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Solubility and dissolution thermodynamics of L-histidine and L-tryptophan in aqueous ethanol solution at five equidistant temperatures

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ABSTRACT

This study highlights the saturated solubilities and dissolution thermodynamical properties of two very important amino acids viz. L-histidine and L-tryptophan having various roles in many field in pure aqueous and aqua-ethanol medium at particular as well as range of temperature employing static gravimetric method which is very systematic and error free. Finding confirms that L-histidine shows more solubility in water rich region and L-tryptophan shows more solubility in organic rich region. L-tryptophan has an extra benzene ring which makes L-tryptophan more covalent than L-histidine moiety. Consequently, solubility of former in water rich region becomes low. In connection with those mentioned properties other various physiochemical parameters like co-solvent diameter, apparent dipole moment, apparent molar volume, solvent diameter etc. are also estimated. All observations are explained clearly on the ground of several solution related interactions namely cavity forming, solvent-solvent, solvent-solute interactions etc. Both total and chemical transfer Gibbs energies as well as entropies are calculated and explained to give support to stability and variation of solubility in both aqueous and aqua-ethanol media.

1. Introduction

Chemicals, pharmaceuticals and cosmetic industries are developed rapidly in modern era with growing demand of human being. In such industries the study on solubility and related solvation thermodynamics of many biochemicals like amino acids are important. Side by side the role of amino acids moves up due to its various biological roles and vast application areas in industrial fields [1–6]. The purification and separation of these amino acids depend heavily on solvation chemistry in industrial fields during their product making. The study of the biological mechanism of these amino acids benefits from the use of thermodynamical indices like transfer entropy and transfer free energy, etc [7,8]. Therefore, a collective understanding on solvation in various solvent system like aqueous [9,10], aqueous-organic [11–17] and aqua-electrolytic solution [18–23] and its thermodynamic must be enhanced for future advancements and from past few years this area now attracts the researchers in a great interest. For example, researchers such as Nozaki, Tanford, and numerous others have embarked on investigations to elucidate the thermodynamics properties of various amino acids [24–27]. By scrutinizing the equilibrium solubility of these amino acids within aqueous organic solvents such as DMF, ethylene glycol, DMSO, ACN, glycerol and 1-butyl-2,3-dimethylimidazolium bromide, these scientists have managed to ascertain crucial insights. Their studies were meticulously designed to explore the intricate interactions at play, ultimately leading them to profound conclusions concerning the relative stability of the amino acids in different solvent systems.

L-histidine and L-tryptophan are considered here because of their attractive as well as important roles in living world [28]. Moreover tryptophan is used for the synthesis of niacin, also known as vitamin B3,

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which is indispensable for proper energy metabolism and DNA synthesis [29]. Furthermore, L-histidine fulfils a distinctive role in maintaining pH homeostasis through proton buffering, facilitating metal-ion chelation, and acting as a scavenger of reactive oxygen [30]. Histidine is precursor for several hormones (thyrotropin releasing hormone) [31] and critical metabolites which affect renal function basically. However, histidine has diverse functional properties, assumes various roles in protein interactions [32]. Notably, it frequently serves as a pivotal residue in enzyme catalytic reactions, playing a crucial role in facilitating and modulating the efficiency of these biochemical processes.

In very recent time solubility behaviour of L-tryptophan has been studied in aqueous methanol system [33]. Even yet, many successful studies on mentioned amino acids have been conducted, but none have addressed comparative account on the solubility and dissolution thermodynamics of L-tryptophan and L-histidine in aqueous and aqueous-ethanol solution. Therefore, our basic research target is the study of effect on addition of ethanol as co-solvent in comparison to pure aqueous solution on the saturated solubility and corresponding thermodynamical parameters of both mentioned amino acids through both temperature and concentration sweeping. In connection with this our aim to compare the saturated solubilities in both aqueous and aqueous ethanol solution between both amino acids and effect of temperature on saturated solubility of both amino acids in pure water as well as in cosolvent system. The change of thermodynamical parameters like transfer Gibbs energy, transfer entropy etc is also focused in this research by both temperature and concentration tuning. Due to its low boiling point, ethanol was a preferred choice for the studied solvent. Additionally, it hastens the crystallisation of both amino acids. In this study, an analytical gravimetric method was employed to determine the saturated solubilities of L-tryptophan and L-histidine in water and aqueous ethanol over a temperature range of 288.15–308.15 K. The obtained results shed light on the solvation energy associated with these amino acids, which is valuable for elucidating the relative stability of the substances in the mentioned solvent system. Additionally, this knowledge contributes to our understanding of the thermodynamic behavior of L-tryptophan and L-histidine in different solvents, providing insights that can be utilized in future industrial applications and growth. By comprehending the solubility characteristics of these substances, researchers and industry professionals can make informed decisions regarding their handling, formulation, and potential applications in various fields.

2. Material and methods

Purchasing source, initial purity, purification method and final purity of all the materials used in our experiment are tabulated in Table 1. At first both used amino acids were perched in completely evacuated desiccator under their melting point for 15 days. After that those were completely dehydrated with the help of temperature-controlled oven by keeping temperature at 380.15 K for 7 days. They were then chilled and stored in a vacuum desiccator for five hours prior to use. No change in weight confirmed to draw the conclusion that there no moisture was present. All solutions were created using triple-distilled water, which had a very low conductivity throughout the entire experiment (0.9 micro siemens/cm).

