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Liposomes on drug delivery system

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ABSTRACT

Liposomes are result of self assembly of phospholipid in an aqueous media resulting in closed bilayered structures. Liposomes are one of unique delivery system which can be use in controlling and targeting drug delivery system. Liposomes are generally classified mainly based structure, method of preparation, composition and application, conventional liposome's, and specialty liposome. Liposomes are formulated, processed and differ in size, composition, charge and lamellarity, depeg upon method of preparation either active loading technique or passive loading technique. The prepared liposomes are characterized for visual appearance, liposome size distribution, lamellarity, liposome stability, entrapped volume and surface charges. Different liposomal formulations are available in market. The liposomes have many applications which increase its importance over other formulations.

KEY WORDS: bilayered, phospholipid, targeting drug delivery system

INTRODUCTION

Liposome, first described in 1965 and initially as models for studying the biological membranes have been considered more frequently as drug carrires for several drugs tp reduce toxicity or to deliver the drug at site of action. Liposomes are now finding application in commercial development as dosage form. Liposomes are spherical vesicles composed of an aqueous core surrounded by a membrane that is usually composed of phospholipids. Liposomes have a size range from nanometres to micrometers. The composition of the aqueous core as well as a lipid membrane gives the liposome the ability to incorporate both hydrophilic and hydrophobic drugs (Chauhan, 2012; Kant, 2012)

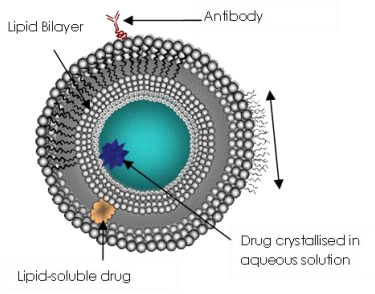

Figure.1.Typical Liposome Structure

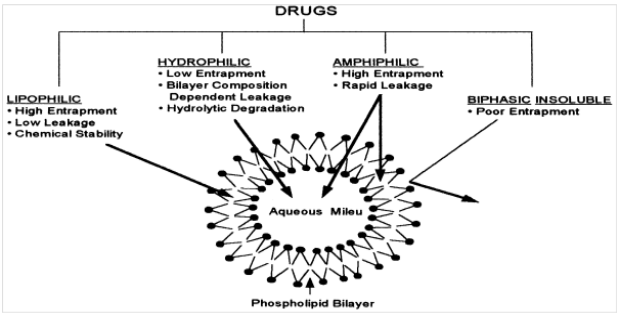

Figure.2.Types of drugs and site of their incorporation into liposomal vesicle

Classification of liposomes (Alving, 1998**):**

Liposomes are classified on the basis of:

A. Structure.
B. Method of preparation.
C. Composition and application.
D. Conventional liposome.
E. Specialty liposome.

Classification Based on Structure:

Table.1.Vesicle Types with their size and number of lipid layers

Vesicle type	Abbreviation	Diameter size	No. of lipid bilayer
Unilamellar	UV	All size ranges	One
Small Unilamellar	SUV	20-40 nm	One
Medium Unilamellar	MUV	40-80 nm	One
Large Unilamellar	LUV	More than 100 nm	One
Giant Unilamellar	GUV	More than 1 µm	One
Oligolamellar	OLV	0.1 – 1 µm	5
Multilamellar	MLV	More than 0.5 µm	5-25
Multi vesicular	MV	More than 1 µm	Multi compartmental structure

Classification based on method of preparation:

Table.2.Different Preparation Methods and the Vesicles Formed by these Methods

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

Classification based on composition and application:

Table.3.Different Liposome with their Compositions

Type of liposome	Abbreviation	Composition
Conventional liposome	CL	Neutral of negatively charge phospholipids and cholesterol
Fusogenic liposome	RSVE	Reconstituted sendai virus enveops
pH sensitive liposomes	-	Phospholipids such as PER or DOPE with either CHEMS or OA
Cationic liposome	-	Cationic lipid with DOPE
Long circulatory liposome	LCL	Neutral high temp, cholesterol and 5-10% PEG, DSP
Immune liposome	IL	CL or LCL with attached monoclonal antibody or recognition sequences

Classification based upon conventional liposome

1. Stabilize natural lecithin (PC) mixtures
2. Synthetic identical, chain phospholipids
3. Glycolipids containing liposome

Classification based upon specialty liposome

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

Materials used for liposome preparation (Chapman, 1974**):**

1. Phospholipids
2. Sphingolipids
3. Sterols
4. Synthetic phospholipids
5. Polymeric materials
6. Polymer bearing lipids
7. Cationic lipids
8. Other substances.

