

Commentary on “Extended Hildebrand Approach: An Empirical Model for Solubility Prediction of Etodolac in 1,4-Dioxane and Water Mixtures”

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Abstract

Several mathematical errors in the published paper by Rathi and Deshpande [J. Solution Chem. **43** (2014) 1886-1903] are identified. The errors concern the incorrect conversion of mass fraction to volume fraction concentrations of 1,4-dioxane, the incorrect conversion of mole fraction solubilities to molar solubilities of etodolac, and the incorrect calculation of the ideal mole fraction solubility of etodolac.

Key Words and Phrases: Etodolac Solubilities; binary solvent mixtures; aqueous-dioxane solvent mixtures; Extended Hildebrand approach

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In a paper published in This Journal Rathi and Deshpande [1] reported the experimental solubilities of binary etodolac in binary aqueous-1,4-dioxane mixtures at 298.15 K. The authors expressed the experimental data at nine binary solvent compositions and in the two mono-solvents in terms of both mole fraction and molar solubilities. The authors used the Extended Hildebrand Approach to interpret their measured experimental data.

The purpose of the present communication is to point out several errors in the published paper. The errors involve both the actual experimental values, as well as the authors' interpretation which contains several miscalculated values. Readers need to be aware of these errors. First, in Table 1 of the published paper [1] the authors give the compositions of the nine binary solvent mixtures in terms of mass fraction and volume fraction ($\phi_{dioxane}$) of 1,4-dioxane. The numerical values that are tabulated in Table 1 for the two concentration units are not consistent with each other. This can easily be shown by converting the tabulated mass fraction composition of 1,4-dioxane to $\phi_{dioxane}$ using the authors' measured densities of the binary solvents (ρ_1) that are given in column 4 of Table 1. The authors did not specify whether the volume fraction concentrations of 1,4-dioxane pertained to the ideal volume fraction of the "solute free" binary solvent mixture or the "solute free" actual volumes of the binary solvent mixture, so I have calculated both numerical values as given below:

$$\phi_{dioxane}^{ideal} = \frac{\text{mass fraction dioxane} / \text{density of dioxane}}{(\text{mass fraction of dioxane} / \text{density of dioxane}) + (\text{mass fraction of water} / \text{density of water})} \quad (1)$$

$$\phi_{dioxane}^{ideal} = \frac{0.1/1.0340}{(0.1/1.0340) + (0.9/0.9998)} \quad (2)$$

$$\phi_{dioxane}^{ideal} = 0.0970 \quad (3)$$

$$\phi_{dioxane}^{actual} \approx \frac{\text{mass fraction of dioxane} / \text{density of dioxane}}{1 / \text{density of binary solvent mixture}} \quad (4)$$

$$\phi_{dioxane}^{actual} \approx \frac{0.1 / 1.0340}{1 / 1.0056} \quad (5)$$

$$\phi_{dioxane}^{actual} = 0.0973 \quad (6)$$

Equation 1 assumes that the volumes of the two solvent components are additive, whereas Eqn. 4 uses the measured density to calculate the volume of the binary solvent mixture. Neither calculated value is close to the volume of fraction of $\phi_{dioxane} = 0.1105$ that the authors given in the second column of Table 1 for a 1,4-dioxane mass fraction of 0.1000. Published applications using the Hildebrand and Extended Hildebrand approach normally use ideal volume fraction compositions for the initial solvent concentration.

In Table 1 of the published paper [1] the authors report the solubility of etodolac in terms of both mole fraction and molar (mol L^{-1}) solubilities. The two sets of experimental values are inconsistent with each other. The molar solubilities of etodolac that are given in column 7 of Table 1 should be much larger than the mole fraction solubilities that are given in column 8. Mole fraction solubilities are converted to molar solubilities by dividing by the molar volume of the saturated solution given in L/mole. What I suspect that the authors have done is to divide by the volume in cm^3/mole as this is the only logical explanation that I have for why the molar solubilities are so very much smaller than the mole fraction solubilities.

Also in the paper [1] the authors calculate the ideal mole fraction solubility of etodolac,

X_{solute}^{ideal} , at 298.15 K based on:

$$\log_{10} X_{solute}^{ideal} = -\frac{\Delta H_{fus} (T_{fus} - 298.15)}{2.303 \times 298.15 R T_{fus}} \quad (7)$$

where R is the universal gas constant, T_{fus} is the melting point temperature of etodolac (given in the paper as 426.89 K), and ΔH_{fus} is the molar enthalpy of fusion of etodolac (given as $91.09 \text{ J g}^{-1} \times 287.35 \text{ g mol}^{-1} = 26175 \text{ J mol}^{-1}$). Substituting numerical values of $\Delta H_{fus} = 26175 \text{ J mol}^{-1}$ and $T_{fus} = 426.89 \text{ K}$ into Eqn. 7 I calculate a value of $X_{solute}^{ideal} = 0.04142$, which differs considerably from the value of $X_{solute}^{ideal} = 0.0071$ that the authors calculated. Clearly there is a problem with either the authors' calculated value of X_{solute}^{ideal} or their measured melting point temperature and/or enthalpy of fusion. The authors' calculated value of X_{solute}^{ideal} is not consistent with the enthalpy of fusion and melting point data reported in their published paper.

