Ultrasonic Studies of Valine in Aqueous Paracetamol Solutions at Different Temperatures

Rajagopal. K, Roy Richi Renold. G*, Mohamed Roshan. M

Abstract— The derived parameters of ultrasonic velocity such as isentropic compressibility (β_S), the change in isentropic compressibility ($\Delta\beta_S$), the relative change in isentropic compressibility ($\Delta\beta_S/\beta_S^0$), the apparent molal compressibility (k_ϕ), the limiting apparent molal compressibility (k_ϕ^0), the transfer limiting apparent molal compressibility ($\Delta_{tr}k_\phi^0$), the hydration number (n_H), and the pair and triplet interaction parameters (k_{AP}, k_{APP}) are computed from the experimentally measured ultrasonic velocity and density data of valine in 0.025 M, 0.05 M, 0.075 M and 0.1 M aqueous paracetamol solutions at 298.15, 303.15, 308.15, 313.15 and 318.15 K. These thermodynamic parameters are used to elucidate the solute–solute and solute–solvent interactions of valine in aqueous paracetamol solutions.

Index Terms— Hydration number · Isentropic compressibility · Limiting apparent molal compressibility · Paracetamol · Ultrasonic velocity

1 INTRODUCTION

Proteins are polymer chains made of amino acids linked together by peptide bonds. They are found in all cells of the body and are the most essential nutrients for the human body. They are important in the sense that they are one of the building blocks of body tissue, and can also serve as a source of fuel for cells. The structure of proteins in various solvents is affected by the complex conformational and configurational factors making it difficult to interpret the nature of interaction directly from studies on proteins in aqueous media. Therefore, investigations on the behavior of model compounds of proteins like amino acids are of great importance. Data on the thermodynamic and transport properties of amino acids in aqueous phase play a key role in the optimization and design of protein molecules. To understand the thermodynamic behavior, the hydration of proteins and non-covalent forces stabilizing their native structure and the solvation property of proteins in solution, amino acids have been used as models where the prediction of the properties of biochemical systems can be had by deriving simple additivity schemes [1].

Recently [2] we have reported the volumetric and viscometric studies of valine in aqueous paracetamol and confirmed the presence of strong solute-solvent interactions in addition to the presence of weak solute-solute interactions. In continuation of our earlier work, in this paper we report data on ultrasonic velocities and densities of valine in aqueous paracetamol at five different temperatures (298.15, 303.15, 308.15, 313.15 and 318.15 K).

Valine [2] is a type of essential amino acid named after the plant valerian, containing an α-amino group (NH_3^+), an α-carboxylic acid group (COO^-), and a side chain isopropyl variable group, classifying it as a non-polar amino acid, which is used to promote normal growth, to repair tissues, to regulate blood sugar, and to provide the body with energy. It helps to stimulate the central nervous system and is much needed for proper mental functioning. The molecular formula is $C_5H_{11}NO_2$ and the chemical structure is shown in Figure-1.

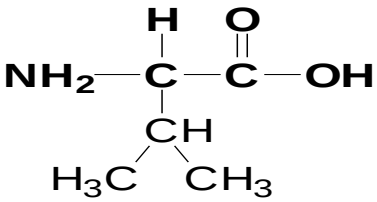

Fig. 1 Chemical structure of Valine

Paracetamol [3], IUPAC name of Paracetamol is N-acetyl-4-aminophenol which is white in colour broadly used as an analgesic (pain reliever) and antipyretic (fever reducer) drug. The molecular formula is $C_8H_9NO_2$. Paracetamol consists of a benzene ring core, substituted by one hydroxyl group and the nitrogen atom of an amide group in the para (1,4) pattern which can take part in interactions with valine. The amide group is acetamide (ethanamide). It is an largely(extensively) conjugated system, as the lone pair on the hydroxyl oxygen, the benzene pi cloud, the nitrogen lone pair, the p orbital on the carbonyl carbon, and the lone pair on the carbonyl oxygen are all conjugated [3]. The presence of two activating groups makes the benzene ring highly reactive towards electrophilic aromatic substitution.

Being a second derivative of free energy, compressibility is another powerful thermodynamic parameter for elucidating the behavior of solute in a solvent as it could sense the solute

- *Rajagopal. K is a Professor of Physics (Rtd.), Government College of Engineering, Tirunelveli, TamilNadu, India.*
- **Roy Richi Renold. G is currently pursuing PhD programme, M.S. University, Tirunelveli and working as a Assistant Professor of Physics, V V College of Engineering, Tisaiyanvilai, Tirunelveli, TamilNadu, India, Ph-09865258904, Fax: 04637-273413, E-mail: richiindia@yahoo.com*
- *Mohamed Roshan. M is working as a Assistant Professor of Physics, Sadakathullah Appa College, Tirunelveli, TamilNadu, India.*

hydration structure at a greater distance from the solute [4]. So the derived thermodynamic parameters of ultrasonic velocity such as isentropic compressibility (β_S), the change in isentropic compressibility ($\Delta\beta_S$), the relative change in isentropic compressibility ($\Delta\beta_S/\beta_S^0$), the apparent molal compressibility (k_ϕ), the limiting apparent molal compressibility (k_ϕ^0), the transfer limiting apparent molal compressibility ($\Delta_{tr}k_\phi^0$), the hydration number (n_H), and the pair and triplet interaction parameters (k_{AP}, k_{APP}) are calculated from the measured data. These parameters are used to interpret the solute–solute and solute–solvent interactions of valine in aqueous paracetamol solutions. The data at temperatures T = (298.15, 303.15, 308.15, 313.15 and 318.15) K provide insight to the drug macromolecular behavior near physiological temperatures. Our group has already reported ultrasonic studies on a number of systems to elucidate the type of interaction [5], [6], [7], [8], [9], [10].

