Studies on Volumetric and Viscometric Properties of Valine in Aqueous Paracetamol Solution Over a Range of Temperature (298.15 to 318.15) K

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ABSTRACT

Density and viscosity values of valine at different concentrations (0.02, 0.04, 0.06, 0.08 and 0.1) M in aqueous paracetamol of concentration (0.025 - 0.1) M insteps of 0.025 M have been used to evaluate various important thermodynamic parameters like apparent molal volume, partial molal volume, the partial molal volume transfer, partial molal expansivity, isobaric thermal expansion coefficients, hydration number, viscosity B-coefficients, B-coefficient transfer, ratio of B-coefficient to partial molal volume, temperature derivative of B-coefficient, salvation number, free energy of activation of viscous flow per mole of solvent and per mole of solute and thermodynamic activation parameter of transfer from ground state to transition state. These thermodynamic parameters have been predicted in terms of solute-solute and solute-solvent interactions and structure making/breaking ability of solutes in the given solution.

Keywords: B-Coefficients; B-Coefficient transfer; Paracetamol; Partial molal volume; Partial molal volume transfer; Valine.

INTRODUCTION

Proteins are natural substances, composed of one or more long chains of amino acids, with high molecular weights ranging from 5,000 to many millions and are the most important constituent of cell membranes and cytoplasm. A direct study of proteins in solution is difficult as their behavior in solutions is governed by a combination of several specific interactions. One of the approaches that reduces the degree of complexity and requires less complex measurement techniques is to study the interactions in systems containing smaller biomolecules, such as amino acids and peptides.

Amino acids which are building blocks of proteins, play a significant role in metabolism and many neurochemical response mechanisms, such as memory, appetite control, and pain transmission [1, 2]. It is well known that drugs used in medicine may alter the metabolism of cells and organs in the human body, or they may kill or inactivate pathogens such as bacteria, viruses and fungi. Eventually, the drug−macromolecule interactions affect the action of a drug in the living organism, as it is based on different physiological processes and nature of the receptors for the drug molecules [3]. Research has further proved that drug solutions produce remarkable effects on the conformation and properties of proteins like denaturation, solubility and dissociation into subunits [4, 5]. The activity of enzymes and four main types of non-covalent interacting forces that could play a major role in drug-protein binding, like hydrogen bonds, van der Waals forces, electrostatic, and hydrophobic interactions [6] may decide the stability of protein structure in biological conditions. Since protein loses its biological activity due to physical factors like temperature, pressure, mechanical shear force, ultrasonic vibration and ionizing radiation, the thermodynamic parameters of binding reaction are the main evidence for confirming acting forces. Therefore, the thermodynamic parameters depend on temperatures are analyzed in order to characterize the acting forces between drug and amino acid [7]. Studies of the effect of concentration of drugs and temperature on the thermodynamic properties of aqueous amino acid solutions have been proven to be very useful in elucidating the various interactions that occur in drug−macromolecule mixtures of solutions that explains the process of absorption of drugs and transport of drugs across biological membranes [8]. In continuation of our previous studies of amino acids in some aqueous drugs [8-11] we report the thermodynamic study of valine in aqueous paracetamol solution, in this paper.

A detailed research survey shows that no one has so far reported thermodynamic study of valine in aqueous paracetamol using volumetric and viscometric studies. In continuation to our previous work on alanine

in aqueous paracetamol [8]**,** in this report we are presenting for the first time the new data and results of volumetric and viscometric properties of valine in aqueous paracetamol, at five different temperatures (298.15 K to 318.15 K) insteps of 5K to provide detailed information about how the macromolecules interact with the drug solutions nearer to physiological temperature.

Valine is a type of essential amino acid named after the plant valerian. It contains 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, used to promote normal growth, to repair tissues, to regulate blood sugar, and to provide the body with energy. It also helps to stimulate the central nervous system and is needed for proper mental functioning. The molecular formula of valine is $C_6H_{13}NO_2$ and its chemical structure is shown in Fig. 1.

Paracetamol [8] was first introduced into medicine as an antipyretic/analgesic by Von Mering in 1893 and has been in use as an analgesic for home medication for over 30 years and is accepted as a very effective treatment for the relief of pain and fever in adults and children. It is the most used medicine after acetylsalicylic acid in many countries as an alternative to aspirin and phenacetin [7, 12]. Its IUPAC name is N-acetyl-4-aminophenol. Its molecular formula is $C_8H_9NO_2$ and the chemical structure is shown in Fig. 1.