A series of ethanol (EtOH) standard solutions with different mole fraction concentrations (0.00, 0.089, 0.207, 0.403, 0.610, 0.779, and 1.00) were prepared individually for each amino acid in order to investigate their solubility and related thermodynamic parameters. The precise amount of EtOH was dissolved in triple-distilled water using stoppered measuring flasks to ensure accurate mixing. The water contents of the ethanol was determined by Karl-Fisher titration and found to be less than 0.03 mol•dm^{-3}.

Glass tubes with stoppers were stuffed with solid tryptophan and solid histidine separately, which was thoroughly mixed for two days. To conduct the tests, a low cum high thermostat was used. The accuracy of the thermostat, which is roughly ± 0.10 K, makes it very skilful to enter a precise temperature. By creating five sets of equilibrated solutions—one for each of the aforementioned amino acids and keeping them at the right temperatures, equilibrium was found. The solutions were continually swirled throughout the experiment for a period longer than 24 h.

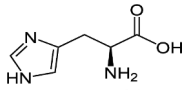
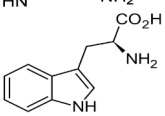
To prepare for the gravimetric technique [34], a stoppered glass test tube was allowed to settle undisturbed at the optimal temperature for a minimum of 7 h before sampling for making it easier for undissolved amino acids to settle. Subsequently, 5 ml of the mixed saturated solution was extracted from each mole fraction composition using a dry pipette. The obtained solutions were filtered using a disposable 0.22 μm HPLC filter, transferred to glass jars, and quickly weighed. In order to dry the solutions for subsequent separation of the L-amino acids, they were evaporated and thoroughly dried in a stove at a temperature of approximately 400.15 K. After being cooled in a dehydrator using silica gel over a 12-hour period, the dried mass was measured through weighing with an analytical balance having accuracy ± 0.1 mg.

3. Discussion

3.1. Solubility

The obtained solubility data for the current amino acids are shown in Table 2 and 3 and presented graphically in Figs. 1-4 and those are explained one by one. The present solubility data also correlated and compared with the literature [39–44] data. The most of the data found in literature showed an excellent agreement in pure water and in pure ethanol solvent system. Only few data were found anomalous. That might be due to use of different quality of amino acids and solvent system or might be their methodical error. Here it is to be mentioned that in the earlier studies only few data are available for the current amino acids in pure water and pure ethanol. But in our studied we have shown in five different temperatures in different mole fraction of concentration of ethanol in aqueous media. In the current study we have shown the respective solvations thermodynamics to justify the current

Table 1
Chemical Compounds, CAS numbers, and their purification.

Sample Name	Structure	Purchase	CAS No.	Initial Purity[z]	Purification Method	Final Purity
L-histidine		SRL, Maharashtra. India.	71-00-1	99 % (mass)	drying in a dehydrator with silica gel	99.5 % (mass)
L-tryptophan		SRL Maharashtra, India.	73-22-3	99 % (mass)	drying in a dehydrator with silica gel	99.5 % (mass)
Ethanol Water	CH_3CH_2OH H_2O	Analytical CSS reagent Merck life Sci. Pvt.	64-17-5 DE2DF72721	99.9 % (mass) 100 %	Distilled under reduced pressure distillation	99.9 % (mass) 100 %

[z] Declared by company.

Table 2
Solubility of L-tryptophan in water and different mole fraction of ethanol mixture at different temperatures at 0.1 MPa[b] and comparison of literature results.

Mole fraction of ethanol	Mole fraction solubility of L-tryptophan × 10^3 at different temperatures (K[#])				
(X_{EtOH})	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K
0.000	1.162 (1.13) [39]	1.192 (1.24) [39]	1.220 (1.37) [39] (1.169) [40] (1.215) [41] (1.034) [42] (1.212) [39]	1.246 (1.54) [39]	1.278 (1.74) [39]
0.089	1.085	1.108	1.113	1.154	1.174
0.207	1.019	1.032	1.055	1.085	1.104
0.403	0.693	0.711	0.741	0.766	0.792
0.610	0.386	0.405	0.438	0.468	0.514
0.779	0.307	0.328	0.343	0.357	0.384
1.000	0.142 (0.14) [39]	0.178 (0.17) [39]	0.209 (0.20) [39]	0.246 (0.24) [39]	0.284 (0.28) [39]

[#] Standard uncertainties u are u(T) = 0.10 K; [b]relative uncertainties $u_r(p)$ = 0.03 and relative uncertainties in solubility $u_r(S \times 10^3)$ = 0.008.

Table 3
Solubility of L-histidine in water and of different mole fraction concentration of ethanol mixture at different temperatures at 0.1 MPa[b.]

