Volumetric, viscometric and refractometric behavior of glycine + {aqueous isoniazid} ternary mixtures at 298.15 K: A drug-amino acid interactions study

S. D. Deosarkar[1*], A. R. Ban[1], R. T. Sawale[1], S. D. Padghan[1], A. J. Pawar and T. M. Kalyankar[2]

[1]School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Nanded- (MS) India
[2]School of Pharmacy, Swami Ramanand Teerth Marathwada University, Nanded-(MS) India

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ABSTRACT

In order to understand molecular interactions between simple amino acid such as glycine and antituberculosis drug isoniazid, the density (ρ), relative viscosity (η_r) and refractive index (n_D) of ternary glycine (0.02-0.34 mol·dm^{-3}) + {aqueous isoniazid (0.02 mol·dm^{-3})} solutions of were measured at 298.15 K. Apparent molar volumes (ϕ_v) were calculated from density data and fitted to Massons relation to get partial molar volume (ϕ^0_v) of glycine at infinite dilution in aqueous 0.02 mol·dm^{-3} isoniazid solution. Viscosity data was analyzed by Jones-Dole relation and viscosity B-coefficient for solute-solvent interaction was determined graphically. Refractive index data was used to calculate specific refraction (R_D). Interactions between solute and co-solute have been interpreted form partial molar volume of transfer ($\Delta_{tr}\phi^0_v$). Measured and derived properties have been interpreted in terms of glycine-water, drug-water and glycine-drug interaction in binary and ternary solutions.

Keywords: Density, Viscosity, Refractive index, Glycine, Isoniazid

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INTRODUCTION

Drug-amino acid molecular interactions are of great significance in view of thermodynamic behavior in biochemical processes and action of bioactive molecules [1]. Glycine can form H-bond with water through -NH$_2$ and –COOH groups. The structure of aqueous glycine solutions changes in presence of drug such as isoniazid. Isoniazid molecule has hydrophilic as well as hydrophobic parts which interact with similar regions in glycine and water molecules. These interactions can be studied through measurement of physicochemical properties such as density, viscosity and refractive index of aqueous drug-amino acid solutions. Apparent molar volumes and partial molar volumes as well as viscosity *B*-coefficient are helpful in understanding solute-solvent interactions [2-3]. Partial molar volume of transfer gives information regarding solute-co-solute interaction. A survey of available literature reveals that molecular interaction studies in aqueous glycine + urea + KBr at different temperatures [4], aqueous glycine + galactose [5] aqueous-alcoholic glycine [6], glycine in aqueous diols [7], and amino acids in aqueous solutions of an antibiotic drug [8] have been carried out.

Objective of present work is to understand structure and interactions in ternary glycine + aqueous isoniazid drug solutions at 298.15 K which is lacking as per the literature available. In continuation with our programme to understand molecular interactions in solutions [9-12], an effort has been made here, to study the density, viscosity and refractive index of ternary solutions of glycine + aqueous isoniazid with varying concentrations of glycine in presence of aqueous 0.02 mol·dm^{-3} isoniazid at 298.15 K and understand structure and molecular interactions therein.

EXPERIMENTAL SECTION

Glycine (*SD fine*, AR Grade) and isoniazid (Figure 1) were used as available. Double distilled water was used for preparation all the solutions. Stock solution of aqueous isoniazid of 0.02 mol·dm^{-3} concentration was prepared in 500 cm^3 calibrated volumetric flask. All other solutions were prepared by dissolving accurate quantities of glycine in aqueous isoniazid stock solution. Density of different solution was determined by using single capillary pycnometer (*Riviera*^{TM}) of 10 cm^3 capacity [13]. Weighing was done on single pan electronic balance (±0.001 g). Pycnometer was suspended in constant temperature water bath for about 15 min to attain the thermal equilibrium and then weighing was done. Average of three weights was taken for density calculation. Viscosity was determined from flow time method using suspended level *U*-type Ostwald viscometer (*Borosilicate*). Viscometer was suspended in constant temperature water bath for about 15 min to attain the thermal equilibrium. Average of three flow times were considered for calculation of relative viscosity of solution. Refractive index measurement was done on Cyber LAB-Cyber Abbe Refractometer (*Amkette Analytics*, ±0.0002). Temperature of solution during refractive index measurements was maintained constant at 298.15 ±0.1 K by water circulation system available with refractometer using specially designed constant temperature water bath. Temperature of sample solution was read on digital thermometer (±0.1 K) attached to the refractometer.
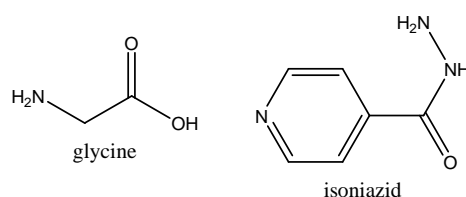
Figure 1: Chemical structures of glycine and isoniazid

