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Ultrasonic Studies of 4-Aminobutyric Acid in Aqueous Metformin Hydrochloride Solutions at Different Temperatures

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Abstract Ultrasonic speeds and density data of 4-aminobutyric acid in 0.05 M, 0.10 M, and 0.15 M aqueous metformin hydrochloride (MFHCl) solutions are measured at 308.15 K, 313.15 K, and 318.15 K. The isentropic compressibility (k_S), the change in isentropic compressibility (Δk_S), the relative change in isentropic compressibility ($\Delta k_S/k_S^0$), the apparent molal compressibility (k_ϕ), the limiting apparent molal compressibility (k_ϕ^0), the transfer limiting apparent molal compressibility (Δk_ϕ^0), the hydration number (n_H), and the pair and triplet interaction parameters (k_{AH}, k_{AHH}) are estimated. The above parameters are used to interpret the solute–solute and solute–solvent interactions of 4-aminobutyric acid in aqueous MFHCl solutions.

Keywords Hydration number · Isentropic compressibility · Limiting apparent molal compressibility · Metformin hydrochloride · Ultrasonic speed

1 Introduction

Information about the origin of the stability of macromolecules such as proteins in aqueous solutions is important for an understanding of their structure and function. The stability of proteins is due to non-covalent forces such as hydrogen bonding, electrostatic interactions, hydrophobic interactions, etc. As proteins are complex molecules,

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the model compound amino acids are considered by many authors in the determination of thermodynamic parameters in aqueous media. Drug macromolecular interactions represent important phenomena in physiological media, such as blood, membranes, and intra and extra-cellular fluids. The processes of drug transport, protein binding, and anesthesia are some examples where drugs and bio-macromolecules appear to interact in an important and vitally significant manner. The mechanisms of these molecular processes are, however, not clearly understood. It has been shown that perceptible thermodynamic changes are associated with the processes of drug–protein binding, anesthesia, etc. In the case of protein binding, anomalous behavior has been noted with respect to certain drugs. Drug action, i.e., drug reaching the blood stream, its extent of distribution, its binding to the receptors, and finally producing physiological action, all depend on various physicochemical properties chiefly detected by various interactions [1,2]. A knowledge of the use of drugs involving physiological and biochemical effects and their mechanism of action at macromolecular/subcellular/organ system levels can be studied in pharmokinetics [3,4]. All pharmokinetic processes involve transport of drugs across biological membranes which can be well understood by transport property measurements, viz., ultrasonic speed, viscosity, diffusion, and thermal conductivity [3].

Metformin hydrochloride (MFHCl), a white crystalline powder, has a molecular formula of ($C_4H_{11}N_5HCl$). It is an antidiabetic and antihyperglycemic agent [5,6] that lowers both basal- and postprandial-elevated blood glucose in patients with non-insulin-dependent diabetes mellitus (Type-2 diabetes), where hyperglycemia cannot be satisfactorily managed by diet alone. In a continuation of earlier work on metformin hydrochloride [7], we report data on ultrasonic speeds and densities of 4-aminobutyric acid in aqueous metformin hydrochloride at three different temperatures (308.15 K, 313.15 K, and 318.15 K). The measured data are used to evaluate the isentropic compressibility (k_S), the change in isentropic compressibility (Δk_S), the relative change in isentropic compressibility ($\Delta k_S/k_S^0$), the apparent molal compressibility (k_ϕ), the limiting apparent molal compressibility (k_ϕ^0), the transfer limiting apparent molal compressibility (Δk_ϕ^0), the hydration number (n_H), and the pair and triplet interaction parameters (k_{AH}, k_{AHH}). These parameters are used to interpret the solute–solute and solute–solvent interactions of 4-aminobutyric acid in aqueous metformin hydrochloride solutions. The data at temperatures $T = (308.15, 313.15,$ and $318.15)$ K provide insight to the drug macromolecular behavior near physiological temperatures.

