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Solubility and transfer Gibbs free energetics of glycine, DL-alanine, DL-nor-valine and DL-serine in aqueous sodium fluoride and potassium fluoride solutions at 298.15 K

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The experimental saturated solubilities of glycine, DL-alanine, DL-nor-valine and DL-serine in aqueous mixtures of NaF and KF solutions at 298.15 K are measured by using an analytical 'formol titrimetry' method. Subsequently, the standard transfer Gibbs free energy, enthalpy for cavity formation, Gibbs free energy for cavity formation and Gibbs free energy for dipole-dipole interaction have been computed. The chemical contribution for the standard transfer Gibbs free energies for the experimental amino acids have been obtained by subtracting the cavity effects and dipole-dipole interaction effects from the total standard transfer Gibbs free energy (ΔG_t^0 (i)). The stability of the studied amino acids in aqueous NaF and KF in terms of thermodynamic parameters are discussed and compared.

Keywords: Solution chemistry, Thermodynamics, Solubility, Amino acids, Electrolytes, Transfer energetics, Formol titrimetry

The solubility data as well as other thermodynamic parameters like Gibbs free energies of the amino acids are vital in biochemical and biophysical processes in human physiology. The detailed studies on amino acid solvation are not only important in protein chemistry, but are also important in chemical, pharmaceutical, food, cosmetics, engineering and biodegradable plastic industries[1-19].

The amino acids studied herein, viz., glycine, DL-alanine, DL-nor-valine and DL-serine with different hydrophobic (CH_3- and CH_3-CH_2-CH_2-) and hydrophilic (-CH_2OH) (Scheme 1) side chains, are the structural units of many proteins[2]. However their biochemical activities and solvation thermodynamics in aqueous and aqueous electrolyte mixtures in living systems are yet to be studied in detail.

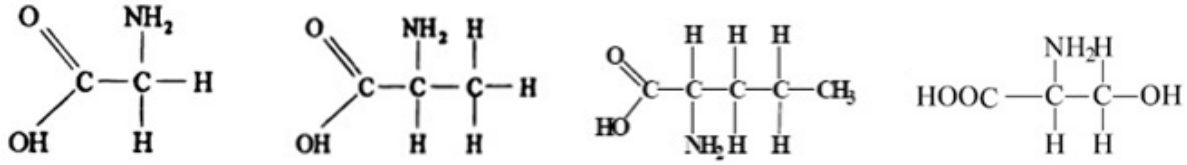
Usually, amino acids are produced by synthesis or fermentation. Their separation from the excess reagents and other impurities in aqueous solution is often done by crystallization or precipitation. The separation cost of these amino acids is about 50% of the total production cost[20]. The separation effect of different salts, cations and anions are hence of potential interest for the separation of amino acids.

Information on the solubility and solvation thermodynamics of amino acids in the presence of different electrolytes is also useful for the rational design of extraction of proteins from the natural sources and also for the purification of proteins.

Herein, we have measured the solubities of the amino acids in aqueous mixtures of NaF and KF solutions and compared with earlier data. We have also evaluated their thermodynamic stability in the light of solute-solvent, solvent-solvent, acid-base and hydrophilic/hydrophobic interactions.

Experimental

Glycine, DL-alanine, DL-nor-valine and DL-serine (>99.8%, Sigma Aldrich) were used after drying in



Glycine DL-alanine DL-nor-valine DL-serine

Scheme 1

vacuum desiccators at 370 K for seven days. Sodium fluoride (NaF) and potassium fluoride (KF) of purity 99.8% were obtained from E. Merck, Bombay, India. The salts were oven dried for 3-4 days and cooled in a vacuum desiccator for seven days prior to use. Triplet distilled water was used throughout the experimental work.

The aqueous solvent mixtures of salts (NaF, KF) of the concentrations of 0.000, 0.100, 0.200, 0.300, 0.500, 1.00 and 1.500 molality were prepared in triply distilled water by accurate weighing.

The solvent mixtures (H_2O+NaF / H_2O+KF) and excess amount of amino acid were placed in well fitted stoppered glass tubes. The glass tubes were incompletely filled to ensure good mixing. A low-cum-high temperature thermostat capable of registering temperatures with an accuracy of ±0.10 K was used for all measurements. A known mass (~0.2-0.3 g) of filtered saturated solution was transferred to a dry conical flask from the solution thermostated at experimental temperature. The saturated solubility of glycine, DL-alanine, DL-nor-valine and DL-serine was measured by the formol titrimetric method[1,13,15-18,21,22] using freshly standardized (0.05 *M*) NaOH solution (GR, E. Merck; >99.0%) and 1% alcoholic phenolphthalein solution as indicator. Excess freshly neutralised formaldehyde (GR, E Merck; >99%) solution was used to mask the amino group of the amino acids. Standardised (0.05 M) NaOH solution from a burette was added to 5 mL formaldehyde with one drop of the indicator to get freshly neutralised formaldehyde. The end point was indicated by the appearance of pink colour. The neutral formaldehyde solution was then added to the pre-neutralised amino acid solution followed by titration with NaOH till the colour changed to pale pink colour. Four sets of measurements were made for the experimental amino acids by equilibrating the solutions at 298.15 K. The solubilities were found to agree to within 3%. The 'formal titrimetric method' for solubility measurements of similar amino acids has been used in earlier studies[1,13,15-18,21,22].

