NEW APPROACH TO THE THERMODYNAMIC ANALYSIS OF POLYMORPHIC SYSTEMS

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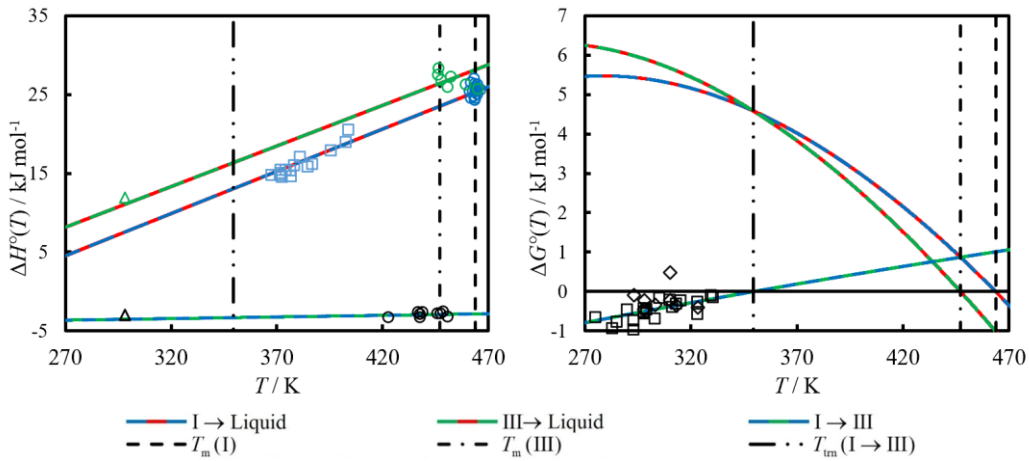
The polymorphic state of compound defines its practically important properties, such as stability, bioavailability, solubility, dissolution rate. Characterization of the thermodynamic relationships between two crystal polymorphs is usually based on experimental melting or solubility data [1]. Due to experimental features and neglecting the heat capacity correction results of these methods may differ significantly.

In this work, we proposed an algorithm for simultaneous treatment of the fusion, solubility and related data to get self-consistent phase diagram for polymorphic compounds. The method combines melting temperatures, enthalpies of fusion, crystallization, dissolution, and solid-solid transitions, equilibrium solubilities, dissolution rates, vapor pressures, and the heat capacity data to achieve their mutual agreement and access ***G*-*T*** and ***H*-*T*** diagrams over a wide temperature range.



Thermodynamic characteristics of phase transitions between crystalline I, crystalline III and liquid carbamazepine. Symbols represent different types of the experimental data used to calculate the diagram.

The proposed approach was tested using our and literature experimental data on several polymorphic systems (see figure). Its ability to distinguish between the reliable and erroneous data make it valuable instrument in the thermodynamic analysis of polymorphism, fusion, and crystallization.

1. L. Yu, Inferring thermodynamic stability relationship of polymorphs from melting data, Journal of pharmaceutical sciences, 84 (1995) 966-974.

This work was supported by the Russian Science Foundation, Project No 25-73-20073.