

AN UPDATED REVIEW ON: LIPOSOMES AS DRUG CARRIERS

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ABSTRACT

Liposomes are sphere-shaped vesicles consisting of one or more phospholipids bilayers. Liposome is suitable and superior carrier and has capacity to encapsulate hydrophilic and lipophilic drugs and protect them from degradation. Liposomes have acquired a number of although the past 30 years as pharmaceutical carriers of great potential. Reason behind this attention that liposome drug delivery system it provides sustained and targeted drug delivery system in medication and cosmetic also hence it minimize number of dose. Now these days liposome frequently used in very sever diseases like cancer, aids, tumor, vaccination etc. The objective of the article is to discussed basic characteristics, method of preparation and marketed formulations of liposomes are discussed. The success of liposomes as drug carriers has been discussed as uses of liposomes in pharmaceutical and cosmetic field

Keywords: Liposome, phospholipids, lamellar, encapsulation, Drug Carriers.

INTRODUCTION

A liposome is a very small or tiny bubble (vesicle), made out of the same material as a cell membrane. Liposomes can be filled with drugs, and used to convey vaccines, drugs, enzymes, or other substances to target cells or organs and drugs for cancer and other diseases. Membranes are usually made of phospholipids, which are molecules that have a head group and a tail group. The head is attracted to water, and the tail, which is made of a long hydrocarbon chain, is repelled by water. A liposome is an artificially-prepared spherical vesicle composed of a lipid bilayer or liposome defined as self-forming structure which consisting of one or more concentric lipid bilayers separated by aqueous buffer compartments ¹.

Composition of liposome

The major Structural Components of Liposomes are:-

1. Phospholipids- Phospholipids are the main constituent of these structures. Phosphatidylcholine (PC), also called lecithin, is biocompatible phospholipids that is found in plants and animals and used widely in liposomal preparation. Moreover, there are other molecules widely used in combination with phospholipids, such as cholesterol ².
2. Cholesterol - Cholesterol molecules in the membrane increases separation between choline head groups which reduces the normal hydrogen bonding and electrostatic interaction.

The unique property of liposomes to entrap drugs both in an aqueous and a lipid phase make such delivery systems attractive for hydrophilic and hydrophobic drugs. Because of advancements in the methods of preparing and formulating liposomes, high-entrapment efficiencies are possible for incorporating drugs into liposomes and creating a very good pharmaceutical impact. Furthermore, such encapsulation reduces drug toxicity while retaining or improving the therapeutic efficacy.

Structure

Liposomes are spherical structures usually found between 15nm and 1000nm in diameter. Many targeting ligands can be attached to their surface to direct them to the appropriate sites within cells; these include, but are not limited to, membrane proteins. It is important to differentiate liposomes from micelles; even though both of these macromolecular complexes are spherical and consist of lipids, a micelle is normally formed from ionized fatty acids, whereas a liposome consists of phospholipids. Furthermore, micelles consist of only a single layer of lipids, with their non-polar carbon tails clustered together at the center (therefore not allowing any water soluble compounds on the interior), whereas liposomes are constructed from a bilayer that does allow charged molecules on the inside. This is due to the presence of the hydrophilic glycerol-phosphate-alcohol heads of phospholipids, which define both the outer and inner surfaces of liposomes.