2 Experimental

Paracetamol (mass fraction purity > 0.990) has been procured from S.D. Fine. Chem. Ltd., Mumbai. L-valine (99% assay, Loba Chemie Pvt Ltd), has been used after drying over P_2O_5 in a desiccator for 72 hrs before use. L-valine of molality (0.02, 0.04, 0.06, 0.08 and 0.1) M has been used as solutes in four different molal (0.025, 0.05, 0.075 and 0.1) concentration of aqueous paracetamol solvents, prepared using doubly distilled deionized water with a conductivity of 1.5×10^{-4} $\Omega^{-1}m^{-1}$. The density and ultrasonic velocity have been measured using single stem pycnometer and single-crystal variable-path multi-frequency ultrasonic interferometer (M-05, Mittal Enterprises, India) operated at 2 MHz whose procedures have been discussed in our earlier report [11].

3 Results

Using the experimentally measured densities and ultrasonic velocities of valine in aqueous paracetamol solutions listed in Tables 1 and 2, adiabatic compressibility (β_S) and the uncertainty associated with β_S [12] has been calculated using equation (1) & (2) and are listed in Table 3.

$$\beta_S = 1/(\rho u^2) \quad (1)$$

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

The following equations (3), (4), (5) and (6) are used to calculate the parameters like change in isentropic compressibility ($\Delta\beta_S$) [13] and relative change in isentropic compressibility ($\Delta\beta_S/\beta_S^0$) [14] and the values are given in Tables in 4 and 5:

$$\Delta\beta_S = \beta_S^0 - \beta_S = A + B\,m \quad (3)$$

$$\beta_S = \beta_S^0 - \alpha\beta_S^0 \quad (4)$$

$$\alpha = (\beta_S^0 - \beta_S)/\beta_S^0 = \Delta\beta_S/\beta_S^0 \quad (5)$$

$$\Delta\beta_S/\beta_S^0 = A' + B'm \quad (6)$$

Where, β_S^0 and β_S are the adiabatic compressibilities of the solvent and solution, respectively. A and B are the intercept and slope values of $\Delta\beta_S$ versus m plot, respectively. Similarly A' and B' stand for the intercept and slope values of ($\Delta\beta_S/\beta_S^0$) versus m plot, respectively.

Using equation (7) the apparent molal compressibility (k_ϕ) values of valine in aqueous paracetamol solution are calculated [15] and are given in Table 6.

$$k_\phi = M\beta_S/\rho - 1000(\beta_0\rho - \beta_S\rho_0)/m\rho\rho_0 \quad (7)$$

Where, M and m are the molar mass and molality of valine; ρ and ρ_0 are the densities of the solute and solvent, respectively.

TABLE 1
Density (ρ) Of Valine In Aqueous Paracetamol Solutions At Different Temperatures

m_A/ (mol·kg^{-1})	ρ x 10^3 / (kg.m^{-3}) at various m_P / (mol·kg^{-1})				
	0.0	0.025	0.05	0.075	0.1
T = 298.15 K					
0.00	0.99706	0.99769	0.99833	0.99900	0.99969
0.02	0.99758	0.99831	0.99896	0.99964	1.00034
0.04	0.99807	0.99890	0.99956	1.00025	1.00096
0.06	0.99853	0.99946	1.00013	1.00083	1.00154
0.08	0.99896	0.99999	1.00067	1.00138	1.00211
0.10	0.99936	1.00049	1.00118	1.00190	1.00264
δρ =	3.5 x 10^{-4}	4.28 x 10^{-4}	4.36 x 10^{-4}	4.43 x 10^{-4}	4.51 x 10^{-4}
T = 303.15 K					
0.00	0.99560	0.99621	0.99685	0.99751	0.99819
0.02	0.99612	0.99682	0.99747	0.99814	0.99883
0.04	0.99661	0.99740	0.99806	0.99874	0.99944
0.06	0.99707	0.99795	0.99862	0.99931	1.00002
0.08	0.99750	0.99847	0.99915	0.99985	1.00057
0.10	0.99791	0.99897	0.99966	1.00037	1.00110
δρ =	3.53 x 10^{-4}	4.21 x 10^{-4}	4.29 x 10^{-4}	4.37 x 10^{-4}	4.44 x 10^{-4}
T = 308.15 K					
0.00	0.99403	0.99463	0.99526	0.99593	0.99660
0.02	0.99455	0.99523	0.99587	0.99655	0.99723
0.04	0.99503	0.99580	0.99645	0.99714	0.99783
0.06	0.99550	0.99634	0.99700	0.99770	0.99840
0.08	0.99595	0.99686	0.99753	0.99824	0.99894
0.10	0.99637	0.99734	0.99802	0.99874	0.99947
δρ =	3.57 x 10^{-4}	4.14 x 10^{-4}	4.22 x 10^{-4}	4.30 x 10^{-4}	4.38 x 10^{-4}
T = 313.15 K					
0.00	0.99228	0.99286	0.99348	0.99412	0.99479
0.02	0.99279	0.99345	0.99408	0.99473	0.99541
0.04	0.99326	0.99401	0.99465	0.99531	0.99600
0.06	0.99370	0.99454	0.99519	0.99586	0.99656
0.08	0.99413	0.99505	0.99571	0.99639	0.99710
0.10	0.99450	0.99553	0.99620	0.99689	0.99761
δρ =	3.40 x 10^{-4}	4.08 x 10^{-4}	4.16 x 10^{-4}	4.23 x 10^{-4}	4.31 x 10^{-4}
T = 318.15 K					
0.00	0.99032	0.99089	0.99150	0.99214	0.99283
0.02	0.99082	0.99147	0.99209	0.99274	0.99344
0.04	0.99130	0.99202	0.99265	0.99331	0.99402
0.06	0.99173	0.99253	0.99318	0.99385	0.99457
0.08	0.99214	0.99306	0.99369	0.99439	0.99511
0.10	0.99252	0.99354	0.99421	0.99489	0.99563
δρ =	3.36 x 10^{-4}	4.05 x 10^{-4}	4.12 x 10^{-4}	4.20 x 10^{-4}	4.27 x 10^{-4}

m_A-stands for molality of valine

m_P-stands formolality of paracetamol

δρ denotes uncertainty in density values

A linear plot of k_ϕ versus m (see the representative plot in Fig. 2) is drawn, from which the limiting apparent molal compressibility (k_ϕ^0) of valine is evaluated [15] using the least-squares method of the following general equation:

$$k_\phi = k_\phi^0 + S_k m \quad (8)$$

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, a measure of solute–solvent interactions. The calculated values of k_ϕ^0 and S_K are listed in Table 7.

