Review Article CODEN: IJPRNK Impact Factor: 5.567 ISSN: 2277-8713
S. S. Upadhye, IJPRBS, 2018; Volume 7(1): 36-55 IJPRBS

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

A REVIEW ON LIPOSOMES

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Accepted Date: 31/12/2017; Published Date: 27/02/2018

Abstract: The liposomes are concentric bilayered vesicle in which an aqueous volume is entirely enclosed by the membranous lipid bilayer mainly composed of the natural or synthetic phospholipids. The liposomes are one of unique drug delivery system which can be use in controlling & targeting drug delivery system. The liposomes are generally classified based upon the structure, method of preparation, composition and application, conventional liposome, and specialty liposome. The liposomes can be filled with drugs & used to deliver the drugs for cancer & other diseases. This review is focused on the various aspects of liposomes like classification, methods of preparation, characterization and applications of liposomes.

Keywords: Liposomes, Phospholipids, Targeting drug delivery system, Bilayered

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Access Online On:

www.ijprbs.com

How to Cite This Article:

S. S. Upadhye, IJPRBS, 2018; Volume 7(1): 36-55

PAPER-QR CODE

INTRODUCTION

The liposomes are the concentric bilayered vesicle in which the aqueous volume is entirely enclosed by the membranous lipid bilayer mainly composed of the synthetic or the natural phospholipids. The name liposome is derived from 2 Greek words, 'Lipos' means fat & 'Soma' means body. At the variety of sizes the liposome can be formed as the uni-lamellar or the multi-lamellar construction & its name relates to its structural building blocks, phospholipids, & not to its size. The liposome does not necessarily have the lipophobic contents such as water, although it usually does. The liposomes are artificially prepared vesicles made up of the lipid bilayer. The liposomes can be filled with the drugs, & used to deliver the drugs for the cancer & other diseases. The liposomes can be prepared by disrupting the biological membranes. For example by sonication method. The liposomes are the micro particulate or the colloidal carriers usually 0.05- 5.0 µm in diameter which form spontaneously when the certain lipids are hydrated in the aqueous media. The liposomes are composed of the relatively biocompatible & biodegradable material & they consist of the aqueous volume entrapped by one or more bilayer of the natural &/or synthetic lipids. The drug with widely varying lipophilicities can be encapsulated in a liposome either in the phospholipids bilayer in the entrapped aqueous volume or at the bilayer interface. [1]

REASONS TO USE LIPOSOMES AS DRUG CARRIERS

Protection- The Liposome-encapsulated drugs are inaccessible to metabolizing the enzymes conversely the body components [such as the erythrocytes or the tissues at the site of injection] are not exposed directly to the full dose of the drug.

Amplification- In vaccine formulations the liposomes can be used as the adjuvant.

Internalisation- The Liposomes are phagocytosed or endocytosed by the cells, by opening up the opportunities to use the 'liposome dependent drugs'. The Lipid based structures [not necessarily liposomes] are also able to bring the plasmid material into the cell through a same mechanism [the non-viral transfection systems].

Solubilisation- The liposomes may solubilize the lipophilic drugs that would otherwise be difficult to be administer by intravenous route

Duration of action- The drug action Liposomes can be prolonged by releasing the drug slowly in the body. By directing the potential targeting options the change in the distribution of the drug through the body. [2]

ADVANTAGES

Some of the advantages of liposome are as follows:

- The increased stability via encapsulation.
- To achieve the active targeting the flexibility to couple with the site specific ligands.
- The site avoidance effect.
- The reduction in toxicity of the encapsulated agents.
- It provides selective passive targeting to the tumor tissues [Liposomal doxorubicin].
- The improved pharmacokinetic effects [reduced elimination, increased circulation life times].
- The increased efficacy & therapeutic index. [3]

CLASSIFICATION OF LIPOSOMES

Liposomes are classified on the basis of:

