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Research Article

Study of associative solvation of isoniazid with bovine serum albumin and glycine in aqueous medium through volumetric and acoustic analysis

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Abstract

Measurements of Density (ρ), speed of sound (u), and viscosity (η) of a pharmacologically significant anti-tuberculosis drug isoniazid with a simplest amino acid Glycine and a poly amino acid Bovine serum albumin (BSA) has been carried out in aqueous medium at normal body temperature of 37^0C and atmospheric pressure. Aston pars Densimeter, Ostwald viscometer, ultrasonic interferometer are used in the concentration range (2×10^{-4} to 2×10^{-3}M) at 310K. The experimental data has been meticulously used to enumerate various parameters which assist to predict valuable information regarding the presence of different kinds of intermolecular interactions possible in both the ternary systems. The results lead to comparative study of associative parameters of (isoniazid + water + Glycine) vs (isoniazid + water + BSA) systems. The experimental outcomes were also interpreted in terms of various volumetric & acoustic parameters such as adiabatic compressibility (β_s), intermolecular free length (Lf), apparent molal volume (φ_v), apparent molal compressibility (φ_κ), specific acoustic impedance (Z), relative association (R_A) etc to establish solute-solvent and solute-solute interactions. The UV –VIS Study justifies the difference in interaction between GLY -BSA and INZ-BSA systems in term of ion-solvent and ion-ion interaction in aqueous medium. Hydrogen bonding and weak van der-Waals attraction are the key players in ternary system and it is observed that these interactions are of higher order when we transit from INZ-GLY system to INZ-BSA system.

Keywords: Isoniazid, Glycine, Bovine Serum Albumin, Ultrasonic velocity, adiabatic compressibility, apparent molal volume, Intermolecular free length, Relative association.

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1. Introduction

Tuberculosis (TB) is potentially serious infectious bacterial diseases that mainly affect the lungs and is caused by mycobacterium Tuberculosis (MTB). Tuberculosis is the second biggest killer globally and WHO declared that TB is a global emergency, the first time that a disease had been labelled as such.

Isoniazid, also known as isonicotinyl hydrazide (INH), is an antibiotic used as a first-line agent for the prevention and treatment of both latent and active tuberculosis [1,2]. With the introduction of Isoniazid, a cure for tuberculosis was first considered possible. It is available worldwide, is inexpensive, and is generally well tolerated. It is on the World Health Organization's List of Essential Medicines and is effective against mycobacteria, particularly Mycobacterium tuberculosis. It is also active against some atypical types of mycobacteria, such as *M. kansasii* and *M. xenopi* [3,4].

Uncommon but more serious side effects include inflammation of nerves, which causes numbness in the arms or legs, and liver inflammation. Isoniazid acts on both intracellular and extracellular mycobacteria [5,6].

Bovine serum albumin (also known as BSA or "Fraction V") is a serum albumin protein derived from cows. Serum albumin is the most abundant protein in blood plasma and serves as a depot protein and transport protein for numerous endogenous and exogenous compounds [7,8]. It occupies a greater proportion in circulating plasma of human system. This is highly indispensable for studying drug-protein binding and probable interactions along with drug liberation, absorption, distribution, metabolism and excretion in terms of pharmacokinetic and pharmacodynamics property [9,11]. Albumin functions primarily as carrier protein for steroids, fatty acids, metal ions, drugs and thyroid hormones in the blood and plays a major role in stabilising extracellular fluid volume by contributing to oncotic pressure of plasma. Since BSA is a small, stable, moderately non-reactive protein, it is often used as a blocker in immunohistochemistry, a process that uses antibodies to identify antigens in cells [12]. This binding of BSA to nonspecific binding sites increases the chance that the antibodies will bind only to the antigens of interest [13]. BSA is also used as a nutrient in cell and microbial culture in order to stabilize some enzymes during the digestion of DNA and to prevent adhesion of the enzyme to reaction tubes, pipet tips, and other vessels. This protein does not affect other enzymes that do not need it for stabilization [14,16].

Glycineis one of the non-essential (also called conditional) amino acids and is helpful to create muscle tissue and convert glucose into energy. It is also needed to maintaining healthy central nervous and digestive systems, and has recently been shown to provide protection via antioxidants from some types of cancer. It is used in the body to help construct normal DNA and RNA strands-the genetic material needed for proper cellular function and formation. [17] It prevents the breakdown of muscle by boosting the body's levels of creatine, a compound that helps build muscle mass. High concentrations of glycine are found not only in the muscles, but in the skin and Connective tissues, as well. Almost 1/3 of collagen, which keeps the skin and connective tissue firm and flexible, is composed of glycine. Without glycine the body would not be able to repair damaged tissues; the skin would become slack as it succumbed to UV rays, oxidation, and free radical damage, and wounds would never heal. Glycine, being a neurotransmitter, plays both stimulatory and depressant roles in the brain boosting mental performance and memory [18,19].

