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Measurement and Correlation of Solubilities of *trans*-Resveratrol in Ethanol + Water and Acetone + Water Mixed Solvents at Different Temperatures

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The solubilities of *trans*-resveratrol in different compositions of ethanol + water mixtures and acetone + water mixtures were measured at different temperatures. The solubilities of *trans*-resveratrol in ethanol + water mixtures increase with increasing mole fraction of ethanol, whereas the solubility curve (the solubilities vs the mole fraction of acetone on solute-free basis) of an acetone + water mixed system presents a maximum. The solubilities of *trans*-resveratrol in both mixture systems increase with increasing temperature. The experimental solubility data were correlated by a three-parameter empirical equation and UNIQUAC model, respectively.

Introduction

Crystallization is the preferred method of purification for the bioactive compounds extracted from herbs, because they have usually high boiling points or thermal instability. Knowledge of solid−liquid equilibrium is of clear importance for the design of separation and purification processes, especially cooling, evaporative, and antisolvent crystallization and the development of thermodynamic models to correlate and predict the solubility of bioactive compounds in pure and mixed solvent systems based on a few experimental data. However, the number of literature references referring to the determination of solubility is relatively limited, particularly with respect to mixed solvent systems, where the solubility behavior can be highly nonideal.

trans-Resveratrol (5-[(1*E*)-2-(4-hydroxyphenyl) ethenyl]-1,3-benzenediol) is a naturally occurring compound usually derived from grape skins, peanuts, and the roots of *Polygonum cuspidatem*.[1] *trans*-Resveratrol is famous for its biological activity, such as potent antimicrobial and antioxidant effects.[2,3] Potential chemopreventive and chemotherapeutic properties of *trans*-resveratrol contribute to human cancer inhibition.[4]

trans-Resveratrol is usually extracted from natural plants. Various volatile solvents could be used to extract *trans*-resveratrol, such as methanol, ethanol, acetone, chloroform, ethyl acetate, and other mixed solvents.[5−9] Some common organic solvents or their mixtures are also efficient to purify *trans*-resveratrol during crystallization. But for considering food and drug safety, an ethanol + water mixture or acetone + water mixture could commendably be substituted for those pernicious organic solvents for crystallization. The solubility of *trans*-resveratrol in binary solvent mixtures at different temperatures is necessary to be measured. The solubility data of *trans*-resveratrol in ethanol + water and acetone + water mixed solvents have not been found in the literature.

In a continuation of our earlier study,[10] the solubilities of *trans*-resveratrol in ethanol + water and acetone + water were measured by an HPLC analytical method at the mole fraction of ethanol of 0.000, 0.100, 0.200, 0.300, 0.400, 0.500, 0.600, 0.700, 0.800, 0.900, and 1.000 on a solute-free basis and at $T = (273.2, 283.2, 293.2, 303.2, 313.2, \text{and } 323.2)$ K. A three-parameter empirical equation and UNIQUAC equation were used to correlate the experimental data.

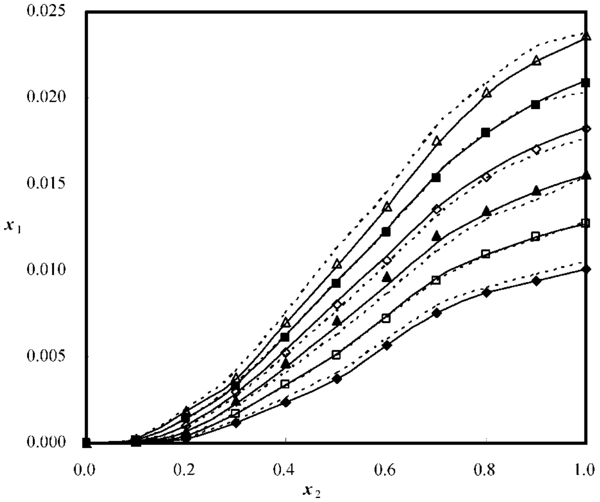

Figure 1. Solubilities of *trans*-resveratrol vs the mole fraction of ethanol on a solute-free basis in ethanol + water mixtures at $T = (273.2, 283.2, 293.3, 303.2, 313.2, \text{and } 323.2)$ K: ♦, $T = 273.2$ K; □, $T = 283.2$ K; ▲, $T = 293.2$ K; ◇, $T = 303.2$ K; ■, $T = 313.2$ K; Δ, $T = 323.2$ K; line, correlated with eq 3 using the parameters in Table 3; dashed line, predicted with the UNIQUAC equation using the parameters in Table 5.

