Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. *76* (1) 129–142 (2011)
JSCS–4106
UDC 547.466.24:532.14:532.13:541.25+54–145.2
Original scientific paper

A volumetric and viscometric study of 4-aminobutyric acid in aqueous solutions of metformin hydrochloride at 308.15, 313.15 and 318.15 K

KRISHA RAJAGOPAL[1] and S. S. JAYABALAKRISHNAN[2]*

[1]*Department of Physics, Government College of Engineering, Tirunelveli-627007 Tamil Nadu and* [2]*Department of Physics, P. S. R. Engineering College, Sivakasi, Tamil Nadu, India*

(Received 16 June 2009, revised 21 September 2010)

Abstract: Density (ρ) and viscosity (η) measurements were performed for 4-aminobutyric acid in 0.05, 0.10 and 0.15 M aqueous metformin hydrochloride at 308.15, 313.15 and 318.15 K. The measured values of density and viscosity were used to estimate some important parameters, such as the partial molal volume, V_ϕ, the standard partial molal volume, $V_\phi^\ominus$, the standard partial molal volume of transfer, $\Delta V_\phi^\ominus$, the hydration number, n_H, the second derivative of the infinite dilution of the standard partial molal volume with temperature $\partial^2 V_\phi^\ominus/\partial T^2$, the viscosity *B*-coefficients, variation of *B* with temperature, d*B*/d*T*, the free energy of activation per mole of solvent $\Delta\mu_1^{\ominus *}$ and solute $\Delta\mu_2^{\ominus *}$ of the amino acid in a ternary system. These parameters were interpreted in terms of solute–solute and solute–solvent interactions and structure making/breaking ability of solutes in the given solution.

Keywords: density; viscosity; standard partial molal volume; hydration number; viscosity *B*-coefficient; free energy activation parameters.

INTRODUCTION

Since several biological processes involve expansion and contraction of proteins molecules resulting from temperature and pressure variations in the living systems, resulting from fever, hypothermia, anaesthesia, *etc*., the study of these processes requires fundamental information about the volumetric properties of proteins.

Amino acids (AA) were considered as model compounds instead of proteins in the presence of aqueous salt solutions to obtain thermodynamic information, as the structure of proteins are highly complicated.[1–5] Some amino acids in the presence of aqueous minerals, such as $CaCl_2$ and NaCl, are available in literature.[6,7]

* Corresponding author. E-mail: krishnanpsr@yahoo.com
doi: 10.2298/JSC090616002R

As pointed out by Iqbal *et al*.,[8] although a great amount of volumetric data for amino acids has been reported in literature, they were obtained at 25 °C; it is understandable that much more relevance and significance can be achieved by studying compounds of biological importance (amino acids) at temperatures close to physiological temperatures, namely 35 °C (308.15 K), which is close to the optimum temperature of several living species. Recently, the results of volumetric and viscometric studies of 4-aminobutyric acid in aqueous solutions of salbutamol sulphate at various temperatures were reported.[9]

A literature survey shows that the study of amino acids in the presence of aqueous metformin hydrochloride has not hitherto been reported. Thus, in this paper, the volumetric and viscometric data of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at three different temperatures (308.15 to 318.15 K) are reported.

Metformin hydrochloride ($C_4H_{11}N_5HCl$) is an antidiabetic and antihyperglycemic agent[10,11] that covers both basal and postprandial elevated blood glucose in patients with non-insulin dependant diabetes mellitus (type 2 diabetes), whose hyperglycemia cannot be satisfactorily managed by diet alone. In continuation of an earlier work on metformin hydrochloride,[12] in this paper, the density (ρ) and viscosity (η) data of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at three different molar concentrations are reported. As hydration effects are known to be very sensitive to temperature,[13–16] both volumetric and viscometric studies are reported at three temperatures, *i.e*., 308.15, 313.15 and 318.15 K. Different physical parameters, such as partial molal volume, $V_\phi^\ominus$, standard partial molal volume, standard partial molal volume of transfer, $\Delta V_\phi^\ominus$, hydration number, n_H, second derivative of infinite dilution of the standard partial molal volume with temperature $\partial^2 V_\phi^\ominus/\partial T^2$ and the viscosity *B* coefficient were calculated using the Jones–Dole equation[17] and the free energies of activation of viscous flow $\Delta\mu_1^{\ominus *}$ and $\Delta\mu_2^{\ominus *}$ per mole of solvent and solutes[18] were, respectively, estimated. All these parameters are used to discuss the solute–solute and solute–solvent interactions occurring in the ternary (4-aminobutyric acid + metformin hydrochloride + water) system as well as the structure making/breaking tendency of the solute (AA) in the given solution.

EXPERIMENTAL

The 4-aminobutyric acid (Otto Chemicals Ltd., Bangalore, minimum assay +99 %) employed in this study was of analytic grade and was used without further purification. However, it was dried over P_2O_5 in a desiccator for 72 h before use. Analytic grade metformin hydrochloride (Accuumen Pharmaceuticals, Pondichery, minimum assay 99.5 %) was used as such without any pre-treatment. Doubly distilled, deionised water with a conductivity of 1.5×10^{-4} Ω^{-1} m^{-1} was used in the experiments and was degassed prior to making the solutions. The densities of the solutions were measured using a single stem pycnometer (Pyrex glass) of bulb capacity of 8×10^{-3} dm^3 having a graduated stem with 5×10^{-7} dm^3 divisions. The marks on the stem were calibrated with doubly distilled water. The weighings were realized

