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Comparison Between Dehydration and Desolvation Kinetics of Fluconazole Monohydrate and Fluconazole Ethylacetate solvate Using Three Different Methods

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Abstract: Purpose. To study the dehydration of fluconazole monohydrate and to determine the kinetics of dehydration using thermogravimetry (TGA). Methods: Fluconazole monohydrate was prepared by crystallization in water. The dehydration process was characterized by differential scanning calorimetry, thermogravimetry, powder X-ray diffractometry and Fourier transform infrared spectroscopy (FTIR). The weight change of the fluconazole monohydrate sample (8-10 mg) was monitored by isothermal TGA at temperatures between 60?C and 70?C with a nitrogen purge of 20 mL/min. Kinetic analysis of isothermal TGA data was done by fitting to various solid-state reaction models. Various heating rates were also employed in different TGA samples, in order to apply Ozawa method to determine the kinetics parameters. Results. Four solid-state reaction models were chosen to interpret the isothermal TGA experiments. These models are: (a) one dimensional diffusion (D1), (b) first order reaction (F1), (c) two-dimensional phase boundary reaction (R2) and (d) three-dimensional phase boundary reaction (R3). Based on statistics, the three-dimensional phase boundary reaction (R3) provides the best fit of the data. The temperature dependence of the rate constants based on the R3 model was subjected to Arrhenius analysis. The activation energies derived ranged from 98-124 kJ/mol, the mean value being 107? 11.44 kJ/mol. For the Ozawa analysis method, activation energy was found to be 117?21 kJ/mol. This agreement in activation energy value strengthens the fitting of the data to R3 model. Conclusion. The dehydration process of fluconazole monohydrate is assumed to follow the kinetics of a three dimensional phase boundary reaction (contracting sphere) i.e. to proceed from the surface of a sphere inward in three dimensions.