, enabling the imaging of different human organs, cells, and tissues using scanning equipment. Variants such as stealth pH-sensitive liposomes, PEGylated liposomes, and paramagnetic thermosensitive liposomes are utilized for diagnostic purposes. The use of liposomes in diagnosis is widespread.[52]

Industrial Uses for Liposomes

Certainly, liposomes have made significant contributions to the food industry. They, along with other carriers like electrophoresis, nanotubes, and inorganic particles, function as vehicles for transporting drugs, genes, and cells. In the context of the food industry, liposomes are employed for delivering food flavors, nutrients, and antimicrobials. This application helps safeguard food products against the growth of harmful bacteria and deterioration, enhancing the quality and safety of various food items.[53]

Future Challenges in Liposomal Delivery [54-56]

Indeed, the commercialization of liposomes faces several challenges, primarily related to their interaction with the reticuloendothelial system, complex manufacturing processes, and the instability of phospholipids. These factors have limited the number of drugs that have successfully reached the commercial manufacturing stage. However, despite these challenges, a few drugs such as Daunoxome, Ambisome, Doxil, and Epaxel have overcome these hurdles and entered the market. Overcoming these challenges is crucial for the broader application and commercial success of liposomal drug delivery systems.

Stability

Liposomes are susceptible to both physical and chemical instabilities. Physical instability can lead to aggregation or fusion of liposomes, altering

their size and structure. Chemical instability primarily arises from the oxidation or hydrolysis of the phospholipids used in their formation, making them unsuitable for long-term storage. Proper storage conditions, such as refrigeration and the use of antioxidants, are essential to mitigate these stability issues and prolong the shelf life of liposomal formulations.

Massive Production

The creation of liposomes involves complex processes such as thin lipid layer formation, sonication, solvent evaporation, and more. These procedures are indeed expensive, difficult to control, and can be challenging to carry out at the laboratory level. Moreover, the production of liposomes often requires specialized equipment and expertise, making it a sophisticated and intricate task in the field of pharmaceutical and research industries.

RESULTS AND DISCUSSION

Liposome drug delivery systems have proven to be highly effective in delivering drugs to the body. They enhance drug absorption, biodistribution, and bioavailability, leading to more efficient therapeutic outcomes. One of the significant advantages of liposomes is their ability to enable targeted drug delivery, minimizing systemic side effects by directing the drug specifically to the intended areas of the body. This targeted approach enhances the efficacy and safety of various pharmaceutical treatments. Liposomes are highly regarded for their safety profile. They have been extensively studied and found to be biocompatible and non-toxic, even at high concentrations. Furthermore, liposomes exhibit low immunogenicity, meaning they do not trigger significant immune responses. This property is particularly advantageous in pharmaceutical applications, as it reduces the risk of allergic reactions or other immune-related complications, ensuring a safer drug delivery system.

Liposomes have proven to be both effective and safe as a drug delivery system for various drugs and compounds. Ongoing research continues to explore their potential in creating new drug formulations and in combination with other drug delivery technologies. The versatility and biocompatibility of liposomes make them a promising avenue in the field of pharmaceuticals.

REFERENCES

1. Sahoo, Sanjeeb K., and Vinod Labhasetwar. "Nanotech approaches to drug delivery and imaging." Drug discovery today 8.24 (2003): 1112-1120.
2. Gabizon, Alberto, et al. "Development of liposomal anthracyclines: from basics to clinical applications." Journal of controlled release 53.1-3 (1998): 275-279.
3. Allen, Theresa M. "Liposomes: opportunities in drug delivery." Drugs 54 (1997): 8-14.
4. Chrai, S. Suggy, R. Murari, and Imran Ahmad. "Liposomes (a review)-Part one: Manufacturing issues." Biopharm-the Applied Technologies of Biopharmaceutical Development 14.11 (2001): 10-+.
5. Wagner, Andreas, and Karola Vorauer-Uhl. "Liposome technology for industrial purposes." Journal of drug delivery 2011 (2011).
6. Iqbal, Md Asif, et al. "Nanostructured lipid carriers system: recent advances in drug delivery." Journal of drug targeting 20.10 (2012): 813-830.
7. Manzoor, Ashley A., et al. "Overcoming limitations in nanoparticle drug delivery: triggered, intravascular release to improve drug penetration into tumors." Cancer research 72.21 (2012): 5566-5575.
8. Wu, Xiaowen, et al. "Investigation on drug entrapment location in liposomes and transfersomes based on molecular dynamics simulation." Journal of molecular modeling 27 (2021): 1-10.