1. Structure.

2. Method of preparation.

3. Composition and application.

4. Conventional liposome.

5. Specialty liposome.

1. Classification Based on the Structure

Table 1: The Vesicle Types with their Size & Number of Lipid Layers

Vesicle type	Abbreviation	No. of lipid bilayer	Diameter size
Unilamellar	UV	One	All size ranges
Small Unilamellar	SUV	One	20-100 nm
Medium Unilamellar	MUV	One	More than 100 nm
Large Unilamellar	LUV	One	More than 100 nm
Giant Unilamellar	GUV	One	More than 1 micrometer
Oligolamellar	OLV	5	0.1 – 1 micrometer

Multilamellar	MLV	5-25	More than 0.5 micrometer
Multi vesicular	MV	Multi compartmental structure	More than 1 micrometer

2. Based on the Method of Preparation

Table 2: The Different Methods of Preparation & the Vesicles Formed by these Methods

Method of preparation	Vesicle type
Single or oligo lamellar vesicle made by reverse phase evaporation method	REVS
Stable pluri lamellar vesicle	SPLV
Multi lamellar vesicle made by reverse phase evaporation method	MLV-REV
Vesicle prepared by extrusion technique	VET
Dehydration- Rehydration method	DRV
Frozen and thawed multi lamellar vesicle	FATMLV

3. Based on the Composition & Application

Table 3: The different Liposome with their Compositions

Type of liposome	Abbreviation	Composition
Conventional liposome	CL	Neutral of negatively charge phospholipids and cholesterol
pH sensitive liposomes	-	The phospholipids such as PER or DOPE with either CHEMS or the OA

Fusogenic liposome	-	Reconstituted sendai virus enveops
Cationic liposome	-	Cationic lipid with DOPE
Immune liposome	IL	CL or LCL with attached monoclonal antibody or recognition sequences
Long circulatory liposome	LCL	Neutral high temp, cholesterol and 5-10% PEG, DSP

4. Based Upon the Conventional Liposome

Table: 4: Conventional Liposome

1	**Stabilize natural lecithin [PC] mixtures**
2	Synthetic identical, chain phospholipids
3	Glycolipids containing liposome

5. Based Upon the Specialty Liposome [4]

Table: 5: Speciality Liposome

1	**Bipolar fatty acid**
2	Antibody directed liposome.
3	Lipoprotein coated liposome
4	Multiple encapsulated liposome.
5	Carbohydrate coated liposome
6	Methyl/ Methylene x- linked liposome.

Method of Preparation of Liposomes

A] Passive Loading Technique

B] Active Loading Technique

Passive Loading Technique		
I] Mechanical Dispersion methods	II] Solvent Dispersion methods	III] Detergent Removal methods
1] Lipid film hydration- **a]Hand shaking ,** **b]Non Hand shaking,** **c]Freeze Drying** **2]Micro emulsification** **3] Sonication** **4] French Pressure Cell** **5] Membrane extrusion** **6] Dried reconstituted vesicles** **7]Freeze-thawed liposomes**	1]Ethanol injection 2] Ether Injection 3]Double Emulsion Vesicles 4] Reverse Phase evaporation vesicles 5]Stable plurilamellar vesicles	1]Detergent Removal from mixed micelles by a] Dialysis b]Dilution c]Column chromatography

Active Loading Technique	
I] Proliposome	II] Lyophilization

A. PASSIVE LOADING TECHNIQUE

I. Mechanical dispersion

1] Lipid Hydration Method

(a) For the preparation of MLV this is the most widely used method. The method consists of drying the solution of lipids so that at the bottom of round bottom flask a thin film is formed & then hydrating the film by adding the aqueous buffer & vortexing the dispersion for some time. At a temperature above the gelliquid crystalline transition temperature Tc of the lipid the hydration step is done or above the Tc of the highest melting component in the lipid mixture. Depending upon their solubilities the compounds to be encapsulated are added either to the aqueous buffer or to the organic solvent containing lipids. The MLV are simple to prepare by this method & the variety of substances can be encapsulated in these liposomes. Low internal volume, low encapsulation efficiency and the size distribution is heterogeneous are the drawbacks of this method.

