International Journal of Thermophysics, Vol. 26, No. 3, May 2005 (© 2005)
DOI: 10.1007/s10765-005-5579-1

Ultrasonic Velocity Studies of Drug Parvon-spas in Mixed Alcohol–Water Solvent Systems at 25°C

V. K. Syal,[1,2] S. K. Thakur,[1] S. Chauhan,[1] and P. Sharma[1]

Received June 29, 2004

Ultrasonic velocities and densities of the drug Parvon-spas in binary mixtures of water with methanol (MeOH), ethanol (EtOH), and propan-1-ol (1-PrOH) have been measured over the complete solvent composition range at 10 mol% intervals at 25°C. Various acoustic parameters such as the acoustic impedance (Z), adiabatic compressibility (β), intermolecular free length (L_f), relative association ($R.A.$), molar volume (V_m), and molar sound velocity (R_m) have been calculated. In addition, excess functions, i.e., excess adiabatic compressibility (β^E), excess intermolecular free length (L_f^E), excess molar volume (V^E), excess ultrasonic velocity (U^E), and excess acoustic impedance (Z^E) for these three solvent mixtures in the absence and presence of the drug have been calculated. A different behavior of these parameters in these alcohol systems has been discussed in terms of the length of the alcohol molecule, the molecular volume, as well as inter/intramolecular interactions of these molecules.

KEY WORDS: aqueous alcohol mixtures; density; drug Parvon-spas; excess functions; ultrasonic velocity.

1. INTRODUCTION

In recent years, measurements of the ultrasonic velocity have been adequately employed in understanding the nature of molecular interactions in pure liquids, liquid mixtures, and solutions [1, 2]. Drug action, although complex, results from various kinds of physicochemical interactions, e.g., ionic or covalent, charge transfer, hydrogen bonding, ion–dipole interactions, hydrophilic interactions, etc. [3, 4]. A knowledge of the use of drugs

[1] Department of Chemistry, Himachal Pradesh University, Shimla-5, India.
[2] To whom correspondence should be addressed. E-mail: vijay_syal@indiatimes.com

involving physiological and biochemical effects, and their mechanism of action at macromolecular/subcellular/organ system levels can be studied in pharmokinetics [5, 6]. All pharmokinetic processes involve transport of drugs across biological membranes, which can be well understood by transport property measurements, viz., ultrasonic velocity, viscosity, diffusion, and thermal conductivity. In the present paper, ultrasonic measurements of the drug Parvon-spas as a solute has been reported which is a kind of narcotic-analgesic drug that selectively relieves pain by acting on the central nervous system (CNS) or on the peripheral pain mechanics, without significantly altering consciousness.

2. EXPERIMENTAL

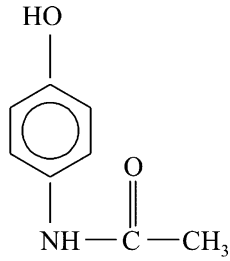
The solvents, methanol, ethanol, and propan-1-ol (extra pure, AR grade, SRL PVT Ltd. Mumbai) were kept overnight in vacuum-dried 4 Å molecular sieves. After decantation, solvent was refluxed for 2 to 3 hours and then distilled slowly through a long fractionating column. By comparing physical constants, e.g., densities, i.e., $\rho_{MeOH} = 0.7848\ g{\cdot}cm^{-3}$ ($0.786\ g{\cdot}cm^{-3}$ [7]), $\rho_{EtOH} = 0.7909\ g{\cdot}cm^{-3}$ ($0.785\ g{\cdot}cm^{-3}$ [8]), and $\rho_{PrOH} = 0.8000\ g{\cdot}cm^{-3}$ ($0.796\ g{\cdot}\ cm^{-3}$ [9]) and ultrasonic velocity values, i.e., $U_{MeOH} = 1107\ m{\cdot}s^{-1}$ ($1102.8\ m{\cdot}s^{-1}$ [7], $1103\ m{\cdot}s^{-1}$ [10]), $U_{EtOH} = 1157\ m{\cdot}s^{-1}$ ($1142\ m{\cdot}s^{-1}$ [11]), and $U_{PrOH} = 1201\ m{\cdot}s^{-1}$ ($1191\ m{\cdot}s^{-1}$ [9]) with literature values, the purity of the above-mentioned solvents was checked.

