

## GENERAL INTRODUCTION

Recently efforts have been made to design novel drug dosage formulations so that more and more drug effectiveness can be achieved compared to the conventional dosage forms. To achieve this goal, controlled release technology discovered few decades ago that developed the commercial methodology by which predecided and reproducible release of a drug up to therapeutic level into a specific environment over a prolonged time period could be maintained. Such drug delivery systems function according to the change in physiological signals within the body and target the drug for the site of action to minimize any side effects. Controlled release medications reduce, the, toxicity and enhance the efficacy, safety and reliability of chemotherapy, which results in improvements in patient compliance and convenience (Langer 1998; Brouwers 1996). Now the drug delivery system concept is well known and is utilized in the treatment of a variety of diseases (Labhasetwar et al. 1997). Nano and micro beads of polymers have been formulated using either synthetic or natural polymeric material (Jagur-Grodzinski 1999; Uhrich et al. 1999; Kumar and Kothari 1999). Drug release from such types of formulated polymeric beads in which a drug is entrapped by polymeric material involves its diffusion through polymeric material slowly in controlled manner. Dispersing a drug in polymeric matrix or covalently attaching drugs to biodegradable polymer may also be able to release them by degradation of such macromolecules. Therapeutic molecules complexed by polymers capable of forming gel may also be released by diffusion. Hence, drug delivery systems require a polymeric matrix which is non-toxic, biocompatible, and biodegradable.

## **1.1 BACKGROUND AND MOTIVATION**

In pharmacology, several drug formulations have matured beyond the stage of promising investigational agents in preclinical and clinical trials to become viable pharmaceutical products, approved for widespread human use. Drug for oral use have been microencapsulated for a variety of reasons. This has been employed to sustain the drug release, to disguise the unpleasant taste of a variety of drugs, to reduce or eliminate gastrointestinal tract irritation, and to separate incompatible drug (Deasy 1984; Kondo 1979). Tablet designed for controlled release oral drug delivery are often nondisintegrating. This can cause local irritation and erratic absorption. Multiple unit dosage forms spread out uniformly in the gastrointestinal tract. This result in a more reproducible drug absorption and reduces local irritation compared to single unit dosage forms. In addition, unwanted intestinal retention of the polymeric material which may occur with non disintegrating tablets on chronic dosing is avoided (Sjoegren et al. 1985). Microcapsules as oval dosage forms, however, may encounter several problems. If microcapsules are to be compressed successfully, good flow properties are essential and the capsule wall must be capable of resisting the severe mechanical stress during compression. Poor flow properties can cause problems in content uniformity. Microcapsules when compressed under high pressure may rupture and lose their protective or sustained release action (Lin 1988). The poor compressibility often requires the addition of large amounts of easily compressible excipients. This dilution could result in a drug content to low in the final dosage forms. Fassihi (1988) studied the consolidation behavior of polymeric behavior and reported both plastic deformation and particle fusion to be operative during compression. The possible fusion of polymeric microparticles during compression could result in a nondisintegrating matrix with the loss of the character of a multiple-unit dosage forms. Nixon and coworker (1977) reported that the tableting of microcapsulated resulted in a nondisintegrating matrix in a reduction of drug

release. We can overcome these problems by developing a delivery system for micro or nano particles in bead form.

Chlorpheniramine maleate (CPM) has been widely used as an antihistamine in treating or preventing respiratory or dermatological allergies. To date, it appears that its absolute bioavailability after oral administration in human has not been reported. Regular dosage forms of CPM be administrated 3-4 time a day or with the contention that sustained or controlled release dosage forms are needed for this drug. The main objective of controlled released dosage forms is to obtain formulation that would allow the drug to remain at the therapeutic levels, can be achieved by using specific polymers that are biocompatible. A wide survey of literature clearly indicate that chitosan has been a subject of much research and has been used for a number of biomedical and bioengineering application due to its unique physical properties. The potential of chitosan in the design of carriers which prolong the drug residence time in the stomach has been reported (Hou et al. 1985). Chitosan matrix formulations appear to float and gradually swell in an acid medium and are suited to oral sustained delivery.

## **1.2 AIMS AND OBJECTIVES**

The aim of our study is to design a formulation of particulate drug delivery system in the form of IPN hydrogel beads for chitosan and amino acids to achieve its application in controlled drug delivery. The objectives of our studies are —

- To prepare beads of chitosan, chitosan-glycine, chitosan-glutamic acid and chitosan-glycine-glutamic acid crosslinked with glutaraldehyde with out drug loading and loading with CPM drug.

To perform comparative study on beads of pure chitosan, chitosan-glycine, chitosan-glutamic acid and chitosan-glycine-glutamic acid crosslinked with different concentrations of glutaraldehyde and having

different composition for chitosan amino acids with out drug loading and loading with CPM drug.

To characterize the prepared beads by FTIR spectroscopy to confirm the crosslinking reaction and drug interaction to crosslinked polymers with in beads.

- To characterize the prepared beads by SEM to determine their size, shape, the surface morphology and internal structure.
- To characterize the prepared beads using DSC to find out the thermal stability of beads.

To characterize the prepared beads using XRD to determine the physical nature of drug after loading into beads.

- To study swelling behaviour of the beads at different time interval as a function of pH concentration of glutaraldehyde, chitosan and amino acids.
- To study drug release of CPM from CPM loaded beads loaded with different amount of drug as a function of pH, concentration of glutaraldehyde, chitosan and amino acids.
- To study the kinetics of CPM release from CPM loaded beads.

### **1.3 THESIS LAYOUT**

The total work has been divided into five chapters.

The first chapter deals with general introduction describing the status of the work, aims and objectives of research.

- The second chapter describes the historical background and literature reviewed.
- The third chapter of this thesis deals with the materials and various experimental method (techniques) used in this study to fulfill the aim and objectives.

The fourth chapter deals with the characterization of raw materials to prepare IPN beads and the comparative study of prepared pure chitosan

beads, chitosan-glycine, chitosan-glutamic acid and chitosan-glycine-glutamic acid beads crosslinked with glutaraldehyde. In this chapter the characterization, swelling behavior, drug release study and kinetics of drug release for formulated pure chitosan beads and different chitosan-amino acid beads are described to differentiate them.

- The fifth chapter describes detailed studies carried out for chitosan-glycine-glutamic acid IPN beads crosslinked with glutaraldehyde. These formulated novel beads are characterized by FTIR, SEM, XRD and thermal drug analysis. The results of swelling behaviour and drug release with release kinetics are described as a function of pH, concentration of glutaraldehyde, chitosan and amino acids.
- In the sixth chapter a discussion about the conclusions and future perspectives has been made.  
Finally, references related to review are listed.
- Lastly, the original graphics obtained from instruments are given in appendix A - C section.