SYNOPSIS

Polymers in the natural form or chemically modified form, find major applications in biomedical and pharmaceutical industries. These polymers are biodegradable and biocompatible. Chemically modified polymers have better properties than the conventional polymers with respect to their stability and processability.

In recent years, polymer based controlled release (CR) technology has emerged as a major multidisciplinary research frontier due to extensive research efforts. Today, the technology finds major applications in the delivery of a wide range of bioactive molecules such as drugs, fertilizers, pesticides and insecticides. The major advantages of CR systems are: (i) increased persistence and lesser quantum and frequency of application, (ii) reduction of toxicity due to avoidance of overloading of drugs, (iii) constant drug concentration in the blood, and (iv) targeting of a drug to specific area of interest.

Production of special formulations such as sustained release, site specific and target release has been a great interest. Controlled release drug delivery system necessarily consists of a barrier, which is generally a polymer. Release of drug from the polymer matrix is controlled by diffusion, permeation and physico-chemical properties of drug and the polymer.

In the present study an attempt has been made to develop newer polymeric networks for the encapsulation of different classes of drugs such as
analgesic, antibiotic and antiasthamatics and investigate the release kinetics. The thesis comprises seven chapters.

Chapter 1 gives an introduction to the controlled release drug delivery systems. Importance and basic characteristics of various polymers and their need for chemical modification is narrated. Classification of polymers according to their sources and uses has been made. Possible uses of these polymers in drug delivery systems and other pharmaceutical industries are covered. Various drug delivery systems such as transdermal membranes, microspheres, nanoparticles etc. are discussed in brief. Production technique and viability of each method is included.

Diffusion of drug from the polymer matrix has been explained using Fick’s diffusion equations. Fick’s first law of diffusion is based on the hypothesis that the rate of transport of a diffusing material through a unit cross-section in unit time, is proportional to the concentration gradient, which is expressed as

\[ F = -D \frac{\partial c}{\partial x} \]

where \( D \) is diffusion coefficient of a drug, \( c \) is concentration of drug, \( x \) is the movement (distance in cm) of the drug perpendicular to the surface of a barrier, and \( F \) is flux. The negative sign of equation signifies that diffusion occurs in the direction of decreasing concentration of the drug.
Fick’s second law of diffusion may be expressed as

\[
dc/dt = D \frac{\partial^2 c}{\partial x^2}
\]

where \(dc/dt\) denotes the concentration gradient from the surface of the layer. The scope of the present investigation is highlighted at the end of the chapter.

Chapter 2 presents details about the experimental procedures and the instruments used in this research. Description of analytical techniques such as Scanning Electron Microscopy (SEM), UV Spectrophotometry, Fourier Transform Infrared (FTIR) spectroscopy, \(^{13}\)C NMR spectroscopy, Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA) is given. Different microencapsulation techniques, film casting, swelling and drying studies, drug content, in vitro drug release profile, antibacterial activity and stability of different chitosan formulations have been described.

Chapter 3 explains the synthesis and characterization of chitosan Schiff’s bases (using acetaldehyde and propionaldehyde) for transdermal delivery of antiasthmatic drugs. The derivatives have been confirmed by FTIR spectroscopy, \(^{13}\)C NMR spectroscopy, DSC and TGA studies. The transdermal membranes containing salbutamol and terbutaline sulphate have been prepared by solvent casting technique. The percentage aldehyde conversion and carbon chain length of aldehyde, affect the film characteristics. Percentage drug content, tensile strength and % elongation of different chitosan derivatives have been determined.
Chapter 4 describes the antibacterial activity and film characterization of thiazolidinone derivatives of chitosan. Thiazolidinone derivatives have been prepared using chitosan Schiff's bases of different aldehydes viz. benzaldehyde, p-chloro benzaldehyde, m-nitro benzaldehyde, 2, 6- dichloro benzaldehyde and N, N- dimethyl amino benzaldehyde using mercaptoacetic acid in presence of zinc chloride. The derivatives have been confirmed by FTIR and \(^{13}\)C NMR spectroscopy. Antibacterial activities of chitosan and modified chitosan are evaluated against *Escherischia coli*, *Salmonella dysentrae*, *Pseudomonas aeruginosa* and *Bacillus subtillis*, using cup plate method, by measuring the zone of inhibition.

Chapter 5 deals with the formation of glutaraldehyde crossinked chitosan beads, incorporated with diclofenac sodium (an analgesic). The presence of drug in the matrix has been confirmed by FTIR spectroscopy. The preparation of beads has been optimized by changing the extent of crosslinking and amount of drug loading. The topographical studies were performed using scanning electron microscopy. The release data has been analyzed using an equation proposed by Peppas,

\[
\frac{M_t}{M_\infty} = kt^n
\]

where \(M_t\) is the amount of drug present at time \(t\), \(M_\infty\) is the amount of drug released at infinite time, \(k\) the rate constant and \(n\) is diffusional exponent.
In chapter 6, we report the development of interpenetrating polymeric network (IPN) beads of chitosan with gelatin and chitosan with egg albumin prepared separately using a common crosslinking agent glutaraldehyde, for the *in vitro* release of an antibacterial agent (cefadroxil). The beads have been characterized by FTIR spectroscopy, SEM and DSC. Both swelling and drying experiments have been performed to compute the diffusion coefficients. The drug release has been evaluated using an equation proposed by Peppas, to understand the transport mechanism. The extent of crosslinking has been studied in terms of the size and release characteristics of the beads.

Chapter 7 presents the summary of the research work. The topics presented in this thesis contain newer approaches to develop the CR devices in the form of transdermal membranes, glutaraldehyde crosslinked beads and IPN beads to encapsulate and release the drugs. The problems that need further investigations are also discussed.