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Analyzing of L-tryptophan thermodynamics and its solubility in aqueous acetonitrile blends at diverse temperatures

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ABSTRACT

This paper delves into an investigation of the solubility characteristics of L-tryptophan within binary solvent systems containing aqueous acetonitrile. The primary emphasis of the study revolves around assessments based on mole fractions. The study utilizes these solubility values to assess thermodynamic constraints, including solution entropies and solution transfer free energetics. The calculated thermodynamic energies are correlated with interaction parameters, including Gibbs free energies and entropies, pertaining to the transfer of L-tryptophanfrom water to binary solvent blends of acetonitrile and water. Mathematical expressions are utilized to determine the transfer Gibbs free energies for chemical interactions, and the consequent entropies are clarified within the framework of solvent-solvent interactions. To expound upon the stability of L-tryptophan within the water-acetonitrile mixed system, we investigate the energetic aspects related to the transfer of chemicals Gibbs free energies. Additionally, standard temperature (298.15 K) is employed to calculate various related physicochemical parameters of solute/solvent.

1. Introduction

An important essential amino acidL-tryptophan thatis required not onlyin the synthesis of proteins but also has been used as precursor in the production of vitamin niacin and serotonin hormone [1]. Eggs, dairy, poultry, and red meat all these are considered as natural source ofit. The numerous organs of human body hinge on consumption of L-tryptophan by the body. The human body cannot produce L-tryptophan naturally and therefore it must be taken from diet and supplements. Part of the L-tryptophan that is absorbed from meals is converted by the body to 5-HTP and subsequently to an important neurotransmitter serotonin [2] which helps nerve cells to communicate with one another. L-tryptophanis used to treat depression, sleeplessness, severe PMS symptoms, and a host of other elements. Major neurotransmitter serotonin (5-HT) regulates several serotonergic functions [3] such as temper, anger, pain, nervousness, laziness, memory, eating habits, addictive behavior etc., and helps in temperature regulation, endocrine function, and motor behavior, among other central nervous system functions. As the characteristic amino acid precursor for 5-HT biosynthesis, tryptophan raises the synthesis of 5-HT in the brain, which may in turn promote 5-HT release and function. To treat mental depression, L-tryptophan is taken in combination with other drugs [4]. In addition, L-tryptophan and lithium are used to get relief from bipolar disorder [5].

Now in order to understand the biological function of L-tryptophan and to make the dietary substances from which we get L-tryptophan as supplements, one of the most needful concepts to know aboutits solubility and its corresponding thermodynamic parameters related to solvation, in electrolytic and several co-solvent mixtures, such as Gibbs energies and entropies, are examples of factors in this context.Supersaturated solutions typically directly contribute to better crystallisation

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processes. The solubility at saturation and the thermodynamics of solvation are essential the development of crystallisation techniques for L-tryptophan. In this context, it is essential to comprehend the thermodynamic parameters associated with solubility and solvation, as well as to assess the stability of L-tryptophan in various solvent systems. Solvation chemistry plays a foremost role also in the purification and separation of L-tryptophan in industrial fields during dietary product production.

Understanding thermodynamic indices like entropies and free energiesare crucial among others, and are beneficial in the investigation of the pathway of biological action of several amino acids [6,7] andthis encourage us to study on this topic. Therefore, to advance future developments, it is imperative to enhance our collective understanding of solvation across diverse solvent systems, including aqueous [8,9], aqueous-organic [10–16], and aqueous electrolytic solutions [17–20], along with a focus on the associated thermodynamics. Over the past few years, this field has drawn a lot of interest from researchers. For example, numerous solute–solvent interactions were resolved by Nozaki, [21], Tanford, [22] and other scientists [19] mainly using the equilibrium solubility. The extraction of numerous amino acids from solutions involving aqueous glycerol, ethylene glycol, urea, methanol, ethanol, acetonitrile, acetone, dimethylformamide, dimethylsulfoxide, and 1-butyl-2,3-dimethylimidazolium bromide serves as a foundation for studying thermodynamic parameters. In each case, the goals of the studies were to get an understanding of the numerous interactions and to draw conclusions regarding assessing the comparative stability of solutes like amino acids within systems comprising pure, dual, and mixed triple solvents. In this context, a recent study by A. Saha et al. delved into the solubility behavior of L-tryptophan in the methanol-water system [23]. Xinbao Li, et al., determined the solubility and discussed the solvent effects of D-tryptophan in pure acetonitrile in different temperature and pressure [24]. However, as of now, there has been no exploration into the thermodynamics governing the solubility and solvation of L-tryptophan in solutions containing both water and acetonitrile.

Acetonitrilewas preferred assolvent only because of diversified applications in versatileorganic synthesis [25]. ACN is also used as an essential solvent in the production of pharmaceuticals [26], acting as a solvent for the crystallisation process, an extraction solvent, and a reaction solvent [27]. The objective of this investigation was to assess the saturated solubilities of L-tryptophan in both water and aqueous acetonitrile (ACN) within a temperature range spanning from 288.15 to 308.15 K, employing a highly accurate analytical gravimetric method.

The results obtained from this study are anticipated to yield valuable insights into the solvation dynamics of L-tryptophan. This understanding is essential for elucidating the factors contributing to the relative stability of L-tryptophan within aqueous ACN systems. The acquired knowledge becomes especially pertinent for refining separation and crystallisation techniques applied to L-tryptophan, whether in the context of aqueous ACN systems or pure ACN. Moreover, establishing a connection between solubility and relevant thermodynamic parameters proves to be a reliable and cost-efficient approach for effectively differentiating and separating L-tryptophan originating from various natural sources.

