Thesis Title Effect of Co-grinding with β-Cyclodextrin and MicrocrystallineCellulose on Physicochemical Properties ofNeedle-form Piroxicam

Name Kanokwon Prasitporn

Degree Master of Science (Pharmacy)

Thesis Supervisory Committee

Satit Puttipipatkhachorn, Ph.D.

Ampol Mitrevej, Ph.D.

Nuttanan Sinchaipanid, Ph.D.

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ABSTRACT

The effect of co-grinding with β-cyclodextrin (β-CD) and microcrys talline cellulose (MCC) on physicochemical properties of needle-form compared to cubic-form piroxicam was investigated. The physicochemical properties were determined by differential scanning calorimetry (DSC), Fourier transformed infrared (FTIR) spectroscopy and powder X-ray diffraction (PXRD) measurement. The needle-form piroxicam melted at 197°C while the cubic-form piroxicam melted at 201°C. The needle-form piroxicam showed different characteristics of FTIR spectra and PXRD pattern from those of cubic-form piroxicam. The solubility and dissolution rate of needle-form piroxicam in 0.1 N HCl was higher than those of the cubic-form piroxicam. The solubilities of both forms of piroxicam increased with β-CD concentration, showing the phase solubility diagrams of A_p type. When the needle-form piroxicam was ground by mortar and pestle, it was changed to the cubic-form. The physical mixtures of either piroxicam polymorph with MCC or β-CD were prepared by gentle trituration in a mortar. The ground mixtures of either piroxicam polymorph with MCC or β-CD were prepared by grinding in a ball

mill. The mixing ratio of piroxicam to MCC was 1:9 % w/w and that of piroxicam to β-CD was 1:1 and 1:2 molar ratios. When the needle-form piroxicam was ground with MCC, it was changed to the cubic-form. The polymorphic change was not observed in case of the cubic-form piroxicam ground with MCC. From DSC and FTIR measurements, the cubic-form piroxicam might form the inclusion complex and/or the hydrogen bonding with β-CD when ground with β-CD at both 1:1 and 1:2 molar ratios. When the needle-form piroxicam was ground with β-CD, it was changed to the cubic-form at the initial stage of grinding and then formed the inclusion complex with β-CD regardless of molar ratio. The dissolution rates of the ground mixture of either piroxicam polymorph with β-CD was higher than those of physical mixtures. The physicochemical characteristics and dissolution behaviours of the ground mixtures of either piroxicam polymorphs with MCC did not significantly changed after storage for 90 days at 45°C and 75%RH. From the results of DSC and PXRD measurements, the crystallization of inclusion complex in the ground mixture of either piroxicam polymorph with β-CD was observed after storage at 45°C and 75%RH for 90 days, nevertheless their dissolution behaviours were not changed. The results from this study demonstrated that both piroxicam polymorphs could form inclusion complex with β-CD in the ground mixture, resulting in higher dissolution rate and the needle-form piroxicam was transformed to the cubic-form piroxicam before forming an inclusion complex.