CHAPTERV-IX

DIVERSE INTERACTIONS OF N-METHYL GLYCINE IN AQUEOUS PARACETAMOL SOLUTION WITH THE MANIFESTATION OF SOLVATION CONSEQUENCE AT DIFFERENT TEMPERATURES INVESTIGATED BY PHYSICOCHEMICAL CONTRIVANCE

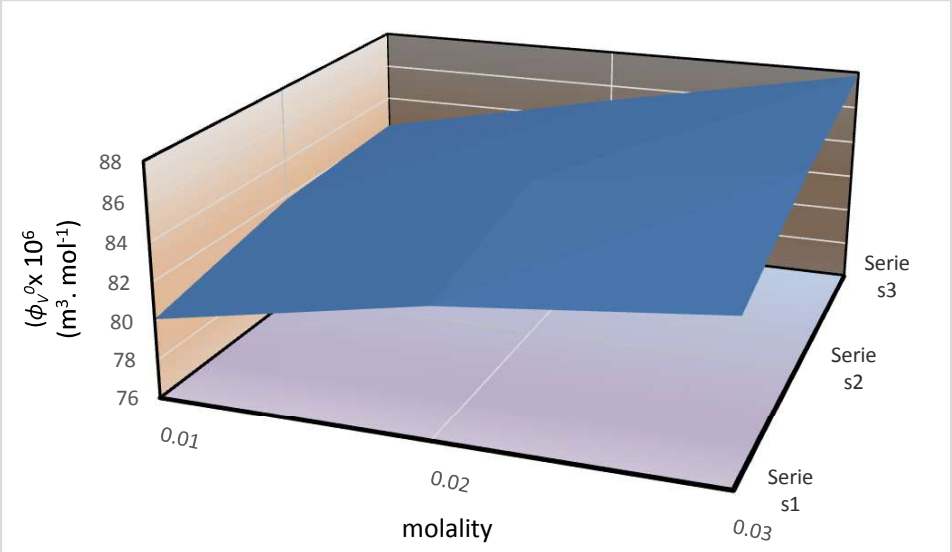


Fig-9.1 Variation of limiting apparent molar volumes (ϕ_V^0) of N-methyl glycine in aqueous solution of paracetamol with molarity and temperature

Keywords: N-methyl glycine, solute-solvent interactions, paracetamol, density, viscosity, limiting apparent molar volume of transfer, refractive index.

9.1 Introduction

The native confirmations of proteins depend on to several non-covalent interactions such as hydrogen bonding, electrostatic and hydrophobic interactions which may originate from surrounding solute and solvent molecules [1, 2]. So physicochemical properties of the proteins are influenced greatly by the presence of surrounding solute and solvent molecules. Physiochemical study of proteins provides many valuable information like hydration, solubility, stabilization and enzyme activity which are taking place in biochemical and physiological processes of living organism [3–5]. The nature of interaction of drug molecules with protein may also be understood from Physiochemical measurements.

World's most popular and most commonly used analgesic and antipyretic medicines from cradle to grave is paracetamol which is readily available and inexpensive also [6-8].

Chemical name of paracetamol is N-para-methyl aminophenol. It was introduced into the market by as an analgesic and antipyretic medicine by McNeil Laboratories mainly for children. After 1961 it became the most frequently sold analgesic medications. Its use as an analgesic is most tolerable than the other non-steroidal drugs (NSAIDs) which should not be used by the people with bronchial asthma, hemophilia, salicylate-sensitized people, peptic ulcer disease, pregnant or breastfeeding women and children under 12 years of age [9, 10]. Currently the use of aspirin as antipyretic and analgesic has been declined due some adverse effects and parallelly the use of paracetamol has been increased. Paracetamol has now been an appropriate analgesic for all age groups.

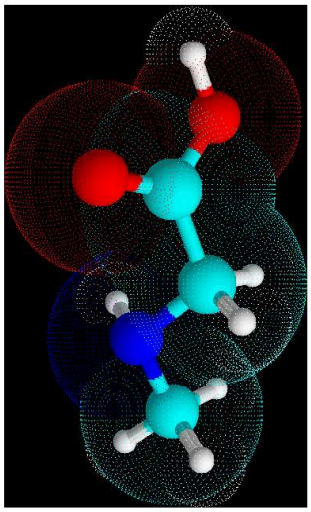
In continuance of our earlier works [11-15], we attempted to examine the nature of solute-solvent/co-solute interactions of N-methyl glycine in aqueous solutions of paracetamol at 298.15 K, 303.15 K and 308.15 K. The densities, viscosities and refractive indices of 0.01, 0.02 and 0.03 m aqueous N-methyl glycine solutions at 298.15 K, 303.15 K and 308.15 K are reported in **Table-9.1** and densities, viscosities and refractive indices of aqueous N-methyl glycine solutions in presence of paracetamol at 298.15 K, 303.15 K and 308.15 K are reported in **Table-9.2**. From the volumetric measurements we calculated limiting apparent molar volume (ϕ_V^0), experimental slopes (S_V^*), transfer volume ($\Delta\phi_V^0$) and from the vicometric measurements we calculated viscosity A and B coefficients to analyse the nature of solute-solvent/ co-solute interactions. The refractive index data helps to find the molar refraction (R_M) which also helps to elucidate the interaction between solute and co-solute in aqueous medium.

