Review Article

Liposomes as a Drug Delivery – An Overview

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ABSTRACT

A lipid entity consisting of one or more phospholipid bilayers is referred to as a liposome. In many scientific disciplines, including mathematics and theoretical physics, chemistry, colloid science, biology, biochemistry, and so on, liposomes are helpful as reagents, tools, and reproduction. Since liposomes' structure is comparable to that of lipid bilayers and cell membranes, they are one of the many drug delivery techniques used to target the medicine to a certain tissue. Both hydrophilic and lipophilic medications can be found within liposomes, which are spherical vesicles composed of phospholipid bilayers. Liposomal formulation has been used in the past to carry out extensive study on a range of drugs and genes for controlled release. The possible use of liposomes in the therapy of cancer has also been investigated. Because liposomes are nontoxic, biodegradable, immunogenic, and biocompatible, they have a number of benefits.

Keywords: Liposomes, drug delivery, drug targeting.

INTRODUCTION

When specific lipids are hydrated in aqueous conditions, they naturally form liposomes, which are microparticulate or colloidal carriers [(1)]. It is a tiny, spherical structure composed of one or more lipid bilayers, usually synthetic or natural phospholipids, encasing a tiny amount of the aqueous phase. Lipid vesicles or just vesicles are other names for it. Because of their size, amphiphilic nature, and biocompatibility, liposomes have been extensively used throughout the years as model biomembranes and as delivery systems for a variety of bioactive substances. Many bioactive substances, such as genetic materials, proteins, DNA, peptides, enzymes, antibacterial and anticancer drugs, vaccines, and vaccine delivery systems, have been studied for liposome-based delivery systems[5]. The use of liposomes in the treatment of human illnesses has increased as a result of accumulating in vivo evidence, which is especially clear in areas like cancer chemotherapy, antimicrobial therapy, vaccines, diagnostic imaging, and the treatment of ophthalmic disorders. Numerous clinical trials conducted on patients with cancer or infections suggest that specific formulations of liposomal medications may have a positive clinical impact.

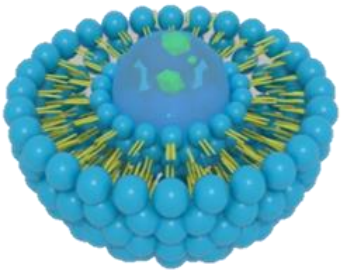

Figure 1: Structure of a Liposome.

Classification of liposomes:

Liposomes are classified into five types based on their composition and intracellular delivery mechanism: conventional, pH-sensitive, cationic, immuno, and long-circulating liposomes. (Table 1)

Techniques for preparing liposomes:

Methods of preparation:

Every liposome preparation technique consists of four primary steps:

1. Lipids dissolved in organic solvent.

2. Elimination of organic solvent.

3. Purification and separation of liposomes.

4. Evaluating the completed product.

Drug loading technique and liposome formation:[5]

These methods are employed in the production of liposomes:

1. Techniques for passive loading.

2. Techniques for active loading.

Three different kinds of passive loading strategies exist:

A. Mechanical dispersion technique.

B. Solvent dispersion technique.

C. Detergent removal methods (removal of non-encapsulated material).

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A. Mechanical dispersion method:

Among the mechanical dispersion techniques are the following:

1.1. Sonication.

1.2. The French pressure cell method.

1.3. Liposomes made using the freeze-drying technique.

1.4. Lipid film hydration by hand shaking and non-hand shaking.

1.5. Micro-emulsification.

1.6. Membrane extrusion.

B. Solvent dispersion technique:

1.1. Ether injection (solvent vaporisation).

1.2. Ethanol injection.

3.3. Reverse phase evaporation technique.

C. Detergent removal methods (removal of non-encapsulated material):

1.1. Dialysis.

1.2. Detergent (cholate, alkyl glycoside, Triton X-100) removal of mixed micelles (absorption).

1.3. Gel-permeation chromatography.

1.4. Dilution.

Table 1: Classification of liposomes based on the composition and mode of drug delivery:

