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Thermodynamic and Solubility Studies of L-Serine and L-Isoleucine in Aqueous Sodium and Potassium Fluoride Solutions

Saroj Chowdhury[1] · Jit Chakraborty[2] · Biplab Ghosh[1] · Avishek Saha[3] · Kalachand Mahali[1] · Adel Noubigh[5] · Sanjay Roy[3,4]

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Abstract
The solubility of L-serine and L-isoleucine was investigated in pure water and in aqueous solutions of different molalities of sodium and potassium fluoride salts (NaF/KF), across a temperature range from 288.15 K to 308.15 K. Salting-in constants of 0.0784 and 0.07436 were obtained for KF + water and NaF + water systems, respectively, indicating an increase in solubility with higher electrolyte molality for L-serine. Conversely, salting-out constants of −0.19424 and −0.13592 were determined for NaF + water and KF + water systems, respectively, suggesting a decrease in solubility with increasing NaF or KF molality for L-isoleucine. The experimental solubility data were utilized to calculate transfer thermodynamic parameters related to solvation. By examining the solubility data and evaluating the thermodynamics associated with the free energetics of solvation, we gained insight into the solvation process and the weak interactions involved in the liquid phase of amino acids.

Keywords L-serine · L-isoleucine · Electrolyte system · Equilibrium thermodynamic modeling · Solution stability

✉ Kalachand Mahali
gourkala@gmail.com

✉ Adel Noubigh
adel.noubigh@nbu.edu.sa

✉ Sanjay Roy
sanjayroyp@gmail.com

[1] Department of Chemistry, University of Kalyani, Kalyani, Nadia 741235, India

[2] Department of Chemistry, JIS College of Engineering, Kalyani, Nadia 741235, India

[3] Department of Chemistry, School of Sciences, Netaji Subhas Open University, Kolkata, West Bengal 700064, India

[4] Department of Chemistry, School of Sciences, Netaji Subhas Open University, Kolkata, West Bengal 741235, India

[5] Center for Scientific Research and Entrepreneurship, Northern Border University, 73213 Arar, Saudi Arabia

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1 Introduction

Understanding solvation phenomena and studying the influence of selective ions on the solubility of important biomolecules are vital for the advancement of bioscience and biochemistry which are utilized by various industries such as chemical, pharmaceutical, and food [1, 2]. The solvation behavior of amino acids holds significant importance not only in biological systems but also in industrial applications [3–5]. However, in order to explain the complexity occurring in solvent systems involving electrolytes, the solubilities of potentially important biomolecules under various temperature conditions in such systems are required. Such investigations can provide valuable insights into solvation phenomena and aid in solvation-related problems. The primary objective of this study is to contribute toward the determination of solubilities and thermodynamic interactions of L-isoleucine and L-serine in aqueous fluoride environments.

Several studies have explored various parameters to elucidate the interactions between cation and anions of the electrolyte and biomolecules in mixed solvent systems [6, 7]. Several investigations have been done previously regarding the amino acids that serves a major role in animal metabolism along with their influence in physiological processes [8–10]. Thermodynamic factors have been employed to explain structural modifications in numerous biomacromolecules, including proteins [11–14]. Notably, electrolytes play an active role in biological systems, particularly in protein folding and unfolding processes, indicating their significance in amino acid solvation phenomena [15, 16]. An important application of ionic salts on the solvation of amino acids lies during the separation of amino acids through the hydrolysis pathway of proteins in electrolyte solutions at optimized pH. This process is frequently employed in amino acid separation and holds practical implications in various fields [17–19].

Numerous works have been carried out worldwide to investigate the solubility and related phenomena of amino acids in various systems, including pure water [20, 21], binary or ternary aqueous-organic mixtures [22–24], completely dehydrated non-aqueous solutions [25, 26] and dilute electrolytic solutions [27–29]. Understanding the solvation chemistry of biomolecules, particularly amino acids that form the fundamental building blocks of proteins, is of paramount importance. However, despite extensive research in this field, there is a lack of supporting valuable data regarding the solvation-related thermodynamic outcomes for protein building units in aqueous solutions of NaF and KF. This study aims to bridge that gap by investigating the solvation-related parameters of L-serine and L-isoleucine in the presence as well as in the absence of fluoride salts of alkali metal ions in aqueous media.

To the best of our knowledge, no comprehensive data exist regarding the solvation behavior of these biologically important and valuable L-amino acids in aqueous sodium and potassium fluoride salts solutions. Therefore, this research effort aims to provide valuable insights into the solvation phenomena of the present solutes in complex electrolytic systems. The possibility of our study extends beyond the determination of solubility. We have also explored the effects of electrolytes on the conformational properties of L-isoleucine and L-serine, as well as the underlying solvation mechanisms. By examining these aspects, we aim to enhance the understanding of the intricate behavior of ions within complex systems. The comprehensive findings obtained through this investigation will assist scientists in deciphering the complex interplay between solvents, electrolytes, and amino acids, ultimately contributing to a more comprehensive understanding of solvation phenomena.

2 Experimental

2.1 Chemicals and Their Purification

In the present investigation, the solutes namely, L-isoleucine and L-serine were obtained from Sigma-Aldrich, ensuring a purity level exceeding 99.8%. To remove any residual moisture, the solutes were subjected to a drying process using a silica gel dehydrator for a duration of 10 days prior to their utilization in the experiment. The electrolytic salts, NaF and KF (both with a purity level of 98%), were procured from E. Merck, India. To eliminate any traces of moisture, the salts were dried in an oven at a temperature of 400.15 K for two weeks. The aqueous electrolyte solutions were prepared by employing triple distilled water, with a maximum conductivity of 1.0 microsiemens/cm. In Table 1, the specifications of the present chemicals are shown.

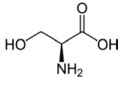
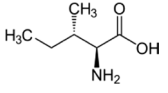
2.2 Preparations of Experimental Solutions

Fluoride salts of sodium (NaF) and potassium (KF) were prepared in five different concentrations: 0.0, 0.25, 0.50, 0.75, 1.0, and 1.25 mol·kg^{-1}. Saturated solutions were prepared by placing approximately 10 mL of each solvent mixture into stoppered glass tubes and shaking until saturation was achieved. These mixtures were then maintained at specific temperatures within a thermostat for 48 h, with periodic shaking and additional solute increments as needed, to ensure complete equilibration. Following this 48-h period, aliquots of the saturated solutions were withdrawn into stoppered conical flasks for solubility measurement. Saturation was confirmed when solution concentrations remained consistent over 48-h intervals.

2.3 Solubility Measurement

In this study, gravimetric technique [2, 30] was employed to measure the solubilities of the studied amino acids in NaF + water solution and KF + water solution. The sample solutions containing a desired concentration of the electrolyte is taken in a stoppered glass tube. This was followed by addition of the amino acids namely, L-serine or L-isoleucine in the stoppered glass tube and vigorous shaking until a mass of amino acid remains constant in the glass tube undissolved which marks the saturation of amino acid in the solution. This solution was kept in a thermostat bath maintained at an experimental temperature for 48 h to attain equilibrium. The solution was shaken occasionally to ensure complete saturation; additional amino acids are added on necessity. After 48 h, the glass tubes were allowed to stand for eight hours to facilitate the settling of undissolved amino acid. Afterward, the excess and undissolved amino acid particles were removed from the obtained liquid (2.5 mL) through filtration using a 0.22 μm HPLC disposable filter (High-performance liquid chromatography, HPLC) and a preheated pipette. The liquid component of the solution was completely evaporated, resulting in amino acid crystals. These pure crystals were subjected to a dehydrator stove at a temperature of 450.15 K. Then, the obtained crystals were kept in a dehydrator followed by cooling to room temperature in a silica gel dehydrator for 12 h. The dried mass was weighed to obtain the solubility data. Three successive measurements under the same conditions were done resulting in three parallel solubility results. The mass of the dehydrated compounds were determined through weighing after undergoing a cooling process.