2. Methods employed in experiments

2.1. Chemical substances and their purification processes

L-tryptophan acquired from Merck, India, (>98.5%, M.P. 563.15 K) was utilized without additional purification following drying in a vacuum desiccator. The supplier of 99.8% acetonitrile was Merck, India. First, ACN was refluxed for six hours with KOH from Merck. Fractional distillation took place after the refluxing process. The complete elimination of any ammonia produced during alkali treatment is ensured by middle fraction collection during distillation. Solutions were made using triple-distilled water, having maximum conductivity of 1.0 μs/cm, and tests were run. Table 1 displays the specific details of the samples used in the study.

2.2. Making of saturated solutions and the procedure for measurement and justification of purity

Compared to other volumetric or titration methods, the thermogravimetric method [17] is more accurate by nature. Consequently, in our study, we employed this method to evaluate the solubility of L-tryptophan in aqueous acetonitrile solvent mixtures. The initial step in this process involves establishing a saturated solution at the required temperature. In order to create the ACN solutions at 0.00, 0.088, 0.204, 0.401, 0.525, 0.684, 0.808, and 0.945 in mole fraction scale, a specific amount of ACN was mixed with water. Triple-distilled water was used to prepare solutions, ensuring thorough mixing with a stoppered measuring flask. Additional L-tryptophan was added to sealed glass tubes and mixed for 1 day interval. The experiment employed a low-cum-high thermostat with a temperature accuracy of ±0.2 K. The sealed tubes were left to stabilize at the specified temperature for seven hrs before sampling for gravimetric analysis. Measurements were taken at designated temperatures. In the process, 2.5 mL of the blended saturated solution was extracted from the upper part using a dry pipette, filtered through a disposable 0.45 μm HPLC filter, transferred to a glass vessel, and promptly weighed. Since the thermal decomposition temperature of free tryptophan is between 491.15 K and 913.15 K, the solution was evaporated until complete dryness and subsequently dried in an oven at 400.15 K for 12 h. After cooling for 24 h in a silica gel-filled dehydrator, the samples were weighed. This procedure was repetitivetill a constant mass was reached. Four successful repetitions later, we were able to maintain a constant mass. By vigorously shaking by shaker (200–250 RPM) the solutions to reach equilibrium. We evaluated the solubility of L-tryptophan in water with acetonitrile across various mole fractions at temperatures of 288.15, 293.15, 298.15, 303.15, and 308.15 K (±0.2 K) separately. A solution was considered saturated or in equilibrium when the concentrations measured at 2-day intervals remained consistent.

A crucial investigation utilizing PXRD was carried out to support the exclusive solid-phase purity of L-tryptophan. X-ray powder diffraction analysis was conducted on recrystallized L-tryptophan samples obtained from aqueous acetonitrile solutions to generate PXRD patterns for both raw materials and residual solids. The results showcase a robust correlation between the diffraction patterns of these recrystallized samples and those of pure L-tryptophan.

It is noteworthy to underscore that the overall crystal phase remains consistent throughout the experiment, indicating the preservation of L-tryptophan's chemical integrity and crystal structure. Additionally, an examination of the solubility of the residual solid phase of L-tryptophan reveals no significant deviations when compared to pure L-tryptophan (Fig. 1).

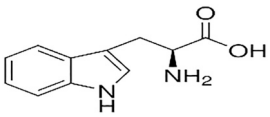
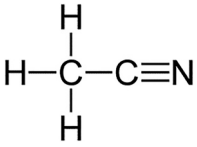
3. Discussion

3.1. Solubility and its significance

Table 2, Figs. 2 and 3 present a comprehensive overview of the mole fraction solubility of L-tryptophan in aqueous acetonitrile across different temperatures and acetonitrile compositions. X_{ACN} denotes the mole fraction of acetonitrile in the solvent mixture. It ranges from 0.088 to 0.945, indicating different compositions of acetonitrile in the solvent. The Table 2 lists solubility values at five different temperatures in Kelvin (K) from 288.15 K to 308.15 K. Temperature can significantly affect solubility, as higher temperatures often increase solute solubility.

The first row, labelled “water,” depicts the solubility of L-tryptophan in pure water, devoid of any acetonitrile. The values denote the solubility (in x 10^{-3}) of L-tryptophan in water at various temperatures. For instance, at 288.15 K, the solubility is 1.159×10^{-3} with a small

Table 1
Specification of chemicals.

Chemical Name	Chemical Structure	Source	Initial Purity [a] (fraction)	Purification Method
Tryptophan		Merck, India	>98.5% (mass)	drying in a dehydrator with silica gel
Acetonitrile		Merck, India	99.8%	Fractional Distillation
Water	H_2O	–	–	Distillation (Triple distilled)

[a] Declared by seller.