Mole fraction of ethanol	Mole fraction solubility of L-histidine × 10^3 at different temperatures (K[#])				
(X_{EtOH})	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K
0.000	3.795 (3.845) [44]	4.182 (4.172) [44]	4.598 (5.036) [40] (4.587) [44] (4.968) [41] (4.959) [43]	5.150 (5.100) [44]	5.701 (5.621) [44]
0.089	3.350	3.550	3.988	4.704	4.905
0.207	0.902	1.086	1.280	1.504	1.722
0.403	0.342	0.380	0.442	0.488	0.591
0.610	0.100	0.114	0.140	0.152	0.174
0.779	0.059	0.066	0.070	0.076	0.084
1.000	0.016	0.020	0.028	0.031	0.039

[#] Standard uncertainties u are u(T) = 0.10 K; [b]relative uncertainties $u_r(p)$ = 0.03 and relative uncertainties in solubility $u_r(S \times 10^3)$ = 0.001.

results and explained the relative stability of the experimental amino acids in the current solvent system as a novel finding (see Tables 4, 5 & 6).

In pure water L-histidine is more soluble than L-tryptophan at a particular temperature [Fig. 4]. Both amino acids contain heterocyclic moiety. But L-tryptophan has an extra benzene ring which makes L-tryptophan more covalent than L-histidine moiety. Consequently, solubility of former in pure water becomes low. This is also supported by their dipole moment values. L-histidine [10.68 D] [35] experience greater dipole–dipole/ion–dipole interaction with water than L-tryptophan [1.378 D] [36]. Beside this L-histidine is effectively solvated by water molecule through H-bonding due to presence of extra nitrogen atom in heterocyclic ring resulting higher solubility. In pure water solubility of both amino acids rises up with enhancement of temperature gradually. Water molecules [0.274 nm] [37] associate together through intermolecular H-bonding. With rising temperature more and more

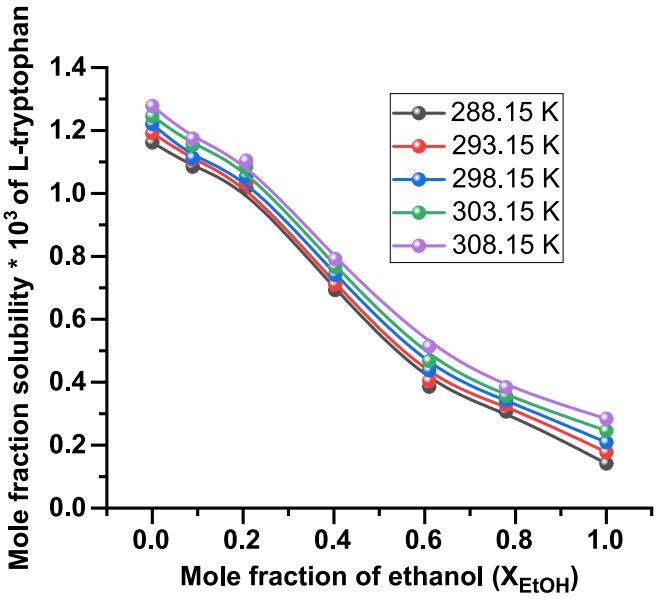


Fig. 1. Solubility variation of L-tryptophan with co-solvent ethanol mole fraction at particular temperature.

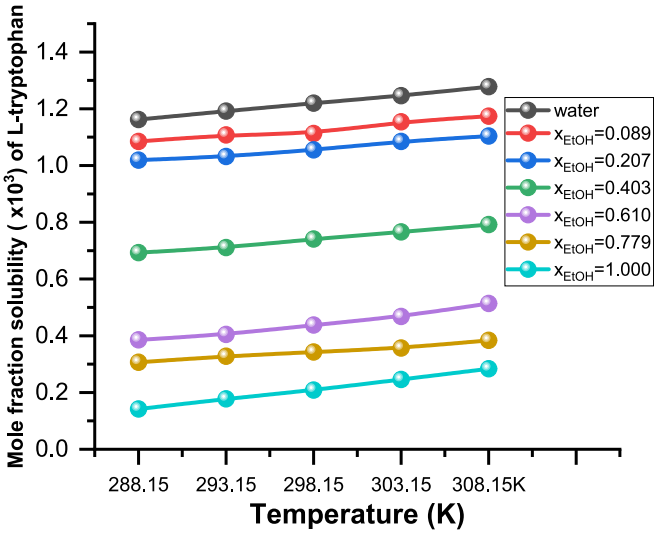


Fig. 2. Alternation of mole fraction solubility of L-tryptophan with the variation of temperature.

water molecules become free to interact with zwitterionic form of amino acid resulting moving up effective ion–dipole interaction which in turn resulting enhancement of solubility.

With rising mole fraction of ethanol, the solubility of both amino acids goes down at a particular temperature. Ethanol acts as anti-solvent for both amino acids. Before addition of ethanol amino acids fruitfully interact with water. But when ethanol (0.44 nm) [38] comes; it replaces amino acids due to its comparable size and structure. Thus, it reduces numbers of available water [0.274 nm] [37] molecule toward amino acids reflecting lesser solvation as well as lowering solubility.