Table 1 Specification of chemical samples

Chemical name	Chemical structure	CAS registry no	Purchased from	Initial purity[a] (fraction)	Purification method
L-serine		56-45-1	Sigma-Aldrich	99.8% (mass)	Dried in a dehydrator with silica gel
L-isoleucine		73-32-5	Sigma-Aldrich	99.8% (mass)	Dried in a dehydrator with silica gel
Sodium fluoride	NaF	7681-49-4	E. Merck, Bombay, India	98% (mass)	Oven dried
Potassium fluoride	KF	7789-23-3	E. Merck, Bombay, India	98% (mass)	Oven dried
Water	H_2O	7732-18-5	Distilled water	–	Distillation

[a]Declared by the supplier

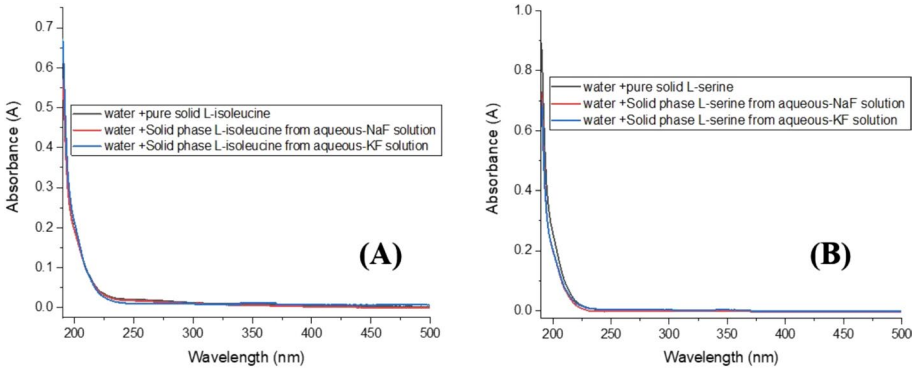


Fig. 1 UV–Vis spectrums of **A** pure L-isoleucine and solid-phase L-isoleucine dried from aqueous–NaF / aqueous–KF solution and **B** pure L-serine and solid-phase L-serine dried from aqueous–NaF /aqueous–KF solution, in pure water (here concentration of KF and NaF were taken 1.00 mol·kg^{-1})

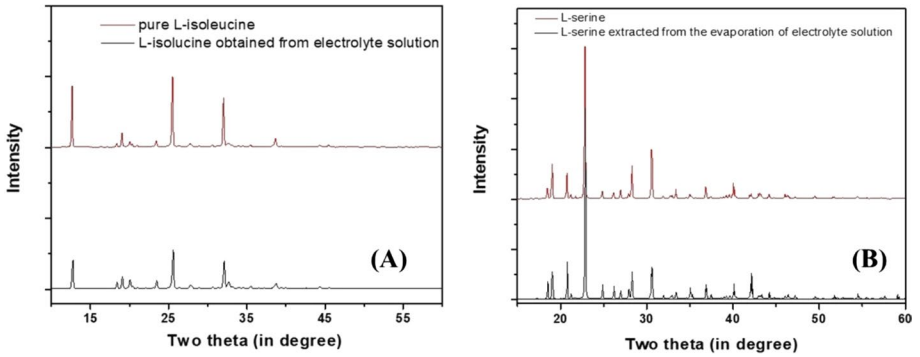


Fig. 2 PXRD data obtained for **A** pure L-isoleucine (Red) and recrystallized L-isoleucine (Black) and **B** pure L-serine (Red) and recrystallized L-serine (Black) obtained from the evaporation of solvent through filtration (here, concentration of KF and NaF were taken 1.00 mol·kg^{-1})

To verify the absence of the electrolytes in the obtained mass, UV–visible spectroscopy, and PXRD studies of the experimental amino acids in pure form and the mass obtained post solvent evaporation were performed as a part of the investigation. The results obtained are presented in Figs. 1 and 2, respectively, which revealed that the UV–Vis spectra of the solid-phase amino acids remained unaltered, indicating that there were no significant chemical changes during the transfer of the solid amino acids into the solution phase. It is noteworthy to mention that the concentration of KF and NaF in water were taken 1.00 mol·kg^{-1}. The clean and well-defined absorption spectra provide strong evidence that the investigated compounds are pure, as they demonstrate the absence of any UV-active impurities or contaminants. Powder X-ray Diffraction (PXRD) analysis was performed on both the original pure amino acids and the amino acids recovered after solvent evaporation via filtration. The resulting PXRD patterns confirm the complete removal of electrolyte particles through the filtration and recrystallization process. Powder X-ray diffraction (PXRD) measurements were performed on amino acid crystals recovered from aqueous NaF and KF solutions at a molality of 1.00 mol·kg^{-1}. This concentration is very close to

the highest investigated electrolyte molality (1.25 mol·kg^{-1}), and no structural changes in the recovered solids are expected within this narrow molality range. Accordingly, the PXRD patterns obtained at 1.00 mol·kg^{-1} are considered representative of the solid-phase behavior across the studied electrolyte concentrations. This further substantiates that the mass obtained after water evaporation consists solely of pure amino acid crystals, indicating that no undesirable reactions or dissociations occurred within the solution during the process.

Saturated aqueous NaF and KF solutions were prepared by dissolving excess electrolyte followed by equilibration for 48 h and filtration through a 0.22-μm membrane to remove undissolved salt particles prior to amino acid solubility measurements. PXRD analysis of the solids recovered after gravimetric evaporation consistently showed diffraction patterns corresponding exclusively to the respective amino acids, indicating that no crystalline electrolyte phases co-precipitated even at higher electrolyte molalities. The mass of the dissolved amino acids was determined using the following methodology. Let the mass of the electrolyte used be represented as S_1. Then, $S_1 = (M \times m \times S_W)$ / 1000 g, which corresponds to the mass of the electrolyte in S_W grams of evaporated solvent water. Here, M is the molecular weight of the electrolyte, and 'm' denotes its molality. The mass of the solid amino acid (S) can then be calculated as $S = (S_3 - S_2 - S_1)$ g, where S_2 is the mass of the empty container, and S_3 is the combined mass of the container, dried electrolyte, and solid amino acid. If S_4 represents the total weight of the jar containing the amino acid-saturated electrolyte solution, the actual amount of evaporated water is $S_W = S_4 - S_3$.

Therefore, the solubility of the amino acid is calculated using the relation:

Solubility $(S_5) = (S \,/\, S_W) \times 1000$ g per kg of water. Consequently, the molality of the amino acid $= S_5 / M$ (where M is the molar mass of the amino acid) in mol/kg of water.

The mole fraction, x, of the amino acid is given as

$$x(\text{mole fraction of L-histidine}) = \frac{\frac{m_{\text{L-histidine}}}{M_{\text{L-histidine}}}}{\frac{m_{\text{water}}}{M_{\text{water}}} + \frac{m_{\text{electrolyte}}}{M_{\text{electrolyte}}} + \frac{m_{\text{L-histidine}}}{M_{\text{L-histidine}}}}.$$

To ensure the reliability of the collected data, each sample mixture was measured in triplicate across all experimental temperatures. The outcomes demonstrated strong consistency, with the uncertainty confined to a narrow range of ± 0.3% to ± 1.2%. Thermodynamic parameters were evaluated using a theoretical mathematical modeling approach.

3 Theoretical Modeling of Solubility

The solubility–temperature dependence of L-serine and L-isoleucine in aqueous fluoride (NaF or KF) solution was quantitatively described using the empirical equation of Heidman et al. [31]. This equation's utility lies in its concise mathematical representation of complex solution interactions, allowing for solubility prediction at different temperatures and facilitating thermodynamic insights into the dissolution process.

$$\ln(x) = A + \frac{B}{T} + C\ln(T), \tag{1}$$

where x is the mole fraction solubility of the amino acid at temperature T (Kelvin), and the solubility–temperature relationship is modeled using an equation with empirically derived constants A, B, and C (obtained by fitting to experimental data). A and B relate to the

temperature dependence of the solution's activity coefficient, reflecting non-ideal behavior. C describes the effect of temperature on the fusion enthalpy and the enthalpy change of the solid-to-liquid transition [32].

Computed amino acid solubilities in various fluoride salt aqueous solutions are comprehensively presented in Tables 2 and 3 and Figs. 3 and 4. Covering 288.15 K to 308.15 K at 101.3 kPa, the computed values strongly agree with experimental data. This concordance indicates the model's accuracy in capturing amino acid solubility behavior within the studied temperature interval. This agreement is essential for the reliability of subsequent analyses or predictions. Accurate solubility modeling is critical for applications like drug formulation, protein purification, and understanding biological

Table 2 Experimental (x_{exptl}) and calculated (x_{calcd}) mole fraction solubility of L-isoleucine in water and fluoride salts aqueous solutions ($p = 101.3$ kPa.[a])