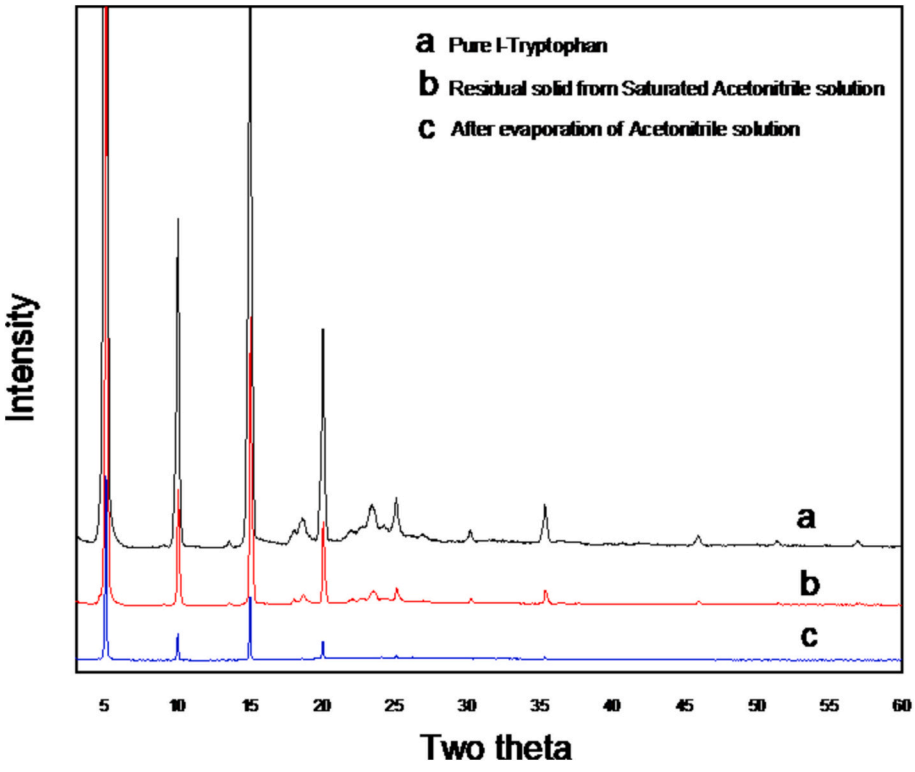


Fig. 1. Comparison of X-ray powder diffraction patterns of (a) pure L- tryptophan and (b) residual solid-phase of L- tryptophan from saturated acetonitrile solution (c) residual solid-phase L- tryptophan after evaporation of acetonitrile solution.

uncertainty of 0.02×10^{-3}.

The subsequent rows correspond to different mole fractions of acetonitrile in the solvent. These rows demonstrate how the presence of acetonitrile affects the solubility of L-tryptophan. For example, at 298.15 K and an acetonitrile mole fraction of 0.088, the solubility is 1.268×10^{-3} with an uncertainty of 0.03×10^{-3}.

As you move from left to right within a given row (same acetonitrile mole fraction), we can see how the solubility changes with increasing temperature. Generally, as the temperature increases, the solubility of L-tryptophan also tends to increase, which is a common trend for most solutes in solvents.

As move from top to bottom (across different rows with increasing acetonitrile mole fraction), one observe how the presence of acetonitrile affects the solubility. Typically, an increase in the mole fraction of acetonitrile results in a decrease in the solubility of L-tryptophan.

The Table 2 also provides uncertainties (expressed as standard deviations or errors) for each solubility value. These uncertainties represent the precision and reliability of the measurements. Smaller uncertainties indicate more precise measurements.

Overall, this Table 2 is essential for understanding the solubility behavior of L-tryptophan in aqueous acetonitrile under different conditions. Researchers can use this data to optimize conditions for processes like crystallisation, extraction, or purification, where controlling solubility is critical to achieving desired outcomes.

In this regards it is to mentioned that a study conducted by Xinbao Li and colleagues regarding the solubility and solvent effects of D-

Table 2
Mole fraction solubility (x 10^3) of L-tryptophan in aqueous acetonitrile at different temperatures (K).

X_{ACN}	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K
water	1.159 ± 0.02	1.236 ± 0.04	1.362 ± 0.05	1.529 ± 0.02	1.746 ± 0.01
0.088	1.036 ± 0.01	1.105 ± 0.02	1.268 ± 0.03	1.439 ± 0.03	1.608 ± 0.02
0.204	0.892 ± 0.02	0.993 ± 0.06	1.112 ± 0.03	1.261 ± 0.02	1.453 ± 0.012
0.401	0.677 ± 0.007	0.759 ± 0.01	0.826 ± 0.007	0.961 ± 0.001	1.074 ± 0.002
0.525	0.550 ± 0.01	0.601 ± 0.02	0.670 ± 0.002	0.772 ± 0.002	0.859 ± 0.009
0.684	0.370 ± 0.01	0.409 ± 0.003	0.445 ± 0.008	0.539 ± 0.006	0.591 ± 0.002
0.808	0.230 ± 0.005	0.264 ± 0.002	0.301 ± 0.002	0.367 ± 0.002	0.402 ± 0.004
0.945	0.078 ± 0.002	0.089 ± 0.002	0.100 ± 0.001	0.152 ± 0.004	0.170 ± 0.005
1.000	0.021 ± 0.001	0.026 ± 0.001	0.038 ± 0.002	0.056 ± 0.001	0.067 ± 0.002

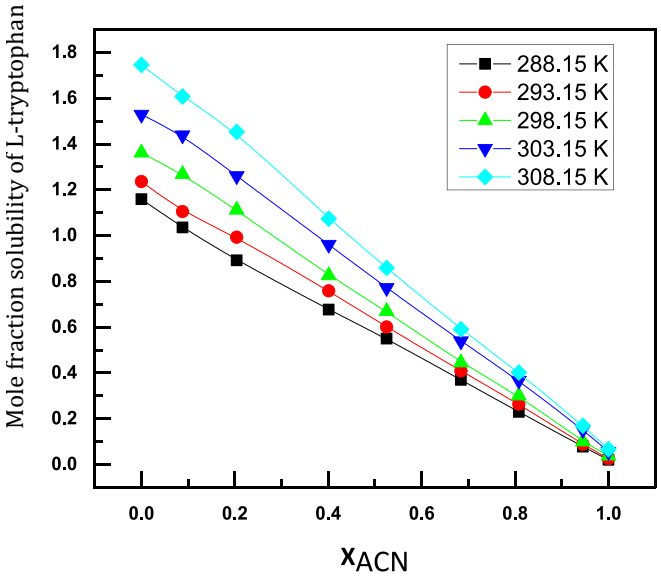


Fig. 2. Variation of solubility of L-tryptophan with mole fraction variation of acetonitrile in water in different experimental temperatures.