At particular mole fraction of co-solvent, the solubility of both amino acids rises up with hike in temperature. In aqua-ethanol solution intermolecular H-bonding, dipole–dipole interaction are major contributing forces responsible for solvent–solvent association. When temperature increment occurs, their union breaks down and consequently a large number of water molecules become free to make new association with present amino acids trough ion–dipole interaction; resulting rising

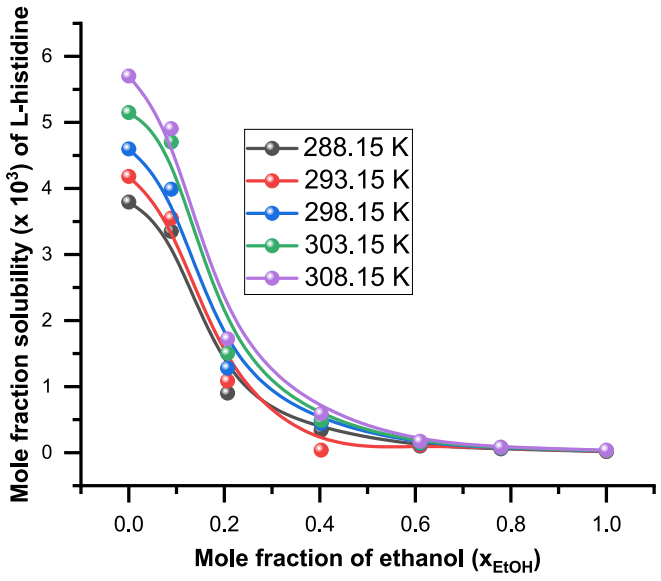


Fig. 3. Solubility variation of L-histidine with ethanol mole fraction at particular temperature.

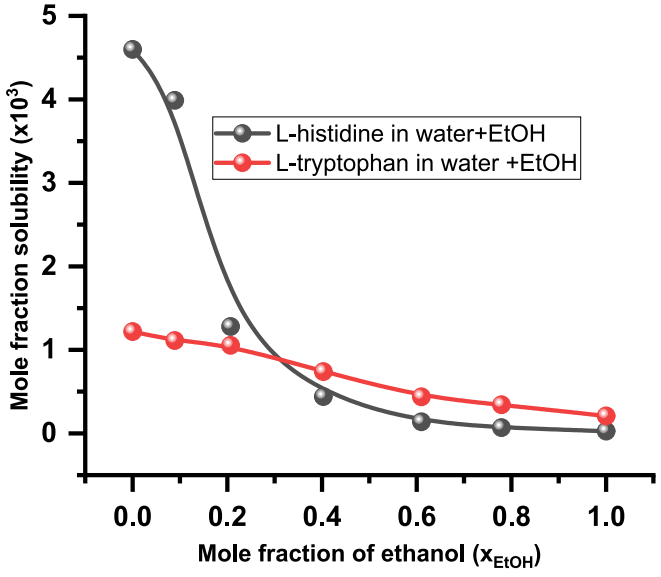


Fig. 4. Solubility comparison of L-histidine and L-tryptophan in mole fraction scale with the variation of ethanol mole fraction at 298.15 K.

solubility gradually.

At lower ethanol mole fraction L-histidine shows greater solubility than L-tryptophan but reverse is seen at higher ethanol concentration. This fact can be explained on the ground of dipole moment difference of both amino acids. Generally greater the dipole moment higher will be the dipole–dipole interaction. L-histidine has greater dipole moment value than L-tryptophan and as a result at lower ethanol mole fraction histidine interacts better with water molecules in comparison with L-tryptophan and when ethanol mole fraction goes on increasing then L-histidine now makes better interaction with ethanol moiety and resulting lowering solubility. The UV–Vis spectroscopic study suggests that there is no any major chemical reactions occur in the solution system with the present experimental solvent systems and the spectrum and explanation were shown in Supplementary Information section.

3.2. Transfer Gibbs energy

Table 5 and Fig. 5 present the changes and comparisons in the total transfer Gibbs free energy ($\Delta G_t^0(i)$), while Table 6 and Fig. 6 display the total chemical transfer Gibbs free energy ($\Delta G_{t,ch}^0(i)$) for the amino acids under investigation. These results demonstrate a positive increase in both parameters as the mole fraction of ethanol increases at a specific temperature. This observation can be attributed to various chemical interactions, including dipole–dipole interactions, cavity formation interactions, dispersion interactions, and other relevant factors. These interactions contribute to the overall thermodynamic behavior and solubility of the amino acids in the ethanol–water system.

The $\Delta G_t^0(i)$ can be expressed into three components: $\Delta G_{t,cav}^0(i)$, $\Delta G_{t,d-d}^0(i)$ and $\Delta G_{t,ch}^0(i)$. In this case, we are assuming that the contribution from dipole-induced dipole interactions ($\Delta G_{t,d-d}^0(i)$) is negligible [38]. Table 6 reveals that the $\Delta G_{t,cav}^0(i)$ values for both L-histidine and l-tryptophan gradually become more negative as the mole fraction of ethanol increases in the binary solvent mixtures. These results indicate that cavity interactions play a significant role in enhancing the stability of L-tryptophan with increasing mole fraction of ethanol. The larger size of ethanol (4.4 Å) [38] compared to water (2.74 Å) [37] implies that the energy changes associated with the creation of cavities for both amino acid moieties in ethanol–water mixtures are more favorable. As a result, the presence of ethanol in the solvent mixture facilitates the formation of cavities, leading to increased stability of L-tryptophan.

