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Study of Thermodynamic Properties of L-Serine and L-Threonine in Aqueous Solutions of 1-(2-Carboxyethyl)-3-methylimidazolium Chloride [HOOCEMIM][Cl]

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Abstract

The stability of amino acids in solutions containing electrolytes and the effect of ambient pH on their biological activity is an important research area. In this research work, the volumetric and transport properties of ionic liquid (IL) aqueous solution with special performance of 1-(2-carboxyethyl)-3-methylimidazolium chloride ([HOOCEMIM][Cl]) were studied. The selected IL acts as an electrolyte and allows the study of systems containing amino acids at acidic pH. In this work, the density, speed of sound and viscosity of binary and ternary solutions of IL in aqueous solution of amino acids in the structure of proteins, namely L-serine and L-threonine within IL molality range of (0.05, 0.07 and 0.09 $mol\cdot kg^{-1}$) were measured at 298.15 K. From these quantities, apparent molar volume, limiting apparent molar volume, apparent molar isentropic compression, limiting apparent molar isentropic compression, transfer standard volumes for amino acids from water to the aqueous IL solutions and viscosity *B*-coefficients were calculated using the equations of Redlich–Meyer and Jones–Dole. Close examination of literature indicates that there is no data for water activity for solution of L-serine + H_2O at 308.15 and 318.15 K. In this way water activity, osmotic coefficient and vapor pressure were measured and using the interaction parameters of Wilson, NRTL, NRF-NRTL and UNIQUAC models, activity coefficient values of L-serine calculated.

Keywords Ionic liquid · 1-(2-Carboxyethyl)-3-methylimidazolium chloride · L-Serine · Aqueous solutions · Volumetric and transport properties · Water activity · Activity coefficient

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1 Introduction

The advancement of biotechnology has largely led to the production of many biomolecules, which has led to the development of effective methods for the separation, concentration and purification of biomolecules. Biomolecules are complex molecules whose behavior in the mixture is affected by many factors such as pH, chemical structure, surface charge distribution, solvent properties, electrolyte type and concentration and even the presence of other biomolecules [1, 2]. Among these factors, the interaction of biomolecules with electrolytes has a potential application in the processes of separation and concentration of biomolecules [3, 4]. Many separation processes of biomolecules, such as adding electrolyte, which is one of the simplest methods of protein precipitation, are widely used in biotechnology and pharmaceutical industries [5, 6]. Also, the extraction of reverse micelles of proteins and amino acids with an electrolyte or solvents that have recently received attention is directly related to the interaction of biomolecules with electrolytes [7, 8]. Investigating the nature of these interactions is very important in designing suitable separation processes. Therefore, the interaction of biomolecules with electrolytes plays a central role in the physicochemical properties of these systems. Due to the complex three-dimensional structure of protein, which makes it difficult to investigate the effect of solvent on these macromolecules, interpreting the behavior of proteins by model compounds such as amino acids and peptides can be a valuable clue for understanding the behavior of biomolecules [9, 10].

Today, ionic liquids (ILs) as organic electrolytes and green solvents have a significant effect on many biochemical and chemical processes [11]. Therefore, due to the increasing importance and use of ILs, these compounds are a suitable option for studying the thermodynamic properties of amino acids due to their unique properties. Also, investigating and understanding the nature of the interaction of these compounds with amino acids is very important in designing suitable processes for the separation of amino acids, peptides and biomolecules. Of course, the design of these processes requires extensive and systematic studies of thermodynamic properties of these systems.

In the present work, the studied ionic liquid is functionalized by –COOH. Close examination of literature indicates that, water activity and solubility of 1-(2-carboxyethyl) -3-methylimidazolium chloride ([HOOCEMIM][Cl]) in presence of L-serine and L-threonine have been investigated in our previous work [12, 13] but no volumetric and transport data are available for these systems. However, volumetric and transport properties of L-serine and L-threonine in binary and ternary aqueous solutions of other ILs were determined in several works [14–21]. We found that, the studied ionic liquid promoted remarkable changes in the solubility of the studied amino acid by reducing the pH of the solution [12].

In this work, the density, speed of sound and viscosity of binary and ternary solutions of IL in aqueous solution of amino acids in the structure of proteins, namely L-serine and L-threonine within IL molality range of (0.05, 0.07 and 0.09 mol·kg^{-1}) were measured at 298.15. From these quantities, apparent molar volume, limiting apparent molar volume, apparent molar isentropic compression, limiting apparent molar isentropic compression, transfer standard volumes for amino acids from water to the aqueous IL solutions and viscosity *B*-coefficients were calculated using the equations of Redlich–Meyer [22] and Jones–Dole [23]. Close examination of literature indicates that there is no data for water activity for solution of L-serine + H_2O at 308.15 and 318.15 K. In this way water activity, osmotic coefficient and vapor pressure were measured and using the interaction parameters of Wilson [24], NRTL [25], NRF-NRTL [26] and UNIQUAC [27] models activity coefficient values of L-serine in aqueous solution were calculated.

2 Experimental Section

2.1 Materials

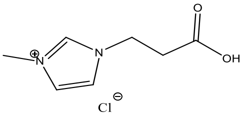
The TSIL has been synthesized. The synthesis method is described in detail in our previous work [12] and its specifications are given in Table 1. TSIL is a brownish yellow solid with melting point of 472.15 K. Other materials used in this research work, L-serine and L-threonine amino acids with molecular mass of 105.09 and 119.12, respectively, and in mass fraction purity > 0.99, are manufactured by Merck. These amino acids were used without further purification. Double distilled and deionized water was used.

2.2 Apparatus and Procedure

Densities and sound velocities were continuously, simultaneously, automatically measured using a commercial density and sound velocity measurement apparatus (Anton Paar DSA 5000 densimeter and sound velocity analyzer). Both of speed of sound and density are extremely sensitive to temperature, so it was kept constant within ± 0.001 K using the Peltier Method. This device determines the density of solutions by electronically measuring the frequency of an oscillating system at the approximate frequency of 3 MHz. The uncertainties of density and speed of sound data measurement by this device is equal to 0.15 $\mathrm{kg{\cdot}m^{-3}}$ and 0.5 $\mathrm{m{\cdot}s^{-1}}$, respectively. The apparatus was calibrated with double distilled deionized and degassed water, and dry air at atmospheric pressure. All solutions were degassed before measurement. The solutions were prepared by weighing with an analytical balance (Shimadzu, 321–34,553, Shimadzu) with an uncertainty of $\pm 10^{-7}$ kg. Before each series of measurements, the device was calibrated using distilled water and dry air.

In this work, the viscosity of the solutions is measured using an Ubbelohde viscometer suspended in a water bath (Julabo, MD-18 V, Germany). This device is able to keep the temperature constant to ± 0.01 K. To make the temperature of the bath uniform and stabilize the temperature better, we connect it to another thermostat (Huber, D-77656, Germany). The dynamic viscosity, η, was calculated by the following relation of $\eta = dK(t-\theta)$, where t is the flow time; K is the viscometer constant; θ is the

Table 1 Characteristics of ionic liquid 1-(2-carboxyethyl)-3-methylimidazolium chloride [HOOCEMIM][Cl]

Structure:	
Name:	1-(2-Carboxyethyl)-3-methylimidazolium chloride
Molecular wight	190.60
Purity:	98%
^{13}C NMR (100 MHz, DMSO-d_6):	δ (ppm): 171.82, 137.56, 123.76, 122.87, 45.25, 35.96, 34.55
^{1}H NMR (400 MHz, DMSO-d_6):	δ (ppm): 8.93 (s, 1H), 7.62 (s, 1H), 7.43 (s, 1H), 5.81 (bs, COOH), 4.37 (t, J = 5.6, 2H), 3.84 (s, 3H), 2.85 (t, J = 5.6, 2H)
FT-IR (cm^{-1}):	3153, 2932, 1734, 1575, 1424, 1168, 633

Hagenbach correction factor; and *d* is the density. The flow times were measured using a stopwatch. The precision of the used stopwatch was 0.01 s. The viscometer constant, *K*, is determined by calibrating at working temperatures with distilled water using viscosity values from the literature. The uncertainty for the dynamic viscosity determination was estimated to be ± 0.006 mPa·s. Each measurement was repeated five times.

The isopiestic method is a simple but highly accurate method for measuring the vapor pressure of a solution with a non-volatile solute, through equilibrium with a solution with a known vapor pressure (as a reference). The isopiestic device used in this research work contained two types of aqueous solution (NaCl as a reference and amino acid sample) which are in contact with each other through the vapor phase and are in thermal contact through an intermediate. The vapor space is emptied of air so that it contains only solvent vapor. Normally, the time needed to establish an equilibrium in the system is at least one week and more time is needed for dilute solutions. Equilibrium occurs when the differences between the mass fractions of each of the two repetitions is less than 0.01 %. The bath of water containing a Julabo temperature controller (Julabo, MB, Germany) was used to keep the isopiestic system at $T = 308.15$ and 318.15 K with an accuracy of 0.1 K. It is estimated that the standard uncertainty of solvent activity to be 0.008.