Experimental Section

Materials. The ivory-white crystalline powder of *trans*-resveratrol (0.98 mass fractions) was supplied by Skyherb Natural Product Co., Ltd. (China). The *trans*-resveratrol was dissolved in a mixture of ethanol and water in a volume ratio of 3:7 and recrystallized thrice at room temperature. The crystal of *trans*-resveratrol was dried in a vacuum oven at $T = 373.2$ K for 12 h and stored in a desiccator to avoid absorbing water. The purity is higher than 0.99 mass fractions, checked by HPLC (Shimadzu LC-10AD). The reference standard of betulin, whose

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Table 1. Solubilities of *trans*-Resveratrol (1) in Different Compositions of Ethanol (2) + Water (3) Mixtures at T = (273.2, 283.2, 293.3, 303.2, 313.2, and 323.2) K[a]

T/K	$10^2 m_1$/(mol·kg^{-1})	$10^3 x_1$	$10^2 m_1$/(mol·kg^{-1})	$10^3 x_1$
	x_2[b] = 0.0000		x_2 = 0.0999	
283.2			0.18 ± 0.01	(3.80 ± 0.15)·10^{-2}
293.2	(1.61 ± 0.10)·10^{-2}	(2.90 ± 0.12)·10^{-3}	0.34 ± 0.01	(7.08 ± 0.08)·10^{-2}
303.2	(2.54 ± 0.02)·10^{-2}	(4.57 ± 0.04)·10^{-3}	0.50 ± 0.01	(10.46 ± 0.18)·10^{-2}
313.2	(3.59 ± 0.10)·10^{-2}	(6.46 ± 0.17)·10^{-3}	0.73 ± 0.03	(15.13 ± 0.71)·10^{-2}
323.2	(5.16 ± 0.09)·10^{-2}	(9.30 ± 0.16)·10^{-3}	1.06 ± 0.01	(22.12 ± 0.10)·10^{-2}
	x_2 = 0.1999		x_2 = 0.2999	
273.2	0.93 ± 0.02	0.22 ± 0.01	4.37 ± 0.10	1.15 ± 0.03
283.2	1.59 ± 0.04	0.38 ± 0.01	6.28 ± 0.10	1.66 ± 0.03
293.2	2.88 ± 0.07	0.68 ± 0.02	9.27 ± 0.03	2.44 ± 0.01
303.2	4.13 ± 0.03	0.98 ± 0.01	11.10 ± 0.13	2.92 ± 0.04
313.2	6.06 ± 0.07	1.43 ± 0.02	12.43 ± 0.04	3.27 ± 0.01
323.2	8.04 ± 0.03	1.90 ± 0.01	14.59 ± 0.09	3.84 ± 0.02
	x_2 = 0.4003		x_2 = 0.4999	
273.2	8.08 ± 0.15	2.36 ± 0.04	11.67 ± 0.11	3.72 ± 0.03
283.2	11.52 ± 0.10	3.36 ± 0.03	15.84 ± 0.11	5.05 ± 0.04
293.2	15.89 ± 0.10	4.62 ± 0.03	22.43 ± 0.16	7.13 ± 0.05
303.2	17.94 ± 0.20	5.22 ± 0.06	25.31 ± 0.31	8.04 ± 0.10
313.2	20.87 ± 0.11	6.07 ± 0.03	29.03 ± 0.20	9.22 ± 0.06
323.2	24.32 ± 0.11	7.06 ± 0.03	32.83 ± 0.17	10.41 ± 0.05
	x_2 = 0.5998		x_2 = 0.6997	
273.2	16.50 ± 0.21	5.72 ± 0.07	20.18 ± 0.12	7.54 ± 0.04
283.2	20.84 ± 0.37	7.21 ± 0.13	25.32 ± 0.23	9.44 ± 0.08
293.2	27.89 ± 0.24	9.63 ± 0.08	32.29 ± 0.19	12.01 ± 0.07
303.2	30.73 ± 0.17	10.59 ± 0.06	36.45 ± 0.38	13.54 ± 0.14
313.2	35.50 ± 0.12	12.22 ± 0.04	41.35 ± 0.29	15.33 ± 0.11
323.2	39.98 ± 0.11	13.74 ± 0.04	47.38 ± 0.20	17.53 ± 0.07
	x_2 = 0.7998		x_2 = 0.8996	
273.2	21.66 ± 0.13	8.69 ± 0.05	21.93 ± 0.23	9.40 ± 0.10
283.2	27.33 ± 0.24	10.93 ± 0.09	27.90 ± 0.34	11.92 ± 0.15
293.2	33.87 ± 0.36	13.52 ± 0.14	34.37 ± 0.34	14.65 ± 0.14
303.2	38.69 ± 0.22	15.41 ± 0.09	39.99 ± 0.10	17.00 ± 0.04
313.2	45.22 ± 0.18	17.97 ± 0.07	46.23 ± 0.20	19.61 ± 0.08
323.2	51.24 ± 0.30	20.31 ± 0.12	52.48 ± 0.23	22.20 ± 0.10
	x_2 = 1.000			
273.2	22.05 ± 0.21	10.06 ± 0.09		
283.2	28.01 ± 0.18	12.74 ± 0.08		
293.2	34.43 ± 0.19	15.62 ± 0.09		
303.2	40.30 ± 0.19	18.23 ± 0.08		
313.2	46.14 ± 0.26	20.81 ± 0.11		
323.2	52.54 ± 0.15	23.63 ± 0.07		

