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Comments on "Solubility of Ethyl Maltol in Aqueous Ethanol Mixtures" (Liu, B.-S.; Liu, R.-J.; Hu, Y.-Q.; Hu, Q.-F. *J. Chem. Eng. Data* 2008, *53*, 2712−2714)

Abolghasem Jouyban*,[†] and William Eugene Acree, Jr.[‡]

Faculty of Pharmacy and Drug Applied Research Center, Tabriz University (Medical Sciences), Tabriz 51664, Iran, Department of Chemistry, University of North Texas, Denton, Texas 76203-5070

Introduction

In a recent paper in this journal, Liu et al.[1] reported the experimental solubilities of ethyl maltol in binary mixtures of ethanol + water at various temperatures. The authors correlated the experimental mole fraction solubilities using a fourth-order polynomial equation derived[2] from the CNIBS/R−K model[3] and evaluated the fitness of the model employing root-mean-square deviations (RMSDs). Liu et al.[1] employed the model at a fixed temperature which is expressed as

$$\ln x_{\mathrm{m}} = f_1 \ln x_1 + f_2 \ln x_2 + f_1 f_2 \sum_{i=0}^{2} S_i (f_1 - f_2)^i \qquad (1)$$

where x_{m}, x_1, and x_2 are the numerical values of the solubility of the solute in the mixture and solvents 1 and 2, respectively; f_1 and f_2 are the volume (mass or mole) fractions of solvents 1 and 2 in the mixture in the absence of the solute; and S_i represent the model constants. The model could be rearranged to eq 2 by replacing f_2 with $1 - f_1$ and further simplified as[2]

$$\ln x_{\mathrm{m}} = \ln x_2 + (\ln x_1 - \ln x_2 + S_0 - S_1 + S_2) f_1 + (-S_0 + 3S_1 - 5S_2) f_1^2 + (-2S_1 + 8S_2) f_1^3 + (-4S_2) f_1^4 \qquad (2)$$

or

$$\ln x_{\mathrm{m}} = B_0 + B_1 f_1 + B_2 f_1^2 + B_3 f_1^3 + B_4 f_1^4 \qquad (3)$$

From a theoretical viewpoint, $B_0 = \ln x_2$, $B_1 = \ln x_1 - \ln x_2 + S_0 - S_1 + S_2$, etc.; however, the fitted coefficients do not exactly match these values, and this causes slightly different errors in the calculations. As an example, the fitted eq 1 to the experimental data of ethyl maltol at 298.15 K yields

$$\ln x_{\mathrm{m}} = -2.528 f_1 - 6.075 f_2 + 6.442 f_1 f_2 - 3.922 f_1 f_2 (f_1 - f_2) + 3.780 f_1 f_2 (f_1 - f_2)^2 \qquad (4)$$

and the corresponding polynomial reported by Liu et al.[1] is

$$\ln x_{\mathrm{m}} = -6.0626 + 17.5415 f_1 - 36.5826 f_1^2 + 37.3772 f_1^3 - 14.7977 f_1^4 \qquad (5)$$

Substituting the constant values of eq 4 into eq 2 yields

$$\ln x_{\mathrm{m}} = -6.0748 + 17.6906 f_1 - 37.1080 f_1^2 + 38.0840 f_1^3 - 15.1200 f_1^4 \qquad (6)$$

Normally the calculated equation coefficients are much closer. Irrespective of the reason why the equation coefficients are slightly different, there is no significant difference between accuracies of eqs 4 to 6.

The aim of this communication is to point out several capabilities of the CNIBS/R−K model (renamed as the Jouyban−Acree model) that journal readers may not have seen. The basic model does contain provisions for representing both the effects of solvent composition and temperature on the solubility of solutes[4]

$$\ln x_{\mathrm{m},T} = f_1 \ln x_{1,T} + f_2 \ln x_{2,T} + f_1 f_2 \sum_{i=0}^{2} \frac{J_i (f_1 - f_2)^i}{T} \qquad (7)$$

where $x_{\mathrm{m},T}$, $x_{1,T}$, and $x_{2,T}$ are the numerical values of the solubility of the solute in the mixture and solvents 1 and 2 at temperature T, respectively, and J_i represent the model constants. The J_i terms could be calculated by regressing $(\ln x_{\mathrm{m},T} - f_1 \ln x_{1,T} - f_2 \ln x_{2,T})$ against $(f_1 f_2)/T$, $[f_1 f_2 (f_1 - f_2)]/T$, and $[f_1 f_2 (f_1 - f_2)^2]/T$ by a no intercept least-squares analysis. The model could be trained using the solubility of a solute in binary solvents at 298.15 K, and then the solubility at higher and lower temperatures could be predicted employing the experimental values of $x_{1,T}$ and $x_{2,T}$ at the temperature of interest. Alternatively, the solubility of various solutes in ethanol + water mixtures at various temperatures could be predicted employing $x_{1,T}$ and $x_{2,T}$ values by using a previously trained Jouyban−Acree model.[5]