Table-9.1: Experimental values of density (ρ), viscosity (η) and refractive index (n_D) of different molality of aqueous N- methyl glycine solution at 298.15 K, 303.15 K and 308.15 K.

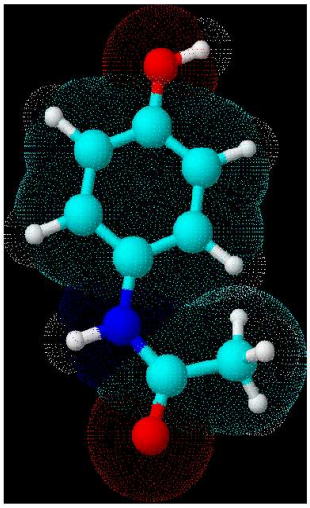
Aqueous solvent molality	$\rho\times10^{-3}$/kg.m^{-3}			η/mP.s			n_D
	298.15 K	303.15 K	308.15 K	298.15 K	303.15 K	308.15 K	298.15 K
0.01 m	0.99756	0.99621	0.99460	0.8956	0.80910	0.6804	1.3319
0.02 m	0.99782	0.99649	0.99486	0.8984	0.8116	0.6831	1.3325
0.03 m	0.99817	0.99679	0.99515	0.9016	0.8140	0.6859	1.3327

Table-9.2: Density (ρ) and viscosity (η) and refractive index (n_D) of different molality of aqueous N- methyl glycine in aqueous paracetamol solution at 298.15 K, 303.15 K and 308.15 K.

Molality Mol.kg-1	$\rho \times 10^{-3}$ kg.m^{-3}			η mP.s			n_D
	298.15 K	303.15 K	308.15 K	298.15 K	303.15 K	308.15 K	298.15 K
0.01m N- methyl glycine solution							
0.013	0.998	0.99664	0.99503	0.9053	0.8179	0.6882	1.3321
0.023	0.99836	0.99700	0.99538	0.9122	0.8242	0.6947	1.3323
0.045	0.999065	0.997725	0.99611	0.9264	0.8373	0.7076	1.3327
0.057	0.99944	0.99811	0.9965	0.9434	0.8537	0.7231	1.3329
0.072	0.99990	0.99859	0.99699	0.9594	0.8703	0.7386	1.3331
0.02m N- methyl glycine solution							
0.013	0.99824	0.996904	0.99527	0.9079	0.8204	0.6909	1.33272
0.023	0.99859	0.99725	0.99562	0.9148	0.8267	0.6974	1.33286
0.045	0.999295	0.99798	0.99635	0.9292	0.8408	0.7110	1.33313
0.057	0.99967	0.998382	0.99676	0.9464	0.8572	0.7262	1.33327
0.072	1.00014	0.99889	0.99726	0.9632	0.8738	0.7423	1.33345
0.03m N- methyl glycine solution							
0.013	0.99858	0.99719	0.99554	0.9111	0.8228	0.6939	1.33319
0.023	0.99892	0.99754	0.99588	0.9181	0.8297	0.7005	1.33332
0.045	0.99962	0.99828	0.99662	0.9334	0.8442	0.7152	1.33358
0.057	0.99999	0.99869	0.99703	0.9506	0.8608	0.7309	1.33372
0.072	1.00046	0.99921	0.99755	0.9674	0.8782	0.7468	1.3339



N-methyl glycine



Paracetamol

Scheme-9.1: Molecular structures of N- methyl glycine and paracetamol

9.2. Experimental methods

9.2.1. Source and purity of samples

The studied N- methyl glycine and co-solute paracetamol of puriss grade was purchased from Sigma-Aldrich, Germany and was used as purchased. The mass purity of salts was ≥0.99. The salts were dried from moisture at 353.15 K for 48 h, and then they were cooled and store in a desiccator prior to use.

9.2.2. Apparatus and procedure

The density (ρ) measurements were done by vibrating-tube Anton Paar Density-Meter (DMA 4500M) with an accuracy of 0.00001 x 10^{-3} ($kg \cdot m^{-3}$). The density meter was calibrated by using double-distilled water and dry air before taking the densities of our studied solutions [16]. The instrument has temperature monitoring system with the precision ±0.01 K.