tryptophan in pure acetonitrile. The comparison between the results of D-tryptophan and L-tryptophan in pure acetonitrile, despite maintaining different experimental conditions, raises interesting points about stereoisomer behavior in solutions.

The fact that L-tryptophan and D-tryptophan are stereoisomers implies that they have the same molecular formula but differ in their spatial arrangement. This dissimilarity can lead to distinct interactions with solvents and affect their solubility characteristics. The factors like molecular polarity and intermolecular forces can influence solubility, and the unique molecular arrangements of stereoisomers may result in different behaviours in a given solution.

It's important to consider the specific properties of each stereoisomer when studying solubility, as subtle structural differences can lead to varying interactions with the solvent molecules. The differences observed between L-tryptophan and D-tryptophan solubility in pure acetonitrile suggest that the stereochemistry of amino acids can indeed impact their solubility profiles.

Further investigations into the solubility of these stereoisomers in aqueous acetonitrile solutions would be valuable, as the presence of water can introduce additional variables and interactions. Overall, the

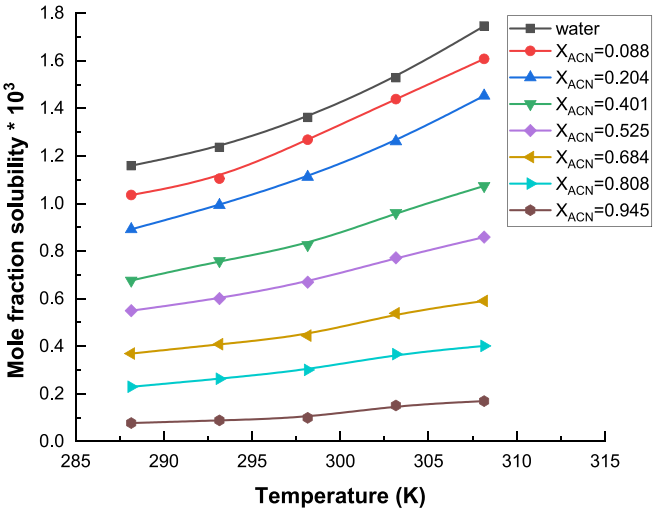


Fig. 3. Variation of mole fraction solubility of L-tryptophan with temperature in different ACN concentrations.

study contributes to our understanding of the intricate relationship between molecular structure, stereoisomerism, and solubility in different solvent environments [24]. Many other researchers also performed thermodynamic analysis of the solubility of many drug molecules in aqueous acetonitrile or in mixed organic solvents for understanding the actual dissolution of the drug molecules [28–32].

One can attribute the solubility behavior of L-tryptophan in water–ACN mixtures to the special characteristics of ACN as a polar aprotic solvent. Compared to water, ACN has less basic and less acidic properties [33] which cause L-tryptophan to dissolve poorly in water-ACN mixtures. The lowering facility of acetonitrile to give or accept hydrogen bonds restricts its ability to solvate L-tryptophan molecules efficiently, which results in decreased solubility. This can be also supported by polarity concept. Being contains hydrocarbon component with a higher covalent character than water, acetonitrile has a lower polarity than water, which reduces the efficiency of H-bonding. But in the solution, co-solvent can form an H-bond with H_2O more easily than it can with L-tryptophan onlybecause of better dipole-dipole interaction exhibit between solvent water and co-solvent acetonitrile. Dipole moment data also supports this fact. The dipole moment value for water, acetonitrile and L-tryptophan are 1.83D, 3.45D [31] and 1.378D [35] respectively. Therefore, a greater acetonitrile concentration in the solution decreases the amount of water molecules that are available for L-tryptophan, which causes L-tryptophan to be less soluble. Wateris therefore shown to be a more effective solvent and acetonitrile is effective antisolvent towards our investigated amino acid L-tryptophan.

Dipole-dipole interaction and intermolecular H-bonding are two of the main contributing factors to solvent-solvent association in aqueous acetonitrile solution. Their union collapse with temperature increases, allowing a huge number of water molecules to re-form associations with the amino acids that are already present in solution mixture through ion-dipole interaction and gradually increasing solubility. Furthermore, as the temperature rises, the kinetic energy of solvent molecules also rises. As a result, solubility of serotonin precursor increases as it can now interact with solvent molecules more successfully.

3.2. Transferred Gibbs free energies and potential stability of L-tryptophan in aqueous acetonitrile environments

Table 3 shows the variation in the Gibbs energies [$\Delta G_s^0(i)$] of L-tryptophan solutions at various solution temperatures (in Kelvin) and acetonitrile mole fractions (X_{ACN}). The maximum reversible work that a system can perform at constant pressure and temperature during a

Table 3
Variations of Gibbs energies of solutions (ΔG_s^0) of L-tryptophan at different solution temperatures (K).