Degrees of interaction of drug with surrounding protein depend on the chemical behaviour of drug particles. This concern potentiates the importance and necessity of studying the interaction between drug and serum albumin at molecular level in terms of acoustical parameters.

2. Material & Methods

Glycine (mass fraction >0.99) was obtained from SD Fine chemicals Ltd, India. BSA and Ionized was procured from Himedia Pvt. ltd. The amino acids were used after recrystallization from (ethanol + water) mixtures and dried in vacuum over P_2O_5 at room temperature for at least 72h. Isoniazid drug was purified by recrystallization to ensure maximum purity and dried in vacuum. The solutions were prepared on a molality basis. The concentrations of amino acids were in the range from (0 to 0.0002) mol×kg^{-1} while concentration of drug Isoniazid varied from (0.02 to 0.1) mol×kg$^{-1.}$ The water used for making the solutions was doubly distilled. The weighing was done using a electronic balance (SHIMADZU AX- 200) Japan with a least count of 0.0001 gm precisely up to 0.00001 g. The standard uncertainty in molality as per stated purities is ru(m)=0.01 (i.e., 1% relative uncertainty). The solutions were prepared with utmost care and stored in special airtight bottles to avoid moisture contamination and evaporation. Measurements of densities and ultrasonic speed were performed by an automated vibrating tube densimeter (Anton Paar DSA 5000 M). The ultrasonic speed is measured using a ultrasonic interferometer model (M-81S, Mittal Enterprises, New Delhi). The temperature was controlled by automatic thermostat at 300.15 K. Before each series of measurements, the densimeter was calibrated with triple distilled water in the experimental temperature range. Both the density and ultrasonic speed extremely sensitive to temperature, so it was controlled to ±1×10^{-3} K by built-in Peltier device. The viscosity was measured in Ostwald's viscometer at the same temperature.

Ultrasonic and volumetric parameters were determined applying following equations.

i) Apparent molar volume ($V_ø$)

The apparent molar volume was calculated by using equation (1)

$$V_ø = \frac{M}{d0} - \left[\frac{d-d0}{d0}\right]\frac{1000}{m} \text{----------(1)}$$

m- Molality in (mol kg $^{-1}$)

M – Molecular mass of the solute (mol kg $^{-1}$)

d_0, d are density of solvent and solute (Kg m^{-3})

ii) Adiabatic compressibility is calculated by using the equation (2)

$$\beta = 1/u^2 d \text{ ---------- (2)}$$

U – Ultrasonic velocity

d- Density of solution

iii) The apparent molar compressibility is calculated by using the relation

$$K_\Phi = \frac{1000}{md\,0}[[\beta - \beta 0] + \beta\phi_v \text{---- (3)}$$

iv) Intermolecular free length has been evaluated by formula

$$L_F = K\sqrt{\beta s} \text{ ---------- (4)}$$

K – Jacobson constant,

β_s---Compressibility parameter of the solution

v) Acoustic impedance is evaluated from the formula

$$Z = d.\ U \quad \text{_____ (5)}$$

d - Density of solution U -ultrasonic velocity

vi) The relative association is a measure of solute-solute or solute- solvent interaction. Relative association is measured by the equation.

$$R_A = (\ d0/d) \quad (\frac{U0}{U})^{1/2} \text{_____ (6)}$$

d_o – density of solvent d- density of solution
U_0 – ultrasonic velocity of solvent,
U – ultrasonic velocity of solution

vii) Solvation no is a measure of structure making and structure breaking tendency of solute in solution. The parameter is calculated by the formula

$$S_n = \frac{M_2}{M_1}\left[1 - \frac{\beta}{\beta_0}\right]\left[\frac{100-x}{x}\right] \text{____ (7)}$$

M_1 – molecular wt of the solvent,
M_2 – molecular wt of solute β
β - Adiabatic compressibility of solution,
β_0 –adiabatic compressibility of solvent

3. Result & discussion

The values of densities (ρ), speeds of Sound (u), and relative viscosity (η_r) of glycine and BSA in aqueous Solutions of isoniazid at 310K temperatures is given in Table 1 and Table 2 respectively.