TABLE 2
Ultrasonic Velocity (u) Of Valine In Aqueous Paracetamol Solutions At Different Temperatures

m_A	u / (ms^{-1}) at various m_P / ($mol{\cdot}kg^{-1}$)				
($mol{\cdot}kg^{-1}$)	0.0	0.025	0.05	0.075	0.1
T = 298.15 K					
0.00	1496.60	1498.90	1500.95	1502.70	1504.15
0.02	1498.50	1500.93	1503.00	1504.55	1505.55
0.04	1500.30	1502.68	1504.71	1506.42	1507.23
0.06	1502.03	1504.29	1506.51	1507.91	1508.90
0.08	1503.70	1505.74	1508.05	1509.38	1510.49
0.10	1505.36	1507.24	1509.38	1511.09	1512
δu =	13.34 x10^{-4}	12.62 x10^{-4}	12.92 x10^{-4}	12.65 x10^{-4}	12.16 x10^{-4}
T = 303.15 K					
0.00	1509.00	1511.32	1513.37	1515.10	1516.62
0.02	1510.82	1513.30	1515.26	1516.77	1517.89
0.04	1512.54	1515.00	1516.90	1518.64	1519.54
0.06	1514.20	1516.52	1518.73	1520.05	1521.11
0.08	1515.81	1517.89	1520.20	1521.44	1522.62
0.10	1517.41	1519.30	1521.50	1523.07	1524.14
δu =	12.80 x10^{-4}	12.07 x10^{-4}	12.52 x10^{-4}	12.07 x10^{-4}	11.64 x10^{-4}
T = 308.15 K					
0.00	1519.68	1522.02	1524.07	1525.82	1527.38
0.02	1521.40	1523.93	1525.89	1527.46	1528.60
0.04	1523.05	1525.50	1527.49	1529.28	1530.16
0.06	1524.60	1527.10	1529.30	1530.67	1531.72
0.08	1526.10	1528.32	1530.69	1531.96	1533.22
0.10	1527.60	1529.67	1531.90	1533.5	1534.64
δu =	12.06 x10^{-4}	11.60 x10^{-4}	12.10 x10^{-4}	11.64 x10^{-4}	11.29 x10^{-4}
T = 313.15 K					
0.00	1528.92	1531.26	1533.30	1535.06	1536.65
0.02	1530.56	1533.01	1535.05	1536.67	1537.79
0.04	1532.12	1534.48	1536.57	1538.38	1539.27
0.06	1533.62	1535.90	1538.18	1539.58	1540.67
0.08	1535.05	1537.10	1539.51	1540.82	1542.06
0.10	1536.54	1538.35	1540.69	1542.32	1543.45
δu =	11.58 x10^{-4}	10.74 x10^{-4}	11.35 x10^{-4}	10.92 x10^{-4}	10.52 x10^{-4}
T = 318.15 K					
0.00	1536.47	1538.80	1540.85	1542.60	1544.25
0.02	1538.09	1540.62	1542.58	1544.15	1545.39
0.04	1539.60	1542.07	1544.06	1545.82	1546.83
0.06	1541.08	1543.44	1545.63	1547.04	1548.17
0.08	1542.50	1544.61	1546.96	1548.2	1549.54
0.10	1543.96	1545.83	1548.09	1549.64	1550.91
δu =	11.38 x10^{-4}	10.61 x10^{-4}	11.13 x10^{-4}	10.62 x10^{-4}	10.27 x10^{-4}

m_A-stands for molality of valine

m_P-stands formolality of paracetamol

δu denotes uncertainty in ultrasonic velocity values

TABLE 3
Adiabatic Compressibility (β_s) Of Valine In Aqueous Paracetamol Solutions At Different Temperatures

m_A	β_S x 10^{11} / (pa^{-1}) at various m_P / ($mol{\cdot}kg^{-1}$)				
($mol{\cdot}kg^{-1}$)	0.0	0.025	0.05	0.075	0.1
T = 298.15 K					
0.00	44.78 (0.081)	44.61 (0.078)	44.45 (0.079)	44.32 (0.077)	44.21 (0.074)
0.02	44.64 (0.081)	44.47 (0.077)	44.31 (0.079)	44.19 (0.077)	44.09 (0.074)
0.04	44.51 (0.081)	44.34 (0.077)	44.18 (0.078)	44.06 (0.077)	43.96 (0.074)
0.06	44.39 (0.080)	44.22 (0.077)	44.05 (0.078)	43.94 (0.076)	43.84 (0.073)
0.08	44.27 (0.080)	44.10 (0.076)	43.94 (0.078)	43.83 (0.076)	43.72 (0.073)
0.10	44.16 (0.080)	43.99 (0.076)	43.83 (0.077)	43.71 (0.076)	43.61 (0.073)
T = 303.15 K					
0.00	44.11 (0.076)	43.94 (0.073)	43.79 (0.075)	43.67 (0.072)	43.55 (0.070)
0.02	43.98 (0.076)	43.80 (0.072)	43.66 (0.075)	43.54 (0.072)	43.44 (0.069)
0.04	43.86 (0.076)	43.68 (0.072)	43.54 (0.074)	43.41 (0.072)	43.31 (0.069)
0.06	43.74 (0.076)	43.57 (0.072)	43.41 (0.074)	43.30 (0.071)	43.20 (0.069)
0.08	43.63 (0.075)	43.46 (0.072)	43.30 (0.074)	43.20 (0.071)	43.09 (0.069)
0.10	43.52 (0.075)	43.36 (0.071)	43.20 (0.074)	43.08 (0.071)	42.98 (0.068)
T = 308.15 K					
0.00	43.56 (0.071)	43.39 (0.069)	43.24 (0.071)	43.12 (0.068)	43.01 (0.066)
0.02	43.44 (0.071)	43.26 (0.068)	43.12 (0.071)	43.00 (0.068)	42.90 (0.066)
0.04	43.32 (0.070)	43.15 (0.068)	43.00 (0.071)	42.88 (0.068)	42.79 (0.066)
0.06	43.22 (0.070)	43.04 (0.068)	42.88 (0.070)	42.77 (0.068)	42.67 (0.066)
0.08	43.11 (0.070)	42.94 (0.068)	42.78 (0.070)	42.67 (0.067)	42.57 (0.065)
0.10	43.01 (0.070)	42.84 (0.067)	42.69 (0.070)	42.57 (0.067)	42.47 (0.065)
T = 313.15 K					
0.00	43.11 (0.067)	42.95 (0.063)	42.80 (0.066)	42.68 (0.063)	42.57 (0.061)
0.02	43.00 (0.067)	42.83 (0.063)	42.68 (0.066)	42.57 (0.063)	42.47 (0.061)
0.04	42.89	42.72	42.57	42.45	42.36

