Commentary on "Effect of β-alanine and the solvent composition on the solubility of solvate of calcium D-pantothenate containing four molecules of methanol and one molecule of water (D-PC·4MeOH·1H$_2$O)"

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Abstract

Cohen equation coefficients reported by Han and coworkers [J. Chem. Thermodyn. 106 (2017) 36-46] were found to provide an incorrect mathematical description of the solubility behavior of calcium D-panthenate solvate as the mole fraction concentration β-alanine approached zero. Reported equation coefficients failed to describe observed trend of increasing calcium D-panthenate solvate solubility with increasing β-alanine mole fraction. The experimental solubility data was reanalyzed and new Cohen equation coefficients calculated. A polemic is also given regarding the authors' interpretation of an observed mathematical relationship between the experimental mole fraction solubility data and the dielectric constant of the binary solvent mixture. The authors' interpreted one of the curve-fit equation coefficients as the energy dissolution barrier. An unit analysis examination shows that the unit of the curve-fit equation coefficient must be J/(mol K) which is inconsistent with energy.

KEY WORDS AND PHRASES

calcium D-panthenate solvate solubility, Cohen equation, mathematical representation

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In a recent paper appearing in *This Journal* Han and coworkers [1] studied the effect that β-alanine and solvent composition has on the solubility of the solvate of calcium D-pantothenate containing four molecules of methanol and one molecule of water (D-PC·4MeOH·1H$_2$O). The authors measured the solubility of the solvate in seven binary aqueous-methanol solvent mixtures, and at different β-alanine concentrations in the binary aqueous-methanol solvent mixture having an initial mole fraction composition of water of $x_1^o = 0.3$. Concentrations of the dissolved solute in the saturated solutions were determined by high-performance liquid chromatographic method. The purpose of the purpose of the present commentary is to point out problems associated with two of the authors' mathematical treatments.

First the authors used the following mathematical form of the Cohen equation:

$$\text{Log } (S/S_0) = -K\,I + \beta \tag{1}$$

to describe the effect that β-alanine has on the solubility of D-PC·4MeOH·1H$_2$O. In Eqn. 1 S and S_0 refer to the solute solubility with no impurity present in the solution and the solute solubility in the solution with impurity, respectively, I is the concentration of the impurity (no units of concentration given), and K and $β$ represent the calculated curve-fit equation coefficients. The problem with this particular mathematical representation is that it fails to properly describe the solubility in the limit as the concentration of dissolved impurity goes to zero. When there is no impurity present S and S_0 must be numerically equal, which is not consistent with Eqn. 1 above. In the absence of impurity, Eqn. 1 gives log $(S/S_0) = β$, and the authors have tabulated several significantly non-zero values of β in Table 6 of their published paper [1]. There may be errors in the authors' tabulated β values. Moreover, the calculated negative numerical values of K that are given in Table 6 are not consistent with the observed solubility behavior of D-PC·4MeOH·1H$_2$O

at different β-alanine. A negative numerical value of K would indicate Log (S/S_0) would be increasing as the concentration of the dissolved impurity increases. In other words, S_0 would decrease with increasing impurity concentration. This is opposite to the solubility behavior given in Table 3 of the published manuscript. At a fixed temperature, the numerical values of the mole fraction solubility of the solute, given as both $10^3 x_B$ and $10^3 x_A$, increase with increasing β-alanine concentration.

Given the failure of the authors' curve-fit equation coefficients to describe the observed solubility behavior, I decided to reanalyze all the measured solubility data given in Table 3. The calculated equation that I obtained by regressing log (S/S_0) versus x_3^o (mole fraction of β-alanine in the solution) yielded the following mathematical equation:

$$\log (S / S_0) = -48.303\,(1.536)\, x_3^o - 0.022(0.006) \tag{2}$$

($N = 8$, $SD = 0.007$ log units, $R^2 = 0.997$; $F = 989.5$)