RESULTS AND DISCUSSION

Experimental and derived physicochemical properties are represented graphically. Experimental density, viscosity and refractive index data of glycine + 0.02 mol·dm^{-3} aqueous isoniazid solutions is presented in Figure 2-4. It is seen form Figure 1-3 that density, viscosity and refractive index of solution increased with concentration of glycine in aqueous 0.02 mol·dm^{-3} isoniazid. Increase in viscosity is attributed to the increase in hydrophilic-ionic and hydrophilic-hydrophilic interactions with increase in glycine concentration which causes more fractional resistance to flow of solution [8].

Figure 2. Variation in density (ρ) with concentration (c) of glycine + aqueous-isoniazid solutions at 298.15 K
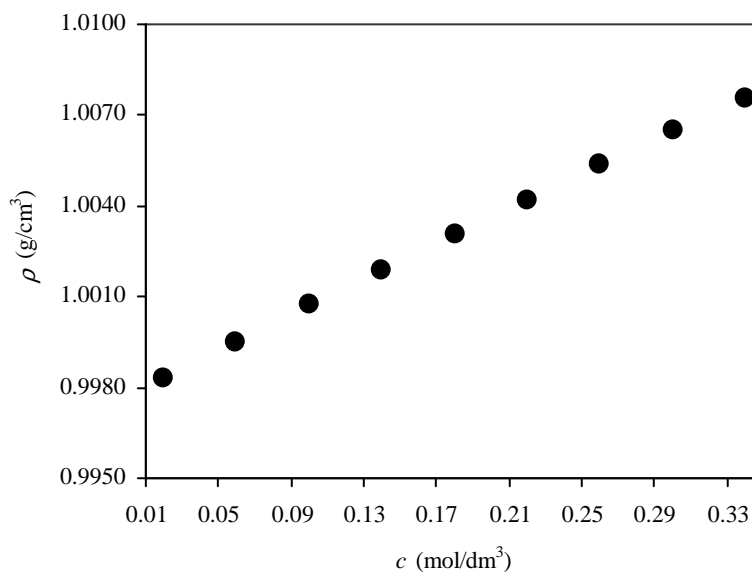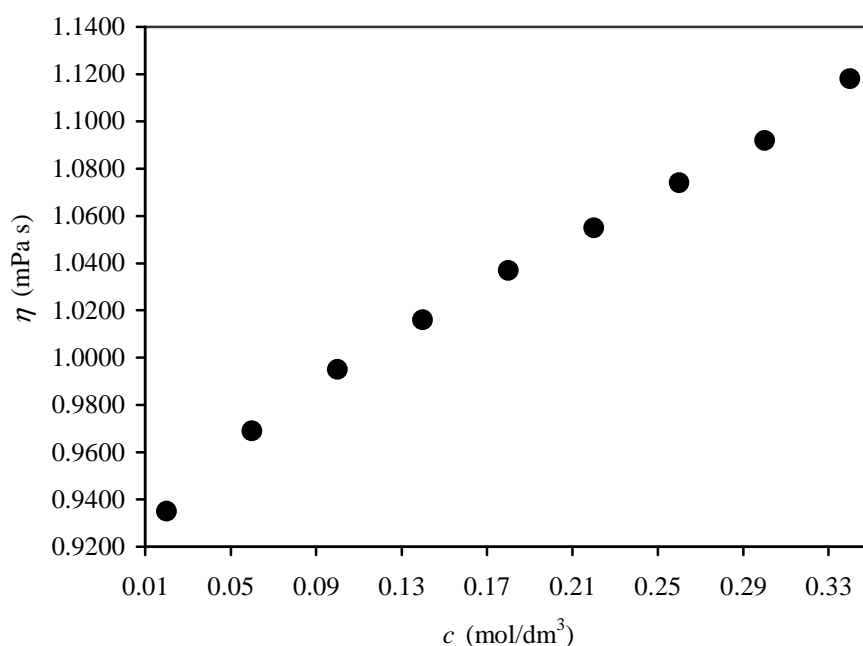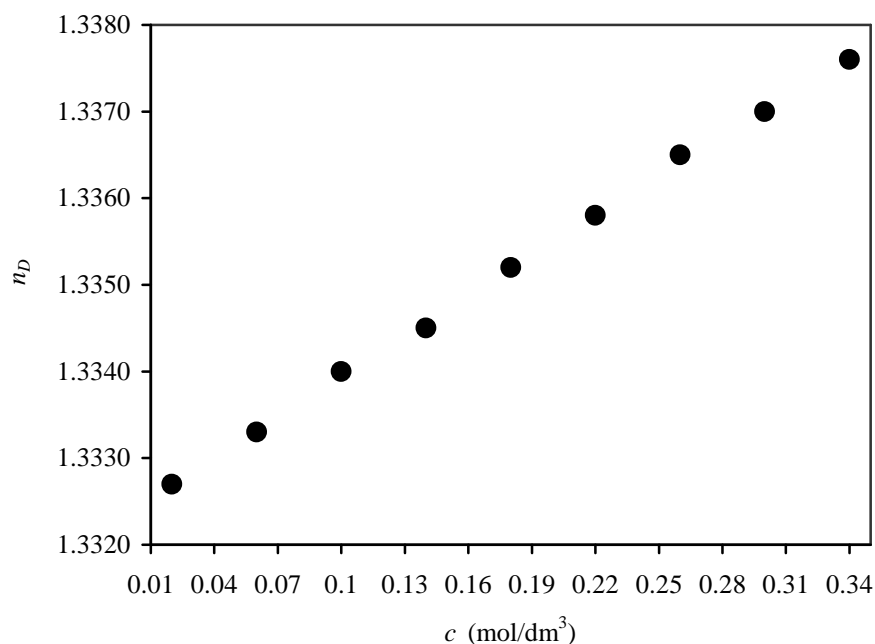
Figure 3. Variation in viscosity (η) with concentration (*c*) of glycine + aqueous-isoniazid solutions at 298.15 K