The viscosity was determined using of Brookfield DV-III Ultra Programmable Rheometer having spindle size-42 fitted. The Rheometer was fitted with Digital Bath TC-500 which has a precision of ±0.001 K. The viscosity was measured after calibrating the Rheometer with doubly distilled water and purified methanol [17]. The uncertainty in viscosity measurements is within ±0.003 mPa·s.

Mass measurements for preparation of stock solutions were done by Mettler AG-285 electronic balance with a precision of ±0.0003 x 10^{-3} kg. The uncertainty in molality of solution is approximately ±0.0001 mol. kg^{-1}. Acceptable precautions were followed to minimize evaporation losses during the measurements.

9.3. Results and discussions

9.3.1. Density

Apparent molar volumes (ϕ_V) of N- methyl glycine in aqueous paracetamol solution were determined from the densities of the solution using the following equation [18]:

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

Where M is the molar mass of N-methyl glycine, ρ_0 and ρ is the densities of solvent and solution respectively and m is the molality of the solution. The ϕ_V values of N-methyl glycine in aqueous paracetamol solution at 298.15 K, 303.15 K and 308.15 K are shown in **Table-9.3** and **9.5** respectively.

Table-9.3: Apparent molar volume, (ϕ_V) and $(\eta/\eta_0-1)/\sqrt{m}$ of 0.01 m, 0.02 m and 0.03 m N- methyl glycine in aqueous paracetamol solution at 298.15 K, 303.15 K and 308.15 K

Molality	ϕ_V x 10^6 (m^3. mol^{-1})	$(\eta/\eta_0-1)/\sqrt{m}$ (mol. $kg^{-1})^{-1/2}$	ϕ_V x 10^6 (m^3. mol^{-1})	$(\eta/\eta_0-1)/\sqrt{m}$ (mol. $kg^{-1})^{-1/2}$	ϕ_V x 10^6 (m^3. mol^{-1})	$(\eta/\eta_0-1)/\sqrt{m}$ (mol. $kg^{-1})^{-1/2}$	R_M
	298.15K		303.15K		308.15 K		
0.01 m N- methyl glycine							
0.013	81.9779	0.097	82.8475	0.097	82.9254	0.1025	24.0760
0.023	82.5861	0.122	82.8701	0.123	83.3881	0.1386	24.0806
0.045	83.6520	0.162	83.4952	0.164	83.6878	0.1885	24.0898
0.057	84.0840	0.176	83.7982	0.183	83.8793	0.2124	24.0939
0.072	84.5290	0.193	84.0372	0.208	83.9781	0.2355	24.0959
0.02 m N- methyl glycine							
0.013	83.5737	0.095	84.1238	0.097	84.5304	0.1021	24.1110
0.023	83.8852	0.120	84.1716	0.123	84.4747	0.1380	24.1119
0.045	84.3100	0.162	84.0420	0.170	84.1249	0.1925	24.1125
0.057	84.6009	0.178	83.9259	0.188	83.8662	0.2140	24.1126
0.072	84.7955	0.197	83.7422	0.212	83.8241	0.2399	24.1131
0.03 m N- methyl glycine							
0.013	84.6007	0.094	85.2365	0.097	86.1321	0.1043	24.1338
0.023	84.7413	0.121	84.5944	0.127	85.5587	0.1404	24.1340
0.045	84.9404	0.166	84.0268	0.175	84.5599	0.2014	24.1343
0.057	85.1125	0.182	83.7691	0.193	84.2069	0.2233	24.1344
0.072	85.1969	0.200	83.4466	0.218	83.8095	0.2463	24.1348

According to Masson (1929), the apparent molar volumes, ϕ_V, vary with the square root of the molal concentration, $\sqrt{m}$ as per following linear equation:

$$\phi_V = \phi_V^0 + S_V^* \sqrt{m} \qquad (2)$$

Where ϕ_V^0 is the limiting apparent molar volume of N- methyl glycine and S_V* is the experimental slope. The plots of ϕ_V against $\sqrt{m}$ of aqueous N-methyl glycine solutions at 298.15 K, 303.15 K and 308.15 K in presence of paracetamol gives a linear line with a slope of S_V* and an intercept of ϕ_V^0.

