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Measurement and Correlation of Solubilities of (*Z*)-2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetic Acid in Different Pure Solvents and Binary Mixtures of Water + (Ethanol, Methanol, or Glycol)

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ABSTRACT: The solubilities of (*Z*)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetic acid in water and alcoholic solvents (methanol, ethanol, 1-propanol, glycol) and the combination of water + alcohols (methanol, ethanol, glycol) of binary mixtures have been experimentally measured in the temperature range from (282 to 330) K using a laser monitoring observation technique. The experimental solubilities in the pure solvents were correlated by modified Apelblat equation. A hybrid model proposed based on Apelblat equation and Jouyban−Acree model was used to correlate the solubility of solute with the variation of both temperature and initial composition of the binary solvent mixtures. With these models the maximum mean percentage deviation is 5.21.

INTRODUCTION

(*Z*)-2-(2-Aminothiazol-4-yl)-2-methoxyiminoacetic acid (formula: $C_6H_7N_3O_3S$, abbreviated as ATMAA, molecular weight: 201.21, CAS Registry No. 65872-41-5) is used as the main intermediate for the synthesis of the third generation of cephalosporin compounds, such as cefotaxime sodium, ceftriaxone, cefepime, cefpirome, and so on. ATMAA is synthesized from ethyl acetoacetate and methyl acetoacetate via a process which includes oximation, methylation, bromination, cyclization, and hydrolysis. Finally, ATMAA is crystallized from the aqueous methanol or ethanol mixtures.[1−4] Purification of ATMAA is realized by recrystallization using alcohols such as methanol, ethanol, 1-propanol, and glycol.[5]

It is obvious that the solubilities of ATMAA in water and alcohols and their mixtures are important basic data for optimizing the production of ATMAA. However, in the open literature the data concerning the solubilities of ATMAA in the above-mentioned solvents are scarce. In the present work, the solubilities of ATMAA in water and the above-mentioned alcoholic solvents and the combination of the binary mixtures of water + alcohol were experimentally measured from (282 to 330) K using a laser monitoring observation technique.

In pure solvents and solvent mixtures with a given composition, the solubility of a solute as a function of temperature can be correlated using modified Apelblat equation.[6,7] In a solvent mixture, however, the solubility of a solute depends not only on temperature but also on the composition of the solvent mixture. Derived from a thermodynamic mixing model, which includes contributions from both two-body and three-body interactions, the combined nearly ideal binary solvent/Redlich−Kister equation suggested by Acree and co-workers[8,9] can be used as a possible mathematical representation for describing the isothermal solubility of a solute in a binary solvent mixture as a function of binary solvent composition.[10,11]

Theoretically, for mixed solvent systems, the solubility is a continuous function of both temperature and initial composition of mixed solvents in a given pressure. To correlate the solubility of a solute with temperature and composition of mixed solvent mixture, the Jouyban−Acree model[12,13] and William−Amidon[14] model can be used. However, both of the models require the temperature dependence of solubilities in monosolvent systems. As a consequence, they are frequently used only for correlating experimental solubility of a solute with the composition of binary solvent mixtures at a constant temperature. In this work, we propose a hybrid model based on Apelblat equation and Jouyban−Acree model to correlate the solubility of a solute with the variation of both temperature and initial composition of binary solvent mixtures. Its accuracy and prediction capability are evaluated using the experimentally obtained solubilities of ATMAA in the combination of water + alcohols (methanol, ethanol, glycol) binary mixtures.

EXPERIMENTAL SECTION

Chemicals. A white crystalline powder ATMAA with a mass fraction higher than 99.3 % was supplied by ShiJiaZhuang HeJia Health Productions Co., Ltd. The chemical structure of ATMAA is shown in Figure 1. Distilled deionizer water was obtained from the market. Methanol, ethanol, 1-propanol, and glycol of analytical reagent grade were purchased from TianJin Damao Chemical Reagent Factory. Their mass fraction purities were better than 99.0 %.

Apparatus and Procedure. The solubility of ATMAA was measured using an apparatus similar to that described as literature.[15] A 300 mL jacketed glass vessel was used to determine the solubility and controlled by a circulated bath (temperature uncertainty of ± 0.05 K). The temperature of the inner chamber

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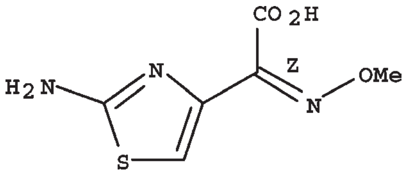

Figure 1. Chemical structure of ATMAA.

of the vessel was measured by a calibrated mercury-in-glass thermometer (uncertainty of ± 0.05 K). The solution was stirred with a magnetic stir bar, and the dissolution of the solute was examined by the laser beam penetrating the vessel. To prevent the evaporation of the solvent, a condenser vessel was introduced. The masses of the samples and solvents were weighed using an analytical balance (sartorius CP224S, Germany) with an uncertainty of ± 0.0001 g. The reported solubilities were the average of three-time repeated measurements. The uncertainty of the experimental solubility values is less than 2.0 %. The uncertainty in the solubility values can be due to uncertainties in the temperature measurements, weighing procedure, and instabilities of the water bath. The procedure of solubility measurement is just like the description of the literature.[16]