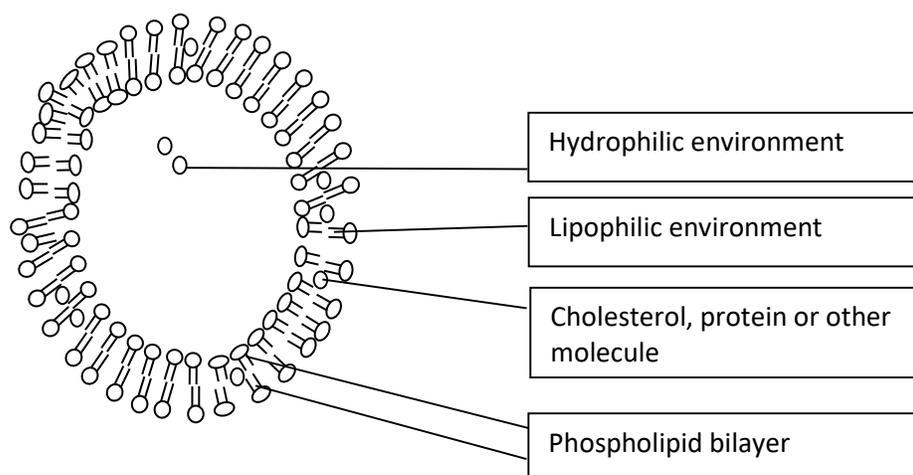


Figure 1: Schematic diagram of liposomes

The liposome can be used as a vehicle for administration of nutrients and pharmaceutical drugs. The sphere like shell encapsulated a liquid interior which may contain many drug such as peptides and protein, hormones, enzymes, antibiotic, anti-fungal and anticancer agents. Liposome properties and

behavior differ considerably with lipid composition, surface charge, size, and the method of preparation. Liposomes have the distinct advantages of being both nontoxic and biodegradable because they are composed of naturally occurring substance.

Classification of liposomes

Classification of liposomes is based on number of lamellae, composition, method of preparation and its size. The liposome size can vary from very small to large (0.025- 2.5 μm). According to their size and number of bilayers, liposomes can also be classified into one of two categories multilamellar vesicles (MLV) and unilamellar vesicles. Unilamellar vesicles can also be classified into two categories - large unilamellar vesicles (LUV) and small unilamellar vesicles (SUV). In unilamellar liposome's, the vesicle has a single phospholipids bilayer sphere enclosing the aqueous solution. In multilamellar liposome's, vesicles have an onion structure. Classically, several unilamellar vesicles will form on the inside of the other with smaller size, making a multilamellar structure of concentric phospholipids spheres separated by layers of water.

Table1: Classification of liposome

No.	Type	Size	No. of lamellae
1.	Multilamellar large vesicles(MLV)	(>0.5 μm)	Multiple
2.	Oligolamellar vesicles(OLV)	0.1-1 μm	Few layer/ multiple
3.	Unilamellar vesicles(UV)	All sizes	Single
4.	Small unilamellar vesicles(SUV)	20-100 nm	Single
5.	Medium sized unilamellar vesicles(MUV)	–	Single
6.	Large unilamellar vesicles(LUV)	>100 nm	Single
7.	Giant unilamellar vesicles(GU)	>1 μm	Single
8.	Multivesicular vesicles(MVV)	usually >1 μm	Multiple

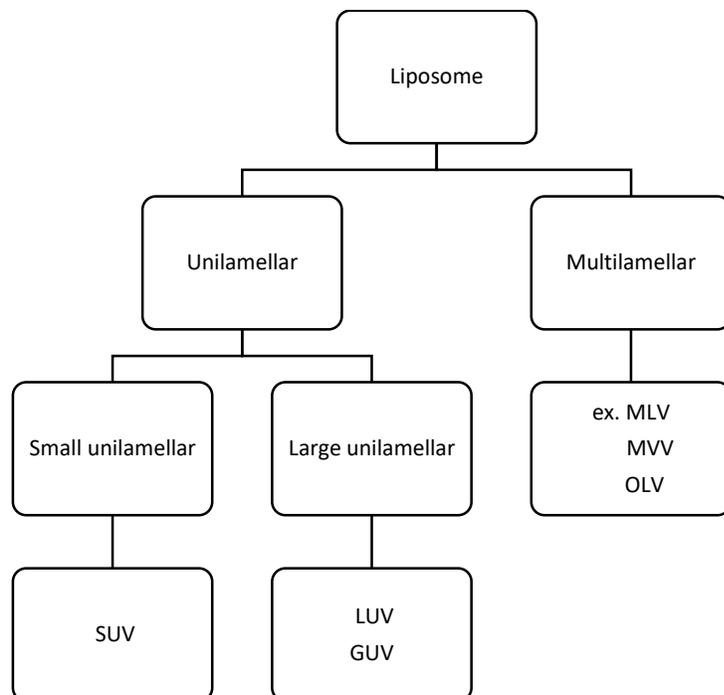


Figure 2: Classification of liposome.

METHODS OF LIPOSOME PREPARATION

General methods of preparation

There are four basic stages which used in all method of preparation of liposome. These are:

1. Drying down lipids from organic solvent.
2. Dispersing the lipid in aqueous media.
3. Purifying the resultant liposome.
4. Analyzing the final product.