by taking the samples in airtight bottles on a high precision electronic balance (A & D model HR300, Japan) with a precision of ±0.1 mg. The reproducibility of the density measurements was $\pm 2.8\times10^{-5}$ kg m^{-3}.[9] Uncertainty values related to measured density data are calculated based JCGM 100:2008. The viscosities were measured by means of a suspended level Ubbelohde viscometer with a flow time of approximately 161 s for distilled water at 308.15 K. The time of flow was measured with a stopwatch capable of recording ±0.01 s. An average of three to four sets of flow times for each solution was taken for the calculation of the viscosity. The overall experimental reproducibility was estimated to be $\pm 1.9\times10^{-3}$ mPa s.[9] As the flow times were greater than 100 s, kinetic energy corrections were not necessary.[19] The pycnometer filled with air bubble free solutions and Ubbelohde viscometer filled with test solutions were allowed to stand for about 30 min in a thermostatic water bath so as to minimize thermal fluctuations. The temperatures of the solutions were maintained to an accuracy of ±0.01 K (Eurotherm, Mittal Enterprises, New Delhi, India) in an electronically controlled thermostated water bath. The data on the density and viscosity for doubly distilled water at the studied temperatures were compared with the literature values (Table I).[20] The fair agreement between the measured and the literature values validated the experimental procedures.

TABLE I. Comparison of experimental density, ρ, and viscosity, η, of water at different temperatures with literature values

T/K	ρ / 10^3 kg m^{-3}		η / mPa s	
	Present work	Literature[20]	Present work	Literature[20]
308.15	0.9940	0.994031	0.718	0.71903
313.15	0.9922	0.992217	0.653	0.65263
318.15	0.9902	0.990216	0.597	0.59716

RESULTS AND DISCUSSION

The experimental densities of the solutions at 308.15, 313.15 and 318.15 K are shown in Table II. The partial molal volumes, V_ϕ of the amino acid were calculated using the following equation:

$$V_\phi = (M/\rho) - 1000(\rho - \rho_0)/(m\rho\rho_0) \quad (1)$$

where M, m, ρ and ρ_0 are the molar mass of the solute, the molality of the solute, and the densities of the solution and solvent (aqueous solution of metformin hydrochloride and water), respectively. The calculated values of V_ϕ are also included in Table II.

The reported values of the apparent molal volume data for amino acids may generally be represented by the linear equation:[21]

$$V_\phi = V_\phi^\ominus + S_V m \quad (2)$$

where $V_\phi^\ominus$ is the standard partial molal volume at infinite dilution ($V_\phi^\ominus = \overline{V}_\phi^\ominus$) and S_V is the experimental slope. However, in those cases where there is a non-linear dependence of V_ϕ on m, as in the present case, the $V_\phi^\ominus$ values are calculated by taking the average of all the data points.[22,23]

The values of $V_\phi^\ominus$ of the amino acid in water at the studied temperatures are given in Table III, together with literature values for comparison. It can be seen from Table III that there is close agreement of the $V_\phi^\ominus$ values of the amino acids

in water reported in this report with the literature values, which further validates the employed experimental procedures.

TABLE II. Values of density, ρ, and partial molal volume, V_ϕ, of 4-aminobutyric acid in aqueous metformin hydrochloride (m_H – molality of metformin hydrochloride; m_A – molality of the amino acid $\delta\rho$ – uncertainty value for density)

m_A / mol kg^{-1}	ρ / 10^3 kg m^{-3}	$V_\phi^\ominus$ / 10^{-6} m^3 mol^{-1}	m_A / mol kg^{-1}	ρ / 10^3 kg m^{-3}	$V_\phi^\ominus$ / 10^{-6} m^3 mol^{-1}
T = 308.15 K					
m_H = 0.00 mol kg^{-1}, $\delta\rho$ = 4.58×10^{-4} kg m^{-3}			m_H = 0.05 mol kg^{-1}, $\delta\rho$ = 3.92×10^{-4} kg m^{-3}		
0.00	0.9940	–	0.00	0.9975	–
0.02	0.9946	73.33	0.02	0.9981	73.18
0.04	0.9952	73.29	0.04	0.9986	75.66
0.06	0.9958	73.25	0.06	0.9991	76.46
0.08	0.9964	73.20	0.08	0.9996	76.83
0.10	0.9970	73.16	0.10	1.0001	77.05
m_H = 0.10 mol kg^{-1}, $\delta\rho$ = 3.99×10^{-4} kg m^{-3}			m_H = 0.15 mol kg^{-1}, $\delta\rho$ = 3.89×10^{-4} kg m^{-3}		
0.00	0.9991	–	0.00	1.0002	–
0.02	0.9996	78.13	0.02	1.0007	78.07
0.04	1.0002	75.58	0.04	1.0013	75.53
0.06	1.0007	76.38	0.06	1.0018	76.32
0.08	1.0012	76.75	0.08	1.0023	76.70
0.10	1.0017	76.97	0.10	1.0027	77.91
T = 313.15 K					
m_H = 0.00 mol kg^{-1}, $\delta\rho$ = 4.58×10^{-4} kg m^{-3}			m_H = 0.05 mol kg^{-1}, $\delta\rho$ = 4.16×10^{-4} kg m^{-3}		
0.00	0.9922	–	0.00	0.9960	–
0.02	0.9928	73.41	0.02	0.9965	78.29
0.04	0.9934	73.37	0.04	0.9971	75.73
0.06	0.9940	73.32	0.06	0.9976	76.53
0.08	0.9946	73.28	0.08	0.9982	75.65
0.10	0.9952	73.24	0.10	0.9987	76.11
m_H = 0.10 mol kg^{-1}, $\delta\rho$ = 3.89×10^{-4} kg m^{-3}			m_H = 0.15 mol kg^{-1}, $\delta\rho$ = 3.91×10^{-4} kg m^{-3}		
0.00	0.9972	–	0.00	0.9988	–
0.02	0.9977	78.23	0.02	0.9993	78.14
0.04	0.9983	75.67	0.04	0.9998	78.11
0.06	0.9988	76.47	0.06	1.0004	76.39
0.08	0.9993	76.85	0.08	1.0009	76.77
0.10	0.9997	78.07	0.10	1.0013	77.99
T = 318.15 K					
m_H = 0.00 mol kg^{-1}, $\delta\rho$ = 4.58×10^{-4} kg m^{-3}			m_H = 0.05 mol kg^{-1}, $\delta\rho$ = 3.89×10^{-4} kg m^{-3}		
0.00	0.9902	–	0.00	0.9943	–
0.02	0.9908	73.50	0.02	0.9948	78.38
0.04	0.9914	73.45	0.04	0.9954	75.81
0.06	0.9920	73.41	0.06	0.9959	76.61
0.08	0.9926	73.37	0.08	0.9964	77.00
0.10	0.9932	73.32	0.10	0.9968	78.23