The solubility of ATMAA in mole fraction (x_A) in different binary solvent mixtures could be obtained from eq 1, and the initial molar fraction concentrations of binary solvent mixtures (x_B^0) were calculated according to eq 2.

$$x_A = \frac{m_A/M_A}{m_A/M_A + m_B/M_B + m_C/M_C} \tag{1}$$

$$x_B^0 = \frac{m_B/M_B}{m_B/M_B + m_C/M_C} \tag{2}$$

where m_A, m_B, and m_C represent the mass of ATMAA (A), water (B), and organic solvent (C = ethanol, methanol, or glycol), respectively. M_A, M_B, and M_C are the respective molecular masses.

RESULTS AND DISCUSSION

Solubility Data. The experimental solubilities of ATMAA in pure solvents and binary solvent mixtures are presented in Tables 1 to 4 and are graphically plotted in Figures 2 to 5 as well. From Tables 1 to 4 and Figures 2 to 5, it can be seen that the solubility of ATMAA in pure solvents and binary solvent mixtures with given initial compositions increases with increasing temperature. The largest solubility of ATMAA is in glycol, and the lowest is in 1-propanol. The higher solubility of ATMAA in glycol is likely due to that glycol has two hydroxyl groups which is easier to form hydrogen bonds than other solvents. Of those solvents used in the work, the lowest polarity of 1-propanol results in the lower solubility of ATMAA. For binary mixtures of water + glycol, thte solubility of ATMAA decreases with increasing water content at a given temperature. However, the solubility of ATMAA shows a maximum at a specific initial composition of water in the binary mixtures of water + (methanol or ethanol). This phenomenon may be related to the formation of hydrates of ATMAA.[5,17]

Table 1. Mole Fraction Solubility of ATMAA in Pure Solvents with the Temperature Range from (282 to 330) K

T/K	$10^3 x_A$	$10^3 x_A^{cal}$ (eq 6)	T/K	$10^3 x_A$	$10^3 x_A^{cal}$ (eq 6)
		Water			
283.67	0.3556	0.3556	307.90	0.7254	0.7208
288.48	0.4157	0.4160	313.25	0.8158	0.8211
293.22	0.4835	0.4814	317.45	0.9105	0.9044
298.36	0.5573	0.5590	322.90	1.015	1.018
303.22	0.6366	0.6386	328.17	1.134	1.133
		Methanol			
283.75	0.2929	0.2955	308.13	0.5568	0.5626
288.17	0.3343	0.3309	312.55	0.6403	0.6352
293.36	0.3802	0.3787	318.05	0.7397	0.7396
298.26	0.4301	0.4311	323.15	0.8534	0.8529
303.10	0.4885	0.4909	328.18	0.9812	0.9827
		Ethanol			
283.12	0.06904	0.06829	308.10	0.1816	0.1822
288.42	0.08311	0.08400	313.30	0.2227	0.2237
293.23	0.1007	0.1014	318.27	0.2759	0.2722
298.17	0.1242	0.1232	323.13	0.3341	0.3298
303.33	0.1506	0.1509	328.18	0.3967	0.4025
		Glycol			
283.11	1.295	1.309	308.44	2.642	2.672
288.68	1.518	1.514	313.66	3.058	3.140
293.41	1.747	1.723	318.42	3.657	3.650
298.26	2.002	1.975	323.15	4.341	4.253
303.46	2.304	2.300	328.65	5.084	5.099
		1-Propanol			
282.85	0.02141	0.01968	308.27	0.08066	0.07781
288.05	0.02490	0.02589	313.13	0.1084	0.1020
293.09	0.03099	0.03391	318.05	0.1419	0.1344
298.30	0.04245	0.04497	323.55	0.1807	0.1832
303.08	0.05937	0.05842	328.13	0.2246	0.2375

Data Correlation. The solubility of solute (A) in the solution can be calculated by the solid−liquid equilibrium equation.[18]

$$\ln x_A \gamma_A = \ln\left(\frac{f_A^s}{f_A^*}\right) = \frac{\Delta_{fus}H_A}{R}\left(\frac{1}{T_{tp,A}} - \frac{1}{T}\right) - \frac{\Delta_{fus}C_{p,A}}{R}\left(\ln\left(\frac{T_{tp,A}}{T}\right) - \frac{T_{tp,A}}{T} + 1\right) \tag{3}$$

where x_A is the solubility of solute (A) in mole fraction; γ_A is the activity coefficient of the solute (A); f_A^* and f_A^s are the fugacity of solute (A) at standard-state and in saturated solution; $\Delta_{fus}C_{p,A}$ is the difference between the heat capacities of solute (A) in the liquid and solid phases; $\Delta_{fus}H_A$ is the enthalpy change upon the melting of solute (A) at its triple-point temperature ($T_{tp,A}$); T and R stand for absolute equilibrium temperature of the saturated solution and the gas constant, respectively.