Mole fraction of Solvent	288.15 K		293.15 K		298.15 K		303.15 K		308.15 K	
X_{ACN}	X_S	ΔG_s^0 (kJ•mol^{-1})	X_S	ΔG_s^0 (kJ•mol^{-1})	X_S	ΔG_s^0 (kJ•mol^{-1})	X_S	ΔG_s^0 (kJ•mol^{-1})	X_S	ΔG_s^0 (kJ•mol^{-1})
water	1.159	16.195	1.236	16.320	1.362	16.357	1.529	16.340	1.746	16.270
0.088	1.036	16.464	1.105	16.593	1.268	16.535	1.439	16.493	1.608	16.480
0.204	0.892	16.823	0.993	16.853	1.112	16.860	1.261	16.826	1.453	16.740
0.401	0.677	17.483	0.759	17.508	0.826	17.597	0.961	17.510	1.074	17.514
0.525	0.55	17.981	0.601	18.077	0.67	18.116	0.772	18.062	0.859	18.087
0.684	0.37	18.931	0.409	19.015	0.445	19.130	0.539	18.968	0.591	19.045
0.808	0.23	20.070	0.264	20.082	0.301	20.099	0.367	19.937	0.402	20.032
0.945	0.078	22.660	0.089	22.732	0.100	22.831	0.152	22.158	0.170	22.237
1.000	0.021	25.804	0.026	25.731	0.038	25.229	0.056	24.675	0.067	24.623

process is described by its Gibbs energy, a thermodynamic property. To comprehend the spontaneity of solute dissolution in the context of solutions, these thermodynamical parameters can be used.

The values in the Table 3 show how the amount of L-tryptophan dissolved in the solution changed in terms of Gibbs energy [$(\Delta G_s^0(i)]$ in kJoule per mole. The energy change related to L-tryptophan dissolution at equilibrium condition at the experimental each temperature in the solvent mixture is represented by $\Delta G_s^0(i)$.

The mole fraction of L-tryptophan (X_S) and acetonitrile (X_{ACN}) changes show how the thermodynamics of dissolution are impacted by varying solvent compositions. Acetonitrile tends to make dissolution less favorable (becomes less negative) as X_{ACN} increases. More spontaneity of dissolution is indicated by a tendency for X_S to become more negative as L-tryptophan concentration rises. It is interesting in determining the Gibbs free energies ($\Delta G_t^0(i)$) associated with cavity-forming interactions, dipole–dipole interactions, and chemical interactions. This effort aims to deepen our understanding of the solvation process and the stability of L-tryptophan. Fig. 4 illustrates the change of $\Delta G_t^0(i)$ with the mole fraction of acetonitrile in aqueous acetonitrile media. This figure makes it evident that as the acetonitrile concentration rises $\Delta G_t^0(i)$ becomes more positive and leads to destabilisation. Additionally, it indicates that L-tryptophan displays enhanced stability in aqueous solutions in comparison to acetonitrile. Stability in this context refers to the ability of L-tryptophan to remain in solution without precipitating out. The stability

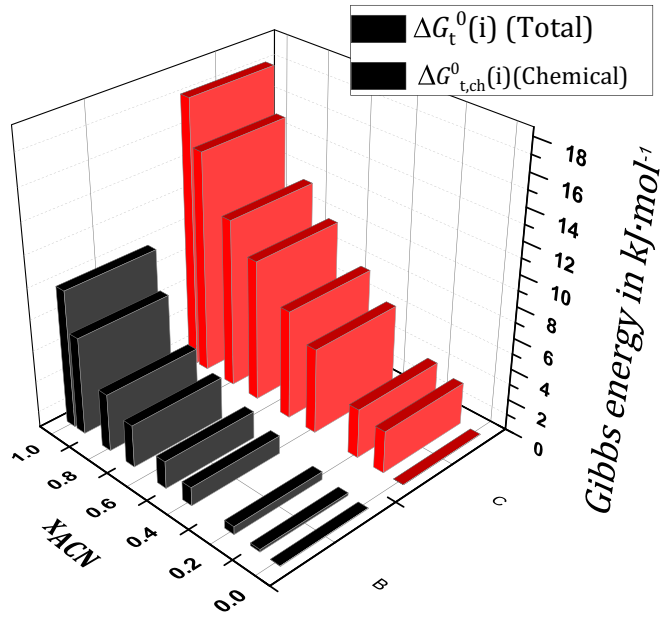


Fig. 4. variation of $\Delta G_t^0(i)$ and $\Delta G_{t,ch}^0(i)$ in kJ•mol^{-1}of L-tryptophan with mole fraction variation of acetonitrile in water at 298.15 K.

and fluctuations also noted in Tables 4 and 5 may be linked to progressive changes in cavity interaction, dipole–dipole interaction, dispersion interaction, hydrophobicity, hydrophilicity, acidity, basicity, and other pertinent factors within the L-tryptophan and mixed solvent system. Notably, dipole-induced dipole interaction is deemed inconsequential in the context of this investigation. The study reveals that as the mole fraction of acetonitrile in the binary solvent mixture increases, $(\Delta G_{t,cav}^0(i))$ exhibits a gradual shift towards more negative values. The outcome of the experiment also suggests that cavity interaction with an increasing mole fraction of acetonitrile gives L-tryptophan increased stability. Given that acetonitrile (0.412 nm) [34,36] has a larger size compared to water (0.274 nm) [37], the energy alteration stemming from the creation of a more advantageous cavity for L-tryptophan becomes evident as the mole fraction of acetonitrile rises in the acetonitrile-water mixture. Fig. 5 portrays the fluctuation in the transfer Gibbs free energy $(\Delta G_{t,cav}^0(i))$ of L-tryptophan concerning the mole fraction concentration of acetonitrile in solvent systems, measured in kJ·mol^{-1} at 298.15 K.

