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Review Article

RECENT UPDATE ON LIPOSOME-BASED DRUG DELIVERY SYSTEM

A. CHARUMATHY[1], U. UBAIDULLA[1], PRIYANKA SINHA[2], GRACE RATHNAM[3]

Department of Pharmaceutics, C. L. Baid Metha College of Pharmacy, Tamil Nadu 600097
Email: ubaidulla@clbaidmethacollege.com

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ABSTRACT

In this review article, liposome a novel drug delivery has been discussed, which is one among the various drug delivery system used to target the drug to a particular tissue. As the structural similarity between lipid bilayer and cell membrane, the liposome can easily penetrate and produce an effective delivery of the drug to such that a free drug would not able to penetrate. Some other drug delivery systems include niosomes, microparticles, resealed erythrocytes, pharmacosomes, etc. The term liposome meaning lipid body. Liposomes can also be able to encapsulate in both hydrophilic and hydrophobic materials and are utilized as drug carriers in drug delivery. This technology is very useful for the treatment of certain diseases. In this review, the preparation, evaluation and the applications of the liposomal drug delivery system for targeting various diseases are elaborately presented.

Keywords: Vaccines, Vesicles, Evaluation of liposomes

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INTRODUCTION

A liposome is a vesicle with at least one lipid bilayer that has a spherical shape. Lipid nanoparticles in mRNA vaccines and DNA vaccines, for example, can be employed as a drug delivery vehicle for nutrients and medicinal pharmaceuticals. Liposomes are vesicles made up of one or more phospholipid bilayers that resemble cell membranes in structure. Liposomes have become valuable medication delivery devices due to their ability to encapsulate hydrophilic or lipophilic medicines. A phospholipid bilayer makes up the majority of cellular membranes. This bilayer has a hydrophilic (water-loving) head group and a lipophilic (fat-loving) tail made comprised of a long hydrocarbon chain that repels water. As a result of having both hydrophilic and hydrophobic components, phospholipids are classed as amphipathic compounds. A phospholipid bilayer makes up the majority of cell membranes. This bilayer is made up of a hydrophilic (or "water-loving") head group and a lipophilic (or "fat-loving") tail made up of a long hydrocarbon chain that repels water. Because phospholipids have both hydrophilic and hydrophobic components, they are categorized as amphipathic molecules. When the head group of the phospholipid bilayer cellular membrane is exposed to water, it is drawn to it and creates a surface facing the water. At the same time, water repels the lipophilic tails, resulting in a surface that opposes the water. One layer of polar head groups faces the external cellular environment, whereas another layer of head groups faces the internal cellular environment within a single cell. The bilayer structure of cell membrane is formed by the hydrocarbon tails attached to both layers of polar head groups facing one other [1].

Liposomes can be made up of mixed-chain phospholipids, such as egg phosphatidyl-ethanolamine, or pure surfactant components, such as dioleoylphosphatidyl-ethanolamine (DOP). A core aqueous solution confined by one or more bilayers is prevalent in liposomes. Natural sources of phospholipid bilayers for liposomes are biologically inert, immunogenic, and have reduced inherent toxicity. A liposome consists of an aqueous solution core surrounded by a hydrophobic barrier in the form of a lipid bilayer; hydrophilic solutes immersed in the core are unable to move easily through the bilayer. The bilayer attracts hydrophobic substances. Hydrophilic or hydrophobic compounds can be put into a liposome. The lipid bilayer can fuse with other bilayers, such as the cell membrane, to carry the molecules to a site of action, allowing the liposome contents to be delivered. Liposomes can be delivered beyond the lipid bilayer by soaking them in a solution of DNA or medicines (which would ordinarily be unable to diffuse through the membrane). Liposomes are small spherical artificial vesicles made from cholesterol and non-toxic phospholipids. Liposomes are attractive drug delivery devices due to their size and hydrophobic and hydrophilic properties. Liposome characteristics vary depending on lipid composition, surface charge, size, and manufacturing process. The 'rigidity' or 'fluidity' of the bilayer, as well as its charge, is determined by the bilayer components chosen. Natural unsaturated phosphatidylcholine species (egg or soybean phosphatidylcholine) produce more permeable and less stable bilayers, whereas saturated phospholipids with long acyl chains (for example, dipalmitoylphosphatidylcholine) generate a hard, relatively impermeable bilayer structure. Lipofection is the process of transforming or transfecting DNA into a host cell using liposomes. Liposomes can also be utilised to transport dyes to textiles, herbicides to plants, enzymes and nutritional supplements to foods, and cosmetics to the skin, in addition to gene and medication delivery [1].