Advantages of liposomes(Deamer, 1980; De Marie, 1994; Crommelin, 1995; Emanuel, 1996**):**

- Provide controlled drug delivery
- Liposomes are biocompatible, completely biodegradable, non toxic and nonimmunogenic..
- Reduced toxicity and increased stability.
- Reduce exposure of sensitive tissues to toxic drugs.
- Enhancement of drug penetration
- Provide sustained release
- Targeted drug delivery or site specific drug delivery
- Alter pharmacokinetics and pharmacodynamics of drug

Disadvantages of liposomes:

- Production cost is high
- Leakage and fusion of encapsulated drug/molecules
- Short half-life

Methods of liposome preparation (Riaz, 1996**):** The correct choice of liposome preparation method depends on the following parameters:

1: The physicochemical characteristics of the material to be entrapped and those of the liposomal ingredients;
2. The nature of the medium in which the lipid vesicles are dispersed.
3. The effective concentration of the entrapped substance and its potential toxicity.
4. Additional processes involved during application/delivery of the vesicles.
5. Optimum size, polydispersity and shelf-life of the vesicles for the intended application; and, batch-to-batch reproducibility and possibility of large-scale production of safe and efficient liposomal product.

Preparation of liposomes (Wen, 2006; Lasic, 1990**):**

The preparation of all types of vesicular systems requires the input of energy generally all the methods of liposome preparation involve three basic stages

1. Drying down of mixture of lipids from an organic solvent.
2. Dispersion of lipids in aqueous media.
3. Separation and purification of resultant liposomes.

Drug can be incorporated intothe aqueous solution or buffer if it is water soluble orincluded in organic solvent if it is hydrophobic.

Applications of liposomes (Emanuel, 1996**):**

- Cancer chemotherapy
- Gene therapy
- Liposomes as carriers for vaccines
- Liposomes as carrier of drug in oral treatment
- Liposomes for topical applications
- Liposomes for pulmonary delivery
- Against Leishmaniasis
- Lysosomal storage disease
- Cell biological application
- Metal storage disease and Ophthalmic delivery of drug.

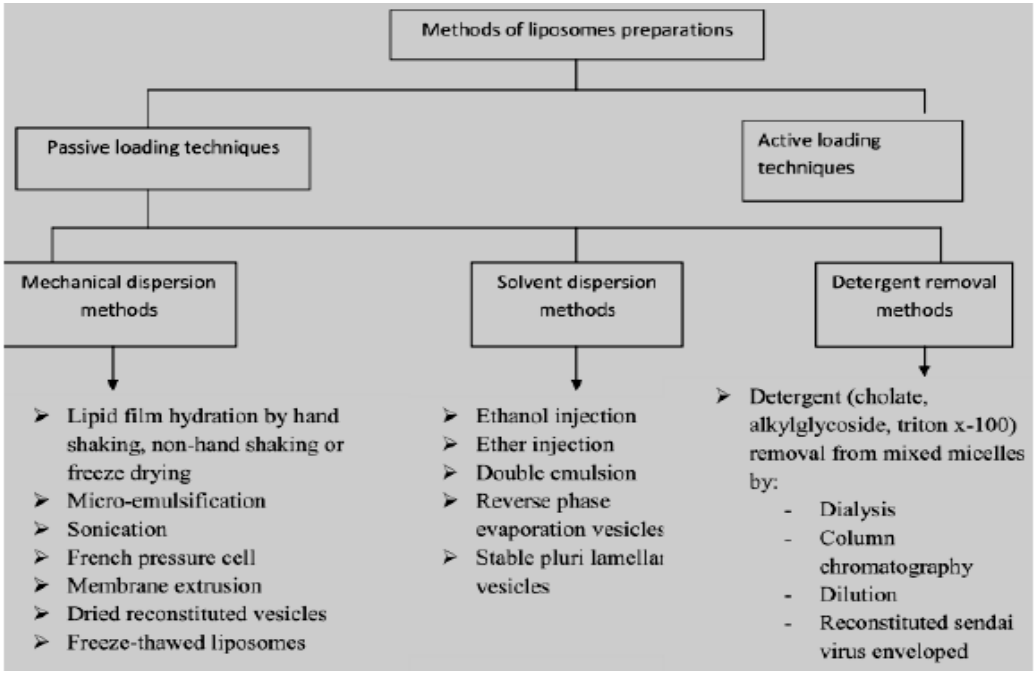

Figure.3.Different methods of liposomes preparations

Table.4.Liposome characterization (Mayhew, 1985)

Characterization parameters	Analytical methods/ instrumentation
Physical Characterization	
Vesicle (Size, shape & Surface morphology, Size distribution)	TEM, Freeze fracture electron microscopy DLS, Zetasizer, TEM, PCR, gel permeation, Exclusion
Surface charge	Free flow electrophoresis
Electric surface potential &pH	Zeta potential measurement, pH Probes
Lamellarity	SAXS, 31NMR, Freeze fracture EM
Phase behavior	DSC, freeze fracture electron microscopy
% Entrapment Efficiency	Minicolumn centrifugation, gel exclusion, ion exachange, protamine aggregation, radiolabelling
Drug release	Diffusion cell/ dialysis
Chemical Characterization	
Concentration	
Phospholipid: Cholestrol: Drug:	Barlett/Stewart assay,HPLC Cholestrol oxidase assay, HPLC Method as in individual monograph
Phospholipid: per oxidation Hydrolysis	UV absorbance, TBA, iodometric, GLC, HPLC, TLC, Fatty Acid Conc.
Cholestrol auto-oxidation	HPLC, TLC
Anti-oxidant degradation	HPLC, TLC
pH	pH meter
Osmolarity	Osmometer
Biological characterization	
Sterility	Aerobic/anaerobic culture
Pyrogenicity	Rabbit fever response(LAL test)
Animal toxicity	Monitoring survival rates, Histopathology