[a] Expanded uncertainties (±) were calculated using standard deviation, SD·coverage factor k; k = 2. [b] Mole fraction of ethanol on a solute-free basis.

purity was > 0.99 mass fractions, was purchased from Sigma Chemical Corporation (USA).

Ethanol and acetone were of analytical grade and purchased from Sinopharm Chemical Reagent Co., Ltd. (China), and dehydrated with molecular sieves of (3 to 4) Å before use. The purities of these solvents, determined by gas chromatography, were > 0.998 mass fraction. Deionized water was distilled by using a quartz sub-boiling purifier. The pH value of pure water was 6.4, determined by pH Scan 2.

Solubility Measurement. Binary solvent mixtures were prepared by mass using a Sartorius CP225D analytical balance with an accuracy ± 0.01 mg. The uncertainty of compositions of mixed solvents was 0.0003 on mole fraction. The 15 cm^3 centrifuge tubes (PBS) with caps were used to prepare saturated solutions (about 10 cm^3) of *trans*-resveratrol with excess solid solute in mixed solvents. The tube was gastight when the turncap with a sizable rubber band was screwed on. Then the tubes were directly placed in a constant temperature thermostatic bath (THJD-0510W, China) with a temperature stability of ± 0.05 K and a temperature uncertainty of 0.1 K. The tubes were allowed to settle about 36 h in the dark to ensure solid−liquid equilibrium and stabilization of the configuration of *trans*-resveratrol before sampling. For each tube, two samples of approximately (0.1 to 1) mL were withdrawn from the clear saturated solution using preheated glass syringes. The glass syringe with saturated solution was weighted with an uncertainty of ± 0.01 mg. The relative uncertainty of the experimental solubility is within 2.5 %. More details of the experimental setup have already been described before.[10]

The solubility of *trans*-resveratrol was monitored by HPLC. The HPLC system (Shimadzu Corporation, Kyoto, Japan) was composed by a degasser (DGU-4A), solvent delivery module (LC-10AT), UV detector (SPD-10A), and 20 μL injector loop. The chromatographic analysis was performed on a Diamonsil C_{18} column (150 mm × 4.6 mm, 5 μm) and a mobile phase composed of acetonitrile and water in a volume ratio of 40:60 at a flow rate of 0.8 mL·min^{-1} and detective wavelength at 303 nm.[11] The reference standard solution containing about 60 μg·mL^{-1} of *trans*-resveratrol was prepared in methanol.