Further analysis of the ($\Delta G_{t,d-d}^0(i)$) values (Table 6) reveals for L-histidine that become more positive (i.e., less stabilized) compared to L-tryptophan as the mole fraction of ethanol increases. This phenomenon can be attributed to the larger dipole moment value of L-histidine in comparison to L-tryptophan. Additionally, this observation is supported by the hard-sphere diameter of the amino acids. The larger dipole moment of L-histidine implies stronger dipole–dipole interactions, which contribute to a less favorable stabilization in the presence of ethanol. On the other hand, L-tryptophan exhibits a smaller dipole moment, resulting in weaker dipole–dipole interactions and a relatively more favorable stabilization with increasing mole fraction of ethanol. This trend is consistent with the differences in the hard-sphere diameters of the amino acids, further supporting the influence of molecular size and dipole moment on their interactions with ethanol in the solvent mixture.

Fig. 6 illustrates the relationship between the variation of $\Delta G_{t,ch}^0(i)$ of L-tryptophan and the mole fraction of ethanol in aqueous-organic solvent systems. The $\Delta G_{t,ch}^0(i)$ exhibit an increasing trend as the mole fraction of ethanol is enhanced. This observation suggests that the presence of ethanol in the solvent system leads to the destabilization of L-tryptophan. The destabilization of L-tryptophan can be attributed to the disruption of extensive hydrogen bonding between water molecules and the hydrophilic heads of L-tryptophan upon the introduction of ethanol into the aqueous solution. As the mole fraction of ethanol increases in water, the hydroxyl groups from water molecules preferentially form hydrogen bonds with ethanol molecules rather than with L-tryptophan. Consequently, the interactions between solvent molecules (ethanol and water) become more favorable compared to the interactions between solute molecules (L-tryptophan) or solute–solvent interactions. This result also can be attributed to the fact that ethanol possesses a lower dielectric constant compared to water. The lower dielectric constant of ethanol implies weaker electrostatic interactions between the solute and solvent molecules, leading to reduced stability for L-tryptophan. Based on the results, the stability order of L-tryptophan in the solvent systems investigated can be ranked as follows: water–ethanol < water.

In Fig. 6, the comparative bar diagram shows that L-histidine exhibits less destabilization compared to L-tryptophan when the mole fraction of ethanol increases. This difference in destabilization can be

Table 4
Variation of Gibbs free energies of solutions (ΔG_s^0) of L-histidine and L-tryptophan in aqueous ethanol solvent mixtures.

288.15 K		293.15 K		298.15 K		303.15 K		308.15 K	
S (mole fraction solubility × 10^3)	ΔG_s^0 kJ/mol	S (mole fraction × 10^3)	ΔG_s^0 kJ/mol	S (mole fraction × 10^3)	ΔG_s^0 kJ/mol	S (mole fraction × 10^3)	ΔG_s^0 kJ/mol	S (mole fraction × 10^3)	ΔG_s^0 kJ/mol
L-histidine	13.3537		13.3487		13.3413		13.2793		13.2379
3.795		4.182		4.598		5.150		5.701	
3.350	13.6525	3.550	13.7481	3.988	13.6942	4.704	13.5076	4.905	13.6232
0.902	16.7959	1.086	16.6348	1.280	16.5112	1.504	16.3816	1.722	16.3050
0.342	19.1192	0.038	19.1942	0.442	19.1469	0.488	19.2185	0.591	19.0448
0.100	22.0650	0.114	22.1285	0.140	21.9967	0.152	22.1583	0.174	22.1775
0.059	23.3291	0.066	23.4606	0.070	23.7149	0.076	23.9053	0.084	24.0432
0.016	26.4553	0.020	26.3705	0.028	25.9862	0.031	26.1655	0.039	26.0089
L-tryptophan									
1.162	16.1891	1.192	16.4079	1.220	16.6302	1.246	16.8559	1.278	17.0689
1.085	16.3533	1.108	16.5860	1.113	16.8577	1.154	17.0492	1.174	17.2864
1.019	16.5037	1.032	16.7592	1.055	16.9904	1.085	17.2046	1.104	17.4439
0.693	17.4273	0.711	17.6672	0.741	17.8661	0.766	18.0821	0.792	18.2948
0.386	18.8293	0.405	19.0389	0.438	19.1694	0.468	19.3239	0.514	19.4025
0.307	19.3778	0.328	19.5528	0.343	19.7755	0.357	20.0063	0.384	20.1495
0.142	21.2250	0.178	21.0425	0.209	21.0035	0.246	20.9449	0.284	20.9223

Table 5
Thermodynamic coefficients a, b and c and variation of transfer Gibbs free energy ($\Delta G_t^0(i)$) and transfer entropy ($T\Delta S_t^0(i)$) in kJ/mol.