Table 1: Values of Densities, ρ, and Speeds of Sound, u, and relative viscosity (η_r) of Glycine in Aqueous Solutions of Isoniazid at 310K Temperatures and Experimental Pressure, p = 0.1 MPa

[INZ], M	[Gly]	ρ/(kg.m^{-3})	u/(m.s^{-1})	η_r /(kg/m.s)
0.02M	0.000M	1002.6855	1516.00	0.919897
	0.002M	1002.8424	1521.68	0.955206
	0.004M	1002.9992	1523.99	1.058989
	0.006M	1003.1168	1524.63	1.122354
	0.008M	1003.2736	1525.05	1.168499
	0.010M	1003.4304	1525.47	1.229006
0.04M	0.000M	1005.3711	1520.00	0.963814
	0.002M	1005.5279	1524.42	1.032419
	0.004M	1005.6847	1525.05	1.093921
	0.006M	1005.8023	1525.68	1.152516
	0.008M	1005.9591	1526.94	1.124142
	0.010M	1006.1160	1527.36	1.139884
0.06M	0.000M	1008.0566	1524.00	0.966392
	0.002M	1008.2134	1525.26	1.041829
	0.004M	1008.3703	1526.10	1.110173
	0.006M	1008.4879	1526.71	1.144278
	0.008M	1008.6447	1527.76	1.189161
	0.010M	1008.8015	1528.62	1.212109
0.08M	0.000M	1010.7421	1518.09	1.000309
	0.002M	1010.8990	1525.64	1.040161
	0.004M	1011.0558	1526.10	1.144408
	0.006M	1011.1734	1527.93	1.20182
	0.008M	1011.3302	1528.60	1.237954
	0.010M	1011.487	1531.66	1.293986
0.10M	0.000M	1013.4277	1526.52	1.002887
	0.002M	1013.5845	1527.15	1.049182
	0.004M	1013.7413	1528.84	1.093627
	0.006M	1013.8589	1529.47	1.136884
	0.008M	1014.0158	1530.31	1.248313
	0.010M	1014.1726	1531.49	1.325506

Table 2: Values of Densities, ρ, and Speeds of Sound, u, and relative viscosity (η_r) of BSA in Aqueous Solutions of Isoniazid at 310K Temperatures and Experimental Pressure, p = 0.1 MPa

[INZ],M	[BSA]	ρ/(kg.m^{-3})	u/(m.s^{-1})	η_r /(kg/m.s)
0.02M	0.000M	1002.6855	1516.00	0.922145
	0.002M	1015.6232	1524.00	1.0698076
	0.004M	1028.5608	1528.00	1.0773815
	0.006M	1041.4984	1532.00	1.0834589
	0.008M	1054.4360	1535.40	1.0881172
	0.010M	1067.3737	1539.16	1.1002932
0.04M	0.000M	1005.3711	1520.00	0.9640206
	0.002M	1018.3087	1524.00	1.0673238
	0.004M	1031.2463	1528.00	1.0747074
	0.006M	1044.1839	1532.00	1.0806977
	0.008M	1057.1216	1536.00	1.0853552
	0.010M	1070.0592	1540.00	1.0973006
0.06M	0.000M	1008.0566	1524.00	0.9965979
	0.002M	1020.9942	1528.60	1.056397
	0.004M	1033.9319	1531.84	1.0648712
	0.006M	1046.8695	1532.00	1.0919258
	0.008M	1059.8071	1538.10	1.1135942
	0.010M	1072.7447	1541.68	1.1293224
0.08M	0.000M	1010.7421	1526.10	1.0423713
	0.002M	1023.6798	1529.26	1.0761001
	0.004M	1036.6174	1531.58	1.092061
	0.006M	1049.5550	1536.63	1.1137287
	0.008M	1062.4926	1539.81	1.1210892
	0.010M	1075.4303	1542.10	1.1405871
0.10M	0.000M	1013.4277	1527.15	1.065567
	0.002M	1026.3653	1528.42	1.0971634
	0.004M	1039.3029	1532.00	1.1099712
	0.006M	1052.2406	1536.21	1.1190219
	0.008M	1065.1782	1539.58	1.1408407
	0.010M	1078.1158	1541.05	1.1832129

Variation of different thermodynamic parameters such as β, Z, L_f, R_A,Vφ, Kφ at different concentrations **Glycine** and BSA in Aqueous Solutions of Isoniazid at T=310K is given in Table 3 and Table 4 respectively.

