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# Notes

## Study of Kirkwood-Buff integrals of selected polar and nonpolar amino acids in aqueous-streptomycin sulphate solutions at 298.15 K

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The Kirkwood-Buff (K-B) integrals play a pivotal role in understanding the physiochemical action of drugs on proteins. The Kirkwood-Buff theory can be used to characterize the intermolecular interactions of amino acids with drug by directly calculating $G_{11}$, $G_{22}$ and $G_{12}$ parameters which represent solute-solute, solvent-solvent and solute-solvent interactions respectively. The K-B integrals of nonpolar amino acids glycine, L-alanine, L-valine, L-isoleucine and polar amino acids L-histidine and L-arginine in aqueous-streptomycin sulphate solutions (1% and 2% streptomycin sulphate in water, *w*/*w*) have been calculated from experimental data of ultrasonic speed and density at 298.15 K. All the results obtained by theoretical calculations are in good agreement with those of experimental results.

**Keywords:** Kirkwood-Buff integrals, Amino acids, Streptomycin sulphate, Apparent molar volumes, Densities, Ultrasonic speeds

The study of thermodynamic stability of the native structure of protein has proved to be quite challenging and still remains a subject of extensive investigation[1]. Owing to the complexities arising from direct thermodynamic study on proteins, investigations of the behaviour of model compound of proteins like amino acids and peptides in aqueous and mixed aqueous solvents make it easy to understand the factor governing their stability[2,3]. To understand the chemistry of biological system, it is important to study properties of amino acids in aqueous-drug solutions[4]. Most of the compounds of medicinal interest undergo a number of complicated interactions of varied nature[5,6]. Drug action has been widely recognized to be the ultimate consequence of physicochemical interactions between the drug and functionally important biomolecules in living organisms. Drugs when administered in the body interact with receptor made up of protein and change their conformation. This makes the body to respond in a particular way. Although various clinical researches are available to optimize the drug dose in human body, the physiochemical study of these drugs with amino acids are still in initial stages[7,8]. Only few reports are available in literature on amino acid-drug interaction[9–18].

Streptomycin sulphate is one such important drug whose physiochemical interaction with protein is not studied in detail yet. It is an antibiotic used to treat a number of bacterial infections including tuberculosis, plague, endocarditis, rat bite fever, etc. Streptomycin binds with highly conserved structure formed by the 16S rRNA, which interacts with ribosomal protein S12. This may lead to the destabilization of its structure which in turn affects the binding of streptomycin with ribosome. This makes the study of amino acid-aqueous streptomycin even more important. In our earlier investigations we studied solute-solute and solute-solvent interactions of nonpolar amino acids glycine/L-alanine/L-valine/L-isoleucine[19] and polar amino acids L-histidine/L-arginine[20] with water and aqueous-streptomycin sulphate [1% (0.0069 mol $kg^{-1}$) and 2% (0.0137 mol $kg^{-1}$) streptomycin sulphate in water] solvents by using physicochemical methods using experimental density ($\rho$), ultrasonic speed ($u$) and viscosity ($\eta$) data.

But there exists one theory which can directly assess all three interactions, i.e., solute-solute, solute-solvent and solvent-solvent simultaneously, known as Kirkwood-Buff theory (K-B theory)[21]. Although people have done work on the theoretical estimation of thermodynamic properties of liquid mixtures[22–32], there are only few reports on theoretical estimation of thermodynamic properties of amino acids[33,34]. In the present study, we have applied K-B theory to evaluate the solute-solute, solute-solvent and solvent-solvent interaction parameters of four nonpolar amino acids: glycine/L-alanine/L-valine/L-isoleucine and two polar amino acids: L-histidine/L-arginine and have studied their interaction with aqueous-streptomycin sulphate (1% and 2% streptomycin sulphate in water, *w*/*w*). The experimental density and ultrasonic speed data at 298.15 K required for the calculations have been taken from our previous studies[19,20].

The Kirkwood-Buff (K-B)[21] theory is considered as the most important theory of solutions. K-B theory provides a link between microscopic structures and macroscopic (thermodynamic) properties such as compressibility, partial molar volumes and derivatives of the chemical potentials, in terms of K-B integrals, $G_{ij}$, (volume per central molecule)

