Review article

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A MINI REVIEW: LIPOSOMES

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ABSTRACT

In mid-60s, liposomes were introduced by Bangham and coworker. Liposomes is a spherical shaped vesicles with layers of phospholipid bilayer. The phospholipid bilayer consists of hydrophilic head and hydrophobic tail. Nowadays, liposomes consist of many function.The invention of liposome is to optimise several properties such as control release of drug, prolong the duration of drug in body, slower the clearance of drug from body, triggered release and deliver of DNA substances. One of the significant function of liposome is it act as Novel Drug Delivery System (NDDS). The aims of NDDS is to delivery active drug at the rate that needed by human body and stay inside of body for extended period of time. Drugs are formulated as liposomes is to increase the therapeutic range of the drugs. The reason liposomal drug is advance than free drug is because the liposome contain of phospholipid bilayer which is alike to the cell membrane. Hence, the delivery of liposome to the body can be done effectively. The formulations of liposomes have progressed from the conventional liposome (first generation) to advance generation liposome (second generation). There are many variety of liposomes, it can be unilamellar vesicles, multimellar vesicles and giant unilamellar vesicles. This review is majorly discuss about the classification of liposomes, formation of liposomes, method of preparation of liposomes, stability of liposomes, advantages and disadvantages of liposomes.

Keywords: Liposomes, Classification of liposome, Formation of liposome

INTRODUCTION

In 1965, Bangham and his coworker discovered the first liposomal product which is Doxil®. [1] They have stated that liposomes are small sized, sphere-shaped vesicles consist of phospholipid bilayer which is made up by cholesterol, non toxic phospholipid and surfactant. Liposomes have phospholipid bilayer, this make the transport of drug to be easy. Because the nature of phospholipid that is amphipatic that contain hydrophobic and hydrophilic nature in aqeous solution. The phospholipid bilayers membranes of liposomes are able to generate spherical structure with hydophilic compartment internally when the lipsomes are introduced in hydrophilic solution. The hydrophilic drug is stored in centre of the liposome and hydrophobic drug is stored in hydrophobic region in the liposome. [2]

The types components that made up the phospholipid bilayer of liposome will affect the rigidity, fluidity, stability and charge of the bilayer. For example, unsaturated phosphatidycholine species such as from protein of natural source (egg or soybean) will produce the liposomes that have phospholipid bilayer that more permeable but less stable. On the other hand, long acyl chains in phospholipid bilayer will form a rigid but impermeable phospholipid bilayer. [3]

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CLASSIFICATION OF LIPOSOME

Generally, liposome is classified into 2 classes based on number and size bilayer.

(1) Multilamellar vesicles (MLV).

(2) Unilamellar.

Then, unilamellar vesicle is then classified into Large Unilamellar Vesicles (LUV) (0.1-20µm) and Small Unilamellar Vesicles (SUV) (25-100nm). [6]

Then, liposome is classified based on the chemical composition.

As, Conventional Liposomes (CL), pH-responsive liposomes, cation liposomes, long circulating liposomes and immuno-liposomes. Next, liposome classified as method of preparation which is reverse phase evaporation vesicles (REV), Ether Injection Vesicles (EIV) and French press vesicles (FPV). [4]

FORMATION OF LIPOSOME

Phospholipid bilayer formation is due to the uncomfortable interaction between hydrophobic and hydrophilic phase. The uncomfortable interaction

problem can be solved by folding hydrophobic and hydrophilic phase into closed vesicles. The other reason for formation of bilayer is when the bilayer is in closed concrete vesicle, the surface tension will be minimize and stability can be achieved. [4]