9. Akbarzadeh, Abolfazl, et al. "Liposome: classification, preparation, and applications." Nanoscale research letters 8 (2013): 1-9.
10. Nakhaei, Pooria, et al. "Liposomes: structure, biomedical applications, and stability parameters with emphasis on cholesterol." Frontiers in bioengineering and biotechnology 9 (2021): 705886.
11. Pavelić, Željka, Nataša Škalko-Basnet, and Ivan Jalšenjak. "Characterisation and in vitro evaluation of bioadhesive liposome gels for local therapy of vaginitis." International journal of pharmaceutics 301.1-2 (2005): 140-148.
12. Sahoo, Sanjeeb K., and Vinod Labhasetwar. "Nanotech approaches to drug delivery and imaging." Drug discovery today 8.24 (2003): 1112-1120.
13. Grazia Calvagno, Maria, et al. "Effects of lipid composition and preparation conditions on physical-chemical properties, technological parameters and in vitro biological activity of gemcitabine-loaded liposomes." Current drug delivery 4.1 (2007): 89-101.
14. Amadi, Sepan T., et al. "Structure, dynamics, and substrate-induced conformational changes of the multidrug transporter EmrE in liposomes." Journal of Biological Chemistry 285.34 (2010): 26710-26718.
15. Garg, Tarun, et al. "Scaffold: a novel carrier for cell and drug delivery." Critical Reviews™ in Therapeutic Drug Carrier Systems 29.1 (2012).
16. Hua, Jing, et al. "In vivo imaging of choroidal angiogenesis using fluorescence-labeled cationic liposomes." Molecular vision 18 (2012): 1045.
17. Lu, Xin-Yi, et al. "Application of liposome encapsulation technique to improve anti-carcinoma effect of resveratrol." Drug development and industrial pharmacy 38.3 (2012): 314-322.
18. Modi, Sweta, Tian-Xiang Xiang, and Bradley D. Anderson. "Enhanced active liposomal loading of a poorly soluble ionizable drug using supersaturated drug solutions." Journal of controlled release 162.2 (2012): 330-339.
19. Chahar, Praveen, and Kenneth C. Cummings III. "Liposomal bupivacaine: a review of a new bupivacaine formulation." Journal of pain research (2012): 257-264.
20. Deamer, David W., and Victor Gavino. "Lysophosphatidylcholine acyltransferase: purification and applications in membrane studies." Annals of the New York Academy of Sciences 414.1 (1983): 90-96.
21. Juliano, R. L., and H. N. McCullough. "Controlled delivery of an antitumor drug: localized action of liposome encapsulated cytosine arabinoside administered via the respiratory system." Journal of Pharmacology and Experimental Therapeutics 214.2 (1980): 381-387.
22. Shaheen, Sharif Mohammad, et al. "Liposome as a carrier for advanced drug delivery." Pak J Biol Sci 9.6 (2006): 1181-1191.
23. Fielding, Robert M. "Liposomal drug delivery: advantages and limitations from a clinical pharmacokinetic and therapeutic perspective." Clinical Pharmacokinetics 21.3 (1991): 155-164.
24. Sharma, Amarnath, and Uma S. Sharma. "Liposomes in drug delivery: progress and limitations." International journal of pharmaceutics 154.2 (1997): 123-140.
25. Gregoriadis, Gregory. "Engineering liposomes for drug delivery: progress and problems." Trends in biotechnology 13.12 (1995): 527-537.
26. Deshmukh, Rutuja Ravindra, et al. "A review on: liposomes." World J Pharm Pharm Sci 5.3 (2016): 506-517.