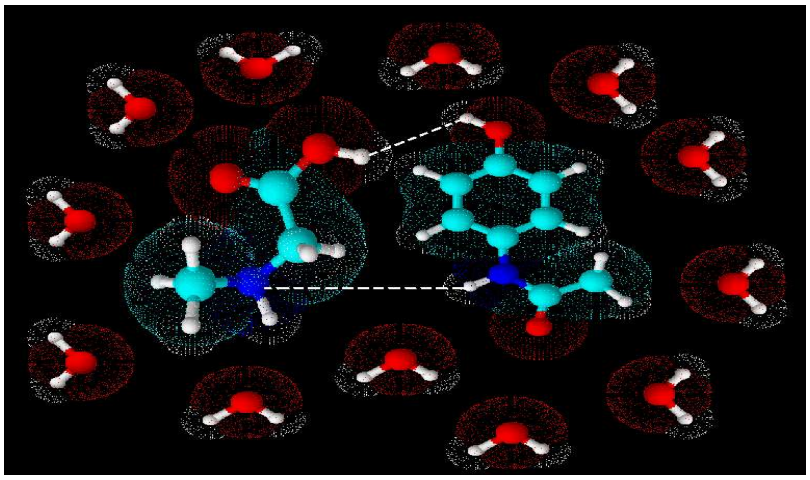
The values of ϕ_V^0 and S_V* of N-methyl glycine in aqueous paracetamol solutions at 298.15 K, 303.15 K and 308.15 K are mentioned in **Table-9.4** and **Figure-9.1.**

Table-9.4: Limiting apparent molar volumes (ϕ_V), experimental slopes (S_V*), viscosity A, *B*-coefficients *of* aqueous N- methyl glycine solution in paracetamol at different temperatures.

Temperature(K)	ϕ_V^0 x 10^6 (m^3. mol^{-1})	$\Delta\phi_V^0$ (m^3. mol^{-1})	S_V^* x 10^6 (m^3. $mol^{-3/2}$.$kg^{1/2}$)	*B* ($kg^{1/2}$. $mol^{-1/2}$)	*A* (kg. mol^{-1})
0.01 m N-methyl glycine					
298.15K	80.114	1.001	16.544	0.6182	0.0286
303.15K	81.794	1.571	7.854	0.7029	0.0127
308.15K	82.288	1.253	6.534	0.8494	0.0086
0.02 m N-methyl glycine					
298.15K	82.69	3.568	7.854	0.6572	0.0211
303.15K	84.471	4.238	-2.39	0.7389	0.0127
308.15K	85.155	4.12	-5.045	0.8804	0.0043
0.03 m N-methyl glycine					
298.15K	84.157	5.044	3.873	0.6856	0.0178
303.15K	86.381	6.158	-11.03	0.7716	0.0104
308.15K	87.816	6.761	-15.074	0.9232	0.0017

The ϕ_V^0 value indicates the extent of solute-solvent interaction [19]. It is observed that ϕ_V^0 values for N- methyl glycine solutions in paracetamol are positive and increase with the increasing molarities N-methyl glycine and also with temperature which is shown in **Table-9.4** and **Fig-9.1**.

The tendency indicates the presence of strong solute-solvent interactions which increase with molarity of N-methyl glycine and temperatures. The interaction arises from the hydrophilic-hydrophilic group interaction between solute and co-solute molecules. The interaction of N- methyl glycine with paracetamol in aq. medium is displayed in **Scheme-9.2**. With increasing temperature the secondary solvation layer is released into the bulk solvent leading to the expansion of solution. As a result, the ϕ_V^0 values of N-methyl glycine in aqueous paracetamol solutions increase with increase in temperature.



Scheme-9.2: Molecular interactions between N- methyl glycine with paracetamol in aqueous medium

The parameter S_V^* defines the pair-wise interaction of solvated species in solution [20]. The S_V^* values of N-methyl glycine in aqueous paracetamol solution at different temperatures are reported in **Table-9.4**. The S_V^* value in our present study is least in 0.03 m N- methyl glycine at 308 K and highest in 0.01 m N- methyl glycine at 298.15 K. So, S_V^* values decrease with increasing temperature and molality. This trend is exactly reverse than the ϕ_V^0 values explained earlier where ϕ_V^0 values increase with increasing concentrations of N-methyl glycine and temperatures. This weakening of S_V^* values signify the presence of poor solute-solute interactions. The smaller S_V^* values than the corresponding ϕ_V^0 signifies that the solute-solvent interaction is stronger than the solute-solute interaction.