3 Results and Discussion

The measured density, speed of sound and viscosity data for binary systems of [HOOCEMIM][Cl] + H2O and ternary systems of [HOOCEMIM][Cl] + L-serine + H_2O and [HOOCEMIM][Cl] + L-threonine + H_2O at a temperature of 298.15 K are reported in Tables 2, 3, 4 and 5. Using these data and the following relations, the apparent molar volume (V_φ), isentropic compressibility (κ_S) and apparent molar isentropic compression ($K_{S,\Phi}$) of solutions considered are obtained, and the relevant results are given in these tables:

Table 2 Molality (*m*), density (*d*), speed of sound (*u*), apparent molar volume (V_φ), isentropic compressibility (κ_s) and apparent molar isentropic compression ($K_{S,\Phi}$) for [HOOCEMIM][Cl] + H_2O solution at 298.15 K and total experimental pressure (p_{total}) of 85.7 kPa

m_{IL}/ (mol·kg^{-1})	10^{-3} *d*/ (kg·m^{-3})	*u*/ (m·s^{-1})	10^6 V_φ/m^3·mol^{-1}	10^{10} ·κ_s/ (Pa^{-1})	10^{14} ·$K_{S,\Phi}$/ (m^3·mol^{-1}·Pa^{-1})
0.0000	0.99704	1496.6		4.48	
0.0355	0.99869	1500.2	144.1	4.45	– 1.65
0.0536	0.99953	1502.1	144.22	4.43	– 1.63
0.0827	1.00083	1504.9	144.51	4.41	– 1.58
0.0957	1.00140	1506.2	144.72	4.40	– 1.57
0.1105	1.00206	1507.7	144.76	4.39	– 1.56
0.1278	1.00282	1509.4	144.88	4.38	– 1.55
0.1422	1.00345	1510.8	144.90	4.37	– 1.54
0.1588	1.00418	1512.5	144.91	4.35	– 1.53

Standard uncertainties (σ) for each variable are σ(*m*) = 0.0001 mol·kg^{-1}; σ(*d*) = 0.15 kg·m^{-3}; σ(*u*) = 0.5 m·s^{-1}; σ(p_{total}) = 6 kPa; σ(*T*) = 0.01 K

Table 3 Molarity (c_{IL}), density (d) and viscosity (η) for [HOOCEMIM][Cl] + H2O solution at 298.15 K and total experimental pressure (p_{total}) of 85.7 kPa

c_{IL}/ (mol·dm^{-3})	10^{-3}·d/ (kg·m^{-3})	η/ (mPa·s)
([HOOCEMIM][Cl] + H_2O)		
0.0352	0.99869	0.895
0.0530	0.99953	0.901
0.0815	1.00083	0.910
0.0941	1.00140	0.914
0.1084	1.00206	0.919
0.1250	1.00206	0.926
0.1389	1.00345	0.932
0.1548	1.00418	0.939

Standard uncertainties (σ) for each variable are $\sigma(c_{\mathrm{IL}}) = 0.0001$ mol·kg^{-1}; $\sigma(d) = 0.15$ kg·m^{-3}; $\sigma(p_{\mathrm{total}}) = 6$ kPa; $\sigma(\eta) = 0.006$; $\sigma(T) = 0.01$ K

$$V_{\varphi} = \frac{M}{d} - \frac{\left(d - d_0\right)}{mdd_0}, \tag{1}$$

$$\kappa_S = \frac{1}{du^2}, \tag{2}$$

$$K_{S,\Phi} = \frac{\left(\kappa_S d_0 - \kappa_{S0} d\right)}{mdd_0} + \frac{\kappa_S M}{d}, \tag{3}$$

where m, M, d, d_0 and κ_{S0} are molality of solution (in mol·kg^{-1}), molar mass of the IL (in kg·mol^{-1}), densities (in kg·m^{-3}) of solution and pure solvent and κ_{S0} the isentropic compressibility of pure solvent, respectively. The apparent molar volume at infinite dilution (V_{φ}^{0}) is obtained by fitting the values of the apparent molar volume in the dilute region with the Redlich–Meyer equation [22], that is, Eq. 4. At infinite dilution, each ion is almost surrounded by solvent molecules and is separated from other ions. Therefore, the values are not affected by ion–ion interactions and this quantity will be a measure of ion–solvent interactions [28].

$$V_{\varphi} = V_{\varphi}^{0} + S_{v} m^{1/2} + B_{v} m. \tag{4}$$

In this equation, S_{v} and B_{v} are adjustable parameters. The values of V_{φ}^{0}, S_{v} and B_{v} at each temperature are reported in Table 6. Apparent molar isentropic compressions in dilute region, $m_1 < 0.1$ mol·kg^{-1} ($K_{S,\Phi}^{0}$) for the studied binary and ternary systems can be obtained by fitting the apparent molar isentropic compression values for IL aqueous solutions at the studied temperature using Eq. 5. Calculated values for $K_{S,\Phi}^{0}$ are reported in Table 7.

$$K_{S,\Phi} = K_{S,\Phi}^{0} + S_{k} m^{1/2} + B_{k} m. \tag{5}$$

where S_k and B_k are the fitting coefficients. The experimental and calculated values of the apparent molar volume from the Redlich–Meyer equation versus the molality of the IL for the binary aqueous IL system are shown in Fig. 1 and are compared with the results of our previous work on 1-carboxymethyl-3-methylimidazolium chloride ([HOOCMMIM]

Table 4 Molality (m), density (d), speed of sound (u), apparent molar volume (V_{φ}), isentropic compressibility (κ_s) and apparent molar isentropic compression ($K_{S,\Phi}$) for [HOOCEMIM][Cl] + L-serine + H_2O and [HOOCEMIM][Cl] + L-threonine + H_2O solutions at 298.15 K and total experimental pressure (p_{total}) of 85.7 kPa

$m_{\text{amino acid}}$/(mol·kg^{-1})	10^{-3}·d/ (kg·m^{-3})	u/ (m·s^{-1})	10^6 V_{φ}/m^3·mol^{-1}	10^{10}·κ_s/ (Pa^{-1})	10^{14}·$K_{S,\Phi}$/ (m^3·mol^{-1}·Pa^{-1})
L-serine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]					
0.0000	0.99938	1502.0		4.44	
0.0484	1.00151	1505.0	60.96	4.41	−2.98
0.0678	1.00237	1506.3	60.79	4.40	−2.98
0.1029	1.00391	1508.5	60.74	4.38	−2.97
0.1386	1.00548	1510.7	60.67	4.36	−2.95
0.1716	1.00693	1512.7	60.64	4.34	−2.94
0.2122	1.00870	1515.2	60.61	4.32	−2.93
0.2616	1.01084	1518.3	60.57	4.29	−2.91
0.3009	1.01255	1520.7	60.53	4.27	−2.89
L-serine in aqueous solutions of 0.09 mol·kg^{-1} [HOOCEMIM][Cl]					
0.0000	1.00110	1505.7		4.41	
0.0565	1.00360	1509.4	60.69	4.37	−3.01
0.0700	1.00420	1510.2	60.60	4.37	−3.00
0.0858	1.00490	1511.2	60.56	4.36	−2.99
0.0987	1.00547	1512.0	60.53	4.35	−2.98
0.1421	1.00738	1514.8	60.48	4.33	−2.97
0.1762	1.00888	1516.9	60.44	4.31	−2.96
0.2123	1.01046	1519.2	60.39	4.29	−2.94
0.3658	1.01712	1528.7	60.30	4.21	−2.89
L-threonine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]					
0.0000	0.999225	1501.7		4.44	
0.0409	1.000882	1505.0	78.51	4.41	−3.17
0.0609	1.001718	1506.6	78.02	4.40	−3.15
0.0749	1.002303	1507.7	77.81	4.39	−3.12
0.0908	1.002992	1508.9	77.37	4.38	−3.11
0.1007	1.003411	1509.7	77.26	4.37	−3.09
0.1306	1.004706	1511.9	76.76	4.35	−3.06
0.1515	1.005601	1513.4	76.57	4.34	−3.03
0.1691	1.006354	1514.7	76.44	4.33	−3.01
0.1992	1.007616	1516.9	76.38	4.31	−2.98
L-threonine in aqueous solutions of 0.07 mol·kg^{-1} [HOOCEMIM][Cl]					
0.0000	1.00018	1503.7		4.42	
0.0392	1.00182	1507.0	77.12	4.40	−3.34
0.0610	1.00275	1508.8	76.87	4.38	−3.32
0.0752	1.00336	1509.9	76.58	4.37	−3.3
0.0904	1.00402	1511.1	76.40	4.36	−3.29
0.1021	1.00452	1512.1	76.30	4.35	−3.27
0.1291	1.00567	1514.2	76.18	4.34	−3.24
0.1516	1.00662	1515.9	76.13	4.32	−3.21
0.1684	1.00734	1517.2	76.07	4.31	−3.19
0.2041	1.00885	1519.9	76.00	4.29	−3.15

Table 4 (continued)

Standard uncertainties (σ) for each variable are $\sigma(m) = 0.0001$ mol·kg^{-1}; $\sigma(d) = 0.15$ kg·m^{-3}; $\sigma(u) = 0.5$ m·s^{-1}; $\sigma(p_{\text{total}}) = 6$ kPa; $\sigma(T) = 0.01$ K

Table 5 Molarity (c_{IL}), density (d) and viscosity (η) for [HOOCEMIM][Cl] + L-serine + H_2O and [HOOCEMIM][Cl] + L-threonine + H_2O solutions at 298.15 K and total experimental pressure (p_{total}) of 85.7 kPa