(b) By hydrating the lipids in the presence of an immiscible organic solvent [petroleum ether, diethyl ether] the MLVs with high encapsulation efficiency can be prepared. By vigorous vortexing or sonication the contents are emulsified. by passing a stream of nitrogen gas over the mixture the organic solvent is removed. After the removal of organic solvent the MLVs are formed immediately in the aqueous phase. [5-7]

2] Microemulsification

For preparing the small lipid vesicles in the commercial quantities by microemulsifying lipid compositions using very high shear forces generated in the homogenizing apparatus operated at a high pressures at the selected temperature this method is provided. To produce a micro emulsion of small vesicles suitable for biological application At least 20 circulations [approx 10 minutes] but not greater than 200 circulations [100 minutes] are sufficient.

3] Sonication

Either with the probe sonicator or the bath type sonicator under an inert atmosphere the MLVs are sonicated. The main disadvantages of this method are very low internal volume/encapsulation efficiency, possibly degradation of the phospholipids & compounds to be encapsulated, exclusion of the large molecules, metal contamination from the probe tip & presence of the MLV alongwith the SUV. Oezden and Hasirci [1991] recently prepared the polymer coated liposomes by this sonication method.[8]

4] French Pressure Cell Method

The method consists of the extrusion of the MLV at 20,000 psi at 4°C through the small orifice. Over the sonication method this method has several advantages. The method is rapid, reproducible, and simple & involves the gentle handling of the unstable materials. The resulting liposomes are somewhat larger than the sonicated SUVs. The disadvantages of this method are that the working volumes are relatively small [about 50 mL maximum] & the temperature is difficult to achieve. [9]

5] Membrane extrusion

Through the polymer filter having the web-like construction providing the network of the interconnected, tortuous-path capillary pore & the membrane thickness of at least about 100 microns, the suspension of the heterogeneous size liposomes is passed. The processed liposomes have selected average size less than about 0.4 microns, &the narrow size distribution.[10]

6] Dried reconstituted vesicles

The preformed liposomes are added to the aqueous solution containing the active agent or are mixed with the lyophilized protein, followed by the dehydration of mixture. [11]

7] Freeze-Thaw Method

The SUVs are rapidly frozen & are followed by slow thawing. The brief sonication disperses aggregated materials to the LUV. Due to the fusion of SUV during the processes of freezing & or thawing there is formation of unilamellar vesicles. By increasing the phospholipid concentration & by increasing the ionic strength of the medium this type of fusion is strongly inhibited. From 20 to 30% the encapsulation efficiencies were obtained. [12-14]

II. Solvent dispersion

1] Ethanol Injection Method

To the vast excess of buffer the lipid solution of ethanol is rapidly injected. The MLVs are formed immediately. The disadvantages of this method are that the population is heterogeneous [30-110 nm], the liposomes are very dilute, it is difficult to remove all the ethanol because it forms the azeotrope with water & the possibility of the various biologically active macromolecules to inactivation in the presence of even low amounts of the ethanol.[15]

2] Ether Infusion Method

To an aqueous solution of the material to be encapsulated at 55-65°C or under reduced pressure, the solution of lipids dissolved in the ether/methanol mixture or diethyl ether is slowly injected. The subsequent removal of the ether under vacuum leads to the formation of the liposomes. The main disadvantages of this method are that the population is heterogeneous [70-190 nm] & the exposure of the compounds to be encapsulated to the organic solvents or high temperature.[16-17]

3] Double emulsification

An active ingredient is first dissolved in the aqueous phase [w1] which is then emulsified in the organic solvent of the polymer to make the primary w1/o emulsion is done in this process. Further this primary emulsion is mixed in an emulsifier-containing aqueous solution [w2] to make the w1/o/w2 double emulsion. The removal of the solvent leaves the microspheres in the aqueous continuous phase, by making it possible to collect them by centrifuging or by filtering. [18-20]