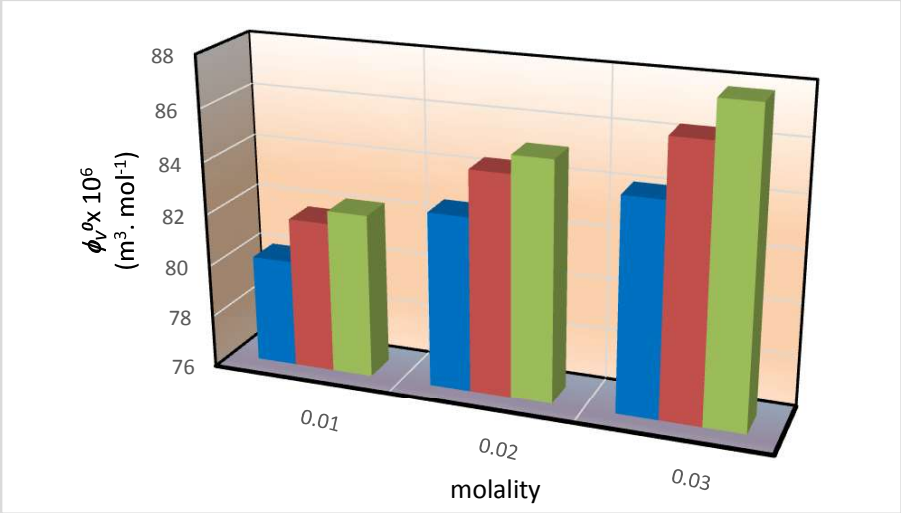


Fig-9.1: Variation of limiting apparent molar volumes (ϕ_V^0) *of* N- methyl glycine solution in paracetamol solution at different temperatures.

The variation of ϕ_V^0 with temperature of N- methyl glycine in paracetamol solution follows the polynomial [21];

$$\phi_V^0 = a_0 + a_1T + a_2T^2 \quad (3)$$

Where T is the temperature in K and a_0, a_1 and a_2 are the coefficients. Values of the coefficients of the above equation for N- methyl glycine in paracetamol solution are reported in **Table-9.5**.

The limiting apparent molar expansibilities (Φ_E^0) can be determined by the following equation [22]:

$$\Phi_E^0 = (\delta\phi_V^0/\delta T)_P = a_1 + 2a_2T \quad (4)$$

The values of Φ_E^0 of N-methyl glycine in paracetamol solution at 298.15 K, 303.15 K and 308.15 K are evaluated and reported in **Table-9.5.**

Table-9.5: Values of empirical coefficients (a_0, a_1, and a_2) of 0.01 m, 0.02 m and 0.03 m N-methyl glycine in paracetamol solution at 298.15 K, 303.15 K and 308.15 K

Molality of N- methyl glycine	$a_0 \times 10^6$ ($m^3.\ mol^{-1}$)	$a_1 \times 10^6$ ($m^3.\ mol^{-1}.\ K^{-1}$)	$a_2 \times 10^6$ ($m^3.\ mol^{-1}.\ K^{-2}$)	$(\delta\Phi_E^0/\delta T)_P$
0.01m	-2161.8	14.59	-0.0237	-0.0474
0.02m	-1951	13.19	-0.0214	-0.0428
0.03m	-1473.2	9.926	-0.0158	-0.0316

The S_V^* is not the only parameter for estimating the structure-making or breaking nature of any solute [30]. Hepler proposed a different technique to inspect the structure-making and breaking ability of the solute in aqueous solution from the following thermodynamic expression [23];

$$(\delta\Phi_E^0/\delta T)_P = (\delta^2\phi_V^0/\delta T^2)_P = 2a_2 \quad (5)$$

According to Hepler the structure making solutes should have positive $(\delta\Phi_E^0/\delta T)_P$ values, whereas structure-breaking solutes should have negative values[24, 25]. The $(\delta\Phi_E^0/\delta T)_P$ values of N-methyl glycine in paracetamol solution have been provided in **Table-9.5.** It is apparent that $(\delta^2\phi_V^0/\delta T^2)_P$ values are negative for N-methyl glycine in paracetamol solution which signifies that paracetamol perform as structure breaker in aq. nicotinic acid solution.

The limiting apparent molar volume of transfer, $\Delta\phi_V^0$ for N- methyl glycine in paracetamol solution may be expressed as follows:

$\Delta\phi_V^0$ (N- methyl glycine) $=\phi_V^0$ (N- methyl glycine in paracetamol) $-\phi_V^0$ (in water) (6)

The $\Delta\phi_V^0$ value provide the idea about the nature solute–solvent interactions. The limiting apparent molar volume of transfer may be analyzed in the light of co-sphere overlap model given by Friedman and Krishnan [26]. According to the model positive $\Delta\phi_V^0$ value specifies the existence of hydrophilic–hydrophilic, ion- hydrophilic and ion–ion interactions, whereas the negative $\Delta\phi_V^0$ value specifies the hydrophobic–hydrophobic interactions [27, 28]. The interactions between N-methyl glycine and paracetamol in aqueous medium may be of following categories.

i) Ionic-ionic interaction of the H^+ ion of water and N- methyl glycine with the $-COO^-$ ion of N- methyl glycine

ii) H-bond between -COOH (N- methyl glycine) and -OH (paracetamol) and also with water.

iii) Ionic-hydrophilic interaction of polar end of water with $-COO^-$ ion of N- methyl glycine and -OH group of paracetamol.

iv) Ionic– hydrophilic interactions of -COOH (N-methyl glycine) and -OH (paracetamol) with the H^+ and OH^- ion of water.

(v) Hydrophobic-hydrophobic interaction of non-polar part of N- methyl glycine and paracetamol.