Figure 4. Variation in refractive index (n_D) with concentration (*c*) of glycine + aqueous-isoniazid solutions at 298.15 K

Density data were fitted to Eq. 1 and apparent molar volumes (φ_v) were calculated [14-15]. The molar concentration of glycine was converted to molal concentration using standard formula.

$$\varphi_v = \frac{M}{\rho} + \frac{10^3(\rho_0 - \rho)}{m\rho\rho_0} \qquad\qquad (1)$$

Where,

ρ_0= density of water/aqueous drug solution in which glycine solutions were prepared

ρ=density of experimental solution

M= molar mass glycine (75.07 g·mol^{-1})

m= molal concentration of glycine

Variation in the calculated φ_v with concentration of glycine is presented in Figure 5. It is seen that apparent molar volumes (φ_v) are large and positive and increase with concentration of glycine for all solutions which is due to presence of strong solute-solvent interactions.

Figure 5. Variation in apparent molar volumes (φ_v) with concentration (c) of glycine + aqueous-isoniazid solutions at 298.15 K
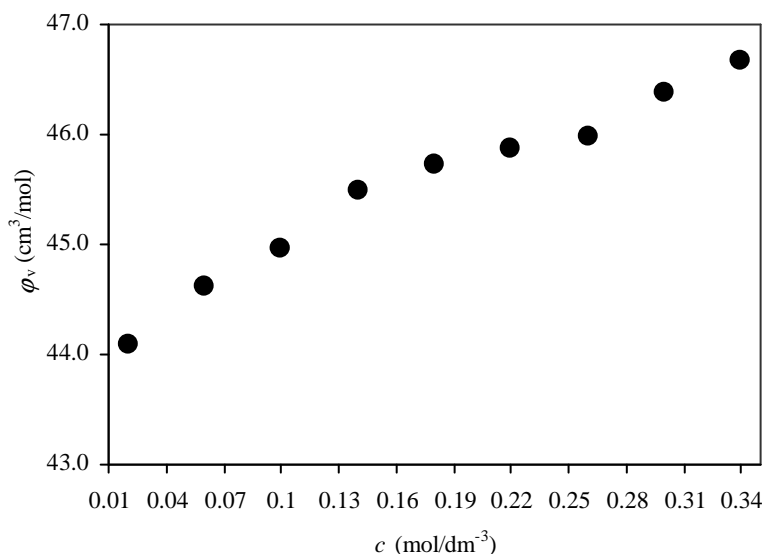
Dependence of φ_v values on concentration of glycine is fitted to the Massons linear relation [16-17], Eq. 2.

$$\varphi_v = \varphi_v^0 + S_v \sqrt{c}$$

(2)

Where,
φ_v^0= intercept representing solute-solvent interactions (partial molar volume) and
S_v= experimental slope representing solute-solute interactions

From the plot of φ_v and $\sqrt{c}$ (Figure 6), S_v and φ_v^0 were determined. The φ_v increased with concentration of glycine. From the Massons plot, partial molar volume at infinite dilution, φ_v^0 is found to be 43.25 cm³·mol⁻¹ and the value of S_v was found to be 5.70 cm³·kg^{3/2}·mol^{-3/2}. Large and positive value of φ_v^0 indicates existence of strong solute-solvent interactions in solution and positive value of S_v indicates presence of solute-solute interactions in solution.

Figure 6. Variation φ_v with $\sqrt{c}$ (Massons relation) for determination of partial molar volume (φ_v^0) of glycine in aqueous-isoniazid solutions at 298.15 K
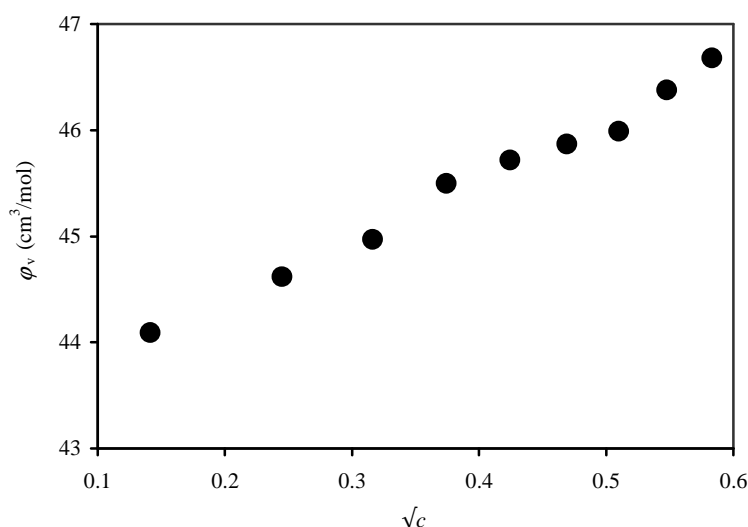
Relative viscosity ($\eta_r = \eta/\eta_0$) was calculated using Eq. 3:

$$\eta_r = \frac{\rho_s t_s}{\rho_o t_o} \tag{3}$$

Where, ρ_0 is density of water/aqueous drug solution, ρ_s is density of experimental solution, t_o and t_s are flow times for water/aqueous drug solution and experimental solution respectively.

Calculated relative viscosities with concentration are presented in Figure 7. It is seen that relative viscosity increased with concentration of glycine. Relative viscosity data was fitted to Jones-Dole [18-20] empirical expression (Eq. 4).

$$\eta_r - 1/\sqrt{c} = A + B\sqrt{c} \tag{4}$$

Where, η is viscosity of solution, η_o is viscosity of solvent, $\eta_r = \eta/\eta_o$ is relative viscosity and c=concentration of solution. And A and B are viscosity coefficients determined as intercept and slope of the plot η_r-1/$\sqrt{c}$ versus $\sqrt{c}$ (Figure 8).