Result and Discussion

High-performance liquid chromatography was adapted to determine the concentration of a saturated solution of *trans*-resveratrol in different solvents. To check the reliability of the HPLC analysis method, known masses of *trans*-resveratrol were

Table 2. Solubilities of *trans*-Resveratrol (1) in Different Compositions of Acetone (2) + Water (3) Mixtures at T = (273.2, 283.2, 293.3, 303.2, and 313.2) K[a]

T/K	$10m_1$/(mol·kg^{-1})	10^2x_1	$10m_1$/(mol·kg^{-1})	10^2x_1
	x_2[b] = 0.0998		x_2 = 0.2000	
273.2	0.23 ± 0.01	(5.07 ± 0.10)·10^{-2}	5.53 ± 0.04	1.42 ± 0.01
283.2	0.37 ± 0.01	(8.11 ± 0.18)·10^{-2}	6.16 ± 0.05	1.58 ± 0.01
293.2	0.58 ± 0.02	(12.80 ± 0.33)·10^{-2}	7.04 ± 0.19	1.80 ± 0.05
303.2	0.83 ± 0.01	(18.27 ± 0.15)·10^{-2}	7.89 ± 0.21	2.01 ± 0.05
313.2	1.03 ± 0.02	(22.70 ± 0.42)·10^{-2}	8.29 ± 0.27	2.11 ± 0.07
	x_2 = 0.3000		x_2 = 0.3959	
273.2	11.72 ± 0.13	3.40 ± 0.04	18.66 ± 0.19	5.95 ± 0.06
283.2	12.98 ± 0.21	3.75 ± 0.06	19.99 ± 0.36	6.34 ± 0.11
293.2	14.62 ± 0.14	4.21 ± 0.04	21.43 ± 0.38	6.77 ± 0.11
303.2	15.57 ± 0.31	4.47 ± 0.09	22.41 ± 0.15	7.06 ± 0.04
313.2	16.24 ± 0.11	4.65 ± 0.03	22.89 ± 0.45	7.20 ± 0.13
	x_2 = 0.4991		x_2 = 0.5954	
273.2	22.71 ± 0.37	7.94 ± 0.12	25.03 ± 0.66	9.49 ± 0.23
283.2	24.37 ± 0.40	8.48 ± 0.13	26.45 ± 0.78	9.97 ± 0.26
293.2	25.44 ± 0.60	8.82 ± 0.19	27.24 ± 0.58	10.24 ± 0.19
303.2	26.18 ± 0.30	9.05 ± 0.09	27.82 ± 0.51	10.43 ± 0.17
313.2	26.89 ± 0.28	9.27 ± 0.09	28.69 ± 0.65	10.72 ± 0.22
	x_2 = 0.6902		x_2 = 0.7983	
273.2	25.30 ± 0.80	10.36 ± 0.29	23.52 ± 0.55	10.52 ± 0.22
283.2	26.53 ± 0.55	10.80 ± 0.20	24.55 ± 0.84	10.93 ± 0.33
293.2	27.56 ± 0.75	11.18 ± 0.27	25.30 ± 0.46	11.23 ± 0.18
303.2	27.89 ± 0.61	11.30 ± 0.22	26.12 ± 0.84	11.55 ± 0.33
313.2	28.73 ± 0.84	11.60 ± 0.30	26.70 ± 0.37	11.78 ± 0.14
	x_2 = 0.8982		x_2 = 1.000	
273.2	20.75 ± 0.17	10.08 ± 0.07	15.92 ± 0.29	8.46 ± 0.14
283.2	21.75 ± 0.70	10.51 ± 0.30	16.17 ± 0.19	8.58 ± 0.09
293.2	22.17 ± 0.48	10.69 ± 0.21	16.42 ± 0.31	8.71 ± 0.15
303.2	22.98 ± 0.50	11.04 ± 0.22	16.55 ± 0.36	8.77 ± 0.17
313.2	23.34 ± 0.32	11.19 ± 0.13	16.74 ± 0.32	8.86 ± 0.16