	(0.066)	(0.062)	(0.065)	(0.063)	(0.061)
0.06	42.79 (0.066)	42.62 (0.062)	42.47 (0.065)	42.36 (0.063)	42.26 (0.061)
0.08	42.69 (0.066)	42.53 (0.062)	42.37 (0.065)	42.26 (0.062)	42.16 (0.060)
0.10	42.59 (0.066)	42.43 (0.062)	42.28 (0.065)	42.16 (0.062)	42.06 (0.060)
T = 318.15 K					
0.00	42.77 (0.065)	42.61 (0.061)	42.47 (0.064)	42.35 (0.061)	42.24 (0.059)
0.02	42.66 (0.065)	42.49 (0.061)	42.35 (0.064)	42.24 (0.061)	42.14 (0.059)
0.04	42.56 (0.065)	42.39 (0.061)	42.25 (0.063)	42.13 (0.061)	42.03 (0.059)
0.06	42.46 (0.064)	42.29 (0.061)	42.14 (0.063)	42.04 (0.060)	41.93 (0.059)
0.08	42.36 (0.064)	42.20 (0.061)	42.05 (0.063)	41.95 (0.060)	41.84 (0.058)
0.10	42.27 (0.064)	42.11 (0.060)	41.96 (0.063)	41.85 (0.060)	41.74 (0.058)

Parenthesis indicates uncertainity in βs values

The hydration number (n_H) represented in Table 8, gives details about the number of water molecules hydrated to valine, calculated using following equation (9) given by Millero et al. [16].

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

where β_S^0 is the adiabatic compressibility of the aqueous paracetamol solution and V_b^0 is the molar volume of bulk water which is taken to be the molar volume of water in paracetamol solution.

The transfer partial molal compressibilities ($\Delta_{tr}k_\phi^0$) from water to aqueous paracetamol solutions are calculated using the following equation and are listed in Table 9.

$$\Delta_{tr}k_\phi^0 = k_\phi^0(\textit{valine in solution}) - k_\phi^0(\textit{valine in water}) \quad (10)$$

Friedman and Krishnan [17], Franks et al.[18] and Rajagopal et al.[5], [6], [7], [8], [9], [10] have used McMillan–Mayer theory of solutions proposed by Kozak et al.[19] to analyse the solute–cosolute interactions in the salvation sphere. According to this theory, at infinite dilution, $\Delta_{tr}k_\phi^0$ can be expressed as

$$\Delta_{tr}k_\phi^0 = 2K_{AP}m_P + 3K_{APP}m_P^2 \quad (11)$$

Where, A stands for valine, P stands for paracetamol, and m_P is the molality of paracetamol. The constants K_{AP} and K_{APP} are pair and triplet interaction coefficients, respectively, and are given in Table 10.

4 Discussion

The effectiveness of solute-solvent interactions [20] indicates a greater association of molecules which is substantiated by an increase in the ultrasonic velocity in any solution with the addition of a solute (see Table 2). The adiabatic compressibility (β_S) decreases [21] with the increase in the concentration of valine, paracetamol and temperature of the solution.

The decrease in adiabatic compressibility with an increase in concentration of valine may be attributed to (i) an increase in the number of incompressible molecules/zwitterions in (ternary system) solution and (ii) the formation of the compact structure of zwitterions–aquatic dipoles and zwitterions–ions structures in the solutions [10]. The decrease in adiabatic compressibility values with increasing temperature may be atributed to the changes occurring in the water structure around zwitterions–ions [22]. Water is considered to be an equilibrium medley of two structures such as an ice-like structure and a close-packed structure [10]. The compressibility of liquid water is given by

$\beta_S = \beta_\alpha + \beta_{relax}/(1 + \omega^2\tau^2)$,

where β_α is an instantaneous part of the compressibility and β_{relax} is a relaxational part of the compressibility.

ω is the angular frequency

τ is the relaxation time and is of the order of 10^{-11} s corresponding to β_{relax} .

where the relation, $\omega\tau < 1$. Thus,

$\beta_S = \beta_\alpha + \beta_{relax}$

Due to thermal expansion β_α increases and due to thermal burst of the ice-like structure β_{relax} decreases when the temperature increases. Thus, the decrease in compressibility with increase in temperature may be ascribed to the corresponding decrease in β_{relax} which is dominant over the corresponding increase in β_α. The values of $\Delta\beta_S$ and $\Delta\beta_S/\beta_S^0$ listed in Tables 4 & 5 shows an increasing trend of variation with an increase in concentration of solute (valine) which may be related to an increase in the incompressible part in a solution and the variation with temperature may be attributed to the thermal rupture of the water structure [10].