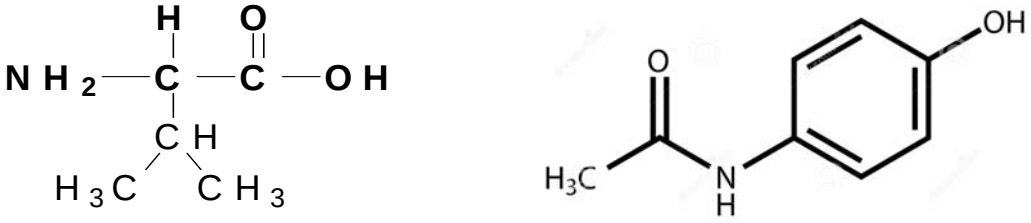

Fig. 1: Chemical structure of Valine & Paracetamol

From the experimentally measured density and viscosity data, different physical thermodynamic parameters like apparent molal volume, V_φ, partial molal volume, V_φ^0, the partial molal volume transfer, $\Delta_{tr}V_\varphi^0$, partial molal expansivity, E_2^0, hydration number, n_H, Viscosity B Coefficients, B-Coefficient transfer, ΔB_{tr}, Ratio of B Coefficient to partial molal volume, (B/V_φ^0), temperature derivative of B-coefficient, dB/dT, and free energy of activation of viscous flow per mole of solvent, $\Delta\mu_1^{0*}$ and per mole of solute of valine in aqueous paracetamol solution are evaluated respectively. All these parameters are used to discuss the solute-solute and solute-solvent interactions occurring in the ternary (valine + paracetamol + water) system and the structure making/breaking tendency of the solutes in the given solvent.

EXPERIMENTAL:

Paracetamol (mass fraction purity > 0.990) procured from S.D. Fine. Chem. Ltd. Mumbai, valine (99% assay, Loba Chemie Pvt Ltd), has been used after drying over P_2O_5 in a desiccator for 72 hrs before use. 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 procedure of measuring density and viscosity of the solutions using single stem pycnometer and suspended ubbelhode viscometer have been reported in elsewhere [13].

RESULTS:

The experiment values of densities and viscosities of the ternary solutions at T= 298.15, 303.15, 308.15, 313.15 and 318.15K are listed in Table 1.

Using density data's (Table 1), the apparent molal volume, V_φ of valine in aqueous paracetamol solution has been calculated by using the relation [8],

$$V_\varphi = (M/\rho)\text{-}1000\ (\rho - \rho_0)\ /m\ \rho\ \rho_0 \qquad (1)$$

Where M is the molar mass of the solute, m is the molality of solute (valine), ρ and ρ_0 are the densities of the ternary solution and the solvent (aqueous paracetamol) respectively.

The partial molal volumes, V_φ^0 and the experimental slope, S_v have been evaluated by least squares fitting the data of V_φ versus molality to the following equation [8],

$$V_\varphi = V_\varphi^0 + S_v\ m \qquad (2)$$

Where the intercept, V_{φ}^{0}, is the infinite dilution value that is equal to the partial molal property at infinite dilution. It gives information about solute – solvent interactions and S_v is the experimental slope that gives information about the solute-solute interactions. The V_{φ}^{0} values of valine in pure water at all the studied temperatures are found to agree fairly well with the reported literature values (Table 2) and thus validating our experimental setup.

The partial molal volumes of transfer, $\Delta_{tr}V_{\varphi}^{0}$ at infinite dilution of valine from water to aqueous paracetamol solutions have been calculated using the following relation [8, 9] and are listed in Table 2, along with standard deviation of linear regression, σ.

$$\Delta_{tr}V_{\varphi}^{0} = V_{\varphi}^{0}{}_{\text{ in aq.-Paracetamol}} - V_{\varphi}^{0}{}_{\text{ in water}} \qquad (3)$$

Where $V_{\varphi}^{0}{}_{\text{ in water}}$ is the partial molal volumes of valine in water and $V_{\varphi}^{0}{}_{\text{ in aq.Paracetamol}}$ is the partial molal volumes of valine in aqueous paracetamol (Table 2). The variations of $\Delta_{tr}V_{\varphi}^{0}$ value with molality of paracetamol are graphically represented in Fig. 2.

Table 1: Densities, ρ, and viscosities, η, of solutions of valine in Paracetamol + water solvents at different temperatures.

