Korean Chem. Eng. Res., 62(2), 173-180 (2024)
https://doi.org/10.9713/kcer.2024.62.2.173
PISSN 0304-128X, EISSN 2233-9558

Experimental Study and Correlation of the Solid-liquid Equilibrium of Some Amino Acids in Binary Organic Solvents

Mustafa Jaipallah Abualreish*, and Adel Noubigh*,†**

**Department of Chemistry, Faculty of Science, Northern Border University, Arar, Kingdom of Saudi Arabia.*
***Department of Chemistry; Faculty of Science and Technology; Omdurman Islamic University; Sudan.*
(Received 5 January 2024; Received in revised from 5 February 2024; Accepted 14 February 2024)

Abstract – Under ordinary atmospheric circumstances, the gravimetric technique was used to measure the solubility of L-cysteine (L-Cys) and L-alanine (L-Ala) in various solvents, including methyl alcohol, ethyl acetate, and mixtures of the two, in the range o 283.15 K to 323.15 K. Both individual solvents and their combinations showed a rise in the solubility of L-Cys and L-Ala with increasing temperature, according to the analyzed data but when analyzed at a constant temperature in the selected mixed solvents, the solubility declined with decreasing of initial mole fractions of methyl alcohol. To further assess, the relative utility of the four solubility models, we fitted the solubility data using the Jouyban-Acree (J-A), van't Hoff-Jouyban-Acree (V-J-A), Apelblat-Jouyban-Acree (A-J-A), and Ma models followed by evaluation of the values of the RAD information criteria and the RMSD were. The dissolution was also found to be an entropy-driven spontaneous mixing process in the solvents since the thermodynamic parameters of the solvents were determined using the van't Hoff model. In order to support the industrial crystallization of L-cysteine and L-alanine and contribute to future theoretical research, we have determined the experimental solubility, correlation equations, and thermodynamic parameters of the selected amino acids during the dissolution process.

Key words: L-cysteine, L-alanine, Solubility, Mixed solvents, Thermodynamic modeling, Thermodynamic properties

1. Introduction

Amino acids such as L-cysteine and L-alanine are integral part of human body and found in many proteins [1,2]. Their chemical structures are shown in Figure 1, and comprehensive information is also given in Table 1. Because of their versatility, amino acids are considered essential in many fields, including cosmetics, food, medicine, and fine chemicals [3-6]. The solubility and thermodynamic properties of biomolecules are crucial physicochemical features that influence the efficacy of purification and separation techniques from solutions. Chemical structure, ionic strength [7], experimental temperature [8], solvent polarity [9], media acidity or alkalinity [10,11], and concentration of electrolytes in aqueous solutions [12], are some variables that affect the solubility of a biomolecule. The Thermodynamics of solvation is also greatly affected by these parameters.

Proteins rely on amino acids as their building blocks, which are essential for the metabolism of all living organisms [4,13-15]. Crystallization is often used in commercial amino acid synthesis procedures to purify the synthesized product. While designing crystallization procedures, understanding of ge the solubility of the solute is crucial, since it determines both the starting concentration and the final concentration of the solute in the solvent. L-Cys and L-Ala solubility have recently been shown in various solvents and aqueous solvent combinations [16,17]. Our comprehensive literature search revealed no information on the solubility of L-Cys and L-Ala in methyl alcohol and ethyl ethanoate mixed binary solutions at the indicated temperatures.

The solubility of L-Cys and L-Ala in methyl alcohol plus ethyl ethanoate solvent mixtures was measured gravimetrically at atmospheric pressure and temperatures ranging from 283.15 to 323.15 K. The experimental solubilities of L-Cys and L-Ala were correlated using the J-A, V-J-A, A-J-A, and Ma models to determine the impact of temperature and solvent composition on solubility. Additionally, the dissolving processes of L-Cys and L-Ala had their thermodynamic parameters computed, which included changes in molar enthalpy (ΔH°_{sol}), molar entropy (ΔS°_{sol}), and Gibbs free energy (ΔG°_{sol}).

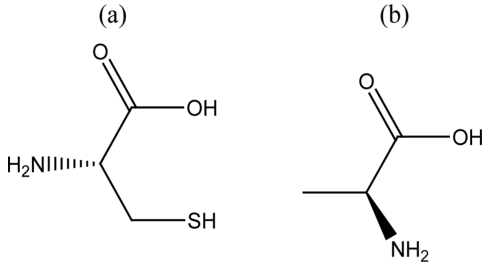

Fig. 1. Molecular structure of L-cysteine (a) and L-alanine (b).

† To whom correspondence should be addressed.
E-mail: adel.anoubigh@ipest.rnu.tn; adel.noubigh@nbu.edu.sa

Table 1. Description of solutes and solvents used in the experiments

Chemicals	Purity (%)	Source	CAS no.
L-cysteine	≥ 99.0	Heibei Huayang Biological technology Co.,Ltd.	52-90-4
L-alanine	≥ 0.990	Heibei Huayang Biological technology Co.,Ltd.	56-41-7
methyl alcohol	≥ 99.5	Sinopharm Chemical Regent Co. Ltd	67-56-1
Ethyl acetate	≥ 99.5	Sinopharm Chemical Regent Co. Ltd	141-78-6

2. Experimental

2-1. Materials

L-cysteine and L-alanine was purchased from Heibei Huayang Biological Technology Co., Ltd. with their mass fraction purity more than 0.98. Reagents of analytical quality, including methyl alcohol and ethyl ethanoate, were obtained from Sinopharm Chemical Reagent Co. Ltd. and used without further purification. Their mass fraction purities exceeded 0.995. Comprehensive details regarding all materials employed in the experiments are listed in Table 1.