TABLE II. Continued

m_A / mol kg^{-1}	ρ / 10^3 kg m^{-3}	V_ϕ^0 / 10^{-6} m^3 mol^{-1}	m_A / mol kg^{-1}	ρ / 10^3 kg m^{-3}	V_ϕ^0 / 10^{-6} m^3 mol^{-1}
T = 318.15 K					
m_H = 0.10 mol kg^{-1}, $\delta\rho$ = 3.91×10^{-4} kg m^{-3}			m_H = 0.15 mol kg^{-1}, $\delta\rho$ = 3.82×10^{-4} kg m^{-3}		
0.00	0.9955	–	0.00	0.9972	–
0.02	0.9960	78.32	0.02	0.9977	78.23
0.04	0.9965	78.28	0.04	0.9982	78.19
0.06	0.9971	76.55	0.06	0.9987	78.15
0.08	0.9976	76.94	0.08	0.9992	78.11
0.10	0.9980	78.16	0.10	0.9997	78.07

TABLE III. Values of standard partial molal volume, $V_\phi^\ominus$ / 10^{-6} m^3 mol^{-1}, of 4-aminobutyric acid in aqueous metformin hydrochloride (m_H – molality of metformin hydrochloride; standard error is given in parentheses)

T / K	m_H / mol kg^{-1}				Literature
	0.0	0.05	0.10	0.15	
308.15	73.25	75.84	76.76	76.91	74.18[24,25], 71.6[26]
	(0.00)	(0.85)	(1.10)	(1.29)	
313.15	73.32	76.46	77.06	77.48	74.1[27], 72.8[26]
	(0.00)	(0.99)	(1.30)	(0.09)	
318.15	73.41	77.21	77.65	78.15	–
	(0.00)	(1.31)	(0.96)	(0.00)	

The standard partial molal volume of transfer, $\Delta V_\phi^\ominus$, for 4-aminobutyric acid for pure water and for the metformin hydrochloride–water mixtures were calculated using Eq. (3):

$$\Delta V_\phi^\ominus = \Delta V_\phi^\ominus \text{ (in a mixture)} - \Delta V_\phi^\ominus \text{ (in pure water)} \quad (3)$$

The results are given in Table IV. It can be seen from Tables III and IV that the values of $V_\phi^\ominus$ and $\Delta V_\phi^\ominus$ for 4-aminobutyric acid are positive and increase monotonically with the molal concentration of metformin hydrochloride and temperature.

TABLE IV. Values of the standard partial molal volume of transfer, $\Delta V_\phi^\ominus$ / 10^{-6} m^3 mol^{-1}, of 4-aminobutyric acid in aqueous metformin hydrochloride solutions (m_H –molality of metformin hydrochloride)

T / K	m_H / mol kg^{-1}		
	0.05	0.10	0.15
308.15	2.59	3.51	3.66
313.15	3.14	3.74	4.16
318.15	3.80	4.24	4.74

The value of $V_\phi^\ominus$ is by definition free from solute–solute interaction and therefore provides information regarding solute–solvent interactions.[28] The posi-

tive $\Delta V_\phi^\ominus$ may be qualitatively interpreted as follows. It is well known that solute–solute interactions are absent at infinite dilution and therefore the observed standard partial molal volume of transfer $\Delta V_\phi^\ominus$ are due to the solute–solvent interactions. The nature of interactions between amino acids and metformin hydrochloride can be classified as follows:[29,30]

i) Ion–ion interactions between $C_4H_{11}N_5H^+$ of the co-solute and the COO^- group of AAs.

ii) Ion–ion interactions between Cl^- of the co-solute and the NH_3 group of AAs.

iii) Ion–non polar group interactions between the co-solute and AAs.