m_A /	T/K									
(mol·kg^{-1})	298.15	303.15	308.15	313.15	318.15	298.15	303.15	308.15	313.15	318.15
	ρ x10^{-3} / (kg.m^{-3})					η / (m.Pa.s)				
	valine in water									
0	0.99706	0.99560	0.99403	0.99228	0.99032	0.8900	0.7969	0.7187	0.6522	0.5968
0.02	0.99758	0.99612	0.99455	0.99279	0.99082	0.8971	0.8030	0.7241	0.6569	0.6010
0.04	0.99807	0.99661	0.99503	0.99326	0.99130	0.9047	0.8098	0.7301	0.6624	0.6059
0.06	0.99853	0.99707	0.99550	0.99370	0.99173	0.9128	0.8171	0.7367	0.6683	0.6113
0.08	0.99896	0.99750	0.99595	0.99413	0.99214	0.9201	0.8234	0.7423	0.6733	0.6158
0.1	0.99936	0.99791	0.99637	0.99450	0.99252	0.9271	0.8296	0.7476	0.6781	0.6200
	valine in 0.025 m_P/(mol·kg^{-1}) aqueous Paracetamol									
0	0.99769	0.99621	0.99463	0.99286	0.99089	0.8994	0.8050	0.7258	0.6585	0.6024
0.02	0.99831	0.99682	0.99523	0.99345	0.99147	0.9070	0.8119	0.7319	0.6640	0.6073
0.04	0.99890	0.99740	0.99580	0.99401	0.99202	0.9147	0.8186	0.7380	0.6694	0.6122
0.06	0.99946	0.99795	0.99634	0.99454	0.99253	0.9229	0.8252	0.7444	0.6751	0.6174
0.08	0.99999	0.99847	0.99686	0.99505	0.99306	0.9300	0.8318	0.7502	0.6798	0.6218
0.1	1.00049	0.99897	0.99734	0.99553	0.99354	0.9373	0.8386	0.7554	0.6852	0.6263
	valine in 0.05 m_P/(mol·kg^{-1}) aqueous Paracetamol									
0	0.99833	0.99685	0.99526	0.99348	0.99150	0.9075	0.8124	0.7324	0.6644	0.6079
0.02	0.99896	0.99747	0.99587	0.99408	0.99209	0.9151	0.8191	0.7384	0.6697	0.6127
0.04	0.99956	0.99806	0.99645	0.99465	0.99265	0.9227	0.8258	0.7444	0.6751	0.6176
0.06	1.00013	0.99862	0.99700	0.99519	0.99318	0.9308	0.8325	0.7510	0.6807	0.6229
0.08	1.00067	0.99915	0.99753	0.99571	0.99369	0.9384	0.8392	0.7566	0.6856	0.6273
0.1	1.00118	0.99966	0.99802	0.99620	0.99421	0.9453	0.8458	0.7619	0.6908	0.6316
	valine in 0.075 m_P/(mol·kg^{-1}) aqueous Paracetamol									
0	0.99900	0.99751	0.99593	0.99412	0.99214	0.9171	0.8205	0.7395	0.6708	0.6133
0.02	0.99964	0.99814	0.99655	0.99473	0.99274	0.9248	0.8275	0.7452	0.6759	0.6180
0.04	1.00025	0.99874	0.99714	0.99531	0.99331	0.9321	0.8339	0.7514	0.6815	0.6230
0.06	1.00083	0.99931	0.99770	0.99586	0.99385	0.9404	0.8406	0.7581	0.6870	0.6282
0.08	1.00138	0.99985	0.99824	0.99639	0.99439	0.9488	0.8481	0.7641	0.6919	0.6327
0.1	1.00190	1.00037	0.99874	0.99689	0.99489	0.9550	0.8540	0.7685	0.6972	0.6370
	valine in 0.10 m_P/(mol·kg^{-1}) aqueous Paracetamol									
0	0.99969	0.99819	0.99660	0.99479	0.99283	0.9260	0.8286	0.7469	0.6773	0.6194
0.02	1.00034	0.99883	0.99723	0.99541	0.99344	0.9338	0.8358	0.7525	0.6823	0.6239

0.04	1.00096	0.99944	0.99783	0.99600	0.99402	0.9412	0.8420	0.7585	0.6879	0.6290
0.06	1.00154	1.00002	0.99840	0.99656	0.99457	0.9497	0.8488	0.7654	0.6935	0.6341
0.08	1.00211	1.00057	0.99894	0.99710	0.99511	0.9570	0.8563	0.7713	0.6984	0.6389
0.1	1.00264	1.00110	0.99947	0.99761	0.99563	0.9645	0.8625	0.7759	0.7036	0.6428

m_A molality of Valine

m_P molality of Paracetamol

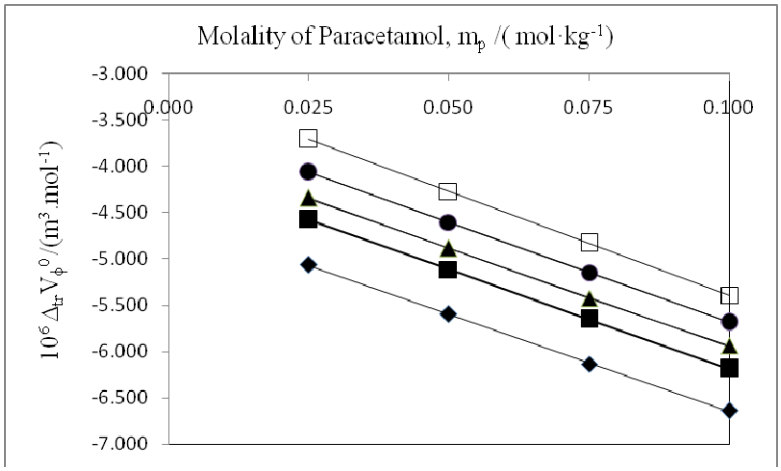

Fig. 2: Variations of transfer volume, $\Delta_{tr}V_{\varphi}^{0}$ versus Molality of Paracetamol, m_P, for valine in Paracetamol + water solutions at temperatures, T/K=298.15, ♦; T/ K=303.15, ■; T/K=308.15, ▲; T/K=313.15, ●; T/K=318.15, ; □

