SUMMARY AND CONCLUSIONS

Physicochemical properties of different liposomes, *viz.*, size, PDI, surface charge, thermal behavior, and membrane micro viscosity as well as their encapsulation efficiency and release behavior of curcumin were pronouncedly influenced by liposome composition along with pH and temperature of the medium. All the studied liposomes (SPC, DPPC, DPPG and DPPC+DPPG) were found to be stable in terms of size, PDI and zeta potential values. Size of liposomes did not vary significantly with temperature in terms of composition, albeit the minimum size was evidenced at ~40°C corresponding to phase transition temperature of the saturated phospholipids. All the systems turned out to be more rigid with increasing acidity of the medium as revealed from DSC results; this was due to increased hydrogen bonding among phospholipid molecules. Maximum anisotropy value of curcumin for SPC liposome reflected its higher binding affinity compared to the other systems. Increase in membrane microviscosity of the vesicles (except DPPC) with the rise in pH of the medium could be rationalized on the basis of the ionizing tendency of curcumin in basic environment and its ability (in neutral form) to disrupt bilayer packing at high concentration. Entrapment efficiency, however decreased with increasing pH of the medium due to the acidic nature of drug. Entrapment efficiency and release kinetics studies revealed opposite phenomenon with respect to liposome composition. SPC exhibited fastest drug release and lowest entrapment efficiency owing to its fluid nature. Curcumin loaded liposomes exhibited pronounced antibacterial activity against the Gram positive bacteria *Bacillus amyloliquefaciens*. Experimental evidences led to conclude that the optimization of the lipid composition and formulation conditions like pH is necessary to prepare liposomes with enhanced stability and efficient drug carrier property. *In vivo* studies of the curcumin loaded liposomes, to evaluate different pharmacokinetic parameters, could be considered as one of the future perspectives.

Studies on the interaction of 2G, 4G and 6G PAMAM dendrimers with different liposome substrates were done using absorbance, size analysis, zeta potential measurements and AFM measurements on solid supported bilayers. Increase in absorbance and size of the liposome is due to the adhesion of the individual liposomes, where the dendrimers acted as “glue”. Maxima in the absorbance and size were due to the maximum adhesion of liposomes, after which

the size decreases, due to the formation of liposome dendrimers complexes, probably "dendriosomes". Charge reversal during the zeta potential measurements reveal the electrostatic interaction among the liposome and dendrimers, which are significant when they are opposite in terms of surface charge. Further enhancement of zeta potential due to dendrimer addition was due to hydrogen bond/ hydrophobic interactions. Bilayer disruption of vesicles was observed upon addition of dendrimer to negatively charged surface of liposomes, as revealed by AFM measurements.

The manuscript describes the interaction between negatively charged liposomes with cationic PAMAM dendrimer and also to study the different biophysical properties of dendrimer-liposome aggregates. The type and strength of the interaction is dependent on charge and size of the liposomes as well as the dendrimer generation. The larger size of DHP+DPPC, DPP+DPPC and DPPEth+DPPC in the gel state than for DMPG+DPPC in the same state is rationalized through the lateral packing of lipid molecules within the membrane, due to the stronger van der Waals interactions between the hydrocarbon chains. Zeta potential of the liposome depends on the electron density on phosphate group of phospholipids and head group moietyof phosphate group [DHP, -H; DMPG, $-CH_2CH(OH)CH_2OH$; DPP, -H; DPPEth, $-CH_2CH_3$]. Here all the liposomes have net negative charges, thus the electrostatic interactions with the cationic dendrimers play an important role. The higher generation dendrimers causes greater disturbances in a lipid bilayer and interacts more effectively with liposomes. The formation of dendrimer-liposome aggregates by higher concentrations of dendrimers were also visualized by TEM, FF-TEM and AFM studies. The increase in the fluorescence anisotropy shows that the liposomal membranes become more rigid, reflecting the fact that dendrimers had probably moved into the liposome bilayer via palisade layer. The differential scanning calorimetry and fluorescence anisotropy showed that the dendrimers interact not only with the hydrophilic part of the membranes but also the hydrocarbon chain. The binding constant for the formation of dendrimer-liposome aggregates depends on the head group moiety of the liposome and the generation of the dendrimers. The cytotoxicity and hemolysis results show that liposomes and dendrimer-liposome complexes are non-toxic in healthy human blood cell lymphocyte as well as human RBCs. In conclusion, it is clear that the exploration of the dendrimer-liposome aggregates as a potential drug carrier has significant perspectives.

DPPC and negatively charged lipids in different sets of combination were used to prepare stable liposome dispersions. Through the comprehensive investigation on the impact of negatively charged lipid on the zwitterionic DPPC were evaluated from monolayer studies where it was concluded that anionic lipids exerts prominent influence on DPPC monolayer. Associative interactions were found for some specific composition; however, the system with 30 mol % anionic lipids did respond to produce stable liposome dispersions. Other lipid combinations were unable to form stable monolayer. This was further scrutinized by measuring as reflected through the existence of positive deviation the Gibbs free energy, found relatively less stable monolayer other than the 30 mole% comprising anionic lipids. Binary monolayer formation was also dependent on lipid composition. In case DMPG, it forms more stable mixed monolayer than the other anionic lipids. The lift-off area of DHP and DPPEth is lower than that of other lipids due directly connected with phosphate group. Also the bilayer disintegration kinetics were explored for stable liposomal systems DPPC and anionic lipids in molar ratio (7:3). Disintegration of bilayer to the interracially adsorbed monolayer also depended on lipid composition. In case of DMPG, due to presence of hydroxyl group it form intra or inter molecular hydrogen bonding. Thus DMPG lipid takes more time to disintegrate. However two shed further lights on the structure on the adsorbed monolayer, investigations like the Brewster angle microscopy (BAM) and polarization modulation infrared reflection-adsorption spectroscopy (PMIRRAS) and atomic force microscopy (AFM) studies are important. This would eventually shed lights on the structure of aggregates at the microscopic level as well as the molecular structures in these aggregates. These are considered to be the future perspectives.