According to the co-sphere overlap model,[31] the first two types of interactions will produce positive $\Delta V_\phi^\ominus$ values, whereas the last type of interactions results in negative $\Delta V_\phi^\ominus$. The observed positive $\Delta V_\phi^\ominus$ values in this work can thus be related to the predominance of first two types of ion–ion interactions over the last ion–non polar interactions. Similar conclusions were drawn by Yan *et al.*[4] in their studies of AAs in aqueous $CaCl_2$ solutions. Due to the interactions between the ions in metformin hydrochloride and the zwitterionic centres of 4-aminobutyric acid, the electrostriction of the water molecules lying in the proximity of the NH_3^+ and the COO^- centres of the amino acids would be diminished and consequently lead to a positive volume contribution.[32,33] Alternatively the standard partial molal volume of the amino acid may be considered[34] to be the sum of van der Waal's volume (V_{VW}) and the volume associated with voids (V_S) or empty space minus the volume due to shrinkage (V_S) that arises due to the electrostriction of solvent caused by the hydrophilic groups present in the amino acid. The presence of metformin hydrochloride in water decreases the extent of the electrostriction caused by the amino acid, which results in a decrease in the shrinkage volume. Assuming that V_{VW} and V_V are not significantly affected by the presence of metformin hydrochloride, an increase in the $V_\phi^\ominus$ values and, hence, in the $\Delta V_\phi^\ominus$ values may be attributed to a decrease in the electrostriction effect. This electrostriction effect is reflected in the values of the hydration number, calculated using the standard equations in the literature,[35–38] which are listed in Table V. It should be noted here that the difference between the molal volume of electrostricted water, $V_E^\ominus$, and molar volume of bulk water, $V_B^\ominus$, at 308.15 K reported by Lark *et al.*[36] and Romero *et al.*[39] was used in the present calculations of n_H at all the studied temperatures. It can be seen from Table V that the hydration number n_H of the amino acid decreases with increasing concentration of metformin hydrochloride and of temperature, which again substantiate an increase in solute-co-solute interactions. Furthermore, this establishes the fact that metformin hydrochloride has a dehydration effect on 4-aminobutyric acid. Wadi and Ramasami[3] reported a similar decrease in n_H values for a few amino acids with increasing concentration of sodium sulphate and temperature.

TABLE V. Values of hydration number, n_H, of 4-aminobutyric acid in aqueous metformin hydrochloride solutions (m_H –molality of metformin hydrochloride; a – using $V_\phi^\ominus$(int) = = (0.7/0.6)$V_\phi^\ominus$(cryst); b – using $V_\phi^\ominus$(int) = (0.7/0.634) $V_\phi^\ominus$(cryst))

T / K	m_H / mol kg^{-1}					
	0.05		0.10		0.15	
	a	b	a	b	a	b
308.15	3.62	2.33	3.39	2.10	3.36	2.06
313.15	3.47	2.17	3.32	2.02	3.21	1.92
318.15	3.28	1.98	3.17	1.87	3.05	1.75

The transfer volumes of 4-aminobutyric acid may also be expressed by the McMillan Mayer theory[40] of solutions, which permits the formal separation of the effects due to interactions between pairs of solute molecules and those due to interactions between three or more solute molecules by the following equation.

$$\Delta V_\phi^\ominus = 2V_{AH}m_H + 3V_{AHH}m_H^2 + \ldots \quad (4)$$

where A stands for the amino acid and H stands for metformin hydrochloride. V_{AH} and V_{AHH} are the pair and triplet volumetric interaction parameters, respectively. Using the above equation, the volumetric interaction parameters were estimated and are given in Table VI. It can be seen that the V_{AH} values are positive while the V_{AHH} values are negative. The large positive V_{AH} values suggest domination of pair interactions for 4-aminobutyric acid over triplet volumetric interaction parameters. Similar reports are available in the literature by for some amino acids in aqueous solutions of $MgCl_2 \cdot 6H_2O$.[37]

TABLE VI. Values of pair and triplet interaction coefficients, V_{AH} and V_{AHH}, of 4-aminobutyric acid in aqueous metformin hydrochloride solutions

T / K	V_{AH} / 10^{-6} m^3 kg mol^{-2}	V_{AHH} / 10^{-6} m^3 kg^2 mol^{-2}
308.15	4.7542	–0.0405
313.15	4.8720	–0.0280
318.15	5.2224	–0.0192

The structure making/breaking property of the solute (AA) in aqueous metformin hydrochloride may be determined from the temperature dependence of the standard partial molal volume at infinite dilution. This study was further used to interpret the effect of the hydrocarbon chain on the structure of water using the general hydrophobicity criteria proposed by Hepler.[41] According to the criteria, the behaviour of the second derivative of the infinite dilution standard partial molal volume with temperature is related to the hydrophobic or hydrophilic character of the solute. When $\partial V_\phi^\ominus/\partial T > 0$ and $\partial^2 V_\phi^\ominus/\partial T^2 < 0$, the solute has hydrophilic character. However when $\partial V_\phi^\ominus/\partial T > 0$ and $\partial^2 V_\phi^\ominus/\partial T^2 < 0$, the solute has hydrophobic character.[42] In order to obtain the hydrophilic or hydrophobic character of 4-aminobutyric acid in aqueous metformin hydrochloride solutions, the

experimental values of $V_\phi^\ominus$ were related to temperature T using the following quadratic equation:[43]

$$V_\phi^\ominus = a + bT + cT^2 \quad (5)$$

The coefficients a, b and c were determined and Eq. (5) has the following forms for the amino acid at three concentrations of metformin hydrochloride reported in this work.

$$\begin{aligned} V_\phi^\ominus &= 288.52 - 1.4914\,T + 0.0026\,T^2 \text{ (for } m_H = 0.05) \\ V_\phi^\ominus &= 617.95 - 3.5435\,T + 0.0058\,T^2 \text{ (for } m_H = 0.10) \\ V_\phi^\ominus &= 234.78 - 1.1286\,T + 0.0020\,T^2 \text{ (for } m_H = 0.15) \end{aligned} \quad (6)$$

Thus, from Eq. (6), it can be observed that the values of $\partial^2 V_\phi^\ominus/\partial T^2$ are positive for all three concentrations of metformin hydrochloride, indicating the structure-making ability of 4-aminobutyric acid in aqueous metformin hydrochloride solutions.[44] This further supports the supposition that the charged end groups of amino acids are the predominant factors for the temperature dependence of $V_\phi^\ominus$ values of amino acid.

