Rawin Imchalee 2014: Production of Cocrystal between Sulfamethoxazole Drug and L-Malic Acid Using Gas Anti-Solvent (GAS) Process. Master of Engineering (Chemical Engineering), Major Field: Chemical Engineering, Department of Chemical Engineering. Thesis Adivisor: Associate Professor Manop Charoenchaitrakool, Ph.D. 165 pages.

The objective of this research was to enhance the dissolution rate of a poorly water–soluble antibiotic drug, sulfamethoxazole (SMX), by forming cocrystal with L-Malic acid (MA). Gas Anti-Solvent (GAS) technique with the use of dense carbon dioxide as an anti-solvent was applied for cocrystallization. The effects of SMX to MA mass ratio (2:1, 1.5:1 and 1:1), temperature (35°C and 45°C) and drug concentration in acetone (30%SAT, 50%SAT and 70%SAT) on % drug content, particle morphology and dissolution rate were investigated. Production of SMX–MA cocrystal by slow evaporation technique was also conducted in order to compare the obtained results. It was found that SMX-MA cocrystal could be successfully produced by both GAS and slow evaporation techniques. Based on the XRD analysis, the cocrystal formation was confirmed by the appearance of two new peaks at 2θ = 6.8 and 13.8. Results from the FTIR analysis also confirmed that there was hydrogen bond formation in the SMX-MA cocrystal. In the GAS process, it was found that drug content of the product was dependent on the SMX to MA ratio. As the SMX to MA ratio decreased from 2:1 to 1:1, % drug content in the product was decreased. The effect of SMX to MA ratio on the % drug content was valid for both 35°C and 45°C. In addition, an increase in drug concentration resulted in a lower threshold pressure, but higher amount of product. Two distinct colors (white and pale yellow) of the GAS products were observed. It was found that the size of the white product was slightly smaller than the pale yellow product at the same operating condition. The melting point of the GAS product was in between those of the drug and co-former. The heat of melting of the GAS product was also lower compared to the drug and co-former. In the dissolution studies, it was found that 90% of SMX in the cocrystal obtained from GAS could be dissolved within 4.2 min, whereas the times required to dissolve 90% of the drug in the physical mixtures were 8.2 min (ratio 1:1) and 25 min (ratio 2:1), and up to 28 min for the commercial micronized SMX. On the other hand, the times required to dissolve 90% of the drug in the cocrystal from slow evaporation could go up to 12 min depending on the SMX to MA ratio. The enhanced in the dissolution rate of the GAS product could be attributed to the reduction in degree of crystallinity as observed from the XRD results.

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