SUMMERY AND CONCLUSIONS

CHAPTER 1 focused on the effect of the fatty acids on the physicochemical stability of the NLC formulations. In this work SLC, TS and four different FAs were used for the preparation of NLC formulations. Conventional hot homogenization followed by ultrasonication technique was used for the preparation of NLC systems. Before preparing the formulations, some suitable lipid compositions were taken by considering the mutual miscibility for the mixed lipidic systems. The mutual miscibility among the lipidic systems were assessed by the langmuir monolayer approach. It was observed that, presence of 20% FA provides the maximum stability to the mixed lipidic systems. Prepared NLC formulations were characterized using DLS, DSC, FF-TEM, UV-Visible spectroscopy, fluorescence spectroscopy. The average size of the NLC formulations were found in the range of 300 – 500 nm. The formulations were found to be stable for 45 days. A natural polyphenolic compound curcumin was used as a model drug for the prepared formulations. The miscibility of curcumin with the lipid systems was also assessed by the Langmuir monolayer approach. The repulsive interaction of curcumin with the lipid systems indicated the accumulation of the incorporated curcumin on the palisade layer of the studied formulations. Curcumin loaded NLC formulations were further characterized using the mentioned analytical approach. Enhancement in the size and reduction in the zeta potential value indicated the accumulation of curcumin on the palisade layer of the studied formulations. No significant change in the thermal properties were observed for the curcumin loaded NLC from the base NLC formulations. The observation indicated the retention of the internal morphology of the NLC formulation in the presence of curcumn. The spectroscopic investigation gives information regarding the polarity of the environment of loaded curcumin. The observed polarity signifies the surface accumulation of it. The crystallinity of the NLC formulations were also found to get influenced by the different FAs. It was observed that, SA was found to provide the mostly compact system. On the other hand LA comprised formulations were found to be fluidic in nature. The drug incorporation and the drug release property of the studied formulations were also get influenced by the crystallinity of the formulations. Being less crystalline, LA comprising formulations were found to give maximum drug incorporation efficiency and faster release of the incorporated drug. On the other hand, the compact nature of the SA loaded formulations was not allowed curcumin to get incorporated easily and also slow down the release phenomenon of the incorporated curcumin. The biological activity of the

curcumin loaded formulations was also studied against *Bacillus amyloliquefaciens*. The antibacterial activity of the curcumin loaded formulations was found to be higher than the native curcumin. Conventional cup plate method was used for the investigation of the antibacterial activity of the studied formulations.

CHAPTER 2 was primarily focused in the improvement of the drug incorporation and the drug loading capacity of the amphiphilic drug to the NLC formulation. In the present study CHR and prepared LCDs of CHR were used as drug. LCDs were prepared by incorporating long hydrocarbon chain to native CHR. CP, TP and OA were used in the molar ratio 2:2:1 for the preparation of the NLC formulation. The lipid ratio was obtained by analyzing the mutual interaction among the lipids by Longmuir monolayer system. Langmuir monolayer approach was also employed to understand the mutual miscibility among CHR and LCDs separately with the selected lipid system. CHR and LCDs were found to show repulsive and associative interaction with the lipid systems respectively. The base and the drug loaded formulations were characterized by DLS, DSC, TEM, FF-TEM, AFM to investigate the physicochemical stability of the formulations. The prepared formulations were found to be stable for 90 days. DLS, DSC, TEM, FF-TEM and AFM studies indicated that the CHR get accumulated on the palisadelayer of NLC formulations. On the other hand, LCDs get incorporated in the core of NLC formulations. The enhanced lipophilicity of the LCDs were mainly responsible for the observation. The incorporation efficiency and the drug loading capacity of the LCDs were found to be higher than the native CHR. The incorporation efficiency and the drug loading capacity of the LCDs on the NLC formulations were found to get enhanced with increasing the hydrocarbon chain. Maximum incorporation efficiency and drug loading were observed for CHR18. Release of native CHR and LCDs from NLC systems was also studied. LCDs were found to show sustain release in comparison to the native CHR. CHR18 was found to show the most sustained release profile among the other studied LCDs. CHR and LCDs loaded NLC formulations were also subjected for the anticancer activity studies against human neuroblastoma (SHSY5Y) cell line. The activity of the LCD loaded NLC formulations were found to be higher than the CHR loaded NLC formulations. Promising drug incorporation efficiency, drug loading capacity and anticancer activity of the LCD loaded NLC formulations prove them as the advantageous alternate of CHR loaded NLC formulation.

