Sasiwimon Phothipanyakun 2014: Dissolution Rate Enhancement of Poorly Water-Soluble Drugs using Gas Anti-Solvent Process. Master of Engineering (Chemical Engineering), Major Field: Chemical Engineering, Department of Chemical Engineering. Thesis Advisor: Associate Professor Manop Charoenchaitrakool, Ph.D. 171 pages.

In this research, Gas Anti-Solvent (GAS) technique with the use of dense carbon dioxide as an anti-solvent was applied to co-precipitate poorly water-soluble drugs and hydrophilic polymer. Mefenamic acid (MEF) and sulfamethoxazole (SMX) were used as model drugs, whereas polyvinylpyrrolidone K30 (PVP K30, M_W ~ 40,000) was used as polymer. The effects of drug to polymer ratio, temperature, solution concentration and type of solvent (only for the case of MEF) on the %Drug content, particle size and morphology were investigated. In the case of MEF, it was found that an increase in drug to polymer ratio resulted in a higher %Drug content. However, temperature and solution concentration had no significant effect on the %Drug content when the amount of polymer in the solution was lower or equal to the drug. The type of solvent had a major effect on particle morphology. It was also found that an increase in drug to polymer ratio or temperature resulted in a larger particle size. The dissolution rate of the MEF-PVP K30 composites was found to be 7 times and 3 times greater than those of the unprocessed MEF and physical mixture, respectively. In the case of tablet dissolution studies, it was found that the dissolution rate of MEF-PVP K30 composites was faster than that of physical mixture. The composite tablet could achieve 65% MEF dissolved in 300 mins, whereas the physical mixture tablet could dissolve only 25% in 300 mins. Based on the Fourier transformed infra-red (FTIR) analysis, it was found that there was no interaction between MEF and PVP K30. In the case of SMX, it was also found that an increase in drug to polymer ratio resulted in a higher %Drug content. The effect of precipitation temperature on %Drug content was only observed when the amount of drug in the solution was greater than the polymer. However, the solution concentration had no significant effect on the %Drug content. In addition, it was found that the precipitated composites were irregular in shape with a broad particle size distribution when the amount of polymer was higher or equal to the drug was applied. On the other hand, when the amount of polymer was lower than the drug was used, the precipitates had prism-like morphology with large particle size which was similar to the precipitation of pure drug. In addition, it was found that the dissolution rate of SMX-PVP K30 composites was similar to that of the physical mixture, but was 5-6 times faster than that of commercial micronized SMX. Unlike MEF-PVP K30 composites, it was found that there was an interaction between SMX and PVP K30 in the composite.

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