The viscosity data obtained in both water and aqueous metformin hydrochloride solutions as a function of the amino acid concentration and the temperature:

$$\eta_r = \eta / \eta_0 \quad (7)$$

are given in Table VII, where η and η_0 are the viscosities of the solution and solvent, respectively.

The viscosity B-coefficients were evaluated by fitting the η_r values to the Jones–Dole Equation by the least squares method[17] as follows:

$$\eta_r = \eta / \eta_0 = 1 + Bc \quad (8)$$

where c is the molar concentration (calculated from the molality data). The values of viscosity B-coefficient are summarized in Table VIII.

TABLE VII. Values of viscosity (η / mPa s) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions (m_H – molality of metformin hydrochloride; m_A – molality of amino acid)

m_A / mol kg^{-1}	m_H / mol kg^{-1}			
	0.00	0.05	0.10	0.15
	T = 308.15 K			
0.00	0.718	0.728	0.739	0.750
0.02	0.723	0.730	0.741	0.752
0.04	0.728	0.737	0.749	0.760
0.06	0.731	0.740	0.752	0.764
0.08	0.735	0.744	0.756	0.768
0.10	0.742	0.750	0.762	0.773

TABLE VII. Continued

m_A / mol kg^{-1}	m_H / mol kg^{-1}			
	0.00	0.05	0.10	0.15
		T = 313.15 K		
0.00	0.653	0.661	0.675	0.680
0.02	0.655	0.663	0.678	0.683
0.04	0.660	0.669	0.684	0.689
0.06	0.662	0.672	0.687	0.692
0.08	0.666	0.676	0.690	0.696
0.10	0.672	0.681	0.696	0.701
		T = 318.15 K		
0.00	0.597	0.607	0.613	0.622
0.02	0.599	0.609	0.615	0.625
0.04	0.603	0.613	0.620	0.630
0.06	0.605	0.617	0.623	0.633
0.08	0.609	0.620	0.626	0.636
0.10	0.614	0.624	0.631	0.641

TABLE VIII. Values of the viscosity B-coefficient (B / 10^{-3} m^3 mol^{-1}) of 4-aminobutyric acid in water and in aqueous metformin hydrochloride (m_H – molality of metformin hydrochloride; standard error is given in parentheses)

T / K	m_H / mol kg^{-1}				Literature
	0.00	0.05	0.10	0.15	
308.15	0.315	0.3187	0.3236	0.3330	0.299[45],
	(0.023)	(0.027)	(0.021)	(0.025)	0.316[46]
313.15	0.310	0.3143	0.3187	0.3283	0.285[46]
	(0.028)	(0.020)	(0.028)	(0.017)	
318.15	0.306	0.3096	0.3142	0.3247	–
	(0.024)	(0.009)	(0.019)	(0.021)	

The literature viscosity B-coefficient values for 4-aminobutyric acid in water are also given in Table VII for comparison. There is close agreement between the viscosity B-coefficient values reported in this work with literature values.

Viscosity B-coefficients are important for a number of reasons.[47] Their application in two research areas is of interest. First, the viscosity B-coefficient provides information about the solvation of solutes and its effects on the structure of the solvent in the near environment of the solute molecules. Furthermore, some activation parameters of viscous flow can be obtained using the viscosity B-coefficient. The viscosity B-coefficient, originally introduced as an empirical term, was found to depend on solute–solvent interactions and on the relative size of the solute and solvent molecules.[48] Larger and positive viscosity B-coefficient values indicate a structure making action (hydrophobic and hydrogen bonded actions) of the solute on solvents.[22] It can be seen from Table VIII that the viscosity B-coefficient values are positive, indicating the structure-making ability of

4-aminobutyric acid and the presence of strong ion–solvent interactions. The viscosity *B*-coefficient values decrease with increasing temperature; hence, their temperature derivatives[49], *i.e.*, d*B*/d*T*, are negative. The sign of d*B*/d*T* gives the information of structure making/breaking property of the solute in the solvent media,[50] rather than simply the viscosity *B*-coefficient. It can be seen from Table VIII that d*B*/d*T* are negative for 4-aminobutyric acid, thereby showing the structure-making ability of amino acid. Thus, 4-aminobutyric acid can be classified as a structure maker in aqueous metformin hydrochloride solutions. The charged groups of the amino acid in the present investigation electrostatically influenced the surrounding water, resulting in the formation of a solvent structure through hydrophobic hydration. These conclusions are in excellent agreement with the conclusions drawn from $\partial^2 V_\phi^\ominus/\partial T^2$ discussed earlier.