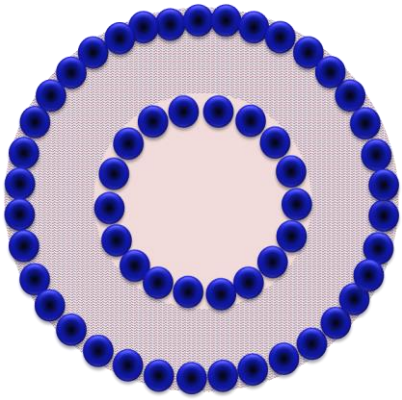

Figure 1: Very Small, Single Layer liposome

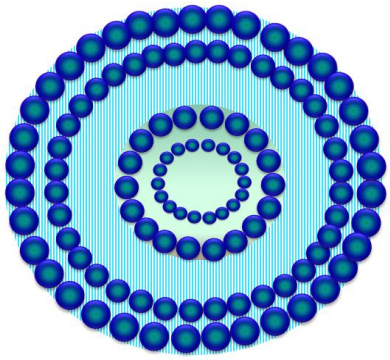

Figure 2: Large Vesicle, Multilayer Liposome [10]

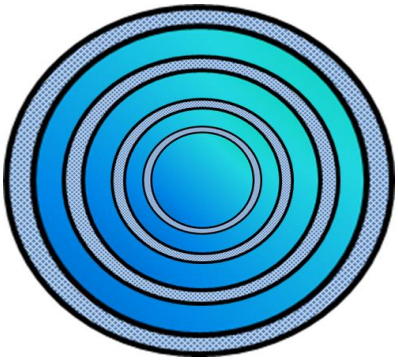

Figure 3: Multilayer Liposome (MLV)

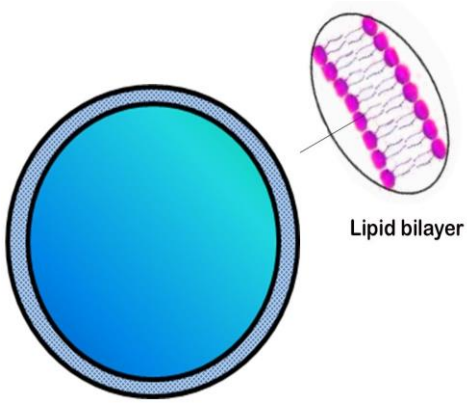

Figure 4: Large Unilamellar Vesicle (LUV)

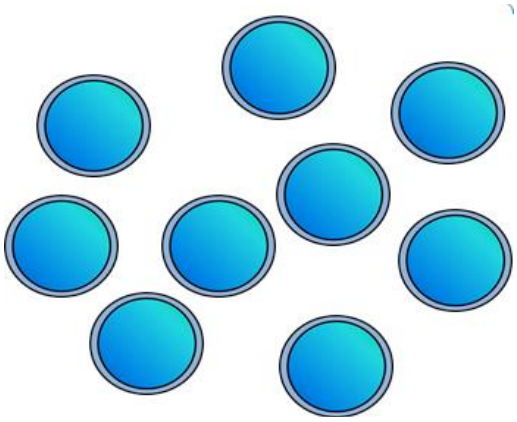

Figure 5: Small Unilamellar Vesicle (SUV)

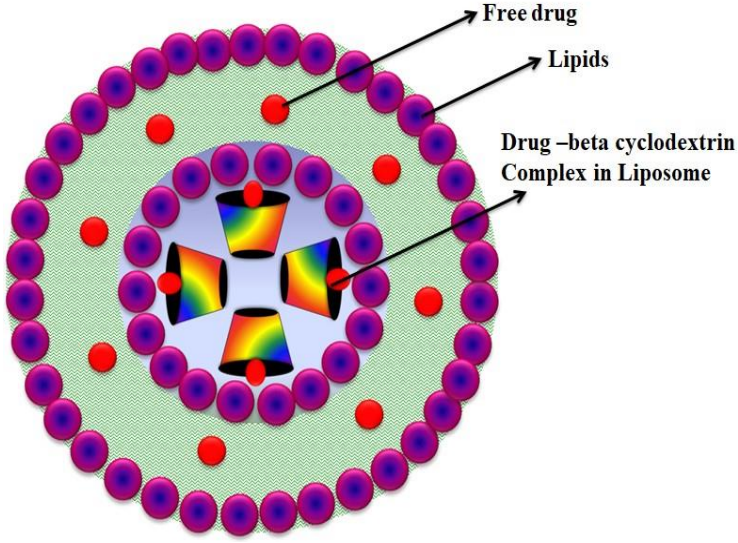

Figure 6: Structure of drug -beta cyclodextrin in liposome

Main group of phospholipids use for liposome preparation:

- ✓ Phospholipid from natural sources.
- ✓ Phospholipid modified from natural sources.
- ✓ Semi-synthetic phospholipid.
- ✓ Fully-synthetic phospholipid,
- ✓ Phospholipid with non-natural head groups. [14]

PREPARATION OF LIPOSOME

Liposome can be formed by general method preparation and specific methods preparation.