The variation of V_{φ}^{0} with temperature [8] for valine in aqueous paracetamol solution can be expressed by the following equation,

$$V_{\varphi}^{0} = a + bT + cT^{2} \qquad (4)$$

Where a, b and c may be estimated by the least squares fitting of partial molal volume in the above equation. The Hepler's constant [8, 14], $\partial^2 V_{\varphi}^{0}/\partial T^2$ pertains the results about the structure making / breaking properties of solute in aqueous paracetamol solution. From these criteria the positive ($\partial^2 V_{\varphi}^{0}/\partial T^2$) values show the structure making ability of solute where as the negative values are related to the structure breaking ability of solute. The values of Hepler's constant are given in Table 3.

From the following equation (5) the partial molal expansivity [8] has been calculated from partial molal volumes and are listed in Table 3.

$$E_2^{0} = (\partial V_{\varphi}^{0}/\partial T)_P \qquad (5)$$

The hydration number n_H has been evaluated from the volumetric data using the following standard equation used in literature [9, 11].

$$n_H = V_{\varphi}^{0}(\text{elect}) / (V_E^{0} - V_B^{0}) \qquad (6)$$

Where $V_{\varphi}^{0}(\text{elect})$ is the electrostriction partial molar volume due to the hydration of amino acids, V_E^{0} is the molal volume of the electrostricted water and V_B^{0} is the molar volume of bulk water. Millero et al. [15] reported the values of $(V_E^{0} - V_B^{0})$ ≅-3.3 $cm^3 \cdot mol^{-1}$ at T = 298.15 K, while actual is $(V_E^{0} - V_B^{0})$ ≅-4 $cm^3 \cdot mol^{-1}$ at T = 308.15 K. Also by Lark et al. [16] this value $(V_E^{0} - V_B^{0})$ has been retained at the other studied temperatures, and suggested to evaluate n_H values and listed in Table 2.

The viscosity B-Coefficients have been calculated by fitting the measured viscosity values to the Jones-Dole equation [17] by a least squares method as follows.

$$\eta_r = \eta / \eta_0 = 1 + B \cdot c \qquad (7)$$

Table 2: Partial molal volume, V_{φ}^{0}, and Transfer volumes, $\Delta_{tr}V_{\varphi}^{0}$, Viscosity *B* coefficients, *B,* and transfer *B* coefficients, $\Delta_{tr}B$, Ratio of *B* coefficient to partial molal volume, B/V_{φ}^{0}, free energy of activation of solvent, $\Delta\mu_1^{0*}$, free energy of activation of solute, $\Delta\mu_2^{0}$*, and standard deviations of linear regression, σ for valine in aqueous Paracetamol solution at different temperatures.

