SUMMARY AND CONCLUSION

Detail studies involving the composition, functionality and structure of the adsorbed BLES films in the absence and presence of three additives, *viz.*, cholesterol, low density lipoprotein (LDL) and serum protein were performed. The study includes the pathophysiological amount of these materials found in lungs in disease. The additives altered the bilayer and film packing, surface activity and structures of surfactant, suggesting possible molecular rearrangement and disordering of surfactant in disease. Since excess cholesterol or its esters may actually arrive inside the lung through LDL transport, it is cholesterol that is the most potent inactivator of LS, than leaked soluble serum proteins, since lipids are far more hydrophobic and more difficult to remove from films during dynamic cycling. Whole serum, serum proteins and its lipid components may specifically interact with the surfactant films and bilayers by either separate mechanisms, or synergistically. In future studies, specific lipid components of serum such as HDL, one of the major studies requires the specific separation of serum lipid and serum protein fractions and observing their structure function correlations in inactivating surfactant. The specific molecular rearrangements observed in our study of domains in films need to be further explored in detecting the exact composition of the variety of domain structures using possibly fluorescently labeled cholesterol, LDL and serum proteins. However these studies need to be conducted in a manner using similar sets of biophysical methods which yield structure function correlates of bilayers and films, as well as uses pathophysiological amounts of materials, so that an over simplification of the models in previous studies can be rectified.

While considering the lipids mixtures as novel drug delivery system, nanostructured lipid carriers (NLCs) were formulated by using Span 65, soy lecithin and stearic acid dispersed in aqueous Tween 40 or Tween 60 solution. Tween 60 provides better stabilization than Tween 40 because of its longer hydrocarbon chain. Hydrocarbon chains of Tween 60 could penetrate to greater extent than Tween 40 into the NLC matrices. TEM study confirmed the spherical morphology of the NLCs with smooth surface. Higher amount of LIDO could be

encapsulated into the NLC than PRO.HCl. LIDO resides in the core of the NLC for its relatively higher hydrophobic nature. PRO.HCl, being ionic, preferentially adsorbs over the NLC surface. Apart from the DLS studies, DSC and spectroscopic investigations on the drug loaded NLC further supported such proposition. Because of its larger lipophilicity LIDO could be entrapped to greater extent compared to PRO.HCl. *In vitro* drug release study revealed that the lipidic matrices could act as promising vehicles for two most widely used local anaesthetics with controlled and prolonged release. Biphasic release behaviour was experienced by all the combinations. In order to further explore the viability, the formulations may be subjected to *in vitro* studies under biological condition. Besides, the *in vivo* studies as well as some clinical trials are warranted which are considered as the future perspectives.

The impact of saturation and unsaturation in the fatty acyl hydrocarbon chain on the physicochemical properties of nanostructured lipid carriers (NLCs) was investigated to develop delivery systems loaded with the anticancer drug, ursolic acid (UA). The findings reveal the influence of saturated and unsaturated lipids and fatty acids on the particle size, polydispersity index, ζ potential, encapsulation efficiency, *in vitro* release behavior and *in vitro* cytotoxicity of the formulations. The studies of surface pressure (π) − area (A) isotherms of pure components, mixed lipids, and mixed lipids with ursolic acid suggest that ursolic acid alters the interfacial organization of lipids. The spherical morphology of NLCs with a smooth surface was observed for all the formulations. Significant differences in crystal structure between NLCs comprising saturated and unsaturated lipids were noted, whereby the crystallinity of UA was lost because of its incorporation into the NLCs. Release of the drug was sustained for all the NLCs; unsaturated lipids exhibited drug release faster than that of saturated components. The most useful finding from this report is the significant difference between the cytotoxicity of free UA and UA-loaded NLCs, which demonstrates the superiority of UA-loaded NLCs over free UA in penetrating the cell membrane. UA in saturated and unsaturated lipids and fatty acid comprising NLCs showed comparable cytotoxicity in human leukemic cell line K562 and melanoma cell line B16 and enhanced anticancer activity. Conclusively, both saturated and unsaturated lipid-containing NLCs formulated in this study may be used as potential delivery systems for UA with improved anticancer activity.

Orcinol glucoside-loaded nanostructured lipid carrier (NLC) coated with polyethylene glycol - 25/55 - stearate (PEG-25/55-SA) were formulated and evaluated for oral delivery of orcinol glucoside (OG) to improved *in vitro* cytotoxicity against GIT cell lines such as Hepatocellular carcinoma (HepG2), hepatocyte-derived carcinoma (Huh-7), humancolorectal carcinoma (HCT-116) and human gastric adenocarcinoma AGS cells. The findings reveal the influence of PEG-25/55- stearate on particle size, polydispersity index, zeta potential, encapsulation efficiency, *in vitro* release behavior and *in vitro* cytotoxicity of the formulations. Spherical morphology with smooth surface was experienced for all the formulations. Significant difference in crystal structure between conventional and PEGylated NLCs were noted whereby the crystallinity of OG was lost due to its incorporation in the NLCs. Release of the drug was sustained for all the NLCs; PEGylated NLCs exhibited slower drug release than non-PEGylated NLCs. The most valuable findings from this report is the significant difference between the cytotoxicity of free OG and OG loaded in PEGylated and non-PEGylated NLCs, which demonstrates the superiority of OG-NLCs over free OG in penetrating cell membrane. OG in PEGylated NLCs showed comparable cytotoxicity in GIT cell lines such as Hepatocellular carcinoma (HepG2), hepatocyte-derived carcinoma (Huh-7), human colorectal carcinoma (HCT-116) and human gastric adenocarcinoma AGS cells, and enhanced anticancer activity. Conclusively, orcinol glucoside could be a potent anticancer drug candidate for gastrointestinal tract cancer and both PEGylated and non-PEGylated NLCs formulated in the present study may be used as potential oral delivery systems for OG with improved anticancer activity.

As extension of the present work, specific lipid components of serum such as HDL, one of the major studies requires the specific separation of serum lipid and serum protein fractions and observing their structure function correlations in inactivating surfactant are considered to be significant. Besides the potential of nanostructured lipid carrier (NLC) as drug delivery system the *in vitro* and *in vivo* study in different cancer cell line and cancer animal models respectively are warranted in order to ensure the superiority of the formulated drug delivery systems.