The interactions of categories (i), (ii), (iii) and (iv) have positive contributions to ϕ_V^0 values while interaction of types (v) has negative contribution to ϕ_V^0 values [29-31]. The positive $\Delta\phi_V^0$ value indicates that the hydrophilic–hydrophilic and ion–ion interactions are in domination over hydrophobic-hydrophobic and ionic–hydrophobic interactions. It is also seen that $\Delta\phi_V^0$ values are increasing with increasing molality of N- methyl glycine. The intermolecular distance between N-methyl glycine and paracetamol decreases with increasing concentration of N-methyl glycine as a result the hydrophobic-hydrophobic and ionic–hydrophobic interactions increase with molality. Similar result can also be obtained from the following expression given by Franks et al [32]:

$$\phi_V^0 = \phi W + \phi V - \phi S \quad (7)$$

Where ϕW is corelated with van der Waals volume, ϕV is the volume corelated with voids or empty space and ϕS is corelated with shrinkage volume due to electrostriction. The value ϕW and ϕV will remain same for the same class of solutes in aqueous solutions and only the volume due to electrostriction will vary. The hydrophilic–hydrophilic, ion–ion and ion-hydrophilic interactions will increase with increasing molality of N- methyl glycine and as a result ϕS value will decrease [33]. For this reason, ϕ_V^0 values increase with increasing molality of N- methyl glycine.

The volumetric pair wise and triple ion interactions may be estimated from the following equation given by McMillan–Mayer [34];

$$\Delta\phi_V^0 = 2Y_{XY}m + 3Y_{XYY}m^2 \quad (8)$$

Where Y_{AB}, Y_{ABB} and $\Delta\phi_V^0$ are pair and triple ion interaction coefficients, limiting apparent molar volume of transfer respectively and X and Y represent N-methyl glycine and paracetamol respectively. The coefficients Y_{AB} and Y_{ABB} are estimated by putting the $\Delta\phi_V^0$ values at diverse molarities of N- methyl glycine in presence of paracetamol in the above expression and mentioned in **Table-9.6**. It is observed that Y_{XY} values are positive whereas Y_{XYY} values are negative for N- methyl glycine in presence of paracetamol in aqueous medium at different temperatures. The positive values of Y_{XY} suggest that existing interactions in our studied solutions are mostly pair wise which arises from hydrophilic–hydrophilic and ion–ion interactions between solute and co-solute in aqueous medium [35].

Table-9.6: Pair, V_{AB}, and Triple, V_{ABB}, interaction coefficients of N- methyl glycine in aqueous solution of paracetamol at 298.15 K, 303.15 K and 308.15 K temperatures.

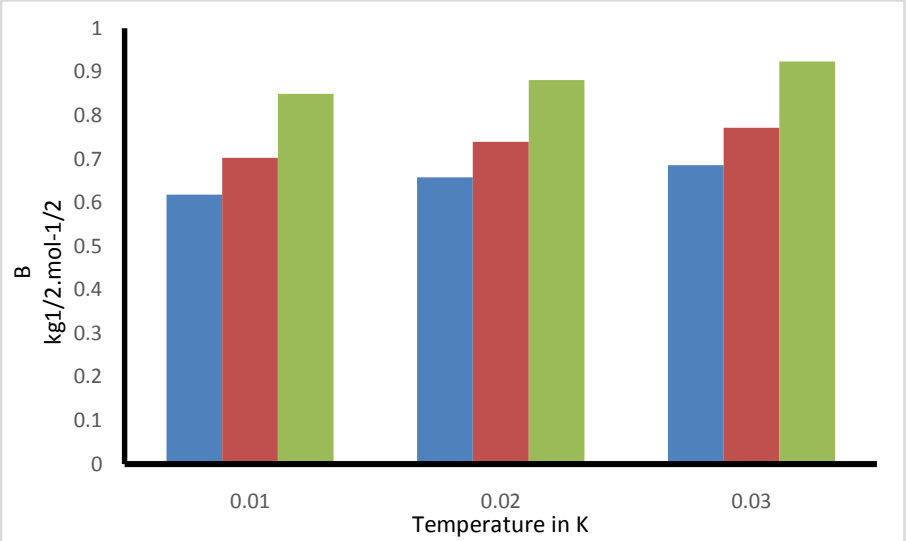
V_{AB} $m^3 \cdot mol^{-2} \cdot kg$	V_{ABB} $m^3 \cdot mol^{-2} \cdot kg^2$	V_{AB} $m^3 \cdot mol^{-2} \cdot kg$	V_{ABB} $m^3 \cdot mol^{-2} \cdot kg^2$	V_{AB} $m^3 \cdot mol^{-2} \cdot kg$	V_{ABB} $m^3 \cdot mol^{-2} \cdot kg^2$
298.15 K		303.15 K		308.15 K	
78.0000	-372.23	99.3100	221.1200	102.3700	-187.77