$$G_{ij} = \int_0^\infty (g_{ij}(r) - 1) 4\pi r^2 \mathrm{d}r \quad \ldots (1)$$

where subscripts *i* and *j* refer to the two components that may be the same or different and $g_{ij}$ is the pair correlation function, denoting the probability of finding a molecule of species *i* in a volume element at a distance *r* from the centre of a molecule of species *j*. Since these integrals are directly related to radial distribution function, they are very sensitive to molecular interactions. These integrals basically convey information on the tendency of solute molecules to attract one another. Thus, this theory may be used to compute the thermodynamic quantities based on the knowledge of the pair correlation function. The K-B theory is an exact theory of solutions which does not involve the assumption of pairwise additivity of the total potential energy and is applicable to both spherical as well as nonspherical molecules. This theory is traditionally applied to the study of hydrophobic phenomena[35]. The K-B integrals $G_{ij}$ as functions of mole fraction of amino acids indicate a change in association between solute and solvents[36]. Therefore, its value should be important for determining preferential solvation. It is difficult to directly calculate the integrals proposed by Kirkwood and Buff. Ben-Naim[22] was the first to suggest the reverse process that the measure of the thermodynamic quantities could provide an insight into the microstructure of the solutions, albeit in an integrated form. Matteoli and Lepori provided the first illustration of this idea by calculating the K-B integrals for various aqueous mixtures[37].

The K-B integrals are computed as follows. For the calculation purpose solute, i.e., amino acids are considered as 1 and solvent as 2. For solutions having 1% and 2% streptomycin co-solute, calculations were adjusted accordingly. $G_{12} = G_{21}$, $G_{11}$ and $G_{22}$ represent solute-solvent, solute-solute and solvent-solvent interaction parameter, respectively. Following equations were used to calculate these K-B parameters[22,37]

$$G_{12} = G_{21} = \mathrm{R}Tk_\mathrm{T} - \left(\tilde{V}_1\tilde{V}_2/DV\right) \quad \ldots (2)$$

where *V* is the molar volume of the mixture, *T* is the absolute temperature, *R* is the universal gas constant, $\tilde{V}_2$ is the partial molar volume of solvent, $\tilde{V}_1$ is the apparent molar volume ($V_\phi$) of amino acid and $k_\mathrm{T}$ is isothermal compressibility of the solution calculated (assuming it to be equal to isentropic compressibility, $k_\mathrm{s}$) as follow

$$V_\phi = \frac{1000(\rho_\mathrm{o} - \rho)}{m\rho\rho_\mathrm{o}} + \frac{M}{\rho} \quad \ldots (3)$$

$$k_\mathrm{T} = k_\mathrm{s} = \frac{1}{u^2\rho} \quad \ldots (4)$$

where m is the molal concentration of the solute (amino acid), $\rho$ and $\rho_\mathrm{o}$ are the densities of the solution and the solvent (aqueous-streptomycin sulphate), respectively; and *M* is the molar mass of the solute (amino acid), *u* is the ultrasonic speed. The $k_\mathrm{S}$ values of solvents have been used assuming these to be equal to the $k_\mathrm{T}$ of solutions, as their difference contribute negligibly to the $G_{ij}$ values[38,39]. The parameter *D* in eqn 1 can be calculated using the following equation

$$D = 1 + x_1(\partial \ln\gamma_1/\partial x_1)_{\mathrm{P,T}} \quad \ldots (5)$$

where $x_1$ and $\gamma_1$ are the mole fraction and activity coefficient of the solute. The $\partial \ln\gamma_1/\partial x_1$ term used in eqn 5, can be obtained by plotting $\ln\gamma_1$ as a function of mole fraction of amino acid and evaluating the required slopes. The same could have been obtained by using the data of solvent activity coefficients and its mole fraction. Following equation has been used for calculating the activity coefficient values[32]

$$\ln\gamma_1 = x_2\, w/kT \quad \ldots (6)$$

where *w* varies very slightly with mole fraction and its value can be taken equal to $10^{-21}$, *k* is the Boltzmann constant, $x_2$ is the mole fraction of solvent. Solute-solute and solvent-solvent interaction parameters, i.e., $G_{11}$ and $G_{22}$ can be calculated using solute-solvent interaction parameter $G_{12}$

$$G_{11} = G_{12} + \left(1/x_1\right)\{\left(\tilde{V}_2/D\right) - V\} \quad \ldots (7)$$

$$G_{22} = G_{12} + \left(1/x_2\right)\{\left(\tilde{V}_1/D\right) - V\} \quad \ldots (8)$$

## Results and discussion

The K-B integrals for nonpolar amino acids glycine/L-alanine/L-valine/L-isoleucine and polar amino acids L-histidine/L-arginine in water and in aqueous streptomycin solvents (1 and 2% streptomycin sulphate in water) at 298.15 K along with experimental data used in calculations are listed in Tables 1–3. The variations of $G_{12}$, $G_{11}$ and $G_{22}$ with