I note that the authors did use their calculated value of $X_{solute}^{ideal} = 0.0071$ to compute the activity coefficient of etodolac in the saturated solutions, e.g., $\gamma_{solute}^{obs} = X_{solute}^{ideal} / X_{solute}^{exp}$. The authors' expressed the calculated activity coefficients as $\log_{10} \gamma_{solute}^{obs}$. Using the authors' value of $X_{solute}^{ideal} = 0.0071$ for the ideal mole fraction solubility of etodolac and $X_{solute}^{exp} = 0.0001126$ for the mole fraction solubility of etodolac in water, I obtain a value of $\log_{10} \gamma_{solute}^{obs} = 1.7997$, which differs from the value $\log_{10} \gamma_{solute}^{obs} = 2.7978$ that the authors report in the last column of Table 1 [1]. Clearly there is a problem with the authors' tabulated numerical value. The rest of the numerical values in the last column of Table 1 are similarly off by one \log_{10} unit as well, assuming that $X_{solute}^{ideal} = 0.0071$ was correct.

It is possible to evaluate the "quality" of the authors' experimental density data for each of the nine binary solvent compositions at which the density was measured. There is both published

experimental density and excess molar volume data in the published literature. Both Ouerfelli et al. [2] and Aminabhavi and Gopalakrishna [4] measured densities of binary aqueous-1,4-dioxane mixtures at 298.15 K over the entire concentration range. It is difficult to compare the densities directly; however, as each research group performed measurements at different mixture concentrations. What I have done is to convert the 1,4-dioxane mass fractions given in the first column of Table 1 [1] to mole fractions, X_{dioxane} and X_{water} , and then use these values to calculate the excess volumes, V^{ex} , for each solvent composition according to Eqn. 8 below:

$$V^{\text{ex}} = \frac{X_{\text{dioxane}} MW_{\text{dioxane}} + X_{\text{water}} MW_{\text{water}}}{\rho_{\text{mixture}}} - \frac{X_{\text{dioxane}} MW_{\text{dioxane}}}{\rho_{\text{dioxane}}} - \frac{X_{\text{water}} MW_{\text{water}}}{\rho_{\text{water}}} \quad (8)$$

where MW_i and ρ_i refer to the molar mass and density of the respective solvent component i . Tabulated in Table 1 of this commentary are the results of my calculations. The excess molar volumes that I calculate are extremely small and would indicate the water and 1,4-dioxane form a nearly ideal binary solvent mixture as far as excess molar volumes is concerned. Ouerfelli and coworkers [2], Iulian and Ciocirlan [3], Aminabhavi and Gopalakrishna [4], and Morcom and Smith [5] report excess molar volumes of $V^{\text{ex}} = -0.626 \text{ cm}^3 \text{ mol}^{-1}$, $V^{\text{ex}} = -0.629 \text{ cm}^3 \text{ mol}^{-1}$, $V^{\text{ex}} = -0.624 \text{ cm}^3 \text{ mol}^{-1}$ and $V^{\text{ex}} = -0.601 \text{ cm}^3 \text{ mol}^{-1}$, respectively, at $X_{\text{dioxane}} = 0.50$. The experimental densities reported by Rathi and Deshpande [1] do not appear to be of sufficient “quality” for excess molar volume calculations.

As an informational note readers should be various cautious of explanations and equations based on or derived from incorrectly calculated values of ϕ_{dioxane} and $X_{\text{solute}}^{\text{ideal}}$. I also suspect that the numerical values of the solubility parameters in the third column of Table 1 are also miscalculated. Normally the solubility parameter of the solvent, $\delta_{\text{binary mixture}}$, is calculated as [6,7]:

$$\delta_{binary\ mixture} = \phi_{solvent\ 1} \delta_{solvent\ 1} + \phi_{solvent\ 2} \delta_{solvent\ 2}$$

an initial volume fraction average of the solubility parameters of the two mono-solvents ($\delta_{solvent\ 1}$ and $\delta_{solvent\ 2}$) that make up the binary solvent mixture. I cannot reproduce the solubility parameters of the binary solvent mixture that the authors give in Table 1 of their published paper [1].

Table 1. Calculated Excess Molar Volumes, V^{ex} , of Binary Aqueous-1,4-Dioxane Mixtures using the Measured Densities, $\rho_{mixture}$, from Rathi and Deshpande [1]

$m_{dioxane}$	$X_{dioxane}$	X_{water}	$\rho_{mixture}$ (g cm ³)	V^{ex} (cm ³ mol ⁻¹)
0.0000	0.0000	1.0000	0.9998	0
0.1000	0.0222	0.9778	1.0032	-0.0016
0.2000	0.0486	0.9514	1.0066	-0.0030
0.3000	0.0806	0.9194	1.0101	-0.0065
0.4000	0.1200	0.8800	1.0135	-0.0076
0.5000	0.1698	0.8302	1.0169	-0.0083
0.6000	0.2347	0.7653	1.0203	-0.0085
0.7000	0.3230	0.6770	1.0237	-0.0079
0.8000	0.4499	0.5501	1.0272	-0.0106
0.9000	0.6479	0.3521	1.0306	-0.0075
1.0000	1.0000	0.0000	1.034	0

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