Results and discussion

The solvent parameters of aqueous salts solution are listed in Table 1. The solubilities (*S*) of the amino acids at 298.15 K (in mol kg^{-1}) are summarised in Table 2. The solubilities in the aqueous- electrolyte as well as in water were used to compute standard free energies of solution ($\Delta G_t^0(s)$), using the Eq. (1)[23],

$$\Delta G_t^0(s) = RT \ln (S_R/S_s) \quad \ldots (1)$$

where the subscripts R and s are for water and aqueous-electrolyte respectively. The standard total transfer Gibbs energies (ΔG_t^0 (i)), in mole fraction scale were calculated by the Eq. (2),

$$\Delta G_t^0(i) = \Delta G_t^0(s) - RT \ln (M_s/M_R) \quad \ldots (2)$$

where M_s and M_R refer to the molar mass of electrolytes (NaF, KF) mixture and reference solvent (water) respectively. $\Delta G_t^0(i)$ are listed in Table 2. Now $\Delta G_t^0(i)$ is the sum of the following terms (assuming dipole-induced dipole term to be negligible)[21],

$$\Delta G_t^0(i) = \Delta G_{t,cav}^0(i) + \Delta G_{t,d-d}^0(i) + \Delta G_{t,ch}^0(i) \quad \ldots (3)$$

where $\Delta G_{t,cav}^0(i)$ stands for the Gibbs energies of transfer due to the contribution of the cavity effect involving the creation of cavities for the species in water and such aquo-ionic solvents, $G_{t,d-d}^0(i)$ for Gibbs energies of transfer due to dipole–dipole interaction effect involving interactions between dipolar zwitter-ionic amino acid and solvated electrolyte molecules, and, $\Delta G_{t,ch}^0(i)$ the chemical part of transfer Gibbs energy which arises from acid-base or short range dispersion interaction, hydrophilic (H_IH) or hydrophobic (H_bH) hydration and structural effects. $\Delta G_{t,cav}^0(i)$ values were computed using the scaled particle theory[24], assuming the solutes and solvent molecules as equivalent hard sphere models as dictated by their respective diameters (vide Table 1).

The equations[18,21] used for cavity calculation are as follows:

$$\Delta G_{cav}^0 = G_C + RT \ln (RT/V_S) \quad \ldots (4)$$

where

$$G_C = RT[-\ln (1-Z) + \{3X/(1-Z)\}\sigma_X + \{3Y/(1-Z)\}\sigma_X^2 + \{9X^2/4(1-Z)^2\}\sigma_X^2]$$

$$Z = \pi N_A/6V_S (Z_R\sigma_R^3 + Z_S\sigma_S^3)$$

$$X = \pi N_A/6V_S (Z_R\sigma_R^2 + Z_S\sigma_S^2)$$

$$Y = \pi N_A/6V_S (Z_R\sigma_R + Z_S\sigma_S)$$

$$V_S = M_S/d_S$$

Herein N_A is Avogadro's number, Z_R and Z_s are the mole fraction of water and salts respectively. σ_x, σ_R and σ_s are the hard sphere diameters of amino acids, water and co-solvent respectively. M_s is the molar mass of the electrolyte solvents and 'd_s' stands for molar density of the same.

Table 1—Solvent parameters (mole fraction of salt (Z_s), water ((Z_R), molar mass (M_S), density (d_s), molar volume (V_s), solvent diameter (σ_s) σ_{s-x}, μ_s, isothermal expansibility constant (α) and dipole moment (D) of the water+salt systems at 298.15 K

Molality	Mole fraction, Z_s	Mole% salt	Mole fraction, Z_R	Molar mass, M_S	Density, d_s (kg dm^{-3})	Molar vol., V_s (dm^3 mol^{-1})	Dipole moment, μ_s (D)	α ($\times 10^{-3}$)
NaF								
0.000	0.0000	0.000	1.0000	18.01500	0.99700[a]	18.06921	1.830	0.257[a]
0.100	0.0018	0.180	0.99820	18.05816	0.99981	18.06159	1.841	0.257
0.200	0.0035	0.353	0.99647	18.09963	1.00251	18.05431	1.852	0.257
0.300	0.0054	0.538	0.99462	18.14399	1.00540	18.04654	1.864	0.257
0.500	0.0089	0.893	0.99107	18.22910	1.01094	18.03183	1.887	0.257
1.000	0.0177	1.770	0.98230	18.43936	1.02463	17.99612	1.942	0.257
1.500	0.0263	2.630	0.97370	18.64554	1.03805	17.96208	1.996	0.257
KF								
0.000	0.0000	0.000	1.0000	18.01500	0.99700[a]	18.0692	1.830	0.257[a]
0.100	0.0018	0.180	0.99820	18.08714	0.99967	18.0931	1.842	0.257
0.200	0.00353	0.353	0.99647	18.15646	1.00223	18.1160	1.854	0.257
0.300	0.00538	0.538	0.99462	18.23060	1.00498	18.1402	1.866	0.257
0.500	0.00893	0.893	0.99107	18.37287	1.01024	18.1866	1.890	0.257
1.000	0.0177	1.770	0.98230	18.72433	1.02325	18.2988	1.949	0.257
1.500	0.0263	2.630	0.97370	19.06897	1.03600	18.4063	2.008	0.257