Classification of liposomes

Liposomes can range in size from extremely small (0.025 m) to very massive (2.5 m) vesicles. Liposomes may also contain one or more bilayer membranes. The size of the vesicle is an important factor in regulating the half-life of liposomes in circulation, and both the size and number of bilayers influence the quantity of drug encapsulation in the liposomes.

Liposomes can also be divided into two groups based on their size and number of bilayers:

- Multilamellar vesicles (MLV)

Vesicles in multilamellar liposomes have an onion structure. Traditionally, a multilamellar structure of concentric phospholipid spheres separated by layers of water is formed by unilamellar vesicles forming on the inside of each other with lower sizes.

- Unilamellar vesicles (ULV)

The vesicle has a single phospholipid bilayer sphere enclosing the aqueous solution in unilamellar liposomes [2, 3].

Advantages of liposomal drug delivery

The pharmacokinetic and pharmacodynamic features of medications encapsulated in a liposomal or lipid drug delivery system are

improved to the point where they can be used on a regular basis. Provides tumour tissues with selective passive targeting. Liposomes improved the drug's effectiveness and therapeutic index. Encapsulation in a liposome enhanced stability. For systemic and non-systemic applications, liposomes are non-toxic, flexible, biocompatible, totally biodegradable, and non-immunogenic. It provides sustained release. It direct the interaction of the drug with cell [2].

Disadvantages of liposomes as a drug delivery system

Low solubility. Sometimes phospholipid undergoes oxidation and hydrolysis-like reaction. Short half-life. Leakage and fusion of encapsulated drug/molecules. Production cost is high. Quick uptake by cells of the reticuloendothelial system. Allergic reactions may occur to liposomal constituents. Problem to targeting to various tissues due to their large size [2].

Preparation of liposomes

General method of preparation:

All the methods of preparing the liposomes involve four basic stages:

1. Drying down lipids from organic solvent.

2. Dispersing the lipid in aqueous media.

3. Purifying the resultant liposome.

4. Analyzing the final product.

Liposomes can be made in a variety of ways. Dimensions, composition (various phospholipids and cholesterol concentrations), charge (due to the charges of the contributing phospholipids), and structure can all change (multilamellar liposomes consisting of several concentric bilayers, separated by aqueous compartments or unilamellar liposomes, consisting of only one phospholipid bilayer surrounding one aqueous compartment). Because of this, high-yield DNA integration is possible, making these liposomes more suitable for gene and antisense treatment. pH-sensitive liposomes may be better for delivering encapsulated compounds into the cytoplasm of target cells because they destabilise and become fusion-active at mildly acidic pH. Because of their positive charge, the latter liposomes allow for high-yield DNA inclusion, while their pH-dependent behaviour promotes fusion with endosomes, allowing for easier DNA release into the cytoplasm [3-5].

Methods of liposome preparation

The following methods are used for the preparation of liposome:

1. Passive loading techniques:

Passive loading techniques include three different methods:

a. Mechanical dispersion method:

The following are types of mechanical dispersion methods:

I. Sonication.

- ✓ Probe sonication.
- ✓ Bath sonication.

II. French pressure cell: extrusion.

III. Freeze-thawed liposomes.

IV. Lipid film hydration.

V. Micro-emulsification.

VI. Membrane extrusion.

VII. Dried reconstituted vesicles.

b. Solvent dispersion method.

- ➢ Ether injection (solvent vaporization).
- ➢ Ethanol injection.
- ➢ Reverse phase evaporation method.

c. Detergent removal method (removal of non-encapsulated material).