Solvent systems having 100 to 0 mol% of water with methanol (MeOH), ethanol (EtOH), and propan-1-ol (PrOH) at 10 mol% intervals have been prepared and investigated. Solutions containing a fixed amount of drug (0.250 g in 40 ml of a solvent/ solvent system) have also been prepared and studied.

The densities of the pure solvents and various mixtures have been measured with a specially designed sealable-type pycnometer of $20\ cm^3$ volume, in a water thermostat precise to $\pm 0.05^{\circ}C$. The ultrasonic velocity in pure solvents as well as in various mixtures was measured using an ultrasonic interferometer (Model-81, supplied by Mittal Enterprises, New Delhi) operating at a frequency of 1 MHz.The temperature was maintained at $25 \pm 0.05^{\circ}C$ by circulating thermostat water around the cell with the help of a Tulu pump. The calibration of the cell was made by measuring ultrasonic velocities of different pure non-aqueous solvents like ethylmethylketone, acetonitrile, and acetone at $25^{\circ}C$.

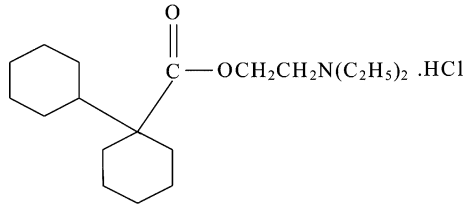
The studied drug Parvon spas (Jagsonpal Pharmaceuticals Ltd., Faridabad-121003) capsules containing paracetamol – 400 mg, dicyclomine hydrochloride – 10 mg, and Dextropropoxyphene hydrochloride – 65 mg having the following structures [12] were used as such after drying in an oven:

1. Paracetamol [$C_8H_9NO_2$]



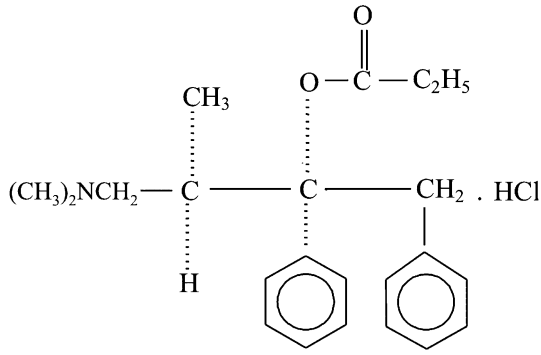
N-(4-hydroxyphenyl)acetamide.

2. Dicyclomine hydrochloride [$C_{19}H_{35}NO_2HCl$]



2-(diethylamino) ethyl[bicyclohexyl]-1-carboxylate hydrochloride

3. Dextropropoxyphene hydrochloride[$C_{22}H_{29}NO_2HCl$]



[(1S,2R)-1-benzyl-3-dimethyl-amino-2-methyl-1-phenylpropylpropionate hydrochloride]

The uncertainties of the density and ultrasonic velocity measurements were estimated to be ±0.2% and ±0.5%, respectively. The sources of error may be purity of the drug supplied and measurement of data. The measured data presented in the various tables for density and ultrasonic velocity are the average values of 7 to 10 determinations.

3. DISCUSSION

The experimental values of ultrasonic velocity and density for MeOH–water, EtOH–water, and PrOH–water with and without drug are presented in Tables I to VI. From these tables, it is evident that the density values decrease with an increase of the alcohol content for all the studied solvent systems. However, these values increase with the addition of drug in all studied systems. This behavior has been found to be similar to that reported by Maity et al. [13] for EtOH–water and MeOH–water solvent systems. From perusal of these tables, it is evident that the ultrasonic velocity increases with the addition of MeOH in MeOH–water mixtures up to 20 mol% of MeOH, and then decreases with further addition of MeOH. However, for EtOH and PrOH mixtures, maxima in the ultrasonic velocity are obtained at 10 mol% of EtOH and PrOH. Such maxima in the ultrasonic velocity have also been reported [13] at 16 mass% MeOH and 25 mass% EtOH in MeOH–water and EtOH–water mixtures, respectively, which show close agreement between the experimental values of this study and literature results. Also, in acetonitrile (AN) + water mixtures [14] there occurs a maximum at 10 mol% of AN which has been ascribed to the fact that in higher water regions of these solvent mixtures, the extent of hydrogen bonding is considerably affected by the addition of co-solvent AN and AN acts as a structure breaker.