2-2. Apparatus and procedures

Within the temperature range of 283.15 K to 323.15 K and pressures of 0.1 MPa, this research investigated the solid-liquid equilibrium of L-Cys and L-Ala using the gravimetric technique, previously published in details [18-22].

The process involved, placing the excess drug of the solid sample (AA) and a predetermined quantity of chosen solvents into a double-jacketed glass container with a specified temperature control (±0.05 K). Water circulation was maintained throughout the glass container to uphold the specified temperature. The mixed solution was continuously stirred for over 12 hours to attain dissolution equilibrium. Subsequently, the solid-liquid solution was allowed to stratify for 12 hours, stirring was halted, and precipitation occurred. Following this, a 5 mL sample was extracted from the upper liquid layer, transferred to a double dish, weighed, and subjected to a 12-hour drying process at 323.15 K. The experimental solubility was measured thrice to minimize errors. The validity of the entire setup has been verified with previously published works [18-22].

The mole fraction solubility of AA (designated as x_{AA}^{exptl}) in the chosen binary solvents was determined using Eq. (1), while the methyl alcohol mole fraction (denoted as x_M) used in Eq. (2) to calculate in every system including a mixture of solvents.

$$x_{AA}^{exptl} = \frac{m_2/M_1}{m_1/M_1 + m_2/M_2 + m_3/M_3} \quad (1)$$

$$x_M = \frac{m_2/M_2}{m_2/M_2 + m_3/M_3} \quad (2)$$

In this case, m_1, m_2 and m_3 stand for the masses of AA, methyl alcohol, and ethyl ethanoate, independently; M_1, M_2, M_3 designate the molar masses of AA, methyl alcohol, and ethyl ethanoate, respectively.

3. Results and Discussion

3-1. Solubility data

Prior research has shed light on the solubility of L-Cys and L-Ala in methyl alcohol and ethyl ethanoate between 283 K and 323 K [16, 17]. Figure 2 displayed the study findings and observations. With a significant relative error of around 2% between them, these numbers align with our findings.

Tables 2-3 and Figure 3 showed resulting L-Cys and L-Ala solubility data of each binary system. The results show that at a given temperature, the experimental solubility of selected amino acids increased monotonically with an increasing mole fraction of methyl alcohol. There was a temperature-dependent increase in the solubility of L-Cys and L-Ala, even when the solvent composition remains constant.

3-2. Thermodynamic modelling

Several models have successfully correlated the solubility of solid solutes in mixtures of solvents. The experimental solubilities of AA in methyl alcohol, ethyl ethanoate, and (methyl alcohol + ethyl ethanoate) solvent mixtures were associated in this work while using the J-A model, V-J-A model, A-J-A model and Ma model. The J-A model, V-J-A model, A-J-A model and Ma model are related to solubility or solution thermodynamics. Their physical implications may involve predicting and understanding the interaction pattern of

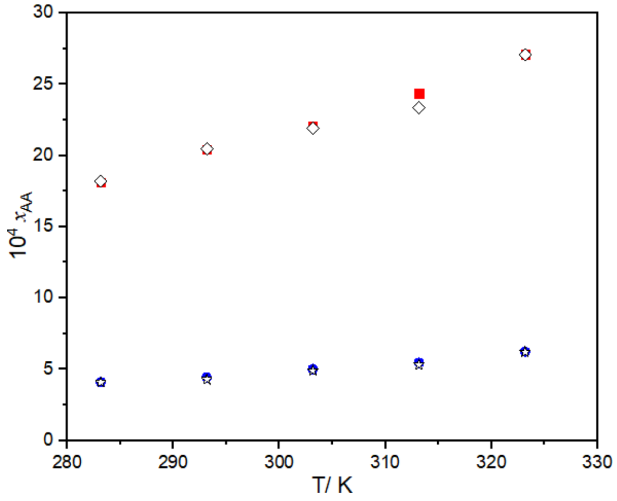

Fig. 2. Graphical comparison of experimental solubilities of selected amino acids in methyl alcohol with literature values [16,17] at various temperatures: this work (■, L-cysteine; ●, L-alanine) and literature (◇, L-cysteine; ☆, L-alanine).

Table 2. Experimental (x_{explt}) and calculated (x_{calcd}) mole fraction solubility of L-cysteine in (methyl alcohol + ethyl acetate) mixture at several temperatures and p=101.3 kPa[a]

		J-A model	V-J-A model	A-J-A model	Ma Model		J-A model	V-J-A model	A-J-A model	Ma Model
T /K	$10^4 x_{explt}$	$10^4 x_{calcd}$				$10^4 x_{explt}$	$10^4 x_{calcd}$			
	0.0					0.20				
283.15	0.240	0.240	0.240	0.235	0.228	0.686	0.679	0.665	0.670	0.656
293.15	0.290	0.290	0.290	0.331	0.336	0.831	0.804	0.914	0.891	0.906
303.15	0.580	0.580	0.580	0.469	0.482	1.304	1.415	1.229	1.192	1.225
313.15	0.670	0.670	0.670	0.666	0.673	1.626	1.610	1.621	1.604	1.625
323.15	0.890	0.890	0.890	0.949	0.918	2.174	2.055	2.103	2.168	2.117
	0.4					0.6				
283.15	2.080	2.037	1.989	2.030	1.994	5.683	5.590	5.445	5.622	5.533
293.15	2.508	2.360	2.583	2.538	2.574	6.457	6.354	6.708	6.631	6.695
303.15	3.262	3.645	3.298	3.202	3.277	8.278	8.641	8.151	7.914	8.049
313.15	4.160	4.081	4.145	4.073	4.120	9.688	9.543	9.782	9.541	9.619
323.15	5.087	4.994	5.136	5.214	5.121	11.392	11.227	11.607	11.599	11.431
	0.8					1.0				
283.15	12.161	12.140	11.626	12.323	12.151	18.120	18.120	18.120	18.562	18.382
293.15	13.673	13.650	13.702	13.824	13.891	20.410	20.410	20.410	20.060	20.110
303.15	16.249	16.465	15.973	15.721	15.889	22.100	22.100	22.100	21.998	22.143
313.15	18.090	18.061	18.440	18.088	18.175	24.350	24.350	24.350	24.429	24.517
323.15	20.592	20.561	21.100	21.021	20.787	27.107	27.107	27.107	27.424	27.270