- ➢ Dialysis.
- ➢ Detergent (cholate, alkyl glycoside, Triton X-100) removal of mixed micelles (absorption).
- ➢ Gel-permeation chromatography.

2. Active loading technique.

- ➢ Solvent-Assisted Active Loading Technology (SALT) [6].

Passive loading techniques

The drug is encapsulated in these passive loading techniques by integrating an aqueous phase of a water-soluble (hydrophillic) drug or an organic phase of a lipid-soluble drug at a specified time during the liposome production. The passive loading approach, which is better suitable for lipid-soluble medicines with high similarity to the lipid membrane, can achieve a high drug encapsulation efficiency. This lesson begins with a lipid solution in an organic solvent and then progresses to a lipid dispersion in water. The components are typically mixed by co-dissolving the lipids in an organic solvent and then film deposition under vacuum to separate the organic solvent. The solid lipid mixture is hydrated with the use of an aqueous buffer after the leftover solvent is removed. Liposomes are formed when lipids spontaneously expand and hydrate. The most recent delivery method used by medical researchers is liposomal encapsulation technology (LET) [7].

Mechanical dispersion method

Variety of components are typically integrated in these methods by co-dissolving the lipids in an organic solvent and then separating the organic solvent by film deposition under a vacuum. The solid lipid mixture is hydrated with an aqueous phase after all of the solvents has evaporated. Liposomes are formed when lipids spontaneously expand and hydrate.

Sonication

The method of sonication is likely the most often employed for SUV preparation. Under a passive atmosphere, MLVs are sonicated with a bath-type sonicator or a probe sonicator. The main drawbacks of this approach are its limited internal volume/encapsulation efficacy, the possibility of phospholipids and substances to be encapsulated degrading, the removal of big molecules, metal contamination from the probe tip, and the existence of MLV alongside SUV. There are two types of sonication.

Probe sonication

A sonicator's tip is immersed directly in the liposome dispersion. In this approach, the energy input into lipid dispersion is extremely high. Because the coupling of energy at the tip causes localized heat, the vessel must be immersed in a water/ice bath. More than 5% of the lipids can be de-esterified during sonication for up to 1 hour. Titanium will also peel off and pollute the solution while using the probe sonicator.

Bath sonication

In a bath sonicator, the liposome dispersion is placed in a cylinder. In comparison to sonication by dispersal directly utilising the tip, controlling the temperature of the lipid dispersion is usually easier using this method. The substance being sonicated can be kept safe in a sterile vessel separate from the probe units or in an inert atmosphere [8].

French pressure cell

MLV is extruded through a small opening in a French pressure cell. The proteins do not appear to be as arrogant during the French press vesicle method as they do during sonication, which is an essential aspect. The SUVs formed by sonication or detergent removal tend to recall imprisoned solutes substantially longer than the French press vesicle. The method entails handling unstable materials with care. Liposomes formed as a result are larger than

sonicated SUVs. The method's disadvantages are that the high temperature is difficult to achieve and that the working quantities are minimal (about 50 ml as the maximum) [8].

Freeze-thawed liposome

SUVs are quickly frozen and then slowly thawed. Sonication disperses aggregated materials to LUV in a short amount of time. UV is created as a result of the fusion of SUV during the freezing and thawing processes. By increasing the phospholipid concentration and the medium's ionic strength, this type of synthesis is strongly inhibited. The encapsulation efficacies from 20% to 30% were obtained [8].

Lipid film hydration method

The most frequent and simple method for preparing MLV is to dissolve the phospholipids in organic solvents such as dichloromethane, chloroform, ethanol, and a chloroform-methanol mixture (2:1 v/v; 9:1 v/v; 3:1 v/v). When a solvent is evaporated under vacuum at 45-60 °C, a thin and homogenous lipid film is produced. In order to totally eliminate the leftover solvent, nitrogen gas is used. In the hydration process, a solution of distilled water, phosphate buffer, phosphate saline buffer at pH 7.4, and the normal saline buffer is utilised. At a temperature of 60-70 °C, the hydration process took anywhere from 1 to 2 h. The liposomal suspension is left overnight at 4 °C to achieve complete lipid hydration. All types of lipid mixes can be hydrated using the lipid-film hydration method [8].