Once more, as acetonitrile concentration increases, the $(\Delta G_{t,d-d}^0(i))$ values (Table 5 and Fig. 5) for L-tryptophan progressively turn in positive direction, representing less stabilisation. Dipole moment values that correspond to these stabilisation and destabilisation can be used to explain these phenomena. L-tryptophan, water, and acetonitrile have dipole moment values of 1.378D, 1.83D, and 3.45D, respectively. According to these findings, the dipole-dipole interaction between acetonitrile and water improves in comparison to that between L-tryptophan and acetonitrile. Consequently, dipole–dipole interaction weakens with increasing acetonitrile concentration, causing destabilisation in this medium. This causes a positive increment in $\Delta G_{t,d-d}^0(i)$values.

$\Delta G_{t,ch}^0(i)$ value of our concerned amino acid is calculated by deducting $\Delta G_{t,cav}^0(i)$and $\Delta G_{t,d-d}^0(i)$from $\Delta G_t^0(i)$. In water-acetonitrile mixtures, the $\Delta G_{t,ch}^0(i)$ value is related to the short-ranges chemical interactions. These interactions encompass various forces between L-tryptophan and solvent molecules, encompassing various interactions.

Fig. 4 illustrates the change in $\Delta G_{t,ch}^0(i)$ of L-tryptophan with acetonitrile composition. The value gradually rises up with the enhancement of acetonitrile concentration leading to destabilisation of L-tryptophan. This phenomenon can be elucidated by considering the principles of solvent-solvent and solvent-solute interactions. Due to the increased hydrocarbon content of L-tryptophan, H_2O molecules form H-bonds with acetonitrile more readily than with tryptophan; as a result, solvent–solvent interaction becomes more advantageous than solute–solute and solvent–solute interaction causing positive increment of $\Delta G_{t,ch}^0(i)$ value. This explanation is also true for interpreting the variation ΔG_s^0. The outcome corroborates the L-tryptophan solubility data in the experimental solvent system.

Result of dissolution procedure and the variation of chemical transfer free energy $\Delta G_{t,ch}^0(i)$ are also supported by enthalpy change values

Table 4
Values of coefficients a, b and c used in least square method for computation of total transfer Gibbs free energy and entropy of solutions considering at various temperatures (K).

X_{ACN}	*a* (kJ•mol^{-1})	*b* (kJ•mol^{-1}•K^{-1})	*c* (kJ•mol^{-1}•K^{-1})	ΔG_t^0(i) (kJ•mol^{-1})	$T\Delta S_t^0(i)$ (kJ•mol^{-1})
water	−210.19	5.0698	−0.75645	0.000	0.000
0.088	−119.18	3.0567	−0.45660	0.171	1.439
0.204	−120.66	3.1113	−0.46511	0.514	2.153
0.401	−93.57	2.4888	−0.37141	1.177	0.643
0.525	−102.45	2.6855	−0.40037	1.748	−0.173
0.684	−129.84	3.3242	−0.49578	2.710	−0.078
0.808	14.76	0.1439	−0.02215	3.677	2.342
0.945	−353.94	8.6209	−1.29142	6.236	9.515
1.000	40.52	0.0457	−0.01704	8.839	21.416

Relative error of $\Delta G_t^0(i)$ and $\boldsymbol{T\Delta S_t^0(i)}$ lies in the range of ± (0.25 to 2.5) %.

Table 5
Gibbs energies of transfer $\Delta G_t^0(i)$,Gibbs energies of transfer due to cavity formation $\Delta G_{t,cav}^0(i)$,Gibbs energies of transfer due to dipole-dipole interaction $\Delta G_{t,d-d}^0(i)$,Gibbs energies of transfer due to chemical types interaction $\Delta G_{t,ch}^0(i)$ and enthalpy, $\Delta H_{t,cav}^0(i)$and entropies of transfer$T\Delta S_t^0(i)$,entropies of transfer due to cavity formation $T\Delta S_{t,cav}^0(i)$,entropies of transfer due to dipole-dipole interaction$T\Delta S_{t,d-d}^0(i)$and entropies of transfer due to chemical interaction $T\Delta S_{t,ch}^0(i)$of l-tryptophan in H_2O + ACN mixture at 298.15 K in kJ•mol^{-1}.

X_{ACN}	ΔG_t^0 (kJ•mol^{-1})	$\Delta G_{t,cav}^0(i)$ (kJ•mol^{-1})	$\Delta G_{t,d-d}^0(i)$ (kJ•mol^{-1})	$\Delta\Delta G_{t,ch}^0(i)$ (kJ•mol^{-1})	$\Delta H^0{}_{soln}$ (kJ•mol^{-1})	$\Delta H_{t,cav}^0$ (kJ•mol^{-1})	$T\Delta S_t^0$ (kJ•mol^{-1})	$T\Delta S_{t,cav}^0$ (kJ•mol^{-1})	$T\Delta S_{t,d-d}^0$ (kJ•mol^{-1})	$T\Delta S_{t,ch}^0(i)$(kJ•mol^{-1})
water	0.000	0.000	0.000	0.000	5.207	0.000	0.000	0	0.000	0
0.088	0.171	−4.351	1.816	2.706	4.599	−0.608	1.439	3.743	−0.641	−1.663
0.204	0.514	−2.640	0.009	3.145	6.113	0.906	2.153	3.546	−0.003	−1.390
0.401	1.177	−4.309	0.029	5.457	7.374	2.167	0.643	6.476	−0.010	−5.823
0.525	1.748	−5.268	0.046	6.970	8.653	3.446	−0.173	8.714	−0.013	−8.874
0.684	2.710	−6.410	0.072	9.048	11.107	5.900	−0.078	12.31	−0.016	−12.372
0.808	3.677	−7.241	0.095	10.823	13.909	8.702	2.342	15.943	−0.016	−13.585
0.945	6.236	−8.103	0.121	14.218	18.336	13.129	9.515	21.232	−0.013	−11.704
1.000	8.839	−8.436	0.132	17.143	20.626	15.419	21.416	23.855	−0.011	−2.428