Molality of NaF	0.00		0.25		0.50	
T/K	$10^2 \cdot x_{exptl}$ [b]	$10^2 \cdot x_{calcd}$ [b]	$10^2\, x_{exptl}$	$10^2\, x_{calcd}$	$10^2\, x_{exptl}$	$10^2 \cdot x_{calcd}$
288.15	0.530	0.530	0.476	0.475	0.432	0.433
293.15	0.540	0.543	0.488	0.488	0.451	0.450
298.15	0.560	0.556	0.501	0.502	0.471	0.468
303.15	0.570	0.569	0.516	0.516	0.486	0.486
308.15	0.580	0.583	0.530	0.530	0.502	0.504
Molality of NaF	0.75		1.00		1.25	
T/K	$10^2 \cdot x_{exptl}$ [b]	$10^2 \cdot x_{calcd}$ [b]	$10^2\, x_{exptl}$	$10^2\, x_{calcd}$	$10^2\, x_{exptl}$	$10^2 \cdot x_{calcd}$
288.15	0.397	0.396	0.356	0.347	0.265	0.268
293.15	0.415	0.415	0.367	0.369	0.293	0.289
298.15	0.434	0.435	0.379	0.392	0.309	0.312
303.15	0.456	0.455	0.415	0.416	0.333	0.336
308.15	0.477	0.475	0.450	0.441	0.361	0.362
Molality of KF	0.00		0.25		0.50	
T /K	$10^2 \cdot x_{exptl}$ [b]	$10^2 \cdot x_{calcd}$ [b]	$10^2\, x_{exptl}$	$10^2\, x_{calcd}$	$10^2\, x_{exptl}$	$10^2 \cdot x_{calcd}$
288.15	0.530	0.530	0.486	0.486	0.471	0.470
293.15	0.540	0.543	0.501	0.501	0.485	0.485
298.15	0.560	0.556	0.517	0.516	0.500	0.500
303.15	0.570	0.569	0.531	0.531	0.515	0.515
308.15	0.580	0.583	0.545	0.547	0.530	0.530
Molality of KF	0.75		1.00		1.25	
T /K	$10^2 \cdot x_{exptl}$ [b]	$10^2 \cdot x_{calcd}$ [b]	$10^2\, x_{exptl}$	$10^2\, x_{calcd}$	$10^2\, x_{exptl}$	$10^2 \cdot x_{calcd}$
288.15	0.415	0.417	0.356	0.347	0.352	0.348
293.15	0.440	0.439	0.367	0.369	0.365	0.366
298.15	0.465	0.462	0.379	0.392	0.377	0.384
303.15	0.481	0.486	0.415	0.416	0.407	0.403
308.15	0.496	0.510	0.450	0.441	0.427	0.423

[a]Standard uncertainty u is $u(T) = 0.01$ K. The relative standard uncertainty u is $u_r(p) = 0.05$, $u_r(x_{explt}) = 0.05$.
[b]x_{explt} is the experimentally determined solubility of L-isoleucine; x_{calcd} is the calculated solubility of L-isoleucine by Eq. (1)

Table 3 Experimental ($x_{\mathrm{exp\,lt}}$) and calculated (x_{calcd}) mole fraction solubility of L-serine in water and fluoride salts aqueous solutions ($p = 101.3$ kPa.[a])

Molality of NaF	0.00		0.25		0.50	
T/K	$10^2{\cdot}x_{\mathrm{exptl}}$ [b]	$10^2{\cdot}x_{\mathrm{calcd}}$ [b]	$10^2\,x_{\mathrm{exptl}}$	$10^2\,x_{\mathrm{calcd}}$	$10^2\,x_{\mathrm{exptl}}$	$10^2{\cdot}x_{\mathrm{calcd}}$
288.15	6.447	6.470	6.639	6.664	7.032	7.034
293.15	6.680	6.663	6.908	6.937	7.198	7.267
298.15	6.912	6.857	7.331	7.217	7.669	7.503
303.15	7.117	7.055	7.500	7.502	7.669	7.743
308.15	7.206	7.254	7.741	7.794	7.976	7.986
Molality of NaF	0.75		1.00		1.25	
T/K	$10^2{\cdot}x_{\mathrm{exptl}}$ [b]	$10^2{\cdot}x_{\mathrm{calcd}}$ [b]	$10^2\,x_{\mathrm{exptl}}$	$10^2\,x_{\mathrm{calcd}}$	$10^2\,x_{\mathrm{exptl}}$	$10^2{\cdot}x_{\mathrm{calcd}}$
288.15	7.221	7.242	8.070	8.060	8.277	8.310
293.15	7.518	7.517	8.217	8.215	8.490	8.450
298.15	7.840	7.798	8.364	8.371	8.545	8.589
303.15	8.021	8.083	8.509	8.527	8.729	8.729
308.15	8.126	8.375	8.698	8.684	8.867	8.868
Molality of KF	0.00		0.25		0.50	
T/K	$10^2{\cdot}x_{\mathrm{exptl}}$ [b]	$10^2{\cdot}x_{\mathrm{calcd}}$ [b]	$10^2\,x_{\mathrm{exptl}}$	$10^2\,x_{\mathrm{calcd}}$	$10^2\,x_{\mathrm{exptl}}$	$10^2{\cdot}x_{\mathrm{calcd}}$
288.15	6.447	6.470	6.497	6.484	6.563	6.575
293.15	6.680	6.663	6.724	6.728	6.895	6.835
298.15	6.912	6.857	6.961	6.977	7.050	7.102
303.15	7.117	7.055	7.226	7.231	7.361	7.374
308.15	7.206	7.254	7.500	7.489	7.670	7.652
Molality of KF	0.75		1.00		1.25	
T/K	$10^2{\cdot}x_{\mathrm{exptl}}$ [b]	$10^2{\cdot}x_{\mathrm{calcd}}$ [b]	$10^2\,x_{\mathrm{exptl}}$	$10^2\,x_{\mathrm{calcd}}$	$10^2\,x_{\mathrm{exptl}}$	$10^2{\cdot}x_{\mathrm{calcd}}$
288.15	6.597	6.696	6.774	6.957	6.900	7.233
293.15	7.226	7.026	7.359	7.271	7.728	7.536
298.15	7.345	7.367	7.907	7.594	8.100	7.847
303.15	7.673	7.718	7.938	7.925	8.239	8.164
308.15	7.857	8.079	8.078	8.266	8.264	8.489

[a]Standard uncertainty u is $u(T) = 0.01$ K. The relative standard uncertainty u is $u_r(p) = 0.05$, $u_r(x_{\mathrm{exptl}}) = 0.05$.
[b]x_{exptl} is the experimentally determined solubility of L-serine; x_{calcd} is the calculated solubility of L-serine by Eq. (1)

processes, enabling the prediction of amino acid behavior in different solution environments. The parameters characterizing the solubility-temperature relationship, derived from the modified empirical equation, are listed in Table 4.

The applicability and precision of different models were evaluated by root mean square deviation (RMSD) and relative average deviation (RAD). They were quantified through Eqs. (2) and (3), respectively.

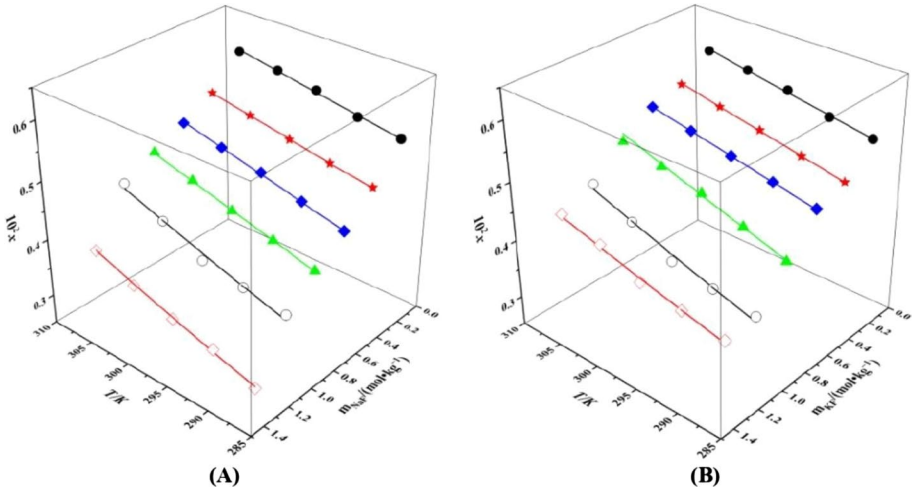


Fig. 3 Comparison of experimental and calculated mole fraction solubility of L-isoleucine in water and **A** aqueous sodium fluoride and **B** aqueous potassium fluoride salt solutions. (Symbols represent experimental data; lines represent correlations using Eq. (1)). Legend: ●, pure water; ★ 0.25 mol·kg^{-1};◆, 0.5 mol·kg^{-1};▲, 0.75 mol·kg^{-1};○, 1.0 mol·kg^{-1};◇, 1.25 mol·kg^{-1}