Property	T/K						T/K				
	298.15	303.15	308.15	313.15	318.15		298.15	303.15	308.15	313.15	318.15
	valine in water						*Literature values of valine in water*				
$10^6 .V_{\varphi}^{0}$ /(m^3·mol^{-1})	90.581	90.715	91.090	91.455	91.905		90.65[a]	90.98[a]	91.42[b]	91.58[b]	91.93[b]
10 . σ for equation 5	0.004	0.056	0.266	0.213	0.196						
$10^6 .S_v$ /(m^3·mol^{-1} kg^{-1})	35.602	34.691	29.204	38.419	37.444						
$10^3 .B$ /(m^3·mol^{-1})	0.430	0.424	0.419	0.414	0.410		0.447[c], 0.423[d]		0.418[e]	0.413[f]	0.408[f]
σ for equation 5	0.064	0.062	0.071	0.065	0.07						
B / V_{φ}^{0}	4.75	4.67	4.60	4.53	4.46						
n_H	3.64	3.61	3.52	3.43	3.31						
$\Delta\mu_1^{0*}$/ (kJ·mol^{-1})	9.16	9.04	8.93	8.83	8.74						
$\Delta\mu_2^{0*}$/ (kJ·mol^{-1})	78.11	78.22	78.48	78.71	79.08						
	valine in 0.025 / 0.05 m_P/(mol·kg^{-1}) aqueous Paracetamol										
$10^6 .V_{\varphi}^{0}$ /(m^3·mol^{-1})	85.519	86.143	86.747	87.395	88.199		84.983	85.604	86.207	86.853	87.636
10 . σ for equation 5	0.003	0.056	0.064	0.075	0.331		0.003	0.056	0.064	0.075	0.285
$10^6 .S_v$ /(m^3·mol^{-1} kg^{-1})	35.220	34.343	33.851	32.984	28.796		35.143	34.267	33.775	32.910	28.981
$10^6 . \Delta_{tr}V_{\varphi}^{0}$/($m^3$·$mol^{-1}$)	-5.062	-4.572	-4.343	-4.060	-3.706		-5.598	-5.111	-4.883	-4.602	-4.269
$10^3 .B$ /(m^3·mol^{-1})	0.427	0.420	0.414	0.408	0.403		0.424	0.417	0.410	0.403	0.398
σ for equation 5	0.06	0.016	0.086	0.063	0.072		0.061	0.004	0.091	0.048	0.093
$\Delta_{tr}B .10^3$ / (m^3·mol^{-1})	-0.003	-0.004	-0.005	-0.006	-0.007		-0.006	-0.007	-0.009	-0.011	-0.012
B / V_{φ}^{0}	4.99	4.88	4.77	4.67	4.57		4.99	4.87	4.76	4.64	4.54
n_H	4.91	4.75	4.60	4.44	4.24		5.04	4.89	4.74	4.58	4.38
$\Delta\mu_1^{0*}$/ (kJ·mol^{-1})	9.20	9.07	8.96	8.86	8.77		9.22	9.10	8.99	8.89	8.80
$\Delta\mu_2^{0*}$/ (kJ·mol^{-1})	76.85	76.87	77.00	77.11	77.36		76.21	76.22	76.20	76.16	76.39
	valine in 0.075 / 0.1 m_P/(mol·kg^{-1}) aqueous Paracetamol										
$10^6 .V_{\varphi}^{0}$ /(m^3·mol^{-1})	84.447	85.066	85.667	86.311	87.076		83.944	84.529	85.155	85.769	86.517
10 . σ for equation 5	0.003	0.056	0.064	0.075	0.203		0.135	0.056	0.114	0.075	0.19
$10^6 .S_v$ /(m^3·mol^{-1} kg^{-1})	35.065	34.191	33.698	32.836	28.658		34.986	34.113	33.241	32.760	29.223
$10^6 . \Delta_{tr}V_{\varphi}^{0}$/($m^3$·$mol^{-1}$)	-6.134	-5.649	-5.423	-5.144	-4.829		-6.637	-6.186	-5.935	-5.686	-5.388
$10^3 .B$ /(m^3·mol^{-1})	0.423	0.415	0.407	0.401	0.396		0.421	0.413	0.405	0.398	0.392
σ for equation 5	0.115	0.078	0.162	0.051	0.086		0.057	0.077	0.15	0.059	0.112
$\Delta_{tr}B .10^3$ / (m^3·mol^{-1})	-0.007	-0.009	-0.012	-0.013	-0.014		-0.009	-0.011	-0.014	-0.016	-0.018
B / V_{φ}^{0}	5.01	4.88	4.75	4.65	4.55		5.02	4.89	4.76	4.64	4.53
n_H	5.18	5.02	4.87	4.71	4.52		5.30	5.16	5.00	4.85	4.66
$\Delta\mu_1^{0*}$/ (kJ·mol^{-1})	9.26	9.14	9.02	8.92	8.83		9.29	9.17	9.06	8.95	8.86
$\Delta\mu_2^{0*}$/ (kJ·mol^{-1})	75.85	75.72	75.56	75.64	75.87		75.36	75.22	75.06	74.99	75.06

a – Ref 18, b – Ref 19, c – Ref 20, d – Ref 21, e – Ref 22, f – Ref 11.

where η_r is the relative viscosity of the solution, η and η_o are the viscosities of solution (Valine + aqueous paracetamol) and the solvent (paracetamol + water) respectively. m is the molality of valine in aqueous paracetamol solution, B is the Jones–Dole coefficients and, c is the molarity (calculated from molality data), respectively. The viscosity B-Coefficients of valine in water at the studied temperatures are listed in Table 2 along with the standard derivations of linear regression, σ, agree fairly well with literature values, thus proving experimental procedures [20, 23, 24]. The temperature derivative of B Coefficient (dB/dT), gives the structure making / breaking property of the solute which is calculated from viscosity B-Coefficients and are listed in the Table 2.

Table 3: Partial molar expansivity E_2^0, Temperature derivative of B-coefficient, dB/dT, and Hepler's constants ($\partial_2 V_\varphi^0/\partial T^2$), of valine in aqueous Paracetamol solution at different temperatures.

m_P/	$10^6\ E_2^0$/	$\partial^2 V_\varphi^0/\partial T^2$ /	dB/dT /
($mol \cdot kg^{-1}$)	($m^3 \cdot mol^{-1} \cdot K^{-1}$)	($m^6 . mol^{-2} \cdot k^{-2}$)	($m^3 \cdot mol^{-1} \cdot K^{-1}$)
0.00	0.067	0.00178	-0.00100
0.025	0.132	0.00115	-0.00120
0.05	0.131	0.00105	-0.00132
0.075	0.13	0.00096	-0.00136
0.1	0.127	0.00090	-0.00146

