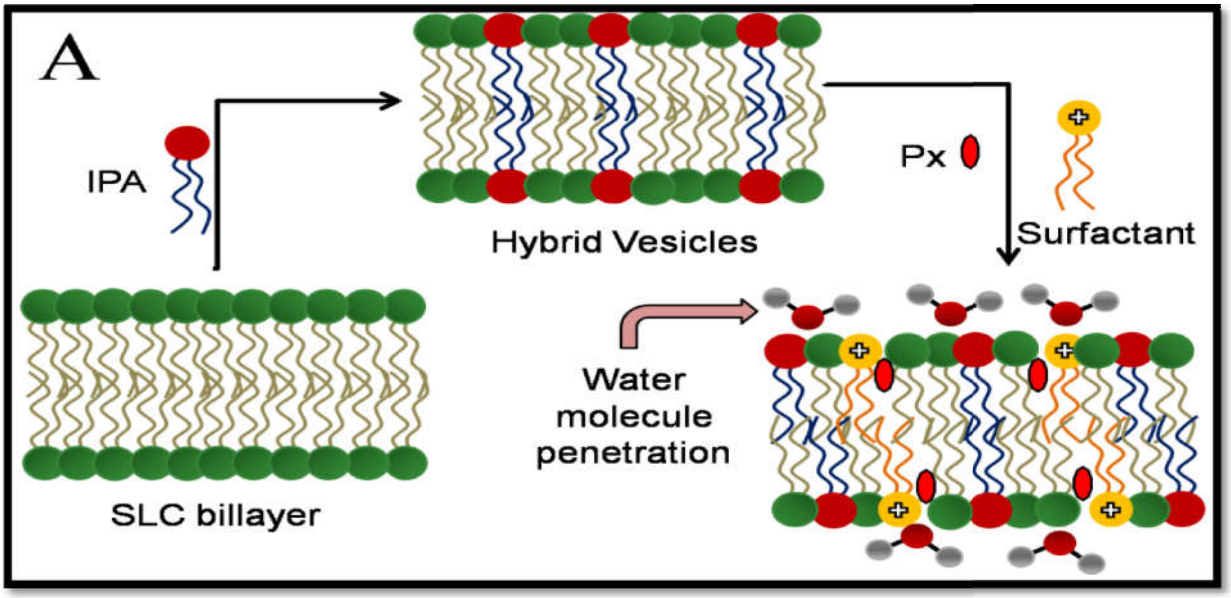
ABSTRACT

The research work embodied in this thesis entitled **"PHYSICOCHEMICAL STUDIES ON LIPOSOME MIMETIC SYSTEMS AND THEIR COMPLEXES WITH BIOLOGICALLY RELEVANT POLYMERS"** is primarily focused on to develop stable, non toxic and biodegradable drug delivery medium, viz liposome mimetic system, known as vesicles with the aid of naturally occurring phospholipids soylecithin (SLC) and synthetic amphiphiles. Finally their interaction with biological macromolecules like dendrimer has been investigated. The whole thesis work is divided into three chapters and their brief discussion is given below.

Chapter I describes the physicochemical characterization of vesicles. vesicles were prepared at different ratio of soylecithin (SLC) and IPA with additional30 mol% cholesterol (with respect to SLC and IPA) in PBS. Impact of IPA on SLC monomolecular film was studied by Langmuir monolayer technique (surface pressure – area isotherms). Hydrodynamic size (d_h), zeta potential (Z. P.) and polydispersity index (PDI) which describes the dispersion behaviour vesicles were measured through dynamic light scattering (DLS) technique. Vesicles Morphological properties also successfully recognized by electron microscopic (normal TEM as well as FF-TEM) studies. Thermotropic behaviours of the bilayers were scrutinized by differential scanning calorimetry (DSC). Structural changes of bilayer, caused by IPA, were further scrutinized by using fluorescence spectroscopy using 1, 6-diphenyl-1, 3, 5-hexatriene (DPH) and 7-hydroxycoumarin (7HC) as the fluorescent probes to get knowledge about the micro viscosity of the bilayer wall. Entrapment efficiency (E. E.) of the vesicles using cationic dye methylene blue (MB) was also evaluated. Such systems are expected to have superior properties as potent vectors for drug delivery.

Chapter II illustrates physicochemical investigation on cationic hybrid vesicles and its toxicity relate to Neuroblastoma cell line. As biological cell membranes are