In order to obtain the relationship between the viscosity *B*-coefficient and free energy activation parameters, the Eyring simple model[51] was followed, wherein the molecules move one-by-one from their equilibrium positions through their transition-states, in which intermolecular bonds are stretched, to other equilibrium positions. For a pure liquid, it was found that:[51]

$$\eta_0 = (hN_A/\overline{V}_1^\ominus)\exp(\Delta\mu_1^{\ominus *}/RT) \quad (9)$$

where h is the Planck constant, N_A is the Avogadro's number, η_0 is the viscosity of the solvent, R is the gas constant and $\Delta\mu_1^{\ominus *}$ is the contribution per mole of solvent to the free energy of activation for viscous flow of the solution. When a solution flows, both the solute and the solvent molecules move under the shearing force. The activation energy per mole of solution can be written:

$$\Delta G^{\ominus *} = x_1\Delta\mu_1^{\ominus *} + x_2\Delta\mu_2^{\ominus *} \quad (10)$$

where x_1 and x_2 are the mole fraction of the solvent and solute, respectively. $\Delta\mu_2^{\ominus *}$, as defined by Eq. (10), includes any change in the free energy of activation of the solvent molecules caused by the presence of the solute, as well as the contribution from the movement of the solute itself. According to the Feakins *et al.*,[52] the viscosity *B*-coefficient is related to $\Delta\mu_2^{\ominus *}$ by Eq. (11):

$$B = (\overline{V}_1^\ominus - \overline{V}_2^\ominus)/1000 + (\overline{V}_1^\ominus/1000)(\Delta\mu_2^{\ominus *} - \Delta\mu_1^{\ominus *})/\mathrm{RT} \quad (11)$$

Eq. (11) can be rearranged to give:

$$\Delta\mu_2^{\ominus *} = \Delta\mu_1^{\ominus *} + RT/(1000B - (\overline{V}_1^\ominus - \overline{V}_2^\ominus)) \quad (12)$$

where $\overline{V}_1^\ominus = \Sigma x_i M_i/\rho$ is the mean volume of the solvent and $\overline{V}_2^\ominus$ ($V_\phi^\ominus$) is the standard partial molal volume of the solute at infinite dilution. The terms x_i and M_i denote the mole fractions and molecular weights of water (1) and metformin hydrochloride (2). The calculated values of $\Delta\mu_1^{\ominus *}$, $\Delta\mu_2^{\ominus *}$and $\overline{V}_1^\ominus$ are given in Table IX.

TABLE IX. Values of activation free energy of the solvent, $\Delta\mu_1^{\ominus *}$, solute, $\Delta\mu_2^{\ominus *}$, and mean molal volume of the solvent $V_\phi^\ominus$ of aqueous metformin hydrochloride solutions (m_H – molality of metformin hydrochloride)

m_H / mol kg^{-1}	$\Delta\mu_1^{\ominus *}$/ kJ mol^{-1}	$\Delta\mu_2^{\ominus *}$/ kJ mol^{-1}	$V_\phi^\ominus$/ 10^{-6} m^3 mol^{-1}
		T = 308.15 K	
0.00	26.629	78.955	18.123
0.05	26.671	79.574	18.193
0.10	26.723	80.136	18.296
0.15	26.776	81.277	18.409
		T = 313.15 K	
0.00	26.814	79.180	18.156
0.05	26.858	80.047	18.220
0.10	26.908	80.415	18.331
0.15	26.961	81.623	18.434
		T = 318.15 K	
0.00	27.013	79.534	18.193
0.05	27.064	80.391	18.251
0.10	27.106	80.879	18.363
0.15	27.161	82.015	18.464

It may be seen from Table IX that the values of $\Delta\mu_2^{\ominus *}$ are positive and larger than $\Delta\mu_1^{\ominus *}$, indicating the structure-making ability of the solute[52] (namely the amino acid) in aqueous metformin hydrochloride, again supplementing the earlier findings through the $\partial^2 V_\phi^\ominus/\partial T^2$ and dB/dT studies. Furthermore, the larger $\Delta\mu_2^{\ominus *}$ values indicate the presence of stronger ion–solvent interactions. In other words, the formation of the transition state is less favoured in the presence of the amino acid. This means that the formation of the transition state is accompanied by the rapture and distortion of the intermolecular forces in the solvent structure. Similar results were obtained by Mishra *et al.*[53] for glycine in aqueous solutions of transition metal chlorides.

According to transition state theory,[46] every solvent molecule in one mole of solution must pass through the transition state and interact more or less strongly with solute molecules. The activation free energy $\Delta\mu_2^{\ominus *}$ includes the free energy of transfer of solute from the ground state to the transition state solvents ($\Delta G_2^\ominus(1\rightarrow 1')$) and the free energy of the solute through its own viscous transition state ($\Delta G_2^\ominus(2\rightarrow 2')$). The values ($\Delta G_2^\ominus(1\rightarrow 1')$) may be calculated using methods similar to those reported elsewhere.[18,52] These values are given in Table X.

The positive $\Delta\mu_2^{\ominus *}$ and $\Delta G_2^\ominus(1\rightarrow 1')$ values are larger than the $\Delta\mu_2^{\ominus *}$ values. Furthermore, both $\Delta\mu_2^{\ominus *}$ and $\Delta G_2^\ominus(1\rightarrow 1')$ increase with increasing concentration of the co-solute, as well as with increasing temperature. This suggests that the formation of transition state is less favoured in the presence of amino acids. This is due to the breaking and distortion of intermolecular bonds, which effectively means that more solute–solvent bonds must be broken to form the transition

state. Similar reports are available in literature for α-amino acids in aqueous sodium acetate solution.[53]

TABLE X. Values of the thermodynamic activation parameter transfer ($\Delta G_2^{\ominus}(1\rightarrow1')$ / kJ mol^{-1}) of 4-aminobutyric acid from the ground state to the transition state in aqueous metformin hydrochloride solutions