Method of liposome preparation and drug loading

The following methods are used for the preparation of liposome:

1. Passive loading techniques
2. Active loading technique.

Passive loading techniques include three different methods:

1. Mechanical dispersion method.
2. Solvent dispersion method.
3. Detergent removal method (removal of non-encapsulated material) ³.

Mechanical dispersion method

a) The following are types of mechanical dispersion methods:

1. Sonication.
2. French pressure cell: extrusion.
3. Freeze-thawed liposomes.
4. Lipid film hydration by hand shaking, non-hand shaking or freeze drying.
5. Micro-emulsification.
6. Membrane extrusion.
7. Dried reconstituted vesicles ⁴.

b) . Solvent dispersion methods:

1. Ethanol injection
2. Ether injection

Sonication

Disruption of LMV suspensions using sonic energy (sonication) typically produces small, unilamellar vesicles (SUV) with diameters in the range of 15-50nm. The most common instrumentation for preparation of sonicated particle is bath and probe tip sonicators.

a) Probe sonication. The tip of a sonicator is directly engrossed into the liposome dispersion. The energy input into lipid dispersion is very high in this method. The coupling of energy at the tip results in local hotness; therefore, the vessel must be engrossed into a water/ice bath. Throughout the sonication up to 1 h, more than 5% of the lipids can be de-esterified. Also, with the probe sonicator, titanium will slough off and pollute the solution.

b) Bath sonication. The liposome dispersion in a cylinder is placed into a bath sonicator. Controlling the temperature of the lipid dispersion is usually easier in this method, in contrast to sonication by dispersal directly using the tip. The material being sonicated can be protected in a sterile vessel, dissimilar the probe units, or under an inert atmosphere ⁵.

French pressure cell: extrusion

French pressure cell involves the extrusion of MLV through a small orifice ³. The method involves the extrusion of MLV at 20,000 psi at 4°C through a small orifice The method involves gentle handling of unstable materials. The method has several advantages over sonication method ⁶. The resulting liposomes are rather larger than sonicated SUVs. The drawbacks of the method are that the high temperature is difficult to attain, and the working volumes are comparatively small (about 50 mL as the maximum) ⁴.

Advantages of the french pressure cell: extrusion method:

An important feature of the French press vesicle method is that the proteins do not seem to be significantly pretentious during the procedure as they are in sonication⁷. An interesting comment is that French press vesicle appears to recall entrapped solutes significantly longer than SUVs do, produced by sonication or detergent removal⁸. The resulting liposomes are somewhat larger than sonicated SUVs.

Freeze thaw method

In this method, SUVs are rapidly frozen and followed by slow thawing. The brief sonication disperses aggregated materials to LUV. The formation of unilamellar vesicles is due to the fusion of SUV during the process of freezing or thawing. This type of fusion is strongly inhibited by increasing the ionic strength of the medium and by increasing the phospholipids concentration. The encapsulation efficiencies from 20–30% were obtained. The disadvantages with the method are divalent metal ions; sucrose and high ionic strength salt solutions cannot be entrapped efficiently.

Lipid film hydration by hand shaking, non-hand shaking or freeze drying.

When preparing liposomes with mixed lipid composition, the lipids must be dissolved and mixed in organic solvent to assure a homogeneous mixture of lipids. Usually this process is carried out using chloroform or chloroform: methanol mixture. The purpose is to obtain a clear lipid solution for complete mixing of lipids. Typically lipid solutions are prepared at 10–20 mg lipid/ml of organic solvent, although higher concentrations may be used if the lipid solubility and mixing are acceptable. Once the lipids are thoroughly mixed in the organic solvent, the solvent is removed to yield a lipid film. For small volumes of organic solvent (<1ml), the solvent is evaporated by using dry nitrogen stream in a fume hood. For larger volumes, the organic solvent should be removed by rotary evaporation yielding a thin lipid film on the sides of round bottom flask. The lipid film is thoroughly dried to remove residual organic solvent by placing the vial or flask on a vacuum pump overnight. If the use of chloroform is objectionable, an alternative is to dissolve the lipids in tertiary butanol or cyclohexane. The lipid solution is transferred to containers and frozen by placing the containers on a block of dry ice or swirling the container in a dry ice-acetone or alcohol (ethanol or methanol) bath. Care should be taken when using the bath procedure that, the container can withstand sudden temperature changes without cracking. After complete freezing, the frozen lipid cake is placed on a vacuum pump and lyophilized until dry (1–3 days depending on volume). The thickness of the lipid cake should not be more than the diameter of the container being used for lyophilisation. Dry lipid films or cake can be removed from the vacuum pump; the container should be closed tightly, tapped and stored frozen until ready to hydrate.