Type	Fabrication	Comments
1.Conventional liposomes	Negatively or neutrally charged phospholipids and cholesterol.	If contents do not disperse from the endosome, they are eventually transported to lysosomes through coated-pit endocytosis. This process is beneficial for RES targeting and allows for rapid and full absorption by RES. Additionally, the contents have a brief half-life of circulation and their pharmacokinetics depend on dosage.
2.Ph-sensitive liposomes	Dioleoyl phosphatidyl ethanolamine and other phospholipids Phosphatidylethanolamine combined with oleic acid or cholesterol hemi-succinate.	It can do coated-pit endocytosis and, at low pH, fuse with endosomes or cell membranes to release their contents in the cytoplasm. It can be used for both macromolecule and weak-based intracellular administration and has the same biodistribution and PK as CL.
3.Cationic liposomes	Cationic lipids; DDAB, DOGS, DOSPA, DOTMA, DMRIE, and DORIE with DOPE	likely to merge with endosome membranes; appropriate for delivering negatively charged macromolecules (DNA, RNA, oligos); simple to formulate; physically unstable; transfection actively declines with time; hazardous at high concentrations; mostly limited to local delivery.
4.Long-circulating liposomes	High Tc neutral lipids, cholesterol, and 5–10% PEG-DSPE, GMI, or HPI; ≤ 0.1µm in size.	Long circulation half-life (about 40 hours), dose-independent PK up to 10µmol/mouse lipid dosage, hydrophilic surface coating, poor opsonization and hence low rate of absorption by RES.
5.Immuno-liposomes	CL or LCL with a recognition sequence or antibody attached.	The release of material extracellularly near the target tissue, receptor-mediated endocytosis, cell-specific binding (targeting), and the potential for drug diffusion across the plasma membrane to produce an effect.

Table 2: Based on the quantity and size of lamellae:

Type	Usual Size	Characteristics
1.Multilamellar vesicles (MLV)	>0.1 µm	Greater encapsulation of lipophilic medicines (1-4 1/mole lipid). mechanically stable after extended storage; quickly removed by RES; effective in focusing on RES cells: easiest to prepare: by hydrating lipids in the presence of an organic solvent.
2.Large unilamellar vesicles (LUV)	- >0.1 µm	Single-phase evaporation (REV), ether injection, detergent dialysis, or "active loading methods" can produce single bilayers with high macromolecule capture and high aqueous volume to lipid ratios (7 l/mole lipid); these bilayers are suitable for hydrophilic medications. It is swiftly removed by RES.
3.Small unilamellar vesicles (SUV)	- ≤0.1 µm	Single bilayer: synthesized by solvent injection or active loading techniques, or by sonicating or gas extruding MLV or LUV to a smaller size; homogenous in size, thermodynamically unstable, prone to aggregation and fusion at low or no charge; restricted macromolecule capture; low aqueous volume to lipid ratio (0.2-1.5 1/mole lipid); extended circulation half-life.

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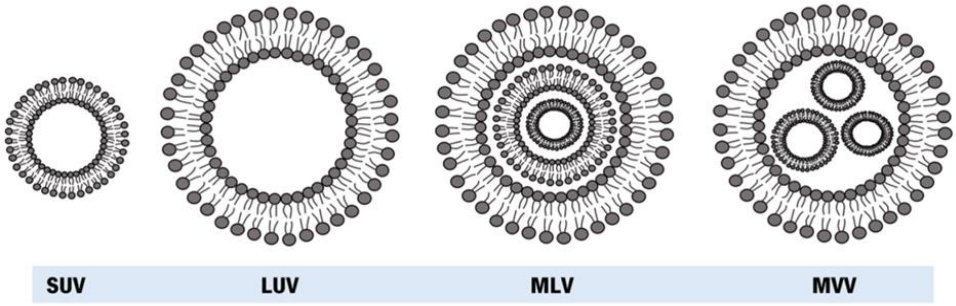

Figure 2: The classification of liposomal cells is based on lamellarity and size, with SUV (Small Unilamellar Vesicles), LUV (Large Unilamellar Vesicles), MLV (Multilamellar Vesicles), and MVV (Multi Vesicular Vesicles).[10]

Table 3: Merits and Demerits:

Merits	Demerits
1) Liposomes enhanced the drug's therapeutic index and efficacy (actinomycin-D)	1) Insufficient solubility
2) Liposome encapsulation increased stability.	2) Small half-life
3) For both systemic and non-systemic delivery, liposomes are non-toxic, flexible, biocompatible, completely biodegradable, and non-immunogenic.	3) Phospholipids can occasionally experience reactions akin to hydrolysis and oxidation.
4) Liposomes reduce the encapsulating agent's toxicity (amphotericin B, Taxol)	4) Drug/molecule encapsulation leakage and fusion
5) Liposomes have a site avoidance effect that helps lessen the amount of hazardous drug exposure to delicate tissues.	5) High cost of production
6) Flexibility in combining with ligands appropriate to a certain location to accomplish active targeting	6) Reduced stable numbers

The mechanical dispersion method:

Sonication:[1,2,5,15]

SUV preparation involves sonicating MLVs using probe or bath sonicators in a passive atmosphere, but has limitations like limited volume/encapsulation efficacy, potential degradation, removal of large molecules, metal pollution, and MLV presence.[10]

a) Probe sonication: Liposome dispersion is achieved by submerging the vessel in an ice or water bath, requiring a high energy input. Over 5% of lipids can be deesterified for up to an hour, but titanium can contaminate the fluid.

b) Bath sonication: A bath sonicator is used to spread liposome dispersion across a cylinder, allowing easier temperature control and storage in an inert atmosphere, sterile tank, or separate probe units.

The French pressure cell method:[1,2,5,15]

In this procedure, multilamellar vesicles (MLVs) are forced through a narrow aperture at high pressure to form small unilamellar vesicles (SUVs). The French pressure cell made of stainless steel can withstand pressures between 20,000 and 40,000 psi. A pressure chamber, an output pressure relief valve, a piston, a bottom seal, a valve closure, and other parts are housed in the cell's body. The cell is turned upside down once the piston has been inserted a brief distance into the body. The bottom seal is driven down, and the pressure chamber closes. The cell is placed in a hydraulic press, which creates pressure while holding it upright. The valve is opened to let the fluid exit the pressure chamber drop by drop at a flow rate of 0.5 to 1 millilitres per minute once enough pressure has been generated. Operational temperature, pressure, and lipid composition all affect the size of the liposome that is generated.

Liposomes made using the freeze-drying technique:[1,2,5,6,8,10]

Here, organic solvents—specifically, tert-butanol—are used since their freezing point is higher than the freeze dryer's operating temperature. Tert-butanol is a safe organic solvent that doesn't damage the lyophilizer's rubber seals. This method starts with dissolving cholesterol and phospholipids in tert-butanol, then freeze-drying the mixture to produce a lipid cake. Hydrophilic drugs that dissolve in water are dissolved in aqueous solutions. After that, it is combined with the dry lipid cake. To create liposome multilamellar vesicles (MLVs) and unilamellar vesicles (ULVs), the mixture is hydrated and agitated.

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Preparing liposomes by handshake method:[1,2,5,6]

This method is widely used to produce liposome multilamellar vesicles (MLVS). Different charged particles, cholesterols, and phospholipids are added to a solvent mixture of methanol:chloroform (2:1). After that, the mixture is poured into a round-bottom flask and placed on top of a vacuum-pressured, 60 rpm rotating rotary evaporator. The organic solvent evaporates and forms a thin layer at 30°C or above. After the film forms, the rotation will continue for a further half hour. Subsequently, the evaporator is filled with nitrogen gas and disconnected from the vacuum source. Up until the pressure outside the flask is equal to the pressure inside the evaporator, pressure will increase. After that, the flask is placed in a freeze dryer to extract the organic solvent. A porous cake will be the end product. After adding 5 mL of the saline phosphate buffer solution containing the material to be encapsulated, nitrogen gas is poured into the flask. Reattaching the flask to the evaporator, it starts spinning at 60 revolutions per minute. Until the lipid that has stuck to the flask walls is gone, the flask is spun. Following the achievement of a consistent, particle-free, milky white suspension, it is let to stand for two hours at room temperature.