$c_{\text{amino acid}}$ / (mol·dm^{-3})	10^{-3}·d/ (kg·m^{-3})	η/ (mPa·s)
L-serine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]		
0.0000	0.99938	0.908
0.0482	1.00150	0.917
0.0675	1.00238	0.922
0.1022	1.00390	0.931
0.1374	1.00549	0.939
0.1697	1.00688	0.946
0.2953	1.01249	0.972
L-serine in aqueous solutions of 0.09 mol·kg^{-1} [HOOCEMIM][Cl]		
0.0000	1.00110	0.922
0.0564	1.00360	0.928
0.0698	1.00420	0.933
0.0854	1.00490	0.937
0.0982	1.00547	0.940
0.1745	1.00888	0.960
0.2098	1.01046	0.970
0.3583	1.01712	1.005
L-threonine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]		
0.0000	0.99922	0.908
0.0606	1.00172	0.920
0.0744	1.00230	0.925
0.0901	1.00299	0.931
0.0998	1.00341	0.936
0.1292	1.00471	0.948
0.1496	1.00560	0.957
0.1668	1.00635	0.963
0.1961	1.00762	0.973
L-threonine in aqueous solutions of 0.07 mol·kg^{-1} [HOOCEMIM][Cl]		
0.0000	1.00018	0.915
0.0391	1.00182	0.928
0.0748	1.00336	0.939
0.0898	1.00402	0.944
0.1013	1.00452	0.947
0.1499	1.00662	0.962
0.1663	1.00734	0.967
0.2010	1.00885	0.977

Standard uncertainties (σ) for each variable are $\sigma(c_{\text{IL}}) = 0.0001$ mol·kg^{-1}; $\sigma(d) = 0.15$ kg·m^{-3}; $\sigma(p_{\text{total}}) = 6$ kPa; $\sigma(\eta) = 0.006$; $\sigma(T) = 0.01$ K

Table 6 Limiting apparent molar volume (V_φ^0) and adjustable parameters S_V and B_V of Eq. 4 along with standard deviations ($\sigma(V_\varphi)$) for [HOOCEMIM][Cl] + H_2O, [HOOCEMIM][Cl] + L-serine + H_2O and [HOOCEMIM][Cl] + L-threonine + H_2O solutions at 298.15 K

$10^6 \cdot V_\varphi^0$ ($m^3 \cdot mol^{-1}$)	$10^6 \cdot S_V$ ($m^3 \cdot kg \cdot mol^{-2}$)	$10^6 \cdot B_V$ ($m^3 \cdot kg^{1/2}$ $mol^{-3/2}$)	$10^6 \cdot \sigma(V_\varphi)$ ($m^3 \cdot mol^{-1}$)
[HOOCEMIM][Cl] + H_2O			
143.89	– 1.14	11.69	0.04
L-serine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]			
61.52	– 3.35	2.90	0.03
L-serine in aqueous solutions of 0.09 mol·kg^{-1} [HOOCEMIM][Cl]			
61.15	– 2.47	1.78	0.01
L-threonine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCMMIM][Cl]			
82.14	– 21.35	18.51	0.07
L-threonine in aqueous solutions of 0.07 mol·kg^{-1} [HOOCMMIM][Cl]			
79.52	– 15.18	16.39	0.04

Table 7 Limiting apparent molar isentropic compression ($K_{S,\Phi}^0$) and adjustable parameters S_κ and B_κ of Eq. 5 along with standard deviations ($\sigma(K_{S,\Phi})$) for [HOOCEMIM][Cl] + H_2O, [HOOCEMIM][Cl] + L-serine + H_2O and [HOOCEMIM][Cl] + L-threonine + H_2O solutions at 298.15 K

$10^{14} \cdot K_{S,\Phi}^0$ ($m^3 \cdot mol^{-1} \cdot Pa^{-1}$)	$10^{14} \cdot S_\kappa$ ($kg^{1/2} \cdot m^3 mol^{-3/2} \cdot Pa^{-1}$)	$10^{14} \cdot B_\kappa$ ($kg \cdot m^3 \cdot mol^{-2} \cdot Pa^{-1}$)	10^{14} $\sigma(K_{S,\Phi})$ ($m^3 \cdot mol^{-1} \cdot Pa^{-1}$)
[HOOCEMIM][Cl] + H_2O			
– 1.75	0.41	0.50	0.006
L-serine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]			
– 2.98	– 0.13	0.52	0.004
L-serine in aqueous solutions of 0.09 mol·kg^{-1} [HOOCEMIM][Cl]			
– 3.05	0.15	0.18	0.003
L-threonine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]			
– 3.26	0.28	0.80	0.004
L-threonine in aqueous solutions of 0.07 mol·kg^{-1} [HOOCEMIM][Cl]			
– 3.36	– 0.21	1.48	0.005

[Cl]) [14]. Also, to better show the effect of ILs on the studied amino acids, the experimental and calculated values of apparent molar volume from Eq. 4 were drawn according to the molality of amino acids for ternary systems [HOOCEMIM][Cl] + L-serine + H_2O and [HOOCEMIM][Cl] + L-threonine + H_2O in different molality of the studied IL and temperature in Fig. 2. As can be seen from Table 2 and Fig. 1, the apparent molar volume increases with increasing concentration for both ionic liquids. The increase in the apparent molar volume with the increase in molality is the result of the decrease in the water molecules around the IL. The V_φ of [HOOCEMIM][Cl] is larger than that of [HOOCMMIM][Cl], which is due to the bulkiness of the carboxyethyl group compared to carboxymethyl. Figure 2 and Table 4 show that the apparent molar volume decreases with the increase of amino acids in the IL solution. This decrease in V_φ can be attributed to the phenomenon that the addition of amino acid to the system (IL + water) causes strong interaction between

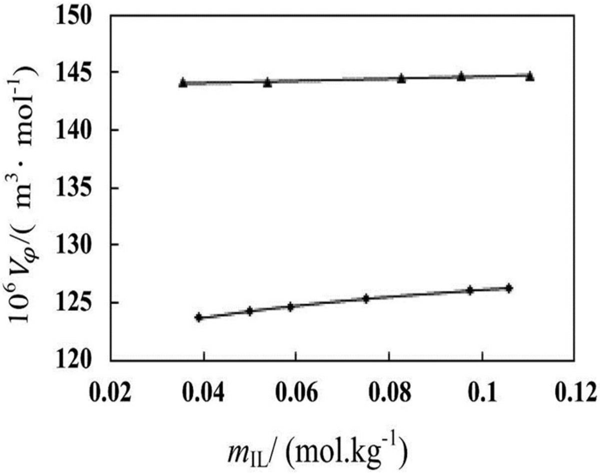


Fig. 1 Experimental and calculated values of apparent molar volume (V_φ) from Redlich–Meyer equation versus the IL molality for aqueous binary solutions of ILs at 298.15 K: filled triangle, [HOOCEMIM][Cl] + H_2O; filled diamond, [HOOCMMIM][Cl] + H_2O from our previous work [14]; and the lines calculated from the Redlich–Meyer (Eq. 4)

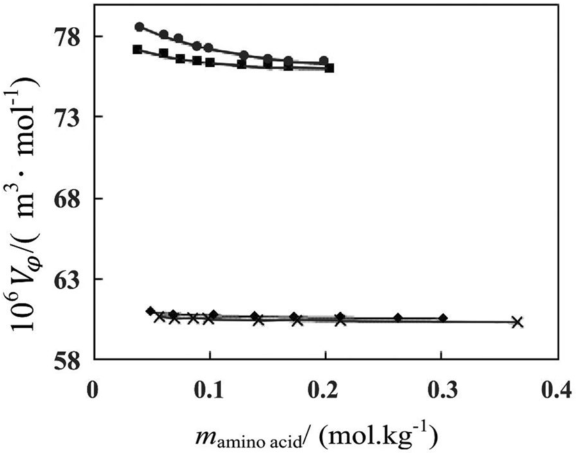


Fig. 2 Experimental and calculated values of apparent molar volume (V_φ) from Redlich-Meyer equation versus the amino acid molality for aqueous ternary solutions at 298.15 K and different molality of IL (m_{IL}): filled diamond, $m_{\text{IL}}=0.05$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-serine + H_2O; ×, $m_{\text{IL}}=0.09$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-serine + H_2O; filled circle, $m_{\text{IL}}=0.05$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-threonine + H_2O; filled Square, $m_{\text{IL}}=0.07$ mol·kg.$^{-1}$ for [HOOCEMIM][Cl] + L-threonine + H_2O; and the lines calculated from the Redlich–Meyer (Eq. 4)

the ionic species of the IL and the dipolar ion part of amino acid molecules as well as water molecules. More information about these interactions can be obtained from the standard volumes of transfer ($\Delta_t V^0$) which is calculated using the apparent molar volume at infinite dilution. The $\Delta_t V^0$ of amino acids from water to aqueous solution of IL is calculated from the following relationship:

$$\Delta_t V^0(\text{water} \rightarrow \text{aqueous IL}) = V_\varphi^0(\text{in aqueous IL}) - V_\varphi^0(\text{in water}). \quad (6)$$

The values of V_φ^0 for amino acids L-serine and L-threonine in aqueous solution and temperature of 298.15 K are 60.6 and 76.81 cm^3.mol^{-1}, respectively, which are reported in the reference [29]; the obtained results for the $\Delta_t V^0$ are given in Table 8. This Table clearly shows that $\Delta_t V^0$ is positive. Positive values can be justified using the cosphere overlap model [28, 30]. Based on this model, interactions between IL and amino acids can be divided into four categories [30]:

1. Hydrophilic–ion interactions.
2. Hydrophilic–hydrophilic interactions.
3. Interaction between hydrophilic and hydrophobic.
4. Hydrophobic–hydrophobic interaction.