For regular solutions, the activity coefficient in eq 3 can be calculated using eq 4:[19]

$$\ln \gamma_A = \alpha + \frac{\beta}{T} \tag{4}$$

Table 2. Mole Fraction Solubility of ATMAA in Water (B) + Methanol (C) with the Temperature Range from (282 to 330) K

T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)	T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)
$x_B^0 = 0$					
283.75	0.2929	0.2901	308.13	0.5568	0.5878
288.17	0.3343	0.3298	312.55	0.6403	0.6676
293.36	0.3802	0.3834	318.05	0.7397	0.7818
298.26	0.4301	0.4419	323.15	0.8534	0.9047
303.10	0.4885	0.5084	328.18	0.9812	1.044
$x_B^0 = 0.08605$					
283.04	0.2913	0.2783	307.65	0.6160	0.5722
288.27	0.3463	0.3248	312.55	0.7025	0.6592
293.32	0.4081	0.3769	317.54	0.8002	0.7607
298.27	0.4749	0.4356	322.80	0.9170	0.8839
303.36	0.5442	0.5053	328.16	1.048	1.029
$x_B^0 = 0.3230$					
283.23	0.3071	0.3182	307.96	0.6270	0.6606
288.10	0.3563	0.3688	312.87	0.7203	0.7596
293.26	0.4150	0.4303	318.17	0.8330	0.8817
298.39	0.4838	0.5006	323.20	0.9467	1.014
302.72	0.5460	0.5680	327.96	1.069	1.155
$x_B^0 = 0.5381$					
283.09	0.3354	0.355	308.40	0.7311	0.7539
288.29	0.3873	0.4170	313.64	0.8801	0.8733
293.13	0.4569	0.4829	318.26	1.040	0.9919
298.44	0.5381	0.5655	323.16	1.229	1.133
303.45	0.6203	0.6544	328.14	1.406	1.293
$x_B^0 = 0.6387$					
282.67	0.3544	0.3540	308.17	0.7940	0.7616
288.20	0.4204	0.4212	312.83	0.9171	0.8681
293.33	0.5049	0.4930	318.60	1.074	1.017
298.50	0.5912	0.5755	323.50	1.243	1.160
303.45	0.6857	0.6653	328.64	1.436	1.328
$x_B^0 = 0.7111$					
283.08	0.3465	0.3549	308.42	0.7732	0.7635
287.91	0.4054	0.4138	313.25	0.9271	0.8743
293.00	0.4819	0.4846	318.16	1.095	1.000
298.02	0.5676	0.5641	323.24	1.296	1.146
303.44	0.6661	0.6618	328.14	1.488	1.303
$x_B^0 = 0.8770$					
283.22	0.3304	0.3358	308.48	0.6890	0.7326
288.36	0.3857	0.3975	313.24	0.7789	0.8379
293.17	0.4474	0.4632	318.40	0.8758	0.9652
298.45	0.5233	0.5452	323.20	0.9808	1.097
303.22	0.6017	0.6288	328.00	1.096	1.243
$x_B^0 = 1$					
283.67	0.3556	0.3292	307.90	0.7254	0.7035
288.48	0.4157	0.3867	313.25	0.8158	0.8187
293.22	0.4835	0.4509	317.45	0.9105	0.9190
298.36	0.5573	0.5295	322.90	1.015	1.063
303.22	0.6366	0.6134	328.17	1.134	1.217

Table 3. Mole Fraction Solubility of ATMAA in Water (B) + Ethanol (C) with Temperature Range from (282 to 330) K

