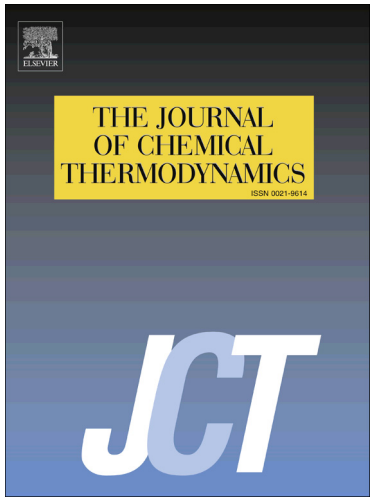

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Thermodynamic and molecular investigation into the solubility, stability and self-assembly of gabapentin anhydrate and hydrate

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Abstract

Solubility of gabapentin anhydrate/monohydrate in alcohol-water mixtures was experimentally determined. An interesting trend of the solubility was found, which showed both maximum and minimum solubility with different solvent compositions at one temperature. Molecular dynamics simulations were carried out to explore the effect of solvent composition on the solubility, indicating that the water association played an important role. Critical water activity and the transition temperature of gabapentin anhydrate/hydrate were also determined, and a relationship between them was established to investigate the factors influencing the hydration. Furthermore, the ternary phase diagram of (gabapentin-ethanol-water) at 293.15 K was built by slurry experiments for further understanding of the crystal form transformation, which confirmed the stability regions of anhydrate/monohydrate and verified the above established relations. Then the dehydration/hydration process in the solution can be predicted and controlled, thus obtaining