Table 3: Variation of thermodynamic parameters at different concentrations Glycine in Aqueous Solutions of Isoniazid and T=310K

[INZ],M	[Gly]	β x10^{-10}	Z x 10^{6}	L_f x10^{-11}	R_A	V φ	K φ x 10^{-10}
0.02M	0.000M	4.33947	1.5200	4.3772	1.011632	-----	8.8357
	0.002M	4.30644	1.5260	4.3605	1.010529	-47.74536	8.7698
	0.004M	4.29273	1.5285	4.3536	1.010177	-24.26241	8.7433
	0.006M	4.28863	1.5293	4.3515	1.010154	-16.36975	8.7359
	0.008M	4.28560	1.5300	4.3499	1.010219	-12.47207	8.7311
	0.010M	4.28257	1.5307	4.3484	1.010284	-10.13341	8.7263
0.04M	0.000M	4.30513	1.5281	4.3598	1.013451	--------	8.7892
	0.002M	4.27954	1.5328	4.3469	1.012629	-61.06138	8.7383
	0.004M	4.27532	1.5337	4.3447	1.012647	-30.91834	8.7311
	0.006M	4.27128	1.5345	4.3427	1.012625	-20.80599	8.7239
	0.008M	4.26355	1.5360	4.3387	1.012504	-15.79821	8.7094
	0.010M	4.26054	1.5367	4.3372	1.012569	-12.79350	8.7046
0.06M	0.000M	4.27115	1.5362	4.3426	1.015269	---------	8.7432
	0.002M	4.26341	1.5377	4.3387	1.015146	-74.30646	8.7287
	0.004M	4.25806	1.5388	4.3359	1.015118	-37.53882	8.7191
	0.006M	4.25415	1.5396	4.3340	1.015100	-25.21861	8.7121
	0.008M	4.24763	1.5409	4.3306	1.015025	-19.10665	8.7001
	0.010M	4.24222	1.5420	4.3279	1.014993	-15.43942	8.6904
0.08M	0.000M	4.29300	1.5344	4.3537	1.019291	----------	8.8113
	0.002M	4.24995	1.5422	4.3318	1.017765	-87.48117	8.7243
	0.004M	4.24675	1.5429	4.3302	1.017821	-44.12413	8.7191
	0.006M	4.23608	1.5450	4.3247	1.017533	-29.60780	8.6982
	0.008M	4.23174	1.5459	4.3225	1.017543	-22.39752	8.6906
	0.010M	4.21420	1.5492	4.3136	1.017023	-18.07130	8.6559
0.10M	0.000M	4.23446	1.5470	4.3239	1.020115	----------	8.7142
	0.002M	4.23032	1.5479	4.3218	1.020132	-100.5860	8.7071
	0.004M	4.22033	1.5498	4.3167	1.019915	-50.67454	8.6878
	0.006M	4.21638	1.5506	4.3147	1.019893	-33.97373	8.6807
	0.008M	4.21108	1.5517	4.3120	1.019864	-25.67095	8.6711
	0.010M	4.20394	1.5532	4.3083	1.019759	-20.68923	8.6578

Table 4: Variation of thermodynamic parameters at different concentrations BSA in Aqueous Solutions of Isoniazid and T=310K