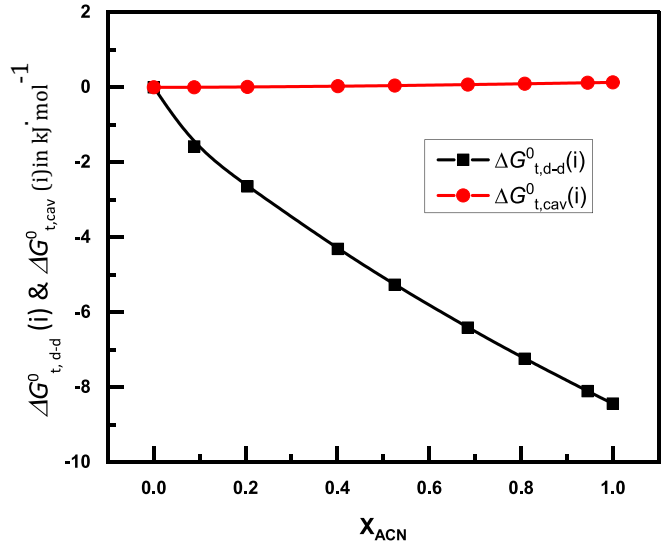


Fig. 5. variation of $\Delta G_{t,d-d}^0(i)$ and $\Delta G_{t,cav}^0(i)$in kJ•mol^{-1}of L-tryptophan with mole fraction variation of acetonitrile in water at 298.15 K.

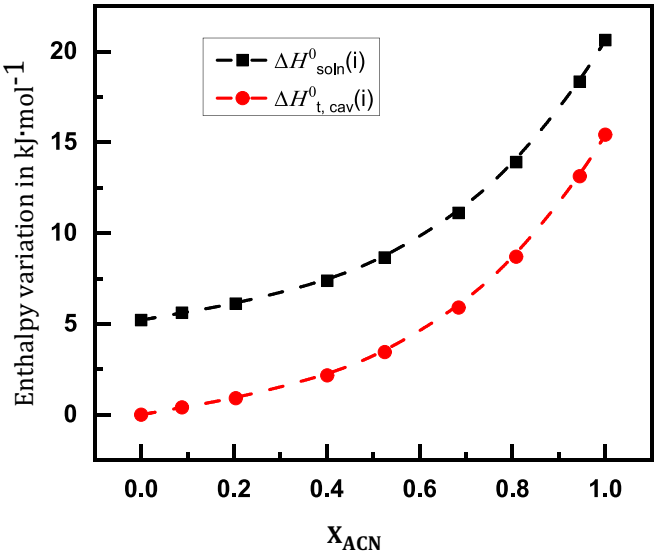


Fig. 6. variation of $\Delta H^0{}_{soln}$ and $\Delta H_{t,cav}^0(i)$in kJ•mol^{-1} of L-tryptophan with mole fraction variation of acetonitrile in water at 298.15 K.

(Table 5 and Fig. 6). This value, given in kJ•mol^{-1}, represents the change in enthalpy during the transfer of L-tryptophan into the solvent mixture. It is a measure of the heat involved in the transfer process. The measured data in Table 4 implies that the dissolution process is endothermic in nature. Lowering solubility with increasing acetonitrile concentration indicates to the point that in order to produce better solvent-solute interaction more heat energy is needed. This also supports the notion that the stability of L-tryptophan is higher in a pure aqueous solution compared to a water-acetonitrile mixture.

3.3. Amino acids induce interactions between solvents, characterized by transfer entropy

Entropies of transfer given in kJ•mol^{-1}, describe the change in entropy during the transfer of L-tryptophan into the solvent mixture. Entropy is a measure of disorder or randomness. Entropies of transfer provide an overall measure of the change in randomness during the transfer.

Entropies of transfer due to cavity formation could represent the change in entropy associated with creating space for L-tryptophan in the solvent mixture. Table 5 shows positive rise for this value and it indicates that L-tryptophan fit more in the cavity created by acetonitrile owing tolarger size of acetonitrile (0.412 nm) compare to water moiety. (0.274 nm) Consequently, solvent-co-solvent interaction is somewhat diminished in terms of cavity interaction leading to increment of free water molecules causing greater randomness which in turn reflect positive rise of that value at experimental temperature.

Entropies of transfer arising from dipole-dipole interactions might reflect the change in entropy associated with dipole-dipole interactions between L-tryptophan and the solvent mixture. Table 5 reflects negative increment of this valueat low concentration of acetonitrileleading to greater solvent-solvent interaction in presence of L-tryptophan. This phenomenon is attributed to their respective dipole moment values. Specifically, the dipole moment values for ACN, H_2O, and L-tryptophan are 3.45D, 1.83D, and 1.378D, respectively. The greater dipole moment of acetonitrile compared to water implies stronger dipole-dipole interactions between water and acetonitrile molecules, resulting in reduced randomness and a consequent negative rise in values. But at very high acetonitrile concentration positive rise are shown gradually and this is occurred due to self-association of acetonitrile leading to lowering solvent-solvent interaction.