TABLE 4
Change In Adiabatic Compressibility (β_S) Of Valine In Aqueous Paracetamol Solutions At Different Temperatures

m_A (mol·kg^{-1})	$\Delta\beta_S \times 10^{12}$ / (pa^{-1}) at various m_P / (mol·kg^{-1})				
	0.0	0.025	0.05	0.075	0.1
T = 298.15 K					
0.02	1.368	1.423	1.428	1.369	1.239
0.04	2.657	2.702	2.693	2.682	2.499
0.06	3.886	3.907	3.958	3.860	3.725
0.08	5.062	5.036	5.108	4.981	4.900
0.10	6.215	6.151	6.169	6.172	6.025
T = 303.15 K					
0.02	1.292	1.351	1.325	1.262	1.149
0.04	2.507	2.573	2.532	2.534	2.360
0.06	3.670	3.703	3.747	3.636	3.510
0.08	4.787	4.765	4.833	4.698	4.610
0.10	5.886	5.817	5.867	5.824	5.710
T = 308.15 K					
0.02	1.212	1.277	1.252	1.202	1.084
0.04	2.361	2.417	2.399	2.413	2.228
0.06	3.446	3.546	3.588	3.485	3.350
0.08	4.490	4.512	4.599	4.479	4.404

0.10	5.518	5.510	5.561	5.530	5.422
T = 313.15 K					
0.02	1.144	1.187	1.186	1.150	1.019
0.04	2.223	2.252	2.269	2.283	2.096
0.06	3.251	3.264	3.334	3.239	3.112
0.08	4.232	4.200	4.298	4.189	4.099
0.10	5.218	5.135	5.223	5.205	5.085
T = 318.15 K					
0.02	1.116	1.181	1.157	1.108	0.998
0.04	2.159	2.219	2.202	2.208	2.037
0.06	3.160	3.205	3.245	3.157	3.018
0.08	4.116	4.102	4.188	4.053	3.978
0.10	5.079	5.012	5.076	5.025	4.939

The apparent molal compressibility (k_ϕ) is known to be very sensitive to changes in solvation, hydrogen bonding, and structural changes of water in the watery medium since it is related to the second pressure differential of the partial molal free energy of the solute. The negative values of k_ϕ (see Table 6) indicate the presence of strong interactions between solute–solvent molecules[5], [6], [7], [8], [9], [10], thereby complimenting our conclusions drawn from our earlier volumetric and viscometric studies of this system [2]. From definition k_ϕ^0 values are free from solute–solute interactions and therefore only provide details about strong solute–solvent interactions. Normally, electrolytes in aqueous solution has negative limiting apparent molal compressibility (k_ϕ^0), and the magnitude depends upon the charges of cations (electrostriction)[10].

TABLE 5
Relative Change In Adiabatic Compressibility (β_S/β_S^0) Of Valine In Aqueous Paracetamol Solutions At Different Temperatures

m_A	$(\Delta\beta_S/\beta_S^0) \times 10^3$ at various m_P / (mol·kg^{-1})				
(mol·kg^{-1})	0.0	0.025	0.05	0.075	0.1
T = 298.15 K					
0.02	3.054	3.189	3.212	3.088	2.803
0.04	5.933	6.057	6.059	6.052	5.652
0.06	8.679	8.759	8.904	8.709	8.425
0.08	11.305	11.289	11.491	11.237	11.083
0.10	13.879	13.790	13.879	13.924	13.627
T = 303.15 K					
0.02	2.929	3.076	3.027	2.890	2.637
0.04	5.684	5.855	5.782	5.804	5.418
0.06	8.321	8.427	8.558	8.326	8.059
0.08	10.853	10.845	11.038	10.758	10.586
0.10	13.343	13.240	13.398	13.337	13.110
T = 308.15 K					
0.02	2.781	2.944	2.896	2.787	2.520
0.04	5.421	5.571	5.548	5.597	5.180
0.06	7.911	8.172	8.297	8.081	7.790
0.08	10.308	10.399	10.635	10.387	10.239
0.10	12.667	12.697	12.860	12.825	12.606
T = 313.15 K					
0.02	2.654	2.764	2.772	2.695	2.395
0.04	5.155	5.243	5.301	5.348	4.925
0.06	7.540	7.601	7.790	7.589	7.310
0.08	9.817	9.779	10.042	9.814	9.630
0.10	12.104	11.955	12.203	12.195	11.946
T = 318.15 K					
0.02	2.609	2.771	2.724	2.615	2.362
0.04	5.046	5.207	5.186	5.214	4.824
0.06	7.387	7.521	7.640	7.455	7.147
0.08	9.623	9.626	9.862	9.570	9.418
0.10	11.874	11.761	11.952	11.866	11.693

TABLE 6
Apparent Molal Compressibility (k_ϕ) Of Valine In Aqueous Paracetamol Solutions At Different Temperatures

m_A	$k_\phi \times 10^{15}$ / (m^3 . mol^{-1} . Pa^{-1}) at various m_P / (mol·kg^{-1})				
(mol·kg^{-1})	0.0	0.025	0.05	0.075	0.1
T = 298.15 K					
0.02	-27.83 (0.05)	-29.97 (0.06)	-30.33 (0.06)	-30.70 (0.06)	-31.22 (0.06)
0.04	-25.66 (0.04)	-27.21 (0.05)	-27.51 (0.05)	-27.91 (0.05)	-28.37 (0.05)
0.06	-23.80 (0.04)	-25.38 (0.04)	-25.83 (0.05)	-26.33 (0.05)	-26.57 (0.04)
0.08	-22.10 (0.04)	-23.82 (0.04)	-24.14 (0.04)	-24.35 (0.04)	-25.09 (0.04)
0.10	-20.76 (0.04)	-22.42 (0.04)	-22.67 (0.04)	-23.28 (0.04)	-23.75 (0.04)
T = 303.15 K					
0.02	-24.68 (0.05)	-26.48 (0.05)	-26.90 (0.05)	-27.22 (0.05)	-27.63 (0.05)
0.04	-22.56 (0.04)	-24.29 (0.04)	-24.82 (0.05)	-25.12 (0.04)	-25.53 (0.04)
0.06	-20.84 (0.04)	-22.39 (0.04)	-22.75 (0.04)	-23.27 (0.04)	-23.71 (0.04)
0.08	-19.30 (0.03)	-20.93 (0.04)	-21.18 (0.04)	-21.58 (0.04)	-22.10 (0.04)
0.10	-18.14 (0.03)	-19.70 (0.04)	-20.22 (0.04)	-20.58 (0.04)	-21.12 (0.04)
T = 308.15 K					
0.02	-21.20 (0.04)	-22.83 (0.05)	-23.28 (0.05)	-23.66 (0.05)	-23.90 (0.05)
0.04	-19.33 (0.04)	-21.04 (0.04)	-21.36 (0.04)	-21.83 (0.04)	-22.36 (0.04)
0.06	-17.62 (0.03)	-19.91 (0.04)	-20.29 (0.04)	-20.72 (0.04)	-21.27 (0.04)
0.08	-16.20 (0.03)	-18.05 (0.04)	-18.36 (0.04)	-19.03 (0.04)	-19.50 (0.04)
0.10	-15.10 (0.03)	-16.90 (0.04)	-17.30 (0.04)	-17.83 (0.04)	-18.27 (0.04)
T = 313.15 K					
0.02	-18.06 (0.04)	-19.71 (0.04)	-20.02 (0.05)	-20.59 (0.05)	-20.78 (0.04)
0.04	-16.07 (0.03)	-17.70 (0.04)	-18.23 (0.04)	-18.53 (0.04)	-19.15 (0.04)
0.06	-14.43 (0.03)	-15.87 (0.03)	-16.36 (0.04)	-16.80 (0.04)	-17.41 (0.04)
0.08	-13.02 (0.03)	-14.64 (0.03)	-14.91 (0.04)	-15.57 (0.03)	-16.00 (0.03)
0.10	-12.00 (0.03)	-13.68 (0.03)	-14.16 (0.03)	-14.81 (0.03)	-15.20 (0.03)
T = 318.15 K					
0.02	-16.77 (0.04)	-18.16 (0.04)	-18.64 (0.04)	-18.96 (0.04)	-19.44 (0.04)
0.04	-14.82 (0.03)	-16.34 (0.04)	-16.70 (0.04)	-17.17 (0.04)	-17.61 (0.04)
0.06	-13.18 (0.03)	-14.83 (0.03)	-15.25 (0.04)	-15.72 (0.03)	-16.07 (0.03)
0.08	-11.74 (0.03)	-13.31 (0.03)	-13.78 (0.03)	-14.16 (0.03)	-14.64 (0.03)
0.10	-10.86 (0.03)	-12.45 (0.03)	-12.93 (0.03)	-13.30 (0.03)	-13.89 (0.03)