[INZ] , M	[BSA]	β x10^{-10}	Z x 10^{6}	L_f x10^{-11}	R_A	V φ	K φ x 10^{-13}
0.02M	0.000M	4.33947	1.5200	4.3772	1.011632	---------	10.00406
	0.002M	4.23933	1.5478	4.3264	1.022889	-110.4231	9.93542
	0.004M	4.16412	1.5716	4.2878	1.035015	-86.1421	9.88347
	0.006M	4.09095	1.5955	4.2500	1.047121	-77.53613	9.83192
	0.008M	4.02288	1.6189	4.2145	1.059345	-72.86306	9.78843
	0.010M	3.95472	1.6428	4.1786	1.071469	-69.77392	9.74066
0.04M	0.000M	4.30513	1.5281	4.3598	1.013451	---------	9.98778
	0.002M	4.22815	1.5519	4.3207	1.025594	-123.4067	9.93542
	0.004M	4.15328	1.5757	4.2823	1.037717	-92.4719	9.88347
	0.006M	4.08043	1.5996	4.2445	1.049821	-81.652	9.83192
	0.008M	4.00952	1.6237	4.2075	1.061905	-75.87481	9.78078
	0.010M	3.94049	1.6478	4.1711	1.073970	-72.12537	9.73004
0.06M	0.000M	4.27115	1.5362	4.3426	1.015269	----------	9.93542
	0.002M	4.19169	1.5606	4.3020	1.027266	-136.322	9.87571
	0.004M	4.12175	1.5838	4.2660	1.039550	-98.76883	9.83398
	0.006M	4.06996	1.6038	4.2391	1.052521	-85.74675	9.83192
	0.008M	3.98843	1.6300	4.1964	1.064117	-78.8713	9.75404
	0.010M	3.92205	1.6538	4.1613	1.076273	-74.46505	9.70879
0.08M	0.000M	4.24807	1.5424	4.3309	1.017505	----------	9.90804
	0.002M	4.17706	1.5654	4.2945	1.029819	-136.322	9.86713
	0.004M	4.11246	1.5876	4.2612	1.042309	-98.76883	9.83732
	0.006M	4.03511	1.6127	4.2209	1.054160	-85.74675	9.77274
	0.008M	3.96953	1.6360	4.1865	1.066419	-78.8713	9.73241
	0.010M	3.91012	1.6584	4.1550	1.078869	-74.46505	9.70351
0.10M	0.000M	4.23097	1.5476	4.3221	1.019975	---------	9.89439
	0.002M	4.17074	1.5687	4.2913	1.032711	-161.9498	9.87804
	0.004M	4.09959	1.5922	4.2545	1.044913	-111.265	9.83192
	0.006M	4.02701	1.6166	4.2167	1.056953	-93.87355	9.77808
	0.008M	3.96071	1.6399	4.1818	1.069168	-84.81894	9.73535
	0.010M	3.90571	1.6614	4.1527	1.081809	-79.10943	9.71676

Table 5: Values of viscosity A-coefficients, B-coefficients of Jones-Dole`s equation of INZ solution in BSA and GLY

Concentration	INZ-BSA Mixture		INZ-GLY Mixture	
	A ($dm^{3/2}$ $mol^{-1/2}$)	B(dm^3 mol^{-1})	A ($dm^{3/2}$ $mol^{-1/2}$)	B(dm^3 mol^{-1})
0.002M	1.045	0.513	1.182	-0.484
0.004M	1.089	-0.047	1.203	-0.356
0.006M	1.098	-0.086	1.188	-0.312
0.008M	1.124	-0.102	1.255	-0.461
0.010M	1.145	-0.098	1.227	-0.367

Spectroscopic study:-

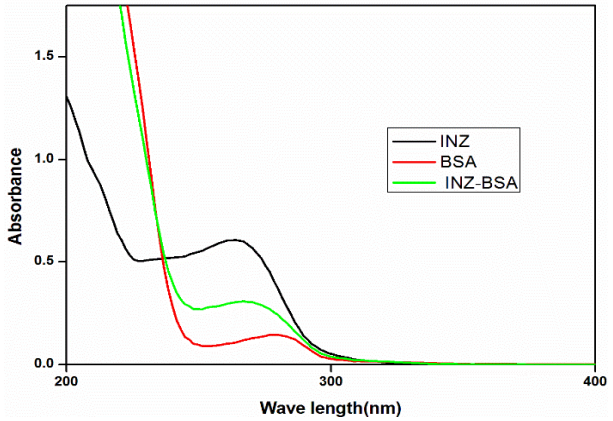


Figure 1: Comparative UV-VIS Spectra of Isoniazid, BSA and INZ-BSA Complex in aqueous Medium

The comparative spectra of Isoniazid, BSA and INZ-BSA complex in aqueous medium was observed in Carry 100 UV-VIS spectrophotometer (figure1). The λ_{max} of Isoniazid is found at 260 nm. In case of BSA λ_{max} peak is observed at 277 nm. After mixing both the Isoniazid peak and peak of BSA get shifted and a new peak is created at 270 nm. This indicates a considerable association between the drugs.

