ABSTRACT

The research work presented in this thesis entitled "**PHYSICOCHEMICAL INVESTIGATION ON NANOSTRUCTURED LIPID CARRIERS**" is mainly directed to the improvement and modification of the second generation solid lipid nano particles or commonly known as nanostructured lipid carrier (NLC). In this thesis, various lipid systems and their different combinations were used for the development of novel drug delivery systems for a variety of drugs and active organic molecules with potential biological activities. The overall work presented in this thesis has been divided into four chapters. In addition to this, a brief introduction has also been presented.

CHAPTER 1 describes the effect of four different fatty acids (FAs), *viz.*, lauric acid, myristic acid, palmitic acid and stearic acid on the physicochemical behavior of the NLC. In this work the NLCs were prepared using soy lecithin, tristearin and FAs. The lipid composition for the NLC formulations was fixed by understanding their mutual miscibility using Langmuir monolayer approach. Detailed and comprehensive set of characterization of the prepared NLC formulations were carried out using dynamic light scattering, differential scanning calorimetry, TEM, FF-TEM. Curcumin a natural polyphenolic compound with large number of biological activity was incorporated into the NLC formulations. The effect of different FAs on the drug loading, entrapment efficiency and the release kinetics of curcumin from NLC were also investigated in detail. To get information regarding the potentiality of curcumin loaded NLC, the drug loaded NLC formulations were subjected for the antibacterial activity against *Bacillus amyloliquefaciens* isolated from soil.

CHAPTER 2 depict a comprehensive set of work representing a detailed physicochemical characterization and anti cancer activity of chrysin (CHR) and long chain derivatives of chrysin (LCD) loaded NLC. In this work cetyl palmitate, tripalmitine and oleic acid have been used for the preparation of NLC formulations. The lipid composition for NLC formulations was fixed using the Langmuir monolayer approach. In this work, the lipophilicity of CHR was enhanced by introducing long hydrocarbon chain in CHR molecule. The base NLC, CHR loaded NLC and the LCD loaded NLC formulations were subjected for the evaluation of solution phase and thermal behavior in order to get idea regarding stability of the formulations.

The drug loading capacity, drug incorporation efficiency and the release kinetics of CHR and LCDs were also studied and compared. The potency of CHR and LCDs as the anticancer drug being incorporated into NLC was also studied by analyzing *in vitro* cytotoxicity study on human neuroblastoma cancer cell line (SHSY5Y) using MTT assay approach.

CHAPTER 3 primarily deals with the potentiality and subsequent anticancer activity of the IPA modified NLC formulations (NLC_{IPA}) loaded with oleanolic acid (OLA). In this work a conventional NLC formulation comprised of SLC, TS and PA with molar ratio 2 : 2 : 1 (M / M / M) was taken and the natural phospholipid SLC from the lipid composition was partially substituted by synthetically prepared ion pair amphiphile (IPA). The stability of the IPA modified formulations were studied by analyzing the solution phase and thermal properties by detailed physicochemical characterizations. The dynamic light scattering, differential scanning calorimetry, TEM, FF-TEM and AFM technique were used for the detailed characterization for the studied NLC and NLC_{IPA} formulations. OLA was used as a drug in this study. The drug loading capacity, entrapment efficiency and the release kinetics of OLA from the conventional NLC as well as NLC_{IPA} formulations were also studied and compared side by side. Drug loading, entrapment and the release kinetics of the IPA modified formulations were found to improve significantly in comparison to the conventional NLC. Anticancer activity of OLA loaded NLC and NLC_{IPA} formulations were also studied using three different GIT cancer cell lines by MTT assay technique. Observed higher activity of the OLA loaded NLC_{IPA} established it as a advantageous alternate of NLC in delivering anticancer drug like OLA.

In **CHAPTER 4**, the conventional NLC formulations were subjected for the polymer induced surface modification and developed as a suitable drug delivery for the water soluble drug pyrazinamide. Nonionic polymer PEG 2000 was used for the surface modification. HSPC, TS and OA having the molar ratio 2 : 2 : 1 was used for the preparation of the NLC formulations. The polymer was introduced in the formulations in combination with the dispersion medium of the NLC systems. 2 mM aqueous Tween 60 solution was used as the dispersion medium for the studied formulation. PYZ, a hydrophilic drug had been successfully incorporated in the studied formulations. The base and the drug loaded formulations were subjected for detailed characterization. Solution phase and thermal stability of the surface modified formulations were more stable than the conventional formulations. EE% and DL% of the NLC_{PEG} formulations

were found to be higher than the conventional NLC formulations. In addition to this the release of the incorporated PYZ was also became sustained in case of the surface modified formulations. The presence of the polymer layer over the surface modified NLC_{PEG} formulation effectively enhanced the EE% and DL%. The exclusion rate of the drug also reduced in the presence of PEG 2000 layer.