Parenthesis indicates the standard deviation.

The hydration of cations (water-loosing compressibility due to coulombic attraction) [12] leads to the negative values of k_ϕ^0. The values of k_ϕ^0 are negative and high at low temperatures which are attributed to the strong attractive interactions between the drug and water, and the k_ϕ^0 values become less negative with increase in temperature indicating that the electrostriction reduces and some water molecules are released to the bulk water, rendering the solutions more compressible at higher temperatures [23], [24], [25].

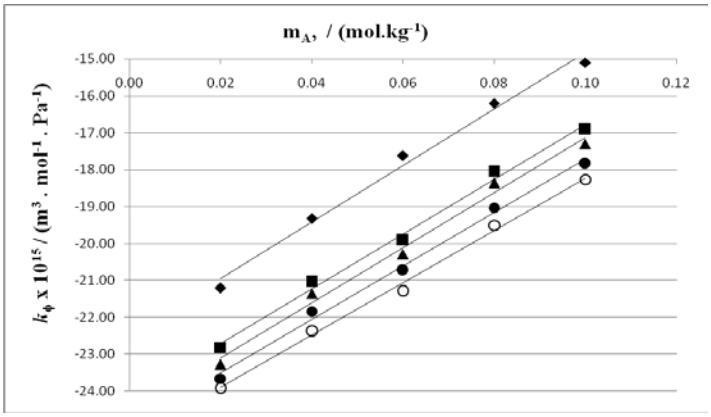

Fig. 2 Plot of apparent molal compressibility (k_ϕ) versus molality of amino acid (m_A) at various molal concentrations of aqueous paracetamol solutions at T = 308.15 K: 0.00 M, 0.025 M, 0.05 M, 0.075 M, and 0.1 M

The k_ϕ^0 values decrease directly in proportion with the concentration of paracetamol in solution (see Table 8), indicating that the co-solute–solvent interactions decrease with increasing concentration of paracetamol in solution [10]. A similar conclusion was draawn by Doyel M. Bhattacharya et al. [21] for antihelmintic drugs in aqueous solutions.

According to Frank J. Millero et al. [26] on the basis of the continuum model of a solution, the limiting apparent molal adiabatic compressibility, k_ϕ^0, of a solute may be expressed as

$$k_\phi^0 = k_\phi^0(\text{int}) + n_H\left(k_{\phi h}^0 + k_{\phi b}^0\right) \quad (12)$$

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

TABLE 7

Limiting Apparent Molal Compressibility, k_ϕ^0, And Slope, S_K, Of Valine In Aqueous Paracetamol Solutions At Various Temperatures

Temp(K)	k_ϕ^0 x 10^{15} / (m^3 . mol^{-1} . Pa^{-1}) & S_K x 10^{15} / (kg. m^3. mol^{-2}. Pa^{-1})									
	m_P = 0 M / mol·kg^{-1}		m_P = 0.025 M / mol·kg^{-1}		m_P = 0.05 M / mol·kg^{-1}		m_P = 0.075 M / mol·kg^{-1}		m_P = 0.1 M / mol·kg^{-1}	
298.15	-29.34	8.854	-31.31	9.248	-31.70	9.350	-32.04	9.203	-32.46	9.108
	(0.044)		(0.076)		(0.072)		(0.081)		(0.086)	
303.15	-26.01	8.172	-27.83	8.462	-28.28	8.506	-28.60	8.409	-28.95	8.223
	(0.051)		(0.058)		(0.069)		(0.06)		(0.061)	
308.15	-22.49	7.665	-24.20	7.419	-24.60	7.472	-24.95	7.230	-25.30	7.062
	(0.045)		(0.034)		(0.043)		(0.032)		(0.026)	
313.15	-19.27	7.585	-20.85	7.554	-21.25	7.521	-21.62	7.261	-22.00	7.154
	(0.053)		(0.067)		(0.065)		(0.076)		(0.053)	
318.15	-17.94	7.421	-19.35	7.228	-19.76	7.165	-20.16	7.164	-20.55	7.036
	(0.058)		(0.049)		(0.054)		(0.046)		(0.057)	

Parenthesis indicates the standard deviation.

