

Review Article

Liposomes – A Novel Drug Delivery System

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Abstract: In this review article, discussion was made about liposomes. These are the one amongst the various drug delivery system used to target the drug to particular tissue. Liposomes were spherical shaped vesicles that consist of phospholipids and cholesterol. Due to their size and hydrophobic and lipophilic character they are very promising system for drug delivery. This novel drug delivery system aims to target the drug directly onto the site of action. Liposomes are very biocompatible and stable and they also have unique property to entrap both the hydrophilic drug and the lipophilic drug to its compartment and lead to the controlled release effect. In this article various techniques for the preparation of liposomes, advantages and limitations was discussed in detail. Liposomal gel preparation and evaluation was also elaborated.

Keywords: Drug delivery system using liposomes, Components of liposomes.

INTRODUCTION

Liposome were derived from the two Greek words “Lipos which means fat and Soma means body”. The term liposome means lipid body [1]. It has been derived on the basis of name of sub cellular particles known as ribosome. Because of the structure their similarity between the lipid bilayer and the cell membrane, the liposomes can penetrate effectively and deliver drug such that a free drug would not penetrate. The various other drug delivery devices include niosomes, micro particles, resealed erythrocytes, pharmacosomes etc. Liposomes were first made by A.D Bangham in the early 1960's. Their size ranges from 25 to 500 nm.

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This is a concise picture of various liposome-based products available in the market and liposome technologies which are involved in the development of these products. Liposome-based products which are under ongoing clinical trials as monotherapy or in the combination with other therapies are also covered [3].

Advantages of liposomes

- Liposomes have direct interaction of drug with cell.
- Liposomes are biodegradable and biocompatible.
- Liposomes reduce the exposure of sensitive tissues to toxic drugs.
- It is suitable for delivery of the hydrophobic, amphipathic and hydrophilic drugs.
- Protect the encapsulated drug from the external environment.

Disadvantages of liposomes

- Production cost is high.
- Oxidation of phospholipids may occur.
- It is less stable.
- It has low Solubility.

Structural components of liposomes

There are two components of liposomes. They are

Phospholipids

Glycerol containing phospholipids are most commonly used component of liposome formulation. They represent greater than 50% of weight of lipid in the biological membrane. They are derived from the phosphatidic acid. The back bone of the molecule is the glycerol moiety. At the C3 -OH group is esterified to phosphoric acid. OH at C1 and C2 are esterified with the long chain. Fatty acid gives the lipid nature. One of the remaining OH groups of phosphoric acid may be further esterified to a wide range of organic alcohols including glycerol, choline, ethanol amine, and inositol. Thus, the parent compound of is the phosphoric ester of glycerol [4].

Examples

- Phosphotidyl choline (Lecithin)-PC
- Phosphotidyl ethanolamine (Cephalin)-PE
- Phosphotidyl serine (PS)
- Phosphotidyl inositol (PI)
- Phosphotidyl Glycerol (PG)

Cholesterol

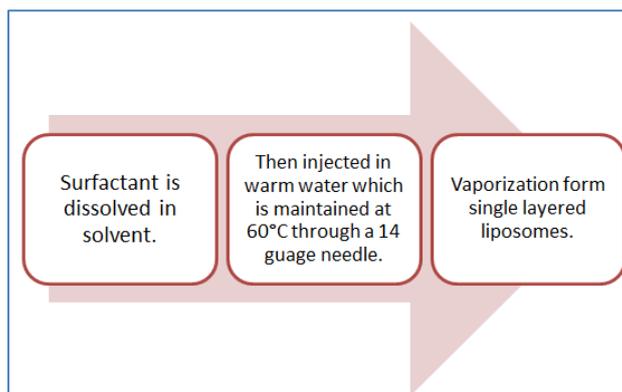
It includes decreasing the fluidity or microviscosity of the bilayer. It reduces the permeability of the membrane to water soluble molecules. It improves the fluidity and stability of biological membrane. The interaction and destabilization of liposomes was prevented by cholesterol [5].

METHODS OF PREPARATION

Ether injection method

In this method Liposomes are slowly introducing the solution of surfactant dissolved in the diethyl ether into warm water maintained at 60°C. The mixture of Ether is injected through 14-gauge needle into an aqueous solution. So vaporization of ether leads to the formation of single layered vesicles. The vesicle ranges from 50-1000nm [6-8].