[a]Standard uncertainty u is $u(T) = 0.01$ K. The relative standard uncertainty u is $u_r(p) = 0.05$, $u_r(x_{explt}) = 0.02$.

Table 3. Experimental (x_{explt}) and calculated (x_{calcd}) mole fraction solubility of L-alanine in (methyl alcohol + ethyl acetate) mixture at several temperatures and p=101.3 kPa[a]

		J-A model	V-J-A model	A-J-A model	Ma Model		J-A model	V-J-A model	A-J-A model	Ma Model
T /K	$10^4 x_{explt}$	$10^4 x_{calcd}$				$10^4 x_{explt}$	$10^4 x_{calcd}$			
	0.0					0.20				
283.15	0.810	0.810	0.810	0.825	0.797	0.997	1.0478	0.972	1.069	1.046
293.15	1.108	1.108	1.108	1.069	1.090	1.358	1.370	1.304	1.337	1.361
303.15	1.451	1.451	1.451	1.395	1.442	1.732	1.746	1.715	1.686	1.735
313.15	1.810	1.810	1.810	1.831	1.855	2.172	2.125	2.217	2.142	2.170
323.15	2.319	2.319	2.319	2.415	2.326	2.782	2.665	2.821	2.737	2.670
	0.4					0.6				
283.15	1.606	1.608	1.605	1.645	1.621	2.588	2.470	2.582	2.532	2.512
293.15	2.070	2.000	2.007	1.974	1.996	2.976	2.919	3.014	2.915	2.929
303.15	2.474	2.466	2.474	2.393	2.437	3.346	3.484	3.484	3.396	3.425
313.15	2.895	2.912	3.009	2.926	2.951	3.842	3.992	3.989	3.997	4.015
323.15	3.564	3.557	3.615	3.604	3.547	4.673	4.751	4.529	4.747	4.713
	0.8					1.0				
283.15	3.626	3.418	3.701	3.512	3.512	4.101	4.101	4.101	4.222	4.247
293.15	3.901	3.852	4.048	3.892	3.890	4.430	4.430	4.430	4.528	4.491
303.15	4.350	4.466	4.402	4.372	4.372	5.010	5.010	5.010	4.928	4.873
313.15	4.956	4.981	4.762	4.971	4.974	5.462	5.462	5.462	5.432	5.407
323.15	5.659	5.792	5.126	5.708	5.721	6.231	6.231	6.231	6.055	6.116

[a]Standard uncertainty u is $u(T) = 0.01$ K. The relative standard uncertainty u is $u_r(p) = 0.05$, $u_r(x_{explt}) = 0.02$.

solutes with solvents at various conditions. It included examining the effects of temperature, pressure, and composition on solubility in mixed solvents. The subsequent section provides detailed insights into the specifics of the selected models.

3-2.1 Jouyban-Acree model

To accurately depict dissolution in binary solvents, it was crucial to consider not only temperature but also the influence of solvent composition on solubility. Hence, the Jouyban-Acree method was recommended [23,24].

$$\ln x_{AA} = x_B^0 \ln(x_{1,T})_B + x_C^0 \ln(x_{2,T})_B + x_B^0 x_C^0 \sum_0^2 \frac{J_i}{T} (x_B^0 - x_C^0)^i \quad (3)$$