The Jouyban−Acree model has provided accurate predictions for the solubility of drugs in mixed solvents at various temperatures. Considering this capability, we have fitted the model to the solubility of ethyl maltol in ethanol + water mixtures at various temperatures and calculated the model constants along with the mean deviation (MD) values defined by

$$\mathrm{MD} = \frac{\sum \left(\frac{|x_{\mathrm{m,Calc}} - x_{\mathrm{m,Obs}}|}{x_{\mathrm{m,Obs}}} \right)}{N} \qquad (8)$$

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* Author to whom correspondence should be addressed. E-mail: ajouyban@hotmail.com. Fax: +98 411 3363231.

[†] Faculty of Pharmacy and Drug Applied Research Center.

[‡] University of North Texas.

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Table 1. Mean Deviation (MD %) for Various Equations Investigated in This Work for Back-Calculated and Predicted Solubilities Before * and After ** Corrections on the Original Article[1,13]

	back-calculated			predicted	
T (K)	eq 1 or 2	eq 3 with the reported B_0 to B_4 terms	eq 9	eq 9 trained with data at 25 °C	eq 10
293.15*	6.4	17.3	55.2	28.1	17.3
293.15**	1.6	1.8	36.5	10.5	10.6
298.15	0.8	0.9	21.1	-	15.5
303.15	1.3	1.3	10.9	7.3	20.7
308.15	0.5	0.6	4.8	12.7	25.0
313.15	2.1	2.1	6.4	17.3	26.8
318.15	2.3	2.2	10.5	19.5	28.5
323.15	3.2	3.2	12.8	20.6	29.6
328.15	3.4	3.5	13.7	21.2	30.3
333.15	4.0	4.1	12.7	20.4	27.7
Overall MD %	2.1	2.2	14.4	16.2	23.9

in which N is the number of data points in each set. The $100 \cdot \mathrm{MD}$ values could be directly compared with the experimentally obtained relative standard deviation (RSD) values for assessing the accuracy of a model for representing the data. The fitted model using all data points was

$$\ln x_{\mathrm{m},T} = f_1 \ln x_{1,T} + f_2 \ln x_{2,T} + 2194.927\left[\frac{f_1 f_2}{T}\right] + 2066.349\left[\frac{f_1 f_2 (f_1 - f_2)}{T}\right] + 1916.914\left[\frac{f_1 f_2 (f_1 - f_2)^2}{T}\right] \qquad (9)$$

Equation 9 is a statistically significant correlation ($F = 766$, $p < 0.0005$) and mathematically describes the solubilities at various temperatures using a single model. It enables one to predict the solubilities at other temperatures and solvent compositions using interpolation/extrapolation techniques. The MD from this calculation was 14.4 % ($N = 81$). Details of MDs at the different temperatures are listed in Table 1 in which the MDs are the same for eqs 1 to 3. It is also possible to train the Jouyban−Acree model employing the solubility data at 298.15 K and then predict the solubilities at other temperatures. The calculated MD for the predicted solubilities at temperatures other than 298.15 K was 16.2 % ($N = 72$).

Alternatively, one may use a generally trained version of the Jouyban−Acree model for predicting the solubility of ethyl maltol at various temperatures. The trained version of the model for predicting the solubility of solutes in ethanol + water mixtures at various temperatures was[5]

$$\ln x_{\mathrm{m},T} = f_1 \ln x_{1,T} + f_2 \ln x_{2,T} + 1667.856\left[\frac{f_1 f_2}{T}\right] + 1117.347\left[\frac{f_1 f_2 (f_1 - f_2)}{T}\right] + 447.426\left[\frac{f_1 f_2 (f_1 - f_2)^2}{T}\right] \qquad (10)$$

and the obtained MD for the predicted solubilities was 23.9 %. It should be noted that none of the ethyl maltol data were used in the training process of eq 10. However, they provided reasonably accurate predictions employing just two experimental data points in monosolvents at each temperature. The acceptable prediction error range should be defined concerning the experimental RSD values. Ideally an error level less than the experiment RSD value is preferred. From a practical point-of-view, an error level of ~30 % has been suggested as an acceptable error range for fitted solubility data[6,7] for many applications.