Preparing liposomes by non-shaking vesicles:[1,2,5,8]

Lipid-soluble medications, phospholipids, and cholesterols are dissolved in a 1:1:2 chloroform-methanol mixture. The mixture is injected with nitrogen. A thin layer of lipids accumulates and covers the whole bottom of the flask. It is drying gradually. Water-saturated nitrogen is sprayed over it. The lipid layer is then passed over by adding 10–20 ml of a 0.2 M sucrose solution in distilled water that has been previously degassed at the flask's edge. After adding nitrogen and sealing it, the flask is kept at 37°C for two hours. It's crucial to avoid stirring the flask when performing this procedure. The suspension is formed and then centrifuged at 12000 g for 10 minutes at room temperature. Multilamellar vesicles form a layer on the mixture's surface.

Pro-liposome technique:

This method involves filling a 100 mL round bottle flask with sorbitol or sodium chloride powder. The flask is connected to an evaporator, which is slowly rotated to guarantee that the powder and solvent are well combined. The flask is filled with 5 ml of lipid solution (60 mg of lipid in 1 ml of chloroform) via the intake tube. The flask is then lowered into a water bath that is heated to between 50 and 55°C in order to create a 100 kPs vacuum. The temperature decreases when the powder absorbs all of the solvent. Add another 5 millilitres of the lipid solution with caution. The hoover is released when the temperature hits 30°C. After a complete drying process, the flask is connected to a lyophilizer and left to overnight at room temperature. When administering the powder, vials are filled with it and 10 mL of distilled water is added. The mixture is then mixed for 30 seconds on a whirl mixer at temperatures higher than the lipid transition point.

Technique for dispersing a solvent:

Ether injection technique:

In this process, diethyl ether is used to dissolve the lipid solution. This mixture is slowly injected into an aqueous solution of the substance to be encapsulated at a temperature between 55 and 65°C, vaporising the organic solvent. It is found that the produced unilamellar vesicles have a diameter of 50–200 nm. The primary benefit of this method is the exceedingly gentle handling of fragile lipids with a very little chance of oxidative damage.[1,3,10]

Ethanol injection (solvent vaporisation):

This method entails dissolving lipids in ethanol and quickly infusing the resulting mixture into an excess buffer solution that contains the material that has to be entrapped. Ethanol is diluted in water quickly and thoroughly to produce a homogeneous distribution of SUVS in the medium. The primary benefits include its ease of usage and speed, as well as the fact that it doesn't break down delicate lipids. [(10)]

Reverse phase evaporation technique:

This method uses an aqueous solution as well as a lipid inorganic solvent, and sonication is employed to produce a water-in-oil emulsion. The organic solvent in the emulsion is extracted by spinning under low pressure in a rotary evaporator. At this point, the lipid only partially forms a monolayer of phospholipid bilayer around the microdroplets in the aqueous phase. Next, the emulsion is shaken hard with a vortex mixer to invert it. The water droplets collide as a result, forming a continuous phase. Lipid components form another monolayer, or the second half of the lipid bilayer, when they come into contact with neighbouring vesicles, which results in the formation of LUVs.[1,2,5,6,8,10]

Detergent removal methods (removal of non-encapsulated material):

Dialysis:

Lipids are solubilized through dialysis using detergents at critical micelle concentrations (CMC), forming LUVs. Lipo-Prep is commercial equipment for detergent removal, and equilibrium dialysis involves submerging bags in detergent-free buffer.[8,10,15]

Dilution:

A diluted micellar solution containing detergent and phospholipids undergoes a spontaneous conversion from polydispersed micelles to vesicles. Detergent adsorbers, like XAD-2 beads or Bio-beads SM2, are used to remove the detergent, potentially eliminating exhausted detergents.[8,10,15]

LIPOSOMAL EVALUATION

The physical, chemical, and biological characteristics of liposomes made using various processes or techniques need to be investigated since they affect the behaviour of liposomes in vivo.