T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)	T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)
$x_B^0 = 0$					
283.12	0.06904	0.06691	308.10	0.1816	0.1819
288.42	0.08311	0.08234	313.30	0.2227	0.2252
293.23	0.1007	0.09965	318.27	0.2759	0.2767
298.17	0.1242	0.1215	323.13	0.3341	0.3386
303.33	0.1506	0.1497	328.18	0.3967	0.4182
$x_B^0 = 0.2285$					
283.09	0.09968	0.09000	308.31	0.2215	0.2418
288.07	0.1206	0.1096	313.34	0.2640	0.2935
293.13	0.1422	0.1338	318.25	0.3293	0.3541
298.21	0.1669	0.1633	323.35	0.4192	0.4300
303.21	0.1924	0.1984	328.15	0.5187	0.5155
$x_B^0 = 0.5285$					
283.12	0.1406	0.1680	308.28	0.4510	0.4294
288.45	0.1919	0.2072	313.34	0.5195	0.5111
293.13	0.2556	0.2478	318.25	0.6154	0.6026
298.21	0.3199	0.2994	323.25	0.7412	0.7098
303.15	0.3850	0.3582	328.15	0.8688	0.8302
$x_B^0 = 0.7194$					
283.15	0.2004	0.2428	308.51	0.6300	0.6076
288.23	0.2536	0.2965	313.25	0.7463	0.7067
293.17	0.3234	0.3572	318.29	0.8704	0.8247
298.40	0.4115	0.4314	323.35	1.029	0.9571
303.55	0.5191	0.5154	328.15	1.214	1.096
$x_B^0 = 0.7929$					
283.15	0.2534	0.2700	308.53	0.6901	0.6707
288.62	0.3112	0.3348	313.67	0.8127	0.7863
293.21	0.3903	0.3977	318.39	0.9496	0.9039
298.40	0.4783	0.4788	323.35	1.099	1.040
303.51	0.5807	0.5698	328.15	1.283	1.184
$x_B^0 = 0.8566$					
282.79	0.2927	0.2847	308.53	0.7165	0.7143
288.07	0.3504	0.3512	313.26	0.8366	0.8244
293.04	0.4214	0.4234	318.39	0.9927	0.9556
298.24	0.5039	0.5095	323.25	1.152	1.091
303.33	0.6084	0.6050	328.15	1.336	1.239
$x_B^0 = 0.9530$					
282.98	0.3280	0.3016	308.41	0.7040	0.7456
288.49	0.3985	0.3760	313.57	0.7999	0.8678
293.53	0.4746	0.4543	318.35	0.9097	0.9904
298.27	0.5347	0.5373	323.07	1.023	1.120
303.25	0.6139	0.6343	328.05	1.157	1.265
$x_B^0 = 1$					
283.67	0.3556	0.3093	307.90	0.7254	0.7325
288.48	0.4157	0.3753	313.25	0.8158	0.8564
293.22	0.4835	0.4489	317.45	0.9105	0.9609
298.36	0.5573	0.5386	322.90	1.015	1.105
303.22	0.6366	0.6330	328.17	1.134	1.253

Table 4. Mole Fraction Solubility of ATMAA in Water (B) + Glycol (C) with Temperature Range from (282 to 330) K

T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)	T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)
		$x_B^0 = 0$			
283.11	1.295	1.301	308.44	2.642	2.675
288.68	1.518	1.508	313.66	3.058	3.146
293.41	1.747	1.719	318.42	3.657	3.660
298.26	2.002	1.974	323.15	4.341	4.266
303.46	2.304	2.301	328.65	5.084	5.114
		$x_B^0 = 0.2851$			
283.16	1.189	1.256	308.31	2.455	2.484
288.25	1.387	1.432	313.17	2.812	2.859
293.35	1.605	1.639	318.32	3.342	3.327
298.13	1.866	1.866	323.15	3.939	3.844
303.22	2.156	2.150	328.15	4.590	4.471
		$x_B^0 = 0.3825$			
283.10	1.057	1.093	308.28	2.219	2.160
288.49	1.253	1.256	313.56	2.522	2.512
293.31	1.465	1.428	318.06	2.924	2.862
298.14	1.701	1.628	323.15	3.367	3.323
303.15	1.949	1.869	328.25	3.870	3.866
		$x_B^0 = 0.4765$			
283.12	0.9394	0.9365	308.58	1.808	1.867
288.71	1.089	1.084	313.52	2.003	2.147
293.33	1.248	1.226	318.12	2.344	2.450
298.26	1.427	1.402	322.97	2.726	2.819
303.34	1.618	1.612	327.75	3.163	3.240
		$x_B^0 = 0.6027$			
282.87	0.7851	0.7481	308.72	1.511	1.509
288.56	0.9177	0.8697	313.21	1.679	1.711
293.23	1.056	0.9859	318.22	1.958	1.971
298.23	1.205	1.129	323.17	2.283	2.268
303.35	1.358	1.300	327.95	2.661	2.600
		$x_B^0 = 0.6523$			
283.10	0.7102	0.6910	308.41	1.315	1.375
288.61	0.8011	0.8001	313.55	1.485	1.586
292.96	0.9084	0.8996	318.42	1.757	1.818
298.37	1.035	1.042	322.64	2.040	2.048
303.55	1.168	1.202	328.05	2.341	2.386
		$x_B^0 = 0.7757$			
284.09	0.5402	0.5752	308.39	1.090	1.115
287.69	0.6219	0.6338	313.02	1.253	1.267
293.24	0.7212	0.7367	318.57	1.463	1.476
298.32	0.8268	0.8461	323.55	1.760	1.694
303.49	0.9465	0.9747	329.54	2.149	1.998
		$x_B^0 = 0.8374$			
282.97	0.4877	0.5020	308.54	0.9787	1.008
288.24	0.5667	0.5792	313.09	1.112	1.141
292.94	0.6482	0.6582	318.39	1.305	1.320
298.32	0.7481	0.7622	322.76	1.504	1.487
303.62	0.8572	0.8810	327.85	1.722	1.709