According to this model, the first two types of interactions lead to positive and the third and fourth types of interactions lead to negative values [30]. In general, it can be said that it will be positive when the sum of the interactions of the first and second categories are dominant compared to the interactions of the third and fourth categories. These interactions cause water molecules to be released in the solution and consequently it will be positive [30]. The positive values for the systems [HOOCEMIM][Cl] + L-serine/ L-threonine + H_2O indicates the predominance of the first two classes of interactions to the interactions are in the third and fourth categories.

Table 2 shows that the obtained values for apparent molar isentropic compression are negative and become less negative as the concentration of IL increases. The negative values indicate that the compressibility of the hydration layer around the ions is lower than the bulk of the solvent, and this is due to the hydration of the ions at low concentrations [31]. By increasing the concentration of the IL, the ion–solvent interaction becomes weaker and the compressibility of the water molecules around the dissolved ions increases, and as a result, it becomes less negative. In Fig. 3, the experimental and calculated values of apparent molar isentropic compression from Eq. 3 are plotted versus the IL molality and compared with the results obtained from our previous work for [HOOCMMIM][Cl] [14]. This figure shows that $K_{S,\Phi}$ becomes less negative with increasing chain length. This issue can be attributed to the reduction of the ion–solvent interactions due to the reduction of the hydration of the IL and the electrostatic interaction with water, resulting in the release of some water molecules into the solution mass [32]. The plot of the change of $K_{S,\Phi}$ in different molality of IL is shown in Fig. 4 for ternary systems. In general, $K^0_{S,\Phi}$ for ionic species are large negative, positive for hydrophobic solutes, and small negative for polar species [33]. The results obtained in Table 7 show that all the values calculated for $K^0_{S,\Phi}$ are marginally negative. Negative values indicate that the water molecules surrounding the solute are more resistant to condensation than the solution [33].

Table 8 Standard volumes of transfer ($\Delta_t V^0$) of amino acid transfer from water to aqueous solutions of [HOOCEMIM][Cl] at 298.15 K

System	$10^6 \cdot \Delta_t V^0$ ($m^3 \cdot mol^{-1}$)
L-serine in aqueous solutions of 0.05 $mol \cdot kg^{-1}$ [HOOCEMIM][Cl]	0.91
L-serine in aqueous solutions of 0.09 $mol \cdot kg^{-1}$ [HOOCEMIM][Cl]	0.54
L-threonine in aqueous solutions of 0.05 $mol \cdot kg^{-1}$ [HOOCEMIM][Cl]	5.27
L- threonine in aqueous solutions of 0.07 $mol \cdot kg^{-1}$ [HOOCEMIM][Cl]	2.65

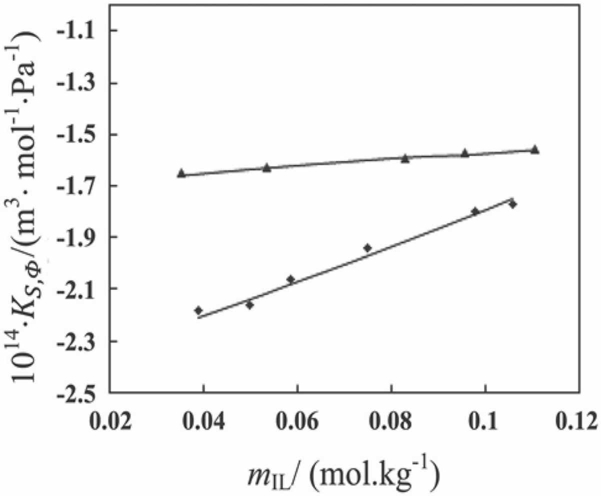


Fig. 3 Experimental and calculated values of apparent molar isentropic compression ($K_{S,\Phi}$) from Eq. 5 versus the IL molality for aqueous binary solutions of ILs at 298.15 K: filled triangle, [HOOCEMIM][Cl] + H_2O; filled diamond, [HOOCMMIM][Cl] + H_2O from our previous work [14]; and the lines calculated from the Eq. 5

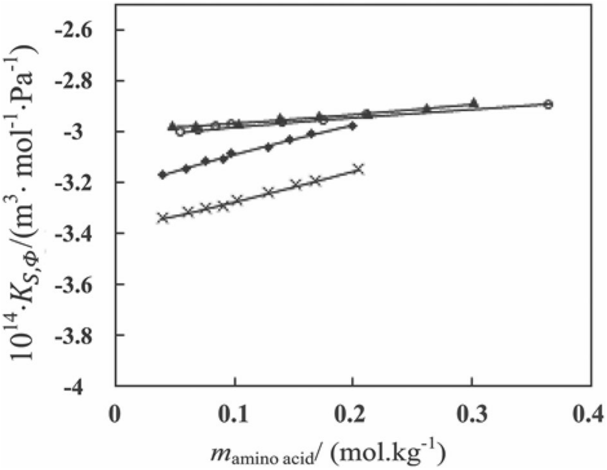


Fig. 4 Experimental and calculated values of apparent molar isentropic compression ($K_{S,\Phi}$) from Eq. 5 versus the amino acid molality for aqueous ternary solutions at 298.15 K and different molality of IL (m_{IL}): filled triangle, $m_{\mathrm{IL}} = 0.05$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-serine + H_2O; open circle, $m_{\mathrm{IL}} = 0.09$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-serine + H_2O; filled diamond, $m_{\mathrm{IL}} = 0.05$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-threonine + H_2O; ×, $m_{\mathrm{IL}} = 0.07$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-threonine + H_2O; and the lines calculated from Eq. 5

The relative viscosity data (η_r) of binary and ternary systems were fitted with the Jones–Dole model [23] of Eq. 6 in order to calculate the viscosity B-coefficients, which provides information about the solvent–solute interactions.

$$\eta_r = \frac{\eta}{\eta_0} = 1 + Bc. \tag{7}$$

Table 9 Viscosity B coefficient along with standard deviations ($\sigma(\eta)$) for [HOOCEMIM][Cl] + H_2O, [HOOCEMIM][Cl] + L-serine + H_2O and [HOOCEMIM][Cl] + L-threonine + H_2O solutions at 298.15 K

System	B ($dm^3.mol^{-1}$)	$\sigma(\eta)$ (mPa·s)
[HOOCEMIM][Cl] in water	0.2681	0.002
L-serine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]	0.2412	0.0009
L-serine in aqueous solutions of 0.09 mol·kg^{-1} [HOOCEMIM][Cl]	0.2409	0.004
L-threonine in aqueous solutions of 0.05 mol·kg^{-1} [HOOCEMIM][Cl]	0.3427	0.004
L- threonine in aqueous solutions of 0.07 mol·kg^{-1} [HOOCEMIM][Cl]	0.3421	0.001

In this model, c and η_0 are molarity and the viscosity of pure solvent where aqueous solution of IL is considered as a solvent in ternary systems. B-coefficients values along with standard deviation values are reported in Table 9. As we know, Jones–Dole B-coefficient is a measure of ion–solvent interactions, and positive Jones–Dole coefficient values indicate that ion–solvent interactions are strong. In other words, the positive B-coefficient in the studied systems means that the solvent is a structure builder, i.e. solutes causes regularization of the solvent structure [33]. Also, the standard deviations obtained for viscosity in Table 9 show the efficiency of Eq. 6 for fitting the viscosity values. Figure 5 shows the changes in the viscosity of the solutions in the studied systems according to their molarity. The drawn lines show the viscosity calculated from Eq. 7 with the parameters listed in Table 9 and are in good agreement with the experimental viscosity data.