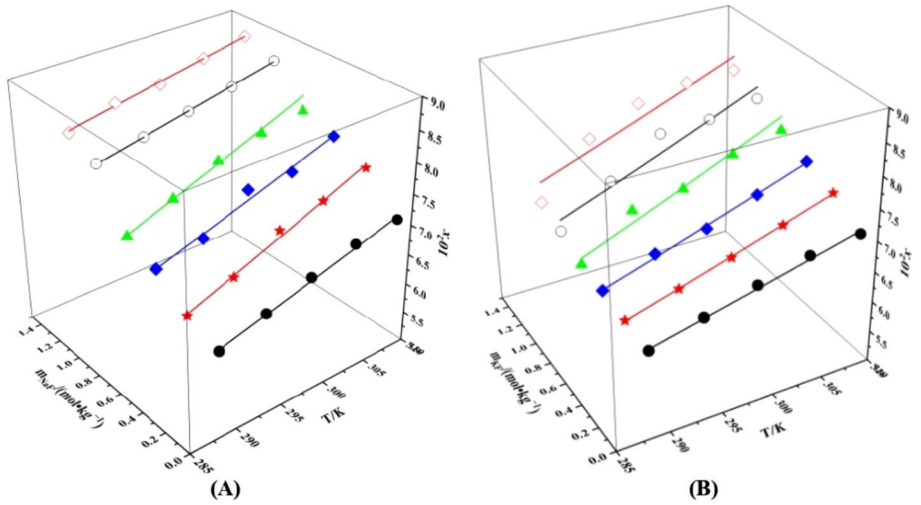


Fig. 4 Comparison of experimental and calculated mole fraction solubility of L-serine in water and **A** aqueous sodium fluoride and **B** aqueous potassium fluoride salt solutions. (Symbols represent experimental data; lines represent correlations using Eq. (1)). Legend: ●, pure water;★, 0.25 mol·kg^{-1};◆, 0.5 mol·kg^{-1};▲, 0.75 mol·kg^{-1};○, 1.0 mol·kg^{-1};◇, 1.25 mol·kg^{-1}

Table 4 Estimated parameters, RAD, and RMSD of Eq. (1) for L-serine and L-isoleucine in various aqueous salts solutions

Molality of NaF	L-isoleucine				
	A	*B*	*C*	10^4RMSD	10^2 RAD
0.00	− 13.327	1.232	1.427	0.10	0.38
0.25	− 14.629	1.211	1.638	0.01	0.08
0.50	− 18.189	1.132	2.250	0.02	0.34
0.75	− 20.906	1.110	2.714	0.05	0.24
1.00	− 25.786	0.986	3.553	0.44	1.74
1.25	− 31.388	0.848	4.496	0.09	0.88
Molality of KF	L-isoleucine				
	A	*B*	*C*	10^4RMSD	10^2 RAD
0.00	− 13.327	1.232	1.427	0.10	0.38
0.25	− 15.263	1.201	1.754	0.02	0.10
0.50	− 15.529	1.198	1.795	0.01	0.03
0.75	− 22.563	1.081	3.016	0.04	1.08
1.00	− 25.786	0.986	3.553	0.44	1.74
1.25	− 22.231	1.066	2.925	0.12	1.07
Molality of NaF	L–serine				
	A	*B*	*C*	10^4RMSD	10^2 RAD
0.00	− 12.423	1.247	1.709	0.20	0.59
0.25	− 15.955	1.189	2.338	0.65	0.60
0.50	− 13.394	1.246	1.896	1.31	0.85
0.75	− 14.914	1.229	2.169	0.26	0.94
1.00	− 8.842	1.349	1.116	0.02	0.12
1.25	− 8.006	1.376	0.974	0.18	0.28
Molality of KF	L–serine				
	A	*B*	*C*	10^4RMSD	10^2 RAD
0.00	− 12.423	1.247	1.709	0.20	0.59
0.25	− 14.929	1.216	2.152	0.02	0.14
0.50	− 15.554	1.199	2.265	0.28	0.44
0.75	− 18.583	1.148	2.803	2.08	1.59
1.00	− 17.242	1.157	2.573	5.96	2.07
1.25	− 16.167	1.188	2.390	10.57	2.81

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

$$\mathrm{RAD} = \frac{1}{n} \times \sum_{i=1}^{n} \left|\frac{x_{\mathrm{exptl}} - x_{\mathrm{calcd}}}{x_{\mathrm{exptl}}}\right|. \tag{3}$$

The variable n refers to the total of 5 experimental data points in this study. The terms x_{calcd} and x_{exptl} stand for the computed and experimental solubility values, respectively. Table 3 also contains the root mean square deviations (RMSD) and relative average deviation (RAD).

The validity of the computed solubility values is substantiated by the error analysis presented in Table 4. The root mean square deviation (RMSD) and relative average deviation (RAD) values, which quantify the model's prediction error, are low. The maximum RMSD and RAD values are 0.44×10^{-4} and 1.74×10^{-2} for L-isoleucine, and 10.57×10^{-4} and 2.81×10^{-2} for L-serine. This indicates that the model's predictions closely match the experimental data. This close agreement between computed and experimental solubility is crucial because it confirms the reliability of the empirical equation. A reliable equation can then be confidently used for further calculations, predictions of solubility under different conditions, and for gaining a deeper understanding of the underlying thermodynamic processes.

The results shown in Tables 2, 3, and 4 and Figs. 3 and 4 clearly demonstrate that amino acids become more soluble in fluoride salt solutions as the temperature increases. This means that as the temperature of the solution increases, a greater amount of the amino acid is able to dissolve. This aligns with the basic scientific idea that higher temperatures provide more energy, helping to break down the crystal structure of the solute and improving how it interacts with water. Interestingly, fluoride salts have opposite effects on the two amino acids studied: they decrease the solubility of L-isoleucine (a "salting-out" effect) but increase the solubility of L-serine (a "salting-in" effect). For L-isoleucine, this drop in solubility is likely due to the fluoride ions competing for water molecules, which reduces the amount of water available to dissolve the amino acid. On the other hand, L-serine seems to benefit from higher fluoride salt concentrations, possibly because of a different kind of interaction with the solvent. Finally, the study confirms that the modified empirical equation used to model these solubility changes is effective. Its strong fit with the experimental data highlights its usefulness in predicting how solubility behaves under varying conditions of temperature and fluoride concentration.

4 Discussion

4.1 Discussion on Solubility Results

Numerous studies in the area of amino acid research have demonstrated that the nature of solubility of amino acids is significantly altered by variations in temperature and other physicochemical parameters [33, 34]. In our study, we conducted an assessment of the equilibrium solubility of L-serine and L-isoleucine in two distinct ternary solvent systems: aqueous NaF and aqueous KF. Solubility investigations were done at five equidistant different temperatures, and the corresponding data are presented in Tables 2 and 3. Remarkably, the findings for these amino acids in pure aqueous medium align closely with previous reports [35]. The obtained solubility data exhibit a low variation of only maximum of 3.0% across multiple observations, indicating a good level of accuracy. Analysis of solubility for L-isoleucine and L-serine, as presented in Tables 2 and 3 and Figs. 3 and 4, reveals that solubility increases with enhancement in temperature in the presence of both the electrolytes. Specifically, Fig. 5 illustrates the variation in solubility of the present L-amino acids at a temperature of 298.15 K. It is noteworthy to mention that the solubility

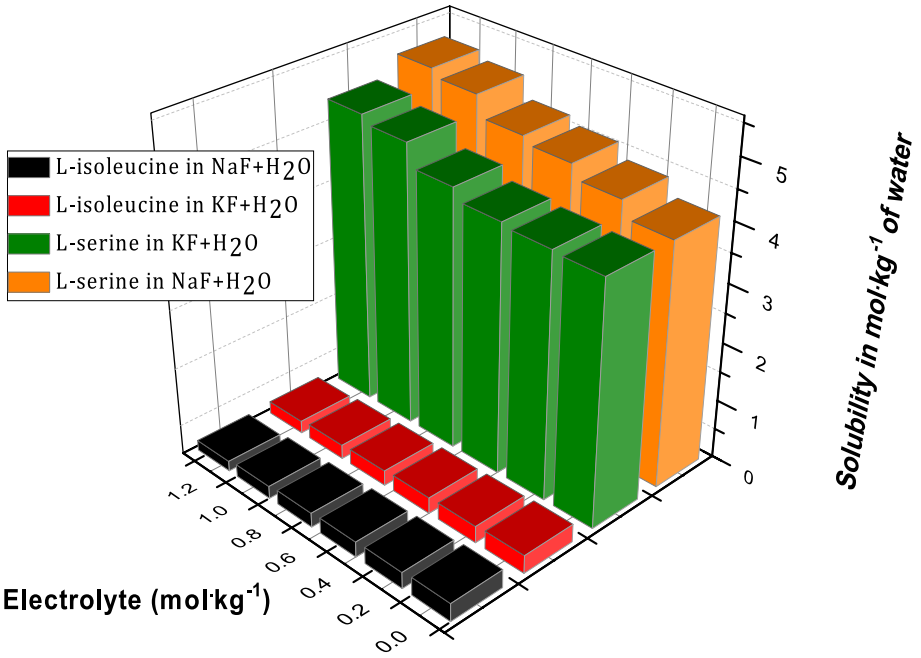


Fig. 5 Solubility of L-serine and L-isoleucine in aqueous NaF/KF solutions of different compositions at 298.15 K

of L-isoleucine exhibits a decreasing trend with increasing electrolyte content, particularly in the NaF + water solvent system compared to the KF + water solvent system. The electrolytic ions also exhibit chaotropic and kosmotropic effects with water molecules present in the system. The smaller ions also referred to as kosmotropes disrupts the hydrogen bonds present between the water molecules due to their stronger electrostatic interactions. On the other hand, the larger ions also called chaotropes accumulate the water molecules and facilitate hydrogen bonding between them [27].