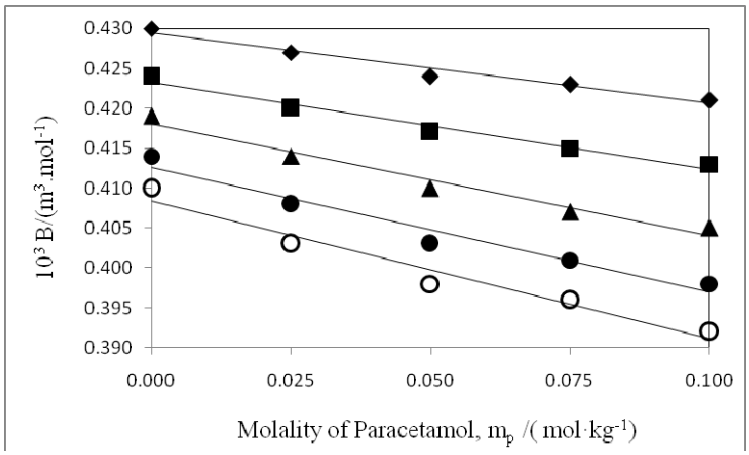

Fig. 3: Variations of Jones-Dole coefficient, B vs. Molality of Paracetamol, m_P, for valine in Paracetamol + water solutions at temperatures, T/K=298.15, ♦; T/K =303.15, ■; T/K=308.15, ▲; T/K=313.15, ●; T/K=318.15, ; ○

The solvation number B/V_φ^0, is the ratio of viscosity B-Coefficients to the partial molar volume V_φ^0 that is used to judge the solvation of any solute is evaluated and listed in Table 2.

The relation (7) has been used to calculate viscosity B-coefficients of transfer, $\Delta_{tr}B$, of valine from water to aqueous paracetamol solutions, and is listed in Table 2.

$$\Delta_{tr}B = B_{\text{in aq.-Paracetamol}} - B_{\text{in water}} \quad (7)$$

Using the following Eqns. (8), (9) and (10) from Feakins et al.[25] and Eyring et al. [26], the viscosity data are used to estimate the free energy of activation per mole of the solvent ($\Delta\mu_1^{0*}$) and solute ($\Delta\mu_2^{0*}$).

$$B = (\overline{V}_1^0 - \overline{V}_2^0)/1000 + \overline{V}_1^0/1000\ RT\ (\Delta\mu_2^{0*} - \Delta\mu_1^{0*}) \quad (8)$$

$$\Delta\mu_1^{0*} = RT \ln\left(\eta_0 \overline{V}_1^0 / hN\right) \quad (9)$$

Equation (9) can be rearranged as

$$\Delta\mu_2^{0*} = \Delta\mu_1^{0*} + RT/\overline{V}_1^0[1000\ B - (\overline{V}_1^0 - \overline{V}_2^0)] \quad (10)$$

Where $\overline{V}_1^0 = (\Sigma x_i m_i/\rho)$ is the mean value of the solvent and $\overline{V}_2^0 = V_\phi^0$ is the partial molal volume at infinite dilution of the solute, where h is Plank's constant, N_A is avogadro's number, η_o is the viscosity of the solvent and R is the gas constant. The calculated values of $\Delta\mu_1^{0*}$ and $\Delta\mu_2^{0*}$ are also given in Table 2.

Mc Millan-Mayer theory of solutions [8, 27, 28] has been used to express thermodynamic transfer functions of amino acids which permits the formal separation of the effects due to the interaction between the pairs of the solute molecules and those due to interactions between three or more molecules by the equations (11) and (12).

$$\Delta_{tr} V_\varphi^0\ (\text{water to aqueous Paracetamol solution}) = 2V_{AP}\, m_P + 3V_{APP}\, m_P^2 + \text{----} \quad (11)$$

$$\Delta_{tr} B\ (\text{water to aqueous Paracetamol solution}) = 2\eta_{AP}\, m_P + 3\,\eta_{APP}\, m_P^2 + \text{----} \quad (12)$$

When A stands for valine and B stands for paracetamol and m_P is the molality of paracetamol in water (cosolute). The constants V_{AP} / η_{AP}, V_{APP} / η_{APP} are pair and triplet volumetric/viscometric interaction parameters obtained by fitting data to equation (11) & (12). The evaluated parameters V_{AP} / η_{AP}, V_{APP} / η_{APP} for volumes and viscosities are summarized in Table 4.

Table 4: Values of pair (V_{AP}, η_{AP}) and triplet (V_{APP}, η_{APP}) of valine in aqueous Paracetamol solution at different temperatures.

T/K	$V_{AP} x10^6$ /	$V_{APP} x10^6$ /	$10^3 \eta_{AP}$/	$10^3 \eta_{APP}$/
	($m^3 .mol^{-2} .kg$)	($m^3 .mol^{-3} .kg^2$)	($m^3 .mol^{-2} .kg$)	($m^3 .mol^{-3} .kg^2$)
	From volume		From viscosity	
298.15	-112.640	584.670	-0.0675	0.1556
303.15	-101.530	519.947	-0.0875	0.2267
308.15	-96.440	491.283	-0.1100	0.2667
313.15	-89.995	453.430	-0.1350	0.3822
318.15	-81.995	405.430	-0.1550	0.4711

DISCUSSION:

On volumetric data:

It is seen from Table 1 that the value of density increases in the ternary system when there is an increase of concentration of solute. This may be due to the presence of strong solute solvent interactions. In other words, the increase in density is the result of the enhanced structure of solvent mixture due to the presence of added solute (valine) [29].