In the CHAPTER 3, a well stabilized conventional NLC (SLC : TS : PA, 2:2:1, M/M/M) formulation was taken and NLC_{IPA} was prepared by partially replacing SLC by synthetically prepared IPA. The ratio of SLC/IPA was optimized by analyzing their mutual miscibility

using Langmuir monolayer approach. SLC/IPA ratio 40: 60, 30: 70 and 20: 80 were selected for the preparation of NLC_{IPA}. Prepared NLC_{IPA} were characterized along with the conventional NLC formulation using DLS, DSC, TEM, FF-TEM and AFM. The stability of the IPA modified NLC formulations were found to be higher than the conventional NLC formulations. IPA lowers the lipid modification and enhances the stability of $NLC_{IPA.}$ Among the studied NLC_{IPA}, formulation having SLC/IPA ratio 30 : 70 was found to have least structural disorder and the maximum stability. OLA as model drug was introduced into the studied systems. OLA loaded formulations were also subjected for detailed physicochemical characterization. The characterization of the drug loaded formulation indicated the surface accumulation of OLA on NLC and $NLC_{IPA.}$ The amphiphilic character of OLA was responsible for its surface accumulation. Due to the surface accumulation of OLA, shell enriched type NLC and NLC_{IPA} were proposed for the studied formulations. The EE% and DL% of the NLC_{IPA} were found to get increased in comparison to the conventional NLC formulation. Control and sustained release of OLA was observed for NLC_{IPA}. Anticancer activity of OLA loaded conventional NLC and NLC_{IPA} were studied on Hepatocellular carcinoma (HepG2), hepatocyte-derived carcinoma (Huh-7) and colorectal carcinoma (HCT-116) cell lines. Considerably higher activity was observed for NLC_{IPA} in comparison to the conventional NLC. Considering the obtained results, it can be conclude that the IPA is an advantageous alternate of conventional phospholipid. The presence of IPA enhances the physicochemical stability and performance of OLA loaded NLC_{IPA}.

CHAPTER 4 mainly focused in the preparation and characterization of NLC_{PEG} systems developed for the delivery of the water soluble drug, PYZ. Non ionic polymer, PEG 2000 was employed for the preparation of NLC_{PEG} systems. HSPC, TS and OA with a molar ratio 2 : 2: 1, M/M/M was taken for the preparation of NLC and NLC_{PEG}. The nonionic polymer was introduced in aqueous 2 mM Tween 60 solution which was the dispersion medium for the studied formulation. 0.01 (W/V)% PEG 2000 was found to be optimum for the physicochemical stability of NLC_{PEG}. NLC_{PEG} formulations were found to be more stable than the conventional NLC formulations. Significant lowering in lipid modification and size enhancement signified the stability of NLC_{PEG}. PEG 2000 was found to form an additional layer over the palisade layer of the lipid system and significantly improves the steric stability of NLC_{PEG} systems. PYZ was taken as the water soluble drug for this work and successfully incorporated in the NLC and NLC_{PEG} formulations. Physicochemical characterization of PYZ loaded formulations signified the formation of shell enriched NLC and NLC_{PEG}. EE% and DL% of NLC_{PEG} were found to be higher than the conventional NLC . Release of PYZ from

NLC_{PEG} was sustained than the conventional NLC. The presence of PEG 2000 layer gives a better hold over the release of PYZ. Hence, NLC_{PEG} systems were advantageous over the conventional NLC for the delivery of PYZ..