In addition, from Figs. 3 and 4, it is evident that the increase in solubility of the solute amino acid first increases slowly up to 298.15 K and then rises steeply in higher electrolytic concentration mainly from 1 molal electrolyte concentration. This is mainly attributed to the intense hydrogen bonding between the water molecules and the entropy factor at low temperatures which results in mild changes in solubility. With increasing temperature beyond room temperature, the breaking of hydrogen bonds among water molecules enhances interactions between water and L-isoleucine resulting in increased solubility. In addition, the presence of excess Na^+ and K^- ions in the solution triggers the solubility of the amino acid by ion–dipole interactions. All these factors together comprehend toward the solubility of L-isoleucine in the solution at room 298.15 K.

Under the same experimental conditions, it was observed that the equilibrium solubility of L-serine rises with electrolyte concentration, with a more pronounced effect in the aqueous NaF system compared to the aqueous KF system. Conversely, the solubility of L-isoleucine showed a decreasing order with increasing electrolyte concentration, with a stronger effect observed in the aqueous KF system compared to the aqueous NaF system. The relative solubility (S_S/S_R) represents the ratio of amino acid solubility in solution of salt (S_S) to pure water (S_R).

Table 5 Relative solubility (S_S/S_W) and $\log_{10}(S_S/S_W)$ of L-isoleucine and L-serine in water and water + NaF and water + KF in different compositions of NaF and KF at different temperatures under atmospheric pressure, $p = 0.1$ MPa[a]

Molality of NaF/KF mol·kg^{-1}	Relative solubility and $\log_{10}(S_S/S_R)$									
	Relative solubility (S_S/S_W) 288.15 K	$\log_{10}$ (S_S/S_R) at 288.15 K	Relative solubility (S_S/S_W) 293.15 K	$\log_{10}$ (S_S/S_W) at 293.15 K	Relative solubility (S_S/S_W) 298.15 K	$\log_{10}$ (S_S/S_W) at 298.15 K	Relative solubility (S_S/S_W) 303.15 K	$\log_{10}$ (S_S/S_W) at 303.15 K	Relative solubility (S_S/S_W) 308.15 K	$\log_{10}$ (S_S/S_W) at 308.15 K
L-isoleucine in NaF + H_2O solvent system										
0.25	0.8981	−0.0467	0.8999	−0.0458	0.9042	−0.0437	0.9053	−0.0432	0.9063	−0.0427
0.50	0.8148	−0.0890	0.8312	−0.0803	0.8492	−0.0710	0.8534	−0.0689	0.8573	−0.0669
0.75	0.7494	−0.1253	0.7648	−0.1165	0.7819	−0.1068	0.7996	−0.0971	0.8153	−0.0887
1.00	0.6708	−0.1734	0.6759	−0.1701	0.6830	−0.1656	0.7272	−0.1384	0.7688	−0.1142
1.25	0.4998	−0.3012	0.5382	−0.2691	0.5765	−0.2392	0.6429	−0.1919	0.7054	−0.1516
L-isoleucine in KF + H_2O solvent system										
0.25	0.9177	−0.0373	0.9240	−0.0343	0.9327	−0.0303	0.9327	−0.0303	0.9323	−0.0304
0.50	0.8893	−0.0510	0.8930	−0.0492	0.9020	−0.0448	0.9037	−0.0440	0.9054	−0.0432
0.75	0.7839	−0.1057	0.8110	−0.0910	0.8392	−0.0761	0.8439	−0.0737	0.8466	−0.0723
1.00	0.7416	−0.1298	0.7562	−0.1214	0.7758	−0.1102	0.7788	−0.1086	0.7792	−0.1084
1.25	0.6644	−0.1776	0.6713	−0.1731	0.6800	−0.1675	0.7140	−0.1463	0.7296	−0.1369
L-serine in NaF + H_2O solvent system										
0.25	1.0318	0.0136	1.0367	0.0156	1.0654	0.0275	1.0581	0.0245	1.0804	0.0336
0.50	1.0976	0.0404	1.0834	0.0348	1.1186	0.0487	1.0840	0.0350	1.1161	0.0477
0.75	1.1294	0.0528	1.1356	0.0552	1.1455	0.0590	1.1381	0.0562	1.1388	0.0565
1.00	1.2738	0.1051	1.2506	0.09712	1.2292	0.0896	1.2138	0.0841	1.2267	0.0887
1.25	1.3093	0.1171	1.2960	0.1126	1.2589	0.1000	1.2481	0.0962	1.2529	0.0979
L-serine in KF + H_2O solvent system										
0.25	1.0083	0.0036	1.0069	0.0030	1.0075	0.0033	1.0165	0.0071	1.0441	0.0187
0.50	1.0191	0.0082	1.0345	0.0147	1.0215	0.0092	1.0369	0.0158	1.0697	0.0293
0.75	1.0248	0.0106	1.0880	0.0366	1.0676	0.0284	1.0846	0.0353	1.0980	0.0406

Table 5 (continued)

Molality of NaF/KF mol·kg^{-1}	Relative solubility and $\log_{10}(S_S/S_R)$									
	Relative solubility (S_S/S_W) 288.15 K	$\log_{10}$ (S_S/S_R) at 288.15 K	Relative solubility (S_S/S_W) 293.15 K	$\log_{10}$ (S_S/S_W) at 293.15 K	Relative solubility (S_S/S_W) 298.15 K	$\log_{10}$ (S_S/S_W) at 298.15 K	Relative solubility (S_S/S_W) 303.15 K	$\log_{10}$ (S_S/S_W) at 303.15 K	Relative solubility (S_S/S_W) 308.15 K	$\log_{10}$ (S_S/S_W) at 308.15 K
1.00	1.0543	0.0230	1.1097	0.0452	1.1562	0.0630	1.1253	0.0513	1.1316	0.0537
1.25	1.0754	0.0316	1.1700	0.0682	1.1870	0.0744	1.1717	0.0688	1.1601	0.0645

[a]Standard uncertainties u are $u(T) = 0.10$ K

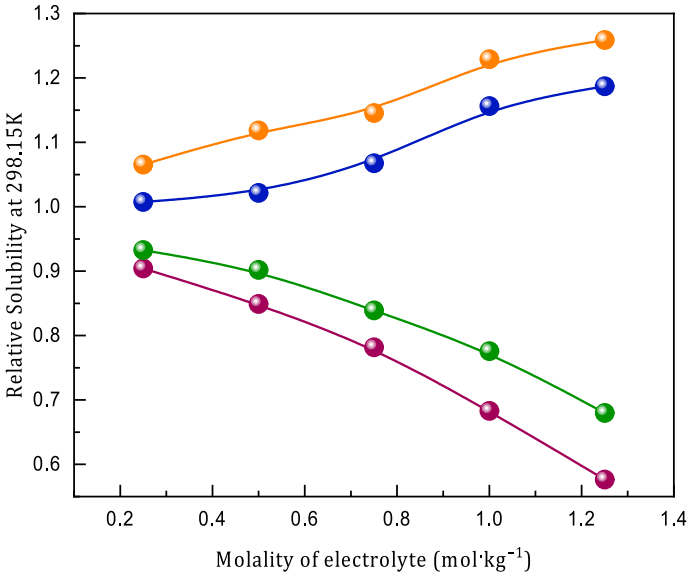


Fig. 6 Relative solubility of L-serine and L-isoleucine in aqueous Na /KF solutions of different compositions at 298.15 K (L-isoleucine in NaF + H_2O (black line), L-isoleucine in KF + H_2O (red line), L-serine in NaF + H_2O (green line), and L-serine in KF + H_2O (blue line)

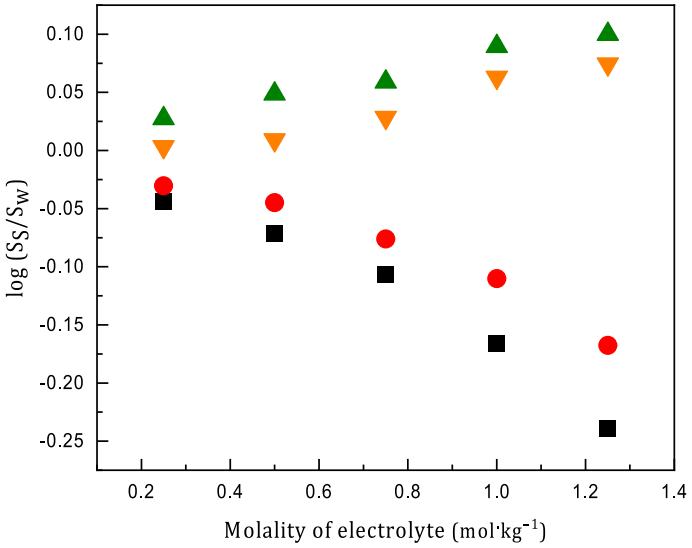


Fig. 7 Variation of $\log(S_S/S_W)$ with salt concentration for L-serine and L-isoleucine in aqueous NaF/KF solutions at 298.15 K (■L-isoleucine in NaF + H_2O, ●L-isoleucine in KF + H_2O, ▲L-serine in NaF + H_2O, ▼L-serine in KF + H_2O)