T / K	m_H / mol kg^{-1}			
	0.00	0.05	0.10	0.15
308.15	52.326	52.903	53.413	54.501
313.15	52.366	53.189	53.507	54.662
318.15	52.521	53.327	53.773	54.854

CONCLUSION

In summary, volumetric and viscometric data are reported for 4-aminobutyric acid in different concentrations of aqueous metformin hydrochloride solutions. The standard partial molal volume $V_{\phi}^{\ominus}$, standard partial molal volume of transfer $V_{\phi}^{\ominus}$, hydration number n_H, second derivative of the standard partial molal volume at infinite dilution with temperature $\partial^2 V_{\phi}^{\ominus}/\partial T^2$ were determined and are reported. These results showed that 4-aminobutyric acid acts as structure maker in aqueous metformin hydrochloride solutions and that strong solute–solvent interactions occur in the reported systems. The viscosity B-coefficient, variation of the viscosity B-coefficient with temperature, dB/dT and the free energy of activation per mole of solute, $\Delta\mu_2^{\ominus *}$, values were also calculated and reported. These results also confirmed the structure-making ability of 4-aminobutyric acid in aqueous metformin hydrochloride.

NOMENCLATURE

List of symbols

B	Viscosity B-coefficient (dm^3 mol^{-1})
C	Molarity of the amino acid (mol dm^{-3})
h	The Planck constant
m	Molality of the amino acid
M	Molar mass of the amino acid
n_H	Hydration number
N_A	Avogadro's number
R	Universal gas constant (8.31441m^3 Pa mol^{-1} K^{-1})
S_V	Slope in Eq. (2)
t	Flow time of solution in viscometer
T	Temperature (K)
V_{ϕ}	Partial molal volume of the amino acid
$V_{\phi}^{\ominus}$	Standard partial molal volume of the amino acid
$V_1^{\ominus}$	Standard mean volume of the solvent
$V_2^{\ominus}$	Standard partial molal volume of the solute
$V_B^{\ominus}$	Standard partial molal volumes of water in the hydration shell of a solution

$V_E^{\ominus}$ Standard partial molal volumes of water in the bulk state
$\Delta V_\phi^{\ominus}$ Standard partial molal volume of transfer for the amino acid

Greek letters

η Viscosity (mPa s)
ρ Density (kg m^{-3})
$\Delta\mu_1^{\ominus *}$ Standard free energy of activations for viscous flow of solvent
$\Delta\mu_2^{\ominus *}$ Standard free energy of activations for viscous flow of solution

Subscripts

1 Binary solvent property
2 Solute property

ИЗВОД

ВОЛУМЕТРИЈСКЕ ОСОБИНЕ И ВИСКОЗНОСТ 4-АМИНОБУТЕРНЕ КИСЕЛИНЕ У ВОДЕНОМ РАСТВОРУ МЕТФОРМИН ХИДРОХЛОРИДА НА 308,15, 313,15 И 318,15 K

K. RAJAGOPAL[1] и S.S. JAYABALAKRISHNAN[2]

[1]*Department of Physics, Government College of Engg. Tirunelveli-627007 Tamil Nadu и*
[2]*Department of Physics, P.S.R. Engg. College, Sivakasi, Tamil Nadu, India*

Извршена су мерења густина (ρ) и вискозности (η) 4-аминобутерне киселине у 0,05, 0,10 и 0,15 M воденом раствору метформин хидрохлорида на 308,15, 313,15 и 318,15 K. Измерене вредности густина и вискозности су коришћене за израчунавање особина смеса, као што су парцијална моларна запремина V_ϕ, стандардна парцијална моларна запремина $V_\phi^{\ominus}$, стандардне парцијалне моларне запремине прелаза $\Delta V_\phi^{\ominus}$, хидрацијског броја n_H, другог извода парцијалне моларне запремине при бесконачном разблажењу са температуром $\partial^2 V_\phi^{\ominus}/\partial T^2$, коефицијента вискозности B, промену B са температуром dB/dT, слободне енергије активације по молу растварача $\Delta\mu_1^{\ominus *}$ и растворене амино киселине $\Delta\mu_2^{\ominus *}$ у тернерном систему. Резултати су интерпретирани са аспекта интеракција растворак–растворак и растворак–растварач и могућности настанка/разградње структура растворка у испитиваним растворима.

(Примљено 16. јуна 2009, ревидирано 21. септембра 2010)

REFERENCES

1. A. Ali, S. Hyder, S. Sabir, D. Chand, A. K. Nain, *J. Chem. Thermodyn.* **38** (2006) 136
2. A. Ali, S. Khan, F. Nabi, *J. Serb. Chem. Soc.* **72** (2007) 495
3. R. K. Wadi, P. Ramasami, *J. Chem. Soc. Faraday. Trans.* **93** (1997) 243
4. Z. Yan, J. Wang, W. Kong, J. Lu, *Fluid Phase Equilib.* **215** (2004) 143
5. T. S. Banipal, G. Sehgal, *Thermochim. Acta* **265** (1995) 175
6. Z. Yan, J. Wang, W. Kong, J. Lu, *Fluid Phase Equilib.* **215** (2004) 130
7. A. Soto, A. Arce, K. Mohammed, *Biophys. Chem.***74** (1998) 165
8. M. Iqbal, T. Ahmed, *Indian J. Chem.* **32A** (1993) 119
9. K. Rajagopal, S. S. Jayabalakrishnan, *Chin. J. Chem. Eng.* **17** (2009) 796
10. L. D. Hu, Y. Liu, X. Tang, Q. Zhang, *Eur. J. Pharm. Sci.* **64** (2006) 185
11. G. Corti, M. S. Lirri, F. Maestrelli, N. Manine, P. Mura, *Eur. J. Pharm. Sci.***68** (2008) 303
12. K. Rajagopal, S. S. Jayabalakrishnan, *J. Pure. Appl. Ultrason.* **28** (2006) 81
13. D. P. Kharakoz, *Biophys. Chem.* **34** (1989) 115