Micro-emulsification method

To make small vesicles from concentrated lipid suspension, a device called a microfluidizer is used. Lipids can be added to the fluidizer in the form of a suspension of big MLVs. The suspension is pumped through the 5 mm screen at a very high pressure using this apparatus. Then a lengthy micro channel is forced, causing two streams of fluid to clash at a straight angle and at a very high velocity. The collected fluid can be circulated through the pump and interaction chamber until spherical vesicles are formed [8].

Membrane extrusion

MLVs are reduced in this procedure by passing them through a membrane filter with predetermined bore size. Membrane filters come in two varieties. There are two types of nucleation tracks: tortuous bath and nucleation track. For sterile filtering, the former is utilised. Between the criss-cross strands in the matrix, a random bath forms. When trying to transmit liposomes through a membrane with a diameter bigger than the channel diameter, they are impacted. The nucleation track is made out of a thin continuous polycarbonate sheet. Because they are made up of straight-sided pore holes that are bored from one side to the other, they will provide less barrier to liposome transit. Both LUVs and MLVs can be processed with this method [8].

Dried reconstituted vesicles

In the DRV technique, a dispersion of empty SUVs is freeze-dried before being dispersed with an aqueous solution containing the substance to be entrapped. This causes solid lipids to hydrate in a finely reduced-sized form. However, rather of drying the lipids from an organic solution, the freeze-drying procedure is used to freeze and lyophilize a performed SUVs dispersion. This results in an ordered membrane structure as opposed to a random matrix structure that can rehydrate, fuse, and reseal to create vesicles with high encapsulation efficiency when water is added. The water-soluble hydrophillic materials to be entrapped are added to the empty SUV dispersion and dried simultaneously, ensuring that the material for inclusion is present in the dried precursor lipid prior to the final step of adding watery medium [9].

Drug loading in liposomes

Drug loading can be performed passively (i.e., the drug is encapsulated during liposome creation) or actively (i.e., the drug is encapsulated during liposome formation) (i.e., after liposome formation). Hydrophobic medicines, such as amphotericin B taxol or annamycin, can be directly incorporated into liposomes during vesicle formation, and drug-lipid interactions control the degree of uptake and retention. 100% drug solubility in the liposome membrane is frequently achieved, however, this is contingent on the drug's solubility in the membrane. The ability of liposomes to capture aqueous buffer containing a dissolved drug during vesicle formation is required for the passive encapsulation of water-soluble medicines. The trapped volume circumscribed in the liposomes and medication solubility restrict the trapping efficacy (usually 30 percent). Water-soluble medicines with protonizable amine functionalities, on the other hand, can be actively entrapped using pH gradients, with trapping efficacy approaching 100 percent [9].

Freeze-protectant for liposomes (lyophilization)

Before being delivered to the target place, natural extracts are frequently damaged because to oxidation and other chemical processes. Freeze-drying has long been a regular method in the manufacturing of pharmaceuticals. The vast majority of these items are made from simple aqueous solutions that have been lyophilized. Although traditionally, water is the only solvent that must be removed from a solution using the freeze-drying method, many pharmaceutical products are still created utilising a process that involves freeze-drying from organic co-solvent systems. Freeze-drying (lyophilization) is the process of removing water from frozen items at extremely low pressures. The procedure is typically used to dry thermo-labile items that would be destroyed by heat-drying. With regard to liposomal stability, the technology offers much too much potential as a way to overcome long-term stability issues. Studies have shown that entrapped materials may leak throughout the freeze-drying process and that when liposomes are freeze-dried in the presence of significant levels of trehalose (a carbohydrate often found at high concentrations in organisms), they retain up to 100% of their original components. Trehalose is an effective cryoprotectant (freeze-protectant) for liposomes, as evidenced by this study. Pharmaceutical equipment companies sell freeze-driers in a variety of sizes, from small laboratory models to huge industrial systems [9].

