Chapter 7: Summary & Conclusion

7.1 SUMMARY

Nanoparticulate drug delivery has attracted a lot of attention of formulation scientists and their biofabrication in order to target or control the release of biomolecules are revolutionizing the entire arena of pharmaceutical sciences besides other areas. Meloxicam, a nonsteroidal anti-inflammatory agents was selected as a model drug owing to its inherent properties like low aqueous solubility and low bioavailability. It was hypothesized that improvement of dissolution profile shall improve its oral bioavailability and therefore, nanoparticles containing the drug was sought to be formulated using Chitosan as a matrix forming agent for nanoparticulate system.

The drug identification studies showed that drug (Meloxicam) supplied by Intas Pharmaceuticals, Ahmedabad matches with the standard for identification and purity. Procedures were adopted for identification of drug as well as the polymer (Chitosan) which was obtained from Leo Chem, Bangalore. The identification Studies includes, FTIR, DSC, XRD of Pure drug and Chitosan and they were in concordance with the standard.

The solubility profile of drug in different solvents shows that drug is highly lipophilic in nature and is almost insoluble in water although it was slightly soluble in phosphate buffer and soluble in dimethylformamide. The absorption maximum of MLX in Dimethyl formamide (DMF) was measured by UV spectrophotometer and found to be 376.5 nm which is concordant with standard \( \lambda_{\text{max}} \) of 376.5 nm. The FTIR of drug confirms the presence of different functional groups in drug giving different peaks. The DSC thermogram of drug showed a sharp peak at 245 °C, which comes in the Standard range 242-245°C, showing crystalline nature of drug. All these observations confirm the identity and purity of drug. The standard curve of drug was prepared in 0.1N HCL, Distilled water, Dimethyl formamide (DMF), Phosphate Buffer pH 6.8, Phosphate Buffer pH 7.4 and the absorbance data obtained subjected to linear regression and graphically shown in Table 6, 7, 8, 9,10 and 16 and Figure 23, 24, 25, 26 and 27. The correlation coefficient was found to be almost 0.99 indicating good linearity.

In the present study, Polymeric nanoparticles were prepared using Emulsion Cross-linking technique to overcome poor aqueous solubility and low oral bioavailability. The
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W/O emulsion containing drug and chitosan in aqueous phase was crosslinked with aldehyde groups of gluteraldehyde with amine group of chitosan. The physicochemical properties like zeta sizes, zeta potential, polydispersity index of formulated nanoparticles were evaluated. The preparation of MLX nanoparticles was initiated by optimizing the drug:polymer on the basis of size, polydispersity index and encapsulation efficiency. The final optimized formulation was found to be MC8, MLX: Chitosan (10:400) with mean size of 84±1.7 nm and having polydispersity index of 0.086. The shape and surface morphology of the nanoparticles were evaluated by the use of scanning electron microscopy (SEM). The SEM photomicrograph revealed that the carrier system was more spherical in shape and uniformly distributed without any aggregation or adhesion of nanoparticles.

The crystalline state evaluation was done by DSC of Meloxicam (plain drug), optimized formulations MC8. The DSC thermogram revealed that crystalline state was apparently unaltered following sonication operation. The formulations characterized for percent drug release and saturation solubility. The drug release study revealed that increase in surface area may have enhanced the dissolution rate. From the Noyes-Whitney equation the increased surface area and saturation solubility due to decreased radius resulted in increased dissolution velocity. The percent drug release obtained was more than 90% in case of MLX nanoparticles as compared to pure drug which was only 30%. The bioavailability of drug is dissolution rate limited, so particle size reduction can significantly improve the performance of drug.

In vivo study of optimized formulation MC8 of MLX nanoparticles in rats were also performed for anti-inflammatory, antiulcer and antiarthritic activities using the models carrageenan Induced Paw Edema, Pylorus Ligation method and Fomaldehyde induced Arthritis respectively. There was significant enhancement in oral bioavailability of meloxicam as compared to the pure drug as at every time point higher plasma drug concentration was observed with nanoparticles formulation and Cmax and Tmax could not be achieved during the study period of 2 hours.
7.2 CONCLUSION

After studying the results found by our research we can say that the nanoparticles of Meloxicam with smaller particle size can be effectively produced by using Emulsion cross linking technique. The nanoparticles produced by this technique resulted in marked increase in solubility and dissolution rate of the drug and the particle size obtained (84 nm) was suitable even for i.v. administration. This technique was shown to be simple and adequate for drug particle size reduction and did not seem to alter the crystalline state of the drug. Nanoparticles were prolonged blood circulation time of drug and observed different pharmacokinetic parameters as compared to Meloxicam solution. The bioavailability has been found to be increased. These results suggested that Meloxicam nanoparticles would be good candidate with improved bioavailability. In future work, the development of stealth nanoparticles laced with functionalized surface coatings capable of eliciting passive or active targeting as per the requirement can be regarded as the future step in the nanoparticles research.