CHAPTER I

INTRODUCTION

Phospholipids , proteins and water are the major components of cell membrane. Among those, phospholipids are commonly considered as the structurally determining constituents of biological membranes. This view is supported by the fact that phospholipids when disperse in aqueous media can form a variety of highly organized structures simultaneously . Such structures consist of lamellar bilayers separated by layers of water and are called *liposomes* . Water content and temperature mostly affect an organization of liposomal structures. In lipid bilayers, hydrocarbon chains are interacting hydrophobically and lipid polar headgroups are facing water. Most models of biological membranes postulate a lipid bilayer or liposome as an essential building unit of the membrane.

The presence of striking similarities between liposomes and biological cells has stimulated researchers to use the liposomal system as an experimental model for biomembranes. General rules on selective permeability with respect to molecular size and polarity can be deduced from studies on the swelling and shrinkage behavior of liposomes in solution of various solutes. These rules resemble very much to those found for biomembranes. Furthermore, temperature effects on

several of these permeability processes appear to be identical when pure lipid bilayers are compared to biomembranes. These results support the hypothesis that lipid bilayers determine to a large extent the barrier function of the biomembranes . It is a well known fact that the chemical composition of biomembranes is generally quite complicated. Fortunately, therefore, the liposome systems offer possibilities for studying the molecular interactions and barrier functions of isolated and selected membrane constituents because other components such as cholesterols, fatty acids as well as proteins can be used and incorporated easily to lipid bilayers in exact ratio.

Besides phospholipids, a major lipid constituent of many biological membranes, in particular the surface membrane of mammalian cells, is cholesterol. The major sterol in such cells is cholest-5-en-3β-ol .Mammalian cell membranes such as liver plasma membranes, erythrocyte membranes and myelin sheath contain high levels of cholesterol : phospholipid in molar ratio of 0.83, 0.90 and 1.32, respectively. The sterol to lipid ratio of 1:1 is normally found to be the limiting amount of sterol which can be associated with lecithin in liposomal structures prepared by sonication method. It has been shown by X - ray diffraction study when molar ratio is beyond 1:1 that cholesterol appears in a crystalline form and clusters of pure cholesterol can readily be observed, [Demel, R.A. and De. Kruyff, B. 1976].

Magnetic resonance technique is one of the physical techniques for studying cholesterol containing lipid bilayers and results obtained from such technique have suggested that cholesterol shows a structural role in stabilizing the membrane fluidity depending on temperature and fatty acid compositions [Marsh, D. and Ian, G. P. S., 1973; Mantripragada, B. S. and Thompson, E. T., 1990]. From various studies there should be concluded that, cholesterol fluidizes the gel phase and has a condensing effect on the liquid crystalline phase of lipid bilayers.

The difference of the cholesterol effects on lecithins above and below their liquid crystalline transition is found to arise from the different effect of cholesterol on the packing of the bilayers supported by the cholestane spin probe separation in an experiment of Marsh, D and Ian, G.P.S.; (1973). Moreover, cholesterol level in the cell surfaces may thus be implemented to regulate normal and abnormal cell growth and differentiation processes.

Many functional changes in mammalian cell appear to be mediated through the cell membrane.It has been expressed that many biological problems concern possible modulation of membrane properties by fluidity changes consequent on interaction with small molecules or with protein [Alister, E.M. et al., 1976].

The fluidity of the lipid bilayer component of biological membranes has been shown by many studies to influence a variety of membrane function in the following.

Grof, P. and Belagyi, J. (1983) had shown by using the spin - labelling technique that local anaesthetics interacted strongly with the polar headgroups of the phospholipid chains and produced an increase of the fluidity of the membrane.

Study on ESR of the membrane organization of erythrocytes from patients with Düchenne muscular dystrophy had been performed by Sato, B. and his coworker (1978) and they suggested that the fluidity of these membranes was similar to those of normal eryhrocytes when investigated near the polar region, however, was quite different in non polar region.

Moreover, fluorescence polarization of 1,6-diphenyl-1,3,5-hexatriene (DPH) was used to study the interaction of DDT with model and native membranes, [Madeira, M.C.A. and Madeira, M.C.V. ; 1990]. In the experiment, cholesterol induced ordering effect in DMPC bilayer, however, cholesterol concentration up to 30 mole % or more did not prevent insecticide interaction of DDT which produced fluidizing effect eventhough DDT did not disturb the fluid native membranes, it disordered membranes enriched cholesterol.

In recent years, Sarkar, N.S. et al. (1993) had indicated that fenvalerate, a commonly used pyrethroid insecticide, was found to decrease the DPH fluorescence polarization value of synaptosomal and microsomal membrane. This effect was implied that it made the membrane more fluid supported by DSC thermogram profile and shown that the acyl chain region of the lipid possibly between C_{10} and C_{16} region was weakened .

From these studies, it is ascertained that fluidity is one of the prerequisite and important parameters for maintaining membrane properties .