The main advantages that the Jouyban−Acree model have over the polynomial model for representing the solubility of solutes in binary solvent mixtures are: 1) a uniform mathematical representation of solubility and other physicochemical properties; 2) the calculated equation coefficients for binary solvent mixtures can be combined to estimate solute solubility in ternary and higher-order multicomponent systems;[8] and (3) the model contains provisions for correlating experimental solubility as a function of both temperature and solvent composition. For illustrational purposes, we have assumed a rather simple temperature dependence of S_i/T which has been successful in correlating densities,[9] surface tensions,[10] acid dissociation constants,[11] and viscosity[12] as a function of temperature. There is no reason that one cannot assume a more complex temperature variation such as $S_i + S'_i/T$ if need be. In using the

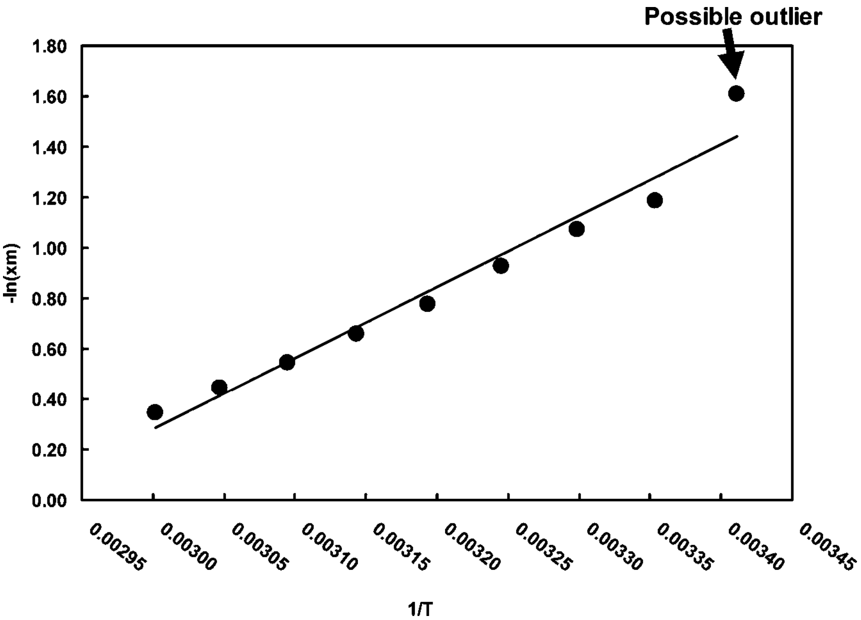

Figure 1. van't Hoff plot of solubility of ethyl maltol at $f_{\mathrm{ethanol}} = 0.4771$ to detect a possible outlier.

Jouyban−Acree model as a mathematical representation, we encourage users to consider a temperature-dependent form for the equation coefficients (such as S_i/T or $S_i + S'_i/T$), as it may be possible to include temperature and composition dependence into a single mathematical correlation.

The basic model has the capability of providing a generally trained model, such as eq 10 to predict the unmeasured solubilities, and can be used to detect possible outliers in experimental data sets for redetermination. As an example, the solubility data of ethyl maltol in 0.4771 mol fraction of ethanol at 293.15 K[1] produced the highest deviation from the predicted solubility. Careful examination of the reported data reveals that this experimental value is likely an experimental and/or typographical error. If fact, the equation coefficients reported in the manuscript do not reproduce the experimental ethyl maltol solubility data that are reported in Table 1 of the original article for 293.15 K. Using the authors' equation coefficients, the calculated mole fraction solubility of ethyl maltol at an ethanol mole fraction of 0.4771 should be 0.0464. The van't Hoff plot (see Figure 1) suggests that this datum is likely a mistyped data. There appears to be a duplicate entry of ethyl maltol mole fraction solubility of 0.0246 in Table 1 for ethanol mole fractions of 0.2811 and 0.4471. The authors' reported deviations between experimental and back-calculated values are wrong. The deviations that are given in the Table 1 of the article are ($x_{\mathrm{m,Obs}} - x_{\mathrm{m,Calc}}$), and not $10^3(x_{\mathrm{m,Obs}} - x_{\mathrm{m,Calc}})$ as the column headings state.

During the review process of this commentary, Liu et al. revised the experimental data, and by including the corrected data,[13] the MD values at 293.15 K dramatically decreased for all numerical methods discussed above and also MD of all temperatures for the back-calculated data by eq 9, since the outlier points could change the numerical values of the model. This observation is more evidence for the advantages of the proposed models, especially previously trained models to estimate the unmeasured solubilities and also to detect possible outliers.

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