Table 6 Salting-in/ salting-out constants of L-isoleucine and L-serine in aqueous NaF/KF solutions at 298.15 K#

Amino acids	K_{si} (salting-in / salting-out)at 298.15 K in NaF	K_{si} (salting-in / salting-out) at 298.15 K in KF
L-isoleucine	− 0.19424 ± 0.0224	− 0.13592 ± 0.01758
L-serine	0.07436 ± 0.00662	0.07840 ± 0.01050

Standard uncertainties u are u(T) = 0.10 K#

Table 5 provides the relative solubility values for various salt concentrations (Fig. 6). The results suggest that the inclusion of sodium fluoride or potassium fluoride leads to a salting-in effect on L-serine, while causing a salting-out effect on L-isoleucine (Fig. 7). The salting-in/out constants listed in Table 6 provide further evidence supporting the experimental solubility variations of the studied amino acids in the current analysis. It is vital to mention that both the structural characteristics of the solutes and the properties of the electrolytes play a combined role in influencing their solubility. The pronounced salting-in effect observed for L-serine in studied NaF solution, as compared to aqueous KF solution, aligns with our previous investigation [36]. Furthermore, Eq. 4 can be applied to calculate the salting-in/out constant (K*si*) [37].

$$\log_{10}\left(S_S/S_W\right) = K_{si}C. \tag{4}$$

In Eq. 4, the symbol "*C*" represents the molality of the electrolyte in the mixture.

The determination of the salting-in constant (Setchenow constants, K*si*) at a temperature of 298.15 K involved the calculation of the linear relationship between the logarithm of the relative solubility ($\log(S_S/S_R)$) and the concentration of electrolyte (*C*) [38].

These calculated K_{si} values align with the solubility patterns described in Table 5 and 6, lending further credibility to the findings. By examining the sign of K_{si}, valuable insights can be gained regarding the dominant interactions taking place in the medium. Positive K_{si} values indicate a salting-in effect, while negative values suggest a salting-out effect [27, 29, 37, 38]. The research conducted by Held and his team examined the complex formation in aqueous solutions, exploring diverse interactions involving different amino acids and the anions present in the electrolytes [39]. The differences in solubility and the occurrence of salting-in or salting-out effects among electrolytic salt solutions can be ascribed to the distinct interactions between amino acids and the negative components of the electrolytes. Tables 5 and 6 demonstrate that solubility exhibits a significant increase with varying experimental solution temperatures, and the results vary depending on the nature of the electrolytic ions and the hydrocarbon backbone of the zwitterionic molecules under different conditions. The substantial variation in solubility can be attributed to factors such as the difference in the size of the solute, solute structure, cosolvent diameter, and the presence of solvated electrolyte ions. These factors collectively contribute to the observed solubility variations on a larger scale. The solubility of the current solutes, along with their relative solubilities at specific temperatures, provides a comprehensive summary of the "salting-in/out" effect in a particular electrolyte content. Across all electrolyte concentrations, L-serine demonstrates greater solubility when compared to L-isoleucine. This difference can be attributed to the structural dissimilarities between the two amino acids. L-serine contains an additional −OH group, enhancing its polarity in comparison to L-isoleucine, which lacks such a group. In our previous research [2], we have observed a

similar solubility trend. This solubility trend in electrolytic solutions, which involves positive and negative ions of varying sizes, can be explained by the interactions of dispersion and hydrogen bonding, influenced by the size factor of different amino acids. Our study has found that L-serine (with a size of 0.593 nm) [11] has stronger hydrogen bonding interactions. The sizes of NaF and L-serine are more favorable for the formation of ion-pair complexes. Additionally, the amine group present in amino acids contributes to the formation of intermolecular hydrogen bonds with both water and electrolytes, further influencing the observed solubility behavior in our current study. In a mixed solvent environment, hydrogen bonding interactions play a vital role in facilitating the formation of ion-pair complexes [40]. These complexes consist of amino acids and electrolyte ions and can exhibit complex structures. In the mixed solvent system of H_2O + amino acid + electrolyte, the presence of ionic amino alkanoic acid (A^-A^+) can lead to the formation of soluble ion-pair complexes. This phenomenon can be attributed to cavity-forming interactions (such as in Na^+ or K^+) as well as the anion X of the electrolyte (such as F^-). These interactions significantly influence the solubility behavior and promote the formation of stable complexes within the system. The solubility behavior of amino acids can be influenced by the effect of salting-in/out, which varies on studied electrolyte. The specific interactions between electrolyte ions and the zwitterionic forms of amino acids play a significant role in determining their solubility behavior, ultimately leading to either a salting-in or salting-out effect. Therefore, understanding the interplay between the electrolyte ions and the zwitterionic structures of amino acids is crucial for comprehending the solubility patterns observed in these systems. Though amino acid can form in different species, such as protonated, neutral, zwitterionic, and deprotonated, depend on pH and ionic strength of solutions [41]. The pH studies of both the electrolytic solutions were done and the obtained data are provided in the supplementary information section, Table S3. It is evident from the pH data that with increase in electrolytic component in the solution, the solution turned slightly basic for both NaF and KF solution.

In this work, the solubility was measured by assuming neutral condition of amino acid. To justify our solubility data measured by the present analytical gravimetric method we compared the earlier results [11, 35] which excellently corroborated with the present study and the detail were shown in Supplementary Information as Table S2 and in Figures S1 and necessary references were cited in supplementary information section. Figure S1 shows the mole fraction solubility of L-isoleucine in pure water at different temperatures in the present study and from earlier literatures [Supplementary References: 11–20]. From Table S2 and in Figure S1, it was found that there are very few extra deviated solubility results at 298.15 K and at 323.15 K. These might be due to usage of different experimental methods and conditions.

It is evident from the present findings that L-serine is more soluble in NaF system than in aqueous KF solvent system. Though, in the case of L-isoleucine, the observed experimental solubility of the KF-water system was marginally higher than the solubility of the water-NaF system (Tables 3 and 4). Increased dispersion interactions with the larger cation K^+ and the L-isoleucine may have contributed to the results of higher solubility.

4.2 Stability (Ability of Solute to Remain in Solution Without Precipitating Out) in Light of Short Range Chemical Interaction

Understanding the short range interactions among solutes, such as amino acids, and solvents is vital, particularly in the context of biologically important compounds and

Table 7 Standard Gibbs energies of solution (ΔG_S^0) on the molal scale for the solubilities of L-isoleucine and L-serine in aqueous NaF/KF mixtures at different temperatures (K)[#]

288.18 K		293.15 K		298.15 K		303.15 K		308.15 K	
S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})
L-isoleucine in NaF + H_2O									
0.2953	2.9222	0.3027	2.9125	0.3091	2.9104	0.3178	2.8892	0.3265	2.8677
0.2652	3.1797	0.2724	3.1696	0.2795	3.1599	0.2877	3.1400	0.2959	3.1198
0.2406	3.4129	0.2516	3.3632	0.2625	3.3154	0.2712	3.2889	0.2799	3.2622
0.2213	3.6132	0.2315	3.5661	0.2417	3.5201	0.2541	3.4530	0.2662	3.3908
0.1981	3.8786	0.2046	3.8672	0.2111	3.8556	0.2311	3.6921	0.2510	3.5414
0.1476	4.5835	0.1629	4.4227	0.1722	4.3605	0.1853	4.2488	0.2012	4.1080
L-isoleucine in KF + H_2O									
0.2953	2.9222	0.3027	2.9125	0.3091	2.9104	0.3178	2.8892	0.3265	2.8677
0.2710	3.1279	0.2797	3.1051	0.2883	3.0830	0.2964	3.0649	0.3044	3.0472
0.2626	3.2033	0.2703	3.1885	0.2788	3.1661	0.2872	3.1444	0.2956	3.1224
0.2315	3.5053	0.2455	3.4230	0.2594	3.3449	0.2682	3.3169	0.2764	3.2944
0.2190	3.6383	0.2289	3.5937	0.2398	3.5396	0.2475	3.5193	0.2544	3.5069
0.1962	3.9017	0.2032	3.8839	0.2102	3.8662	0.2269	3.7384	0.2382	3.6755
L-serine in NaF + H_2O									
3.8255	−3.2143	3.9736	−3.3626	4.1217	−3.5107	4.2534	−3.6488	4.3108	−3.7433
3.9472	−3.2893	4.1193	−3.4504	4.3914	−3.6678	4.5005	−3.7911	4.6576	−3.9416
4.1987	−3.4373	4.3051	−3.5579	4.6104	−3.7884	4.6108	−3.8522	4.8112	−4.0247
4.3204	−3.5057	4.5123	−3.6725	4.7215	−3.8474	4.8406	−3.9748	4.9093	−4.0764
4.8731	−3.7941	4.9694	−3.9080	5.0665	−4.0223	5.1626	−4.1371	5.2882	−4.2669
5.0089	−3.8600	5.1499	−3.9946	5.1889	−4.0814	5.3085	−4.2073	5.4008	−4.3209
L-serine in KF + H_2O									
3.8255	−3.2143	3.9736	−3.3626	4.1217	−3.5107	4.2534	−3.6488	4.3108	−3.7433