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Physical Properties

The particles' size:

Using the techniques described below, liposome particle size and particle size distribution can be determined.[8]

Laser light scattering:

Although it's a quick and easy method, it requires expensive equipment. In this method, a tiny suspension transmits light at a wavelength that is sufficient. The size of liposomes determines how much light they disperse. Therefore, measuring the oscillations in scattered light can help estimate the liposome particle size. One uses the Stokes-Einstein equation to calculate it:

$$D = KT/6\pi\eta\underline{R_h}$$

D = Translational diffusion coefficient

K = Boltzmann constant

T = Absolute temperature

H = Viscosity of solvent

$\underline{R_h}$ = Mean hydrodynamics radius

Transference Electron Microscopy (TEM):

To measure each liposome's particle size, electron microscopy is employed. This method's primary drawback is that it takes a lot of time and requires a strong hoover. It might change the liposomes' structural makeup. Large vesicles are frequently studied using freeze fracture electron microscopy.

Surface charge:

The passive, negative, or natural charge on the liposome surface is caused by the composition of the head groups. The kinetics and range of distribution in vivo, as well as the interaction with target cells, are governed by liposome surface charge. The technique for measuring surface charge is based on MLV free-flow electrophoresis. It uses a cellulose ester plate submerged in a sodium borate buffer with a pH of 8.8. Lipid samples in the approximate amount of moles are added to the plate, which is then electrophoresed for 30 minutes at 4'C. The surface charge of liposomes causes them to split in half.[8]

Percent drug encapsulated:

The quantity of medications included in liposomes makes it easier to predict how each medicine would behave in a biological system. First, separate the free drug friction from the encapsulated drug component in order to compute the percentage of drug encapsulation. The encapsulated drug fraction is then extracted from the liposomes and dissolved in an aqueous solution using the proper detergents.[8]

The following methods were employed to extract the free drug from the sample:

Mini column centrifugation technique:

A syringe without a plunger is used to build the mini-column for each sample. A Whatman GF/B filter pad is used to seal the open end of the syringe once it has been filled with hydrated gel (Sephadex G).

After the syringe barrel is inserted, the centrifuge tube is spun for three minutes at 2000 rpm. This facilitates the collection tube's ability to remove any extra saline solution from the hydrated gel. Next, the liposome sample is dropped onto the gel bed's uppermost section. To close any vacuum spaces between the liposomes in the centrifuge tube, the column is rotated once more for three minutes at 2000 rpm. Next, the extracted material is examined.

Protamine aggregate method:

This method is applied to evaluate just negatively charged liposomes, irrespective of their makeup. A liposome suspension (20 mg/ml) in normal saline and 0.1 mL protamine sulphate is contained in a conical centrifuge tube. It is then blended and left for three minutes. After that, 30 mL of saline are added to the tube, and it is spun for 20 minutes at 2000 rpm. Using standard methods, the liquid supernatant is decanted and checked for the presence of free drug. The liposomal pellets that remain are disrupted by resuspension in 0.6 mi triton X-100. After reaching the proper volume, the drug entrapment volume is tested in accordance with accepted practices.

Phase behaviour:

At this point, temperature liposomes go through a reversible phase shift. Both the steady permeability and the drug entrapment zone are shown by the TC. The technique employed is differential scanning calorimetry, or DSC.

Drug release rate:

An in vitro assay technique is used to measure the liposome's drug release rate, assisting in the assessment of the drug's pharmacokinetics and bioavailability. This method makes use of a suitable buffer in a USP disintegration apparatus. After inserting the liposomes into the apparatus, the sample is taken out at regular intervals and the disintegration apparatus is replenished with the same volume of heated buffer. The sample is tested to determine the substance. An in vitro assay technique is used to measure the liposome's drug release rate, assisting in the assessment of the drug's pharmacokinetics and bioavailability. This method makes use of a suitable buffer in a USP disintegration apparatus. After inserting the liposomes into the apparatus, the sample is taken out at regular intervals and the disintegration apparatus is replenished with the same volume of heated buffer. The sample is tested to determine the substance.

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Chemical Properties

Determination of Phospholipid:

Two assays are commonly used to directly measure the phospholipid content of liposomes: the Bartlett assay and the steward assay.

Bartlett assay:[8]

Due to its great sensitivity, this method of determining phospholipids should yield inaccurate results even in the face of very low phosphate levels. Consequently, double-water and borosilicate glass tubes are used.

1. The sample's lipid bilayer's phosphorous is first hydrolyzed to produce inorganic phosphate.

2. Ammonium molybdate is then added to the inorganic phosphate to create phosphomolybdic acid (PMP).

3. Subsequently, amino naphthyl sulphonic acid is used to the sample in order to quantitatively reduce PMP to a blue chemical.