The addition of drug results in an increase of the ultrasonic velocity, but the general behavior remains the same as for all the studied pure solvent systems. A similar effect has been reported by Syal et al. for the case of sucrose in AN + water [14] and DMSO + water [15] solvent mixtures. This shows that solute–solvent interactions, although present, do not alter the solvent–solvent interactions already present in the binary mixtures. However, an increase in the ultrasonic velocity in any solution with the addition of a solute is indicative of greater association of molecules due to effective solute–solvent interactions [15].

The values of various derived parameters, i.e., specific acoustic impedance (Z), relative association ($R.A.$), adiabatic compressibility (β), intermolecular free length (L_f), molar volume (V_m), and molar sound velocity (R_m) have been calculated using formulae given below and these values

Table I. Density (ρ), Ultrasonic Velocity (U), Specific Acoustic Impedance (Z), Relative Association ($R.A.$), Adiabatic Compressibility (β), Intermolecular Free Length (L_f), Molar Volume (V_m), and Molar Sound Velocity (R_m) for MeOH + Water Solvent System at 25°C

Mol. Frac. of MeOH	$\rho \times 10^{-3}$ ($kg \cdot m^{-3}$)	U ($m \cdot s^{-1}$)	$Z \times 10^{-6}$ ($kg \cdot m^{-2} \cdot s^{-1}$)	$R.A.$	$\beta \times 10^{5}$ (bar^{-1})	$L_f \times 10^{11}$ (m)	V_m ($cm^3 \cdot mol^{-1}$)	$R_m \times 10^{4}$ ($(m \cdot s^{-1})^{1/3} \cdot m^3 \cdot mol^{-1}$)
0.0	0.997	1501.0	1.496	1.0000	4.45	4.34	18.0	2.067
0.1	0.975	1527.0	1.488	0.9723	4.40	4.22	19.9	2.291
0.2	0.9516	1549.0	1.474	0.9445	4.38	4.32	21.9	2.529
0.3	0.9274	1535.0	1.423	0.9232	4.57	4.40	23.9	2.761
0.4	0.9052	1463.0	1.324	0.9157	5.16	4.67	26.1	2.959
0.5	0.8814	1402.0	1.235	0.9043	5.77	4.94	28.4	3.174
0.6	0.8611	1330.0	1.145	0.8992	6.56	5.27	30.6	3.371
0.7	0.8415	1264.0	1.063	0.8937	7.43	5.61	33.0	3.572
0.8	0.8148	1205.0	0.981	0.8793	8.44	5.98	35.8	3.813
0.9	0.8047	1154.0	0.928	0.8810	9.32	6.28	38.0	3.988
1.0	0.7848	1107.0	0.868	0.8712	10.85	6.63	40.8	4.218

Table II. Density (ρ), Ultrasonic Velocity (U), Specific Acoustic Impedance (Z), Relative Association ($R.A.$), Adiabatic Compressibility (β), Intermolecular Free Length (L_f), Molar Volume (V_m), and Molar Sound Velocity (R_m) for Drug Parvon-spas with Concentration 3.72×10^{-2} mol·dm^{-3} in MeOH + Water Solvent System at 25°C