Table 1 — Values of $m$, $x_1$, $\rho$, $u$, $V_\phi$, $k_T$, $G_{12}$, $G_{11}$ and $G_{22}$ for the amino acids in water at 298.15 K

| $m$ (mol kg$^{-1}$) | $x_1$ | $\rho$ (kg m$^{-3}$) | $u$ (m s$^{-1}$) | $10^6 \cdot V_\phi$ (m$^3$ mol$^{-1}$) | $10^{11} \cdot k_T$ (m$^2$ N$^{-1}$) | $10^6 \cdot G_{12}$ (m$^3$ mol$^{-1}$) | $10^6 \cdot G_{11}$ (m$^3$ mol$^{-1}$) | $10^3 \cdot G_{22}$ (m$^3$ mol$^{-1}$) |
|---|---|---|---|---|---|---|---|---|
| Glycine | | | | | | | | |
| 0.0000 | 0.00000 | 997.07 | 1496.9 | | 4.4760 | | | |
| 0.0250 | 0.00045 | 997.86 | 1497.5 | 43.430 | 4.4687 | -0.7821 | -2.1901 | -0.9618 |
| 0.0500 | 0.00090 | 998.63 | 1498.5 | 43.798 | 4.4596 | -0.7885 | -1.0968 | -0.9630 |
| 0.0750 | 0.00135 | 999.38 | 1499.7 | 44.180 | 4.4488 | -0.7951 | -0.7323 | -0.9642 |
| 0.0999 | 0.00180 | 1000.11 | 1501.3 | 44.555 | 4.4364 | -0.8016 | -0.5507 | -0.9653 |
| 0.1249 | 0.00225 | 1000.82 | 1503.1 | 44.929 | 4.4223 | -0.8080 | -0.4412 | -0.9666 |
| 0.1500 | 0.00269 | 1001.51 | 1505.3 | 45.328 | 4.4066 | -0.8149 | -0.3679 | -0.9678 |
| L-Alanine | | | | | | | | |
| 0.0000 | 0.00000 | 997.07 | 1496.9 | | 4.4760 | | | |
| 0.0250 | 0.00045 | 997.79 | 1497.5 | 60.339 | 4.4691 | -1.0866 | -2.1911 | -0.9456 |
| 0.0500 | 0.00090 | 998.49 | 1498.5 | 60.698 | 4.4602 | -1.0927 | -1.0977 | -0.9472 |
| 0.0750 | 0.00135 | 999.17 | 1499.8 | 61.058 | 4.4493 | -1.0988 | -0.7333 | -0.9488 |
| 0.0999 | 0.00180 | 999.83 | 1501.5 | 61.392 | 4.4366 | -1.1045 | -0.5516 | -0.9505 |
| 0.1249 | 0.00225 | 1000.47 | 1503.5 | 61.759 | 4.4218 | -1.1107 | -0.4421 | -0.9521 |
| 0.1500 | 0.00269 | 1001.09 | 1505.9 | 62.117 | 4.4049 | -1.1167 | -0.3689 | -0.9538 |
| L-Valine | | | | | | | | |
| 0.0000 | 0.00000 | 997.07 | 1496.9 | | 4.4760 | | | |
| 0.0250 | 0.00045 | 997.74 | 1497.3 | 90.637 | 4.4705 | -1.6323 | -2.1927 | -0.9166 |
| 0.0500 | 0.00090 | 998.38 | 1498.1 | 90.960 | 4.4629 | -1.6375 | -1.0994 | -0.9190 |
| 0.0750 | 0.00135 | 999.01 | 1499.3 | 91.284 | 4.4530 | -1.6428 | -0.7349 | -0.9214 |
| 0.0999 | 0.00180 | 999.62 | 1500.9 | 91.594 | 4.4408 | -1.6478 | -0.5532 | -0.9238 |
| 0.1249 | 0.00225 | 1000.21 | 1502.9 | 91.909 | 4.4264 | -1.6529 | -0.4437 | -0.9262 |
| 0.1500 | 0.00269 | 1000.78 | 1505.2 | 92.245 | 4.4101 | -1.6584 | -0.3705 | -0.9286 |
| L-Isoleucine | | | | | | | | |
| 0.0000 | 0.00000 | 997.07 | 1496.9 | | 4.4760 | | | |
| 0.0250 | 0.00045 | 997.71 | 1497.2 | 105.737 | 4.4713 | -1.9042 | -2.1935 | -0.9021 |
| 0.0500 | 0.00090 | 998.33 | 1497.9 | 106.073 | 4.4644 | -1.9096 | -1.1002 | -0.9049 |
| 0.0750 | 0.00135 | 998.93 | 1499.0 | 106.411 | 4.4551 | -1.9150 | -0.7357 | -0.9076 |
| 0.0999 | 0.00180 | 999.51 | 1500.5 | 106.757 | 4.4437 | -1.9206 | -0.5541 | -0.9104 |
| 0.1249 | 0.00225 | 1000.07 | 1502.4 | 107.097 | 4.4300 | -1.9261 | -0.4446 | -0.9131 |
| 0.1500 | 0.00269 | 1000.61 | 1504.7 | 107.435 | 4.4140 | -1.9315 | -0.3713 | -0.9159 |
| L-Histidine | | | | | | | | |
| 0.0000 | 0.00000 | 997.07 | 1496.9 | | 4.4760 | | | |
| 0.0199 | 0.00036 | 998.22 | 1501.1 | 97.526 | 4.4459 | -1.7565 | -2.7535 | -0.9094 |
| 0.0399 | 0.00072 | 999.37 | 1504.4 | 97.408 | 4.4213 | -1.7538 | -1.3765 | -0.9118 |
| 0.0599 | 0.00108 | 1000.52 | 1506.8 | 97.294 | 4.4021 | -1.7513 | -0.9190 | -0.9142 |
| 0.0799 | 0.00144 | 1001.68 | 1508.1 | 97.193 | 4.3895 | -1.7490 | -0.6905 | -0.9165 |
| 0.1000 | 0.00180 | 1002.83 | 1508.6 | 97.116 | 4.3815 | -1.7472 | -0.5530 | -0.9189 |
| 0.1199 | 0.00216 | 1003.98 | 1507.9 | 96.973 | 4.3806 | -1.7441 | -0.4623 | -0.9213 |
| L-Arginine | | | | | | | | |
| 0.0000 | 0.00000 | 997.07 | 1496.9 | | 4.4760 | | | |
| 0.0249 | 0.00045 | 998.35 | 1501.7 | 122.927 | 4.4417 | -2.2138 | -2.2033 | -0.8857 |
| 0.0500 | 0.00090 | 999.62 | 1505.6 | 123.117 | 4.4131 | -2.2164 | -1.1011 | -0.8890 |
| 0.0749 | 0.00135 | 1000.89 | 1508.6 | 123.007 | 4.3900 | -2.2137 | -0.7376 | -0.8925 |
| 0.1002 | 0.00180 | 1002.14 | 1510.8 | 123.148 | 4.3718 | -2.2155 | -0.5533 | -0.8959 |
| 0.1251 | 0.00225 | 1003.40 | 1512.4 | 123.066 | 4.3571 | -2.2133 | -0.4447 | -0.8994 |
| 0.1501 | 0.00270 | 1004.64 | 1512.8 | 123.048 | 4.3494 | -2.2122 | -0.3719 | -0.9029 |