Evaluation parameters

1. Particle size and particle size distribution

2. Zeta potential

3. Percentage yield

4. Entrapment efficiency and

5. Drug loading

6. Thermal analysis

7. *In vitro* drug release study

8. *In vivo* drug release study

9. Compatability study (FTIR)

10. Stability

Particle size and particle size distribution

Dynamic light scattering (DLS) was used to determine the mean particle size and polydispersity index (PDI) for each liposomal formulation using a Zetasizer Nano ZS analyzer ZEN 3600. The particle size distribution of the liposomal vesicles population was determined using the PDI. The analysis was carried out at 25 °C using clear folded capillary cells with a detection angle of 173° backscatter and three observations per data point [10].

Zeta potential (Z)

The zeta potential of liposomal vesicles was determined using a Zetasizer Nano ZS analyzer as electrophoretic light scattering. As a measure of dispersion stability, the zeta potential was calculated. Clear folded capillary cells were used for the analysis, which was done at 25 °C. The average of three measurements is used to get each reported result [11].

Percentage yield

Percent yield refers to the percent ratio of actual yield to the theoretical yield. In chemistry, yield is a measure of the quantity of moles of a product formed in relation to the reactant consumed,

obtained in a chemical reaction, usually expressed as a percentage. The amount of product actually made compared with the maximum calculated yield is called the percentage yield [11].

Entrapment efficiency (EE %)

The EE% was determined to evaluate the effect of changing liposomal composition and preparation technique on the properties of liposomes.

Sample preparation

Liposomal dispersions were centrifuged at 14,000g using Amicon Ultra 0.5 ml Centrifugal Filters with a 10 K molecular weight cut-off (Millipore Co.) to remove the non-encapsulated drug. A volume of 400 µl of the supernatant were mixed with 400 µl of ethanol and 800 µl of PBS. Dilution factor was considered for later calculations. Concentration in the supernatant was determined by interpolation in the average calibration curve [12].

Drug loading

Drug loading is the process of incorporation of the drug into a polymer matrix or capsule. Drug release is the reverse process by which the drug molecules are liberated from the solid phase and become available for absorption and pharmacological action [12].

Thermal analysis

The differential scanning calorimetry (DSC) of formulations was carried between −5 °C and 100 °C under an inert atmosphere, with a heating rate of 5 °C/min. Analysis was performed using the differential scanner calorimeter. DSC is a thermal analysis apparatus measuring how physical properties of a sample change, along with temperature against time. This device is a thermal analysis instrument that determines the temperature and heat flow associated with material transitions as a function of time and temperature [12].

***In vitro* drug release studies**

Drug release from liposomes was studied using a dialysis method. Dialysis bags were soaked before use in distilled water at room temperature for 12 h to remove the preservative, followed by rinsing thoroughly in distilled water. *In vitro* release of liposomes was conducted by dialysis in a dialysis sac with 150 ml of phosphate-buffered saline (PBS; pH 5.6) containing 7% (V/V) propylene glycol and 25% (V/V) methanol at 37 °C. Three sacs were prepared as control, conventional liposomes, and PEG-coated liposomes. Liposomal concentrate (equivalent to 2 mg) dispersed in 1 ml of bicarbonate buffer (pH 9) was placed in a dialysis bag. Control bags were prepared and tested along with the liposomal dispersions. Each control bag contained 2 mg drug. Two ends of the dialysis sac were tightly bound with threads. The sac was hung inside a conical flask with the help of a glass rod so that the portion of the dialysis sac with the formulation dipped into the buffer solution. The flask was kept on a magnetic stirrer and stirring was maintained at 100 rpm at 37 °C with thermostatic control. Samples were collected every half an hour over a period of five hours and assayed spectrophotometrically for drug content [12].

***In vivo* experiments**

The animal experimental protocols were in accordance with the guidelines for conducting animal experiments stipulated by our Institution's committee Animal Ethics Committee and in compliance with the Federation of European Laboratory Animal Science Association and the European Community Council Directive (European Community Council Directive, 1986) [13-15].