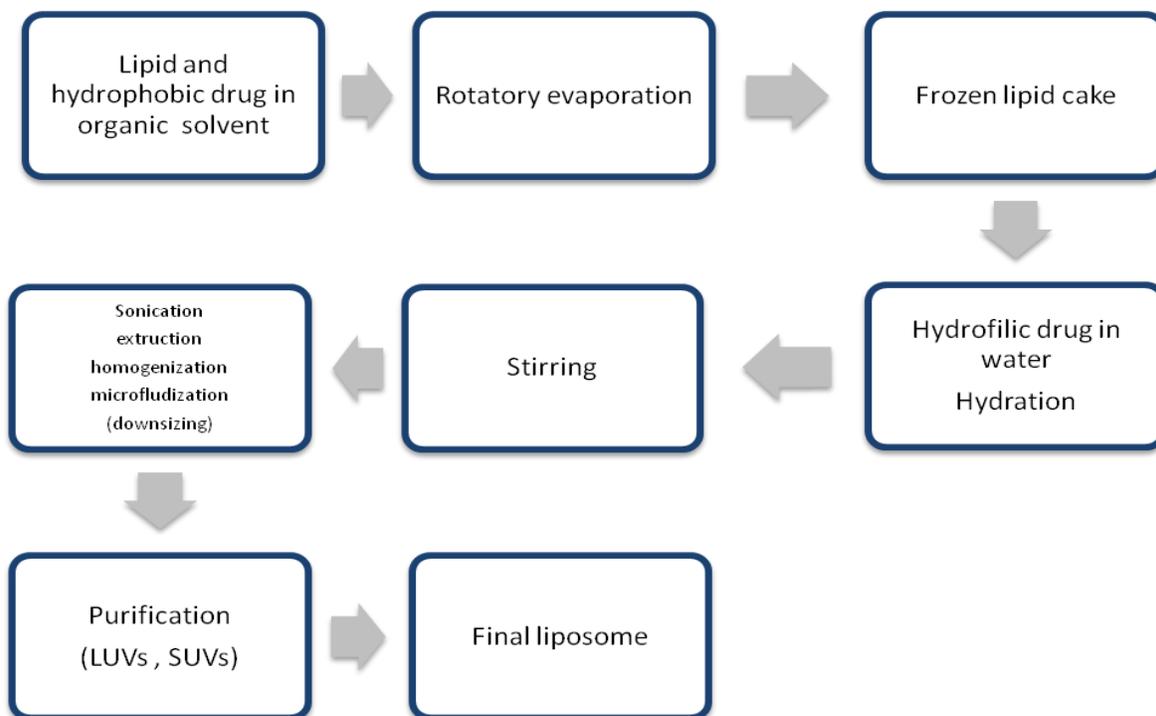


Figure 3: Flow diagram of lipid film hydration method.

Advantages of the lipid film hydration:

It is easy, simple and economic method for the preparation of liposomes.

b. Solvent dispersion methods

Ether Injection Method

A solution of lipids dissolved in diethyl ether or ether/ methanol mixture is slowly injected to an aqueous solution of the material to be encapsulated at 55–65°. The subsequent removal of ether under vacuum leads to the formation of liposomes. The main disadvantage with the method is liposomes produced are heterogeneous in nature (70–190 nm) and the material to be encapsulated will be exposed to higher temperature.

Ethanol injection

A lipid solution of ethanol is rapidly injected to a huge excess of buffer. The MLVs are at once formed. The disadvantages of the method are that the population is heterogeneous liposomes are very dilute, the removal all ethanol is difficult because it forms into azeotrope with water, and the probability of the various biologically active macromolecules inactivate in the presence of even low amounts of ethanol is high⁹.