Here, x_B^0 and x_C^0 measure the proportion of ethyl ethanoate and

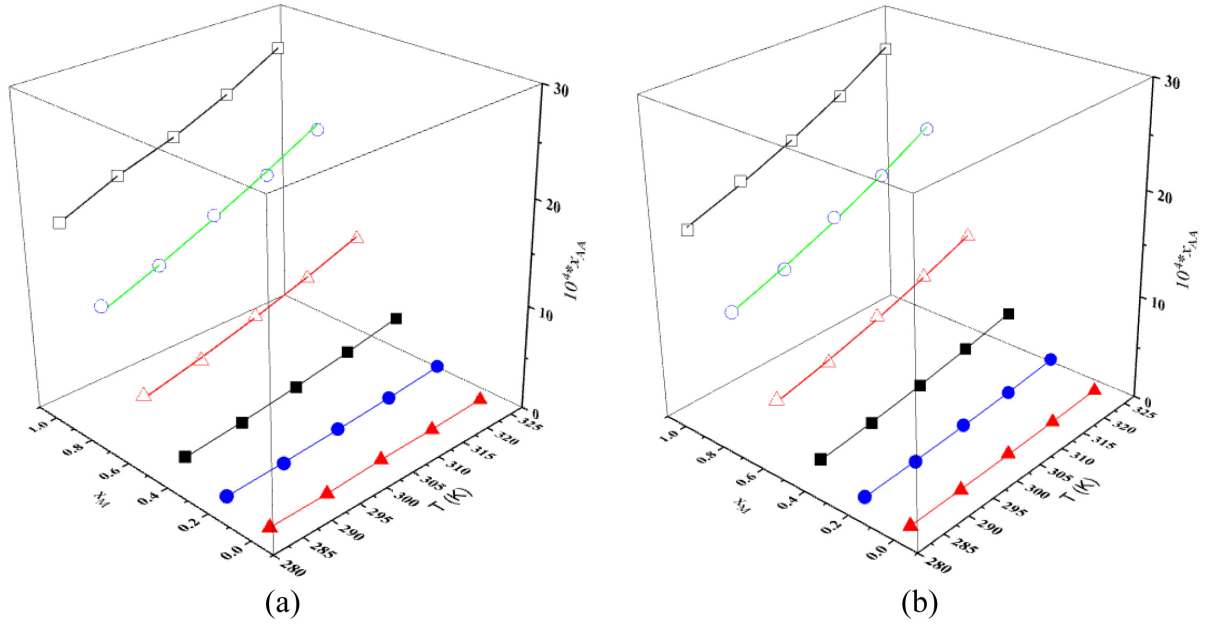

Fig. 3. Mole fraction solubility of L-cysteine in (methyl alcohol + ethyl acetate) binary solvent mixtures at various temperatures: ?, x_M = 0.0; ●, x_M = 0.2; ◆, x_M = 0.4; ★; Δ, x_M = 0.6; ○, x_M = 0.8; ◇, x_M = 1.00; solid line, calculated with van't Hoff – Acree model (a) and Ma model (b).

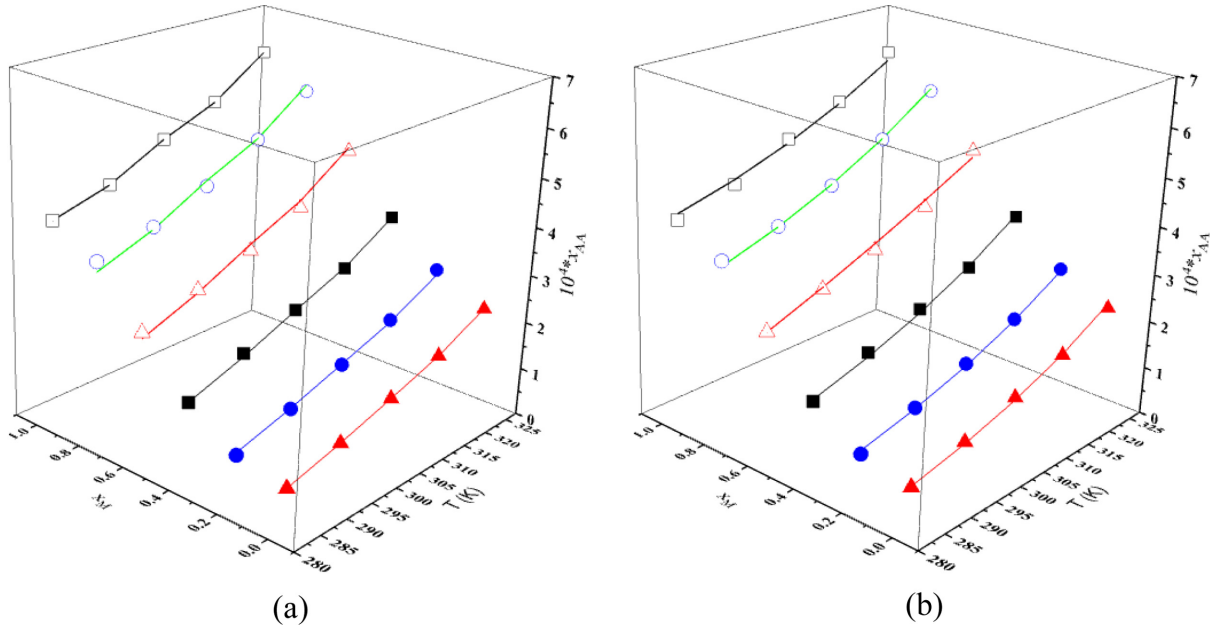

Fig. 4. Mole fraction solubility of L-alanine in (methyl alcohol + ethyl acetate) binary solvent mixtures at various temperatures: ?, x_M = 0.0; ●, x_M = 0.2; ◆, x_M = 0.4; ★; Δ, x_M = 0.6; ○, x_M = 0.8; ◇, x_M = 1.00; solid line, calculated with Acree model (a) and Apelblat−Jouyban−Acree (b).

alcohol in a binary solvent that was free of a solute $x_{1,T}$ and $x_{2,T}$, the *AA* molar fraction solubility in pure ethyl ethanoate and alcohol at a given temperature *T*, respectively; J_i was the model parameter.

3-2-2. van't Hoff-Jouyban-Acree model

The van't Hoff model was the most straightforward equation describing the association between solubility and temperature based on the thermodynamic principles of solid-liquid equilibrium [25].

$$\ln x_{AA} = \frac{A}{T/K} + B \tag{4}$$

Eq. (5) represents the V-J-A model, which was derived by combining the van't Hoff equation with Eq. (3) [26,27].

$$\ln x_{AA} = x_B^0 \ln\left(A_1 + \frac{B_1}{T/K}\right) + x_C^0 \ln\left(A_2 + \frac{B_2}{T/K}\right) + x_B^0 x_C^0 \sum_0^2 \frac{J_i}{T} (x_B^0 - x_C^0)^i \tag{5}$$

3-2-3. Apelblat-Jouyban-Acree model

Apelblat introduced the Apelblat equation, a popular semi-empirical equation [28]. Eq. (3) can be used to explain it [29,30].

$$\ln x_{AA} = A + \frac{B}{T/K} + C\ln(T/K) \tag{6}$$

A, *B*, and *C* in this equation are the empirical constants that may be adjusted in the model. The solubility mole fraction of an amino acid in the solvents being studied at each absolute temperature *T*, was denoted as x_{AA}. Regarding the activity coefficient's volatility, the parameters *A* and *B* indicated that the solution was not optimum. C parameter represented the impact of temperature on the fusion enthalpy.