Using the isopiestic technique and with the following equation, the partial pressure of water (p) for aqueous systems of L-serine has been calculated at 308.15 and 318.15 K [34, 35]:

$$\ln(p) = \ln(a_m p_m) - \frac{(B_m - V_m)(p - p_m)}{RT}. \tag{8}$$

In this equation information of water as the second virial coefficient (B_m) is calculated from the Rard and Platford equation [36]; the state equation of Saul and Wagner [37] is utilized to estimate the vapor pressure (p_m) of water; density of water [38] is utilized to estimate the molar volume (V_m) of it. R and T are, respectively, universal constant of gases and absolute temperature. a_m is the water activity in the solutions studied which is calculated applying the following equation [34, 35]:

$$a_m = \exp(-v_{NaCl} m_{NaCl} \varphi_{NaCl} M_m). \tag{9}$$

In this equation, φ_{NaCl} is the osmotic coefficients of aqueous solution of NaCl which can be estimated using the following equation proposed by Colin et al. [39]:

$$\varphi_{NaCl} = 1 - A\sqrt{m_{NaCl}}\left(1 + 1.2\sqrt{m_{NaCl}}\right)^{-1} + Qm_{NaCl}\exp\left(-2\sqrt{m_{NaCl}}\right) + Bm_{NaCl} + Cm_{NaCl}^2 + Dm_{NaCl}^3 + Em_{NaCl}^4. \tag{10}$$

In Eq. 9 v_{NaCl}, m_{NaCl} and M_m are, respectively, total stoichiometric numbers of anions and cations in NaCl solutions, the molality of aqueous solution of NaCl and molecular mass of water. In Eq. 10, parameters adjusted by Colin et al. (A, Q, B, C, D and E) have, respectively, values of 0.391942, 0.280069, 0.079776, 1.565033 × 10^{-3}, − 2.048323 × 10^{-4} and 8.748618 × 10^{-6} at 298.15 K [39]. The experimental results of osmotic coefficient, activity and partial pressure of water for binary system L-serine + water at temperatures of 308.15 and 318.15 K were calculated and reported in Table 10. As can be seen in this table, with increase in the molality, the activity and

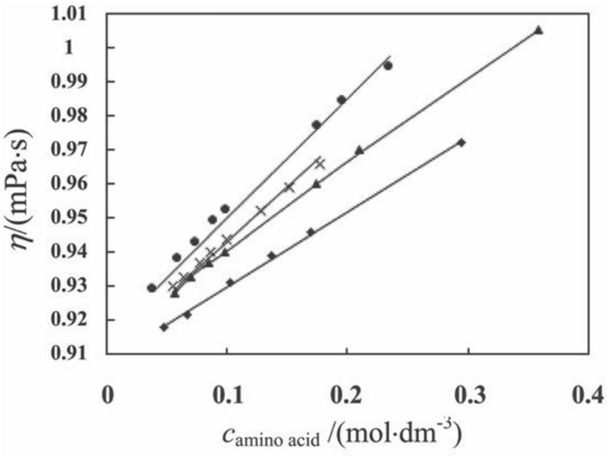


Fig. 5 Experimental and calculated values of viscosity (η) from Eq. 7 versus the amino acid molarity for aqueous ternary solutions at 298.15 K and different molality of IL (m_{IL}): filled diamond, $m_{\text{IL}} = 0.05$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-serine + H_2O; Δ, $m_{\text{IL}} = 0.09$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-serine + H_2O; ×, $m_{\text{IL}} = 0.05$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-threonine + H_2O; filled circle, $m_{\text{IL}} = 0.07$ mol·kg^{-1} for [HOOCEMIM][Cl] + L-threonine + H_2O; and the lines calculated from Eq. 6

partial pressure of water decreases. Figures 6 and 7 show the effect of temperature on the activity and vapor pressure of the solvent for the L-serine system. The water activity data for 298.15 K is taken from our previous work [12]. According to these figures and Table 10, it is clear that the activity and partial pressure of water increases with the increase in temperature. The partial pressure is directly related to the activity of the solvent, the higher the activity of the solvent in the solution, the higher the vapor pressure of the solvent. As can be seen from these figures, changes in vapor pressure due to temperature are more intense than activity.

Water activity data were fitted by local composition models (Wilson [24], NRTL [25], NRF-NRTL [26] and UNIQUAC [27]) using the following relation

$$\ln a_m = \ln\gamma_m^{cal} + \ln x_m, \tag{11}$$

where, x_m and γ_m^{cal} are respectively the water mole fraction and water activity coefficient calculated by Flory–Huggins relation (FL) [41] and aforementioned local composition-based models (LC) as $\ln\gamma_m^{\text{cal}} = \ln\gamma_m^{\text{FL}} + \ln\gamma_m^{\text{LC}}$. Flory–Huggins relation is as follow [41]:

$$\ln\gamma_m^{\text{FL}} = \ln\left(\frac{X_m}{x_m}\right) + 1 - \sum\nolimits_J \frac{X_J}{r_J} \tag{12}$$

where r_J is the number of polymer segments, subscript J denote the component J. X_J is the effective local mole fractions of species J and $X_m = x_m$. The necessary equations of these models are given in the appendix. The results of fitting are given in Table 11 and the efficiency of Wilson model is shown in Figs. 6 and 7. As can be seen from these figures and Table 11, the performance of all models is good in fitting the water activity data. The activity coefficients for the studied system were calculated by the considered local combination models and the results of the NRTL model as an example are shown in Fig. 8. As seen in this figure, the activity coefficient of amino acid increases with increasing temperature.

Table 10 Molality (m), osmotic coefficient (ϕ), water activity (a_{m}) and partial pressure of water (p) for (L-serine + H_2O) at temperatures of 308.15 and 318.15 K and total experimental pressure (p_{total}) of 85.7 kPa

$m_{\text{L-serine}}$/(mol·kg^{-1})	m_{NaCl}/(mol·kg^{-1})	ϕ	a_{m}	p/kPa
T = 308.15 K				
0.8347	0.4207	0.928	0.9861	5.497
0.9250	0.4671	0.930	0.9846	5.489
1.1212	0.5582	0.919	0.9816	5.472
1.2083	0.5972	0.913	0.9803	5.465
1.2523	0.6165	0.910	0.9797	5.462
1.5691	0.7579	0.897	0.9750	5.435
1.5960	0.7713	0.898	0.9745	5.433
1.9015	0.9067	0.891	0.9699	5.407
2.0137	0.9566	0.889	0.9683	5.398
2.1420	1.0046	0.880	0.9666	5.388
2.4218	1.0995	0.855	0.9634	5.371
2.5457	1.1671	0.866	0.9610	5.357
2.6296	1.2006	0.864	0.9599	5.351
2.9549	1.3327	0.859	0.9553	5.325
T = 318.15 K				
0.9150	0.4665	0.936	0.9847	9.362
0.9172	0.4566	0.914	0.9850	9.365
1.1606	0.5637	0.894	0.9815	9.332
1.2603	0.6156	0.900	0.9798	9.315
1.3929	0.6819	0.904	0.9776	9.294
1.7365	0.8373	0.895	0.9724	9.245
1.7645	0.8534	0.898	0.9718	9.239
1.8633	0.9064	0.906	0.9701	9.223
2.0880	0.9603	0.858	0.9682	9.205
4.5493	1.9296	0.832	0.9341	8.880

$\sigma(a_{\mathrm{m}}) = 0.008$; $\sigma(T) = 0.1$ K; $\sigma(p) = 0.005$ kPa; $\sigma(p_{\mathrm{total}}) = 6$ kPa; $(100.u_{\mathrm{r}}(m)) = 1$; σ is standard uncertainty and $u_{\mathrm{r}}(m)$ is relative standard uncertainty of molality

This result is in accordance with the studies conducted by Romero et al. [40] on the effect of temperature on aliphatic amino acids. But there is no interpretation about the effect of temperature on the activity coefficient. It seems that with the increase in temperature, the values of the solute activity coefficient deviate less than the ideal state due to the decrease in the solute–solute interaction.

4 Conclusion

The density, speed of sound and viscosity of binary and ternary solutions of (2-carboxyethyl)-3-methylimidazolium chloride ([HOOCEMIM][Cl]) in aqueous solution of amino acids in the structure of proteins, namely L-serine and L-threonine within ionic liquid (IL) molality range of (0.05, 0.07 and 0.09 mol·kg^{-1}) were measured at 298.15 K. From these quantities, apparent molar volume, limiting apparent molar volume, apparent molar isentropic compression, limiting apparent molar

Fig. 6 Solvent activity according to amino acid molality ($m_{\text{L-serine}}$) for binary system (L-serine + H_2O) at different temperatures: filled square, 298.15 K [42]; open triangle, 308.15 K; ×, 318.15 K; Lines calculated from the Wilson model

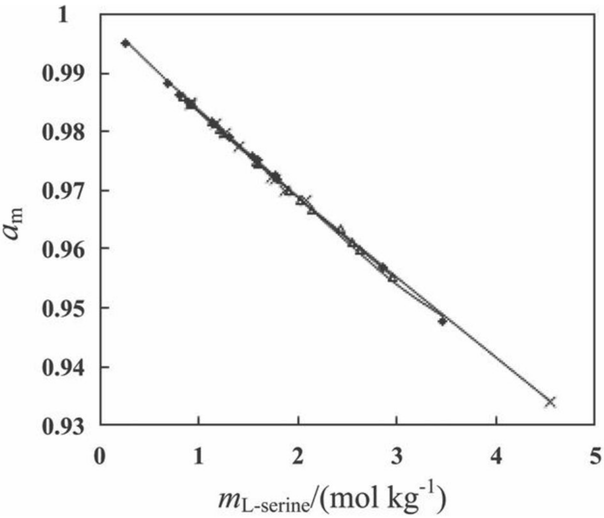
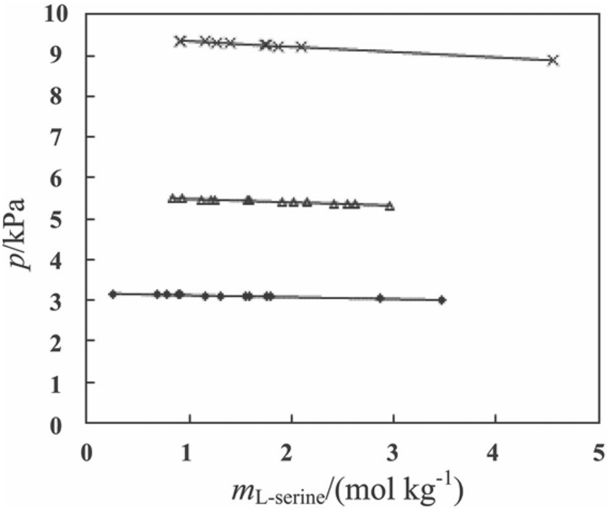