9.3.2. Viscosity calculation

The viscosity data were fit into Jones–Dole equation [36]:

$$(\eta/\eta_0 - 1)/\sqrt{m} = A + B\sqrt{m} \quad (9)$$

Where, η_0 and η are the viscosities of the solvent and solution respectively. A plot of $(\eta/\eta_0 - 1)/\sqrt{m}$ against √m gives a straight line with an intercept "A" and a slope of "B". The $(\eta/\eta_0 - 1)/\sqrt{m}$ values of N- methyl glycine of different molarities in aqueous paracetamol solution are reported in **Table-9.3.** The viscosity coefficients A and B values are reported in **Table-9.4** and the variation of B with temperature of N- methyl glycine is shown in **Fig-9.2.** The viscosity *B*-coefficient signifies solute-solvent interaction and provides valuable information concerning the solvation of the solute in solution [37, 38]. A close inspection reveals that B-value is higher for 0.03 m N-methyl glycine solution at 308.15K and lowest at 0.01 m solution at 298.15 K. So, solute–solvent interactions increase with increasing molarity and temperature. Viscosity A coefficient denotes solute-solute interaction. It is reflected from the **Table-9.4** that the values of *A* coefficient decrease with the increase in molarity and temperature of N-methyl glycine in aqueous solution of paracetamol. Hence solute-solute interaction diminishes with molarity of N-methyl glycine and also with temperature in K.



Variation of viscosity B coefficient with temperature in K *of* aqueous N-methyl glycine in paracetamol solution.

9.3.3 Refractive index calculation

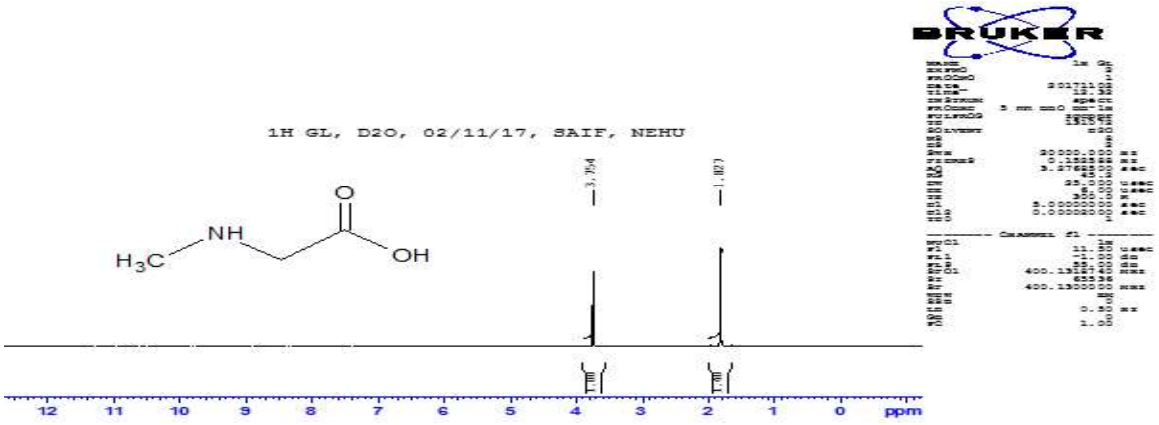
The molar refraction, R_M *for any compound in its aqueous solution* may be determined from the Lorentz–Lorenz relation [39]:

$$R_M = \{(n_D^2-1)/(n_D^2+2)\}\,(M/\rho) \qquad (4)$$

where, R_M, ρ, M and n_D are the molar refraction, density of solution, molar mass and refractive index, respectively. The refractive index of a material is defined as c_0/c, where c is the speed of light in any medium and c_0 the speed of light in vacuum. The light is refracted more for the substance of higher refractive index [40]. According to Deetlefs et al. [41] the molar refraction of a substance will be higher when the molecules in any solution are more tightly packed. The values of R_M are shown in Table-3. The increase in molar refraction values with increase in molarity of N-methyl glycine in aqueous paracetamol solution indicates close packing of molecules in the mixture resulting in maximum solute–solvent interactions.

9.3.4 ^{1}H NMR Spectroscopy

Various spectroscopy may be employed to examine the diverse interaction playing in solution of any compound [42-46]. ^{1}H NMR Spectroscopy of pure N-methyl glycine, paracetamol and their solution are recorded in D_2O at 298.15 K and shown in **Fig-9.3**. Up field chemical shift of protons of methyl group and methylene group of glycine in aqueous solution of paracetamol from its pure form may be regarded due to the involvement of adjacent -NH- and -COOH groups in H-bonding with the -OH group of paracetamol. However higher Δδ for methylene group than the methyl group indicates that -COOH form stronger H-bond with -OH group of paracetamol than the -NH- group. Similar up field chemical shift of protons adjacent to -OH group of paracetamol takes place which may also be considered due to its involvement in H-bonding with favorable groups of N-methyl glycine. The extend of Δδ for protons at o-position of -OH group is larger than the protons at p-position which indicates that -OH is more favorable in forming H-bond than the -NH- group of paracetamol.