4. Spectrophotometric techniques can be used to measure the intensity of the blue colour produced; the value is then plotted on a standard curve to calculate the phospholipid concentration.

b) Steward assay:[8]

Although this assay overcomes the limitations of the Bartlett assay, it is not suitable for use with a combination of unidentified phospholipids.

1. A 0.1 M solution of ammonium ferro-thiocyanate reagent is combined with a known concentration of phospholipids in chloroform to create the standard curve.

2. The same reagent is likewise applied to the sample, and the optical density is determined simultaneously at 485 nm.

3. Plotting the sample's absorbance against the standard curve allows one to calculate the phospholipid concentration.

Cholesterol Analysis:[8]

Qualitative analysis:

Carried out with a capillary column filled with fused silica.

Quantitative analysis:

After applying a reagent containing sulfuric acid, ethyl acetate, and ferric perchlorate to the sample, the absorbance of the purple complex that results is measured at 610 nm. A quantitative measurement of cholesterol can be made between 0-8 µg.

Biological Characterization:[8]

a) Sterility:

Sterile test is carried out in either anaerobic or aerobic cultures.

b) Pyrogenicity:

For pyrogenicity determination, the Limulus amebocyte lysate (LAL) test is utilised.

c) Animal toxicity:

During the toxicity test, animals' pathology, histology, and survival rate are all observed.

Applications of liposomes:

Liposomes with modified surface characteristics:[5,7]

Novel approaches, such the targeted delivery of cancer and other diseased cells, rely on liposomes with modified surface characteristics that are removed from circulation by the immune system. Their inability to leave the bloodstream, or extravasate,

is a significant obstacle in the majority of other applications, although it is beneficial in some topical applications where liposomes are used as localised drug reservoirs or in pulmonary applications where liposomal aerosols are used.

Liposomes in the treatment of cancer: [5,7,10]

The main finding of early studies was that medications encapsulated in liposomes were less toxic; yet, in most cases, the therapeutic molecules were not bioavailable, which led to a significant reduction in both toxicity and efficacy. It was also shown that primary and secondary liver tumours were similar in this regard. It has been shown that a variety of anticancer liposome formulations are less hazardous than the drug in its free form [(17)]. Due to the fact that liposome encapsulation reduces drug molecule distribution to certain organs, there can be both acute and longterm toxicity. Although there was limited potential of utility, human applications frequently showed reduced toxicity and enhanced administration tolerability. Clinical trials are underway for a number of formulations, with differing degrees of success[18].

Liposomes as antimicrobial agents: [5,7,10,16]

Liposomes have been used to administer drugs for leishmaniasis and malaria, among other infectious disorders. Intravenous delivery of liposomes containing neutral glycolipids with a glucose or galactose terminal decreased the growth of erythrocytic Plasmodium bergei forms in mice that had previously received sporozoite injections.

The aminoglycosides gentamicin and amikacin have significantly improved in their ability to cure intracellular mycobacterial infections when encapsulated in liposomes.

Liposomes in the management of arthritis: [5,7]

Liposomes carrying cortisol palmitate remain stable in rheumatoid synovial fluid at 37°C. It was discovered that the length of inflammation was inversely correlated with the amount of liposomal steroids present in the tissue. Several chemicals' absorption and dispersion were investigated.

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Rat hip muscles were injected with liposome-entrapped prednisolone together with free steroid. It has been demonstrated that liposomal prednisolone is more firmly held by the injected tissue. It has been found that liposome-encapsulated aurothiomalate reduces mice's arthritis produced by collagen.

Applications of stealth liposomes in humans: [5,7,19]

Human clinical trials confirmed the encouraging results of doxorubicin-loaded stealth liposomes in preclinical research. Up to a week after injection, the medication was still present in circulating liposomes; drug metabolites were found near the sites of the tumours, suggesting that the liposomes had released the drug. Compared to the control group, which was given free treatment, the medication absorption in tumours was four to ten times higher. When compared to free drug delivery, the medication concentration in lesions was ten times higher, which contributed to the extraordinary efficacy. In summary, it seems that anticancer drugs loaded within stealth liposomes will greatly enhance the therapy of various tumours. Additionally, we think they'll work well for antiviral treatments, infections, and inflammations.

