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Evaluation of Sodium Naproxen Hydrated Forms by Isoconversional Analysis

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Sodium naproxen (SN) exists in an anhydrous form and in four different hydrated forms: one monohydrate (MSN), two dehydrates (DSN and CSN) and one tetrahydrate (TSN). Mechanisms of dehydration have been previously determined by an isothermal method [1, 2]. In this study, their dehydration was followed by an isoconversional analysis (ICA), which is based on a non-isothermal method.

Materials and Methods:

SN (B.P.) was kindly supplied by A.C.R.A.F. (Italy).

Thermogravimetric analysis (TGA) was performed by a Simultaneous Thermal Analyzer (STA 6000, Perkin Elmer, Inc., Waltham, MA, USA), under nitrogen atmosphere (20 mL/min) in a 0.07 ml open aluminium oxide pans. After calibration, samples (approximately 10 mg) were tested in quadruplicate by heating from 293 to 413 K at four different heating rates (5, 10, 20, 40 K/min).

Results:

For each hydrate form, the degree of conversion (% dehydration) was plotted versus temperature at any heating rate. The temperature relative to each conversion degree was then determined and plotted versus temperature. The slope of the regression lines permitted the calculation of the activation energy (E_{att}). The E_{att} ranged approximately from 60 to 80 kJ \cdot mol⁻¹ for the MSN, from 70 to 90 kJ \cdot mol⁻¹ for the DSN, from 28 to 50 kJ \cdot mol⁻¹ for the CSN and from 30 to 70 kJ \cdot mol⁻¹ for the TSN. A dehydration occurring by one-step mechanism has been revealed for the MSN and DSN, while a multi-step mechanism explains the dehydration of CSN and TSN. The results of this study showed a good correlation with those previously determined by applying an isothermal method [1]. In conclusion, the isoconversional analysis may be considered as a simple and fast method to predict the conversional behaviour of pharmaceutical substances and it may be applied to predict the phase transition of complex systems.

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- [2] Kim Y, Rousseau RW. Characterization and solid-state transformations of the pseudopolymorphic forms of sodium naproxen. *Cryst Growth Des.* 2004; 4: 1211–1216. doi:10.1021/cg049917q