Figure 7. Variation in relative viscosity (η_r) with concentration (c) of glycine + aqueous-isoniazid solutions at 298.15 K
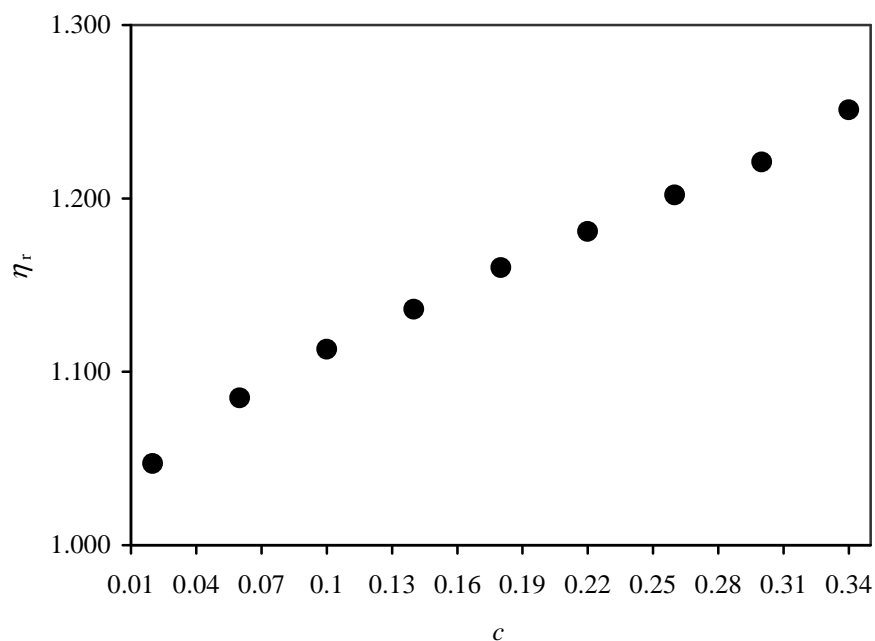

Viscosity B-coefficient gives information about solute-solvent interactions [21], solvation of ions and effect of solute on structure of solvent near the environment of solute [22]. Value of viscosity B-coefficient is found to be 0.20 dm^3·mol^{-1} which are in agreement with value of φ^0_v which indicates presence of strong solute-solvent interactions. Viscosity A-coefficient is found to be 0.30 dm$^{3/2}$·mol$^{-1/2}$ which is positive due to existence of solute-solute interactions.

Temperature independent quantity, *specific refraction (R_D)* which explains electronic polarizability of a substance was calculated by Lorentz and Lorenz [23] equation 5.

$$R_D = \frac{(n_D^2 - 1)}{(n_D^2 + 2)} \times \frac{1}{\rho} \tag{5}$$

Figure 8. Variation in η_r-1/$\sqrt{c}$ with $\sqrt{c}$ for determination of viscosity coefficients as per the Jones-Dole relation
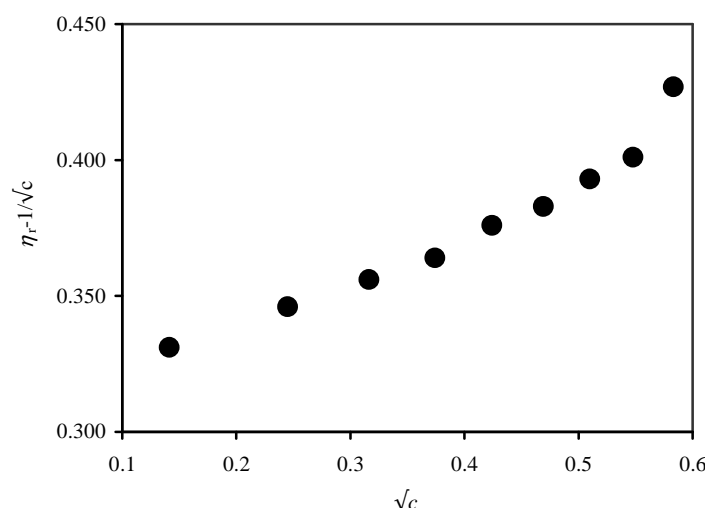
Specific refraction (R_D) of glycine in 0.02 mol·dm^{-3} isoniazid is presented in Figure 9. It is seen that specific refractions increased with increase in concentration of glycine which indicated electronic polarizability of a substance increase with concentration of glycine.