Similarly, the Apelblat model wass constructed by combining the *J-A* model (Eq. 3) with the modified Apelblat equation (Eq. 6) [26, 27].

$$\ln x_{AA} = x_C^0 \ln\left(A_1 + \frac{B_1}{T/K} + C_1\ln(T/K)\right) + x_C^0 \ln\left(A_2 + \frac{B_2}{T} + C_2\ln(T/K)\right) + x_B^0 x_C^0 \sum_0^2 \frac{J_i}{T}(x_B^0 - x_C^0)^i \tag{7}$$

Using Eqs. (5) and (7) at different temperatures, we can determine how the solute dissolved in binary solvent mixtures.

3-2-4. Ma model

To better correlate, the experimental solubility data in solvent mixed at different temperatures, Ma [31,32] suggested the following alternative adjustment to Eq. (7):

$$\ln x_{AA} = E_0 + \frac{E_1}{T} + E_2\ln T + E_3 x_B^0 + E_4\frac{x_B^0}{T} + E_5\frac{(x_B^0)^2}{T} + E_6\frac{(x_B^0)^3}{T} + E_7\frac{(x_B^0)^4}{T} + E_8 x_B^0 \ln T \tag{8}$$

In Eq. (8), E_0 to E_8 represent the parameters of the equation.

Using experimental solubility as input, the model parameters in Eqs. (3), (5), (7), and (8) can be derived using the nonlinear least squares technique in the MATLAB. The following was the objective function formulation:

$$F = \sum_{i=1}^{n}(\ln x_i^{exptl} - \ln\gamma x_i^{calcd})^2 \tag{9}$$

Also, the associated outcomes were evaluated using the RAD and RMSD, described by Eqs. (10) and (11), respectively.

$$RAD = \frac{1}{n}\times\sum_{i=1}^{n}\left|\frac{x_{exptl} - x_{calcd}}{x_{exptl}}\right| \tag{10}$$

$$RMSD = \left[\frac{1}{n}\times\sum_{i=1}^{n}(x_{calcd} - x_{exptl})^2\right]^{1/2} \tag{11}$$

The measured value and the computed value were represented by x_{exptl} and x_{calcd} in Eqs. (10) and (11), respectively, and n was the number of experimental points.

Table 4. Model parameters, ARD and RMSD of AA in mixtures of methyl alcohol + ethyl acetate at 101 k Pa

	L-cysteine	L-alanine
Paramter	J−A model	
J_0	567.992	110.433
J_1	426.614	308.540
J_2	-6.223	-121.846
10^2 × RAD	2.257	1.731
10^3 × RMSD	0.686	0.173
Paramter	V−J−A model	
A_1	-2.484	-6.817
B_1	-1105.010	-246.849
A_2	0.223	0.918
B_2	-3070.124	-2983.019
J_0	572.375	184.818
J_1	472.850	265.467
J_2	-39.395	-109.480
10^2 × RAD	2.173	2.080
10^3 × RMSD	0.528	0.465
Paramter	A−J−A model	
A_1	-120.882	-121.090
B_1	4408.532	4408.544
C_1	17.539	17.313
B_2	-161.758	-146.745
B_2	4116.725	4117.083
C_2	24.187	21.750
J_0	567.992	110.562
J_1	426.614	308.514
J_2	-6.223	-121.818
10^2 × RAD	4.067	2.840
10^3 × RMSD	1.539	0.463
Paramter	Ma Model	
E_0	20.285	66.877
E_1	-4077.183	-5495.510
E_2	-2.936	-10.079
E_3	-97.549	-246.670
E_4	6658.950	12231.800
E_5	720.480	1378.510
E_6	-891.787	-1529.670
E_7	25.917	458.744
E_8	13.981	36.142
10^2 × RAD	3.850	2.018
10^3 × RMSD	1.640	0.307

The J-A, V-J-A, A-J-A, and Ma models were employed while fitting solubility data in binary solvent systems. The appropriate model-specific estimated values can be found in Tables 2 and 3. Table 4 displayed all correlation model's parameters, RAD, and RMSD values. For L-cysteine, the four models exhibited the following overall RAD (percent) and RMSD (×103): J-A model (2.257 and 0.686), V-J-A model (2.173 and 0.528), A-J-A model (4.067 and 1.539), Ma model (3.850 and 1.640), and for L-alanine, J-A model (1.731 and 0.173), V-J-A model (2.080 and 0.465), A-J-A model (2.840 and 0.463), and Ma model (2.018 and 0.307). Regarding L-cysteine and L-alanine, respectively, the J-A and V-J-

A models performed the best among the four models used in this research.