for calculating the mole fraction solubility of D-PC·4MeOH·1H$_2$O at T/K = 283.15 as a function of mole fraction of β-alanine. The standard errors in the slope and intercept are indicated in parenthesis. The statistical information associated with the derived equation is given immediately below the correlation, and includes the number of data points (N), the standard deviation (SD), the squared correlation coefficient (R^2) and the Fisher F-statistic (F). The equation coefficients in Eqn. 2 are significantly different than the values that Han and coworkers report in Table 9 of their manuscript. Careful examination of Eqn. 2 reveals that it predicts the correct trend regarding how the solubility of D-PC·4MeOH·1H$_2$O varies with mole fraction of β-alanine. The near zero value that I calculated for β indicates that the equation will give a correct value of S_0 as the mole fraction of β-alanine approaches zero. Listed in Table 1 are the numerical values of K and β that I

calculated by reanalyzing the authors' experimental data. The K values are given as positive numerical values, because of the negative sign in Eqn. 1. The numerical value of β can be set equal to zero by performing a linear least squares analysis through the origin. Table 2 gives the numerical values of K and the associated statistical information for the linear least squares regression analyses through the origin.

A second problem in the manuscript concerns the authors' interpretations based on what was called the Solubility-Polarity Model. The model mathematical describes the variation in the mole fraction solubility with solvent dielectric constant in terms of an Arrhenius-type equation:

$$x_A = k \exp\left(-\frac{E_x}{R\varepsilon_{mix}(T)}\right) \tag{2}$$

where x_A is the mole fraction solubility of D-PC·4MeOH·1H$_2$O, k is a pre-exponential factor, E_x represents the dissolution energy barrier, R is the universal gas constant, and $\varepsilon_{mix}(T)$ corresponds the relative dielectric constant of binary solvent mixtures at various temperatures which is relevant to the temperature and the composition of the solvents. A careful unit analysis of the argument of the exponential term shows that there is a problem in the authors' interpretation. The relative dielectric constant is a dimensionless quantity, which then requires that E_x must have the same set of units as the universal gas constant (e.g., J·mol^{-1}·K^{-1}). The units of the gas constant are not consistent with the units of energy. The authors tabulated the calculated numerical values of E_x in Table 8 of their paper [1] with units of kJ·mol^{-1}.

It would have been better had the authors described the mathematical relationship between the solubility and dielectric constant in more generalized fashion:

$$x_A = constant_1 \exp\left(-\frac{constant_2}{\varepsilon_{mix}(T)}\right) \tag{3}$$

without trying to rationalize the meanings for the curve-fit equation coefficients. There is no theoretical justification that I am aware of for expressing the mole fraction solubility in terms of Eqn. 3. The units do not correctly work out for E_x to be defined as a dissolution energy barrier.

References

[1]   D. Han, Y. Liu, X. Li, T. Zhang, Z. Li, S. Du, M. Guo, S. Xu, B. Yu, B. Hou, J. Gong, J. Chem. Thermodyn. 106 (2017) 36-46

Table 1. Curve-fit equation coefficients for Eqn. 1 with the concentration of β-alanine given in mole fraction

T/K	K	β	N	SD	R^2	F
263.15	71.835	-0.100	8	0.023	0.972	209.8
268.15	62.630	-0.064	8	0.013	0.988	480.0
273.15	58.893	-0.029	8	0.011	0.990	609.5
278.15	54.056	-0.021	8	0.006	0.997	1867.4
283.15	48.303	-0.022	8	0.007	0.997	989.5
288.15	45.255	-0.017	8	0.006	0.995	1267.4
293.15	42.980	-0.012	8	0.003	0.999	5774.2
298.15	48.071	0.000	8	0.002	0.999	11233
303.15	49.248	-0.021	8	0.008	0.993	847.7

Table 2. Curve-fit equation coefficients for Eqn. 1 with β set equation to zero and the concentration of β-alanine given in mole fraction

T/K	K	N	SD	R^2	F
263.15	94.473	8	0.049	0.982	384.5
268.15	77.161	8	0.031	0.989	645.9
273.15	65.562	8	0.017	0.996	1628.6
278.15	58.919	8	0.011	0.998	3027.1
283.15	53.266	8	0.012	0.997	2145.9
288.15	49.164	8	0.009	0.998	2853.5
293.15	45.789	8	0.006	0.999	6042.6
298.15	48.184	8	0.002	1.000	63379
303.15	53.932	8	0.012	0.997	2218.0

HIGHLIGHTS

- Published Cohen coefficients fail to describe solubility at zero impurity concentration

- Solubility data reanalyzed and new Cohen equation coefficients calculated

- Polemic given regarding authors' mole fraction versus dielectric constant model