CHAPTER 6

Summary and Conclusions

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A mechanistic investigation of emulsion and microemulsion polymerization of polar monomers to produce stable, translucent nanolatex and its subsequent use as a device for drug encapsulation.

In early 19 th century industrial reforms across the globe resulted in the beginning of a new age, called '*Plastic age* ' which witnessed tremendous growth of two closely related classes of man – made materials ' rubbers and plastics '. Modern life is difficult to conceive without these two materials. Plastics and rubbers fall in the general class of materials known as ' Polymers '. Nowadays polymers are finding increasing use in biomedical applications. One such application is the use of polymeric nanoparticles as a device for controlled delivery of the drug at the site of action. This site specific or targeted delivery combined with delivery at an optimal rate will not only improve the efficacy of the drug but also reduce the possibility of unwanted side reaction A polymerisable microemulsion is a well-established route for the production of high molecular weight polymer with a narrow particle size distribution and high specific surface area but suffers the disadvantage of high surfactant concentration. The present work utilizes emulsion polymerisation as an alternative method to increase the solid content of the latex and at the same time retains the inherent advantages of microemulsion polymerisation. Subsequently the conditions were optimized to enhance the % entrapment of an oil soluble drug in the polymeric nanoparticles since higher % entrapment is a prerequisite to a sustained release.

In the first chapter, basic concepts of free radical polymerization are discussed with a special emphasis on the relative importance of various phases involved in emulsion and

microemulsion polymerisation. Literature survey for the past 25 years in the field of microemulsion polymerization is also presented in the first chapter.

The second chapter comprises of the experimental techniques generally used in free radical polymerisation. Optimization of various reaction conditions such as initiator concentration, reaction temperature, monomer – feed composition along with the reaction kinetics is also described in chapter two. Characterisation of the latexes and polymers using DLS, TEM, spectroscopy, viscometry and GPC is also discussed.

In the third chapter the kinetics of homopolymerisation of ethylacrylate and the copolymerisation of ethylacrylate - methylmethacrylate has been discussed for both emulsion and microemulsion media. Following conclusions are drawn from the work

1. The kinetics of emulsion system at [M / S = 10 , 40 and 54] was studied with respect to microemulsion at M / S =1 for ethylacrylate. While the copolymerisation of ethylacrylate – methylmethacrylate in emulsion was carried out at M / S = 10 and 50 with respect to microemulsion system at M / S = 0.66. Transition of the emulsion system into transparent / translucent nanolatexs is attributed to the simultaneous distribution of monomer into the sites created by homogeneous and micellar nucleation resulting into early disappearance of monomer as a separate phase. The rate of particle nucleation was observed to be higher than the rate of particle growth resulting into a larger number of smaller particles stabilized by the available surfactant. Breaking of the same emulsion system with AIBN also supports this observation. AIBN generates lesser number of effective radicals initiating polymerisation, resulting in lower rate of nucleation and higher rate of particle growth. This results into lesser number of larger

size particles, which are not stabilised with the available surfactant, resulting into phase separation. Gel effect dominance was observed in the case of microemulsion polymerisation.

2. The fact that polymer particles are indeed generated by both micellar and homogeneous nucleation in the emulsion polymerisation of polar monomers was confirmed by the study of copolymerisation.

[a] ^{1}H NMR studies showed a drift in composition . Such a drift was more evident for M / S = 50 having the lowest surfactant concentration.

[b] DSC study showed the appearance of two Tg' s for emulsion based samples indicating two different compositions for the polymer chains. Particle size distribution showed a bimodal nature during the nucleation stage Whereas no such drift in composition was observed for microemulsion based copolymers studied below 10 % conversion. Copolymers synthesized in microemulsion also showed a single Tg.

3. The contribution of homogeneous nucleation to the overall process of particle nucleation was observed to be higher for emulsion system compared to microemulsion.

4. In contrast, microemulsion polymerisation studied at lower monomer and higher surfactant concentration resulted into much larger particles, showing effects of coagulation.

5 The role of KPS and AIBN was found to be opposite for emulsion and microemulsion. AIBN initiated system generated larger number of smaller particles compared to KPS in case of microemulsion polymerisation under identical reaction conditions. Whereas emulsion system initiated with KPS produced a stable latex system with smaller particle size. AIBN initiated emulsion system showed phase separation under identical reaction conditions.

6. pH seems to influence the decomposition rate constant of KPS at higher emulsifier concentration thus lowering the fraction of effective radicals initiating polymerisation.

The fourth chapter deals with monomer reactivity of EA – MMA, Sty – MA and Sty – BA in microemulsion considering the effect of monomer partitioning. The following points can be deduced.

1 The concentration of comonomers at the polymerisation loci can be determined from the ratio of concentration of the comonomers at the polymerisation loci, assuming that the sum of the loci concentrations of the comonomers equals unity rather than considering the equivalency of loci and feed concentrations, even for hydrophobic monomers like styrene to overcome the error arising due to the partitioning of the other monomer.

2. Recalculation of the reactivity ratios termed as true reactivity ratios, considering the concentration of monomers at the polymerisation loci and not in the feed leads to very close values for those calculated for bulk polymerisation.

3. Prediction regarding actual copolymerisation locus has been done on the basis of f'_A / f_A and f'_B / f_B ratio.

4. Calculation of loci concentration involving both polar monomers reqiures their concentration at the polymerisation site to be unity.

5. Emulsion copolymerisation shows a greater composition drift compared to microemulsion polymerisation of polar monomers.

The last chapter discuss the use of polymeric nanoparticles to achieve higher % entrapment of a relatively water insoluble drug carbamazepine. The conclusions are as follows-

1. Increase in % of HEMA in the comonomer mixture changed the polymer microstructure from a more discrete to a complete network like structure with a corresponding increase in the % entrapment of the drug. Increase in % of the cross linker made the polymeric matrix more rigid resulting into slower diffusion of the drug molecule and an increase in drug entrapment.

2. In vitro release studies carried out in 1 % SDS solution shows a slower release of the drug initially.