3-3. Thermodynamic parameters

In the solid-liquid phase equilibrium system, the thermodynamic properties of AA in binary solvent mixtures were notably significant. Eq. (12) [33,34] represented the van't Hoff analysis, which can be employed to determine the molar enthalpy ($\Delta H^{\circ}_{\mathrm{sol}}$), molar entropy ($\Delta S^{\circ}_{\mathrm{sol}}$), and Gibbs free energy change ($\Delta G^{\circ}_{\mathrm{sol}}$) of *AA* during the dissolution process:

$$\Delta H^{\circ}_{\mathrm{sol}} = -R\left(\frac{\partial \ln x_{AA}}{\partial(1/T - 1/T_{\mathrm{hm}})}\right) \tag{12}$$

In this expression, T_{hm} denoted the mean harmonic temperature, calculated to be 302.338 K using Eq. (13) whereas x_{AA} represented the AA solubility.

$$T_{mean} = N/\sum_{i=1}^{N}\frac{1}{T_i} \tag{13}$$

In this equation, the experimental temperature, denoted as T_i, N equals the number of the temperature points measured.

The relationship between the absolute temperature's reciprocal (1/*T*) and the (ln x_{AA}) was linear. The slope of the plots of ln x_{AA}versus ($1/T–1/T_{hm}$) was equal to $-\Delta H^{\circ}_{\mathrm{sol}}/R$. By utilizing the following equations, the change in molar enthalpy may be determined ($\Delta H^{\circ}_{\mathrm{sol}}$) from the slope and the Gibbs free energy change $\Delta G^{\circ}_{\mathrm{sol}}$) from the intercept.

$$\Delta H^{\circ}_{\mathrm{sol}} = -R \times \mathrm{slope} \tag{14}$$

$$\Delta G^{\circ}_{\mathrm{sol}} = -RT_{mean} \times \mathrm{intercept} \tag{15}$$

Eq. (16) can be applied to ascertain the molar entropy change ($\Delta S^{\circ}_{\mathrm{sol}}$) during the dissolution process:

$$\Delta S^{\circ}_{\mathrm{sol}} = \frac{\Delta H^{\circ}_{\mathrm{sol}} - \Delta G^{\circ}_{\mathrm{sol}}}{T_{\mathrm{mean}}} \tag{16}$$

Eqs. (17) and (18) [35, 36] offered the respective contributions of entropy (%ξ_{TS}) and enthalpy (%ξ_H) to the Gibbs free energy change ($\Delta G^{\circ}_{\mathrm{sol}}$) of *AA* during the dissolution process.

$$\%\xi_H = \frac{\left|\Delta H^{\circ}_{\mathrm{sol}}\right|}{\left|\Delta H^{\circ}_{\mathrm{sol}}\right| + \left|T \cdot \Delta S^{\circ}_{\mathrm{sol}}\right|} \times 100 \tag{18}$$

$$\%\xi_{TS} = \frac{\left|T \cdot \Delta S^{\circ}_{\mathrm{sol}}\right|}{\left|\Delta H^{\circ}_{\mathrm{sol}}\right| + \left|T \cdot \Delta S^{\circ}_{\mathrm{sol}}\right|} \times 100 \tag{19}$$

In this paper, $\Delta H^{\circ}_{\mathrm{sol}}$, $\Delta S^{\circ}_{\mathrm{sol}}$, $\Delta G^{\circ}_{\mathrm{sol}}$, %$\xi_H$, and %$\xi_{TS}$ for *AA* were calculated for saturated solution systems by using the above Eqs. (14)-(19). The summarized information was presented in Table 5. It was evident that $\Delta S^{\circ}_{\mathrm{sol}} > 0$, $\Delta G^{\circ}_{\mathrm{sol}} > 0$ and $\Delta H^{\circ}_{\mathrm{sol}} > 0$ for all systems. These results pointed to heat absorption and a rise in disorder as defining features of the breakdown process of the selected amino acids (L-Cys and L-Ala). Moreover, in all chosen binary systems of (methyl alcohol + ethyl ethanoate), %ξ_H was observed to exceed %ξ_{TS}, signifying that the impact of heat during dissolution outperformed the contribution of entropy.

Table 5. Thermodynamic functions relative to the dissolution process of L-cysteine and L-alanine in different (methyl alcohol + ethyl acetate) mixed solvents at T_{hm} = 302.338 K

x_{M}	$\Delta_{\mathrm{sol}}H^{\circ}$ (kJ·mol^{-1})	$\Delta_{\mathrm{sol}}G^{\circ}$ (kJ·mol^{-1})	$\Delta_{\mathrm{sol}}S^{\circ}$ (J·mol^{-1}·K^{-1})	%ξ_H	%ξ_{TS}
L-cysteine					
0	26.541	1.913	81.388	51.869	48.109
0.2	22.306	0.450	72.290	50.488	49.490
0.4	17.495	2.941	48.095	54.588	45.412
0.6	13.803	5.218	28.394	61.634	38.346
0.8	10.209	6.945	10.795	75.759	24.225
1	7.497	5.729	5.847	80.907	19.079
L-alanine					
0	20.384	0.837	64.597	51.070	48.930
0.2	17.838	1.327	54.563	51.954	48.046
0.4	14.901	2.209	41.942	54.025	45.982
0.6	11.964	3.094	29.312	57.447	42.553
0.8	9.268	3.733	18.292	62.628	37.372
1	6.919	2.964	13.072	63.646	36.385

Conclusions

Between 283.15 and 323.15 K, the solid−liquid equilibrium of L-Cys and L-Ala in methyl alcohol, ethyl acetate, and (methyl alcohol + ethyl ethanoate) was examined in this work. The experimental findings showed that solvent composition and temperature, altered L-cysteine and L-alanine solubility values across all the solvent systems. A rising mole fraction of methyl alcohol increased solubility. The J−A, V−J−A, A−J−A, and Ma models were used to calculate and correlate the solubility of L-Cys and L-Ala concerning temperature and solvent composition. Neither the RAD nor the RMSD values were higher than 3.22×10^{-2} and 3.09×10^{-4}. Results from the correlation analysis were good for all the models. In addition, $\Delta G^{\circ}_{\mathrm{sol}} > 0$, $\Delta H^{\circ}_{\mathrm{sol}} > 0$, $\Delta S^{\circ}_{\mathrm{sol}} > 0$, showed that L-Cys and L-Ala dissolved in an entropic and heat-absorbing manner. The crystallization technique for L-Cys and L-Ala might be optimized and designed using the experimental solubility data.