the mole fraction, $x_1$ of amino acids are shown graphically in supplementary data, Figs S1–S6.

The variations of K-B interaction parameters, i.e., $G_{12}$, $G_{11}$ and $G_{22}$ with mole fraction ($x_1$) of amino acids, glycine/L-alanine/L-valine/L-isoleucine in water, 1% and 2% aqueous-streptomycin sulphate solvents are shown graphically in Figs S1-S3, respectively. The values of $G_{12}$ for nonpolar amino

Table 2 — Values of $m$, $x_1$, $\rho$, $u$, $V_\phi$, $k_T$, $G_{12}$, $G_{11}$ and $G_{22}$ for the amino acids in 1% streptomycin sulphate + water at 298.15 K

| $m$ | $x_1$ | $\rho$ | $u$ | $10^6 \cdot V_\phi$ | $10^{11} \cdot k_T$ | $10^6 \cdot G_{12}$ | $10^6 \cdot G_{11}$ | $10^3 \cdot G_{22}$ |
|---|---|---|---|---|---|---|---|---|
| (mol kg$^{-1}$) | | (kg m$^{-1}$) | (m s$^{-1}$) | (m$^3$ mol$^{-1}$) | (m$^2$ N$^{-1}$) | (m$^3$ mol$^{-1}$) | (m$^3$ mol$^{-1}$) | (m$^3$ mol$^{-1}$) |
| Glycine | | | | | | | | |
| 0.0000 | 0.00000 | 1001.29 | 1503.8 | | 4.4163 | | | |
| 0.0250 | 0.00045 | 1002.05 | 1504.4 | 44.498 | 4.4094 | -0.8013 | -2.2032 | -0.9666 |
| 0.0500 | 0.00090 | 1002.80 | 1505.3 | 44.883 | 4.4009 | -0.8079 | -1.1033 | -0.9678 |
| 0.0750 | 0.00135 | 1003.52 | 1506.5 | 45.269 | 4.3907 | -0.8146 | -0.7367 | -0.9690 |
| 0.0999 | 0.00180 | 1004.22 | 1508.0 | 45.626 | 4.3790 | -0.8207 | -0.5540 | -0.9702 |
| 0.1249 | 0.00224 | 1004.90 | 1509.8 | 46.003 | 4.3656 | -0.8272 | -0.4438 | -0.9714 |
| 0.1500 | 0.00269 | 1005.56 | 1511.9 | 46.382 | 4.3506 | -0.8338 | -0.3701 | -0.9727 |
| L-Alanine | | | | | | | | |
| 0.0000 | 0.00000 | 1001.29 | 1503.8 | | 4.4163 | | | |
| 0.0250 | 0.00045 | 1001.98 | 1504.3 | 61.404 | 4.4102 | -1.1057 | -2.2041 | -0.9504 |
| 0.0500 | 0.00090 | 1002.65 | 1505.1 | 61.741 | 4.4027 | -1.1114 | -1.1042 | -0.9520 |
| 0.0750 | 0.00135 | 1003.30 | 1506.2 | 62.093 | 4.3937 | -1.1173 | -0.7376 | -0.9537 |
| 0.0999 | 0.00180 | 1003.93 | 1507.5 | 62.452 | 4.3831 | -1.1234 | -0.5549 | -0.9553 |
| 0.1249 | 0.00224 | 1004.54 | 1509.1 | 62.801 | 4.3712 | -1.1293 | -0.4447 | -0.9570 |
| 0.1500 | 0.00269 | 1005.14 | 1511.0 | 63.165 | 4.3576 | -1.1355 | -0.3711 | -0.9587 |
| L-Valine | | | | | | | | |
| 0.0000 | 0.00000 | 1001.29 | 1503.8 | | 4.4163 | | | |
| 0.0250 | 0.00045 | 1001.92 | 1504.1 | 91.726 | 4.4119 | -1.6517 | -2.2057 | -0.9214 |