Table 7 (continued)

288.18 K		293.15 K		298.15 K		303.15 K		308.15 K	
S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})	S (mol·kg^{-1})	$\Delta G_S^0(i)$(kJ·mol^{-1})
3.8572	− 3.2340	4.0012	− 3.3795	4.1528	− 3.5293	4.3234	− 3.6900	4.5007	− 3.8538
3.8987	− 3.2597	4.1105	− 3.4452	4.2104	− 3.5634	4.4105	− 3.7402	4.6112	− 3.9159
3.9204	− 3.2730	4.3234	− 3.5682	4.4004	− 3.6729	4.6133	− 3.8535	4.7334	− 3.9829
4.0331	− 3.3409	4.4094	− 3.6162	4.7656	− 3.8705	4.7862	− 3.9463	4.8782	− 4.0601
4.1139	− 3.3884	4.6491	− 3.7453	4.8924	− 3.9356	4.9838	− 4.0482	5.0008	− 4.1237

#Standard uncertainty u(T)= 0.10 K

eco-friendly solvents. Our first aim was to calculate the Gibbs energies of solution for the studied amino acids and the results are presented in Table 7.

The transfer Gibbs energies of L-isoleucine and L-serine were studied in aqueous electrolytic solutions, aiming to enhance our understanding of these processes. To accomplish this, we employed least-squares methods to determine the coefficients associated with the energy terms [42]. Accurate measurements of the free energy terms were obtained, and the resulting coefficients are determined and summarized in Table 8. These coefficients offer valuable insights into the thermodynamics of the transfer process for the studied systems. Figure 8 illustrates the results obtained for the total transfer Gibbs free energies of the examined amino acids in aqueous electrolytic solutions. For L-isoleucine, a positive trend is observed for the total transfer free energy in both systems. However, contrasting outcomes are observed for L-serine in the two solvent systems. Specifically, the total transfer Gibbs energies for L-isoleucine in the aqueous

Table 8 Gibbs energies of transfer $\Delta G_t^0(i)$, $\Delta G_{t,cav}^0(i)$, $\Delta G_{t,d-d}^0(i)$, and $\Delta G_{t,ch}^0(i)$, enthalpy, $\Delta H_{t,cav}^0(i)$ and entropies of transfer $T\Delta S_t^0(i)$, $T\Delta S_{t,cav}^0(i)$, $T\Delta S_{t,d-d}^0(i)$, and $T\Delta S_{t,ch}^0(i)$ of L-isoleucine and L-serine in $H_2O + NaF$ and $H_2O + KF$ mixture at 298.15 K[#] in kJ•mol^{-1}

NaF/KF (mol·kg^{-1})	$\Delta G_t^0(i)$	$\Delta G_{t,cav}^0(i)$	$\Delta G_{t,d-d}^0(i)$	$\Delta G_{t,ch}^0(i)$	$T\Delta S_t^0(i)$	$\Delta H_{t,cav}^0(i)$	$T\Delta S_{t,cav}^0(i)$	$T\Delta S_{t,d-d}^0(i)$	$T\Delta S_{t,ch}^0(i)$
L-isoleucine in $NaF + H_2O$									
0.00	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
0.25	0.2410	0.0095	0.0008	0.2307	0.1098	0.0012	−0.0083	0.0009	0.1172
0.50	0.3725	0.0193	0.0027	0.3505	1.4912	0.0023	−0.0170	0.0029	1.5053
0.75	0.5542	0.0293	0.0057	0.5192	2.5837	0.0035	−0.0258	0.0061	2.6034
1.00	0.8758	0.0394	0.0097	0.8267	4.3219	0.0047	−0.0347	0.0105	4.3461
1.25	1.3567	0.0490	0.0148	0.7629	6.0000	0.0059	−0.0431	0.0160	6.0271
L-isoleucine in $KF + H_2O$									
0.00	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
0.25	0.1348	−0.0295	0.0020	0.1623	0.4526	−0.0012	0.0283	0.0021	0.4222
0.50	0.2110	−0.0579	0.0080	0.2610	0.4874	−0.0021	0.0558	0.0086	0.4230
0.75	0.3586	−0.0854	0.0172	0.4144	2.4398	−0.0030	0.0824	0.0185	2.3389
1.00	0.5284	−0.1120	0.0296	0.6108	1.3307	−0.0039	0.1081	0.0319	1.1907
1.25	0.6511	−0.1268	0.0447	0.7332	2.8927	−0.0046	0.1322	0.0481	2.7124
L-serine in $NaF + H_2O$									
0.00	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
0.25	−0.1613	0.0102	0.0005	−0.1720	1.8200	0.0013	−0.0089	0.0006	1.8283
0.50	−0.2618	0.0208	0.0018	−0.2844	0.7794	0.0025	−0.0183	0.0020	0.7957
0.75	−0.3954	0.0316	0.0038	−0.4308	0.6565	0.0038	−0.0278	0.0041	0.6802
1.00	−0.5590	0.0425	0.0065	−0.6080	−0.9560	0.0051	−0.0374	0.0070	−0.9256
1.25	−0.6681	0.0529	0.0100	−0.7310	−1.1674	0.0064	−0.0465	0.0107	−1.1316
L-serine in $KF + H_2O$									
0.00	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
0.25	−0.0605	−0.0317	0.0014	−0.0302	1.2671	−0.0013	0.0304	0.0015	1.2352
0.50	−0.0982	−0.0622	0.0056	−0.0416	1.6046	−0.0024	0.0598	0.0061	1.5387
0.75	−0.2546	−0.0917	0.0122	−0.1751	2.2159	−0.0035	0.0882	0.0131	2.1146
1.00	−−0.4361	−0.1201	0.0210	−0.3370	2.6542	−0.0045	0.1156	0.0226	2.5160
1.25	−0.5491	−0.1466	0.0317	−0.4342	2.6862	−0.0053	0.1413	0.0341	2.8011

[a]Standard uncertainty $u(T) = 0.10$ K

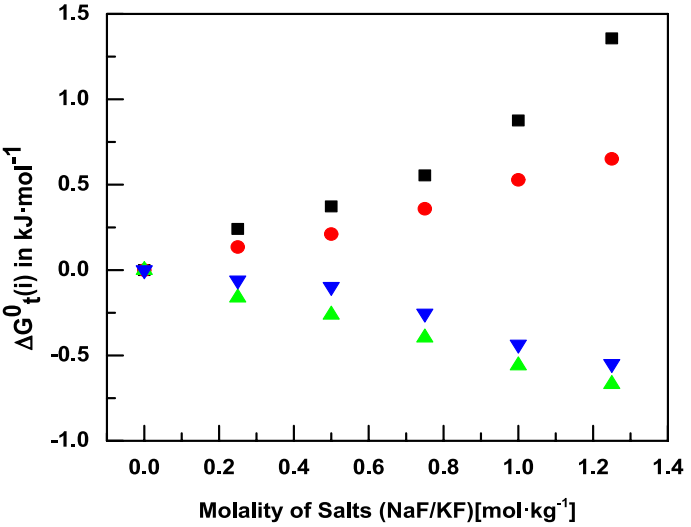


Fig. 8 Variation of $\Delta G_t^0(i)$ with salt concentration for L-serine and L-isoleucine in aqueous NaF/KF at 298.15 K in kJ•mol.$^{-1}$(■L-isoleucine in NaF + H_2O (black), ●L-isoleucine in KF + H_2O (red), ▲L-serine in NaF + H_2O (green), ▼L-serine in KF + H_2O (blue)

KF solvent system exhibit a more negative value compared to the aqueous NaF solution. This implies that L-isoleucine exhibits higher solubility and greater capacity in aqueous KF compared to the aqueous NaF solvent. Conversely, L-serine demonstrates a decreasing (negative) trend in both experimental aqueous electrolyte solutions. It is noteworthy to mention that the presence of larger KF content in the system enhances the solubility and the stability of L-serine over L-isoleucine (Fig. 8). The total transfer Gibbs free energies enhance the free energy for cavity creation and the dipole–dipole interaction energy between the solute and the solvent molecules, consequently, the free energy for chemical reactions, such as dispersion, acid–base, and dipolar interactions, also increases significantly.