Table 4. Continued

T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)	T/K	$10^3\,x_A$	$10^3\,x_A^{cal}$ (eq 12)
		$x_B^0 = 0.9372$			
283.25	0.4164	0.4220	308.35	0.8514	0.8381
288.44	0.4930	0.4866	313.15	0.9791	0.9547
293.20	0.5715	0.5544	318.06	1.148	1.090
298.20	0.6536	0.6357	323.25	1.342	1.254
303.35	0.7454	0.7316	330.25	1.572	1.512
		$x_B^0 = 0.9836$			
283.23	0.3970	0.3845	308.25	0.7719	0.7632
288.25	0.4624	0.4417	313.00	0.8822	0.8678
293.25	0.5290	0.5069	318.03	1.021	0.9935
298.30	0.6022	0.5821	323.15	1.186	1.139
303.33	0.6806	0.6677	330.30	1.383	1.378
		$x_B^0 = 1$			
283.67	0.3556	0.3760	307.90	0.7254	0.7308
288.48	0.4157	0.4296	313.25	0.8158	0.8445
293.22	0.4835	0.4895	317.45	0.9105	0.9453
298.36	0.5573	0.5636	322.90	1.015	1.093
303.22	0.6366	0.6436	328.17	1.134	1.258

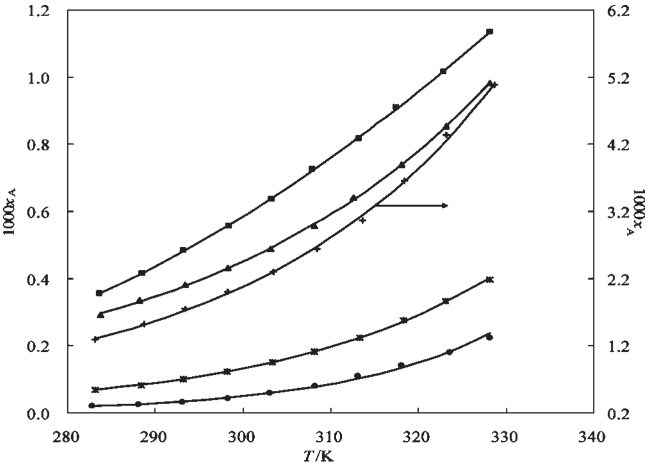

Figure 2. Solubility of ATMAA at different temperatures in pure solvents: ■, water; ▲, methanol; ∗, ethanol; +, glycol; ●, 1-propanol; solid line, calculated by eq 6.

where α and β are empirical constants. Introducing eq 4 into eq 3 results in eq 5:

$$\ln x_A = \left[\frac{\Delta_{fus}H_A}{RT_{tp,A}} - \frac{\Delta_{fus}C_{p,A}}{R}(1 + \ln T_{tp,A}) - \alpha\right] + \left[-\beta - \frac{\Delta_{fus}H_A}{R} + \frac{\Delta_{fus}C_{p,A}}{R}T_{tp,A}\right]\frac{1}{T} + \frac{\Delta_{fus}C_{p,A}}{R}\ln T \tag{5}$$

Which can be rearranged to get eq 6:

$$\ln x_A = a + \frac{b}{T} + c \ln T \tag{6}$$

Equation 6 is the modified Apelblat equation that represents the temperature dependence of solubility of ATMAA (A) in the pure

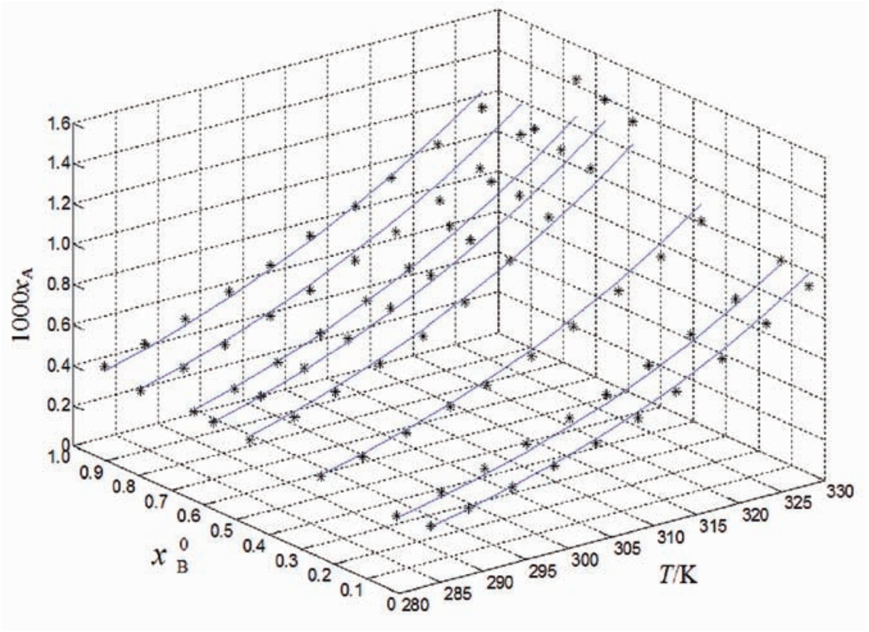

Figure 3. Solubility of ATMAA varying with temperature and initial composition of water (B) + methanol (C) binary mixtures: ∗, experimental data point; blue solid line, calculated by eq 12.