| 0.0500 | 0.00090 | 1002.53 | 1504.7 | 92.109 | 4.4056 | -1.6580 | -1.1059 | -0.9237 |
| 0.0750 | 0.00135 | 1003.12 | 1505.6 | 92.466 | 4.3975 | -1.6639 | -0.7393 | -0.9261 |
| 0.0999 | 0.00180 | 1003.69 | 1506.9 | 92.814 | 4.3876 | -1.6696 | -0.5565 | -0.9285 |
| 0.1249 | 0.00224 | 1004.24 | 1508.5 | 93.183 | 4.3758 | -1.6756 | -0.4464 | -0.9309 |
| 0.1500 | 0.00269 | 1004.77 | 1510.5 | 93.540 | 4.3621 | -1.6815 | -0.3727 | -0.9333 |
| L-Isoleucine | | | | | | | | |
| 0.0000 | 0.00000 | 1001.29 | 1503.8 | | 4.4163 | | | |
| 0.0250 | 0.00045 | 1001.90 | 1503.9 | 106.755 | 4.4129 | -1.9223 | -2.2066 | -0.9070 |
| 0.0500 | 0.00090 | 1002.49 | 1504.3 | 107.035 | 4.4080 | -1.9267 | -1.1067 | -0.9098 |
| 0.0750 | 0.00135 | 1003.06 | 1505.0 | 107.339 | 4.4013 | -1.9315 | -0.7401 | -0.9126 |
| 0.0999 | 0.00180 | 1003.61 | 1506.0 | 107.629 | 4.3933 | -1.9361 | -0.5574 | -0.9154 |
| 0.1249 | 0.00224 | 1004.14 | 1507.3 | 107.934 | 4.3836 | -1.9409 | -0.4472 | -0.9182 |
| 0.1500 | 0.00269 | 1004.66 | 1508.8 | 108.228 | 4.3724 | -1.9455 | -0.3735 | -0.9211 |
| L-Histidine | | | | | | | | |
| 0.0000 | 0.00000 | 1001.29 | 1503.8 | | 4.4163 | | | |
| 0.0198 | 0.00036 | 1002.39 | 1507.0 | 99.438 | 4.3928 | -1.7907 | -2.7838 | -0.9134 |
| 0.0397 | 0.00071 | 1003.50 | 1509.9 | 99.217 | 4.3711 | -1.7862 | -1.3916 | -0.9159 |
| 0.0598 | 0.00108 | 1004.62 | 1512.4 | 99.088 | 4.3518 | -1.7834 | -0.9260 | -0.9183 |
| 0.0799 | 0.00144 | 1005.74 | 1514.5 | 98.969 | 4.3349 | -1.7808 | -0.6947 | -0.9207 |
| 0.1000 | 0.00180 | 1006.86 | 1516.3 | 98.854 | 4.3198 | -1.7782 | -0.5563 | -0.9231 |
| 0.1196 | 0.00215 | 1007.95 | 1517.6 | 98.761 | 4.3077 | -1.7761 | -0.4662 | -0.9254 |
| L-Arginine | | | | | | | | |
| 0.0000 | 0.00000 | 1001.29 | 1503.8 | | 4.4163 | | | |
| 0.0248 | 0.00045 | 1002.51 | 1507.0 | 124.757 | 4.3922 | -2.2465 | -2.2253 | -0.8897 |
| 0.0503 | 0.00091 | 1003.76 | 1509.8 | 124.689 | 4.3705 | -2.2445 | -1.1011 | -0.8933 |
| 0.0752 | 0.00135 | 1004.98 | 1512.1 | 124.574 | 4.3519 | -2.2416 | -0.7391 | -0.8969 |
| 0.1001 | 0.00180 | 1006.19 | 1513.8 | 124.541 | 4.3369 | -2.2403 | -0.5572 | -0.9004 |
| 0.1247 | 0.00224 | 1007.39 | 1515.1 | 124.426 | 4.3243 | -2.2375 | -0.4488 | -0.9040 |
| 0.1502 | 0.00270 | 1008.63 | 1515.8 | 124.322 | 4.3150 | -2.2348 | -0.3739 | -0.9076 |

