5. SUMMARY AND CONCLUSION

In the present study, Preformulation study of drugs and excipients which shows that the drugs and excipients could be used for research work. Drug excipient compatibility study was performed at 40°C/75%RH for 1 week. There is no interaction between drugs and excipient.

Plain Chitosan and Gelatin nanoparticles were prepared by Ionic gelation method and ethanol precipitation method respectively. Formulations were optimized based on particle size, drug loaded nanoparticles were prepared. PEGylation of polymers was done in two steps; Intermediate PEG-Epoxide was prepared followed by grafting of polymer with PEG-Epoxide. Drug entrapment was optimized by changing drug to polymer ratio. Drug loaded Pegylated Chitosan and Gelatin nanoparticles were prepared and checked for particles size. There was no change in particles size of non drug loaded non PEGylated nanoparticle and drug loaded PEGylated nanoparticles.

Lyophilization study was performed to select the best cryoprotect for formulation. Sucrose, mannitol and dextrose were chosen for the study in the proportion of 1:1, 1:2 and 1:3. Based on particle size, flowability and dispersibility, sucrose in 1:1 was chosen as the best cryoprotectant for the formulation.

Lyophilized formulations were characterized for particle size, % drug entrapment, drug content, scanning electron microscopy. In-vitro study was performed by dialysis bag method for 120-168 hrs.

Stability study of PEGylated nanoparticles was done at 2-8°C and 30±2°C/60±5% humidity for the period of 1 year. Pharmacokinetic study was performed on Sprague Dawley rat. Cell line study was performed on MCF-7 breast cancer cell line.

Polymeric nanoparticles were prepared from naturally obtained hydrophilic, biodegradable and easily available polymers like gelatin and chitosan. Method of preparation for chitosan
nanoparticles did not include any organic solvents and method of preparation of gelatin polymers includes lower concentration of gluteraldehyde. Overall formulations do not include risk of toxic materials.

The size of nanoparticles is helpful to target the tumor tissues by EPR effect. It justifies that the formulations are having better targeting potentials. Hence, the anticancer drug loaded formulations have reduction in side effects of anticancer drugs. Optimized formulations have better drug entrapment. In lyophilisation study, cryoprotectant ratio was optimized and nanoparticles: sucrose in ratio of 1:1 proportion found to be the best cryoprotectant among all ratios of different cryoprotectant. Stability study of drug loaded PEGylated gelatin and drug loaded PEGylated chitosan nanoparticles are stable for one year at 2-8°C with ambient humidity.

The drug loaded PEGylated gelatin nanoparticles and drug loaded PEGylated chitosan nanoparticles obeys zero order kinetics and follows Higuchi’s diffusion controlled model, also the drug entrapped within matrix.

Pharmacokinetic data showed that the PEGylated formulations show long circulating properties of nanoparticles as well as better anticancer activities of drugs. Cell line study showed effects due to free drug and drug entrapped within the PEGylated nanoparticles. Hence it proves the targeting potential of PEGylated polymeric nanoparticles loaded with anticancer drugs.

Anastrozole loaded PEGylated gelatin Nanopartilces are having high entrapment with good in-vivo and pharmacokinetic behavior. Docetaxel loaded PEGylated Gelatin nanoparticles are having less entrapment with very good pharmacokinetic behavior. So, amongst all the six formulations Anastrozole loaded PEGylated Gelatin Nanoparticles and Docetaxel loaded PEGylated Gelatin nanoparticles are chosen as better formulations. Both formulations showed prolonged action upto 1 week (Once a week), reduced dosing frequency, more patient compliance, site specificity (reduced side effects) and longer circulation time (more efficient).