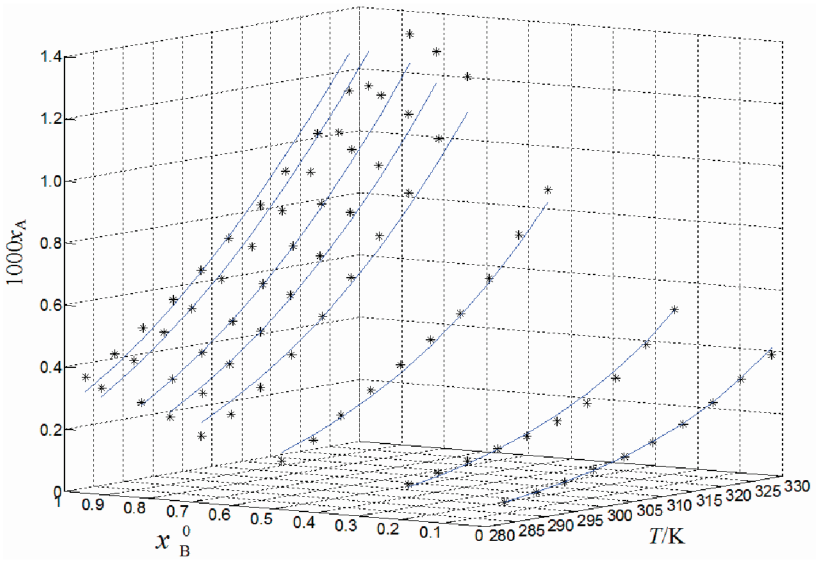

Figure 4. Solubility of ATMAA varying with temperature and initial composition of water (B) + ethanol (C) binary mixtures: ∗, experimental data point; blue solid line, calculated by eq 12.

solvent systems or the mixed solvent systems with a given initial composition.

Jouyban—Acree model is perhaps one of the more versatile models to describe the solubility of a solute with the variation of both temperature and initial composition of binary solvent mixtures:

$$\ln x_A = x_B^0 \ln(x_A)_B + x_C^0 \ln(x_A)_C + x_B^0 x_C^0 \sum_{i=0}^{n} \frac{J_i}{T} (x_B^0 - x_C^0)^i \tag{7}$$

In which T is the absolute temperature, and J_i is the model constant, x_B^0 and x_C^0 refer to the initial mole fraction of the binary solvent mixtures. $(x_A)_i$ is the mole fraction solubility of the solute in pure solvent i. n refers to the number of "curve-fit" parameters used and can be equal to 0, 1, 2, and 3, respectively. Substitution of $(1 - x_B^0)$ for x_C^0 in eq 7 with $n = 2$ and subsequent rearrangements result in eq 8:

$$\begin{aligned} \ln x_A = {} & \ln(x_A)_c + [\ln(x_A)_B - \ln(x_A)_C]x_B^0 \\ & + (J_0 - J_1 + J_2)\,\frac{x_B^0}{T} + (3J_1 - J_0 - 5J_2)\,\frac{(x_B^0)^2}{T} \\ & + (8J_2 - 2J_1)\,\frac{(x_B^0)^3}{T} + (-4J_2)\,\frac{(x_B^0)^4}{T} \end{aligned} \tag{8}$$

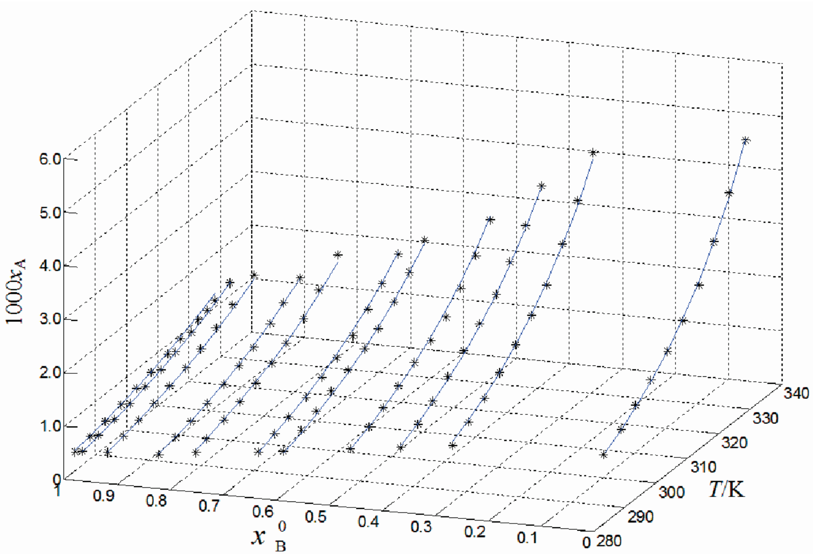

Figure 5. Solubility of ATMAA varying with temperature and initial composition of water (B) + glycol (C) binary mixtures: ∗, experimental data point; blue solid line, calculated by eq 12.