2 Experimental

Metformin hydrochloride procured from Accumen Pharmaceutical Ltd., Pondicherry (minimum assay 99.5 %) was used without any pretreatment, after drying it in a vacuum oven. The amino acid used in the study (4-aminobutyric acid) was of analytical grade (Otto Chemicals Ltd., Bangalore, minimum assay 99+ %), and was used without further purification. However, it was dried over P_2O_5 in a desiccator for 72 h before use. Doubly distilled deionized water with an electrical conductivity of $1.5\,\mu S \cdot m^{-1}$ was used in our experiments and was degassed prior to preparing solutions. The densities of the solutions were measured using a single-stem pycnometer (pyrex glass)

Table 1 Comparison of experimental densities (ρ) and ultrasonic speeds (u) of water with literature values

Temp (K)	$\rho \times 10^{-3}$ (kg · m^{-3})		u (m · s^{-1})	
	Experimental value	Literature value	Experimental value	Literature value
308.15	0.9940	0.994031 [9]	1520.4	1519.83 [10]
313.15	0.9922	0.992217 [9]	1528.0	1528.88 [10]
318.15	0.9902	0.990216 [9]	1535.2	1536.42 [10]

with a 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 carried out by putting the samples in air-tight bottles and weighing them on a high precision electronic balance (Model HR 300, Japan) with a precision of ±0.1 mg. The necessary buoyancy corrections were applied in all cases. The reproducibility of density measurements was $\pm 2.8 \times 10^{-4}$ g · cm^{-1} [8]. The ultrasonic speeds in solvents and in solutions were measured using a single-crystal variable-path multi-frequency ultrasonic interferometer (M-84, Mittal, India) operated at 2 MHz. An average of five readings was taken as the final value of the speed of sound. The reproducibility in ultrasonic speed measurements was within ±0.03 %. Water from a thermostated bath circulated through the brass jacket surrounding the cell and the quartz crystal. The jacket was well insulated, and the temperature of the solution under study was maintained within ±0.01 K. The thermostated water was maintained at a desired temperature for about 30 min prior to measurements at each temperature, so as to minimize thermal fluctuations. The experimental values of ultrasonic speed and density in water are compared with literature values (see Table 1). The close agreement demonstrates the reliability of our experimental measurements.

3 Results

Experimental data on ultrasonic speeds and densities of 4-aminobutyric acid in aqueous metformin hydrochloride solutions are given in Tables 2 and 3, respectively.

The measured values of density and ultrasonic speed are used to calculate the isentropic compressibility (k_S) using the following equation and are given in Table 4:

$$k_S = 1/(u^2\rho) \tag{1}$$

The uncertainty in k_S [11] values have been obtained using the following equation and is given in parentheses in Table 4:

$$\delta k_S = k_S[(2\delta u/u)^2 + (\delta\rho/\rho)^2]^{1/2} \tag{2}$$

The change (Δk_S) [12] and relative change ($\Delta k_S/k_S^0$) [13] in isentropic compressibility are calculated using the following equations:

$$\Delta k_S = k_S^0 - k_S = A + Bm \tag{3}$$

Table 2 Ultrasonic speed (u, $\mathrm{m \cdot s^{-1}}$) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at different temperatures

m_A ($\mathrm{mol \cdot kg^{-1}}$)	u ($\mathrm{m \cdot s^{-1}}$)			
	$m_H = 0.00$ M	$m_H = 0.05$ M	$m_H = 0.10$ M	$m_H = 0.15$ M
$T = 308.15$ K				
0.0000	1520.4	1527.4	1529.0	1530.0
0.0200	1521.8	1528.7	1530.3	1531.2
0.0400	1523.0	1530.1	1531.4	1532.2
0.0600	1524.3	1531.5	1532.6	1533.3
0.0800	1525.6	1532.9	1533.8	1534.4
0.1000	1527.0	1534.2	1535.0	1535.6
	$\delta u = 10.5 \times 10^{-4}$	$\delta u = 10.0 \times 10^{-4}$	$\delta u = 9.1 \times 10^{-4}$	$\delta u = 8.4 \times 10^{-4}$
$T = 313.15$ K				
0.0000	1528.0	1534.4	1537.8	1541.2
0.0200	1529.4	1535.8	1539.0	1542.3
0.0400	1530.7	1536.9	1540.0	1543.4
0.0600	1532.0	1538.2	1541.1	1544.3
0.0800	1533.3	1539.3	1542.2	1545.4
0.1000	1534.6	1540.6	1543.4	1546.6
	$\delta u = 10.4 \times 10^{-4}$	$\delta u = 9.3 \times 10^{-4}$	$\delta u = 8.4 \times 10^{-4}$	$\delta u = 8.1 \times 10^{-4}$
$T = 318.15$ K				
0.0000	1535.2	1539.2	1541.0	1543.8
0.0200	1536.5	1540.4	1542.0	1544.7
0.0400	1537.7	1541.4	1543.0	1545.6
0.0600	1538.9	1542.6	1543.8	1546.5
0.0800	1540.1	1543.7	1544.7	1547.3
0.1000	1541.3	1545.0	1545.8	1548.2
	$\delta u = 9.3 \times 10^{-4}$	$\delta u = 8.8 \times 10^{-4}$	$\delta u = 7.2 \times 10^{-4}$	$\delta u = 6.7 \times 10^{-4}$