acids in water and aqueous-streptomycin sulphate are negative and decrease with increase in amino acid concentration, which indicates significant solute-solvent interactions and the structure breaking ability of these nonpolar amino acids (Figs S1a, S2a, S3a). It has been reported that there exists hydrophilic-ionic interaction between OH/NH/$NH_2$ groups of streptomycin sulphate and zwitterions of these amino

Table 3 — Values of $m$, $x_1$, $\rho$, $u$, $V_\phi$, $k_T$, $G_{12}$, $G_{11}$ and $G_{22}$ for the amino acids in 2% streptomycin sulphate + water at 298.15 K

| $m$ | $x_1$ | $\rho$ | $u$ | $10^6 \cdot V_\phi$ | $10^{11} \cdot k_T$ | $10^6 \cdot G_{12}$ | $10^6 \cdot G_{11}$ | $10^3 \cdot G_{22}$ |
|---|---|---|---|---|---|---|---|---|
| (mol kg$^{-1}$) | | (kg m$^{-1}$) | (m s$^{-1}$) | (m$^3$ mol$^{-1}$) | (m$^2$ N$^{-1}$) | (m$^3$ mol$^{-1}$) | (m$^3$ mol$^{-1}$) | (m$^3$ mol$^{-1}$) |
| Glycine | | | | | | | | |
| 0.0000 | 0.00000 | 1005.43 | 1507.2 | | 4.3783 | | | |
| 0.0250 | 0.00045 | 1006.16 | 1507.8 | 45.627 | 4.3719 | -0.8215 | -2.2159 | -0.9712 |
| 0.0500 | 0.00090 | 1006.88 | 1508.6 | 46.010 | 4.3639 | -0.8281 | -1.1097 | -0.9724 |
| 0.0750 | 0.00135 | 1007.57 | 1509.8 | 46.393 | 4.3543 | -0.8347 | -0.7410 | -0.9736 |
| 0.0999 | 0.00180 | 1008.23 | 1511.2 | 46.768 | 4.3430 | -0.8412 | -0.5572 | -0.9749 |
| 0.1249 | 0.00224 | 1008.88 | 1512.9 | 47.170 | 4.3305 | -0.8481 | -0.4464 | -0.9761 |
| 0.1500 | 0.00269 | 1009.51 | 1515.0 | 47.565 | 4.3161 | -0.8549 | -0.3723 | -0.9774 |
| L-Alanine | | | | | | | | |
| 0.0000 | 0.00000 | 1005.43 | 1507.2 | | 4.3783 | | | |
| 0.0250 | 0.00045 | 1006.09 | 1507.7 | 62.452 | 4.3727 | -1.1244 | -2.2168 | -0.9551 |
| 0.0500 | 0.00090 | 1006.73 | 1508.5 | 62.828 | 4.3654 | -1.1308 | -1.1106 | -0.9567 |
| 0.0750 | 0.00135 | 1007.35 | 1509.6 | 63.217 | 4.3563 | -1.1374 | -0.7419 | -0.9584 |
| 0.0999 | 0.00180 | 1007.94 | 1511.0 | 63.596 | 4.3455 | -1.1438 | -0.5581 | -0.9600 |
| 0.1249 | 0.00224 | 1008.51 | 1512.7 | 63.987 | 4.3332 | -1.1505 | -0.4473 | -0.9617 |
| 0.1500 | 0.00269 | 1009.07 | 1514.7 | 64.384 | 4.3192 | -1.1572 | -0.3732 | -0.9634 |
| L-Valine | | | | | | | | |
| 0.0000 | 0.00000 | 1005.43 | 1507.2 | | 4.3783 | | | |
| 0.0250 | 0.00045 | 1006.03 | 1507.4 | 92.681 | 4.3745 | -1.6687 | -2.2185 | -0.9262 |
| 0.0500 | 0.00090 | 1006.61 | 1508.0 | 93.023 | 4.3687 | -1.6742 | -1.1123 | -0.9286 |
| 0.0750 | 0.00135 | 1007.18 | 1508.9 | 93.326 | 4.3609 | -1.6791 | -0.7436 | -0.9310 |
| 0.0999 | 0.00180 | 1007.72 | 1510.2 | 93.648 | 4.3510 | -1.6844 | -0.5598 | -0.9334 |
| 0.1249 | 0.00224 | 1008.24 | 1511.9 | 93.975 | 4.3390 | -1.6897 | -0.4490 | -0.9359 |