The basic stages for liposome preparation is divided into 4 general steps.

(a) Dissolve the lipids in organic solvent

(b) Lipid is added in aqueous media.

(c) Purifying the resultant lipsome

(d) Evaluate the final product.

Organic solvent is used to dissolve the lipid. Then let the solvent to dry up. It will leave a small film of the lipids on the surface of the wall of container. Lipid is added with aqueous solution. The mixture of the solution is stirred aggressively.

Multi lamellar vesicle is obtained. Then MLVs are undergo sonicate to become SUVs. Then SUVs are sonicate again and undergo evaporation to get LUVs. During SUVs, drug can be dissolved in the aqueous solution. If the drug is hydrophilic then it can be added directly but if the drug is hydrophobic then organic solvent have to be included while adding. [5]

Among all type of preparation, thin-film preparation is the most easy way and many people use this method. [11]

TYPES OF SONICATION

Probe sonication:

The tip of sonicator is straight away in contact with the liposomal solution. Hence, the energy is very high and will give rise in temperature of the solution.

It has the greater rish of contamination as the tip of sonicator is straight away is immerse into the liposomal solution.

Bath sonication:

The control of temperature of liposomal solution is more easy. (1) Stealth liposomes Stealth liposomes is liposomes that coated by polyethylene glycol (PEG). PEG is a synthetic water loving polymer.

PEG coating function is to enhance the stability and the half-life of liposomes. PEG coating will avoid liposome recognition by reticuloendothelial system (RES) by prevent protein adsorption and opsonization of liposomes. [7]

In stealth liposomes, the active drug molecules are attached to the PEG. This makes liposomes become more stable, increase the safety, and increase efficacy.

PEGylation is the process in making stealth liposome. [12]

Advantages of liposomes

- ✓ Liposomes can act effectively in distribution throughout human body and target to specific receptors.
- ✓ Liposomes can protect drug from degradation.
- ✓ Liposomes is fastly absorb by mononuclear phagocyte system (MPS). [8]
- ✓ Increase solubility of hydrophobic drugs and amphiphilic drugs.
- ✓ Sustained release form and can act locally.
- ✓ Can transfer hydrophilic drug in rapid manner,
- ✓ Good penetration into body tissue.
- ✓ Site-avoidance mechanism. [1]

Disadvantages of liposomes

- ✓ Cost to produce is high. Because price for raw material is high.
- ✓ Need professional to produce.
- ✓ Equipment to produce liposomes is costly. [9]

Liposomes targeting Liposomes have 2 types of targeting which is passive targeting and active targeting. In passive targeting, the liposome administered to the body is rapidly metabolize in blood and absorbed by reticuloendothelial system in liver spleen. Then, macrophages are exploited when liposomes is target to the antigens to macrophages as initial step in the range of immunity.

In active targeting, the targeting agents is target to the surface of liposomal such that the interaction with the target. [13]

Stealth liposomes are liposomes that suitable targeting to target cell by active targeting. This is because stealth liposomes with PEG coating have protective hydrophilic layer and prolonged circulation time. [15]

CONCLUSION

It is obvious that liposomes bring plenty of benefits to pharmaceutical industry. Liposomes bring improvement to drug delivery system. The uses of liposomes include of chemo-therapy, gene therapy, vaccines with liposomes as carrier, oral intake drug with liposomes as carrier, topical applications with liposomes as carrier, aerosol drug (pulmonary delivery drug) with liposomes, metal storage disease

and so on. [5] It is believe that in the future liposomes will have a great improvement in delivery of drug.

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