L-isoleucine exhibited an increasing (positive) trend of chemical transfer Gibbs free energy in both electrolytic solvent systems, while L-serine displayed a decreasing (negative) tendency. Figure 8 illustrates that L-isoleucine is seemingly less stable than L-serine in terms of chemical interactions in both electrolytic solvent systems. The results suggest that L-isoleucine exhibits positive (increasing) trends, whereas L-serine shows negative (decreasing) trends at higher concentrations of electrolyte–water systems. These findings indicate that the dissolution process of L-serine is more pronounced compared to L-isoleucine (Table 8 & Fig. 9). Furthermore, L-serine is likely to be more stable in aqueous NaF compared to aqueous KF. When considering the hydrated electrolytic ions and the solute, the size of L-serine appears to be a better match for water-NaF solvent systems, resulting in the formation of a more stable ion-pair complex [11]. In H_2O-NaF solutions, the formation of a stable ion-pair complex involves a combination of hydrophobic and electrostatic interactions, which are more favorable for the ion-pair complex formed by water-NaF and L-serine. This could explain why L-serine is more likely to exhibit stability in the H_2O-NaF solvent system compared to the H_2O-KF system. However, on the other hand, the

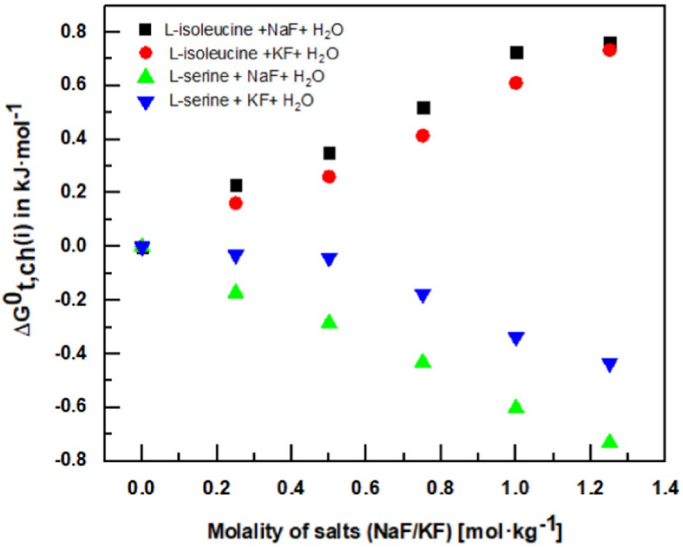


Fig. 9 Variation of $\Delta G^{0}_{t,ch}(i)$ with salt concentration for L-serine and L-isoleucine in aqueous NaF /KF at 298.15 K in kJ•mol.$^{-1}$ (L-isoleucine in NaF + H_2O (black line), L-isoleucine in KF + H_2O (red line), L-serine in NaF + H_2O (green line), L-serine in KF + H_2O (blue line)

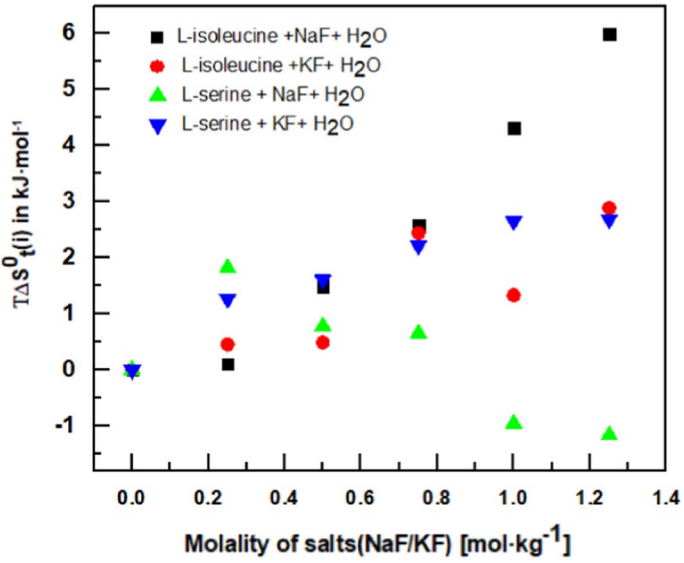


Fig. 10 Variation of $T\Delta S^{0}_{t}(i)$ with salt concentration for L-serine and L-isoleucine in aqueous NaF /KF at 298.15 K in kJ•mol^{-1} (■L-isoleucine in NaF + H_2O, ●L-isoleucine in KF + H_2O, ▲L-serine in NaF + H_2O, ▼L-serine in KF + H_2O)

alkyl residues present in the structure of L-isoleucine render it somewhat unstable in the realm of mixed aqueous electrolytic solvent systems.

4.3 Involved Solvent–Solvent Interactions in Solution

The transfer entropies investigated in this study are intricately linked to the intermolecular interactions occurring between solvents as they undergo a transition from a single solvent to a mixed binary electrolyte solvent system. To determine the comprehensive standard transfer entropy, we employed the least-squares approach, a robust mathematical method widely utilized in statistical analysis [22]. The results of these calculations can be found in Table 8 and Fig. 10.

The combined influence of transfer entropy associated with cavity formation, transfer entropy linked to dipole–dipole interactions, and entropy associated with chemical interactions among solvent molecules collectively engenders a multifaceted pattern of variation, as detected from the observations presented in Table 8. The transfer entropies contribute to the overall entropy changes during the solvent transition process, and their intricate interplay provides further closes to the behavior of solvents in mixed binary electrolyte solvent systems.

Figure 11 provides a graphical representation of the variation of transfer entropies due to non-covalent types of interactions, studied in the electrolyte solution. Both amino acids exhibit a nonlinear pattern of change in both electrolyte systems. With increasing concentrations of KF, the transfer entropy shows a more positive value, indicating higher disorder. Conversely, in the NaF-water system, the transfer entropy becomes more negative, following a reverse trend. Specifically, in the case of L-serine and the NaF-water system, the solvent–solvent interaction reaches a maximum negative value at higher molality concentrations. Conversely, in

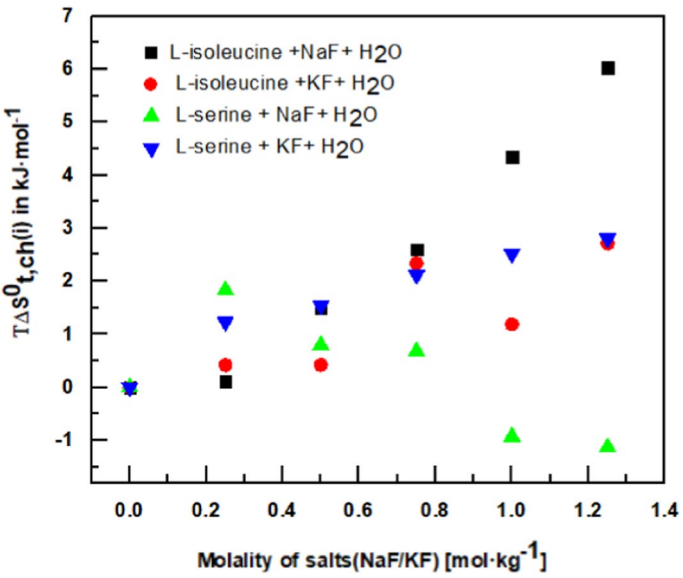


Fig. 11 Variation of $T\Delta S^0_{t,ch}(i)$ with concentration of salts for L-serine and L-isoleucine in aqueous NaF /KF at 298.15 K in kJ•mol.$^{-1}$ (■L-isoleucine in NaF + H_2O, ●L-isoleucine in KF + H_2O, ▲L-serine in NaF + H_2O, ▼L-serine in KF + H_2O)

the KF-water system, the corresponding amino acid exhibits a modest yet consistent positive increment in value. These findings highlight the complex and nonlinear nature of solvent–solvent interactions and their impact on the observed transfer entropies in electrolyte solutions.

5 Conclusion

The experimental study finds that L-serine exhibits higher solubility than the comparatively larger L-isoleucine in both electrolytic solutions under the same experimental conditions. The greater solubility of L-serine in the NaF-water solvent system suggests an easier dissolution process compared to the KF-water system. On the other hand, L-isoleucine is relatively less soluble in both electrolytic solutions due to the size mismatch. The salt-in/salting-out constants provide excellent support for these results. The overall findings suggest that the solvation is more favorable for L-serine in the KF-water system than in the NaF-water system. Conversely, for L-isoleucine, it is more favorable in the NaF-water system than in the KF-water system. The decreasing transfer Gibbs free energies further suggest that the dissolution process and hence the potential stability of L-serine is more spontaneous in the NaF-water solvent system compared to the KF-water system. On the other hand, the positive increment of transfer Gibbs free energies for L-isoleucine indicates a non-spontaneous dissolution and lower stability of L-isoleucine in both experimental electrolytic solutions. In addition, the low root mean square deviation (RMSD) and relative average deviation (RAD) values obtained in this study confirm the applicability and accuracy of the modified Heidman empirical equation for modeling the temperature-dependent solubility of L-serine and L-isoleucine in aqueous sodium and potassium fluoride solutions. This robust agreement between the model and experimental data supports the continued use of this equation for predictive solubility analyses and thermodynamic investigations.

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Data Availability No datasets were generated or analyzed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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