| 0.1500 | 0.00269 | 1008.76 | 1513.9 | 94.278 | 4.3253 | -1.6945 | -0.3749 | -0.9384 |
| L-Isoleucine | | | | | | | | |
| 0.0000 | 0.00000 | 1005.43 | 1507.2 | | 4.3783 | | | |
| 0.0250 | 0.00045 | 1006.01 | 1507.2 | 107.648 | 4.3757 | -1.9381 | -2.2193 | -0.9118 |
| 0.0500 | 0.00090 | 1006.57 | 1507.5 | 107.884 | 4.3715 | -1.9417 | -1.1131 | -0.9147 |
| 0.0750 | 0.00135 | 1007.11 | 1508.1 | 108.122 | 4.3656 | -1.9454 | -0.7444 | -0.9176 |
| 0.0999 | 0.00180 | 1007.64 | 1509.1 | 108.390 | 4.3580 | -1.9495 | -0.5606 | -0.9204 |
| 0.1249 | 0.00224 | 1008.15 | 1510.3 | 108.625 | 4.3489 | -1.9531 | -0.4498 | -0.9233 |
| 0.1500 | 0.00269 | 1008.65 | 1511.7 | 108.898 | 4.3384 | -1.9573 | -0.3757 | -0.9262 |
| L-Histidine | | | | | | | | |
| 0.0000 | 0.00000 | 1005.43 | 1507.2 | | 4.3783 | | | |
| 0.0199 | 0.00036 | 1006.50 | 1510.2 | 101.025 | 4.3563 | -1.8190 | -2.7859 | -0.9176 |
| 0.0402 | 0.00072 | 1007.60 | 1512.8 | 100.706 | 4.3366 | -1.8128 | -1.3824 | -0.9202 |
| 0.0598 | 0.00108 | 1008.66 | 1514.9 | 100.567 | 4.3200 | -1.8098 | -0.9314 | -0.9226 |
| 0.0798 | 0.00144 | 1009.74 | 1516.5 | 100.463 | 4.3063 | -1.8074 | -0.6996 | -0.9250 |
| 0.1004 | 0.00180 | 1010.85 | 1517.6 | 100.378 | 4.2954 | -1.8054 | -0.5573 | -0.9275 |
| 0.1203 | 0.00216 | 1011.92 | 1518.2 | 100.307 | 4.2874 | -1.8036 | -0.4662 | -0.9298 |
| L-Arginine | | | | | | | | |
| 0.0000 | 0.00000 | 1005.43 | 1507.2 | | 4.3783 | | | |
| 0.0248 | 0.00045 | 1006.61 | 1510.1 | 126.043 | 4.3564 | -2.2693 | -2.2381 | -0.8942 |
| 0.0499 | 0.00090 | 1007.79 | 1512.5 | 126.178 | 4.3375 | -2.2710 | -1.1163 | -0.8976 |
| 0.0748 | 0.00135 | 1008.97 | 1514.4 | 125.999 | 4.3216 | -2.2670 | -0.7473 | -0.9012 |
| 0.1002 | 0.00180 | 1010.17 | 1515.8 | 125.870 | 4.3085 | -2.2639 | -0.5598 | -0.9049 |
| 0.1249 | 0.00224 | 1011.33 | 1516.7 | 125.792 | 4.2984 | -2.2617 | -0.4507 | -0.9085 |
| 0.1502 | 0.00270 | 1012.52 | 1517.0 | 125.678 | 4.2917 | -2.2589 | -0.3761 | -0.9121 |

acids[19]. The values of $G_{12}$ for these amino acids in all the three solvents follow the order: glycine > L-alanine > L-valine > L-isoleucine, which in turn indicates that the order of solute-solvent interactions in these systems decreases with increase in hydrophobic character in the side chain of amino

acids. Also, the values of $G_{12}$ for these amino acids become more negative on addition of streptomycin sulphate and decrease further with increase in the concentration of streptomycin. This indicates that the solute-solvent interaction (hydrophilic-ionic interaction) increases with increase in added streptomycin sulphate concentration. These findings further support our conclusions from previous experimental studies[19].