4] Reverse-phase evaporation

Several phospholipids [pure/mixed with cholesterol] can be used in this method. To the round bottom flask the lipid mixture is added & the solvent is removed under the reduced pressure by the rotary evaporator. The system is purged with the nitrogen & the lipids are re-dissolved in the organic phase. This is the phase that the reverse phase vesicles will be formed. The isopropyl ether & diethyl ether are the usual solvents of choice. The aqueous phase (contains compound to be encapsulated) is added after the lipids are re-dissolved in this phase. The system is kept under continuous nitrogen & the 2 phase system is sonicated until the mixture becomes the clear one-phase dispersion. on the rotary evaporator the mixture is then placed & the organic solvent is removed until the gel is formed. The non encapsulated material is removed. The resulting liposomes are called REV [Reverse-phase Evaporation Vesicles]. The large unilamellar & oligolamellar vesicles formed have the ability to encapsulate the large macromolecular vesicles having high efficiency.[21]

III. Detergent removal

At their critical micelles concentrations the detergents have been used to solubilize lipids. The micelles become progressively richer in phospholipid and finally combine to form LUVs as the detergent is removed. By dialysis the detergents were removed. The advantages of detergent dialysis method are production of liposome populations which are homogenous in size & excellent reproducibility. The main disadvantage of this method is the retention of the traces of detergent(s) within the liposomes.

B. ACTIVE LOADING TECHNIQUE

I] Proliposome

In Proliposome, lipid and drug are coated onto 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.

II] Lyophilization

The Freeze-drying [lyophilization] involves the removal of water from the products in the frozen state at extremely low pressures. To dry products that Riaz 75 are thermo labile & would be destroyed by heat-drying the process is generally used. The technique has the great potential as the method to solve the long term stability problems with respect to the liposomal stability. During the process of the freeze- drying & on the reconstitution. It is exposed that the leakage of the entrapped materials may take place. [22-24]

PHARMACOKINETICS OF LIPOSOMES

- Through the various routes the liposomal drugs can be applied but mainly the i.v. & topical administration is preferred. The liposome can interact with the cell by any of the following methods, after reaching in the systemic circulation or in the local area.
- The endocytosis by phagocytotic cells of the R.E.S such as macrophages & Neutrophils
- The adsorption to the cell surface either by specific interaction with cell surface components or by non specific weak hydrophobic or by electrostatic forces.
- The Fusion with a plasma cell membrane by insertion of the lipid bilayer of the liposome into the plasma membrane with simultaneous release of the liposomal contents into the cytoplasm.
- The transfer of the liposomal lipids to the cellular or sub cellular membrane or vice versa without any association of the contents of liposome.
- What mechanism is operative & more than one may operate at the same time, it is often difficult to determine.[25]

PHARMOCODYNAMICS OF LIPOSOME ENCAPSULATED DRUGS

The general approach to continue the action of drugs to the particular site in the body is to deposit drug bearing liposome directly into the site where the therapy is desired. As the liposomes are large & do not easily cross the epithelial or the connective barriers they are likely to remain at the site of the local administration. The liposomes will then slowly release into the targeted site or perhaps create the local drug level higher than the systemic level. The drug loaded liposomes might interact directly with the cells in the targeted site, without producing

the release. To maximize the amount of effective drug at the target site, while minimizing the drug levels at other sites and thus decreasing systemic toxicity is the goal of this approach. For example the SUV injected into the skin can persist interact at the site for the 600 hours. & the release of the entrapped markers from the liposomes occurs only after the cellular uptake & intracellular space remain intact.[26]

MECHANISM OF LIPOSOME FORMATION

The phospholipids are amphipathic having affinity for both aqueous & polar moieties molecules as they have a hydrophobic tail & the hydrophilic or polar head. The hydrophobic tail is composed of 2 fatty acid chain containing 10-24 carbon atom & 0-6 double bonds in each chain. The macroscopic structures most often formed include the hexagonal, lamellar or cubic phases dispersed as the colloidal nanoconstructs [artificial membranes] referred to as the hexasomes, liposomes, or cubosomes. The most common natural polar phospholipids are the phosphatidylcholine. These are the amphipathic molecules in which the glycerol bridge links to the pair of the hydrophobic acyl hydrocarbon chains with the hydrophilic polar head group, the phosphocholine. The amphipathic nature of the phospholipids & their analogues render them the ability to form the closed concentric bilayers in presence of the water. The liposomes are formed when the thin lipid films or the lipid cakes are hydrated & stacks of the lipid crystalline bilayers become fluid & swell. The hydrated lipid sheets detach during the agitation & self-close to form the large, multi-lamellar vesicles which prevent the interaction of water with the hydrocarbon core of the bilayer at the edges. [25]