m_H molality of metformin hydrochloride
δu uncertainty in ultrasonic speed values

$$k_S = k_S^0 - \alpha k_S^0 \tag{4}$$

$$\alpha = k_S^0 - k_S/k_S^0 = \Delta k_S/k_S^0 \tag{5}$$

$$\Delta k_S/k_S^0 = A' + B'm \tag{6}$$

where k_S^0 and k_S are the isentropic compressibilities of the solvent and solution, respectively. A and B are the intercept and slope values of Δk_S versus m plot (see Fig. 1), respectively. Similarly A' and B' stand for the intercept and slope values of $(\Delta k_S/k_S^0)$ versus m plot (see Fig. 2), respectively. The values of Δk_S and $(\Delta k_S/k_S^0)$ are listed in Tables 5 and 6.

The apparent molal compressibility k_ϕ values of 4-aminobutyric acid in aqueous metformin hydrochloride solution is obtained using the following equation [14] and are listed in Table 7.

Table 3 Density (ρ) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at different temperatures

m_A (mol · kg^{-1})	$\rho \times 10^{-3}$ (kg · m^{-3})			
	$m_H = 0.00$ M	$m_H = 0.05$ M	$m_H = 0.10$ M	$m_H = 0.15$ M
$T = 308.15$ K				
0.0000	0.9940	0.9975	0.9991	1.0002
0.0200	0.9946	0.9981	0.9996	1.0007
0.0400	0.9952	0.9986	1.0002	1.0013
0.0600	0.9958	0.9991	1.0007	1.0018
0.0800	0.9964	0.9996	1.0012	1.0023
0.1000	0.9970	1.0001	1.0017	1.0027
	$\delta\rho = 4.6 \times 10^{-4}$	$\delta\rho = 3.9 \times 10^{-4}$	$\delta\rho = 4.0 \times 10^{-4}$	$\delta\rho = 3.9 \times 10^{-4}$
$T = 313.15$ K				
0.0000	0.9922	0.9960	0.9972	0.9988
0.0200	0.9928	0.9965	0.9977	0.9993
0.0400	0.9934	0.9971	0.9983	0.9998
0.0600	0.9940	0.9976	0.9988	1.0004
0.0800	0.9946	0.9982	0.9993	1.0009
0.1000	0.9952	0.9987	0.9997	1.0013
	$\delta\rho = 4.6 \times 10^{-4}$	$\delta\rho = 4.2 \times 10^{-4}$	$\delta\rho = 3.9 \times 10^{-4}$	$\delta\rho = 3.9 \times 10^{-4}$
$T = 318.15$ K				
0.0000	0.9902	0.9943	0.9955	0.9972
0.0200	0.9908	0.9948	0.9960	0.9977
0.0400	0.9914	0.9954	0.9965	0.9982
0.0600	0.9920	0.9959	0.9971	0.9987
0.0800	0.9926	0.9964	0.9976	0.9992
0.1000	0.9932	0.9968	0.9980	0.9997
	$\delta\rho = 4.6 \times 10^{-4}$	$\delta\rho = 3.9 \times 10^{-4}$	$\delta\rho = 3.9 \times 10^{-4}$	$\delta\rho = 3.8 \times 10^{-4}$

m_H molality of metformin hydrochloride
$\delta\rho$ uncertainty in density values

$$k_\phi = \left(\frac{Mk_S}{\rho}\right) - \frac{1000(k_S\rho_0 - k_S^0\rho)}{m\rho\rho_0} \tag{7}$$

where M and m are the molar mass and molality of 4-aminobutyric acid; ρ and ρ_0 are the densities of the solute and solvent, respectively.