A perusal of Figs S1b, S2b and S3b shows that the values of $G_{11}$ are nearly same in magnitude for all the four nonpolar amino acids in each solvent. This indicates that the solute-solute interactions between amino acid molecules are not much affected by addition of streptomycin sulphate in these systems. The $G_{11}$ values show sudden increase from $x_1 = 0.0005$ to $x_1 = 0.015$ of amino acids and then gradually increase with further increase in $x_1$ for rest of the compositions. This indicates that the solute-solute interactions between amino acid molecules increase with increase in amino acid concentration.

The values of $G_{22}$ (which represents solvent-solvent interactions) decrease with increase in the concentration of amino acid in each system, which indicates the structure breaking ability of these nonpolar amino acids (Figs S1c, S2c, S3c). The values of $G_{22}$ for these amino acids in all the three solvents follow the order: glycine < L-alanine < L-valine < L-isoleucine, which in turn indicates the order of solvent-solvent interactions in these systems. This is due to the reason that solute-solvent interactions increase with decrease in hydrophobic character in the side chain of amino acids, resulting in decreased solvent-solvent interactions.

The variations of K-B interaction parameters, i.e., $G_{12}$, $G_{11}$ and $G_{22}$ with mole fraction ($x_1$) of amino acids, L-histidine/L-arginine in water, 1% and 2% aqueous-streptomycin sulphate solvents are shown in Figs S4-S6, respectively. The values of $G_{12}$ for nonpolar amino acids in water and aqueous-streptomycin sulphate are negative and increase with increase in amino acid concentration, which indicates significant solute-solvent interactions and the structure making ability of these polar amino acids (Figs S4a, S5a, S6a). It has been reported that there exists hydrophilic-ionic interaction between OH/NH/$NH_2$ groups of streptomycin sulphate and zwitterions of these amino acids. The values of $G_{12}$ for these amino acids in all the three solvents follow the order: L-histidine > L-arginine, which in turn indicates that the order of solute-solvent interactions in these systems decreases with increase in hydrophobic character in the side chain of amino acids. Also, the values of $G_{12}$ for these amino acids become more negative on addition of streptomycin sulphate and decrease further with increase in the concentration of streptomycin. This indicates that the solute-solvent interactions (hydrophilic-ionic interaction) increase with increase in added streptomycin sulphate concentration. These findings further support our conclusions from previous experimental studies[20].

The values of $G_{11}$ are nearly same in magnitude for both the polar amino acids in each solvent (Figs S4b, S5b, S6b). This indicates that the solute-solute interactions between amino acid molecules are not much affected by the addition of streptomycin sulphate in these systems. The $G_{11}$ values show sudden increase from $x_1 = 0.0005$ to $x_1 = 0.015$ of amino acids and then gradually increase with further increase in $x_1$ for rest of the compositions. This indicates that the solute-solute interactions between amino acid molecules increase with increase in amino acid concentration.

The values of $G_{22}$ (which represents solvent-solvent interactions) decrease with increase in the concentration of amino acid in each system, which indicates that the solvent-solvent interactions decrease with increase in amino acid concentration (Figs S4c, S5c, S6c). The values of $G_{22}$ for these amino acids in all the three solvents follow the order: L-histidine < L-arginine, which in turn indicates the order of solvent-solvent interactions in these systems. This is due to the reason that solute-solvent interactions are stronger in L-histidine than those in L-arginine.

In summary, using the Kirkwood-Buff theory, the K-B integrals of nonpolar amino acids glycine, L-alanine, L-valine, L-isoleucine and polar amino acids L-histidine and L-arginine in aqueous-streptomycin sulphate solutions have been calculated from experimental data of ultrasonic speed and density at 298.15 K. The results indicated that there exists hydrophilic-ionic interaction between OH/NH/$NH_2$ groups of streptomycin sulphate and zwitterions of these amino acid. The values of $G_{12}$ for these amino acids in all the three solvents follow the order: glycine > L-alanine > L-valine > L-isoleucine for nonpolar and L-histidine > L-arginine for polar, which decrease with increase in hydrophobic character in the side chain of amino acids.

## Supplementary data

Supplementary data associated with this article are available in the electronic form at http:// www.niscair.res.in/jinfo/ijca/IJCA_58A(02)281-287_SupplData.pdf.

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