14. D. P. Kharakoz, *Biochem.* **36** (1997) 10276
15. M. Sakurai, T. Nakumaura, N. Takenaka, *Bull. Chem. Soc. Jpn.* **67** (1994) 352
16. M. Kikuchi, M. Sakurai, N. Nitta, *J. Chem. Eng. Data* **41** (1996) 1439
17. G. Jones, M. Dole, *J. Am. Chem. Soc*. **51** (1929) 2950
18. B. S. Lark, P. Patyar, T. S. Banipal, *J. Chem. Thermodyn.* **39** (2007) 344
19. Z. Yan, J. Wang, J. Lu, *Biophys. Chem.* **99** (2002) 199
20. A. Pal, S. Kumar, *Indian J. Chem.* **44A** (2005) 469
21. J. A. Reddick, W. B. Bunger, T. K. Sakano, *Organic solvents*, Vol. II, 4th ed., Wiley Interscience, New York, 1986
22. X. Ren, X. Hu, R. Lin, H. Zong, *J. Chem. Eng. Data* **43** (1998) 700
23. Z. Yan, J. Wang, W. Kong, J. Lu, *Fluid Phase Equilib.* **215** (2004) 143
24. R. Bhat, J. C. Ahulwalia, *J. Phys. Chem.* **89** (1985) 1099
25. M. N. Islam, R. K. Wadi, *Phys. Chem. Liq.* **41** (2003) 533
26. R. K. Wadi, R. K. Goyal, *J. Solution Chem*. **21** (1992) 163.
27. M. M. Bhattaacharyya, M. Sengupta, *J. Indian Chem. Soc.* **62** (1985) 959
28. T. V. Chalikian, A. V. Sarvazyan, K. J. Breslauer, *J. Phys. Chem.* **97** (1993) 13017
29. K. Belibagli, E. Ayranci, *J. Solution. Chem.* **19** (1990) 867
30. R. Bhat, N. Kishore, J. C. Ahluwalia, *J. Chem. Faraday Trans. 1* **84** (1988) 2651
31. S. Li, W. Sang, R. Lin, *J. Chem. Thermodyn.* **34** (2002) 1761
32. H. L. Friedman, C. V. Krishnan, in *Water: A comprehensive Treatise*, Vol. 3, F. Franks, Ed., Plenum Press, New York, 1973, p. 1
33. Q. Liu, X. Hu, R. Lin, W. Sang, S. Li, *J. Chem. Eng. Data* **46** (2001) 522
34. C. Zhao, P. Ma, J. Lu, *J. Chem. Thermodyn.* **37** (2005) 37
35. M. Natarajan, R. K. Wadi, H. C. Gaur, *J. Chem. Eng. Data* **35** (1990) 87
36. F. Franks, M. A. Quickenden, D. S. Reid, B. Watson, *Trans Faraday. Soc.* **66** (1970) 582
37. B. S. Lark, P. Patyar, T. S. Banipal, *J. Chem. Thermodyn.* **38** (2006) 1592
38. A. Pal, K. Kumar, *J. Mol. Liq.* **121** (2005) 148
39. F. J. Millero, G. K. Ward, F. K. Lepple, E. V. Hoff, *J. Phys. Chem.* **78** (1974) 1636
40. C. M. Romero, F. Negrete, *Phys. Chem. Liq.* **42** (2004) 261
41. W. G. McMillan, J. E. Mayer, *J. Chem. Phys.* **13** (1945) 276
42. L. Hepler, *Can. J. Chem.* **47** (1969) 4613
43. *Water A: Comprehensive Treatise*, Vol. IV, F. Franks, Ed., Plenum Press, New York, 1978
44. A. Pal, S. Kumar, *J. Mol. Liq.* **109** (2004) 23
45. B. S. Lark, P. Patyar, T. S. Banipal, N. Kishore, *J. Chem. Eng. Data* **49** (2004) 553
46. R. K. Wadi, R. K. Goyal, *J. Chem. Eng. Data* **37** (1992) 377
47. M. M. Bhattacharyya, M. Sengupta, *Z. Phys. Chem. (N.F.)* **133** (1982) 79
48. H. D. B. Jenkins, Y. Marcus, *Chem. Rev.* **95** (1995) 2695
49. T. C. Bai, G. B. Yan, *Carbohydr. Res.* **338** (2003) 2921
50. J. M. Tsangins, R. B. Martin, *Arch. Biochem. Biophys.* **112** (1965) 267
51. T. S. Sharma, J. C. Ahluwalia, *Chem. Soc. Rev.* **2** (1973) 203
52. S. Glasstone, K. Laidler, H. Eyring, *The Theory of Rate Processes*, McGraw Hill, New York, 1941, p. 477
53. D. Feakins, F. M. Bates, W. E. Waghorne, K. G. Lawrence, *J. Chem. Soc. Faraday Trans.* **89** (1993) 3381
54. A. P. Mishra, S. K. Gautam, *Indian J. Chem. A* **40** (2001) 100.