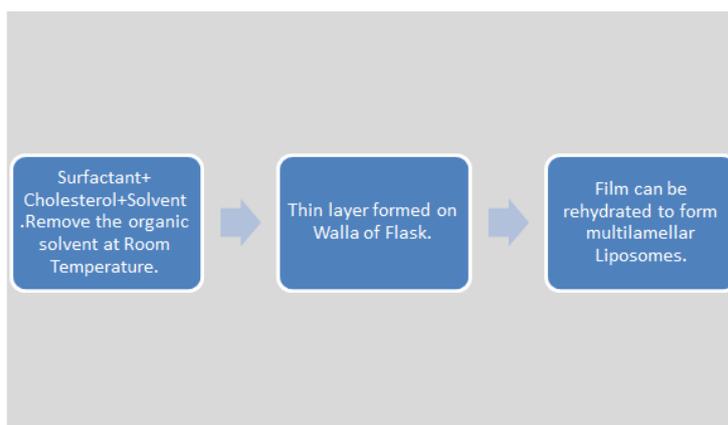
Preparation Method



Thin Film Hydration Technique

The mixture of surfactant and cholesterol are dissolved in a volatile organic solvent (diethyl ether, chloroform or methanol) in a round bottomed flask. The solvent is evaporated at the room temperature (20°C) by using rotary evaporator leaving a thin layer of solid mixture which is deposited on the wall of flask. The dried film could be again rehydrated with aqueous phase at 0-60°C with gentle agitation. This process forms typical multilamellar liposomes[9].

Preparation Method



CHARACTERIZATION OF LIPOSOMES

Determination of Size Distribution, Poly Dispersity Index (PDI) and Zeta Potential

The prepared liposomes are dispersed in deionised water and sonicated for 30 mins. The resultant dispersion was diluted and observed for particle size and zeta values by using Malvern zeta sizer [10].

Drug Content

The suspension equivalent to 5 mg was separately taken into 10ml volumetric flask and the volume was made with methanol to disrupt the vesicles by thoroughly shaking for 10 minutes and from this 0.1 ml of solution was taken and suitable dilutions were made and the concentration of drug was analysed using UV spectrophotometer at 271 nm [11,16].

Entrapment Efficiency

The determination of the entrapped drug is identified by using 50% n-propanol or 0.1% Triton X-100 and analysing the resultant solution by appropriate assay method of drug [12, 15].

Drug Diffusion Studies

The Drug diffusion studies were performed by the using Franz diffusion cell. A known amount of liposomal, ethosomal and transferosomal suspension was separately pipetted out and transferred to the donor compartment and 25 ml of the pH 7.4 Phosphate buffer was taken in the receptor compartment. The temperature and stirring speed was adjusted to 37C and 100 rpm, respectively. At predetermined time intervals of 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 hours aliquots of 5 ml of samples were withdrawn and the same volume was replaced with fresh medium to maintain sink conditions. The samples were further analysed using UV Spectrophotometer at 271 nm [13-18].

Liposomal gel preparation

On the basis of the factorial design approach, the liposome batch (LPE) was selected for the further formulation studies of 13 liposomal gels. Gel was prepared using carbopol® 934 NF. The proper quantity of carbopol 934 powder was dispersed into the distilled water followed by continuous stirring with a glass rod to avoid the formation of in dispersible lumps and then allowed to hydrate for 24 hours at room temperature for swelling. Its formulations were prepared by incorporation of liposome's containing fluconazole were mixed into the carbopol gel with a mechanical stirrer (25 rpm, 2 m). The dispersion was neutralized using 0.5% w/w triethanolamine. Control gels were also made under the same 14 conditions [14, 15, 19-27].

Evaluation of liposomal gels

- PH Measurement Gel: The pH of gel was measured by pH meter.
- Viscosity: Viscosity was determined by Brookfield viscometer, spindle s64.
- Drug Content of Formulated Gels: Drug content was estimated by dissolving 100mg of formulation in methanol and filtered. The volume was made up to 100m; and the absorbance was measured at 212nm.
- In Vitro Diffusion Study: It was carried out by using Franz diffusion cell with cellophane dialysis membrane of grade 110.

Applications of liposomes

- Tumour therapy-Carrier of small cytotoxic molecule and vehicles used for macromolecule such as cytokines.
- Immunological adjuvants in vaccines-Liposomes used in immunoadjuvant, immunodiagnosis.
- Liposomes as protein drug delivery-They are used to enhanced drug solubilisation
- Pulmonary Application –They are useful tools for pulmonary delivery of drugs due to their solubilisation capacity12.
- Site specific targeting-The immunoliposomes are able to recognize and binds to target cells with greater specificity.
- Gene therapy-Liposomes are used widely in gene applications to cure diseases.
- In Cosmetology.

CONCLUSION

Liposomes have been used in the broad range of pharmaceutical applications. They show particular promise as intracellular delivery systems for anti-sense molecules, ribosomes, proteins, and DNA. Liposomes with increased drug delivery to the disease area by ability of long circulation residence times are now reaching the clinical acceptance. Also, liposomes promote the targeting of particular diseased cells within the disease site. Finally, liposomal drugs exhibit reduced toxicities and retain enhanced efficacy compared with other complements. Based on the pharmaceutical applications and the available products, the liposomes have definitely established their position in modern delivery systems also.

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