Table 5. Parameters for ATMAA in Pure Solvents by the Modified Apelblat Equation

solvent	A	B	C	MPD
water	88.1722	−6395.32	−13.0261	0.35
methanol	−150.593	4345.18	22.5125	0.51
ethanol	−164.386	3941.10	24.9517	0.87
glycol	−226.561	7637.27	34.1750	1.06
1-propanol	−278.358	7826.95	42.4896	0.05

Table 6. Parameters for ATMAA in Aqueous Binary Solvent Mixtures by the Hybrid Model

solvent	A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_8	A_9	MPD
water + methanol	−108.588	2299.89	16.3484	111.382	−5301.38	1449.49	−2196.45	959.792	−16.5223	4.94
water + ethanol	−203.960	5631.36	30.9000	335.380	−14646.9	891.947	−586.401	−75.0799	−50.1166	5.21
water + glycol	−221.258	7380.94	33.3950	128.979	−4899.18	−2185.09	2290.22	−882.051	−19.5165	2.55

In eq 8, the temperature dependence of the solubility of a solute in a pure solvent i $((x_A)_i)$ can be described with the modified Apelblat equation:

$$\ln(x_A)_B = a_1 + \frac{b_1}{T} + c_1 \ln T \tag{9}$$

$$\ln(x_A)_C = a_2 + \frac{b_2}{T} + c_2 \ln T \tag{10}$$

Introducing $(x_A)_i$ from eqs 9 and 10 into eq 8, and subsequent rearrangements result in eq 11:

$$\ln x_A = a_1 + \frac{b_1}{T} + c_1 \ln T + [a_1 - a_2]x_B^0 + (b_1 - b_2 + J_0 - J_1 + J_2)\frac{x_B^0}{T} + (3J_1 - J_0 - 5J_2)\frac{(x_B^0)^2}{T} + (8J_2 - 2J_1)\frac{(x_B^0)^3}{T} + (-4J_2)\frac{(x_B^0)^4}{T} + (c_1 - c_2)x_B^0 \ln T \tag{11}$$

Equation 11 can be rearranged to eq 12 by introducing a constant term and can be further simplified as:

$$\ln x_A = A_1 + \frac{A_2}{T} + A_3 \ln T + A_4 x_B^0 + A_5\frac{x_B^0}{T} + A_6\frac{(x_B^0)^2}{T} + A_7\frac{(x_B^0)^3}{T} + A_8\frac{(x_B^0)^4}{T} + A_9 x_B^0 \ln T \tag{12}$$

This equation is referred as a hybrid model, which can simultaneously correlate the solubility of a solute with both temperature and initial mole fraction of binary solvent mixtures. A_1 to A_9 are the model parameters.

The parameter values of eqs 6 and 12 are directly obtained by Microsoft Excel using the linear least-squares method from the experimental data. The validity of the models is evaluated by calculating the mean percentage deviation (MPD) using eq 13.

$$\text{MPD} = \frac{100}{N}\sum\frac{|x_A^{\text{cal}} - x_A|}{x_A} \tag{13}$$

where x_A^{cal} is the solubility calculated from the modified Apelblat equation and the hybrid model and N is the number of experimental points.

The solubility of ATMAA in pure solvents and binary solvent mixtures has been predicted by the modified Apelblat equation and the hybrid model, respectively, and is listed in Tables 1 to 4 and plotted in Figures 2 to 5. The values of their parameters are presented in Tables 5 and 6 together with the MPD. The maximum MPD for the modified Apelblat equation is 1.06. The MPDs for the hybrid model in water + (methanol, ethanol, or glycol) are 4.94, 5.21, and 2.55. This findings showed that the modified Apelblat equation can represent the solubility of ATMAA in pure solvents well, and the hybrid model fitted very well to the experimental solubility data of ATMAA in the binary water + (methanol, ethanol, or glycol) solvent mixtures at all initial composition ranges of water content between (282 and 330) K.

■ CONCLUSION

The solubility of ATMAA in water and alcoholic solvents and the binary combinations of water + alcohol has been experimentally measured. The solubility of ATMAA was found to increase with increasing temperature.

In the pure solvents used in this study, the solubility of ATMAA follows the following order: glycol > water > methanol > ethanol > 1-propanol. In the binary water + (methanol, ethanol, or glycol) solvent mixtures it is also a function of the initial composition of water. Increasing the initial content of water results in a decrease of its solubility in water + glycol. For the water + (methanol or ethanol) systems, a maximum solubility at a specific content of water is observed.

The hybrid model proposed based on Apelblat equation and Jouyban−Acree model can provide an accurate mathematically representation of the solubility of ATMAA with both temperature and solvent composition. The hybrid model can be used to predict the solubility of ATMAA in the water + (methanol, ethanol, or glycol) binary solvent mixtures with any water content at temperatures between (282 and 330) K.

The experimental solubility and the correlation equations presented in this work can be used as essential data and models in the practical process of synthesis and purification of ATMAA.

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■ REFERENCES

(1) Ge, H. Y.; Zhang, J.; Fang, Z. J. Preparation of Aminothiazoly Loximate and the Analysis of Technological Process. *Jiangsu Chem. Ind.* **2005**, *33*, 47–50.