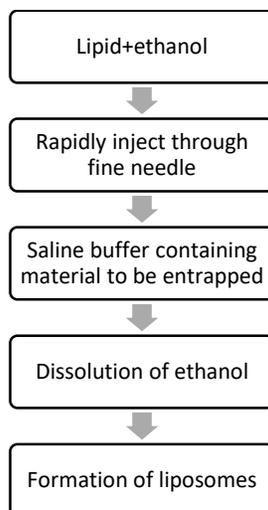


Figure 4: Flow diagram of ethanol injection method

Detergent Removal Method

The detergents at their critical micelle concentrations have been used to solubilize lipids. As detergent is removed the micelles become progressively rich in phospholipid and finally combine to form LUVs. The detergents can be removed by dialysis. The advantages of detergent dialysis method are excellent reproducibility and production of liposomes which are homogenous in size. The main drawback of the method is the retention of traces of detergent within the liposomes. A commercial device called LIPOPREP which is a version of dialysis system available for the removal of detergents. Other techniques have been used for the removal of detergents: (a) by using Gel Chromatography involving a column of Sephadex G-259 (b) by adsorption or binding of Triton X-100 (detergent) to Bio-Beads SM-210 (c) by binding of octylglucoside (detergent) to Amberlite.

Active loading technique

Industrial Production of Liposomes

In above preparation methods described in the literature, only a few have potential for large scale manufacture of liposomes. The main issues faced to formulator and production supervisor are presence of organic solvent residues, physical and chemical stability, sterility, size and size distribution and batch to batch reproducibility. Liposomes for parenteral use should be sterile and pyrogen free. For human use, precautions for sterility must be taken during the entire preparation process: that is,

- 1) The raw materials must be sterile and pyrogen free,
- 2) Preparation in sterile system: working areas equipped with laminar flow and
- 3) Use of sterile containers. Some issues related to phospholipids need attention.

The liposomes which prepared with egg yolk phospholipids are not very stable. The cost of purified lipids is very high. Recently, liposomes have been prepared using synthetic and polymerizable lipids. The liposomes prepared from polymerizable phospholipids are exposed to UV light. The polymerization process takes place in the bilayer(s). Such liposome preparations usually have better storage stability. It should be noted that such materials usually are phospholipid and their metabolic fates have yet to be established.

(i) Detergent Dialysis: A pilot plant under the trade name of LIPOPREP II-CIS is available from Diachema, AG, Switzerland. The production capacity at higher lipid concentration (80 mg/ml) is 30 ml liposomes/minute. But when lipid concentration is 10-20 mg/ml 100 mg/ml then up to many litres of liposomes can be produced.

(ii) Microfluidization A method based on microemulsification/homogenization was developed for the preparation of liposomes. A pilot plant based on this technology can produce about 20 gallon/minute of liposomes in 50-200 nm size range. The encapsulation efficiency up to 75% could be obtained.

(iii) Aqueous dispersions of liposomes often have tendency to aggregate or fuse and may susceptible to hydrolysis and or oxidation. Two solutions have been proposed:

a) Proliposomes: In proliposomes, lipid and drug are coated into a soluble carrier to form free-flowing granular material Which on hydration forms an isotonic liposomal suspension. The proliposome approach may provide an opportunity for cost-effective large scale manufacture of liposomes containing particularly lipophilic drugs.

(b) Lyophilization: Freeze-drying (lyophilization) involves the removal of water from products in the frozen state at extremely low pressures. The process is generally used to dry products that are thermolabile and would be destroyed by heat-drying. The technique has a great potential as a method to solve long term stability problems with respect to liposomal stability. It is exposed that leakage of entrapped materials may take place during the process of freeze- drying and on reconstitution.³