The limiting apparent molal compressibility (k_ϕ^0) of 4-aminobutyric acid is evaluated using an equation in [14], from a linear plot of k_ϕ versus m (see the representative plot in Fig. 3) using the least-squares method of the following general equation:

$$k_\phi = k_\phi^o + S_K m \tag{8}$$

Table 4 Compressibility (k_S) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at different temperatures

m_A (mol · kg^{-1})	$k_S \times 10^{11}$ (Pa^{-1})			
	$m_H = 0.00$ M	$m_H = 0.05$ M	$m_H = 0.10$ M	$m_H = 0.15$ M
$T = 308.15$ K				
0.0000	43.52(0.127)	42.97(0.128)	42.81(0.119)	42.71(0.114)
0.0200	43.41(0.127)	42.87(0.128)	42.71(0.119)	42.62(0.114)
0.0400	43.31(0.127)	42.77(0.127)	42.63(0.118)	42.54(0.114)
0.0600	43.21(0.126)	42.67(0.127)	42.54(0.118)	42.45(0.113)
0.0800	43.11(0.126)	42.57(0.127)	42.45(0.118)	42.37(0.113)
0.1000	43.01(0.125)	42.48(0.126)	42.36(0.117)	42.29(0.113)
$T = 313.15$ K				
0.0000	43.16(0.126)	42.64(0.120)	42.40(0.113)	42.15(0.102)
0.0200	43.06(0.126)	42.54(0.119)	42.31(0.113)	42.06(0.109)
0.0400	42.96(0.125)	42.45(0.119)	42.23(0.112)	41.98(0.109)
0.0600	42.86(0.125)	42.36(0.119)	42.15(0.112)	41.91(0.109)
0.0800	42.76(0.124)	42.28(0.118)	42.07(0.112)	41.83(0.109)
0.1000	42.66(0.124)	42.18(0.118)	41.99(0.118)	41.75(0.108)
$T = 318.15$ K				
0.0000	42.85(0.120)	42.45(0.115)	42.30(0.104)	42.07(0.099)
0.0200	42.75(0.119)	42.36(0.115)	42.22(0.103)	42.00(0.099)
0.0400	42.65(0.119)	42.28(0.114)	42.14(0.103)	41.93(0.099)
0.0600	42.56(0.119)	42.19(0.114)	42.08(0.103)	41.86(0.099)
0.0800	42.47(0.118)	42.11(0.114)	42.01(0.103)	41.80(0.098)
0.1000	42.38(0.118)	42.02(0.113)	41.93(0.102)	41.73(0.098)

m_H molality of metformin hydrochloride
Parentheses indicates uncertainty in k_S values

where S_K is the experimental slope that is a measure of solute–solute interactions and k_ϕ^0 is the partial molal parameter at infinite dilution is a measure of solute–solvent interactions. The calculated values of k_ϕ^0 and S_K are listed in Table 8.

Furthermore, the number of water molecules (n_H) hydrated to 4-aminobutyric acid are calculated using a method given by Millero et al. [15]:

$$n_H = -k_\phi^0(\text{elec})/k_S^0 V_b^0 \tag{9}$$

where k_S^0 is the isentropic compressibility of the aqueous metformin hydrochloride solution and V_b^0 is the molar volume of bulk water which is taken to be the molar volume of water in the metformin hydrochloride solution. The calculated n_H values are given in Table 9.

The partial molal compressibilities of transfer (Δk_ϕ^0) from water to aqueous metformin hydrochloride solutions are calculated using the following equation and are listed in Table 10.

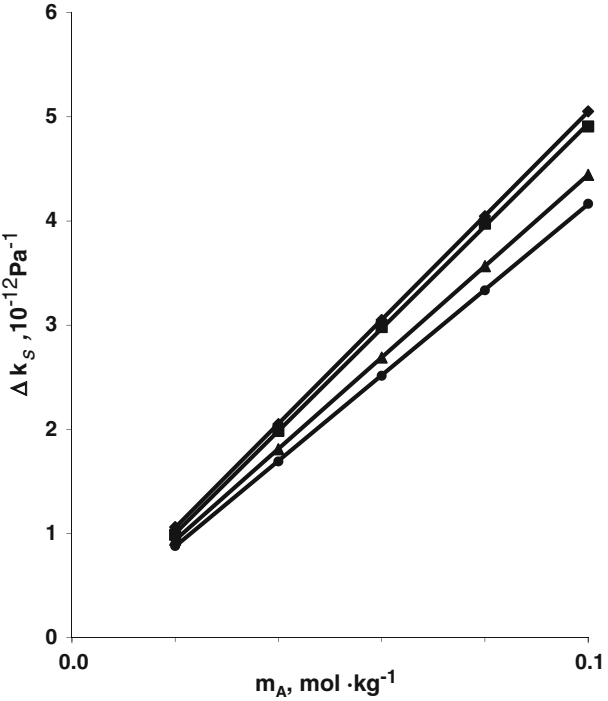

Fig. 1 Plot of change in isentropic compressibility (Δk_S) versus molality of amino acid (m_A) at various molal concentrations of aqueous metformin hydrochloride solutions at $T = 308.15$ K: ♦ 0.00 M, ■ 0.05 M, ▲ 0.10 M, ● 0.15 M

$$\Delta k_\phi^0 = k_\phi^0(\text{4-aminobutyric acid in solution}) - k_\phi^0(\text{4-aminobutyric acid in water}) \tag{10}$$