Molality	σ_s (nm)	σ_{s-x} (nm)[b]			
		Glycine	DL-alanine	DL-nor-valine	DL-serine
NaF					
0.00	0.2740	0.419	0.4450	0.4830	0.4335
0.100	0.2743	0.420	0.4462	0.4842	0.4337
0.200	0.2747	0.420	0.4462	0.4842	0.4339
0.300	0.2750	0.420	0.4462	0.4842	0.4340
0.500	0.2757	0.420	0.4462	0.4842	0.4344
1.000	0.2774	0.421	0.4481	0.4861	0.4352
1.500	0.2790	0.421	0.4481	0.4861	0.4360
KF					
0.00	0.2740	0.4190	0.4450	0.4830	0.4335
0.100	0.2746	0.4190	0.4453	0.4833	0.4338
0.200	0.2751	0.4196	0.4456	0.4836	0.4341
0.300	0.2757	0.4199	0.4459	0.4839	0.4344
0.500	0.2769	0.4205	0.4465	0.4845	0.4349
1.000	0.2797	0.4219	0.4479	0.4859	0.4364
1.500	0.2825	0.4233	0.4493	0.4873	0.4378

[a]Ref. 25; [b]$\sigma_{s-x} = ½(\sigma_s+\sigma_x)$.

Finally, $\Delta G^0_{t,cav}$ (i) represents the difference

$$\Delta G^0_{t,cav}(\text{i}) = {}_s\Delta G^0_{cav}(\text{i}) - {}_R\Delta G^0_{cav}(\text{i}) = {}_sG_C - {}_RG_C + \text{RTln}\,(V_R/V_S) \quad \ldots (5)$$

For the calculation of $\Delta G^0_{t,cav}$ (i) the required solvent parameters are taken from Table 1.

The $\Delta G^0_{t,d-d}$(i) values were calculated by means of the Keesom-orientation expression[25] (Eq. 6),

$$\Delta G^0_{t,d-d}(\text{i}) = ({}_s\Delta G^0_{t,d-d}(\text{i}) - {}_R\Delta G^0_{t,d-d}(\text{i})) \quad \ldots (6)$$

while, ${}_s\Delta G^0_{t,d-d}$(i) in a solvent 's', is given as Eq. 7,

$${}_s\Delta G^0_{d-d}(\text{i}) = -(8\pi/9)N^2\mu_S^2\mu_X^2\sigma_{S-X}^{-3}\ (kT)^{-1}V_S^{-1} = \text{A/T}V_S \quad \ldots (7)$$

where $A = -(8\pi/9)N^2\mu_S^2\mu_X^2\sigma_{S-X}^{-3}\ (k)^{-1}$

and $V_S = M_S/d_S$

Here N stands for Avogadro's number, μ_s and μ_x are the dipole moment of solvent and amino acid molecules respectively (Table 1), σ_{s-x} is the distance at

Table 2—Solubility, standard total transfer Gibbs energies (ΔG_t^0 (i)), transfer Gibbs energies due to cavity formation ($\Delta G_{t,cav}^0$ (i)), Gibbs energies of transfer due to dipole–dipole interaction arising out of highly oriented dipole–dipole interactions between the dipolar zwitterionic amino acid and electrolyte/solvent molecules relative to those in water ($\Delta G_{t,d-d}^0$ (i)), Chemical part of transfer Gibbs energy ($\Delta G_{t,ch}^0$ (i)) and change of enthalpy due to cavity formation ($\Delta H_{t,cav}^0$ (i)) of glycine, DL-alanine, DL-nor-valine and DL-serine from water to water-electrolytes solutions in different compositions at 298.15 K (on mole fraction scale in kJ mol^{-1})