Acknowledgments

The authors gratefully acknowledge the approval and the support of this research study by the grant no. SCIA-2023-12-2150 from the Deanship of the Scientific Research in Northern Border University, Arar, KSA.

Declarations

Conflicts of interest: The authors state that they have no competing financial interests.

References

1. Tseng, H. C., Lee, C. Y., Weng, W. L. and Shiah, I. M., "Solubilities of Amino Acids in Water at Various pH Values Under 298.15 K," *Fluid Phase Equilib.*, **285**, 90-95(2009).
2. Wang, Y., Lin, K., Jia, W. and Yu, Q., "Measurement, and Correlation of Solubility of L-Valine, L-Isoleucine, L-Methionine, and L-Threonine in Water + tert-Butanol from 283.15 to 328.15 K," *J. Chem. Eng. Data*, **66**, 677-683(2021).
3. Roy, S., Guin, P. S., Mahali, K., Houssain, A. and Dolui B. K., "Evaluation and Correlation of Solubility and Solvation Thermodynamics of Glycine, dl-alanine and dl-valine in Aqueous Sodium Sulphate Solutions at Two Different Temperatures," *J. Mol. Liq.*, **234**, 124-128(2017).
4. Roy, S., Hossain, A. and Dolui, B. K., "Solubility and Chemical Thermodynamics of d,l-Alanine and d,l-serine in Aqueous NaCl and KCl Solutions," *J. Chem. Eng. Data*, **61**(1), 132-141(2016).
5. Lammens, T. M., Franssen, M. C. R., Scott, E. L. and Sanders, J. P. M., "Availability of Protein-derived Amino Acids as Feedstock for the Production of Bio-based Chemicals," *Biomass Bioenergy*, **44**(9), 168-181(2012).
6. Thombre, S. M. and Sarwade, B. D., "Synthesis and Biodegradability of Polyaspartic Acid: A Critical Review," *J. Macromol. Sci. A*, **42**(9), 1299-1315(2005).
7. Abualreish, M. J. and Noubigh, A., "Experimental Measurement and Correlation of two α-Amino Acids Solubility in Aqueous Salts Solutions from 298.15 to 323.15 K," *Korean Chem. Eng. Res.*, **58**, 98-105(2020).
8. Abualreish, M. J. and Noubigh, A., "Evaluation of Thermodynamic Properties and Correlation of L-glutamic Acid Solubility in Some Aqueous Chloride Solutions from 298.15 to 323.15 K," *Can. J. Chem*., **97**, 615-620(2019).
9. Romero, C. M. and Oviedo, C. D., "Effect of Temperature on the Solubility of Alpha-amino Acids and Alpha, Omega - Amino Acids in Water," *J. Solution Chem.,* **42**(6), 1355-1362(2013).
10. Lu, J., Wang, X. J., Yang, X. and Ching, C. B., "Solubilities of Glycine and Its Oligopeptides in Aqueous Solutions," *J. Chem. Eng. Data*, **51**, 1593-1596(2006).
11. Pradhan, A. A. and Vera, J. H., "Effect of Acids and Bases on the Solubility of Amino Acids," *Fluid Phase Equilib.*, **152**(1), 121-132(1998).
12. Koseoglu, F., Kilic, E. and Dogan, A., "Studies on the Protonation Constants and Solvation of Alpha-amino Acids in Dioxan-water Mixtures," *Anal. Biochem.*, **277**(2), 243-246(2000).
13. Lu, J., Wang, X. J., Yang, X. and Ching, C. B., "Solubilities of Glycine and Its Oligopeptides in Aqueous Solutions," *J. Chem. Eng. Data*, **51**, 1593-1596(2006).
14. Anfinsen, C. B. and Scheraga, H. A., "Experimental and Theoretical Aspects of Protein Folding," *Adv. Protein Chem.*, **29**, 205-300(1975).
15. Lapamje, S., "In Physico-chemical Aspects of Proteins Denaturation," New York; Wiely Interscience(1978).
16. Han, J., Liu, H., Hu, S., Qiu, J., Yi, D., An, M., Guo, Y., Huang, H., He, H. and Wang, P., "Determination and Correlation of the Solubility of L-cysteine in Several Pure and Binary Solvent Systems," *J. Chem. Eng. Data*, **65**, 2649-2658(2020).
17. An, M., Qiu, J., Yi, D., Liu, H., Hu, S., Han, J., Huang, H., He, H., Liu, C., Zhao, Z., Shi, Y. and Wang, P., "Measurement and Correlation for Solubility of L-Alanine in Pure and Binary Solvents at Temperatures from 283.15 to 323.15 K," *J. Chem. Eng. Data*, **65**, 549-560(2020).
18. Noubigh, A. and Akremi, A., "Experimental Measurements, Equilibrium Study and Model Correlation of Methyl Paraben in Ethanol and Methanol Aqueous Solutions from = (293.15 to 323.15) K," *J. Mol. Liq.*, **293**, 111505(2019).
19. Noubigh, A., "Stearic Acid Solubility in Mixed Solvents of (water + ethanol) and (ethanol + ethyl acetate): Experimental Data and Comparison Among Different Thermodynamic Models," *J. Mol. Liq.*, **296**, 112101(2019).
20. Noubigh, A. and Abderrabba, M., "Thermodynamic Modeling of the Solubility and Preferential Solvation of the Natural Product Vanillic Acid in Some Aqueous Mixtures of Alcohols at Different Temperatures," *J. Chem. Eng. Data*, **67**, 2675-2686(2022).
21. Noubigh, A., Abualreish, M. J., Mogharbel, R. T., Alanazi, A. F., Alanazi, T. S. and Guetat A., "Solubility Measurement of Syringic Acid, Trans-cinnamic Acid, p-coumaric Acid, and Vanillin Constituent of Deverra DC. Genus in (ethyl acetate + ethyl alcohol) Mixtures: Thermodynamic Modeling and Preferential Solvation," **387**, 122710(2023).
22. Noubigh, A., Ben Tahar, L. and Eladeb, A.,"Solubility Modeling and Preferential Solvation of Benzamide in Some Pure and Binary Solvent Mixtures at Different Temperatures," *J. Chem. Eng. Data*, **68**, 1018-1030(2023).
23. Jouyban-Gharamaleki, A., Valaee, L., Barzegar-Jalali, M., Clark, B. J. and Acree, Jr W. E., "Comparison of Various Cosolvency Models for Calculating Solute Solubility in Water–cosolvent Mixtures," *Int. J. Pharm.*, **177**, 93-101(1999).
24. Jouyban, A., "Review of the Cosolvency Models for Predicting Solubility of Drugs in Water-cosolvent Mixtures," *J. Pharm. Pharm. Sci.*, **11**, 32(2007).
25. Zhou, C., Shi, X., Wang, H. and An, N., "Measurement and Correlation of Solubilities of Trans-ferulic Acid in Solvents," *J. Chem. Ind. Eng.*, **58**, 2705-2709(2007).
26. Jouyban, A., Fakhree, M. A. A. and Acree, Jr. W. E., "Comment on 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)," *J. Chem. Eng. Data*, **57**, 1344-1346(2012).
27. Vahdati, S., Shayanfar, A., Hanaee, J., Martínez, F., Acree, Jr. W. E. and Jouyban, A., "Solubility of Carvedilol in Ethanol + propylene Glycol Mixtures at Various Temperatures," *Ind. Eng. Chem. Res.*, **52**, 16630-16636(2013).
28. Apelblat, A. and Manzurola, E., "Solubilities of L-aspartic, DL-aspartic, DL-glutamic, p-hydroxybenzoic, o-anisic, p-anisic, and Itaconic Acids in Water from T=278 K to T=345 K," *J. Chem. Thermodyn.*, **29**, 1527-1533(1997).
29. Sunsandee, N., Hronec, M., Štolcová, M., Leepipatpiboon, N. and Pancharoen, U., "Thermodynamics of the Solubility of 4-acetylbenzoic Acid in Different Solvents from 303.15 to 473.15 K," *J. Mol. Liq.*, **180**, 252-259(2013).
30. Wang, K., Hu, Y., Yang, W., Guo, S. and Shi, Y., "Measurement and Correlation of the Solubility of 2,3,4,5-tetrabromothiophene in Different Solvents," *J. Chem. Thermodyn.*, **55**, 50-55(2012).
31. Du, C. B., Xu, R. J., Han, S., Xu, J., Meng, L., Wang, J. and