Fig. 7 partial pressure of water according to amino acid molality ($m_{\text{L-serine}}$) for binary system (L-serine + H_2O) at different temperatures: filled square, 298.15 K [42]; open triangle, 308.15 K; ×, 318.15 K; Lines calculated from the Wilson model



isentropic compression, transfer standard volumes for amino acids from water to the aqueous IL solutions and viscosity B-coefficients were calculated using the equations of Redlich–Meyer and Jones–Dole. It was found that apparent molar volume (V_φ) decreases with the increase of amino acids in the IL solution. This decrease in V_φ can be attributed to the phenomenon that the addition of amino acid to the system (IL + water) causes strong interaction between the ionic species of the IL and the dipolar ion part of amino acid molecules as well as water molecules. In the systems of [HOOCEMIM][Cl] + L-serine/L-threonine + H_2O, hydrophilic–ion interactions and hydrophilic–hydrophilic interactions are dominant compared to interactions of hydrophilic–hydrophobic and hydrophobic–hydrophobic. The compressibility of the hydration layer around the ions is lower than the bulk of the solvent, and this is due to the hydration of the ions at low concentrations. By increasing the concentration of the

Table 11 Parameters of local composition models obtained from fitting the experimental data of water activity for the system of L-serine + H_2O along with standard deviations (*sd*) at 308.15 and 318.15 K

308.15 K			318.15 K		
Wilson					
E_{mw} ($J \cdot mol^{-1}$)	E_{wm} ($J \cdot mol^{-1}$)	100.*sd*	E_{mw} ($J \cdot mol^{-1}$)	E_{wm} ($J \cdot mol^{-1}$)	100.*sd*
− 23,735.9587	36,445.5603	0.02	− 23,936.0603	36,710.9031	0.04
NRTL					
τ_{mw} ($J \cdot mol^{-1}$)	τ_{wm} ($J \cdot mol^{-1}$)		τ_{mw} ($J \cdot mol^{-1}$)	τ_{wm} ($J \cdot mol^{-1}$)	
− 2.3601	4.1214	0.02	− 2.3416	4.1126	0.04
NRF-NRTL					
4.0036	3.8436	0.02	− 1.8889	3.8645	0.04
UNIQUAC					
Δu_{mw} ($J \cdot mol^{-1}$)	Δu_{wm} ($J \cdot mol^{-1}$)		Δu_{mw} ($J \cdot mol^{-1}$)	Δu_{wm} ($J \cdot mol^{-1}$)	
− 1056.9	1607.04	0.02	− 1009.898	1558.022	0.04

Subscript m and w stand L-serine and water, respectively

$sd = \sqrt{\frac{\sum_i (a_m^{\exp} - a_m^{\mathrm{cal}})^2}{N}}$ where *N*, cal and exp are the number of data points, the calculated values and the experimental data

IL, the ion–solvent interaction becomes weaker and the compressibility of the water molecules around the dissolved ions increases. In ternary systems, the water molecules surrounding the solute are more resistant to condensation than the solution; and the solvent is a structure builder, i.e. solutes causes regularization of the solvent structure. Osmotic coefficient, water activity, vapor pressure and activity coefficient for L-serine + H_2O at 308.15 and 318.15 K were measured and correlated with Wilson, NRTL, NRF-NRTL and UNIQUAC models. It is clear that the activity and partial pressure of water increases with the increase in temperature. The partial pressure is directly related to the activity of the solvent, the higher the activity of the solvent in the solution, the higher the vapor pressure of the solvent. With the increase in temperature, the values of the solute activity coefficient deviate less than the ideal state due to the decrease in the solute–solute interaction.

Appendix 1

Wilson Equation

The coefficient equation of the solvent for Wilson model [24] is as follow:

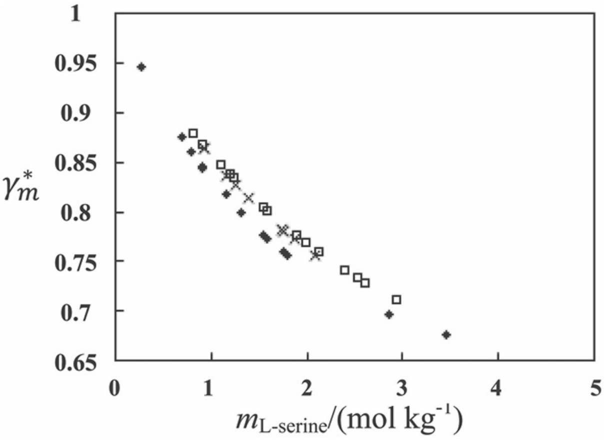


Fig. 8 activity coefficient of L-serine ($\gamma_m{}^*$) calculated from NRTL model for binary system (L-serine + H_2O) at different temperatures: filled diamond, 298.15 K [42]; open square, 308.15 K; ×, 318.15 K; Lines calculated from the Wilson model

$$\begin{aligned}\ln\gamma_m^{*,\text{Wilson}} =& -C\ln(x_m+\exp(-\frac{E_{sm}}{CRT})x_s+\exp(-\frac{E_{Em}}{CRT})\big(x_a+x_c\big)\\ &-\frac{Cx_m\Big(x_a+x_c+x_s-\exp(-\frac{E_{sm}}{CRT}\Big)x_s-\exp(-\frac{E_{Em}}{CRT})\big(x_a+x_c\big)}{x_m+\exp(-\frac{E_{sm}}{CRT})x_s+\exp(-\frac{E_{Em}}{CRT})\big(x_a+x_c\big)}\\ &+\frac{Cx_s\Big(x_s-\exp(-\frac{E_{ms}}{CRT}\Big)\big(x_a+x_c+x_s\big)+\exp(-\frac{E_{Es}}{CRT})\big(x_a+x_c\big)}{x_s+\exp(-\frac{E_{ms}}{CRT})x_m+\exp(-\frac{E_{Es}}{CRT})\big(x_a+x_c\big)}\\ &+\frac{Cx_a\Big(x_c+\exp(-\frac{E_{sE}}{CRT}\Big)x_s-\exp(-\frac{E_{mE}}{CRT})\big(x_c+x_s\big)}{\big(x_c+x_s+x_m\big)\Big(x_c+\exp(-\frac{E_{sE}}{CRT}\Big)x_s+\exp(-\frac{E_{mE}}{CRT})x_m}\\ &+\frac{Cx_c\Big(x_a-\exp(-\frac{E_{mE}}{CRT}\Big)x_a+x_s\Big(\exp(-\frac{E_{sE}}{CRT}\Big)-\exp(-\frac{E_{mE}}{CRT}))}{\big(x_a+x_s+x_m\big)\Big(x_a+\exp(-\frac{E_{sE}}{CRT}\Big)x_s+\exp(-\frac{E_{mE}}{CRT})x_m}\end{aligned} \tag{13}$$

Here, E_{mE}, E_{Em}, E_{sE}, E_{Es}, E_{sm} and E_{ms} are the adjustable parameters of Wilson model; R is the universal constant of gases; C is the coordination number of the model which was set to 10.

NRTL Equation

The activity coefficient equation of the solvent for NRTL model [25] is as follow:

$$\begin{aligned}\ln \gamma_m^{*,\mathrm{NRTL}} =& \frac{(\exp(-\alpha_{sm}\tau_{sm})x_s + \exp(-\alpha_{Em}\tau_{Em})(x_a + x_c))(\exp(-\alpha_{sm}\tau_{sm})x_s\tau_{sm} + (\exp(-\alpha_{Em}\tau_{Em})\tau_{Em}(x_a + x_c)}{(x_m + \exp(-\alpha_{sm}\tau_{sm})x_s + \exp(-\alpha_{Em}\tau_{Em})(x_a + x_c))^2}\\ &+ \frac{\exp(-\alpha_{ms}\tau_{ms})x_s(x_s\tau_{ms} + \exp(-\alpha_{Es}\tau_{Es})(x_a + x_c)(\tau_{ms} - \tau_{Es}))}{(x_s + \exp(-\alpha_{ms}\tau_{ms})x_m + \exp(-\alpha_{Es}\tau_{Es})(x_a + x_c))^2}\\ &+ \frac{\exp(-\alpha_{mE}\tau_{mE})x_a(x_c\tau_{mE} + \exp(-\alpha_{sE}\tau_{sE})x_s)(\tau_{mE} - \tau_{sE}))}{(x_c + \exp(-\alpha_{sE}\tau_{sE})x_s + \exp(-\alpha_{mE}\tau_{mE})x_m)^2}\\ &+ \frac{\exp(-\alpha_{mE}\tau_{mE})x_c(x_a\tau_{mE} + \exp(-\alpha_{sE}\tau_{sE})x_s)(\tau_{mE} - \tau_{sE}))}{(x_a + \exp(-\alpha_{sE}\tau_{sE})x_s + \exp(-\alpha_{mE}\tau_{mE})x_m)^2}\end{aligned} \tag{14}$$

Here, x is mole fraction; subscripts E, m and s denote IL, water and drug, respectively; α is non-randomness factor and in this work its values are set to 0.2 for obtaining the better fitting quality.τ_{mE}, τ_{Em}, τ_{sE}, τ_{Es}, τ_{sm} and τ_{ms} are the adjustable parameters of NRTL model.