The bulk water is more compressible as it has an open structure when compared to electrostricted water. The electrostricted water behaves like bulk water with the addition of paracetamol and this depicts that the limiting apparent molal adiabatic compressibilities of amino acids in mixed solvents becomes smaller than the corresponding ones in water as given in Table 7. S_K values are positive which predicts weak solute–solute interactions. The changes in electrostriction, reflects in the hydration number. In aqueous paracetamol solutions the calculated n_H values from compressibility data (see Table 8) are higher than water and increase with increasing concentration and decrease with increase in temperature. The trend of n_H values from compressibility data shows weak solute–co-solute interactions complimenting our earlier volumetric and viscometric studies [2].

TABLE 8

Hydration Number (n_H) Of Valine In Aqueous Paracetamol Solutions At Various Temperatures

m_P / (mol·kg^{-1})	n_H				
	298.15 K	303.15 K	308.15 K	313.15 K	318.15 K
0.000	3.622	3.211	2.777	2.379	2.215
0.025	3.865	3.436	2.988	2.574	2.389
0.050	3.914	3.491	3.037	2.623	2.440
0.075	3.956	3.531	3.080	2.669	2.489
0.100	4.007	3.574	3.123	2.716	2.537

The limiting apparent molal compressibilities of transfer, $\Delta_{tr}k_\phi^0$, from water to paracetamol at infinite dilution are found to be negative (see Table 9) and increases with the rise in temperature and decreases with increase in paracetamol concentration. The negative value $\Delta_{tr}k_\phi^0$ for valine in aqueous paracetamol solutions result from the overlap of hydration co-spheres of hydrophobic- hydrophobic groups and ionic - hydrophobic / hydrophilic - hydrophobic groups leading to a net decrease in volume which could be explained by the co-sphere overlap model developed by Friedman and Krishnan [27]. The types of the interaction occurring between valine and aqueous paracetamol can be classified as follows [25], [28].

a) The hydrophilic–ionic interaction between OH and NH-CO groups of paracetamol and zwitterions of valine.
b) Hydrophilic–hydrophilic interaction between the OH/NH-CO groups of paracetamol and OH, NH groups in the side chain of acid valine mediated through hydrogen bonding.
c) Hydrophilic–hydrophobic/ionic- hydrophobic interaction between the OH/NH-CO groups of paracetamol molecule and non-polar (isopropyl) group in the side chain of valine molecule.
d) Hydrophobic–hydrophobic group interactions between the non-polar group (Benzene ring) of Paracetamol and non-polar (isopropyl) group in the side chain of valine molecule.

The negative values for $\Delta_{tr}k_\phi^0$ for the ternary system suggest that the disruption of the hydration sphere of the charged centre of the drug and the positive contribution to the

$\Delta_{tr}k_{\phi}^{0}$ gets reduced, a phenomena created by the increased hydrophobic interactions with the carbon skeleton of the paracetamol [10]. These negative values of transfer, attributed to the interactions occurring indicate the dominance of hydrophobic–ionic interactions over those of the hydrophilic–ionic interactions which substantiate the results drawn from volumetric and transport properties [2].

TABLE 9
Transfer Apparent Molal Compressibility ($\Delta_{tr}k_{\phi}^{0}$) Of Valine In Aqueous Paracetamol Solutions At Various Temperatures

Temp (K)	$\Delta_{tr}k_{\phi}^{0}$ x 10^{15} / (m^3 . mol^{-1} . Pa^{-1}) at various m_P / (mol·kg^{-1})			
	0.025	0.05	0.075	0.1
298.15	-1.970	-2.360	-2.700	-3.120
303.15	-1.820	-2.270	-2.590	-2.940
308.15	-1.710	-2.110	-2.460	-2.810
313.15	-1.580	-1.980	-2.350	-2.730
318.15	-1.410	-1.820	-2.220	-2.610

The pair interaction coefficient, K_{AP}, is negative (see Table 10), suggesting that weak interactions occur due to the overlap of hydration spheres of solute–co-solute molecules. The triplet interaction coefficient, K_{APP}, is positive(see Table 10), indicating the predominance of triplet interactions over pair compressibility interaction parameters [29] which substantiates the results detained from volumetric and transport properties [2].

TABLE 10
Pair (K_{AP}) And Triplet (K_{APP}) Interactions Of Valine In Aqueous Paracetamol Solutions At Various Temperatures

Temp (K)	K_{AP}	K_{APP}
	(mol^{-2}.Pa^{-1}.kg)	(mol^{-1}.Pa^{-1}.kg^2)
298.15	-43.400	205.33
303.15	-40.400	188.09
308.15	-37.725	173.73
313.15	-34.675	154.62
318.15	-30.775	130.27

5 Conclusion

In this work, the compressibility data are reported for valine in aqueous paracetamol solutions with different concentrations at different temperatures. The negative values of limiting apparent molal compressibility confirms the presence of strong solute-solvent interactions, the positive value of S_K predicts weak solute–solute interactions and the increasing trend of n_H values shows weak solute–co-solute interactions complimenting our earlier volumetric and viscometric studies [2].

References

[1] K.Rajagopal, S.S.Jayabalakrishnan, "Effect of Temperature on Volumetric and Viscometric Properties of Homologous Amino Acids in Aqueous Solutions of Metformin hydrochloride", Thermodynamics And Chemical Engineering Data, Chinese Journal of Chemical Engineering, 18, 3, 425—445, 2010.

[2] K.Rajagopal, G.Roy Richi Renold, M.Mohamed Roshan, "Studies on Volumetric and Viscometric Properties of Valine in Aqueous Paracetamol Solution Over a Range of Temperature (298.15 to 318.15) K", International Journal of Pharmaceutical Sciences and Research, Vol. 8, 6, 133-142, Jun 2017.

[3] K.Rajagopal, G.Roy Richi Renold, "Studies on Volumetric and Viscometric properties of Alanine in aqueous Paracetamol solution over a range of temperature (298.15 to 318.15) K", International Journal of Advance Engineering and Research Development, Volume 4, Issue 3, April – 2017.)

[4] T.V.Chalikian, A.P.Sarvazyan and K.J.Breslauer, "Hydration and partial compressibility of biological compounds."Biophys. Chem., 51, 2-3, 89-107, 1994.