Drug loading in liposomes

Drug loading can be attained either passively (i.e., the drug is encapsulated during liposome formation) or actively (i.e., after liposome formation). Hydrophobic drugs, for example amphotericin B taxol or annamycin, can be directly combined into liposomes during vesicle formation, and the amount of uptake and retention is governed by drug-lipid interactions. Trapping effectiveness of 100% is often achievable, but this is dependent on the solubility of the drug in the liposome membrane. Passive encapsulation of water-soluble drugs depends on the ability of liposomes to trap aqueous buffer containing a dissolved drug during vesicle formation. Trapping effectiveness (generally <30%) is limited by the trapped volume

delimited in the liposomes and drug solubility. On the other hand, water-soluble drugs that have protonizable amine functions can be actively en-trapped by employing pH gradients⁷, which can result in trapping effectiveness approaching 100%¹⁰. Freeze-protectant for liposomes (lyophilization) Natural excerpts is usually degraded because of oxidation and other chemical reactions before they are delivered to the target site. Freeze-drying has been a standard practice employed to the production of many pharmaceutical products. The overwhelming majority of these products are lyophilized from simple aqueous solutions. Classically, water is the only solvent that must be detached from the solution using the freeze-drying process, but there are still many examples where pharmaceutical products are manufactured via a process that requires freeze-drying from organic co-solvent systems¹¹. Freeze-drying (lyophilization) involves the removal of water from products in the frozen state at tremendously low pressures. The process is normally used to dry products that are thermo-labile and would be demo-lished by heat-drying. The technique has too much potential as a method to solve long-term stability difficulties with admiration to liposom al stability. Studies showed that leakage of entrapped materials may take place during the process of freeze-drying and on reconstitution. Newly, it was shown that liposomes when freeze-dried in the presence of adequate amounts of trehalose (a carbohydrate commonly found at high concentrations in organism) retained as much as 100% of their original substances. It shows that trehalose is an excellent cryoprotectant (freeze-protectant) for liposomes. Freeze-driers range in size from small laboratory models to large industrial units available from pharmaceutical equipment suppliers¹².

Mechanism of transportation through liposome

The liposome drug carriers in vivo and in vitro studies of the contacts with cells have shown that the main interaction of liposomes with cells is either simple adsorption (by specific interactions with cell-surface components, electrostatic forces, or by non-specific weak hydrophobic) or following endocytosis (by phagocytic cells of the reticuloendothelial system, for ex-ample mac rophages and neutrophils). Fusion with the plasma cell membrane by insertion of the lipid bilayer of the liposome into the plasma membrane, with simultaneous release of liposomal content into the cytoplasm, is much rare. The fourth possible interaction is the exchange of bilayer components, for instance cholesterol, lipids, and membrane-bound molecules with components of cell membranes. It is often difficult to determine what mechanism is functioning, and more than one may function at the same time¹³.

ADVANTAGES AND DISADVANTAGES OF LIPOSOME

Advantages

- Liposome can use for delivery of hydrophobic, amphipathic and hydrophilic drugs.
- Protect the encapsulated drug from the external environment.

- Reduced toxicity and increased stability.
- As therapeutic activity of chemotherapeutic agents can be improved through liposome encapsulation.
- Similar to or lower than those required for maximum therapeutic activity.
- Reduce exposure of sensitive tissues to toxic drugs.
- Non ionic can carry both water and lipid soluble drugs ¹⁴.
- Biodegradable drugs can be stabilized from oxidation and improve protein stabilization.
- Controlled hydration and it shows sustained release.
- Targeted drug delivery or site specific drug delivery.
- Stabilization of entrapped drug from hostile environment.
- Alter pharmacokinetics and pharmacodynamics of drugs.
- Can be administered through various routes.
- Can incorporate micro and macromolecules act as reservoir of drugs.
- Therapeutic index of drugs is increased.
- Direct interaction of the drug with cell Biodegradable and flexible ¹⁵.

Disadvantages

- Less stability, Low solubility, Short half life and phospholipids undergoes oxidation, hydrolysis.
- Leakage and fusion, high production cost.
- Quick uptake by cells of R.E.S. allergic reactions may occur to liposomal constituents ¹⁵.
- Phospholipids impulsively form closed structures when they are hydrated in aqueous solutions.
- Such vesicles which have one or more phospholipid bilayer membranes can transport aqueous or lipid drugs, depending on the nature of those drugs.