Table.5.Various Marketed Liposomal Formulations (Payne, 1986)

Trade name	Generic name	Application	Company
Ambisome TM	Amphotericin B	Antifungal activity	NeXstar Pharmaceuticals, Inc., CO
Abelcet TM	Amphotericin B	Antifungal activity	The Liposome Company, NJ
Amphotec TM	Amphotericin B	Antifungal activity	Sequus Pharmaceuticals, Inc., C.A.
Doxil	Doxorubicin	Metastatic ovarian cancer and advanced Kaposi's sarcoma	Sequus Pharmaceuticals, Inc., C.A.
Dauno Xome TM	Daunorubicin	Cancers	NeXstar Pharmaceuticals, Inc., CO
MiKasome	Amikacin	Bacterial infections	NeXstar Pharmaceuticals, Inc., CO
DC99	Doxorubicin	Metastatic breast cancer	Liposome Co., NJ, USA
Epaxal	Hepatitis A Vaccine	Hepatitis A	Swiss Serum Institute,Switzerland
ELA-Max	Lidocaine		Biozone Labs, CA, USA
Myocet™	Doxorubicin	Metastatic breast cancer	zeneus
Depocyt	Cytarabine	Neoplastic and lymphomatous meningitis	enzon pharmaceuticals

CONCLUSION

The development of liposomes as carriers for therapeutic molecules is an ever-growing research area. The possibility of modulating the technological characteristics of the vesicles makes them highly versatile both as carriers of several types of drugs (from conventional chemotherapeutics to proteins and peptides) and in therapeutic applications (from cancer therapy to vaccination). In recent years, several important formulations for the treatment of different diseases have been developed. Liposomes allowed a significant vesicular carrier system for therapeutic effectiveness in terms of duration of action and decrease in dose dose frequency and delivering drugs at a higher

efficacy and lower toxicity. They do, hwo ever have limitations and as far as drug delivery goes there seems to be an emphasis on the use of sterically stabilized liposomes.

REFERENCES

Alving CR, Macrophages, as targets for delivery of liposome encapsulated antimicrobial agents, Adv Drug Delivery Rev, (2),1998, 2-4.

Chapman Allison CJ,Gregoriadis AC, Liposomes as immunological adjuvant, Nature, 1974, 252.

ChauhanTikshdeep, Arora Sonia, Parashar Bharat, Chandel Abhishek, Liposome Drug Delivery: A Review, International Journal of Pharmaceutical and Chemical Sciences, 1(3), 2012, 756.

Crommelin JA, Liposomes Lasic DD, Papahadjopoulos D, Liposomes revisited, Science, 267,1995, 1275-6.

Crow JH, Spargo BJ and Crow LM, Proc. Natl. Acad. Sci, USA, 84, 1987, 1537.

De Marie, Janknegt R,Bakker-Woudenberg, Clinical use of liposomal and lipid complexed Amphotericin B, J. Antimicrob. Chemother, 33,1994, 907-16.

Deamer D,Uster P, Liposome preparation methods and monitoring liposome fusion, In:Baserga R ,Croce C,Royeza G(Eds).Introduction of macromolecules into viable mammalian Cells, Alan R. Liss,New York, 1980, 205-20.

Emanuel N,Kedar E,Bolotin EM,Smorodinsky NI,Barenholz Y, Preparation and characterisationbof doxorubicin-loaded sterically stabilised immunoliposomes, Pharm. Res, 13, 1996, 352-9.

Kant Shashi, Kumar Satinder, Prashar Bharat,A complete review on: Liposomes, International Research Journal of Pharmacy, 3(7), 2012, 11-2.

Lalitha K Lende,Grampurohit ND, Gaikwad DD, Gadhave MV, Jadhav SL, A review on:Liposomal Drug Delivery, WJPPS, 1(4), 2012, 1211.

Lasic DD, On the thermodynamic stability of liposomes, J Colloid Interface Sci, 140, 1990;302-4.

Mayhew E, Nikolopoulos GT, King JJ and Siciliano AA, Pharm. Manufacturing, 2, 1985, 18.

Payne NI, Browning I,Hynes CA.J. Pharm. Sci, 75, 1986, 330.

Riaz M, Liposome preparation method, Pakistan Journal of Pharmaceutical Sciences, (1), 1996, 65-77.

Vyas SP, Khar RK, Targeted and controlled drug delivery: Novel carrier systems, Edition 1, CBS Publishers & Distributors, New Delhi, India, 2006, 421-7.

Weiner N, Martin F and Riox M, Liposomes as drug delivery system, Drug Dev Ind Pharm, 15(10), 1989, 1523–54.

Wen AH, Choi MK and Kim DD, Formulation of Liposome for topical Delivery of Arbutin, Arch Pharm Res 29(12), 2006, 1187-92.