[5] K.Rajagopal, S.S.Jayabalakrishnan, "Ultrasonic Studies of 4-Aminobutyric Acid in Aqueous Metformin Hydrochloride Solutions at Different temperatures", Int J Thermophys, 31, 2225–2238, 2010.

[6] K.Rajagopal, S.S.Jayabalakrishnan, "Ultrasonic Studies of 4-Aminobutyric Acid in Aqueous Salbutamol Sulphate Solutions at Different Temperatures", Thermodynamics And Chemical Engineering Data, Chinese Journal of Chemical Engineering, 18, 4 659-666 2010.

[7] K.Rajagopal, S.Edwin Gladson, "Partial molar volume and partial molar compressibility of four homologous a-amino acids in aqueous sodium fluoride solutions at different temperatures", J. Chem. Thermodynamics, 43, 852–867, 2011.

[8] K.Rajagopal, S.Edwin Gladson, "Thermodynamic Analysis of Homologous α-Amino Acids in Aqueous Potassium Fluoride Solutions at Different Temperatures", J Solution Chem, 41, 646–679, 2012.

[9] K.Rajagopal and J.Johnson, "Intermolecular interaction studies of homologous α-amino acids in aqueous fructose solution at 298.15 K", International Journal of PharmTech Research,Vol.8, No.3, pp 480-498, 2015.

[10] K.Rajagopal, G.Roy Richi Renold, M.Mohamed Roshan, "Ultrasonic Studies Of Alanine In Aqueous Paracetamol Solutions At Different Temperatures", J. Pharm. Sci. & Res. Vol. 9(6), 1017-1025, 2017.

[11] K.Rajagopal, G.Roy Richi Renold, "Effect of Temperature on the Volumetric, Compressibility and Viscometric Properties of Paracetamol in Aqueous Methanol Solution", International Journal of PharmTech Research, Vol.8, No.8, 180-195, 2015.

[12] R.L.Gardas, D.H.Dagade, S.S.Terdale, J.A.P.Countinho, K.J.Patil, "Acoustic and volumetric properties of aqueous solutions of imidazolium based ionic liquids at 298.15 K", J. Chem. Thermodyn. 40, 695 2007.

[13] J.D.Pandey, A.Misra, N.Hasan, K.Misra, "Ultrasonic velocity, density, viscosity and compressibility lowering of urea and its derivatives in water-dioxane mixtures", Acoustics Letters, 15, 105-110, 1991.

[14] I.E.Elpiner, "Ultrasound, Physical Chemical and Biological Effects", Sindair, F.Z., trans., Consultants Bureau, New York, 188, 1964.

[15] R.K.Wadi, P.Ramsami, "Partial molar volumes and adiabatic compressibilities of transfer of glycine and DL-alanine from water to aqueous sodium sulphate at 288.15, 298.15 and 308.15 K", J. Chem. Soc., Faraday Trans., 93, 2, 243-247, 1997.

[16] F.J.Millero, A.L.Surdo, C.Shin, "The apparent molar volumes and adiabatic compressibilities of aqueous amino acids at 25°C", J. Phys. Chem., 82, 784-792, 1978.

[17] H.L.Friedmann, C.V.Krishnan, "Aqueous solutions of simple electrolytes", In: Water. A Comprehensive Treatise, Franks, F., ed., Plenum Press, New York, 1975.

[18] F.Franks, M.Pedley, D.S.Reid, "Solute interactions in dilute aqueous solutions (I) Microcalorimetric situdy of the hydrophobic interaction", J. Chem. Soc. Faraday Trans. I, 72, 359-367, 1976.
[19] J.J.Kozak, W.Knight, W.Kauzmann, "Solute-solute interactions in aqueous solutions", J. Chem. Phys., 48, 675-691, 1968.
[20] V.K.Syal, R.Gautam, S.Chauhan, "Ultrasonic velocity measurements of carbohydrates in binary mixtures of DMSO+H2O at 25°C", Ultrasonics, 36, 619-623, 1998.
[21] Doyel M.Bhattacharya, Sudhakar S.Dhondge, Sangesh P.Zodape, "Solvation behaviour of an antihelmintic drug in aqueous solutions of sodium chloride and glucose at different temperatures", J. Chem. Thermodynamics, 101, 207–220, 2016.
[22] Riyazudeen, G.K. Bansal, "Intermolecular/interionic interactions in l-leucine-, l-asparagine-, and glycylglycine-aqueous electrolyte systems", Thermochim. Acta., 445, 40-48, 2006.
[23] M.Riyazuddeen, Usmani, "Interactions in (glycylglycine + 1 M aqueous glucose/1 M aqueous sucrose) systems at 298.15–323.15 K", Thermochim. Acta., 532, 36–40, 2012.
[24] Nain. R.Pal, P.Sharma, "Volumetric, ultrasonic, and viscometric behaviour of l-histidine in aqueous-glucose solutions at different temperatures", J. Chem. Thermodyn., 43, 603–612, 2011.
[25] R. Bhat, N. Kishor, J. Ahluwalia, "Thermodynamic studies of transfer of some amino acids and peptides from water to aqueous glucose and sucrose solutions at 298.15 K", J. Chem. Soc. Faraday Trans. I, 84, 8, 2651-2665, 1988.
[26] F.J.Millero, G.K.Ward, F.K.Lepple, E.V.Hoff, "Isothermal compressibility of aqueous sodium chloride, magnesium chloride, sodium sulfate, and magnesium sulfate solutions from 0 to 45.deg. at 1 atm", J. Phys. Chem. 78, 1636, 1974.
[27] H.Friedman, C.V.Krishnan, "Thermodynamics of Ion Hydration in Water: A comprehensive treatise", Plenum press, New York, Vol. 3 (Chapter 1), 1-118, 1973.
[28] S.Li, W.Sang, R.Lin, "Partial molar volumes of glycine, L-alanine and L-serine in aqueous glucose solutions at T = 298.15 K", J. Chem. Thermodynamics, 34, 1761-1768, 2002.
[29] T.S.Banipal, G.Singh, "Themodynamic study of some amino acids, diglycine, and lysozyme in aqueous and mixed aqueous solutions", Thermochim. Acta, 412, 63-83, 2004.