SUMMARY
CHAPTER VII

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The Present thesis is aimed at developing drug loaded polymeric micro/nano particles and micro spheres. Mainly antihistamine drug, arthritis drug and anti-cancer drugs have been investigated for the controlled release applications. This area has been quite intensively studied over the past three decades and still there is more scope for the development of these products. Controlled release (CR) of Pharmalogically active agents to the specific site of action at the therapeutically optimal rate and dose regimen has been the major goal in designing such devices. In order to pursue research in this area, the author has developed novel polymeric micro /nano particles as drug delivery systems for antihistamine drug, arthritis drug and anti-cancer drugs. These investigations are presented in six major chapters of this thesis.

**Chapter I.** gives an introduction to the field of controlled drug delivery through polymer matrices. The latest development in the production of Polymeric micro/nano particles, pH sensitive and temperature sensitive Polymeric systems have been explained in brief along with the *in-vitro* drug release studies. This chapter also gives in brief a survey of literature relevant to present study along with the aim of this study.

**Chapter II.** discusses the details on materials used, experimental methods developed and/or adopted for the preparation of micro/nanogels, pH sensitive and temperature sensitive polymeric matrices. The characterization studies of the system under study were carried out by Differential Scanning Calorimetry (DSC), X-ray diffraction studies (X-RD), Fourier transform infrared spectroscopy (FTIR), Scanning electron microscopy (SEM), Transmission Electron Microscopy (TEM), Dynamic Light Scattering (DLS) and *in-vitro* release kinetics have been discussed.

Blends microspheres of Poly (methyl methacrylate) and Poly (ethylene oxide) were prepared by solvent evaporation technique using poly (Vinyl alcohol) as a stabilizer and were characterized and their drug release studies incorporated in **Chapter III.** Nimesulide, an arthritis drug was successfully loaded into these microspheres. The effect of experimental variables such as ratio of
ploy (methyl methacrylate) to Poly (ethylene oxide) on nimesulide encapsulation efficiency, release rate, size and morphology of the microspheres has been investigated. Nimesulide loaded and unloaded microspheres were analyzed using FTIR, DSC, X-RD and SEM techniques. Fourier transforms infrared spectroscopy results were used to explain the nature of blending of constituent polymers. Differential scanning calorimetry and X-RD techniques were used to investigate the crystalline nature of the drug after encapsulation. DSC and X-RD results indicated an uniform dispersion of Nimesulide in the PMMA/PEO blend matrix. Scanning electron micrographs indicated the formation of spherical microspheres with distinct size. Nimesulide was successfully encapsulated up to 85% in the polymeric matrices. In-vitro dissolution experiments performed in PH 7.4 buffer medium indicated a controlled release of Nimesulide from blend microspheres up to 12hrs.

**Chapter IV**, is mainly concerned about the development of pH sensitive blend microspheres of polycaprolactone (PCL) and cellulose acetate phthalate (CAP) for drug release studies. These microspheres were prepared by double emulsion solvent evaporation method. Triprolidine Hydrochloride (TPH), a propylamine, antihistamine drug, was successfully loaded in to these microspheres via in-situ method. The maximum loading of TPH was found to be about 66%. The resulting microspheres were characterized by Differential Scanning Calorimetry (DSC), X-ray diffraction (X-RD), particle size analysis, and Scanning electron microscopic (SEM) studies. The DSC study revealed the blend compatibility of the constituent polymers. X-RD studies showed that the TPH drug particles are molecularly dispersed in the microspheres. Particle size and SEM studies indicated the formation of spherical microspheres with distinct size. The in-vitro release studies revealed that the release of TPH depends upon the pH condition, blend composition, and drug content. The release of TPH from microspheres achieved for more than 10 h.

**Chapter V**, deals with a series of nanogels (NGs) developed from N-vinyl caprolactam and hydroxyethyl methacrylate through free radical emulsion polymerization using methylene bis acrylamide (MBA) as cross linker. Curcumin, an anti cancer drug, was successfully loaded in to these NGs via equilibrium in-situ method. These NGs were characterized by Fourier transform spectroscopy (FTIR), differential scanning calorimetry (DSC), transmission electron microscopy (TEM), and dynamic light scattering experiments (DLS) techniques. The formation of co-polymeric NGs was confirmed by FTIR analysis. DSC results revealed that drug was molecularly dispersed in the nanogel networks. TEM result indicates the formation of nanogels in the spherical form with the
size of 150 nm. The DLS results also support the formation and size of NGs. An in-vitro release study indicated that these NGs may be potentially useful for targeted drug delivery applications.

**Chapter VI,** gives the details of development of temperature and pH-responsive nanogel systems based on poly(N-vinylcaprolactam-co-2-dimethylaminoethylmethacrylate) [poly(NVC-co-DMA)] by using a free radical emulsion polymerization procedure for the responsive drug delivery of 5-Fluorouracil (5-FU). The formations of nanogels confirmed from fourier transform infrared spectroscopy (FTIR) studies. From TEM and DLS studies it was noticed that the nanogels were with spherical in shape and the average diameter of nanogels was about 100 nm. Further, 5-FU, an anti cancer drug, was encapsulated into these nanogels via equilibrium swelling method. The encapsulation efficiencies also calculated and concluded that they were dependent on network structure of nanogels. The DSC results indicated that the 5-FU was molecularly dispersed in nanogels. The temperature/pH-dependent cumulative release properties were investigated for the systems under study for long-term delivery. The nanogels displayed efficient delivery for long-term delivery systems. We provided here a proof of concept for the use of responsive nanogels having an overall size below 100 nm as a cargo system for anti cancer drugs and for controlled release mediated by temperature and pH. The developed nanogels can be applied for tumor targeted drug delivery.

Summary of the present research results were presented in Chapter VII. In conclusion, the study demonstrated successfully the development of microspheres, micro particles, pH sensitive and thermo sensitive polymeric matrices with natural and synthetic polymers. In the course of this study some novel techniques/polymeric systems were developed, which will be useful to the future researchers working in this area. The systems developed in this research are promising CR systems to deliver antihistamine drug, arthritis drug and anti-cancer drugs.

**Future Challenges and Prospectus**

Future needs in this area are multifaceted. There is a great need to develop the effective systems for the delivery of many types of drugs including vaccines, human growth hormones, insulin, anti-tumor agents, contraceptives, genes, etc. Many Polymeric micro/nanoparticles have been developed for this purpose. From polymer chemistry viewpoint, it is important to synthesize newer polymers and copolymers to match the hydrophilic and hydrophobic properties. More research efforts are needed to produce micro/nanoparticles that are free from unwanted toxic residual solvents, using a recently developed supercritical fluid technology. Although many important goals have been reached
in achieving stabilization of drugs in circulation, yet more investigations are needed to develop the newer materials in this area!.

The research on stimuli-responsive polymeric matrices for the drug delivery applications is under active research area to be developed. It requires a strong multidisciplinary approach to develop the marketable products. The future challenge is to develop the functional polymers, which are biodegradable that are useful for parental drug delivery.

**List of publications/ communicated**


**Papers presented in conference/seminars**