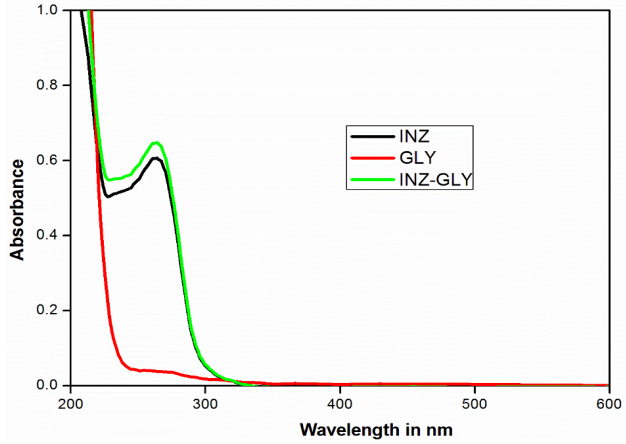


Figure 2: Comparative UV-VIS Spectra of Isoniazid, Glycine and INZ-GLY Complex in aqueous Medium

But the same comparative spectra between Isoniazid, Glycine and INZ-GLY complex in aqueous medium do not show any significant change (figure 2). The λ_{max} of Isoniazid undergoes no shifting indicating no force of attraction from glycine. Glycine molecule being very small and having same amino linkage may not have tendency to associate with Isoniazid.

Variation of apparent molar volume:

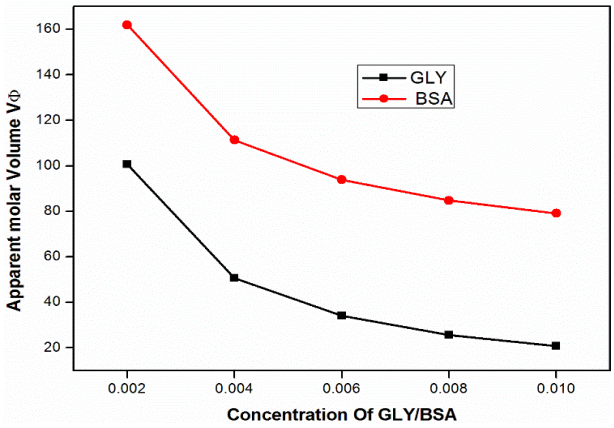


Figure 3: Variation of apparent molar volume with concentration of GLY & BSA with varying concentration of INZ

Variation of apparent molar volume shows similar trend in both cases (figure 3) i.e. with increase of concentration of glycine/BSA the positive value of partial molar volume of Isoniazid decreases due to solute-solvent interaction indicating electrostatic solvation of ions. In aqueous medium there is probability of intra-molecular hydrogen bonding due to ion-dipole interaction decreasing Vϕ value. The positive values ofVϕ indicates the strong solute–solvent interaction. The electrostatic solvation of ions is more pronounced in case of BSA-Isoniazid mixture in aqueous solution having high positive values due to both associative effect and intramolecular hydrogen bonding [20].

Variation of adiabatic compressibility

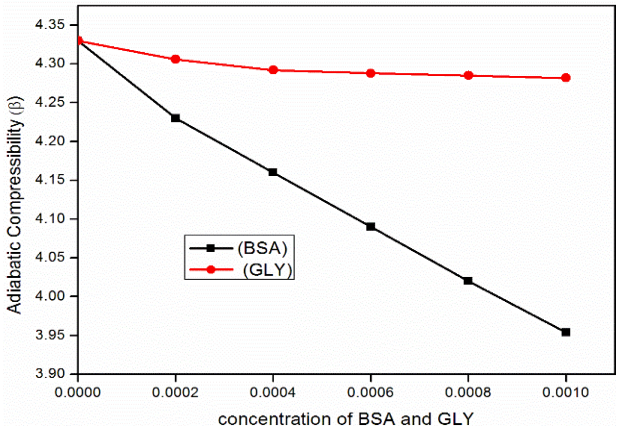


Figure 4: Variation of adiabatic compressibility with concentration of BSA & Glycine

The increase of adiabatic compressibility with decrease of concentration of solution (figure 4) may be due to the dispersion of solvent molecules around ions supporting weak ion solvent interactions. Adiabatic compressibility is more in case of bulky and less polar substituents. β decreases with increasing concentration indicates formation of strong hydrogen bonding between solute and solvent. The decrease in β values with concentration indicates the existence of attractive force between the BSA and Isoniazid in aqueous solution but the decrease in β values in case of glycine and Isoniazid is negligible indicating less association [21].