Mole fraction of EtOH (x_{EtOH})	a (kJ/mol)	b (kJ/mol/K)	c (kJ/mol/K)	$\Delta G_t^0(i)$(kJ/mol)	$T\Delta S_t^0(i)$(kJ/mol)
L-histidine					
0.000	−49.59	1.4477	−0.21705	0.000	0.000
0.089	−31.65	1.0518	−0.15793	0.332	−0.018
0.207	106.66	−1.8847	0.27771	3.163	5.575
0.403	−172.32	4.3165	−0.64486	5.865	−1.044
0.610	124.59	−2.3318	0.34892	8.757	−3.321
0.779	−13.43	0.6205	−0.08706	10.349	−12.946
1.000	246.03	−4.8145	0.71556	12.806	4.757
L-tryptophan	−0.70	0.1377	−0.01397	0.000	0.000
0.000					
0.089	−33.22	0.8590	−0.12130	0.210	−0.729
0.207	−21.97	0.6102	−0.08416	0.371	−0.714
0.403	−13.89	0.4686	−0.06355	1.244	0.348
0.610	−110.24	2.7444	−0.40548	2.575	4.614
0.779	−20.32	0.6732	−0.09456	3.138	1.269
1.000	177.67	−3.4396	0.51146	4.366	17.347

attributed to the lower hydrocarbon character and higher dipole moment value of L-histidine. Due to its lower hydrocarbon character, L-histidine experiences weaker hydrophobic interactions with the surrounding solvent molecules. As a result, the solvent–solvent interactions in the presence of ethanol are less favorable for L-histidine compared to L-tryptophan. The higher dipole moment value of L-histidine also contributes to its stronger interactions with the solvent molecules, which can partially offset the destabilizing effect of ethanol.

3.3. Transfer entropies

Tables 5, 6 and Fig. 7 reflect the variation as well as comparison of total entropy of transfer of our investigated amino acid L-histidine. The variation of mentioned parameter basically arises out through the change of solvent–solvent interactions in presence of solute amino acids. L-histidine show unusual variations with the variation of co-solvent concentration. This solvent–solvent interaction in turn basically depends on two important factors viz dipole moment and size of all constituents present in solution system. With rise of mole fraction of ethanol solvent–solvent interaction initially rise up due to comparable size of both solvent and vice-versa solvent–solute interaction become lower to some extent and as a result negative value of $T\Delta S_t^0(i)$ is shown for L-histidine. But with further rise of ethanol mole fraction the solvent–solute interaction predominate due to rise of hydrophobic interaction between the solvent and solute molecules, resulting positive value of $T\Delta S_t^0(i)$ After reaching a certain mole fraction value with the introduction of more ethanol to the aqua-amino acid system, again solvent-cosolvent interaction predominating and gives rise to negative change to this value (see Fig. 7).

With the increase of ethanol concentration, the solute–solvent dipole–dipole interaction gets more favourable in positive direction (Table 6).

Since ethanol (4.4 Å) is larger than water (2.74 Å), the energy changes involved in the formation of holes for L-histidine moieties in ethanol–water combinations are likely to be more advantageous. As a result, the presence of ethanol in the solvent mixture makes it easier for cavities to form, which increases stability of L-histidine and resulting rising randomness of solvent molecules causing positive increment of $T\Delta S_{t,cav}^0(i)$ values as tabulated in Table 6.

When we move from binary to ternary system $T\Delta S_{t,ch}^0(i)$ values (Fig. 8) shows negative increment because of extent of H-bonding present within the system. Ethanol makes better H-bonding, with water compared to L-histidine molecules due to bearing heterocyclic hydrocarbon part resulting better solvent-co-solvent interaction and this influence the variation of $T\Delta S_{t,ch}^0(i)$ Initially solvent–solvent interaction is somewhat hampered due to cavity size factor. But after a certain

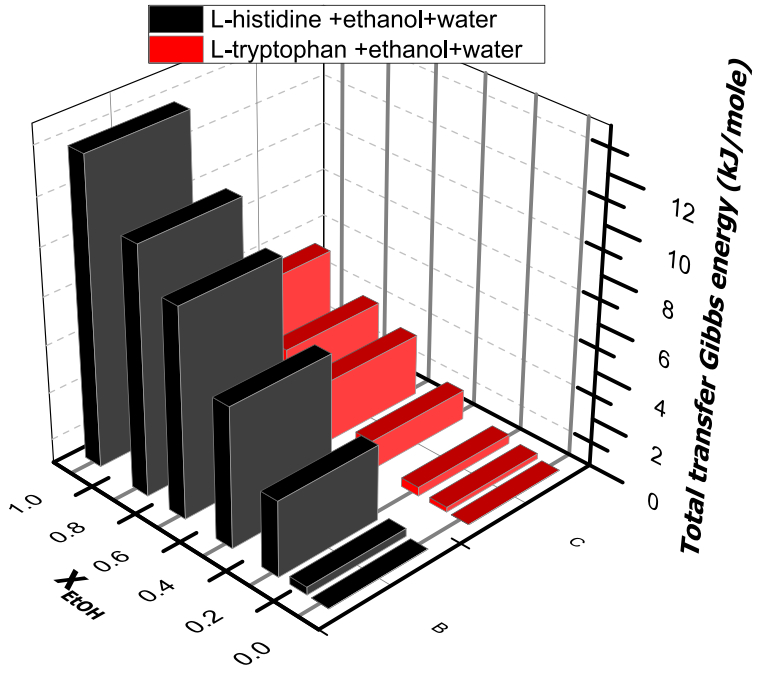


Fig. 5. Alternation and comparison of total transfer Gibbs energy of experimental amino acids with change of ethanol mole fraction at 298.15 K.