Molality	Solubility (mol kg^{-1})	ΔG_t^0 (i) (kJ mol^{-1})	$\Delta G_{t,cav}^0$ (i) (kJ mol^{-1})	$\Delta G_{t,d-d}^0$ (i) (kJ mol^{-1})	$\Delta G_{t,ch}^0$ (i) (kJ mol^{-1})	$\Delta H_{t,cav}^0$ (i) (kJ mol^{-1})
			NaF- H_2O system			
Glycine						
0.000	3.320	0.000	0.000	0.000	0.000	0.000
0.100	2.908	0.323	0.004	− 0.0012	0.3202	0.006
0.200	3.006	0.235	0.008	− 0.0089	0.2359	0.011
0.300	3.112	0.143	0.012	− 0.0252	0.0792	0.016
0.500	3.306	- 0.019	0.020	− 0.0782	0.0392	0.025
1.000	3.342	- 0.074	0.040	− 0.3140	0.2000	0.050
1.500	3.448	- 0.179	0.060	− 0.7420	0.5030	0.077
DL-alanine						
0.000	1.800	0.000	0.000	0.000	0.000	0.000
0.100	1.654	0.204	0.004	− 0.0008	0.2008	0.003
0.200	1.614	0.259	0.008	− 0.0072	0.2582	0.005
0.300	1.568	0.324	0.013	− 0.0209	0.3319	0.011
0.500	1.502	0.419	0.022	− 0.0658	0.4628	0.022
1.000	1.454	0.471	0.043	− 0.2520	0.6800	0.052
1.500	1.429	0.487	0.065	− 0.6080	1.0300	0.083
DL-nor-valine						
0.000	0.677	0.000	0.000	0.000	0.000	0.000
0.100	0.544	0.536	0.005	− 0.0007	0.5317	0.005
0.200	0.502	0.730	0.009	− 0.0059	0.7269	0.012
0.300	0.488	0.794	0.014	− 0.0169	0.7969	0.019
0.500	0.446	1.005	0.024	− 0.0527	1.0337	0.032
1.000	0.408	1.198	0.048	− 0.2030	1.3530	0.069
1.500	0.390	1.282	0.073	− 0.4870	1.6960	0.107
DL-serine						
0.000	0.478	0.000	0.000	0.000	0.000	0.000
0.100	0.492	− 0.077	0.004	− 0.0004	− 0.0806	0.006
0.200	0.508	− 0.163	0.008	− 0.0037	− 0.1673	0.011
0.300	0.522	− 0.236	0.013	− 0.0109	− 0.2381	0.016
0.500	0.536	− 0.313	0.021	− 0.0344	− 0.2996	0.027
1.000	0.567	− 0.481	0.042	− 0.1410	− 0.3820	0.054
1.500	0.588	− 0.599	0.063	− 0.3330	− 0.3290	0.083
			KF- H_2O system			
Glycine						
0.000	3.320	0.000	0.000	0.0000	0.0000	0.000
0.100	2.948	0.284	− 0.013	− 0.0029	0.2999	− 0.012
0.200	3.124	0.131	− 0.024	− 0.0098	0.1648	− 0.025
0.300	3.328	− 0.035	− 0.037	− 0.0231	0.0121	− 0.039
0.500	3.386	− 0.098	− 0.060	− 0.0645	0.0265	− 0.064
1.000	3.405	− 0.158	− 0.115	− 0.2600	0.2170	− 0.121
1.500	3.566	− 0.318	− 0.166	− 0.5850	0.4330	− 0.170

(*Contd.*)

Table 2—Solubility, standard total transfer Gibbs energies (ΔG_t^0 (i)), transfer Gibbs energies due to cavity formation ($\Delta G_{t,cav}^0$ (i)), Gibbs energies of transfer due to dipole–dipole interaction arising out of highly oriented dipole–dipole interactions between the dipolar zwitterionic amino acid and electrolyte/solvent molecules relative to those in water ($\Delta G_{t,d-d}^0$ (i)), Chemical part of transfer Gibbs energy ($\Delta G_{t,ch}^0$ (i)) and change of enthalpy due to cavity formation ($\Delta H_{t,cav}^0$ (i)) of glycine, DL-alanine, DL-nor-valine and DL-serine from water to water-electrolytes solutions in different compositions at 298.15 K (on mole fraction scale in kJ mol^{-1}). (*Contd.*)

Molality	Solubility (mol kg^{-1})	ΔG_t^0 (i) (kJ mol^{-1})	$\Delta G_{t,cav}^0$ (i) (kJ mol^{-1})	$\Delta G_{t,d-d}^0$ (i) (kJ mol^{-1})	$\Delta G_{t,ch}^0$ (i) (kJ mol^{-1})	$\Delta H_{t,cav}^0$ (i) (kJ mol^{-1})
DL-alanine						
0.100	1.886	− 0.126	− 0.013	− 0.0021	− 0.1109	− 0.021
0.200	1.912	− 0.169	− 0.026	− 0.0085	− 0.1345	− 0.036
0.300	1.920	− 0.189	− 0.039	− 0.0200	− 0.1300	− 0.052
0.500	1.938	− 0.232	− 0.064	− 0.0560	− 0.1120	− 0.082
1.000	1.998	− 0.354	− 0.123	− 0.2260	− 0.0050	− 0.148
1.500	2.146	− 0.577	− 0.177	− 0.5080	0.1080	− 0.205
DL-nor-valine						
0.000	0.677	0.000	0.000	0.0000	0.0000	0.000
0.100	0.664	0.038	− 0.015	− 0.0017	0.0547	− 0.021
0.200	0.678	− 0.023	− 0.029	− 0.0069	0.0129	− 0.040
0.300	0.689	− 0.073	− 0.044	− 0.0161	− 0.0129	− 0.059
0.500	0.699	− 0.128	− 0.071	− 0.0451	− 0.0119	− 0.096
1.000	0.714	− 0.228	− 0.137	− 0.1820	0.0910	− 0.178
1.500	0.728	− 0.321	− 0.196	− 0.4090	0.2840	− 0.248
DL-serine						
0.000	0.478	0.000	0.000	0.0000	0.0000	0.000
0.100	0.502	− 0.131	− 0.013	− 0.0011	− 0.1169	− 0.014
0.200	0.544	− 0.340	− 0.025	− 0.0045	− 0.3105	− 0.028
0.300	0.573	− 0.479	− 0.038	− 0.0105	− 0.4305	− 0.043
0.500	0.592	− 0.579	− 0.062	− 0.0298	− 0.4872	− 0.071
1.000	0.633	− 0.792	− 0.120	− 0.1180	− 0.5540	− 0.133
1.500	0.658	− 0.933	− 0.172	− 0.2660	− 0.4950	− 0.186