COMPONENTS OF LIPOSOMES

1) Phospholipids: The most common used component of liposome formulation are glycerol containing phospholipids & represent greater than 50% of the weight of lipid in the biological membranes. These are derived from phosphatidic acid. The glycerol moiety is the back bone of the molecule. At C3 position OH group is esterified to phosphoric acid. OH at C1 & C2 are esterified with long chain. The fatty acid giving rise to the lipidic nature, one of the remaining OH group of phosphoric acid may be further esterified to the wide range of the organic alcohols including glycerol, choline, ethanolamine, serine & inositol. Thus the parent compound of the series is the phosphoric ester of the glycerol. The examples of the phospholipids are –

- Phosphatidyl serine [PS]
- Phosphatidyl inositol [PI]
- Phosphatidyl ethanolamine [cephalin] – PE
- Phosphatidyl choline [Lecithin] – PC
- Phosphatidyl Glycerol [PG] For stable liposomes, saturated fatly acids are used.

The unsaturated fatty acids are not used generally.

2) Sphingolipids: The Backbone is sphingosine or a related base. These are important constituents of plant & animal cells. The head group that can vary from the simple alcohols such as the choline to the very complex carbohydrates.

Most common Sphingolipids is – Sphingomyelin, Glycosphingo lipids.

Gangliosides – It is found on grey matter, used as the minor component for the liposome production. This molecule contains complex saccharides with 1or more Sialic acid residues in their polar head group and thus have 1 or more negative charge at the neutral pH.

These are included in the liposomes to provide the layer of surface charged group.

3) Sterols:

For decreasing the fluidity or Microviscosity of the bilayer reducing the permeability of the membrane to water soluble molecules, the cholesterols & its derivatives are often included in liposomes. Stabilizing the membrane in presence of the biological fluids such as plasma [This effect used in formulation of i.v. liposomes]

4) Synthetic phospholipids

For Example: For saturated phospholipids are

DPPC [Dipalmitoyl phosphatidyl choline], DSPC [Distearoyl phosphatidyl choline],

DPPE [Dipalmitoyl phosphatidyl ethanolamine], DPPS [Dipalmitoyl phosphatidyl serine],

DPPA [Dipalmitoyl phosphatidic acid], DPPG [Dipalmitoyl phosphatidyl glycerol] For E.g.: for unsaturated phospholipids DOPC [Dioleoyl phosphatidyl choline], DOPG [Dioleoyl phosphatidyl glycerol]

5) Polymeric materials

The synthetic phospholipids with the diactylenic group in a hydrocarbon chain polymerizes when it is exposed to U.V leading to the formation of the polymerized liposomes having significantly higher permeability barriers to the entrapped aqueous drugs. For e.g: for other Polymerisable lipids are -lipids containing conjugated diene, methacrylate etc. [27]

CHARACTERIZATION OF LIPOSOMES

I]. Physocochemical methods:

a. Determination of particle size:

By laser light scattering the determination of particle size of liposomes is done

b. TEM [Transmission electron microscopy]:

For maintaining temperature of -196°c in TEM Osmium tetroxide is used

c. X-ray scattering:

It determines shape and size of liposomes.

d. Differential scanning colourimetry:

From crystalline to liquid crystalline & liquid crystalline to amorphous transitions can be studied.

e. Rheology:

The flow characteristics exhibited by rheology are plastic & pseudoplastic. For determining liquid crystalline get elasticity, the mechanical oscillation measurement is the method of choice.

II]. Percent entrapment:

The mostly used method is Minicolumn centrifugation method.

