CHAPTER 7

CONCLUSIONS AND SCOPE OF FUTURE WORK

7.1 CONCLUSIONS

The work presented in this thesis marks the first attempt to model the supersaturation profile, particle size and particle size distribution resulting from a moving droplet in the supercritical antisolvent (SAS) process. This process involves a complex interaction of hydrodynamics, thermodynamics and mass transfer principles.

This model gives insights into the fundamental phenomena taking place in the SAS process. The first insight is on the droplet dynamics as the droplet moves downwards in the precipitator chamber. The solubility of carbon dioxide at supercritical conditions is high in organic solvents and therefore, the size of the droplet increases due to the fast diffusion of carbon dioxide into the droplet. The solvent is continuously coming out from the droplet due to the concentration gradient. It is observed that the droplet size starts to shrink after reaching a maximum. This is because the droplet becomes saturated with carbon dioxide and from that point onwards, both the solvent and carbon dioxide diffuse out from the droplet which leads to shrinking of the droplet.

The simulation results show that supersaturation profile and particle size distributions curves are quite similar in pattern. This confirms that supersaturation is the driving force in SAS micronization as it is in other crystallization processes. It was found that the effects of various process parameters such as solute concentration, nozzle diameter, solution flow rate on particle size distribution are similar to their effects on supersaturation profile. Therefore, it is expected that tuning of supersaturation profiles will yield particle size distributions and average particle size of desired characteristics.
The mathematical model developed in this thesis has been used to simulate the SAS process for two systems namely: (i) rifampicin-dimethyl sulfoxide (DMSO)-CO$_2$ (ii) erythromycin-methanol (MeOH)-CO$_2$. The results show that a higher concentration of rifampicin or erythromycin results in a broader particle size distribution. This effect of solute concentration on particle size distribution is attributed to a change in the supersaturation profile in the moving droplet. Higher concentrations of solute in the droplet require less amount of carbon dioxide to reduce the actual solubility to equilibrium solubility. Therefore, the droplet becomes supersaturated at an early stage and yields a broader particle size distribution. It is also observed that a higher flow rate of solution and small droplet diameters lead to a narrower particle size distribution.

The mathematical model results have been compared with experimental values for erythromycin-MeOH-CO$_2$ system. Although the model has described the effect of the process parameters on particle size distribution, it fails to satisfactorily predict the actual particle size distribution. This is due to the complexity of the SAS process as well as general expressions for nucleation and growth phenomena.

The model presented here is useful to predict the average particle size and particle size distribution micronized through the SAS process if accurate nucleation and growth mechanism expressions are available. At present, there is no evidence of any nucleation and growth kinetics expression correlated for any substance produced by the SAS process.

### 7.2 Scope of Future Work

The SAS process has been used experimentally to produce a wide variety of compounds. But the main focus of researchers has been to produce particles experimentally. Some researchers have made efforts to model the SAS process but did not consider all aspects of the SAS process i.e. hydrodynamics, mass transfer and nucleation and growth. In this work, all these phenomena have been considered. Still there remains a lot to be done in the modeling of the SAS process.

The future work lies in converting this model from descriptive to predictive. For this, we need experimentally correlated solubility of substance and accurate nucleation as well as growth expressions. The solubility of solute plays a great role in the morphology and particle
size of product obtained in the SAS process. This may be done by measuring solubility at
different compositions of the solute-antisolvent mixture and then developing a correlation.
Similarly, to get accurate nucleation and growth expressions, power law expression for
nucleation and growth need to be developed. Further, the SAS process is also used for
encapsulation of pharmaceutical drugs in bio-polymers. A model that looks into possible
effects of process parameters on encapsulation of drugs can also be developed in future
works.