Zhao, H. K., "Solubility Determination and Correlation for 1,8-dinitronaphthalene in (acetone + methanol), (toluene + methanol) and (acetonitrile + methanol) Mixed Solvents," *J. Chem. Thermodyn.*, **94**, 24-30(2016).
32. Ma, H., Qu, Y, Zhou, Z., Wang, S. and Li, L., "Solubility of Thiotriazinone in Binary Solvent Mixtures of Water + methanol and Water + ethanol from (283 to 330) K," *J. Chem. Eng. Data*, **57**, 2121-2127(2012).
33. Ruidiaz, M. A., Delgado, D. R., Martínez, F. and Marcus, Y., "Solubility and Preferential Solvation of Indomethacin in 1,4-dioxane + water Solvent Mixtures," *Fluid Phase Equilib.*, **299**, 259-265(2010).
34. Kalam, M. A., Khan, A. A. and Alshamsan, A., "Solubility of a Poorly Soluble Immunosuppressant in Different Pure Solvents: Measurement, Correlation, Thermodynamics and Molecular Interactions," *J. Mol. Liq.*, **249**, 53-60(2018).
35. Noubigh, A. and Akrmi, A., " Temperature Dependent Solubility of Vanillic Acid in Aqueous Methanol Mixtures: Measurements and Thermodynamic Modeling," *J. Mol. Liq*., **220**, 277-282(2016).
36. Delgado, D. R., Holguin, A. R., Almanza, O. A., Martinez, F. and Marcus, Y., "Solubility and Preferential Solvation of Meloxicam in Ethanol + water Solvent Mixtures," *Fluid Phase Equilib*., **305**, 80-85(2011).

Authors

Mustafa Jaipallah Abualreish: Associate Professor, Faculty of Science, Department of Chemistry, Northern Border University, Arar 91431, Kingdom of Saudi Arabia; Mustafa.Abualreish@nbu.edu.sa

Adel Noubigh: Associate Professor, Faculty of Science, Department of Chemistry, Northern Border University, Arar 91431, Kingdom of Saudi Arabia; adel.noubigh@nbu.edu.sa