Hard sphere diameter of water, NaF and KF are 2.74 Å, 4.64 Å and 5.96 Å (Refs 25, 28 & 29) respectively. The dipole moment values of NaF, KF and water are 8.16 D, 6.60 D and 1.830 D respectively, taken from Refs. 25 & 28.The required diameter of glycine, DL-alanine, DL-nor-valine and DL-serine are 5.64 Å, 6.16 Å, 6.92 Å and 5.93 Å respectively taken from Refs 21 & 29. The dipole moment of glycine, DL-alanine, DL-valine and DL-serine are 15.7 D, 15.9 D, 16.0 D and 11.10 D respectively (Refs 21 & 29).

which the attractive and repulsive interactions between the solvent and solute molecules are equal and is generally equal to ½ (σ_s+ σ_x), where σ_s and σ_x are the hard sphere diameter of solvent and solute molecules respectively. μ_s and σ_s and for such mixed binary solvent system are computed with the variation of mole fraction of the co-solvent as done by Graziano[26]. The quantity was again multiplied by the term X_{sl} following Marcus[25] and Kim *et al.* [27] methods in order to get the $\Delta G_{t,d-d}^0$ (i) term on mole fraction scale.

$$X_{S1} = X_S\,(\mu_s\sigma_s^3) / (\mu_R\sigma_R^3) \quad \ldots (8)$$

X_{S1} is the real mole fraction contribution due to dipole-dipole interaction.

Now, the values $\Delta G_{t,cav}^0$ (i) and $\Delta G_{t,d-d}^0$ (i) are subtracted from ΔG_t^0 (i) to get $\Delta G_{t,ch}^0$ (i) of amino acid and all these values are shown in Table 2. The values of ΔG_t^0 (i) and $\Delta G_{t,ch}^0$ (i) are illustrated in Figs 1 and 2.

The enthalpy change due to cavity forming interaction in water to aqueous electrolytes mixtures ($\Delta H_{t,cav}^0$ (i)) is computed Eqs 9 and 10,

$$\Delta H_{t,cav}^0(\text{i}) = {}_S\Delta H_{\text{cav}}^0(\text{i}) - {}_R\Delta H_{\text{cav}}^0\ (\text{i}) \quad \ldots (9)$$

$$\Delta H_{cav}^0\ (\text{i}) = (\text{A+H+K+E}) \times \text{B} \quad \ldots (10)$$

where

A = $(\pi N_A/6V_S) \times (Z_R\sigma_R^3 + Z_s\sigma_s^3)$;

B = $\sigma_{s\,RT}{}^2/\,(1\text{-A})^2$; =$\sigma_X \times 3\text{Y}/\,(1\text{-A})$

K = $\sigma_x \times 3\text{X}/\,(1\text{-A})$; E=$9\sigma_x^2 \times \text{X}^2/\,(1\text{-A})^2$

X = $(\pi N_A/6V_S) \times (Z_R\sigma_R^2 + Z_s\sigma_s^2)$

Y = $(\pi N_A/6V_S) \times (Z_R\sigma_R + Z_s\sigma_s)$,

Δ = 22/7

Table 3—Comparison of the solubility data for glycine, DL-alanine DL-nor-valine and DL-serine by formol titrimetry method and with earlier results by different analytical techniques in aqueous media in the absence and in the presence of NaCl, NaF, KCl and KF at 298.15 K

Amino acid	Solubility in pure water	Solubility (mol kg^{-1}) in presence of 1.0 mol kg^{-1} of electrolyte			
		NaCl	NaF	KCl	KF
Glycine	3.320[a]	3.33 ± 0.12 (36)	3.342[a]	3.27 ± 0.10 (36)	3.405[a]
	3.339 (17)	3.371 (31)	3.330 (33)	3.281 (19)	3.335 (33)
	3.330 (21)	3.409 (34)		3.496 (31)	
	3.389 (1)			3.372 (34)	
	3.338 (33)				
DL-alanine	1.800[a]	1.87±0.09 (36)	1.454[a]	1.85 ± 0.08 (36)	1.998[a]
	1.800 (17)	1.859 (31)	1.500 (33)	1.841 (19)	1.983 (33)
	1.850 (21)	1.859 (34)		2.01 (31)	
	1.938 (1)	1.859 (35)		1.896 (34)	
	1.895 (33)			1.896 (35)	
DL-nor-valine	0.677[a]	0.564 ± 0.007 (34)	0.408*	0.702 ± 0.013 (34)	0.714[a]
	0.677 (17)		0.422 (33)		0.695 (33)
	0.683 (21)				
	0.751 (1)				
	0.602 (34)				
DL-serine	0.478[a]	0.569 (31)	0.567[a]	0.725 (31)	0.633[a]
	0.477 (31)	0.570 (35)	0.552 (33)	0.726 (35)	0.635 (33)
	0.476 (32)				
	0.479 (33)				