Table 2 indicates that V_φ^0 values are positive there by showing the presence of strong solute– solvent interactions in addition to the weak solute–solute interactions in the studied system [30]. The positive values of V_φ^0 may be attributed to their hydration behavior, results from the following interactions mentioned below [8]: (a) The terminal groups of zwitterions of amino acids, NH_3^+ and COO^- are hydrated in an electrostatic manner but, hydration of R group depends on its nature, which might be hydrophilic, hydrophobic, or amphiphilic; (b) Electrostriction of NH_3^+ group is greater than COO^-group by 10 times ; and (c) The overlap of hydration co-spheres of terminal NH_3^+ and COO^- groups as well as adjacent groups results in volume change.

It is also seen from the table 1 that the V_φ^0 values increase with the increase in concentration of solutes which may be related to the reduction in the electrostriction at the terminals. The solvation effect of valine zwitterions in the solvent [31-34] may also be attributed to the increase in V_φ^0 values (Table 2) with increase in temperature. The hydration number, n_H, relates the number of molecules of water with which an ion can combine in an aqueous solution of given concentration, has been calculated from volumetric data (Table 2) that are high in aqueous paracetamol solutions as compared to water and increase with increasing concentration and decrease with temperature (Fig. 4), which shows decrease in and weak solute–cosolute interactions [9, 10].

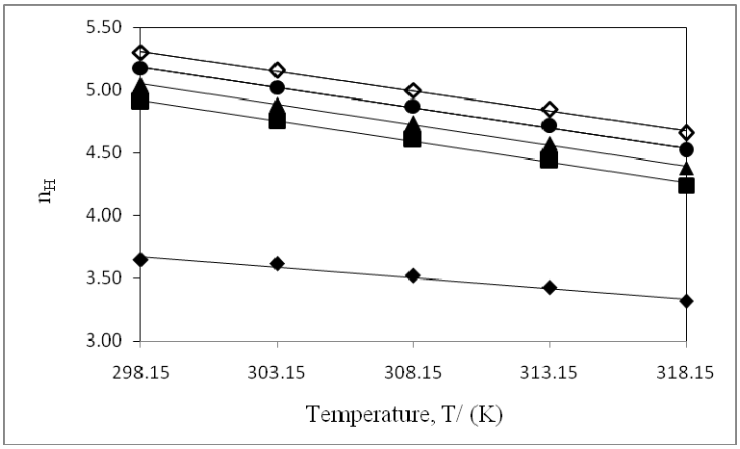

Fig. 4: Hydration number, n_H vs. Temperature, T/K, for valine in Paracetamol + water solutions at concentrations, m_P = 0 M, ♦; m_P = 0.025 M, ■; m_P = 0.05 M, ▲; m_P = 0.075 M, ●; m_P = 0.1 M, ◇

The structure maker properties of the solute [36] are also substantiated by the positive values of second derivatives of V_φ^0 viz $(\partial^2 V_\varphi^0/\partial T^2)_p$ (Table 3). It supports that the charged end groups of amino acids are the major factors for the feature of temperature dependence of V_φ^0 of amino acids [8].

Solute-solvent interactions and the structure making or breaking properties of the solute could be derived from the values of partial molar expansivity E_2^0 [8]. For a structure making solute the partial molar expansivity values are positive whereas for structure breaking solutes the values are negative. In the current study, the positive values of partial molar expansivity (see Table 3) describe the structure making [36] property of the solute (valine) in aqueous paracetamol solvent.

The values of transfer volumes, $\Delta_{tr}V_{\varphi}^{0}$ are negative and they too decrease monotonically with the molar concentration of paracetamol and also increase with temperature as shown in Table 2. The value of $\Delta_{tr}V_{\varphi}^{0}$ is theoretically free from solute-solute interaction and it provides significant information regarding solute-solvent interactions [37]. The negative value $\Delta_{tr}V_{\varphi}^{0}$ for valine in aqueous paracetamol solutions might be obviously explained by the co-sphere overlap model developed by Friedman and Krishnan [38]. The types of the interaction happening between valine and aqueous paracetamol can be segregated as follows [39, 40].

a) The hydrophilic–ionic interaction between OH and NH-CO groups of paracetamol and zwitterions(COO^-, NH_3^+) 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 channeled through hydrogen bonding.

c) Hydrophilic–hydrophobic interaction between the OH/NH-CO groups of paracetamol molecule as well as the non-polar (isopropyl) group in the side chain of valine molecule.

d) Hydrophobic–hydrophobic interactions between the non-polar (Benzene ring) group of Paracetamol and non-polar (isopropyl) group in the side chain of valine molecule.