NRF-NRTL Equation

The activity coefficient equation of the solvent for NRF-NRTL model [26] is as follow:

$$\begin{aligned}&\ln \gamma_m^{*,\mathrm{NRF\text{-}NRTL}} =\\ &\frac{(\exp(-\alpha_{sm}\tau_{sm})x_s + \exp(-\alpha_{Em}\tau_{Em})x_a + \exp(-\alpha_{Em}\tau_{Em})x_c)(\exp(-\alpha_{sm}\tau_{sm})x_s\tau_{sm} + \exp(-\alpha_{Em}\tau_{Em})x_a\tau_{Em} + \exp(-\alpha_{Em}\tau_{Em})x_c\tau_{Em})}{(x_m + \exp(-\alpha_{sm}\tau_{sm})x_s + \exp(-\alpha_{Em}\tau_{Em})x_a + \exp(-\alpha_{Em}\tau_{Em})x_c)^2}\\ &- \frac{(x_a + x_c + x_s)(x_s\tau_{sm} + x_a\tau_{Em} + x_c\tau_{Em})}{(x_a + x_c + x_s + x_m)^2}\\ &+ \frac{(\exp(-\alpha_{ms}\tau_{ms})(x_s\tau_{ms} + \exp(-\alpha_{Es}\tau_{Es})x_a\tau_{ms} + \exp(-\alpha_{Es}\tau_{Es})x_c\tau_{ms} - \exp(-\alpha_{Es}\tau_{Es})x_a\tau_{Es} - \exp(-\alpha_{Es}\tau_{Es})x_c\tau_{Es})}{(x_s + \exp(-\alpha_{ms}\tau_{ms})x_m + \exp(-\alpha_{Es}\tau_{Es})x_a + \exp(-\alpha_{Es}\tau_{Es})x_c)^2}\\ &- \frac{x_s(x_a\tau_{ms} + x_c\tau_{ms} + x_s\tau_{ms} - x_a\tau_{Es} - x_c\tau_{Es})}{(x_a + x_c + x_s + x_m)^2}\\ &+ \frac{(\exp(-\alpha_{mE}\tau_{mE}x_a)(x_c\tau_{mE} + \exp(-\alpha_{sE}\tau_{sE})x_s\tau_{mE} - \exp(-\alpha_{sE}\tau_{sE})x_s\tau_{sE})}{(x_c + \exp(-\alpha_{sE}\tau_{sE})x_s + \exp(-\alpha_{mE}\tau_{mE})x_m)^2}\\ &- \frac{x_a(x_a\tau_{mE} + x_c\tau_{mE} + x_s\tau_{mE} - x_s\tau_{sE})}{(x_a + x_c + x_s + x_m)^2}\\ &+ \frac{(\exp(-\alpha_{mE}\tau_{mE}x_c)(x_a\tau_{mE} + \exp(-\alpha_{sE}\tau_{sE})x_s\tau_{mE} - \exp(-\alpha_{sE}\tau_{sE})x_s\tau_{sE})}{(x_a + \exp(-\alpha_{sE}\tau_{sE})x_s + \exp(-\alpha_{mE}\tau_{mE})x_m)^2}\\ &- \frac{x_c(x_a\tau_{mE} + x_c\tau_{mE} + x_s\tau_{mE} - x_s\tau_{sE})}{(x_a + x_c + x_s + x_m)^2},\end{aligned} \tag{15}$$

where the nonrandomness factor values are set to 0.3 for obtaining the better fitting quality in this work.τ_{mE}, τ_{Em}, τ_{sE}, τ_{Es}, τ_{sm} and τ_{ms} are the adjustable parameters of NRF-NRTL model.

UNIQUAC Equation

The activity coefficient equation of the solvent for UNIQUAC model [27] is as follow:Where

$$\begin{aligned}\ln\left(\gamma_m^*\right) = {} & \ln\left(\frac{\psi_m^*}{x_m}\right) + \frac{z}{2} q_m \ln\frac{\theta_m}{\psi_m^*} + l_m - \left(\frac{\psi_m^*}{x_m}\right)\left(x_w l_w + x_m l_m + x_{ca} l_{ca}\right) \\ & - q_m \ln\left(\theta_w' \exp(\frac{-u_{w,m}}{RT}) + \theta_{ca}' \exp(\frac{-u_{ca,m}}{RT}) + \theta_m'\right) + q_m \\ & + q_m - q_m\left[\left(\frac{\theta_w' \exp(\frac{-u_{m,w}}{RT})}{\theta_w' + \theta_{ca}' \exp(\frac{-u_{ca,w}}{RT}) + \theta_m' \exp(\frac{-u_{m,w}}{RT})}\right) + \left(\frac{\theta_{ca}' \exp(\frac{-u_{m,ca}}{RT})}{\theta_w' \exp(\frac{-u_{w,ca}}{RT}) + \theta_{ca}' + \theta_m' \exp(\frac{-u_{m,ca}}{RT})}\right)\right. \\ & \left. + \left(\frac{\theta_m'}{\theta_w' \exp(\frac{-u_{w,m}}{RT}) + \theta_{ca}' \exp(\frac{-u_{ca,m}}{RT}) + \theta_m'}\right)\right] \\ & - \ln\left(\frac{r_m}{r_w}\right) + 1 - \left(\frac{r_m}{r_w}\right) - \frac{z}{2} q_m\left(\ln\frac{r_m}{r_w}\frac{q_w}{q_m}\right) + 1 - \frac{r_m}{r_w}\frac{q_w}{q_m} + q_m\left(1 - \ln\left(\exp\left(\frac{-u_{w,m}}{RT}\right) - \exp\left(\frac{-u_{m,w}}{RT}\right)\right)\right),\end{aligned} \tag{16}$$

$$l_i = \frac{z}{2}\left(r_i - q_i\right) - \left(r_i - 1\right) \tag{17}$$

z which is the coordination number whose value is equal to 10; and the values of r and q which are parameters related to size can be calculated by the group theory.

Data Availability

All data can be found in the current manuscript.

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Declarations

Conflict of interest The authors declare that there are no conflict of interest.

References

1. Nelson, D.L., Cox, M.M.: Lehninger Principles of Biochemistry, 4th edn., pp. 64–172. W. H. Freeman and Company, New York (2008)
2. Schaefer, M., Sommer, M., Karplus, M.: PH-dependence of protein stability: absolute electrostatic free energy differences between conformations. J. Phys. Chem. B **101**, 1663–1683 (1997). https://doi.org/10.1021/jp962972s
3. Hermann, T.: Industrial production of amino acids by coryneform bacteria. J. Biotechnol. **104**, 155–163 (2003). https://doi.org/10.1016/S0168-1656(03)00149-4