[a]Solubility values from present study. Other solubility values are taken from the references given in brackets.

The variations of $\Delta H^0_{t,cav}$(i) values in kJ mol^{-1} are given in Table 2.

The solubility data (Table 2) of the experimental amino acids indicate that dissolution of glycine is the highest and that of DL-serine is the lowest among the four amino acids in both the aqueous solutions of NaF and KF. The solubility values of such molecules in the current study are compared with the solubilities reported earlier[1, 17, 21, 31, 33- 36] in aqueous media in the absence and in the presence of NaCl, KCl, NaF, and KF at 298.15 K (Table 3). This clearly shows that in most of the cases the values correlate excellently and in some of the cases there is a deviation between the present and the earlier results which may be due to the nature of electrolytes, dimension of the ions and different methods of measurements.

All the studied amino acids show salting-in effect in presence of KF in aqueous-KF whereas only DL-serine shows salting-in effect in aqueous NaF with a regular trend, glycine shows salting out effect initially but in higher concentration of NaF it shows salting- in effect. DL-alanine and DL-serine show salting-out effect in aqueous NaF solution. All the amino acids under study were found to have higher solubilities in the presence of the potassium cation than in the presence of the sodium cation (Table 2).

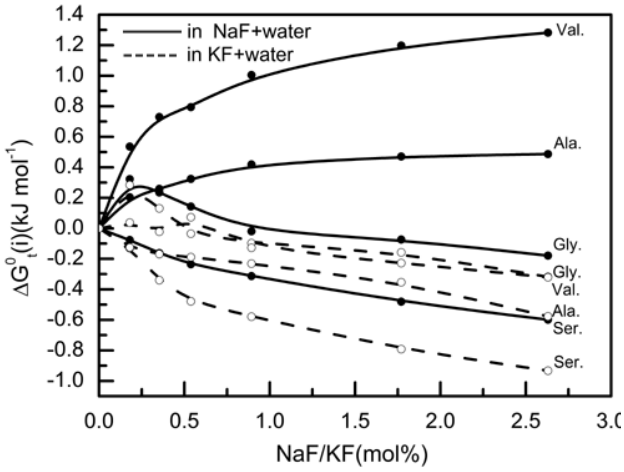


Fig. 1 — Variation of ΔG^0_t (i) in kJ mol^{-1} of glycine, DL-alanine, DL-nor-valine and DL-serine in aqueous mixtures of NaF/KF at 298.15 K.

The effect of the nature of cation on the solubility in aqueous solution of amino acids in the presence of potassium and sodium cations have also been reported[30,31] for glycine, DL-alanine, DL-valine and DL-serine in the presence of both sodium and potassium cations and with different anions also[30-35].

Figure 1 represents the variation of ΔG^0_t (i) of Glycine, DL-alanine, DL-nor-valine and DL-serine in

aqueous mixtures of NaF and KF at 298.15 K. It shows that ΔG_t^0 (i) value (Table 2) shows more positive values for the experimental amino acids in aqueous NaF solution rather than aqueous KF solution. DL-serine shows more negative ΔG_t^0 (i) values for both the solvent systems. The results indicate that the amino acid DL-serine is more stabilized than the other amino acids, i.e. glycine, DL-alanine and DL-nor-valine.

The $\Delta G_{t,cav}^0$ (i) values (theoretically calculated, Table 2) for the amino acids show that glycine is more stable whereas DL-nor-valine shows lesser stability in aqueous mixtures of NaF. The order of stability is as: glycine > DL-serine > DL-alanine > DL-nor-valine. However, in aqueous mixtures of KF, the order of stability is just the reverse. This indicates that the smaller amino acids are stabilized due to easy creation of cavity after its transfer from water to water-NaF mixture and larger amino acids are stabilized due to easy creation of cavity after its transfer from water to water-KF mixture. Here $\Delta G_{t,d-d}^0$ (i) values are guided by the hard sphere diameter of solute and solvent and density of the solvent mixtures. The hard sphere diameter of KF (5.96 Å) is higher than that of NaF (4.64 Å)[28,29] and therefore the former is suitable for cavity creation for the larger amino acids and the latter for the smaller amino acids.

$\Delta G_{t,d-d}^0$ (i) values increase negative in the order: DL-serine < DL-nor-valine < DL-alanine < glycine in both the aqueous electrolytes solvent systems (Table 2). This leads to the conclusion that glycine is more stabilized by the dipole-dipole interaction between the solute and solvent molecules in both the aqueous electrolyte solutions.