The values $T\Delta S^0_{t,ch}(i)$ are computed by subtracting $T\Delta S^o_{t,cav}(i)$and $T\Delta S^0_{t,d-d}(i)$ from $T\Delta S^0_t(i)$. Entropies of transfer attributed to chemical interactions may signify the alteration in entropy associated with distinct chemical interactions such as dispersion forces, H-bonding, acid-base interactions, hydrophobic interactions, etc., occurring between L-tryptophan and the solvent mixture. When ACN is added to water in the presence of L-tryptophan, the monomeric water molecules are somewhat repelled by tryptophan because of its greater bulk and the existence of a more substantial hydrophobic part and L-tryptophan also can not able to make interaction effectively with acetonitrile also due to weak acid-base interaction owing to the fact that ACN exhibiting weak acidic and basic characteristics compare to water. Therefore, both water and acetonitrile able to interact with each other and this leads to lowering of randomness of solvent system. Molecules in experimental organic solvent (ACN) tend tointerfere with the 3D cluster of water molecules, and it can bind to molecules of free water, decreasing thesystem's entropy. This clarifies the disparities in negative increment of $T\Delta S^0_{t,ch}(i)$ values in the current organic solvent (ACN) up to certain concentration as shown in Table 4. But at higher mole fraction value of ACN dimerization of that organic solvent disrupt this regularity and showing positive rise of that value. The variation is represented in Fig. 7.

4. Conclusion

In the current study, an aqueous-ACN solvent system was used to evaluate the solvation properties and related thermodynamics parameters of L-tryptophan at temperatures that maintained an equal distance from one another, as shown in Tables 2–5. The size, dipole moment value, and hydrocarbon component of L-tryptophan are the main basis of explanationfor the experimentally measured variations. In this study, a number of interactions, including dipole-dipole, acid-base, and H-bonding, is significantly influencing the investigated properties. Due to acid-base and dipole-dipole interactions, the solubility of the concerned amino acid decreases with an increase in organic solvent concentration

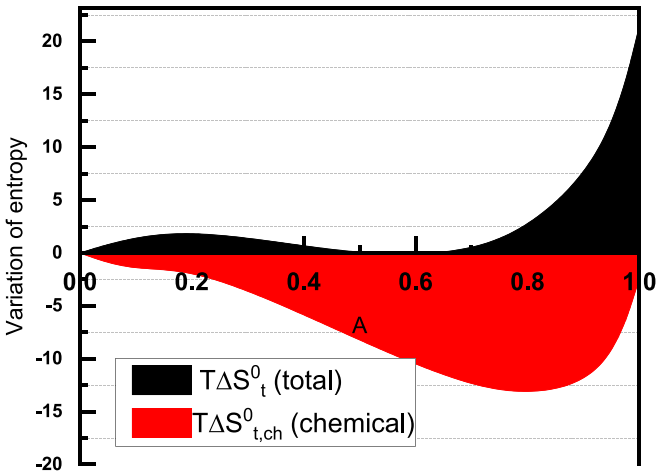


Fig. 7. variation of $T\Delta S^0_t(i)$ and $T\Delta S^0_{t,ch}(i)$ in kJ•mol^{-1}of L-tryptophan with mole fraction variation of acetonitrile in water at 298.15 K.

at any given tabulated temperatures values. However, with the temperature enhancement the solubility of experimental amino acidmoves to higher value gradually indicating their solubility enhancement due to increasing a greater number of free water molecules for crumbling of H-bonding present in between solvent water molecules. Solvent-solute and solvent-solvent interactions in co-solvent environment are the major controlling factors for showing variations for chemical transfer Gibbs energy [$\Delta G^0_{t,ch}(i)$] and chemical transfer enthalpy [$\Delta H^0{}_{soln}$] respectively. The conclusion that the dissolution process is endothermic in nature and that the stability of the pure aqueous solution of tryptophan is greater than that of the water-acetonitrile system is reached by a positive increment of both values. In accordance with the standard transfer Gibbs energies change resulting from short-range chemical interactions in solution, it is observed that L-tryptophan exhibits greater stability in pure water compared to solvent systems mixed with acetonitrile. The driving force behind this behavior is primarily the entropy, which plays a pivotal role in the total solvation course of the experimental molecule in water–acetonitrile solvent mixtures, as evidenced by the consistent negative trend in chemical entropy transfer. Furthermore, the results of this study are important for the industrial and medical fields in addition to the larger field of amino acid research.

CRediT authorship contribution statement

Avishek Saha: Formal analysis, Data curation. **Sourav Ghosh:** Investigation, Formal analysis. **Sintu Ganai:** Methodology, Investigation. **Puspal Mukherjee:** Software, Investigation. **Kalachand Mahali:** Visualization, Validation, Formal analysis. **Bidyut Saha:** Writing – review & editing. **A.M.A. Henaish:** Writing – review & editing, Software. **Partha Sarathi Guin:** Writing – review & editing, Visualization, Validation, Investigation, Formal analysis. **Perwez Alam:** Writing – review & editing. **Sanjay Roy:** Writing – original draft, Supervision.

Declaration of competing interest

The authors assert that they have no competing interests.

Data availability

The article contains complete information regarding the data generated or analyzed throughout the course of this study.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bpc.2024.107195.

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