Amorphization and Dissolution Studies of Acetaminophen-β-Cyclodextrin Inclusion Complexes

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ABSTRACT

In order to improve the solubility and the dissolution rate of acetaminophen, the equimolar inclusion complex of acetaminophen and β-cyclodextrin was prepared by freeze drying, grinding and sealed heating methods. The physical mixture of acetaminophen and β-cyclodextrin was also prepared by means of mechanical mixing. The molecular behaviors of the drug in all samples were characterized by X-ray powder diffraction, fourier transformed infrared spectroscopy and differential scanning calorimetry. The dissolution and the stability studies of the samples were performed. The results showed that the amorphous inclusion complex of acetaminophen in β-cyclodextrin was successfully obtained by freeze drying and grinding methods. These inclusion complexes showed a substantially higher dissolution rate than acetaminophen and physical mixture. The characterization techniques provided useful information to support the amorphousness of the samples as well as the successful inclusion of the drug molecule into the cyclodextrin cavity. Upon storage under certain conditions at a specific time, molecular behaviors of acetaminophen in freeze-dried mixture were partially transformed into the crystalline state, whereas the sealed heating mixture and physical mixture showed little change in their molecular behaviors.

On the basis of these results, the improvement of acetaminophen bioavailability is expected by inclusion complex formation with cyclodextrin. However, from the stability point of view, the retardation of phase transition in order to maintain the amorphous state of the drug should be taken into consideration.

Key words: Acetaminophen, Amorphization, β-Cyclodextrin, Inclusion complexes

INTRODUCTION

The bioavailability of most drugs depends primarily on their dissolution properties. Fast dissolution rate and complete dissolution usually enables better absorption. It is recognized that the internal structure of a compound exerts a profound effect on its dissolution characteristics, i.e., the ease of escaping to the dissolution medium of each molecule depends on the nature of the internal structure. Accordingly, crystalline and amorphous forms of a compound usually show different dissolution behaviors. As the amorphous form of a drug dissolves much more rapidly and completely than its crystalline