Here $\Delta G_{t,d-d}^0$ (i) values, which are obtained after subtraction of ${}_R\Delta G_{t,d-d}^0$ (i) from ${}_S\Delta G_{t,d-d}^0$ (i), depend on dipole moment of solute and co-solvents system. Its value decreased with the increase of hard-sphere diameter of solute and co-solvent.

Since, ΔG_t^0(i) = $\Delta G_{t,cav}^0$(i)+$\Delta G_{t,d-d}^0$(i)+$\Delta G_{t,ch}^0$(i), $\Delta G_{t,ch}^0$ (i) can be obtained by subtracting $\Delta G_{t,cav}^0$ (i) and $\Delta G_{t,d-d}^0$ (i) from ΔG_t^0 (i). Here it is to be noted that in the solute-solvent system the involved chemical interactions may be of different types such as acid-base type interaction, H-bonding interaction, hydrophilic and hydrophobic interactions, hard-soft interaction and dispersion interaction, etc.

Figure 2 represents the variation of $\Delta G_{t,ch}^0$ (i) of the amino acids with the mole% of NaF /KF at 298.15 K. The nature of variation of the curves indicates that the studied amino acids are more stable in aqueous solution of KF than the aqueous solution of NaF. Among the four amino acids, DL-serine shows the highest stability in both the electrolytes solvent systems. The chemical stability order of these amino acids in aqueous NaF is as follows: DL-serine > glycine > DL-alanine > DL-nor-valine. However, the chemical stability order of the amino acids in aqueous KF is as follows: DL-serine > DL-alanine > DL-nor-valine > glycine.

Such type of stability order of the said amino acids may be because of the structural difference arising due to the presence three different side chains in their chemical structure (Scheme 1). The amino acid, DL-serine contains –OH group whereas other two amino acids do not contain OH group. The absence of –OH group in other three amino acids imparts lesser dipole-dipole, hydrophilic and acid-base type chemical interaction with water as well as water-electrolytes mixtures. However such types of interactions are strongly favourable for DL-serine which leads to its highest stability among the four amino acids in both the aqueous electrolytes systems.

DL-alanine is the second most stable in aqueous KF solution in terms of cavity forming and dipole-dipole and chemical interactions. On the other hand, DL-alanine gets second highest stability in terms of dipole-dipole interaction and third highest stability in terms of cavity forming interaction but due to involvement of chemicals interactions, the overall stability becomes third in position among the present amino acids in aqueous NaF solutions. The amino acid glycine shows slight by higher stability in KF solution

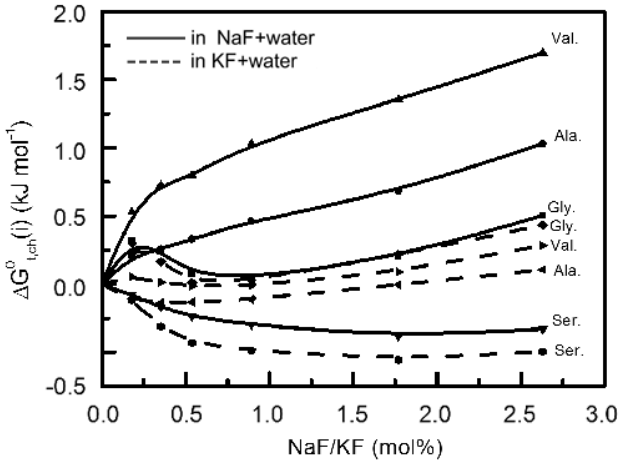


Fig. 2 —Variation of $\Delta G_{t,ch}^0$ (i) in kJ mol^{-1} of glycine, DL-alanine, DL-nor-valine and DL-serine in aqueous mixtures of NaF/KF at 298.15 K.

due to interactions like acid-base, hydrogen bonding, etc. It is to be noted that in aqueous NaF, glycine shows maximum stability in terms of cavity forming and dipole-dipole interactions whereas in cavity forming interaction, glycine shows lowest stability in aqueous KF solution.

Another important point is that in higher content of water, $\Delta G^0_{t,ch}$ (i) value increases and shows a maximum for glycine, which indicates destabilization. This may be due to the breakdown of extensive hydrogen bonding between protic water and hydrophilic head of zwitterionic glycine with the introduction of the larger electrolyte molecules into water. This phenomenon occurs in the case of glycine only and this may be due to the higher charge density (smallest in size) in its vicinity. That is why glycine molecules associate very strongly with water molecules through hydrogen bonding interaction in water- rich regions.

The comparatively larger amino acid, viz., DL-nor-valine is unstable in aqueous NaF solution and in aqueous KF it is comparatively more stable than glycine. The type of stability order of DL-nor-valine may be due to the size factor of the cations present in the salts. Comparatively larger K^+ ion interacts more strongly than Na^+ ion with the larger size DL-nor-valine in terms of dispersion interaction which leads to the observed stability order.

