Stability of Liposomes Produced Using Phospholipids by the Conventional (Film) Method

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Abstract:
Liposomes were produced using the conventional (film) method and the effect of pH on the liposome size was investigated using the Dynamic Light Scattering (DLS) method and fluorescent microscope. The mean sizes of liposomes prepared at pH 5, 8 and 11 were initially in the range of 110 to 150 nm and reduced with time over a period of one week.

1 Introduction
Liposomes are phospholipid-bilayer structures with an aqueous core. They have been used for a wide range of applications in the pharmaceutical and cosmetic industries, including the controlled release of drugs, gene delivery and as model cells. They have therapeutic advantages, such as the ability to deliver large amounts of drugs to specific sites, spare healthy tissue from toxic effects and increase the systematic circulation time of the drug [Erika et al. 2002]. Specific accumulation of liposomal substances in tumor cells may be achieved by attachment of targeting agents to the liposome surface. There are several methods of producing liposomes such as conventional method, extrusion technique [Bangham et al., 1964], supercritical reverse phase evaporation method [Otake et al., 2006], and coacervation (phase separation) technique [Ishii et al., 1995]. Most of these techniques produce symmetric membrane liposomes where the composition of inner and outer leaflets of the bilayer are identical.

The physical stability of liposomes at various pHs are affected due to loss of core material caused by leaking vesicle aggregation and fusion. Hence the stability of liposomes can be determined by investigating the changes in the average particle size and size distribution.

Changes in the average particle size and size distributions of liposomes are strongly affected by (phospho) lipid composition, medium composition and pH. Liposomes which lack a net electrical charge tend to aggregate more the than charged liposomes. Thus, aggregation can be prevented or slowed down by incorporation of a charge carrying lipid into the liposomal formulation.

2 Objectives
The overall objective of this study was to investigate the effect of pH on the stability of liposome dispersions.

3 Production of Liposomes

DOTAP (1,2-dioleoyl-3-trimethylammonium-propane) lipid was obtained in chloroform from Avanti Lipids. Liposomes were prepared using the film technique.

4 Analysis and Discussions

Particle size distribution was measured for both the inverse emulsion and the liposomes using the dynamic light scattering device (Malvern ZET 5004). Emulsion and liposome images were taken using a horizontally mounted Nikon Optiphot-2 epifluorescence microscope equipped with a QImaging QICAM Fast 12-bit color camera and Prior ProScan II automated stage (Fig 1). Initial size of liposomes measured using DLS were 145 nm, 113 nm and 123 nm at pH of 5,8 and 11 respectively(Fig 2).

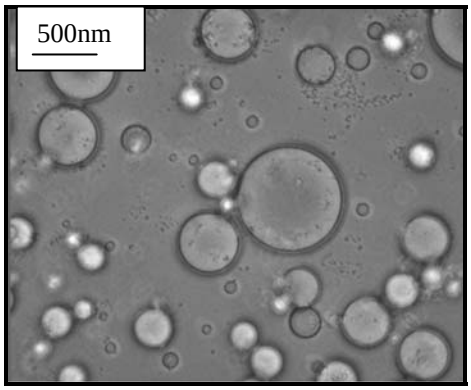

Fig 1: Liposomes produced using film technique (Contrast Fluorescent Microscope)

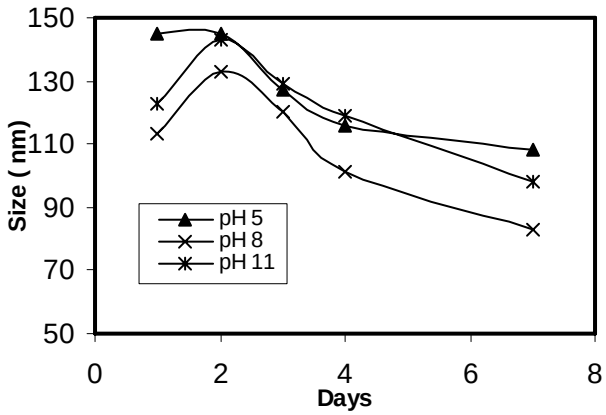

Fig 2: pH Stability of liposomes for a period of a week

5 Conclusions

The mean sizes of liposomes reduced from 145 nm, 113 nm and 123 nm to 108 nm, 83 nm and 98 nm at pH 5, 8 and 11 respectively in 7 days.

6 Acknowledgements

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7 References

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