The formula based on the McMillan–Mayer theory of solutions, proposed by Kozak et al. [16] and further discussed by Friedman and Krishnan [17] and Franks et al. [18] has been used to include the solute–cosolute interactions in the solvation sphere. According to this, at infinite dilution, Δk_ϕ^0 can be expressed as

$$\Delta k_\phi^0 = 2K_{\mathrm{AH}} m_{\mathrm{H}} + 3K_{\mathrm{AHH}} m_{\mathrm{H}}^2 \tag{11}$$

where A stands for 4-aminobutyric acid, H stands for metformin hydrochloride, and m_{H} is the molality of metformin hydrochloride. The constants K_{AH} and K_{AHH} are pair and triplet interaction coefficients, respectively, and are given in Table 11.

4 Discussion

An increase in the ultrasonic speed in any solution with the addition of a solute (see Table 2) is indicative of greater association of molecules due to effective solute–solvent interactions [19]. The isentropic compressibility (k_S) decreases with

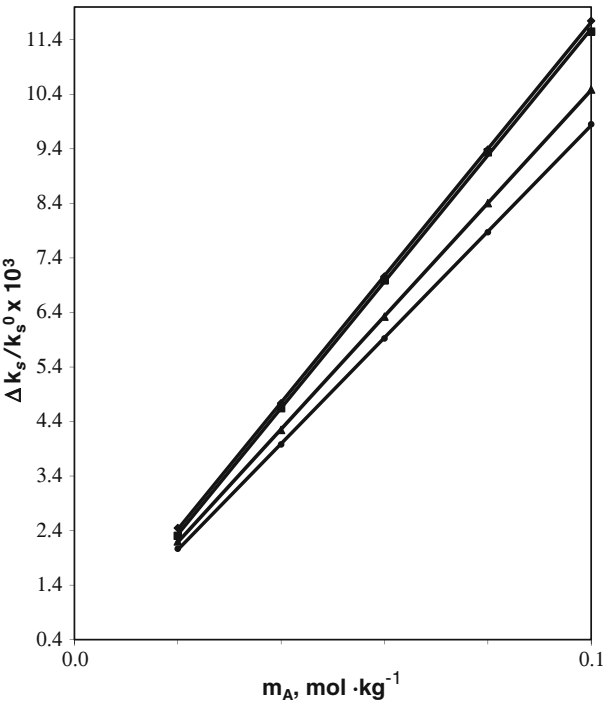

Fig. 2 Plot of relative change in isentropic compressibility ($\Delta k_S/k_S^0$) versus molality of amino acid (m_A) at various molal concentrations of aqueous metformin hydrochloride solutions at $T = 308.15$ K: ♦ 0.00 M, ■ 0.05 M, ▲ 0.10 M, ● 0.15 M

an increase in the concentration of metformin hydrochloride and the temperature (see Table 4). The decrease in compressibility with an increase in concentration may be attributed to (i) an increase in the number of incompressible molecules/zwitterions in solution and (ii) the formation of the compact structure of zwitterions–water dipoles and zwitterions–ion structures in solutions. The decrease in adiabatic compressibility values with increasing temperature may be explained in terms of the changes occurring in the water structure around zwitterions–ions [20]. Water is regarded as an equilibrium mixture of two structures such as an ice-like structure and a close-packed structure. The compressibility of liquid water is given by $k_S = k_\alpha + k_{\text{relax}}/(1 + \omega^2\tau^2)$, where k_α is an instantaneous part of the compressibility and k_{relax} is a relaxational part of the compressibility. The relaxation time, τ, corresponding to k_{relax} is of the order of 10^{-11} s. The relation, $\omega\tau < 1$, holds in the present case, where ω is the angular frequency. Thus, the obtained compressibility is equal to $k_\alpha + k_{\text{relax}}$. With a rise in temperature, k_α increases due to thermal expansion while k_{relax} decreases due to thermal rupture of the ice-like structure. Thus, the decrease in compressibility with temperature may be attributed to the corresponding decrease in k_{relax} which is dominant over the corresponding increase in k_α.