4. Eyal, A.M., Bressler, E.: Mini-review industrial separation of carboxylic and amino acids by liquid membranes: applicability. Process considerations and potential advantages. Biotech. Bioeng. **11**, 287–298 (1993). https://doi.org/10.1002/bit.260410302
5. Belter, P.A., Cussler, E.L., Hu, W.S.: Bioseparation. Willy, New York (1998)
6. Foster, P.R., Dunhill, P., Lilly, M.D.: The precipitation of enzymes from cell extracts of saccharomyces cerevisiae by polyethylene-glycol. Biochem. Biophys. Acta **317**, 505–512 (1973). https://doi.org/10.1016/0005-2795(73)90243-2
7. Marcozzi, G., Correa, N., Luisi, P.L., Caselli, M.: Protein extraction by reverse micelles: a study of the factors affecting the forward and backward transfer of a-chymotrypsin and its activity. Bitechnol. Bioengin. **38**, 1239–1246 (1991). https://doi.org/10.1002/bit.260381017
8. Khoshkbarchi, M.K., Vera, J.H.: Reverse micellar extraction and back extraction of l-lysine with three di alkyl sodium phosphinatesin pentanol/isooctane mixtures. Sep. Sei. Technol. **30**, 2301–2310 (1995). https://doi.org/10.1080/01496399508013113
9. Jaenicke, R.: Stability and stabilization of globular proteins in solution. J. Biotechnol. **79**, 193–203 (2000). https://doi.org/10.1016/S0168-1656(00)00236-4
10. Curtis, R.A., Heinemann, S.M., Blanch, H.W., Prausnitz, J.M.: Hydrophobic forces between protein molecules in aqueous solutions of concentrated electrolyte. Biophys. Chem. **98**, 249–265 (2002). https://doi.org/10.1016/S0301-4622(02)00071-6
11. Tan, Z., Welz-Biermann, U., Yan, P., Liu, Q., & Fang, D.: Thermodynamic properties of ionic liquids - measurements and predictions -. In: Kokorin, A. (ed.) Ionic Liquids: Theory, Properties, New Approaches. (2011). https://doi.org/10.5772/15222
12. Zafarani-Moattar, M.T., Asadzadeh, B., Shahrisa, A., Nazari, MGh.: Investigation of 1-(2-carboxyethyl)-3-methylimidazolium chloride [HOOCEMIM][Cl] ionic liquid effect on water activity and solubility of L-serine at $T = 298.15$ K. J. Chem. Thermodyn. **80**, 49–58 (2015). https://doi.org/10.1016/j.jct.2014.08.016
13. Zafarani-Moattar, M.T., Asadzadeh, B.: The solubility and stability of L-threonine in ionic liquids. J. Mol. Liq. **214**, 364–368 (2016). https://doi.org/10.1016/j.molliq.2015.11.041
14. Zafarani-Moattar, M.T., Asadzadeh, B.: Effect of 1-carboxymethyl-3-methylimidazolium chloride, [HOOCMMIM][Cl], ionic liquid on volumetric, acoustic and transport behavior of aqueous solutions of l-serine and l-threonine at $T = 298.15$ K. J. Mol. Liq. **202**, 79–85 (2015). https://doi.org/10.1016/j.molliq.2014.12.006
15. Xie, H., Zhao, L., Liu, Ch., Cao, Y., QunfangLei, X., Fang, W.: Volumetric property of glycine, L-serine, L-alanine and L-proline in aqueous solutions of 1-phenylpiperazinium tetrafluoroborate. J. Chem. Thermodyn. **99**, 75–81 (2016). https://doi.org/10.1016/j.jct.2016.03.045
16. Rafiee, H.R., Frouzesh, F.: The study of solute–solvent interactions in the ternary amino acid (glycine or L-serine) + ionic liquid (1-butyl-3-methylimidazolium tetra fluoroborate [Bmim][BF4]) + H2O system at different temperatures and ambient pressure: Volumetric study. J. Mol. Liq. **230**, 6–14 (2017). https://doi.org/10.1016/j.molliq.2016.12.116
17. Rafiee, H.R., Frouzesh, F.: Volumetric properties for glycine and L-serine in aqueous solutions of 1-Ethyl-3-methylimidazolium hydrogen sulfate ([Emim][HSO4]) at $T = (293.15–313.15)$ K and ambient pressure. J. Chem. Thermodyn. **102**, 398–405 (2016). https://doi.org/10.1016/j.jct.2016.07.046
18. Brinzei, M., Stefaniu, A., Lulian, O., Ciocirlan, O.: Molecular interactions of two biologically active molecules (L–serine and L-valine) in aqueous [Hmim]Cl solutions: volumetric and viscometric approach. J. Mol. Liq. **341**, 116912 (2021). https://doi.org/10.1016/j.molliq.2021.116912
19. Kaur, H., Thakur, R.C., Kumar, H.: Effect of proteinogenic amino acids l-serine/l-threonine on volumetric and acoustic behavior of aqueous 1-butyl-3-propyl imidazolium bromide at $T = (288.15, 298.15, 308.15, 318.15)$ K. J. Chem. Thermodyn. **150**, 106211 (2020). https://doi.org/10.1016/j.jct.2020.106211
20. Gaba, R., Pal, A., Kumar, H., Sharma, D.: Navjot: volumetric and acoustic studies of amino acids in aqueous ionic liquid solution. J. Mol. Liq. **242**, 739–746 (2017). https://doi.org/10.1016/j.molliq.2017.07.058
21. Patyar, P., Kaur, T., Sethi, O.: Molecular interactions of some amino acids in aqueous 1-butyl-3-methylimidazolium bromide solutions at different temperatures: a volumetric approach. J. Chem. Thermodyn. **125**, 278–295 (2018). https://doi.org/10.1016/j.jct.2018.05.008
22. Redlich, O., Meyer, D.M.: The molal volumes of electrolytes. Chem. Rev. **64**, 221–227 (1964). https://doi.org/10.1021/cr60229a001
23. Jones, G., Dole, M.: The viscosity of aqueous solutions of strong electrolytes with special reference to barium chloride. J. Am. Chem. Soc. **51**, 2950–2964 (1929). https://doi.org/10.1021/ja01385a012

24. Sadeghi, R.: Thermodynamic representation of phase equilibrium behavior of aqueous solutions of amino acids by the modified Wilson model. Fluid Phase Equilib. **260**, 266–274 (2007). https://doi.org/10.1016/j.fluid.2007.07.024
25. Chen, C.C., Zhu, Y., Evans, L.B.: Phase partitioning of biomolecules: solubilities of amino acids. Biotechnol. Prog. **5**, 111–118 (1989). https://doi.org/10.1002/btpr.5420050309
26. Sadeghi, R.: Thermodynamics studies of aqueous solutions containing polyvinylpyrrolidone and some electrolytes, pp. 134–137. Faculty of Chemistry, Universityof Tabriz, Tabriz (2004)
27. Prausnitz, J.M., Lichtenthaler, R.N., Azevedo, E.G.: Molecular Thermodynamics of Fluids-Phase Equilibria, pp. 31–56. Prentice Hall Inc, Hoboken (1999)
28. Shekaari, H., Armanfar, E.: Apparent molar volumes and expansivities of aqueous solutions of ionic liquids, l-alkyl-3-methylimidazolium alkyl sulfate at T = (298.15–328.15) K. Fluid Phase Equilib. **303**, 120–125 (2011). https://doi.org/10.1016/j.fluid.2011.01.001
29. Banipal, T.S., Kaur, D., Banipal, P.K., Singh, G.: Thermodynamic and transport properties of l-serine and l-threonine in aqueous sodium acetate and magnesium acetate solutions at T = 298.15 K. J. Chem. Thermodyn. **39**, 371–384 (2007). https://doi.org/10.1016/j.jct.2006.08.003
30. Fang, S., Ren, D.H.: Effect of 1-ethyl-3-methylimidazolium bromide ionic liquid on the volumetric behavior of some aqueous L-amino acids solutions. J. Chem. Eng. Data **58**, 845–850 (2013). https://doi.org/10.1021/je300953u
31. Zafarani-Moattar, M.T., Sarmad, Sh.: Apparent molar volumes, apparent isentropic compressibilities and viscosity B-coefficients of 1-ethyl-3-ethylimidazolium bromide in aqueous di-potassium hydrogen phosphate and potassium di-hydrogen phosphate solutions at T = (298.15, 303.15, 308.15, 313.15, and 318.15) K. J. Chem. Thermodyn. **54**, 192–203 (2012). https://doi.org/10.1016/j.jct.2012.03.032
32. Zafarani-Moattar, M.T., Sarmad, Sh.: Effect of tri-potassium phosphate on volumetric, acoustic and transport behaviour of aqueous solutions of 1-ethyl-3-methyl imidazolium bromide at T = (298.15 to 318.15). J. Chem. Thermodyn. **42**, 1213–1221 (2010). https://doi.org/10.1016/j.jct.2010.04.025
33. Sadeghi, R., Gholamireza, A.: Thermodynamics of the ternary systems: (water + glycine, L-alanine and L-serine + di-ammonium hydrogen citrate) from volumetric, compressibility, and (vapour + liquid) equilibria measurements. J. Chem. Thermodyn. **43**, 200–215 (2011). https://doi.org/10.1016/j.jct.2010.08.021
34. Robinson, R.A., Stokes, R.H.: Electrolyte Solutions. Butterworths, London (1965)
35. Qiu, X., Huo, B., Wang, Q., Yang, J., Zhu, Zh., Wang, Y., Gao, J.: Isobaric vapor-liquid equilibrium of binary systems of 1-pentanol + butyl butyrate, 1-pentanol + *N*-formylmorpholine, and p-xylene + butyl butyrate at 101.3 kPa. J. Chem. Eng. Data **66**, 2874–2881 (2021). https://doi.org/10.1021/acs.jced.1c00250
36. Pitzer, K.S.: Activity Coefficients in Electrolyte Solutions, 2nd edn. CRC Press Inc, Boca Raton (1991). https://doi.org/10.1201/9781351069472
37. Saul, A., Wagner, W.J.: International equations for the saturation properties of ordinary water substance. J. Phys. Chem. Ref. Data **16**, 893–901 (1987). https://doi.org/10.1063/1.555787
38. Kell, G.S.: Density, thermal expansivity, and compressibility of liquid water from 0°. to 150°. Correlations and tables for atmospheric pressure and saturation reviewed and expressed on 1968 temperature scale. J. Chem. Eng. Data **20**, 97–105 (1975). https://doi.org/10.1021/je60064a005
39. Colin, E., Clarke, W., Glew, D.N.: Evaluation of the thermodynamic functions for aqueous sodium chloride from equilibrium and calorimetric measurements below 154 °C. J. Phys. Chem. Ref. Data **14**, 489–610 (1985). https://doi.org/10.1063/1.555730
40. Romero, C., González, M.E.: Osmotic and activity coefficients of glycine, DL-α-alanine and DL-α-aminobutyric acid in aqueous solutions at temperatures between 288.15 and 303.15 K. Fluid Phase Equilib. **250**, 99–108 (2006). https://doi.org/10.1016/j.fluid.2006.10.012
41. Flory, P.J.: Thermodynamics of high polymer solutions. J. Chem. Phys. **9**, 660–661 (1941). https://doi.org/10.1063/1.1750971
42. Zafarani-Moattar, M.T., Asadzadeh, B., Shahrisa, A., Nazari, MGh.: Study of thermodynamic properties of l-serine in aqueous 1-carboxymethyl-3-methylimidazolium chloride solutions at 298.15 K. Fluid Phase Equilib. **363**, 32–40 (2014). https://doi.org/10.1016/j.fluid.2013.11.017