III]. Determination of percent capture:

Before studying the behavior of this entrapped material in physical or biological systems,

It is clearly essential to measure the quantity of the material entrapped inside liposomes

Leakage through phase separation:

The lipophilic compounds may phase separate from liposomal bilayers .The simple light microscope is the very suitable tool to identify these crystals or the amorphous precipitate in the liposomal dispersions the larger ones form. The maltose crosses when viewed under the light microscope with 2 cross-positioned polarizing light filters. When the phase separation is observed may be estimated by measuring the drug contain phospholipid in a supernatant after 10 to 30 sec .centrifugation and then filter it.

Lekage via permeation membrane:

The leakage of the water soluble compounds out of the liposomes might be estimated by the ultracentrifugation followed by the quantification of the free drug that contain in the supernatant.

IV]. Determination of percentage release:

The choice of marker: For the release of water soluble markers from the liposomes, one would like to use the molecule:

a. That is highly water soluble.

b. That can be easily sepearated from liposomes by conventional methods.

c. That does not pass through interact membranes.

d. With a very low solubility in organic media.

e. That does not associate with membranes in any way so as to destabilize or aggreagate them.

Detection method	Marker	Molecular weight
Enzymatic	Glucose	181
	Isocitrate	258
Fluroscence	Calcein	620
	Flurescein	319
Optical density	Sodium chromate	162
	Cytochrome C	13000
Radiolabel	DNA	millions
	Inulin	5000

V]. Determination of entrapped volume:

The entrapped volume [lit/mol] = 500/3.A.N.R

A= Area of the membrane occupied by one lipid

N=Avegadros no.

R=Radious

VI]. Electron microscopy:

The electron microscopy is alternative to estimate the lamillarity of the liposomes. The sample is quickly frozen to about -200°c & subsequently fractured with the sharp knife in vaccum. The fracture plane falls often in the middle of the membrane, which is one of the weakest region. Finally, an ultrathin metal layer

VII]. Phospholipid quantification:

The Bartlett assay: The principle of this Bartlett assay is based on a colorimetric determination of the inorganic phosphate. The phospholipid content of the liposopmes can be determined after the destruction of the phospholipid with perchloric acid to the inorganic phosphate is converted to the phosphomolybdic acid, colorimetrically this compound can be determined at 830nm.

The Stewart assay:

In this Stewart assay for phospholipid, To form a complex with ammonium ferrothiocynate in organic solution, the ability of phospholipids is utilized. The presence of inorganic phosphate does not interfare with the assay, is the advantage of this method. [28]

APPLICATIONS

In Gene delivery: For gene transfer into the cell in culture the negatively charged or classical liposomes have been used as the vehicles. The cationic lipids are able to interact spontaneously with the negatively charged DNA to form the cluster or the aggregated vesicles along the nucleic acid. At the critical liposome density the DNA is condensed & becomes encapsulated within the lipid bilayer. [29]

Liposomes for pulmonary delivery: The targeted drug delivery to the lungs has evolved to be one of the most widely investigated local or systemic drug delivery approaches. Because of their potential for the localized topical therapy in the lungs, the use of drug delivery system for the treatment of pulmonary diseases is increasing. There by reducing the overall amount of drug given to the patients, this route also makes it possible to deposit the drugs more site specific at high concentrations within the diseased lung, as well as increasing local drug activity while reducing the systemic side effects & first pass metabolism. [30-31]

Liposomes in parasitic diseases: After intravenous management the conventional liposomes are digested by the phagocytic cells in the body. For the targeting drug molecules into these macrophages they are ideal vehicles. The Leishmaniasis is the parasitic infection of the macrophages which affects over 100 million people in the tropical regions & is often deadly.

