Thesis Title The Dissolution Kinetics of Three-Component Solid Mixtures with Various Solubilities.

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ABSTRACT

The dissolution kinetics of MAN-SMX-TMP 3-component solid mixtures was studied. The triangular composition diagram of MAN-SMX-TMP was constructed in order to study various dissolution behaviors of compressed spheres of various compositions of mannitol (MAN), sulfamethoxazole (SMX), and trimethoprim (TMP). The critical flaking line was drawn between 2 critical flaking points (*i.e.*, the composition with a MAN mass fraction of 0.5022 and a SMX mass fraction of 0.4978 and the composition with a MAN mass fraction of 0.4906 MAN and a TMP mass fraction of 0.5094) in order to separate such diagram into nonflaking and flaking regions.

In the case of nonflaking region, there are only 3 dissolution behaviors for MAN-SMX-TMP 3-component mixtures. The observed dissolution rates for each component were found to approximate the calculated values for both 2- and

3-component solid mixtures.

In the case of flaking region, the observed dissolution rate of MAN was found to be the exponential function of the mass fraction ratio of either SMX or TMP to MAN for both 2- and 3-component mixtures. The slope of the profile obtained by plotting the mass fraction ratio of each drug to MAN against the natural logarithm of the observed dissolution rate of MAN, r_{SMX} and r_{TMP}, defined as retarding coefficients of SMX and TMP, respectively, were also used to calculate the dissolution rate of MAN. The observed dissolution rates of MAN appeared to be in good agreement with the calculated values.

Within flaking region, the erosion rate of either SMX or TMP was the product of mass fraction ratio of drug to MAN and the exponential function of such mass fraction ratio. The optimal mass fraction ratio of SMX and TMP to MAN causing maximum erosion rate of SMX and TMP were computed to be the inverse fraction of r_{SMX} and r_{TMP}, respectively. The observed erosion rates of both drugs were found to be in good agreement with the predicted value.

By utilizing the calculated erosion rate of each drug along with its calculated dissolution rate of prime particles, the method of superimposition was developed to predict the dissolution rate of each drug from flaking spheres within flaking region. The ranking in prediction accuracy was higher when the amount of MAN was increased. Besides, it was found that the deviation of the predicted dissolution rates from the observed values were less in the case of TMP than SMX.