Figure 9. Variation in specific refractions (R_D) with concentration (c) of glycine + aqueous-isoniazid solutions at 298.15 K
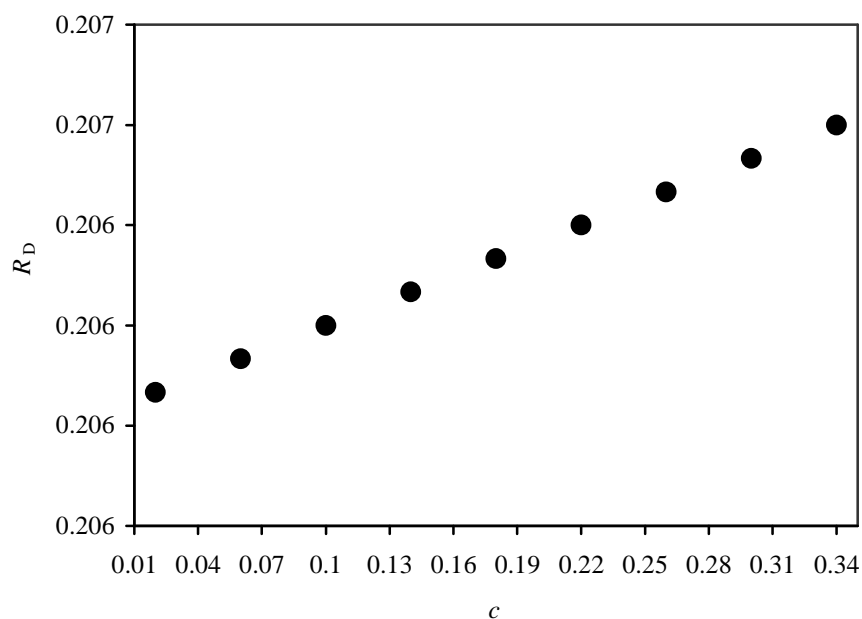
In binary aqueous isoniazid solutions, solute-solvent interaction between hydrophilic parts of drug and polar water molecule exists. The hydrophilic parts of isoniazid get solvated by water molecules. On addition of glycine in aqueous isoniazid solution, glycine through its ionic polar sites and hydrophilic sites interacts with polar water molecules which perturb original structure of aqueous isoniazid solution. This process removes water molecules from hydrated drug which decreases hydration number of drug. Structure of isoniazid in aqueous solution is thus changed due to addition of glycine to binary system. As per the co-sphere overlap model [24] interaction between glycine and isoniazid can be of following types: a) ion-hydrophilic interactions between zwitterionic groups of glycine and –CONHNH$_2$ group of isoniazid, b) hydrophilic-hydrophobic interactions between hydrophobic part of glycine and –CONHNH$_2$ group of drug and c) hydrophobic-hydrophobic interactions between hydrophobic groups of glycine and isoniazid. Positive value of $\Delta_{tr}\phi^0_v$ (43.25–42.97 [25] =0.28 cm^3·mol^{-1}) indicates interactions of the type (a) are relatively dominant over the remaining interactions.

CONCLUSION

Glycine + aqueous isoniazid solutions have been analyzed for intermolecular interactions through measurement of density, viscosity and refractive index at 298.15 K. Apparent molar volumes and partial molar volume of glycine in 0.02 mol·dm^{-3} isoniazid solution was evaluated. Effect of presence of isoniazid on physico-chemical behavior of aqueous glycine solutions with varying glycine concentrations has been studied 298.15 K. Experimental and derived properties revealed the presence of electrostatic and hydrophilic or ionic interactions between solute-solute, solute-solvent and solvent-solvent molecules. Apparent molar volumes and partial molar volume of glycine indicated the presence of strong solute-solvent interactions. The relative viscosity increased with concentration of glycine due to strengthening of glycine-water interactions. The structure of aqueous isoniazid solution changed on addition of glycine. The ion-hydrophilic interaction between ionic part of glycine and hydrophilic part of drug comes into picture on addition of glycine. Also, glycine interacts with polar water molecules through its hydrophilic zwiterionic sites.

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