Applications of stealth liposomes in medicine:[5,7,19]

Larger liposomes (0.2 mm) are required for the former application, while the latter is connected to the ability of small vesicles to leave the circulation. Moreover, stabilised liposomes can be employed as a localised drug depot or as a long-circulating micro-reservoir for prolonged drug release. First, cytosine arabinose has been shown to have improved therapeutic efficacy in the treatment of cancer[20]. On the other hand, the polypeptide vasopressin's action has been shown to demonstrate the subcutaneous/ intramuscular sustained release mechanism[21]. Unlike the free edition, which was only available for a few days, it lasted up to a month.

Peptide present in regular liposomes, and one week for the drug. The introduction of genetically engineered polypeptides and proteins, which are hindered by the body's rapid blood absorption, breakdown, and/or deactivation, should be noted as making these ideas even more crucial. The modified biodistribution of covert liposomes and their localization at sites with permeable blood capillaries, like its usage in tumours, inflammations, and infections may have many more benefits. Stealth liposomes in intact vasculature are distributed to the skin from the liver, spleen, and bone marrow. This means that antivirals and dermatological medications cannot be delivered to certain regions.

Liposomes as an oxygen-carrying fluid:[7]

From the initial idea of encasing haemoglobin in an inert shell, liposome-encapsulated haemoglobin (LEH) has developed into a fluid that has been shown to carry oxygen, can endure in the bloodstream for acceptable amounts of time, and can be produced on a massive scale. The formula for egg lecithin and distearoyl-phosphatidylcholine-based lipid combinations replaced synthetic, non-lipid components to form the outer shell. Studies conducted in vivo have demonstrated that LEH can carry enough oxygen to support life and has a circulation half-life of 16–20 hours. Since most biological membranes, including red blood cells, express carbohydrates, adding a carbohydrate component to the LEH increases its biocompatibility. Ganglioside incorporation into the liposomal bilayer has been demonstrated to lengthen circulation times.

Liposomes for the treatment of respiratory disorders:[7]

Aerosolized liposomes are useful for treating asthmatic bronchial constriction and can be inhaled. Treatment with intravenous injections of liposomal prostaglandin E1 (Lip-PGE1) decreased lung leak and neutrophil buildup in lung lavage in rat models. Rats' acute lung injury was lessened when liposomal alpha-tochopherol was administered intratracheally.

Targeted liposomes:

By attaching amino acid fragments that target certain receptor sites, including those on proteins or antibodies, liposomes can be utilised to target specific cells. In nude mice, targeted sterically stabilised liposomes work better against human breast cancer xerographs than non-targeted liposomes. Because of their increased penetration, capacity to transport macromolecules across the cell membrane, and protection of related agents, liposomes are currently being explored as delivery vehicles for genes and oligonucleotides.[22]

FUTURE PROSPECTS OF LIPOSOMES:

We can anticipate a number of novel anticancer drugs, cytokines, antifungals, antibiotics, and antivirals in conventional and long-circulating liposomes, given the potential medical applications of liposomes. By distributing prostaglandins, their utility may also extend to the cardiovascular field. The distribution of ribozymes and antisense oligonucleotides is particularly promising.

Novel modes of action could involve the following: using liposomes as a long-circulating platform to bind and inactivate different blood-borne toxins; creating localised liposomal depots for different drugs (such as a lipid foam that DepoTech (San Diego, CA, USA) is developing with programmable release of morphine, cytosine, arabinose, or other drugs); saturating different receptors with liposome-bound ligands; and targeting macrophages in lymph nodes and skin. There may be uses for inhaling liposomal aerosols that contain drugs. Artificial blood based on liposomes and allergens encapsulated in liposomes or their extracts could be further contenders for development as allergy therapy desensitizers in the future.

A lot of experts anticipate advancements in two other areas: targeted delivery and immunotherapy. Developing formulas for the treatment of tropical antiparasitic illnesses, such leishmaniasis and malaria, would be far easier, there doesn't seem to be enough business interest to produce such formulations, despite the fact that

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hundreds of millions of people are afflicted. Since lipids are inherently anticancer agents, Eibl and colleagues developed synthetic amphiphilic lipids that can form liposomes or micelles as a cancer treatment. These lipid mutations were also particularly successful in treating tropical parasite infections.