[a] Expanded uncertainties (±) were calculated using standard deviation, SD·coverage factor k; k = 2. [b] Mole fraction of acetone on a solute-free basis.

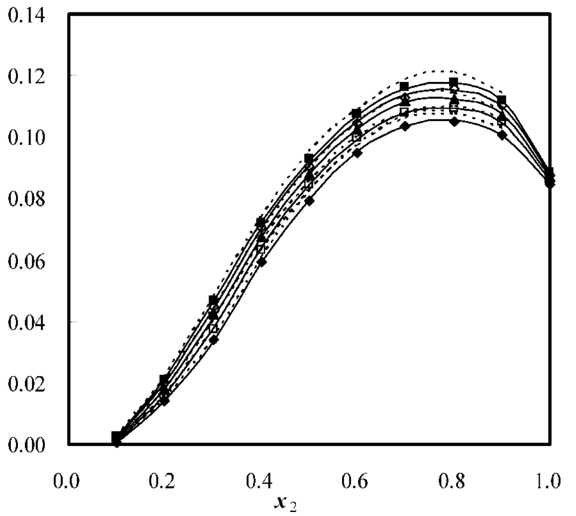

Figure 2. Solubilities of *trans*-resveratrol vs the mole fraction of acetone on a solute-free basis in acetone + water mixtures at T = (273.2, 283.2, 293.3, 303.2, and 313.2) K: ◆, T = 273.2 K; □, T = 283.2 K; ▲, T = 293.2 K; ◇, T = 303.2 K; ■, T = 313.2 K; line, correlated with eq 3 using the parameters in Table 4; dashed line, predicted with the UNIQUAC equation using the parameters in Table 6.

Table 3. Parameters of Equation 3 for *trans*-Resveratrol (1) in Different Solvent Compositions of the Ethanol (2) + Water (3) System

x_2[a]	a	b/K	c	10^3rmsd
0.0000	142.600	−10179.945	−21.234	$8.21 \cdot 10^{-5}$
0.0999	286.566	−16667.148	−42.129	$3.75 \cdot 10^{-3}$
0.1999	283.374	−16150.676	−41.477	0.02
0.2999	358.314	−17937.524	−53.372	0.09
0.4003	280.674	−14279.269	−41.789	0.16
0.4999	293.689	−14769.756	−43.710	0.21
0.5998	178.515	−9430.475	−26.588	0.24
0.6997	131.586	−7278.978	−19.577	0.22
0.7998	98.674	−5828.614	−14.631	0.15
0.8996	108.829	−6290.833	−16.125	0.11
1.0000	111.039	−6377.236	−16.451	0.11

[a] Mole fraction of ethanol on a solute-free basis.

completely dissolved in methanol, and the concentration of solution was measured by HPLC. The average relative uncertainty was 0.19 %.

The solubilities of *trans*-resveratrol in different compositions of ethanol + water mixtures and acetone + water mixtures at different temperatures were measured and listed in Tables 1 and 2. Molalities, m_1 (mol·kg^{-1}), and mole fraction, x_1, values are the average values taken from four test tubes with the same composition of an ethanol + water mixture or acetone + water mixture. The expanded uncertainty (±) for each data point is given in Tables 1 and 2. The experimental data of solubility of *trans*-resveratrol in different compositions of ethanol + water mixtures and acetone + water mixtures were plotted as shown in Figures 1 and 2. The solubility of *trans*-resveratrol in the acetone + water mixture is a maximum, and it is different from that of *trans*-resveratrol in an ethanol + water mixture.