The effectual dose of the drugs mostly different antimonials is not much lower than the toxic one. The liposomes accumulate in the very same cell population which is infected. The best results reported so far in the human therapy are probably the liposomes as carriers for Amphoterecin B in the antifungal therapies. This is the drug of choice in the dispersed fungal infections. [32]

Liposomes for Brain targeting: To design with better site specific action this liposomal technology is quite advanced. The basic reason for the acceptance of the liposomal carrier is due to their controlled profile or the nature of drug release as well as due to their selected targeting mechanism. The surface modified liposomes can be used to directly encapsulate drug molecules to diseased organs or tissues. By conjugation of appropriate targeting vectors like the monoclonal antibody the brain distribution of liposomes can be modulated. The mechanism involved in a concentration of the liposomes in the brain by crossing the blood brain barrier-coupling of the liposomes with brain drug transport vector through the absorptive mediated transcystosis or by the receptor mediated transcystosis. **[**33]

Cancer chemotherapy: A long term therapy of the anticancer drug leads to the several toxic side effects. A liposomal therapy to the cell of tumour has revolutionized the world of cancer therapy with least side effects. It has been said that the stable & small liposomes are targeted passively to the different tumor because they can circulate for longer time & they can extra vasate in tissue with the enhanced vascular permeability. Where the light triggers the release of anticancer drugs, like doxorubicin the light sensitive liposomes have been prepared.. The light triggered system will reduce the potential toxicity & lead to more effective therapy. [34-35]

Liposomes for topical applications: The liposomes are proved to be effective in delivering the drugs in to the skin. The liposomes increase the permeability of the skin for the various entrapped drugs. After the topical application the liposomes can exert different functions. At the site of action they can improve the drug deposition within the skin where the goal is to reduce systemic absorption & thus minimize the side effects .They can provide targeted delivery to the skin appendages in addition to their potential for the transdermal delivery. It is shown in the recent studies that liposomes penetrate effectively into the hair follicles & by massaging the skin thus the hair follicle penetration can be increased which stimulates the *in vivo* movement of the hairs in the hair follicles.**[**36-38]

Liposome for Nasal administration: Good penetration is of little use for nasally administered products, if the formulation is not able to remain in contact with the mucosal surface for the long enough time to enable the penetration to occur. Hence the mucoadhesion is the key characteristic of nasally administered formulations**.** The liposomes coated with the chitosan,

alginates or trimethyl chitosan, which are able to penetrate through the nasal mucosa & offer the enhanced penetration over the uncoated liposomes when delivered as the dry powders. The coating of the liposomes may result in some reduction in the encapsulation efficiency still maintained between 60–69% & the structural integrity of the entrapped protein & its release characteristics were also maintained. **[**39]

The Ophthalmic delivery of drugs: Since it offers advantages as the carrier system the Liposomes have been investigated for the ophthalmic drug delivery. It is biodegradable & biocompatible nano carrier. It can enhance the permeation of the poorly absorbed drug molecules by binding to the corneal surface & by improving residence time. A novel approach was introduced to reduce the drug loss & side effects associated with conventional eye drops, where the liposomes made up of the dimyristoylphosphatidylcholine and are dispersed in contact lens hydrogels made up of the poly-2-hydroxyethyl methacrylate. The contact lens loaded with the hydrogels is transparent in nature & for few days deliver drugs at therapeutic level. **[**40-41]

MARKETED PREPARATIONS OF LIPOSOMES [42]

PRODUCT	DRUG	INDICATION
Cisplatin	Lipoplatin®	Epithelial malignancies
Morphine Sulfate	DepoDur®	Postoperative pain following major surgery
Amphoteracin B	Ambisome™	Fungal infection
Doxorubicin	Myocet®	Recurrent breast cancer
Daunorubicin	DaounoXome™	Kaposi's sarcoma
Doxorubicin	Doxil™	Refractory Kaposi's sarcoma, recurrent breast cancer and ovarian cancer
Verteporfin	Visudyne®	Age-related macular degeneration, pathologic myopia and ocular histoplasmosis
Cytarabine	DepoCyt®	Neoplastic meningitis and lymphomatous meningitis

CONCLUSION

The liposomes have been used in the broad range of pharmaceutical applications. The liposomes are acceptable & superior carriers & have ability to encapsulate the lipophilic & hydrophilic drugs & protect them from degradation. The liposomes are used in the sustain release, diagnostic purpose & intracellular delivery systems for peptides/proteins, antisense molecules, DNA & ribozymes. The numbers of problems are associated with the drug molecule such as the bioavailability, stability degradation; site effect can be overcome by incorporating it into liposome.

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