27. Gaurav, R., and S. Tejal. "Liposomal drug delivery system: an overview." IJPBA 2.6 (2011): 1575-1580.
28. Dua, J. S., A. C. Rana, and A. K. Bhandari. "Liposome: methods of preparation and applications." Int J Pharm Stud Res 3.2 (2012): 14-20.
29. Hwang, Tsong-Long, et al. "Cisplatin encapsulated in phosphatidylethanolamine liposomes enhances the in vitro cytotoxicity and in vivo intratumor drug accumulation against melanomas." Journal of dermatological science 46.1 (2007): 11-20.
30. Prabhu, Prabhakara, et al. "Preparation and evaluation of liposomes of brimonidine tartrate as an ocular drug delivery system." Int. J. Res. Pharm. Sci. 1.4 (2010): 502-508.
31. Lopes, Luciana Biagini, et al. "Interaction of sodium diclofenac with freeze-dried soya phosphatidylcholine and unilamellar liposomes." Revista Brasileira de Ciências Farmacêuticas 42 (2006): 497-504.
32. Sipai, A. B. M., et al. "Liposomes: an overview." J Pharm Sci Innov 1.1 (2012): 13-21.
33. Jadhav, M. P., et al. "Formulation and evaluation of long circulating liposomal amphotericin B: a scinti-kinetic study using 99mTc in BALB/C mice." Indian Journal of Pharmaceutical Sciences 73.1 (2011): 57.
34. Chauhan, T., S. Arora, and B. Parashar. "Chandel." Liposome Drug Delivery. IJPCS 1.3 (2012): 1103-1113.
35. Marie, M. K., and Athmar Dhahir Habeeb. "Preparation and evaluation of salbutamol liposomal suspension using chloroform film method." Mustansiriya Medical Journal 11.2 (2012): 39-44.
36. Anwekar, Himanshu, Sitasharan Patel, and A. K. Singhai. "Liposome-as drug carriers." International journal of pharmacy & life sciences 2.7 (2011).
37. Traïkia, Mounir, et al. "Formation of unilamellar vesicles by repetitive freeze-thaw cycles: characterization by electron microscopy and 31 P-nuclear magnetic resonance." European Biophysics Journal 29 (2000): 184-195.
38. Kumar, Ajay, et al. "Development and characterization of liposomal drug delivery system for nimesulide." Int J Pharm Pharm Sci 2.4 (2010): 87-89.
39. Da Costa, Carla Andréia Miranda, and Ângela Maria Moraes. "Encapsulation of 5-fluorouracil in liposomes for topical administration." Maringá 25.1 (2003): 53-61.
40. Niu, Mengmeng, et al. "Liposomes containing glycocholate as potential oral insulin delivery systems: preparation, in vitro characterization, and improved protection against enzymatic degradation." International journal of nanomedicine (2011): 1155-1166.
41. Mirzaee, M., P. Owlia, and M. R. Mehrabi. "Comparison of the bactericidal activity of amikacin in free and liposomal formulation against gram-negative and gram-positive bacteria." Jundishapur Journal of Natural Pharmaceutical Products 4.1 (2009): 1-7.
42. Hathout, Rania M., et al. "Liposomes as an ocular delivery system for acetazolamide: in vitro and in vivo studies." AAPS pharmscitech 8 (2007): E1-E12.
43. Sharma, Amarnath, and Uma S. Sharma. "Liposomes in drug delivery: progress and limitations." International journal of pharmaceutics 154.2 (1997): 123-140.
44. Gregoriadis, Gregory. "Engineering liposomes for drug delivery: progress and problems." Trends in biotechnology 13.12 (1995): 527-537.
45. John, Dingwoke Francis, et al. "Tolnaftate loaded liposomes-design, and in-vitro evaluation." Universal Journal of Pharmaceutical Research 1.2 (2016): 48-53.

46. van Winden, Ewoud C. "Freeze-drying of liposomes: theory and practice." Methods in enzymology 367 (2003): 99-110.
47. Lo, Yu-li, Jui-chen Tsai, and Jung-hua Kuo. "Liposomes and disaccharides as carriers in spray-dried powder formulations of superoxide dismutase." Journal of controlled release 94.2-3 (2004): 259-272.
48. Alving, Carl R. "Liposomes as carriers of antigens and adjuvants." Journal of immunological methods 140.1 (1991): 1-13.
49. Raj, Silpa, et al. "Nanotechnology in cosmetics: Opportunities and challenges." Journal of pharmacy & bioallied sciences 4.3 (2012): 186.
50. Garg, Tarun, and Amit Kumar Goyal. "Iontophoresis: drug delivery system by applying an electrical potential across the skin." Drug delivery letters 2.4 (2012): 270-280.
51. Imran, Muhammad, et al. "Active food packaging evolution: transformation from micro-to nanotechnology." Critical reviews in food science and nutrition 50.9 (2010): 799-821.
52. Al-Jamal, Wafa'T., and Kostas Kostarelos. "Liposomes: from a clinically established drug delivery system to a nanoparticle platform for theranostic nanomedicine." Accounts of chemical research 44.10 (2011): 1094-1104.
53. Cortesi, Rita, et al. "Liposomes-and ethosomes-associated distamycins: a comparative study." Journal of liposome research 20.4 (2010): 277-285.
54. Elizondo, Elisa, et al. "Liposomes and other vesicular systems: structural characteristics, methods of preparation, and use in nanomedicine." Progress in molecular biology and translational science 104 (2011): 1-52.
55. Garg, Tarun, and Amit K Goyal. "Liposomes: targeted and controlled delivery system." Drug delivery letters 4.1 (2014): 62-71.
56. Akbarzadeh, Abolfazl, et al. "Liposome: classification, preparation, and applications." Nanoscale research letters 8 (2013): 1-9.

HOW TO CITE: Ayush S. Jaiswal *, Rekha Gaukande, Gajanan Sanap, A Review on Liposomes As Drug Delivery System, Int. J. in Pharm. Sci., 2023, Vol 1, Issue 12, 926-936. https://doi.org/10.5281/zenodo.10442217