Table 6
Transfer Gibbs energies ΔG_t^0(i), $\Delta G_{t,cav}^0$(i), $\Delta G_{t,d-d}^0$(i), $\Delta G_{t,ch}^0$(i) and transfer enthalpy, $\Delta H_{t,cav}^0$(i) and transfer entropies $T\Delta S_t^0$(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-histidine and L-tryptophan from H_2O to H_2O-EtOH at 298.15 K in **kJ/mol**.

Mole fraction of EtOH (x_{EtOH})	ΔG_t^0(i) kJ/mol	$\Delta G_{t,cav}^0$(i) kJ/mol	$\Delta G_{t,d-d}^0$(i) kJ/mol	$\Delta G_{t,ch}^0$(i) kJ/mol	$T\Delta S_t^0$(i) kJ/mol	$\Delta H_{t,cav}^0$(i) kJ/mol	$T\Delta S_{t,cav}^0(i)\Delta S_{t,cav}^0$ kJ/mol	$T\Delta S_{t,dd}^0$(i) kJ/mol	$T\Delta S_{t,ch}^0$(i) $T\Delta S_{t,ch}^0$ kJ/mol
L-histidine									
0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
0.089	0.332	−1.228	1.227	0.333	−0.018	−1.241	−0.012	1.341	−1.347
0.207	3.163	−2.489	4.769	0.883	5.575	−2.113	0.379	5.205	−0.009
0.403	5.865	−3.968	8.856	0.977	−1.044	−2.620	1.348	10.409	−12.802
0.610	8.757	−5.112	12.822	1.047	−3.321	−2.791	2.322	13.940	−19.583
0.779	10.349	−5.812	14.119	2.042	−12.946	10.150	15.962	14.002	−42.910
1.000	12.806	−6.434	14.601	4.639	4.757	11.903	18.334	15.166	−28.7431
L-tryptophan									
0.000									
	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
0.089	0.210	−1.339	0.033	1.516	−0.729	−1.54	−0.201	0.036	−0.564
0.207	0.371	−2.690	0.128	2.933	−0.714	−2.62	0.07	0.139	−0.923
0.403	1.244	−4.228	0.257	5.215	0.348	−3.26	0.968	0.280	−0.900
0.610	2.575	−5.383	0.346	7.612	4.614	−3.48	1.903	0.376	2.335
0.779	3.138	−6.064	0.382	8.820	1.269	12.40	18.464	0.377	−17.572
1.000	4.366	−6.624	0.395	10.595	17.347	14.48	21.104	0.409	−4.166

Standard uncertainty in temperature u(T) = 0.10 K; Estimated uncertainties in ΔG_t^0(i) and Δ T ΔS_t^0(i) are about "0.004 kJ/mol and 0.002 kJ/mol respectively.

concentration solvent–solvent interaction predominates over solvent–solute interaction for L-histidine due to comparable size of co-solvent mixture producing negative increment of total $T\Delta S_{t,ch}^0(i)$ values.

When ethanol is introduced, L-tryptophan interacts favourably with ethanol due to their similar sizes, and as a result, the solvent–solute interaction rises and vice-verse solvent-cosolvent interaction moves down producing large number of free solvent molecule creating a positive $T\Delta S_{t,}^0(i)$ value as shown in tabulated in Table 6. Initially, solvent–solvent interaction predominates, leading to a negative $T\Delta S_{t,}^0(i)$ value because at low ethanol concentration L-tryptophan makes unfavourable interaction with both solvent and co-solvent due its low dipole moment value and large size. Two parameters vis $T\Delta S_{t,d-d}^0(i)$ and $T\Delta S_{t,cav}^0(i)$ shows exactly similar variation as shown in L-histidine. The values differ for a particular concentration of ethanol is due to greater dipole moment value and smaller size of L-histidine compared to L-tryptophan. That is why the $T\Delta S_{t,ch}^0(i)$ value differ Basically, with increasing concentration of ethanol, solvent-cosolvent interaction rises up gradually due to large size of L-tryptophan resulting poor holding

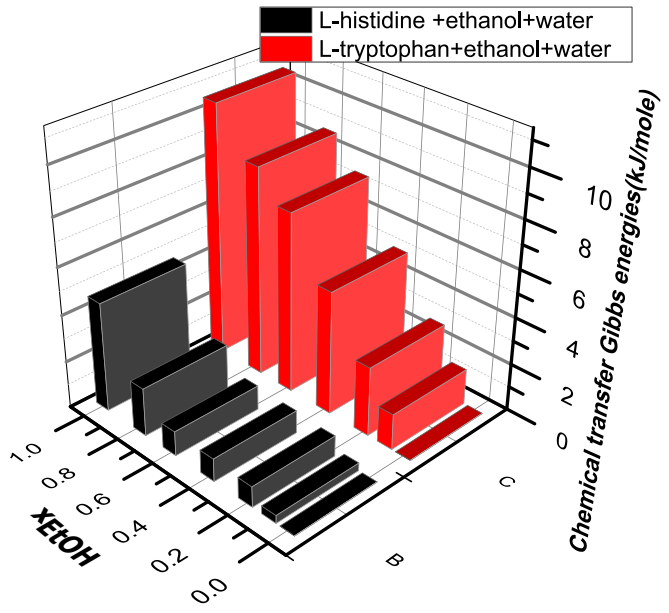


Fig. 6. Alternation and comparison of total chemical transfer Gibbs energy of experimental amino acids with change of ethanol mole fraction at 298.15 K.