(2) Zhang, X. L.; Liang, B.; Quan, S. Q.; Li, X. Y.; Yao, Y. H. Research on a New Synthetic Process of Ethyl-aminothiazoly Loximate and Its Derivative. *J. Nanchang Univ. (Eng. Technol.)* **2000**, *22*, 93–96.

(3) Rominville, R. H.; Strasbourg, A. L. Novel 3-Acetoxymethyl-7-(Iminoacetamido)-Cephalosporanic Acid Derivatives. U.S. Patent US 4376203, 1985.

(4) Kwanishi, T. T.; Kitamachi, T. M.; Kohamanishi, H. T.; Sakai, H. K. Syn-Isomers of 7-[2-Alkoxyimino-2-(2-Amino-Thiazol-4-yl) Acetamido]-3-[Nitrobenzoyl-, or Benzoyl-Oxymethyl]-3-Cephem-4-Carboxylic Acid. U.S. Patent US 4279818, 1981.

(5) Burchield, R. W.; Greenwood. Purification of Syn-(2-Aminothiazol-4-yl) (Methoxyimino) Acetic Acide. U.S. Patent US 4426528, 1984.

(6) Apelblat, A.; Manzurola, E. Solubility of o-acetylsalicylic, 4-aminosalic, 3,5-dinitrosalicylic, and ptoluic acid, and magnesium-DL-aspartate in water from T = (278 to 348) K. *J. Chem. Thermodyn.* **1999**, *31*, 85–91.

(7) Wang, L. H.; Song, Y. T.; Chen, Y.; Cheng, Y. Y. Solubility of Artemisinin in Ethanol + Water from (278.2 to 343.2) K. *J. Chem. Eng. Data* **2007**, *52*, 757–758.

(8) Acree, W. E., Jr. Mathematical Representation of Thermodynamic Properties. Part 2. Derivation of the Comined Nearly Ideal Binary Solvent (NIBS)/Redlich-Kister Mathematical Representation from a Two-Body and Three-Body Interactional Mixting Model. *Thermochim. Acta* **1992**, *198*, 71–79.

(9) Acree, W. E., Jr.; McCargar, J. W.; Zvaigzne, A. L.; Teng, L. L. Mathematical Representation of Thermodynamic Properties. Carbazole Solubilities in Binary Alkane + Dibutyl Ether and Alkane + Tetrahydropyran Solvent Mixture. *Phys. Chem. Liq.* **1991**, *23*, 27–35.

(10) Guo, K.; Yin, Q. X.; Zhang, M. J.; Wang, J. K. Solubility of Losartan Potassium in Different Binary Solvents from (293.15 to 343.15) K. *J. Chem. Eng. Data* **2008**, *53*, 1138–1140.

(11) Zhu, L.; Wang, J. K. Solubility of Tobramycin in Binary Water-Ethanol Solvent. *J. Chem. Eng. Data* **2008**, *53*, 2532–2534.

(12) Jouyban, A. Review of the Cosolvency Models for Predicting Solubility of Drugs in Water-cosolvent Mixtures. *J. Pharm. Pharmaceut. Sci.* **2008**, *11*, 32–58.

(13) Jouyban, A.; Shokri, J.; Barzegar-Jalali, M.; Hassanzadeh, D.; Acree, W. E., Jr.; Ghafourian, T.; Nokhodchi, A. Solubility of Benzodiazepines in Polyethylene Glycol 200 + Water Mixtures at 303.2 K. *J. Chem. Eng. Data* **2010**, *55*, 519–522.

(14) Jouyban, A.; Romero, S.; Chan, H. K.; Clark, B. J.; Bustamante, P. A Cosolvency Model to Predict Solubility of Drugs at Several Temperatures from a Limited Number of Solubility Measurements. *Chem. Pharm. Bull.* **2002**, *50*, 594–599.

(15) Wang, S.; Wang, J. K.; Yin, Q. X. Measurement and Correlation of solubility of 7-aminocephalosporanic acid in aqueous acetone mixtures. *Ind. Eng. Chem. Res.* **2005**, *44*, 3783–3787.

(16) Wu, J. H.; Wang, J. K.; Zhang, M. J. Solubility of Cefazolin Sodium Pentahydrate in Different Solvents Between 278 and 310 K. *J. Chem. Eng. Data* **2005**, *50*, 2026–2027.

(17) Li, Y.; Chow, P. S.; Tan, R. B. H.; Black, S. N. Effect of Water Activity on the Transformation Between Hydrate and Anhydrate of Carbamazepine. *Org. Process Res. Dev.* **2008**, *12*, 264–270.

(18) Prausnitz, J. M.; Lichtenthaler, R. N.; Azevedo, E. G. *Molecular Thermodynamics of Fluid-phase Equilibria*, 3rd ed.; Prentice Hall: Englewood Cliffs, NJ, 1999.

(19) Kondepudi, D.; Prigogine, I. *Modern Thermodynamics*; John Wiley: Chichester, England, 1998.