Comments on “Thermodynamic modeling studies of aqueous solubility of caffeine, gallic acid and their cocrystal in the temperature range of 303 K–363 K”

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Abstract

The activity coefficients reported by Dabir and coworkers [Fluid Phase Equilib. 456 (2017) 65-76] were based on a thermodynamic relationship that failed to properly take into account the solid phase transition that both caffeine and gallic acid exhibited prior to melting. The calculation of activity coefficients for crystalline nonelectrolyte solutes exhibiting a solid phase transition is discussed.

Key Words and Phrases: Caffeine solubility; Gallic Acid Solubility; Activity Coefficients

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In a recent article appearing in *This Journal* Dabir and coworkers [1] determined the aqueous solubility of caffeine, gallic acid and their co-crystal in the temperature range of 303 K - 363 K. As part of the thermodynamic modelling the authors calculated the activity coefficients, γ , of the solutes based on a simplified form of the following thermodynamic relationship for nonelectrolyte solutes:

$$\ln(x\gamma) = -\frac{\Delta H_f}{RT_t} \left(\frac{T_t}{T} - 1 \right) + \frac{\Delta C_p}{R} \left(\frac{T_t}{T} - 1 \right) - \frac{\Delta C_p}{R} \ln \left(\frac{T_t}{T} \right) \quad (1)$$

where x is the mole fraction solubility of the solute, T_t is the triple point temperature, T is the equilibrium temperature at which the solubility measurement was performed, ΔH_f is the solute's molar enthalpy of fusion at the normal melting point temperature, ΔC_p is the difference in the molar isobaric heat capacity of the liquid and crystalline forms of the solute, and R is the universal gas constant. As noted by the authors many times there is very little difference between the triple point temperature and the normal melting point temperature, T_m . The two ΔC_p terms on the right-hand side of Eqn. 1 are opposite in sign, and are often neglected in the activity coefficient calculations. Neglect of the two ΔC_p terms leads to the following mathematical expression:

$$\ln(x\gamma) = -\frac{\Delta H_f}{RT_t} \left(\frac{T_t}{T} - 1 \right) \quad (2)$$

which was used by the authors to calculate the activity the activity coefficients of both caffeine and gallic acid at the solution temperatures of the solubility measurements. As an informational note Dabir et al. [1] reported experimental values of $\Delta H_f = -17.7 \text{ kJ}\cdot\text{mol}^{-1}$ and $\Delta H_f = -65.5 \text{ kJ}\cdot\text{mol}^{-1}$ for the enthalpies of fusion of caffeine and gallic acid, respectively. This corresponds to an

exothermic melting process. Melting is an endothermic process. I have added a negative sign in front of the ΔH_f term in both Eqns. (1) and (2) to be consistent with a positive value for ΔH_f .

The purpose of the following commentary is to inform readers that the thermodynamic relationship used to calculate the activity coefficient of crystalline nonelectrolyte solutes contains additional terms [2, 3]:

$$\ln(x\gamma) = -\frac{\Delta H_f}{RT_t} \left(\frac{T_t}{T} - 1 \right) + \frac{\Delta C_p}{R} \left(\frac{T_t}{T} - 1 \right) - \frac{\Delta C_p}{R} \ln \left(\frac{T_t}{T} \right) - \frac{\Delta H_{trs}}{RT_{trs}} \left(\frac{T_{trs}}{T} - 1 \right) \quad (3)$$

if the solute exhibits a first-order solid-to-solid phase transition between the normal melting point temperature and the equilibrium solution temperature, as was the case for both caffeine and gallic acid. The DSC thermograms shown in Figure 5 show transitions before the melting point temperature. In Eqn. (3) ΔH_{trs} and T_{trs} correspond to the enthalpy and temperature of the first-order transition. The thermodynamic expression to calculate γ in the case of a λ -type transition is more involved, and is discussed in detail elsewhere [4].

While the authors did not report the experimental enthalpies of transition, there is published experimental values in the chemical literature. Suzuki et al. ($\Delta H_{trs} = 3.7 \text{ kJ}\cdot\text{mol}^{-1}$ and $T_{trs} = 423.2 \text{ K}$ [5]), Don et al. ($\Delta H_{trs} = 3.43 \text{ kJ}\cdot\text{mol}^{-1}$ and $T_{trs} = 420.9 \text{ K}$ [6]), Mogalian et al. ($\Delta H_{trs} = 3.00 \text{ kJ}\cdot\text{mol}^{-1}$ and $T_{trs} = 414.9 \text{ K}$ [7]), Manic et al. ($\Delta H_{trs} = 2.6 \text{ kJ}\cdot\text{mol}^{-1}$ and $T_{trs} = 405.8 \text{ K}$ [8]), and Boumrah et al. ($\Delta H_{trs} = 3.29 \text{ kJ}\cdot\text{mol}^{-1}$ and $T_{trs} = 421.5 \text{ K}$ [9]) have determined both the enthalpy of transition and the transition temperature of caffeine. For gallic acid there is one experimental value. Bogel-Lukasik and coworkers [10] reported experimental values of $\Delta H_{trs} = 19.28 \text{ kJ}\cdot\text{mol}^{-1}$ and $T_{trs} = 351.3 \text{ K}$.

Recently there has been a significant increase in the number of research groups publishing experimental solubility data. Researchers must take great care to interpret their measured

solubility data correctly so that incorrect methods are not propagated throughout the published chemical literature. In the past two years I am aware of four additional studies [11-14] that have used Eqns (1) and/or (2) to calculate activity coefficients for crystalline nonelectrolyte solutes that exhibit solid-to-solid phase transitions between the normal melting point temperature and the equilibrium solution temperature. Hopefully this commentary, and reader commentaries [15-17] concerning the earlier three studies will prevent this error from propagating further.

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TABLE OF CONTENTS HIGHLIGHTS

- Caffeine and gallic acid exhibit solid phase transition prior to melting
- Activity coefficient of caffeine was incorrectly calculated
- Activity coefficient of gallic acid was incorrectly calculated
- Correct calculation needs to include the solid phase transition prior to melting