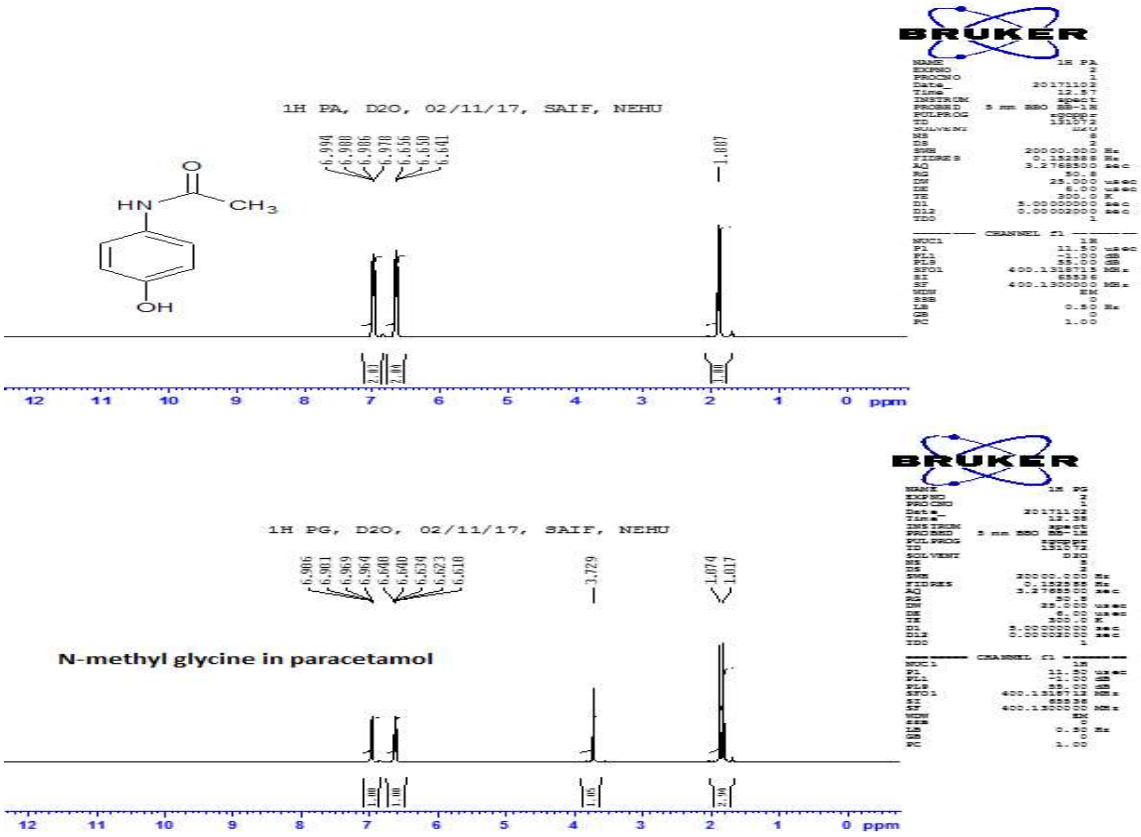


Fig-9.3: ^{1}H NMR spectra of N-methyl glycine, paracetamol and their solution in D2O.

^{1}H NMR data:

N-methyl glycine: [1H NMR (300 MHz, D2O)]: δ 1.827 (3H, s), 3.754(2H, s)

paracetamol: [1H NMR (300 MHz, D2O)]: δ 1.887 (3H, s), 6.656 (2H, d), 6.988 (2H, d)

solution of N-methyl glycine and paracetamol [1H NMR (300 MHz, D2O)]: δ 1.817 (3H, s), 1.874 (3H, s), 3.729(2H, s) 6.634 (2H, d), 6.981 (2H, d).

9.4. Conclusion

The limiting apparent molar volume (ϕ_V^0) and viscosity *B*-coefficient and molar refraction (R_M) values indicate the existence of strong solute–solvent interactions between N-methyl glycine and paracetamol in aqueous medium. The solute–solvent interactions enhances with increasing molality of N-methyl glycine and temperature. On the other hand, the solute-solute interactions diminish with increasing molality of N-methyl glycine and temperature. The nature of solute–solvent interactions was evaluated from the limiting apparent molar volume of transfer (ϕ_V^0) values. It was also observed that the interaction between our studied solute and co-solute in aqueous medium was mostly pair wise. ^{1}H NMR Spectroscopy concretely support our findings obtained from volumetric, viscometric and refractive index study.