Chapter VIII

Summary and Conclusion
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In the field of pharmaceuticals, sustained release drug delivery systems have been introduced to overcome the drawbacks of fluctuating drug levels associated with conventional dosage forms. Moreover, drugs having short plasma half life require repeated administration to cause patient non-compliance. Rational drug therapy, therefore, requires quick attainment of therapeutic drug concentration in blood followed by maintenance of this level over the desired period of time. These considerations have led to the development of oral sustained release dosage forms. The use of biopolymeric matrix devices to control the release of therapeutic agents has become important in the development of modified release dosage forms. The development of improved drug release systems is dependent on the selection of an appropriate carrier capable of controlling the delivery of active agents. Responsive polymers, in particular hydrophilic natural carbohydrate polymers are the promising new versatile carriers for the preparation of oral sustained release systems. These hydrophilic Polymers swell in presence of biological fluids and form a gel layer and enabling the drug to be released from the matrix throughout the gastrointestinal tract. Hence to encourage the research in the field of natural gums, we made an attempt to explore the use of one of the gum exudates of plant origin, gum odina, as a release retarding polymer in oral sustained release drug delivery system. Gum odina was collected from the bark of the tree *Odina wodier*, Roxb, family Anacardiaceae.

Initially toxicity study of gum odina was performed by MTT assay and non toxic nature of gum odina stipulated our interest to develop sustained release drug delivery system using gum odina. Rheological characterization shows pseudoplastic nature of gum odina. Effect of different factors on viscosity of gum odina was also investigated.

In the first part (Part I) of the thesis gum odina was used to develop conventional tablet dosage form. Tramadol hydrochloride was used as a model drug. The powdered drug is
embedded uniformly in the matrix of tablet and compressed to form a tablet, a production method that is relatively simple and cheap. Upon contact with biological fluids, water penetrates the tablet, gradually dissolving the drug, which then diffuses out through the tablet. Effect of different formulation variables and pH of the gastrointestinal tract on invitro release profile was investigated. Compatibility study of the drug in the polymer matrix was analysed by FTIR and DSC. No drug polymer interaction was observed in FTIR. DSC thermogram of tramadol hydrochloride showed a sharp melting endothermic peak at 183.15˚ C, whereas a broad peak was observed in case of gum odina. However, in tablet no such peak was observed which indicates amorphous dispersion of the drug in tablet.

In Part II of the thesis, considering the drawbacks of conventional tablet dosage forms, gum odina was used to prepare microparticles in combination with other polymer, chitosan. If a sustained release product is formulated in the form of tablet which keeps its integrity throughout the gastrointestinal tract, then the location of tablet will vary under different circumstances. This will lead to the variation in the rate of drug delivery to the systemic circulation. In order to circumvent the erratic behaviors like varying gastric emptying and intestinal transit rate of single unit sustained release dosage forms like tablet, microcapsules were chosen as the drug delivery system in the present work for sustained delivery of a model drug diclofenac sodium. In the preparation of microparticles glutaraldehyde was used as a crosslinking agent. Effect of ratio of gum odina and chitosan and glutaraldehyde concentration on the drug entrapment efficiency and in vitro drug release profile was studied. n values of all the formulations is less than 0.43 which indicates Fickian diffusion. Diffusion coefficient decreases with the increase in glutaraldehyde concentration and increase in the chitosan:gum ratio. From these values it is evident that stronger matrix is formed at higher crosslinking density which ultimately decreases drug diffusion.

To assess the viability and validity of the sustaining nature of IPN microparticles, IVIVC study is essential, since prolonged-release products may be specially suited for this kind of study. When the fraction of drug released in pH 6.8 was plotted against the fraction of
drug absorbed, a linear correlation was obtained. Different pharmacokinetic parameters like $C_{\text{max}}$, $t_{\text{max}}$, AUC were measured directly from the plasma concentration vs time profile. From the slope of the terminal linear portion of semi logarithmic plot of concentration vs time curve overall elimination rate constant was determined using trapezoidal method. When the fraction of drug dissolved in pH 6.8 was plotted against the fraction of drug absorbed, a linear correlation was obtained. A higher value of correlation coefficient suggested existence of good correlation between in vitro and in vivo data.

The total assessment of the experimental work was a good indicator that suitable oral sustained release drug delivery systems could be successfully developed using natural polymer like gum odina.