The values of Δk_S and $(\Delta k_S/k_S^0)$ (see Tables 5, 6) show an increasing trend of variation with an increase in concentration which may be attributed to an increase

Table 5 Change in isentropic compressibility (Δk_S) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at different temperatures

m_A (mol · kg^{-1})	$\Delta k_S \times 10^{12}$ (Pa^{-1})			
	$m_H = 0.00$ M	$m_H = 0.05$ M	$m_H = 0.10$ M	$m_H = 0.15$ M
$T = 308.15$ K				
0.0200	1.062	0.988	0.940	0.882
0.0400	2.051	1.986	1.810	1.693
0.0600	3.050	2.982	2.690	2.515
0.0800	4.046	3.974	3.567	3.335
0.1000	5.052	4.908	4.443	4.166
$T = 313.15$ K				
0.0200	1.050	0.990	0.873	0.811
0.0400	2.041	1.855	1.676	1.621
0.0600	3.028	2.785	2.490	2.362
0.0800	4.013	3.644	3.302	3.167
0.1000	4.995	4.569	4.124	3.983
$T = 318.15$ K				
0.0200	0.983	0.874	0.760	0.700
0.0400	1.909	1.678	1.519	1.400
0.0600	2.831	2.548	2.209	2.097
0.0800	3.751	3.360	2.910	2.739
0.1000	4.669	4.238	3.676	3.434

m_H molality of metformin hydrochloride

in the incompressible part in a solution. The variation of the above parameter with temperature may be attributed to the thermal rupture of the water structure.

The apparent molal compressibility (k_ϕ) is related to the second pressure differential of the partial molal free energy of the solute and has proved to be very sensitive to changes in solvation, hydrogen bonding, and water structural changes in the aqueous medium. The values of k_ϕ are negative (see Table 7) which indicates the presence of strong interactions between solute–solvent molecules. The limiting apparent molal compressibility (k_ϕ^0) is generally negative for electrolytes in aqueous solution, and the magnitude depends upon the charges of cations (electrostriction). The negative values are attributed to hydration of cations (water-loosing compressibility due to coulombic attraction) [11]. k_ϕ^0 values are by definition free from solute–solute interactions and therefore provide information regarding strong solute–solvent interactions.

It is found that k_ϕ^0 increase linearly with the concentration of metformin hydrochloride in solution (see Table 8). It indicates that the cosolute–solvent interactions increase with increasing concentration of metformin hydrochloride in solution. A similar observation was made by Kikuchi et al. [21] for some amino acids in aqueous solutions.

Table 6 Relative change in isentropic compressibility($\Delta k_S/k_S^0$) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at different temperatures

m_A (mol · kg^{-1})	$\Delta k_S/k_S^0 \times 10^3$			
	$m_H = 0.00$ M	$m_H = 0.05$ M	$m_H = 0.10$ M	$m_H = 0.15$ M
$T = 308.15$ K				
0.0200	2.447	2.305	2.202	2.069
0.0400	4.735	4.645	4.246	3.980
0.0600	7.058	6.988	6.323	5.925
0.0800	9.384	9.335	8.403	7.871
0.1000	11.745	11.550	10.486	9.851
$T = 313.15$ K				
0.0200	2.439	2.328	2.063	1.929
0.0400	4.750	4.369	3.969	3.861
0.0600	7.066	6.573	5.907	5.635
0.0800	9.384	8.620	7.848	7.571
0.1000	11.707	10.830	9.821	9.540
$T = 318.15$ K				
0.0200	2.301	2.063	1.801	1.668
0.0400	4.475	3.970	3.604	3.338
0.0600	6.652	6.039	5.250	5.010
0.0800	8.833	7.980	6.927	6.554
0.1000	11.016	10.084	8.766	8.229

m_H molality of metformin hydrochloride

Quantitatively, the same results can be viewed on the basis of the continuum model [22] of a solution. As per this model, the limiting apparent molal adiabatic compressibility, k_ϕ^0, of a solute may be expressed as

$$k_\phi^0 = k_{\phi m} + n_H \left(k_{\varphi h}^0 + k_{\varphi b}^0\right) \tag{12}$$

where $k_{\phi m}$ is the intrinsic compressibility of a solute molecule, and $k_{\varphi h}^0$ and $k_{\varphi b}^0$ are the apparent molal adiabatic compressibilities of water in the hydration shell and in the bulk state of a solution.

The bulk water has an open structure when compared to electrostricted water and is therefore more compressible. The electrostricted water behaves like bulk water on the addition of metformin hydrochloride, and this results in the limiting apparent molal adiabatic compressibilities of amino acids in mixed solvents being larger than the corresponding ones in water as depicted in Table 8. The positive values of S_K indicate weak solute–solute interactions. The changes in electrostriction are reflected in hydration numbers. The n_H values calculated from compressibility data (see Table 9) are less in aqueous metformin hydrochloride solutions as compared to water and decrease with increasing concentration and temperature. The decreasing trend of n_H values from compressibility data shows strong solute–cosolute interactions.