According to the solid−liquid phase equilibrium theory, the experimental data of *trans*-resveratrol could be expressed for a nonideal solution[12]

$$\ln\left(\frac{1}{\gamma_1 x_1}\right) = \frac{\Delta_{\text{fus}}H}{RT_{\text{t}}}\left(\frac{T_{\text{t}}}{T} - 1\right) - \frac{\Delta C_p}{R}\left(\frac{T_{\text{t}}}{T} - 1\right) + \frac{\Delta C_p}{R}\ln\frac{T_{\text{t}}}{T} \tag{1}$$

where γ_1 is the activity coefficient of *trans*-resveratrol in a mixed solvent referring to the subcooled liquid; x_1 is the mole fraction

Table 4. Parameters of Equation 3 for *trans*-Resveratrol (1) in Different Solvent Compositions of the Acetone (2) + Water (3) System

$x_2{}^a$	a	b/K	c	10^3 rmsd
0.0999	343.788	−18121.600	−50.811	0.03
0.2000	65.937	−3818.405	−10.022	0.22
0.3000	105.511	−5343.282	−15.925	0.31
0.3959	71.166	−3590.078	−10.846	0.27
0.4991	62.501	−3115.842	−9.559	0.25
0.5954	31.142	−1675.205	−4.877	0.44
0.6902	34.317	−1796.388	−5.349	0.45
0.7983	17.707	−1075.157	−2.856	0.13
0.8982	23.268	−1305.370	−3.705	0.45
1.0000	5.234	−418.429	−1.100	0.09

[a] Mole fraction of acetone on a solute-free basis.

Table 5. Parameters of the UNIQUAC Equation for *trans*-Resveratrol (1) in Different Solvent Compositions of the Ethanol (2) + Water (3) System

$x_2{}^a$	$\Delta\mu_{21}$ / $\mathrm{J \cdot mol^{-1}}$	$\Delta\mu_{12}$ / $\mathrm{J \cdot mol^{-1}}$	$\Delta\mu_{31}$ / $\mathrm{J \cdot mol^{-1}}$	$\Delta\mu_{13}$ / $\mathrm{J \cdot mol^{-1}}$	10^3 rmsd
0.0000			−960.79	3114.14	$8.50 \cdot 10^{-5}$
0.0999	179.09	617.83	178.55	43.53	$3.09 \cdot 10^{-3}$
0.1999	−279.82	523.60	−279.79	103.05	0.06
0.2999	−2650.72	3759.86	−2653.11	26974.63	0.22
0.4003	−3432.31	864.26	1772.88	27955.66	0.32
0.4999	2187.68	1020.58	−3719.28	26326.34	0.54
0.5998	2866.21	914.51	−4186.07	26376.78	0.53
0.6997	2274.74	898.44	−4693.52	26607.33	0.55
0.7998	−2823.81	73942.08	−3569.76	75443.19	0.35
0.8996	−2483.09	28635.28	−4604.74	−254.62	0.42
1.0000	8385.95	−3209.54			0.39
	$\Delta\mu_{23} = 383.15\ \mathrm{J \cdot mol^{-1}}$		$\Delta\mu_{32} = 752.75\ \mathrm{J \cdot mol^{-1}}$		

[a] Mole fraction of ethanol on a solute-free basis.