APPLICATIONS OF LIPOSOMES IN MEDICINE AND PHARMACOLOGY

Applications of liposomes in medicine and pharmacology can be divided into diagnostic and therapeutic applications of liposomes containing various markers or drugs, and their use as a tool, a model, or reagent in the basic studies of cell interactions, recognition processes, and mode of action of certain substances unfortunately, many drugs have a very narrow therapeutic window, meaning that the therapeutic concentration is not much lower than the toxic one. In several cases, the toxicity can be reduced or the efficacy can be enhanced by the use of a suitable drug carrier which alters the temporal and spatial delivery of the drug, i.e., its biodistribution and pharmacokinetics. Advances in liposome design are leading to new applications for the delivery of new biotechnology products, for example antisense oligo-

nucleotides, cloned genes, and recombinant proteins. A vast literature defines the viability of formulating wide range of conservative drugs in liposomes, frequently resultant in improved therapeutic activity and/or reduced toxicity compared with the free drug. Changed pharmacokinetics for liposomal drugs can lead to improved drug bioavailability to particular target cells that live in the circulation, or more prominently, to extravascular disease sites, for example, tumors. Recent improvements include liposomal formulations of all-*trans*-retinoic acid and daunorubicin, as first-line treatment of AIDS related advanced Kaposi's sarcoma. Examples are vincristine, doxorubicin, and amphotericin B. The benefits of drug load in liposomes, which can be applied as (colloidal) solution, aerosol, or in (semi) solid forms, such as creams and gels, can be summarized into seven categories.

Liposomes in parasitic diseases and infections

From the time when conventional liposomes are digested by phagocytic cells in the body after intravenous management, they are ideal vehicles for the targeting drug molecules into these macrophages. The best known instances of this 'Trojan horse-like' mechanism are several parasitic diseases which normally exist in the cell of MPS. They comprise leishmaniasis and several fungal infections. Leishmaniasis is a parasitic infection of macrophages which affects over 100 million people in tropical regions and is often deadly.

The effectual dose of drugs, mostly different antimonials, is not much lower than the toxic one. Liposomes accumulate in the very same cell population which is infected, and so an ideal drug delivery vehicle was proposed. Certainly, the therapeutic index was increased in rodents as much as several hundred times upon administration of the drug in various liposomes. These formulations use mostly ionosphere amphotericin B and are transplanted from very successful and prolific area of liposome formulations in antifungal therapy.

Unfortunately, the drug itself is very toxic and its dosage is limited due to its ionosphere and neurotoxicity. These toxicities are normally related with the size of the drug molecule or its complex.

Obviously, liposome encapsulation inhibits the accumulation of drug in these organs and radically reduces toxicity. Furthermore, often, the fungus exists in the cells of the mononuclear phagocytic system; therefore, the encapsulation results in reduced toxicity and passive targeting.

Liposomes in anticancer therapy

Now a day's liposomal drug delivery system plays good and beneficial role in treatment of the cancer with the help of nanodrug like liposome the treatment of cancer like sever disease become easy fast and effective. Many different liposome formulations of various anticancer agents were shown to be less toxic than the free drug ¹⁶. It was found that the anticancer drugs like doxorubicin and anthracyclins shows less

toxicity when compared to free drug molecules. Anthracyclines are drugs which stop the growth of dividing cells by intercalating into the DNA and therefore kill predominantly quickly dividing cells. These cells are in tumours, but also in gastrointestinal mucosa, hair, and blood cells and therefore this class of drugs are very toxic. The most used and studied is Adriamycin (commercial name for Doxorubicin HCl). In addition to the above mentioned acute toxicities its dosage is limited by its cumulative cardiotoxicity. Many different formulations were tried. In most cases the toxicity was reduced about 50%. Of toxicity includes both, short term and chronic toxicities because liposome encapsulation reduces the distribution of the drug molecules towards those tissues. For the same reason, 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 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 circulation¹⁷. Applications in man showed in general reduced toxicity, better tolerability of administration with not too encouraging efficacy. Several different formulations are in different phases of clinical studies and show mixed results.

OTHER APPLICATION

Respiratory disorders

The liposomes show beneficial effects in the treatment of several respiratory disorders, reason being their better sustained release, improved stability and reduced toxicity than ordinary aerosols. Although, lipid composition, size, charge, drug-lipid ratio along with method of delivery are certain parameters that must be necessitated in order to make liposomal drug delivery effective enough. Liquid or dry form can be taken for inhalation of liposome and release of drug has been reported to occur during nebulization^{18, 19}. Liposomal inhalational reduce toxicity of drug and may provide soothing effect. Eg. Topex-Br for asthma and Alectm for Expanding lung diseases in babies.