Table 7 Apparent molal compressibility (k_ϕ) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at different temperatures

m_A (mol · kg^{-1})	$-k_\phi \times 10^{15}$ (m^3 · mol^{-1} · Pa^{-1})			
	$m_H = 0.00$ M	$m_H = 0.05$ M	$m_H = 0.10$ M	$m_H = 0.15$ M
$T = 308.15$ K				
0.0200	21.60(0.21)	18.16(0.22)	13.71(0.19)	10.82(0.17)
0.0400	20.94(0.10)	17.43(0.11)	13.07(0.09)	10.19(0.08)
0.0600	20.22(0.07)	17.20(0.07)	12.38(0.06)	9.51(0.06)
0.0800	19.86(0.05)	17.09(0.05)	12.05(0.04)	9.18(0.04)
0.1000	19.35(0.04)	16.47(0.04)	11.86(0.03)	8.70(0.03)
$T = 313.15$ K				
0.0200	21.31(0.21)	16.42(0.19)	10.67(0.17)	7.75(0.17)
0.0400	19.90(0.10)	14.41(0.09)	10.07(0.08)	7.78(0.08)
0.0600	19.44(0.07)	14.18(0.06)	9.38(0.05)	7.39(0.05)
0.0800	19.22(0.05)	13.75(0.04)	9.05(0.04)	7.52(0.04)
0.1000	19.09(0.04)	13.76(0.03)	8.57(0.03)	7.31(0.03)
$T = 318.15$ K				
0.0200	18.25(0.19)	10.75(0.18)	5.12(0.15)	2.27(0.14)
0.0400	16.86(0.09)	10.15(0.09)	5.15(0.07)	2.30(0.07)
0.0600	16.41(0.06)	10.38(0.06)	4.77(0.05)	2.34(0.04)
0.0800	16.19(0.04)	9.82(0.04)	4.22(0.03)	1.69(0.03)
0.1000	16.07(0.03)	9.74(0.03)	4.15(0.03)	1.85(0.02)

m_H molality of metformin hydrochloride
Parentheses indicates the standard deviation

The apparent molal compressibilities of transfer, Δk_ϕ^0, from water to metformin hydrochloride at infinite dilution are found to be positive (see Table 10). These positive values of transfer may be attributed to the interactions occurring due to (i) hydrophilic–ionic group interactions between the (–OH) hydroxyl groups of metformin hydrochloride and the zwitterionic center of the amino acid and (ii) hydrophilic–hydrophilic group interactions between the –OH group of metformin hydrochloride and the (–OH) groups of amino acid mediated through hydrogen bonding. Due to these interactions, the electrostriction of neighboring water molecules around the charged centers of 4-aminobutyric acid will be reduced in the presence of metformin hydrochloride. Therefore, the electrostricted water goes out of the hydration spheres of these ions and enters into the bulk which is more compressible [23], thus making a positive contribution to Δk_ϕ^0. This observation means that the dehydration of solute and cosolute is high. Pal et al. [24] also reported positive Δk_ϕ^0 values for glycine from water to aqueous magnesium chloride solutions.

Furthermore, it is seen from Table 11 that the triplet interaction coefficients, k_{AHH}, are negative, whereas pair interaction coefficients, k_{AH}, are only positive. The positive values of the pair interaction coefficients, k_{AH}, in the case of 4-aminobutyric