Diagnostic assays are one more really potential application for liposomes. For example, a number of blood-clotting assays rely on the colloidal instability of distinct cell types or lipid extracts from different sources, such as rabbit brains. As liposomal kits for testing prothrombin times have demonstrated, it is only reasonable to assume that synthetic liposomes with similar, but optimised and always same, lipid composition will lead to more repeatable results (Innovin and Actin by DADE International, Miami, FL, USA).

Membrane-binding proteins called annexins were identified using a very sensitive and accurate technique based on turbidimetry-monitored liposome aggregation. The capacity of liposomes to enhance reactions or to agglutinate is the basis for a number of other diagnostic assays. One antibody, for example, usually carries one labelling group in an ELISA; however, if the ligand is attached to a liposome, it may carry thousands of markers that correspondingly increase the signal. Another illustration is the ability to identify viruses through receptor-ligand interactions that are followed by colour transitions. As an example, a system made up of polyacetylene bilayers functionalized by a sialic-acid analogue—a site-specific ligand for the influenza virus haemagglutinin—experiences a visible colour shift (blue to red) upon binding.

Simpler yet more widely recognised are liposome uses in the food and cosmetics sectors, as well as in the oral delivery of nutrients [e.g. liposomal vitamins, minerals, and herb extracts for oral administration (Biozone Labs, Pittsburgh, CA, USA). These claim that liposomes can solubilize hydrophobic molecules in natural lipid–water systems, act as slow-release capsules, and possibly enhance penetration through mucosal membranes. These claims are hard to prove, but it's safe to say that lecithin has other positive effects, like lowering blood cholesterol levels and reducing stomach irritation. The explosive growth of liposomal cosmetic products—which was sparked in 1987 by Dior's Capture and L'Oreal's Niosomes and Nactosomes (skin-rejuvenating creams) — seems to have stopped because consumers are now drawn to other cutting-edge technologies and agents. In spite of this, there are hundreds of items on the market that bring in well over a billion dollars in sales each year 1, including skin creams, sunscreens, toothpastes, skin-whitening lotions, and perfumes.

In parallel, liposome uses will expand into a number of other sectors, including the coating, diagnostic, and food and nutrition industries. Cheap liposomes will soon mature, despite the fact that the earliest liposome uses were high tech formulations for the pharmaceutical business (and slightly less expensive ones in cosmetics) manufactured from pricey raw materials. Low-purity lipid extracts that cost between US$ 1 and 50 kg[21] and innovative processing techniques (like injecting propylene-glycol directly during mixing and churning or directly hydrating during the process) will make it possible to prepare large amounts of extremely affordable liposomes, which have uses in the food and nutrition sectors as well as in cleansing formulations. Large-scale uses for these liposomes could include cleaning up reactor spills or metal detoxification; it's even feasible that the metal ions could be bonded to the liposomes using chelators affixed to the surface, making the separation process easier. The liposomes can precipitate and the decontaminated water can be safely decanted following metal binding. There have been discussions on a number of alternative possibilities, such as cleaning up oil spills on land and in water.

CONCLUSIONS

Currently, there is rise in the creation of "pharmaceutical" liposomes due to their encouraging pre-clinical outcomes. Liposomes ensure a higher therapeutic index and minimal toxicity, providing greater control over the in vivo fate of drug candidates. Liposomes that circulate for a long time have been designed to be difficult to identify. Liposomes are employed as drug delivery vehicles for specific dosages. Research on the viability of liposomes for protein and peptide delivery will not stop. Numerous liposomal augmentations have already been identified, approved, and highly successful in the pharmaceutical industry. Prospects for liposomal structure-based drug delivery in the future depend on a thorough understanding of the pathophysiology and biochemistry of the ailment, novel developments in their formulation and characterisation, and precise risk assessment and monitoring of liposome exposure. Future commercialization of more advanced and highly stabilized liposomal formulations has even more promise, with a wide range of applications, particularly in the treatment of cancer.

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