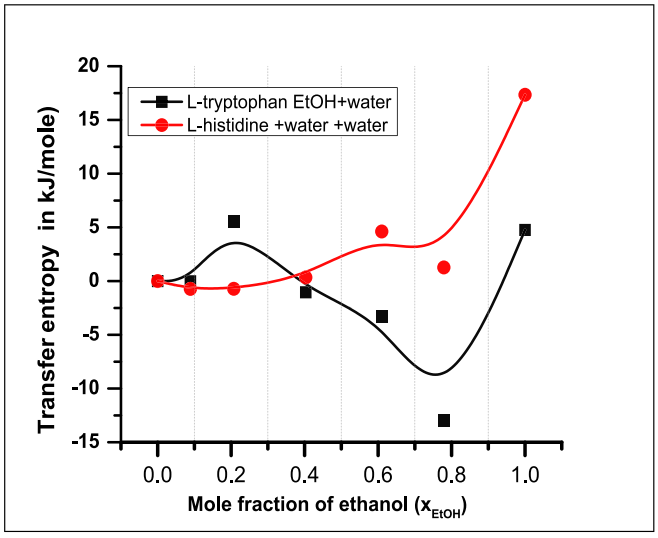


Fig. 7. Variation and comparison of transfer entropy of both amino acids with mole fraction variation of co-solvent ethanol 298.15 K.

solvent water molecule and consequently more water become free to interact with ethanol exhibiting strong H-bonding causing lowering of randomness of water molecule giving negative value of $T\Delta S^{0}_{t,ch}(i)$. But the variation is not following a smooth way due to others complex nature of interactions in solution system.

4. Conclusion

In conclusion, this experimental investigation focused on studying the solubility and solvation thermodynamics of two biologically important amino acids, L-histidine and L-tryptophan, at various temperatures in the presence of different mole fractions of ethanol. Results showed that L-histidine is more soluble in water rich region and L-tryptophan is more soluble in organic rich region. The solubility behavior of these amino acids was examined from multiple perspectives, and the results were supported by a comprehensive analysis of the

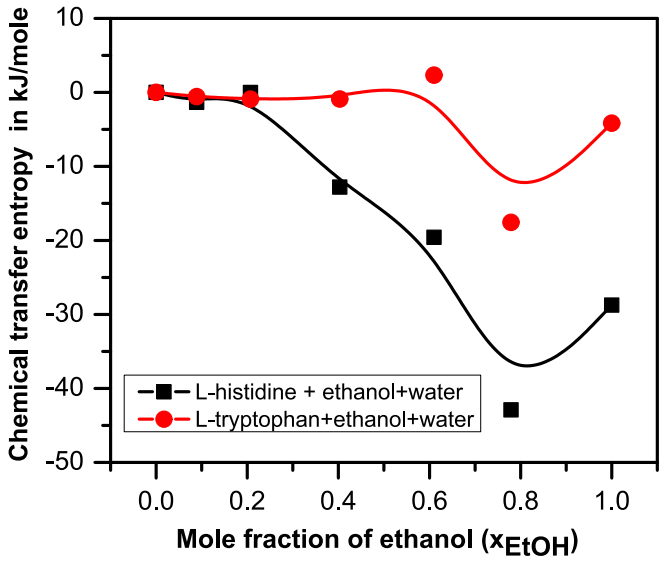


Fig. 8. Variation and comparison of Chemical transfer entropy of both amino acids with mole fraction variation of co-solvent ethanol at 298.15 K.

various interactions between the solvent and solute, as evidenced by the tabular data. Furthermore, the influence of temperature on the solubility of both amino acids was explored, and appropriate explanations were provided. The study also revealed that the chemical stability of the amino acids in the co-solvent mixture depended on the size and dipole moment values of all constituents in the solution. The results of this investigation demonstrated that the standard transfer Gibbs free energy change of solution and standard molar enthalpy change owing to cavity-forming contact both shows positive rising with enhancement of ethanol concentration, demonstrating that the solvation process was non-spontaneous and endothermic in nature. The change of chemical standard transfer Gibbs free energy of solutions revealed that L-tryptophan and L-histidine both are effectively more stable in pure water than in a mixed water–ethanol environment. The negative chemical entropy change suggests lesser solvent–solvent interaction with rising ethanol concentration for both investigated amino acids. Complex interactions responsible for some deviated values than usual which are needs further investigations. These findings contribute to understanding of the solubility and dissolution behavior of amino acids in complex solvent environments, providing valuable insights for future research in the theoretical field by using thermodynamical modelling to show the interactional phenomena in complex aqueous solvent systems and to justify the results for valuable applications.

CRediT authorship contribution statement

Avishek Saha: Conceptualization, Investigation. **Kalachand Mahali:** Conceptualization, Investigation. **Puspal Mukherjee:** Conceptualization, Investigation. **Sintu Ganai:** Conceptualization, Investigation. **Aslam Hossain:** Writing – original draft. **A.M.A. Henaish:** Writing – review & editing. **Simanta Kundu:** Conceptualization, Investigation. **Jahangeer Ahmed:** Writing – review & editing. **Sanjay Roy:** Writing – original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.molliq.2023.122852.

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