Compatability study (FTIR)

Fourier-transform infrared spectroscopy (FTIR) is a technique used to obtain an infrared spectrum of absorption or emission of a solid, liquid or gas. An FTIR spectrometer simultaneously collects high-resolution spectral data over a wide spectral range. Fourier Transform Infrared Spectroscopy (FTIR) is a type of infrared spectroscopy that simultaneously collects high-spectral-resolution data over a wide range and is the preferred method of IR spectroscopy for laboratories. The definition of FTIR comes from the fact that a mathematical process known as Fourier Transform is used to convert raw data into a readable spectrum. FTIR spectroscopy is used to quickly and definitively identify compounds such as compounded plastics, blends, fillers, paints, rubbers, coatings, resins, and adhesives. It can be applied across all phases of the product lifecycle including design, manufacture, and failure analysis [16-19].

Stability

Stability testing is the statistical analysis of how long a pharmaceutical product can be stored without any change in its original chemical composition. Pharmaceutical products when stored for long durations tend to undergo changes and release by-products.

Stability testing provides evidence on how the quality of a drug substance or product varies over a given time period and under the influence of environmental factors including temperature, humidity and light. The studies are designed to include testing of attributes susceptible to change during storage and are likely to influence quality, safety and efficacy [20, 21].

Applications of liposomal drug delivery

Liposome used in the treatment of cancer

Various anticancer drugs in liposome formulations were found to be less hazardous than the free medication. Drugs that stop dividing cells from growing by intercalating into their DNA, killing mostly dividing cells. These cells are in cancers, but also in the gastrointestinal mucosa, hair, and blood cells and consequently this family of medications is particularly hazardous. Its dosage is limited by its cumulative cardiac toxicity, in addition to the above-mentioned acute toxicities. The level of toxicity was reduced by nearly half. Because liposome encapsulation decreases medication distribution, cardiotoxicity involves both short-term and long-term effects. On the other hand, the efficacy was in many cases compromised due to the reduced bioavailability of the drug, especially if the tumour was not phagocytic, or located in the organs of the mononuclear phagocytic system. In some cases, such as systemic lymphoma, the effect of liposome encapsulation showed enhanced efficacy due to the sustained release effect, i.e. longer presence of therapeutic concentrations in the circulation while in several other cases the sequestration of the drug into tissues of the mononuclear phagocytic system actually reduced its efficacy. Applications in man showed in general reduced toxicity, and better tolerability of administration with not too encouraging efficacy [22-26].

Liposomes for brain-targeted drug delivery

Developing a liposome that can pass through the blood-brain barrier (BBB) and reach human glioma. The sulfatide and a monoclonal antibody as the sensory device in order to increase the target ability of the liposome. Egg PC liposomes coated with CHP also were significantly accumulated in brain tumors of the rat. CHP-coated liposomes labeled with [^{14}C]-DPPC were injected by the carotid route into Fisher-344 rats implanted with 9L-gliosarcoma. Each tissue (tumor, ipsilateral and contralateral brain, liver, spleen, kidney and blood) was collected 30 min after injection of the liposome. Tissue distribution of the liposome with or without CHP-coating was investigated. Distribution of the CHP-coated liposome increased by 4.5 times in the tumor and by 2.1 times in the ipsilateral brain and decreased by 4 times in the spleen compared with that of the control liposome. The survival of 9L-glioma-implanted rats was investigated by the use of liposomes in which an antitumor drug (CDDP, c/s-platinum diamino dichloride) was loaded [27-29].

Liposomes in infections and parasitic diseases

Liposomes are digested by phagocytic cells in the body after intravenous administration, they are ideal vehicles for the targeting of drug molecules into these macrophages. The best-known examples of this 'Trojan horse-like' mechanism are several parasitic diseases that normally reside in the cells of the mononuclear