Ophthalmic delivery of drugs

The liposomes have been evidenced to play a good role in treatment of disorders of both anterior and posterior segment of eye. Dry eyes, keratitis, corneal transplant rejection, uveitis, ondothelmitis and proliferative vitro retinopathy are the examples of eye disorders against which liposomes have been found to possess beneficial effects²⁰ [Fujisawa T et al 2012]. It can enhance the permeation of poorly absorbed drug molecules by binding to the corneal surface and improving residence time.

Brain targeting

The liposomes can also be used for brain targeting due to their biocompatible and biodegradable behavior, which is evidenced by the fact that inability of amitriptylline to cross the blood brain barrier (BBB) when given systemically was found to be reversed when administered as liposomal formulation; proving their application in brain targeting^{21,22}.

The basic reason for the acceptance of liposomal carrier is due to their controlled profile or drug release nature as well as due to their selected targeting mechanism. The surface modified liposomes can be used to directly encapsulate drug molecules to diseased tissues or organs.

Fungal Infections

Liposomes can be used as a carrier for drugs such as for amphotericin B, used in the treatment of fungal infection. For amphotericin B has notably beneficial properties as an antifungal medication but its use in practice is limited by its toxicity, particularly ionosphere and neurotoxicity. Using liposomes as carriers to encapsulate the drug helps to prevent the build-up of drugs in problematic organs, such as those in the central nervous system, reducing the risk of toxicity dramatically. Additionally, the liposomes naturally target the mononuclear phagocytic system where the fungus usually exists, leading to passive drug targeting.

Liposome for topical applications

Liposome show very good and specific effect in delivering drugs in to the skin. Liposomes increase the permeability of skin for various entrapped drugs. They can improve drug deposition within the skin at the site of action where the goal is to reduce systemic absorption and thus minimize side effects. They can provide targeted delivery to skin appendages in addition to their potential for transdermal delivery.

In the recent studies, it is shown that liposomes penetrate effectively into hair follicles and thus hair follicle penetration can be increased by massaging the skin, which stimulates the in vivo movement of hairs in the hair follicles.

Liposome in cosmetic:

The effectiveness of liposome encapsulation in cosmetics varies depending on size and amount. In today's skin care, smaller liposomes are used, so they can enter deeper into the skin and deliver the active ingredients for longer. Nanospheres are microscopic fragments used to deliver ingredients into the deep layers of the skin. liposomes can carry almost everything that we should need in order to attain perfect skin. To achieve this, cosmetic companies need to manipulate materials at the atomic level; this is called "nanotechnology".

Some of their benefits include:

- Liposomes (nanosphere) are naturally attracted to skin, and work well with any skin type because of their molecular structure. They are added to moisturizers to keep the skin hydrated.
- The bigger benefits of having them in your skin products come from the ingredients they help your skin absorb, not necessarily the nanospheres themselves.
- It shows very good effect when it encapsulated by any anti-aging ingredient. It reduces wasting of drug
- AGE is a moisturizer which has also been known to have anti-wrinkle qualities. CoQ10, a powerful antioxidant, has also been packed inside into these spheres.
- Vitamin E has also been introduced into nanospheres bubbles. Because of their unique molecular structure, liposomes can carry almost everything that you would need in order to attain perfect skin.

Example; Sesderma C Vit serum liposomal

Sesderma azelac RU liposomal dipigmentation

- Water-soluble vitamins, fat-soluble amino acids, and even chemically created ingredients can be put into these spheres successfully.
- They are being used in most, if not all, of the highest-rated skincare lines on the market. Best of all, the use of these skin care ingredients will also help protect your skin from future damage.²³

CONCLUSION

Liposomes are very useful carrier systems for targeted drug delivery. Liposomes are administrated orally, parenterally and topically as well as used in cosmetic and hair technologies, sustained release formulations, diagnostic purpose and as good carriers in gene delivery various drugs with liposomal delivery systems have been approved. Liposomes with enhanced drug delivery to disease locations, by ability of long circulation residence times, are now achieving clinical acceptance. Liposomal drugs entrapment reduced toxicities and enhanced efficacy compared with free complements. Drugs encapsulated in liposomes can have a significantly altered pharmacokinetics. Based on the pharmaceutical applications and available products, we can say that liposomes have definitely established their position in modern delivery systems.

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