Variation of acoustic impedance:

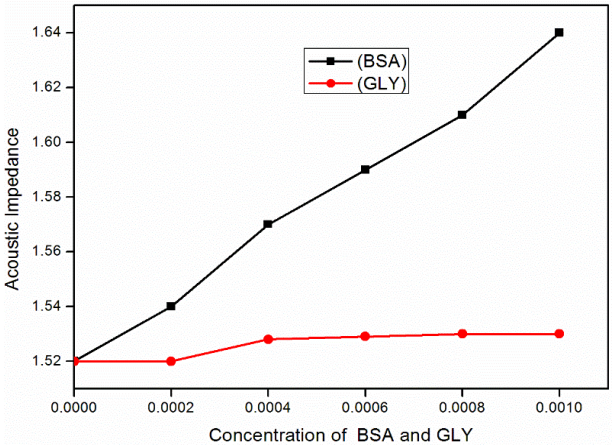


Figure 5: Variation of acoustic impedance with concentration of GLY & BSA with varying concentration of aqueous Solution of INZ.

The increase in Z value explains the dipole-dipole interaction through hydrogen bonding between solute and solvent. It is observed from figure-5 that U and Z show nonlinear increasing variation with concentration of BSA justify no compound formation between BSA and isoniazid ensuing the possibility of association only.

Variation of Intermolecular free length

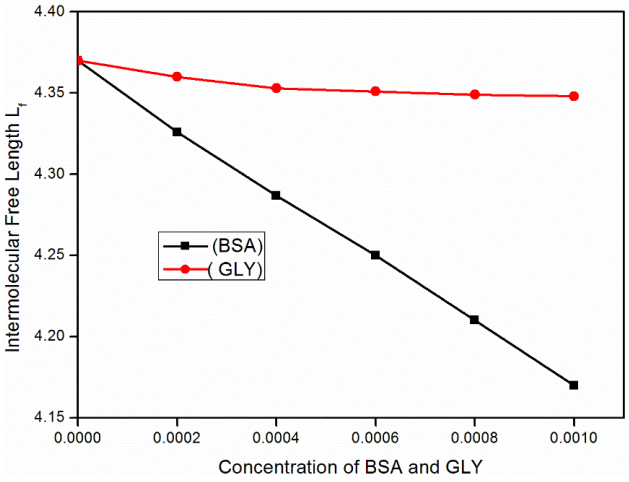


Figure 6: Variation of Intermolecular free length with concentration of GLY & BSA with INZ.

Intermolecular free length decreases (figure 6) almost linearly in BSA-INZ system with enhancing concentration of BSA as L_f depends upon the size of the molecules as well as the distance between the surfaces of molecules. The solute-solute association here expressed with a decreasing trend of intermolecular free length. In the contrary the least attraction between glycine and Isoniazid can be interpreted with minimum variation in aqueous medium [22,23].

Variation of relative association:

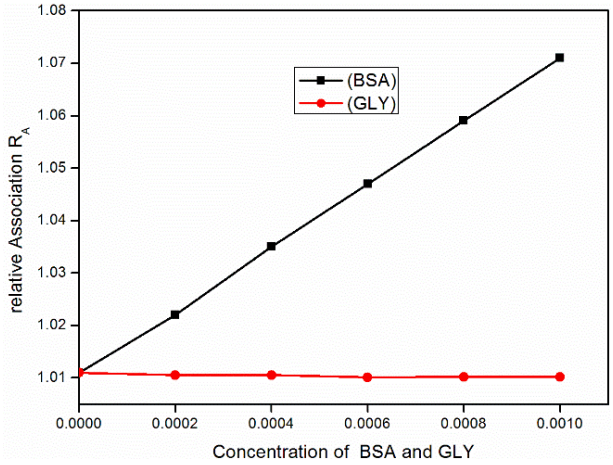


Figure 7: Variation of relative association with concentration of GLY & BSA with varying concentration of aqueous Solution of INZ.

All positive and steady increase in relative association in BSA-Isoniazid system (figure 7) indicates high electrostatic dipole –induced dipole interaction between unlike molecules which result in contraction of volume. This also indicates significant solute-solvent interaction which is almost negligible in glycine-Isoniazid system.

Variation of apparent molar adiabatic compressibility:

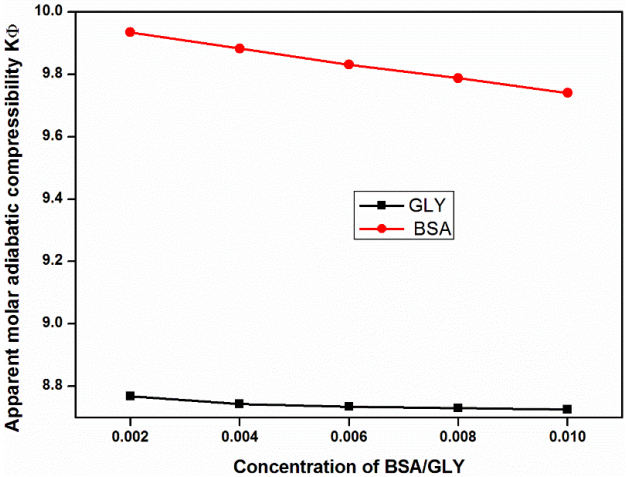
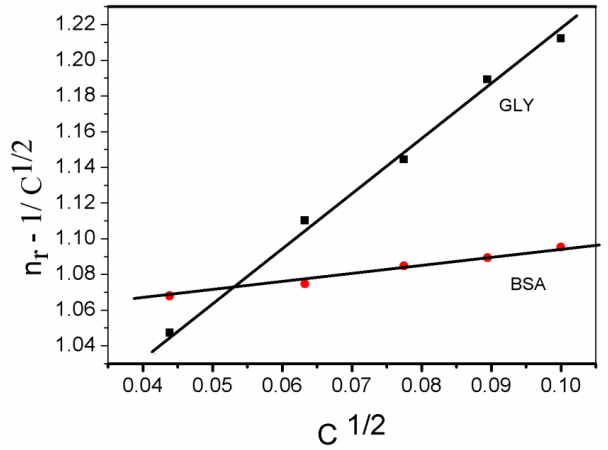


Figure 8: Variation of apparent molar adiabatic compressibility with concentration of GLY & BSA with varying concentration of aqueous Solution of INZ

Apparent molar adiabatic compressibility K_φ is a sensitive measure of solute solvent interactions existing in a solution. Here Kφ have high positive values for BSA-Isoniazid (figure-8) indicating strong association. The positive Kφ values indicate that the solute are loosely attached to solvent molecules and are more compressible. As the value decreases, it indicates weak interaction for glycine-Isoniazid system in aqueous medium. [24,25].

Viscometric measurement:



The relative viscosities η_r of INZ with BSA and INZ with GLY in aqueous medium were calculated by using the equation

$$\eta_r = \eta / \eta_0$$

Where η and η_0 are the viscosities of the solution and solvent respectively

The viscosity data were analysed by using Jones–Dole equation in the form

$$\eta_r = \eta/\eta_0 = 1 + A\sqrt{C} + BC$$

Co-efficient A gives a significant insight into solute−solute interactions while the B parameter which measures the structure making/breaking capacity of an electrolyte in a solution also contain a contribution from structural effects and is responsible for solute–solvent interactions in a solvent. The values of A and B have been determined from the intercept and slope of linear regression of $\frac{\eta_r - 1}{C^{1/2}}$ vs. $c^{1/2}$ curve.

The value of Falkenhagen coefficient A increases with the addition of BSA in to aqueous solution of Isoniazid indicating strong solute-solute interaction. The value of B coefficient decreases in case of BSA-INZ mixture but remain almost constant for INZ-GLY solution which indicates less interaction between solute and solvent.

4. Conclusion

A detailed analysis of various interaction parameters such as acoustic impedance, intermolecular free length, adiabatic compressibility, relative association, apparent molar volume, partial molar volume, apparent molar adiabatic compressibility, partial molar compressibility etc for two systems one containing drug + essential protein and other with drug+ low molecular amino acid is studied in aqueous medium and following facts are accounted.

1) Analysis of UV-VIS spectra shows no significant interaction of INZ with glycine whereas there is a shift of peak of INZ with BSA showing probability of relative association due to the presence of multiple peptide linkage and hydrogen bonding.
2) The parameters like acoustic impedance, intermolecular free length, adiabatic compressibility, relative association and Solvation number calculated to have regular change when INZ associates with varying concentration of BSA indicating a prominent associative interaction between them where as we found almost no change of these parameters for INZ with glycine system.
3) All above observations implies anti-tuberculosis drug isoniazid can be better associated with BSA which is a carrying protein essential for compensation of albumin deficiency of tuberculosis affected patient
4) The result obtained from these studies can thus be helpful for pharmacological application of drug as well as to understand pharmacokinetics process such as transport of drug across biological membranes, drug action and physicochemical properties
5) Clinically it is observed that patients victimised with tuberculosis reveals the deficiency of albumin in blood plasma that leads to the risk of morbidity and mortality and also slows down the transport system of hormones, enzymes, bioinorganic salts, administered drugs. In order to circumvent the hypoalbumineia, the selected anti TB drug must be dosed along with serum albumin.

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