phagocytic system. Liposomes accumulate in the very same cell population which is infected and therefore offer an ideal drug delivery vehicle. These formulations mostly use the ionophore amphotericin B and are relocated from very thriving and prolific areas of liposome formulations in antifungal therapy. These toxicities are normally correlated with the size of the drug molecule or its complex, and liposome encapsulation obviously prevents the accumulation of drug in these organs and drastically reduces toxicity. Similar approaches can be implemented in antibacterial and antiviral therapy. The preparation of antibiotic-loaded liposomes at the reasonably high drug to lipid ratios may not be easy because of the interactions of these molecules with bilayers and high densities of their aqueous solutions, which often force liposomes to float as a creamy layer on the top of the tube. Several other routes, such as topical application or pulmonary (by inhalation) administration are also being considered. The automatic targeting of liposomes to macrophages can be exploited in several other ways, including by macrophage activation and injection. Some usual toxins persuade tough macrophage response which results in macrophage activation. This can be duplicated and improved by the use of liposomes because small molecules with immunogenic properties (haptens) cannot induce an immune response without being attached to a larger particle. Normally, this is done by administration of alum or killed bacteria, and liposomes evidently offer an elegant alternative. Indeed, liposomes are being used in animal vaccination already since 1988, while human vaccinations against malaria are now in clinical trials [30, 31].

Therapeutic applications of liposomes

Liposomes provide superior therapeutic efficacy and safety in comparison to existing formulations. Some of the major therapeutic applications of liposomes in drug delivery include:

Site-avoidance delivery

The cytotoxicity of anti-cancer drugs to normal tissues is attributed to their narrow therapeutic index (TI). Under such circumstances, the TI can be improved by minimizing the delivery of drug to normal cells by encapsulating in liposomes. For eg doxorubicin has a severe side effect of cardiac toxicity, but when formulated as liposomes, the toxicity was reduced without any change in the therapeutic activity.

Site-specific targeting

Delivery of a larger fraction of the drug to the desired (diseased) site, reducing the drug's exposure to normal tissues can be achieved by site-specific targeting. On systemic administration, long-circulating immunoliposomes are able to recognize and bind to target cells with greater specificity. For e. g. in patients with recurrent osteosarcoma, there was an enhanced tumoricidal activity of monocytes, when muramyl peptide derivatives were formulated as liposomes and administered systemically.

Intracellular drug delivery

Increased delivery of potential drugs to the cytosol (where drug receptors are present) can be accomplished by using LDDS. N-(phosphonacetyl)-L-aspartate (PALA) is normally poorly taken up into cells. Such drugs when encapsulated within liposomes, showed greater activity against ovarian tumor cell lines in comparison to free drug.

Sustained release drug delivery

To achieve the optimum therapeutic efficacy, which requires a prolonged plasma concentration at therapeutic levels, liposomes provide sustained release of target drugs. Drugs like cytosine Arabinoside can be encapsulated in liposomes for sustained release and optimized drug release rate.

Intraperitoneal administration

Tumors that develop in the intra-peritoneal cavity can be treated by administering the drug to an intra-peritoneal cavity. But the rapid clearance of the drugs from the intra-peritoneal cavity results in minimized amount of drug at the diseased site. Liposomal encapsulated drugs have a lower clearance rate, when compared to free drug and can provide a maximum fraction of drug in a prolonged manner to the target site.

Immunological adjuvants in vaccines

Liposomes can be used for enhancing the immune response by encapsulating the adjuvants. Depending on the lipophilicity of antigens, the liposome can accommodate antigens in the aqueous cavity or incorporate them within the bilayers. To enhance the immune response of diphtheria toxoid, liposomes were first used as immunological adjuvants [29].

CONCLUSION

Liposomes have been realized as extremely useful carrier systems for targeted drug delivery. The flexibility of their behavior can be exploited for drug delivery through any route of administration and for any drug material irrespective of their solubility properties. The use of liposomes in the delivery of drugs and genes are promising and is sure to undergo further developments in future.

Liposome has been identified as a useful carrier system for targeted drug delivery. The flexibility of the liposome activity can be used for the drug delivery through any route of administration and for the drug with irregular solubility properties. The liposome can be prepared by various methods and some include the thin-film hydration method, solvent injection method, freeze-thaw method, sonication method, and several other methods has been discussed. The evaluation parameters such as entrapment efficiency, particle size, zeta potential and other parameters has been observed. The recent applications of the liposome-based drug delivery system has been studied and they are listed accordingly.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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