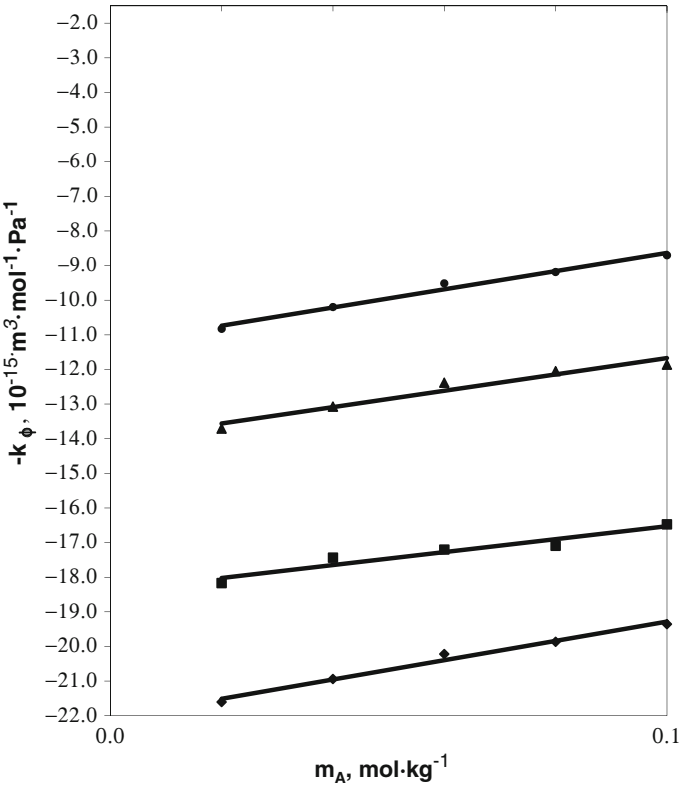

Fig. 3 Plot of apparent molal compressibility ($-k_\phi$) versus molality of amino acid (m_A) at various molal concentrations of aqueous metformin hydrochloride solutions at $T = 308.15$ K: ♦ 0.00 M, ■ 0.05 M, ▲ 0.10 M, ● 0.15 M

Table 8 Limiting apparent molal compressibility, k_ϕ^0, and slope, S_K, of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at various temperatures

Temp (K)	$-k_\phi^0 \times 10^{15}$ ($m^3 \cdot mol^{-1} \cdot Pa^{-1}$)							
	$m_H = 0.00$ M		$m_H = 0.05$ M		$m_H = 0.10$ M		$m_H = 0.15$ M	
308.15	22.07	18.68	18.40	27.77	14.03	23.62	11.26	26.30
	(0.13)	(0.01)	(0.20)	(0.03)	(0.21)	(0.03)	(0.12)	(0.01)
313.15	21.34	25.62	16.30	29.85	11.12	26.09	7.89	5.65
	(0.48)	(0.07)	(0.07)	(0.01)	(0.11)	(0.01)	(0.13)	(0.01)
318.15	18.27	25.12	10.88	11.71	5.55	31.05	2.53	23.68
	(0.47)	(0.07)	(0.01)	(0.03)	(0.18)	(0.02)	(0.23)	(0.03)

m_H molality of metformin hydrochloride
Parentheses indicates standard deviation

acid suggest that interactions occur due to the overlap of hydration spheres of the solute–cosolute molecules. The large positive k_{AH} values suggest the domination of pair interactions for the 4-aminobutyric acid over triplet compressibility interaction parameters [25].

Table 9 Hydration number (n_H) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at various temperatures

m_H (M)	308.15 K	313.15 K	318.15 K
0.00	2.81	2.74	2.36
0.05	2.36	2.10	1.41
0.10	1.79	1.43	0.71
0.15	1.43	1.01	0.32

m_H molality of metformin hydrochloride

Table 10 Transfer limiting molal compressibility (Δk_ϕ^0) of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at various temperatures

Temp (K)	$\Delta k_\phi^0 \times 10^{15}$ ($m^3 \cdot mol^{-1} \cdot Pa^{-1}$)		
	$m_H = 0.05$ M	$m_H = 0.10$ M	$m_H = 0.15$ M
308.15	3.67	8.04	10.81
313.15	5.04	10.22	13.45
318.15	7.39	12.72	15.74

m_H molality of metformin hydrochloride

Table 11 Pair (k_{AH}) and triplet (k_{AHH}) interactions of 4-aminobutyric acid in aqueous metformin hydrochloride solutions at various temperatures

Temp (K)	$k_{AH} \times 10^{15}$ ($m^3 \cdot mol^{-2} \cdot Pa^{-1} \cdot kg$)	$k_{AHH} \times 10^{15}$ ($m^3 \cdot mol^{-1} \cdot Pa^{-1} \cdot kg^2$)
308.15	0.4514	−0.0051
313.15	1.3508	−0.0177
318.15	0.7909	−0.0069

5 Conclusions

In this study, compressibility data are reported for 4-aminobutyric acid in different concentrations of aqueous metformin hydrochloride solutions. The negative values of apparent molal compressibility (k_ϕ) indicate a close-packed structure in metformin hydrochloride solutions. Furthermore, the negative values of the limiting apparent molal compressibility (k_ϕ^0) also indicate the presence of strong solute–solvent interactions. The decreasing trend of n_H values reflects the electrostriction effect and the strong solute–cosolute interactions in the studied system.

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