The values of $\Delta H^0_{t,cav}$ (i) of glycine, DL-alanine, DL-nor-valine and DL-serine in aqueous mixtures of NaF and KF at 298.15 K are presented in Table 2. The order of stability of the amino acids in term of theoretically calculated enthalpy of transfer due cavity forming interaction in KF solution is as follows: DL-nor-valine > DL-alanine > DL-serine > glycine. But the stability order in aqueous NaF solution is glycine > DL-alanine > DL-serine > Dl-nor-valine. Thus, the difference in size of cations is also a guiding factor for the change in transfer enthalpy due to cavity formation for amino acids in such aqueous electrolytes solution.

The above experimental solubility data suggest that all the studied amino acids show salting-in effect in aqueous-KF, whereas glycine and DL-serine show salting-in effect in aqueous NaF solutions. The Gibbs free energy due to acid-base, hydrogen bonding, and dispersion types of interactions shows that all the amino acids are more stable in aqueous KF rather than in aqueous NaF solutions. K^+ imparts stronger dispersion interaction as compared to Na^+ to stabilise larger amino acids.

References

1 Bhattacharyya A & Bhattacharyya S K, *J Sol Chem*, 42 (2013) 2149.
2 Pradhan A A & Vera J H, *Fluid Phase Equilib*, 152 (1998) 121.
3 Nozaki Y & Tanford C, *J Biol Chem,* 238 (1963) 4074.
4 Roy S, Mahali K, Mondal S, Mondal R P & Dolui B K, *Russian J Gen Chem*, 85 (2015) 162.
5 Anfinsen C B & Seheraga H A, *Adv Protein Chem*, 29 (1978) 205.
6 Reading J F, Watson I D & Hedwig G R, *J Chem Thermodyn*, 22 (1990) 159.
7 Banipal T S, Singh G & Lark B S, *J Sol Chem*, 30 (2001) 657.
8 Lapamje S, *Physicochemical Aspects of Proteins Denaturation,* (Wiley Interscience, New York) 1978.
9 Held C, Cameretti L F & Sadowski G, *Ind Eng Chem Res***,** 50 (2011) 131.
10 Hippel V et al., *Structure of Stability of Biological Macromolecules*, (Marcel Dekker, New York) 1969.
11 Roy S, Mahali K, Akhter S & Dolui B K , *Asian J Chem,* 25 (2013) 6661.
12 Roy S, Mahali K, Mondal S & Dolui B K , *Russian J Phys Chem A,* 89 (2015) 654.
13 Roy S, Mahali K & Dolui B K, *J Chem Eng Data,* 60 (2015) 1233.
14 Roy S, Mahali K & Dolui B K , *Biochem Ind J*, 3 (2009) 63.
15 Mahali K, Roy S & Dolui B K , *J Biophys Chem*, 2 (2011) 185.
16 Mahali K, Roy S & Dolui B K , *J Chinese Chem Soc*, 61 (2014) 659.
17 Roy S, Mahali K & Dolui B K , *J Sol Chem,* 42 (2013) 1472.
18 Mahali K, Roy S & Dolui B K , *J Sol Chem*, 42 (2013) 1096.
19 Ferreira L A, Macedo E A & Pinho S P, *Ind Eng Chem Res*, 44 (2005) 8892.
20 Eyal A M & Bressler E, *Biotechnol Bioeng*, 287 (1993) 41.
21 Sinha R & Kundu K K, *J Mol Liq*, 111 (2004) 151.
22 Sinha R, Bhattacharya S K & Kundu K K, *J Mol Liq*, 95 (2005) 122.
23 Chatterjee S & Basumallick I, *J Chinese Chem Soc*, 667 (2007) 667.
24 Pierotti R A, *Chem Rev,* 76 (1976) 717.
25 Marcus Y, *Ion Solvation*, (Wiley, New York) 1985.
26 Graziano G, *J Phys Chem B*, 2632 (2001) 105.
27 Kim J I, Cocal, A, Born H & Comma E A, *Z Phys Chem Neue Folge*, 209 (1978) 209.
28 Hein, Best, Pattison, Arena, *College Chemistry,* 5th Edn, (Brooks/Cole Pub Co, Canada) 1993.
29 David R Lide, *CRC Handbook of Chemistry and Physics,* 85th Edn, (CRC Press, Boca Raton, USA) 2004.
30 Dittrich B & Jayatilaka D, *Struct Bond,* 47 (2012) 27.
31 Khoshkbarchi M K & Vera J H, *Ind Eng Chem Res,* 36 (1997) 2445.
32 Pradhan A & Vera J H, *J Chem Eng Data*, 140 (2000) 45.
33 El-Dossoki F I, *J Sol Chem*, 39 (2010) 1311.
34 Roy S, Guin P S & Dolui B K, *J. Mol Liq*, 211 (2015) 294.
35 Roy S, Hossain A & Dolui B K, *J Chem Eng Data*, 61 (2016) 132.
36 Held C, Reschke T, Müller R, Kunz W & Sadowski G, *J Chem Thermodyn,* 68 (2014) 1.