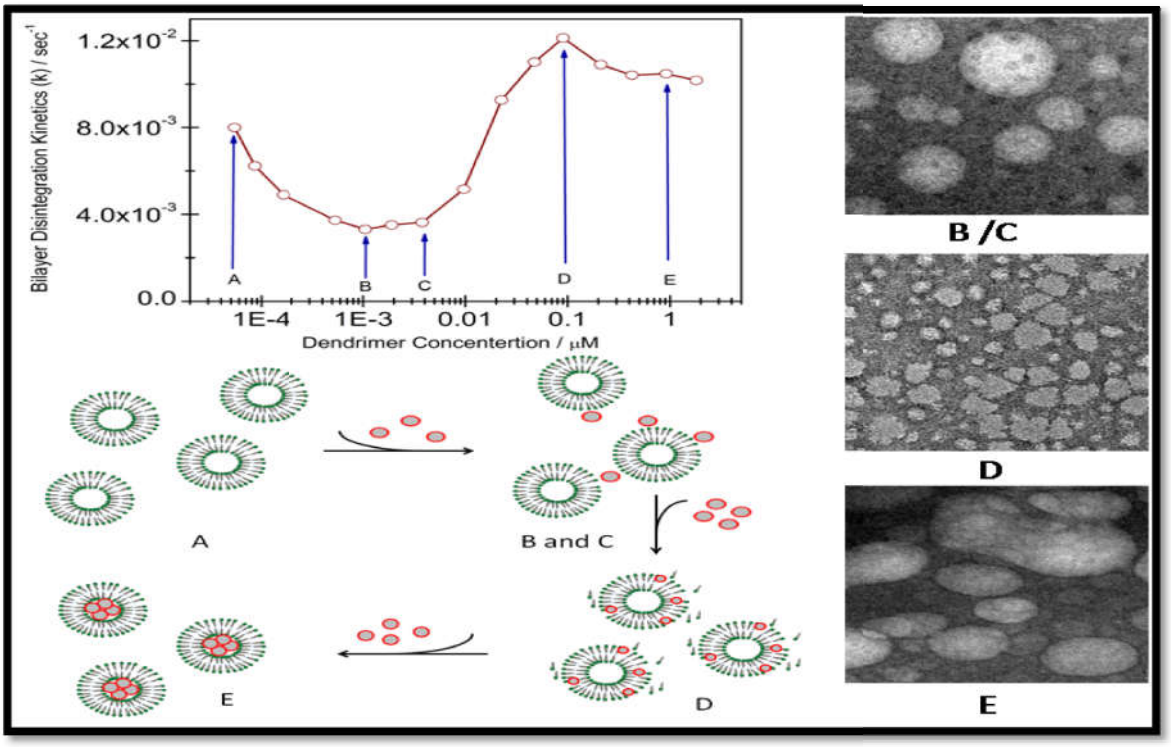
negatively charged, non-toxic, biodegradable vesicles could be served as an excellent drug delivery agent. Cationic vesicles were prepared using bi-tail cationic surfactants with varying hydrocarbon chain length (bis-C_{12} to C_{18}) in combination with soy lecithin (SLC) and ion pair amphiphile (IPA). Bi-tail cationic surfactants were chosen to progressively substitute with previously established three sets of SLC/IPA combinations (1:0, HCV1; 9:1, HCV2 and 7:3, HCV3; M/M). Interaction between hybrid membrane and Piroxicame (Px), a Non Steroidal anti inflammatory Drug were analyzed in the form of monolayer, bilayer and solid supported bilayer.



Finally optimised Px encapsulated formulations were analysed for biological activity. Mutual miscibilities among the components were studied by way of the surface pressure – area measurements. Physicochemical characterizations of the different hybrid vesicles with and without Px were assessed by combined dynamic light scattering, zeta potential, electron microscopy, atomic force microscopy, differential scanning calorimetry, FTIR, UV-VIS absorption and emission sepctroscopic studies. Entrapment efficiency and the release kinetics of Px from the vesicles were analyzed by conventional dialysis bag approach. Finally the toxicity and biocompatiblity of the drug loaded formulations were assessed. And could shed

further light in the development of drug delivery systems in the treatment of brain – tumors targeted drug delivery.

Chapter III presents the physic-chemistry between the interaction of cationic vesicles and PAMAM succinimaci acid, 1, 4-diaminobutane core dendrimers generation 5 (G5-SA) which is negatively charged. Previously prepared cationic vesicle comprised of SLC, IPA and DHDAB in three different combinations was taken to investigate the impact of dendrimers. Increasing hydro dynamic size and reduced Z. P. measurement suggests the formation of vesicles/dendrimers aggregates. The formation of aggregates was further confirmed by turbidity measurement. Morphological state of the vesicles with and without dendrimers was analysed via TEM studies. Vesicles disintegration kinetics measurement also has been done to understand the pattern of interaction using varying concentration of dendrimers. A surface pressure – time isotherm developed due to the vesicle disintegration upon the inclusion of dendrimer. The rate kinetics of such disintegration process was found to be depending on the dendrimers concentration.



The effect of dendrimers on solid supported cationic bilayer was further scrutinized via AFM studies that help to understand stoichiometry depended aggregate formation. Finally DSC studies was performed which specifically enlighten the features of bilayer in presence of dendrimers as well it describe the point of interaction induced by dendrimer on the bilayer region. Steady state fluorescence anisotropy measurements also lead us to recognize that at lower concentration, dendrimer porn to attack on the surface of the bilayer and thereby rigidify membrane packing. However at higher concentration, it interdigited into the bilayer segment. Overall interaction studies put IPA on the map as it tries to restore the bilayer morphology by providing hydrophobic interaction. Bilayer embedded dendrimer forms supramolecular aggregates that can be promoted in the field of drug, gene, and vaccine delivery.