Usually the values of $V_{\varphi}{}^{0}{}_{tr}$ increase as a result of the reduction in the electrostriction at terminals by positive contribution of the interactions of type (a) and (b), whereas it decreases due to disruption of side group hydration by the charged end by negative contribution from the interactions of type (c) and (d) which are mentioned earlier [8]. In the present investigation the observed negative $\Delta_{tr}V_{\varphi}^{0}$ values (see Table 1) show the dominance of hydrophilic–hydrophobic group and hydrophobic–hydrophobic group interactions in the systems [8, 41]. The increase in the magnitude of $\Delta_{tr}V_{\varphi}^{0}$ with temperature increments may be attributed to a decreased thermal agitation and strengthening of various interactions [42].

On viscometric property:

The viscosity values listed in the Table 1, increase with increase in concentration of solute (valine). When a solute is dissolved in a solvent, a few of the solvent molecules are usually attracted to the solute as the result of solute-solvent interaction and therefore the viscosity is increased [8]. Generally, the increase in viscosity of the solution while adding the solute points out the structure making ability of solutes [42]. The detailed information about the solvation of the solutes and their possible effects on the structure of the solvent in the environment close to the solute molecule is provided by the viscosity B-coefficients. As an empirical term the viscosity B-coefficient is calculated and it always depends upon solute-solvent interactions and on the relative size of the solute and solvent molecules. The positive values of B-coefficient in the present system (see Table 1) points out the strong solute-solvent interactions and also the solute's structure making ability [43].

Apart from giving information pertaining to viscosity B coefficients, the sign of (dB/dT) is reported widely in literature to identify the structure making / breaking property of the solute in the solvent media [43]. As *B* values decrease with increase in temperature (Fig. 3), its first derivatives of temperature (dB/dT) are negative (see Table 3) there by showing the structure making ability of amino acids (valine). Thus it is concluded that valine is a structure maker in aqueous paracetamol solutions. These results wonderfully agree with the conclusions drawn from volumetric studies.

Moreover, the solvation of any solute can be gauged from the magnitude of $B/V_{\varphi}{}^{0}$ and are listed in Table 2. A value between 0 and 2.5 reveals the unsolvated spherical species; and any higher value(>2.5) is an indication of solvated ones. In the current scenario, the values of $B/V_{\varphi}{}^{0}$ is > 2.5 thereby confirming the presence of solvated [19] spherical species in the studied systems.

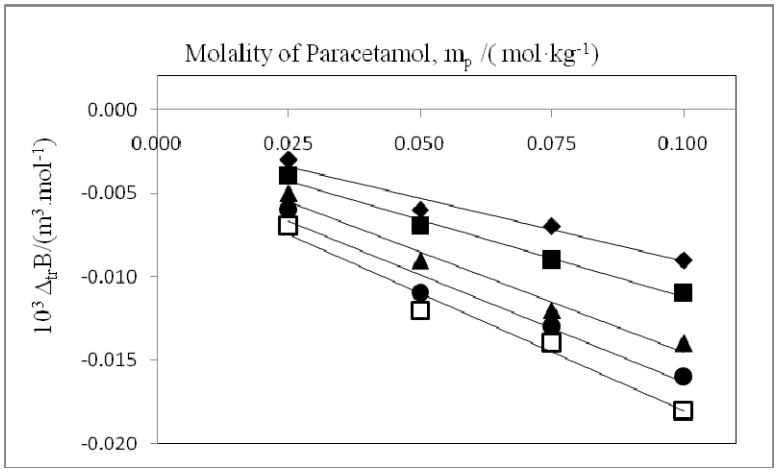

Fig. 5. Variations of Jones-Dole coefficient, $\Delta_{tr}B$ vs. Molality of Paracetamol, M_s for valine in Paracetamol + water solutions at temperatures, T/K=298.15, ♦; T/ K=303.15, ■; T/K=308.15, ▲; T/K=313.15, ●; T/K=318.15, ; □

The detailed analysis (Fig. 5) regarding $\Delta_{tr}B$ and molality of Paracetamol shows that $\Delta_{tr}B$ values are negative and decreases with concentration and temperature in all cases. The nature of variation in $\Delta_{tr}B$ is directly related to the dominance of hydrophobic –hydrophobic interactions over the hydrophilic– hydrophilic interactions [36].

Furthermore, when viscous flow's activation parameters are obtained by utilizing B-Coefficients [44], the values of $\Delta\mu_2^{0*}$ are positive and usually larger than $\Delta\mu_1^{0*}$(Table 2) proving the structure making ability of the solute [25] and thereby supplements the earlier findings by $\partial^2 V_\varphi^0/\partial T^2$ and dB/dT studies. Also, larger $\Delta\mu_2^{0*}$ values indicate the presence of stronger solute-solvent interactions. The positive values of V_{ABB}/η_{ABB} indicate the dominance of the triplet interactions over the doublet interactions V_{AB}/η_{AB} in the present system.

CONCLUSION:

The density and viscosity of valine in aqueous paracetamol solution are measured and reported for different concentrations at five different temperatures. Several thermodynamic parameters are calculated and the volumetric study shows that valine is structure maker in aqueous paracetamol which is substantiated by viscometric studies and also the results show the presence of strong solute–solvent and weak solute–cosolute interactions.

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