Conclusion and Future scope of the Research work

6.1 Conclusion

In this thesis, strong effect has given on the development of polymeric controlled drug delivery systems. Chitosan has been chosen as the starting material. Chitosan is naturally occurring second most abundant biopolymers after cellulose. Chitosan is deacetylated form of chitin which is the major structural elements of crustaceans (crabs, lobsters and shrimps). Chitosan is well-known biomaterials because of its high biocompatibility, biodegradability, antibacterial and non-antigenicity and blood coagulation properties. This thesis represents the modification of chitosan for designing advance drug delivery systems.

Chemical modification of chitosan has been carried out through the grafting of polyurethane chain on chitosan backbone. Polyurethane grafted on chitosan with a different degree of substitution. Chitosan shows highly hydrophilic nature but grafting of polyurethane chain make them hydrophobic as compared to pure chitosan. Hydrophobicity of the copolymers gradually increases with the increase in the degree of substitution. Copolymers with the high degree of substitution are found to be insoluble in acetic acid/DMF mixture indicating highly crosslinked behavior. Controllable hydrophilic/hydrophobic nature of the copolymers makes them suitable for drug delivery applications. Mechanical properties of the copolymers also enhance. The copolymers show higher elongation of break as compared to the native chitosan indicating highly flexible in nature. The antibacterial drug, Tetracycline hydrochloride has been used as model drug to understand the drug release kinetics from pure chitosan and its graft copolymers. *In vitro,* Drug release kinetics reveals that pure chitosan shows burst release whereas the graft copolymers deliver the drug in a sustained manner. Sustained release behavior of the graft copolymers is attributed the poor swelling ability and crosslinked polymeric structure which

slow down the diffusion nature of the drug from the polymeric network. The most interesting finding of this work is that drug release kinetics can be tuned by controlling the degree of substitution. Bio-and hemocompatibility of the graft copolymers has been checked in terms of platelet function for their possible use as drug delivery vehicles. Graft copolymers are found to be better biocompatible in nature than pure chitosan. Polyurethane-grafted-chitosan is a promising candidate for controlled drug delivery purpose.

In this study polyurethane is grafted on chitosan backbone slight changing in the reaction condition of the previous synthesis technique. In the previous study, the degree of substitution was very high; therefore, the graft copolymers show poor solubility which restricts them to form hydrogel. In the present study, Polyurethane graft copolymers are synthesized with low degree of substitution. The graft copolymers are designed in brush like architecture. The graft copolymers are able to form hydrogel in the diluted acetic acid medium. Hydrogel can be prepared with higher concentration and at high temperature with the copolymers as compared to the pure chitosan. The high solubility and instant gelling properties of pure chitosan restrict them for their use as an injectable hydrogel. The great advantage of graft copolymers is that they can be used as an injectable hydrogel which is confirmed by the *In vivo* gelation study in animal model. Graft copolymers are fabricated in the form of hydrogels and scaffolds for their possible use in drug delivery applications. Hydrogels of graft copolymers possess high gel strength as compared to pure chitosan as compared to the pure chitosan. Antibacterial drug, Tetracycline hydrochloride was loaded in hydrogels and scaffolds for the investigation of *In vitro* drug release kinetics. *In vitro* drug release behavior shows that both the hydrogels and scaffolds slow down the drug release kinetics as compared to pure one. The zone of inhibition formation with drug loaded

hydrogels of graft copolymer and pure chitosan also supports the *In vitro* release kinetics. The drug release kinetics can be controlled by controlling the degree of substitution using both hydrogels and scaffolds of brush copolymers. Cytotoxicity assessment using NIH 3T3 fibroblast cell has been carried out through the proliferation of the cells on the surface of the hydrogels and scaffolds of graft copolymers and pure one. Cell viability is found to be higher in graft copolymers as compared to pure chitosan indicating better biocompatible nature. It is interesting to note that the cell viability is higher in case of scaffolds as compared to hydrogels in both graft copolymers and pure one. How the cells are proliferated in scaffolds were investigated through the SEM of the cell seeded scaffolds. It is observed that the uniform pore structure in graft copolymers helps to proliferate the cells inside the pores as opposed to the surface proliferation of cell on pure chitosan scaffold. So, scaffolds of graft copolymers can be used for the tissue engineering purpose such as bone regeneration. Henceforth, the developed polyurethane-graft-chitosan brush copolymers have the potential to be used as injectable hydrogel for controlled drug delivery and tissue engineering.

In another study, main focus has been given on the enhancement of mechanical strength of chitosan and to obtain controlled drug systems. Hydrogels and scaffolds of chitosan nanohybrids have been developed for controlled drug delivery applications. Two types of nanofillers of opposites charges (30B (-Ve and LDH (+Ve)) were used to prepare nanohybrids. The mechanical stability of the hydrogel and scaffolds has been significantly enhanced using nanofillers in both cases hydrogels and scaffolds. LDH based nanohybrid shows higher mechanical strength as compared to 30B because of homogenous dispersion and higher interactions with chitosan matrix. Nanohybrids are explored for drug

delivery study using both hydrogels and scaffolds taking Tetracylcine hydrochloride (antibacterial drug) as a model drug. *In vitro*, drug release kinetics exhibits that the nanohybrids release the drug in more sustained manner as compared to the pure chitosan. LDH based nanohybrid shows more sustained release behavior as compared to 30B one because the interaction of drug molecules with LDH nanohybrid is greater as compared to the 30B one, thereof, slower diffusion of drug molecules from the LDH based matrix is observed. Cytotoxicity assay suggests that the nanohybrids do not show any kind of toxic nature to NIH 3T3 cells indicating the biocompatible nature of the nanohybrids. So, developed nanohybrids are deserving candidates for controlled drug delivery applications.

The thesis containing the research work on chitosan based drug delivery systems have the potential to be used as drug delivery vehicles. The research work included in this thesis has important future which is noted under the headline of Future scope of the work.

6.2 The future scope of the work

The scopes of the research work carried out during the PhD programme are summarized below:

- ✓ Polyurethane-chitosan brush injectable hydrogel will be used to check the antitumor activity in the animal model using anticancer drug.
- ✓ Highly mechanically stable chitosan nanohybrid scaffolds will be used for bone regeneration in animal model.
- ✓ Hydrogel of chitosan nanohybrid with sufficient gel strength will be checked for wound healing in the animal model.