Table 6. Parameters of the UNIQUAC Equation for *trans*-Resveratrol (1) in Different Solvent Compositions of the Acetone (2) + Water (3) System

$x_2{}^a$	$\Delta\mu_{21}$ / $\mathrm{J \cdot mol^{-1}}$	$\Delta\mu_{12}$ / $\mathrm{J \cdot mol^{-1}}$	$\Delta\mu_{31}$ / $\mathrm{J \cdot mol^{-1}}$	$\Delta\mu_{13}$ / $\mathrm{J \cdot mol^{-1}}$	10^2 rmsd
0.0999	−801.85	−310.16	−801.23	153.20	0.01
0.2000	−5445.18	26684.95	2644.35	1373.51	0.04
0.3000	−5203.43	25942.82	4779.01	2042.54	0.10
0.3959	34219.84	40676.12	−5217.93	2255.53	0.14
0.4991	673.50	25193.01	−5952.06	3420.04	0.21
0.5954	19093.98	1919.29	−6193.44	3268.61	0.19
0.6902	4275.96	1284.28	−6609.96	2978.21	0.27
0.7983	499.59	2096.20	−7664.37	3697.52	0.25
0.8982	−3365.70	101281.84	−8292.54	120726.09	0.19
1.0000	−4028.46	64136.49			1.28
	$\Delta\mu_{23} = 2746.16\ \mathrm{J \cdot mol^{-1}}$		$\Delta\mu_{32} = -387.40\ \mathrm{J \cdot mol^{-1}}$		

[a] Mole fraction of acetone on a solute-free basis.

solubility of *trans*-resveratrol; $\Delta_{\mathrm{fus}}H$ is the enthalpy of fusion of *trans*-resveratrol; ΔC_p is the change of the heat capacity; T is the absolute temperature; T_{t} is the triple-point temperature of *trans*-resveratrol; and R is the gas constant. Given a temperature, the solubility of *trans*-resveratrol is only a function of its activity coefficient in solution. The activity coefficient of *trans*-resveratrol in solution determines its solubility as the solvent composition changes. The experimental data of solubility were correlated by following two methods.

Three-Parameter Empirical Equation. The activity coefficient of *trans*-resveratrol is given by[13]

$$\ln \gamma_1 = A + \frac{B}{T/\mathrm{K}} \tag{2}$$

where A and B are constants. Introducing γ_1 from eq 2 into eq 1 and subsequent rearrangement results in[10]

$$\ln x_1 = a + \frac{b}{T/\mathrm{K}} + c \ln T/\mathrm{K} \tag{3}$$

where a, b, and c are empirical parameters. They were obtained by nonlinear least-squares fit and listed in Tables 3 and 4 together with the root-mean-square deviations (rmsd) for two mixed solvent system. The rmsd's are defined as

$$\mathrm{rmsd} = \left[\frac{1}{n}\sum_{i=1}^{n}(x_{1,i}^{\mathrm{calcd}} - x_{1,i}^{\mathrm{exptl}})^2\right]^{1/2} \tag{4}$$

where $x_{1,i}^{\mathrm{calcd}}$ is the solubility calculated by eq 3 using the parameters in Tables 3 and 4; $x_{1,i}^{\mathrm{exptl}}$ is the experimental value of mole fraction solubility of *trans*-resveratrol; and n is the number of experiment points.

UNIQUAC Equation. In chemical literature, there are assumptions commonly employed: the first one is that ΔC_p at T_{f} is equal to zero. For most substances, there is a little difference between the triple-point temperature and the normal melting point temperature. Also, there is a negligible difference between the enthalpies of fusion at these two temperatures. Therefore, normal melting temperature (T_{m}) can be substituted for triple-point (T_{t}) temperatures. Therefore, a simplified form of eq 1 can be stated

$$\ln\left(\frac{1}{\gamma_1 x_1}\right) = \frac{\Delta_{\mathrm{fus}}H}{RT_{\mathrm{m}}}\left(\frac{T_{\mathrm{m}}}{T} - 1\right) \tag{5}$$

The melting point of *trans*-resveratrol was determined by differential scanning calorimetry (Q100, TA Corporation) at a heating rate of 5 $\mathrm{K \cdot min^{-1}}$ under nitrogen flow. This machine was calibrated against supplied standards. The melting point of *trans*-resveratrol is $T_{\mathrm{m}} = 541.3$ K. The uncertainty of the melting point is 0.5 K. However, due to the decomposition of *trans*-resveratrol close to the melting point, it was difficult to accurately determine the $\Delta_{\mathrm{fus}}H$ values. Thus, $\Delta_{\mathrm{fus}}H$ was estimated by using the method[14]

$$\Delta_{\mathrm{fus}}H = T_{\mathrm{m}} \cdot (56.5 - R \ln \sigma) \tag{6}$$

where R is the universal gas constant and σ is the rotational symmetry of the molecule. σ of *trans*-resveratrol is equal to 1. The enthalpy of fusion of *trans*-resveratrol was 30.6 $\mathrm{kJ \cdot mol^{-1}}$.

The activity coefficient of *trans*-resveratrol in eq 5 can be calculated by the UNIQUAC equation[12]

$$\ln \gamma_i = \ln \frac{\phi_i}{x_i} + \left(\frac{z}{2}\right) q_i \ln \frac{\theta_i}{\phi_i} + l_i - \frac{\phi_i}{x_i}\sum_{j=1}^{m} x_j l_j - q_i \ln\left(\sum_{j=1}^{m} \theta_j \tau_{ji}\right) + q_i - q_i \sum_{j=1}^{m} \frac{\theta_j \tau_{ij}}{\sum_{k=1}^{m} \theta_k \tau_{kj}} \tag{7}$$

where

$$\phi_i = \frac{r_i x_i}{\sum_{j=1}^{m} r_j x_j}, \qquad \theta_i = \frac{q_i x_i}{\sum_{j=1}^{m} q_j x_j}$$

$$l_j = \frac{z}{2}(r_j - q_j) - (r_j - 1)$$

The coordination number z is set equal to 10. r_i and q_i are the structural parameters of pure solvent i. The structural parameters of *trans*-resveratrol were calculated by the functional group approach.[15]

$$r = \sum_{i=1}^{m} n_i \cdot R_i, \qquad q = \sum_{i=1}^{m} n_i \cdot Q_i \tag{8}$$

where m is the number of functional groups in the molecule and n is the repeating number of each function group. The structural parameters, R_i and Q_i of function group i, were taken from the literature. Two adjustable parameters, τ_{ij} and τ_{ji}, are expressed by

$$\tau_{ij} = \exp\left(-\frac{\Delta\mu_{ij}}{RT}\right), \qquad \tau_{ji} = \exp\left(-\frac{\Delta\mu_{ji}}{RT}\right) \tag{9}$$

where $\Delta\mu_{ij}$ and $\Delta\mu_{ji}$ are interaction parameters. For a system with two solvents and a solute, two solvent−solvent interaction parameters were taken from the literature[16] and four solvent−solute interaction parameters were fitted to the experimental data by a nonlinear least-squares method at the same solvent composition. The interaction parameters obtained in this work are given in Tables 5 and 6 together with the root-mean-square deviations (rmsd).

As can be seen from Tables 3 to 6 and Figures 1 and 2, the results correlated by the empirical equation and UNIQUAC equation are satisfactory. However, the empirical model gave better results than the UNIQUAC model. It may be for two reasons: First, the interaction parameter $\Delta\mu_{ij}$ in eq 9 may depend on temperature. Second, two solvent−solvent interaction parameters which were obtained from fitting the VLE data may be unsuitable to the SLE systems. Those interaction parameters listed in Tables 5 and 6 could be used to predict the solubilities of *trans*-resveratrol at different temperatures.

Figures 1 and 2 showed some regular conclusions obviously: (1) the solubilities of *trans*-resveratrol in both fixed solvent compositions increase slightly with increasing temperature. (2) At the same temperature, the solubilities of *trans*-resveratrol increase with increasing mole fraction of ethanol in the mixture. However, the solubility of *trans*-resveratrol in acetone + water mixed solvents presents a maximum at $x_2 = 0.8$ (solute-free). (3) The mixture with the volume ratio of ethanol/water = 3: 7 ($x_2 = 0.\ 1169$) used for crystallization of *trans*-resveratrol is reasonable.

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