Mol. Frac. of MeOH	$\rho \times 10^{-3}$ (kg·m^{-3})	U (m·s^{-1})	$Z \times 10^{-6}$ (kg·m^{-2}·s^{-1})	$R.A.$	$\beta \times 10^{5}$ (bar^{-1})	$L_f \times 10^{11}$ (m)	V_m (cm^3·mol^{-1})	$R_m \times 10^4$ ((m·s^{-1})$^{1/3}$·m^3·mol^{-1})
0.0	0.9974	1503.0	1.499	1.0000	4.44	4.33	18.0	2.067
0.1	0.9836	1542.0	1.516	0.9777	4.27	4.25	19.7	2.278
0.2	0.9710	1570.0	1.524	0.9594	4.17	4.20	21.4	2.489
0.3	0.9472	1567.0	1.484	0.9365	4.30	4.26	23.4	2.722
0.4	0.9432	1553.0	1.464	0.9353	4.39	4.31	25.0	2.897
0.5	0.9251	1528.0	1.413	0.9224	4.62	4.42	27.0	3.112
0.6	0.9036	1467.0	1.325	0.9133	5.14	4.66	29.2	3.319
0.7	0.8810	1393.0	1.227	0.9059	5.85	4.97	31.6	3.524
0.8	0.8488	1290.0	1.095	0.8954	7.07	5.47	34.4	3.744
0.9	0.8239	1223.0	1.007	0.8848	8.11	5.86	37.1	3.971
1.0	0.7898	1119.0	0.837	0.8736	9.86	6.54	40.5	4.206

Table III. Density (ρ), Ultrasonic Velocity (U), Specific Acoustic Impedance (Z), Relative Association ($R.A.$), Adiabatic Compressibility (β), Intermolecular Free Length (L_f), Molar Volume (V_m), and Molar Sound Velocity (R_m) for EtOH + Water Solvent System at 25°C

Mol. Frac. of EtOH	$\rho \times 10^{-3}$ ($kg \cdot m^{-3}$)	U ($m \cdot s^{-1}$)	$Z \times 10^{-6}$ ($kg \cdot m^{-2} \cdot s^{-1}$)	$R.A.$	$\beta \times 10^{5}$ (bar^{-1})	$L_f \times 10^{11}$ (m)	V_m ($cm^3 \cdot mol^{-1}$)	$R_m \times 10^{4}$ ($(m \cdot s^{-1})^{1/3} \cdot m^3 \cdot mol^{-1}$)
0.0	0.9970	1501.0	1.496	1.0000	4.45	4.34	18.1	2.067
0.1	0.9655	1626.0	1.569	0.9429	3.91	4.07	21.5	2.533
0.2	0.9372	1549.0	1.451	0.9302	4.44	4.34	25.2	2.913
0.3	0.9078	1460.0	1.325	0.9189	5.17	4.67	29.1	3.299
0.4	0.8838	1400.0	1.237	0.9072	5.81	4.94	33.0	3.696
0.5	0.8635	1344.0	1.160	0.8985	6.40	5.21	37.1	4.089
0.6	0.8442	1304.0	1.100	0.8873	6.96	5.43	41.2	4.503
0.7	0.8310	1261.0	1.047	0.8833	7.56	5.66	45.2	4.888
0.8	0.8161	1229.0	1.003	0.8749	8.11	5.86	49.5	5.302
0.9	0.8033	1198.0	0.962	0.8686	8.67	6.06	53.8	5.711
1.0	0.7909	1157.0	0.915	0.8651	9.44	6.32	58.2	6.105

Table IV. Density (ρ), Ultrasonic Velocity (U), Specific Acoustic Impedance (Z), Relative Association ($R.A.$), Adiabatic Compressibility (β), Intermolecular Free Length (L_f), Molar Volume (V_m), and Molar Sound Velocity (R_m) for Drug Parvon-spas with Concentration 3.72×10^{-2} mol·dm^{-3} in EtOH + Water Solvent System at 25°C

Mol. Frac. of EtOH	$\rho \times 10^{-3}$ (kg·m^{-3})	U (m·s^{-1})	$Z \times 10^{-6}$ (kg·m^{-2}·s^{-1})	$R.A.$	$\beta \times 10^{5}$ (bar^{-1})	$L_f \times 10^{11}$ (m)	V_m (cm^3·mol^{-1})	$R_m \times 10^4$ ((m·s^{-1})$^{1/3}$·m^3·mol^{-1})
0.0	0.9974	1503.0	1.499	1.0000	4.44	4.33	18.0	2.067
0.1	0.9656	1629.0	1.573	0.9424	3.89	4.06	21.5	2.534
0.2	0.9374	1564.0	1.466	0.9274	4.36	4.29	25.2	2.922
0.3	0.9071	1470.0	1.333	0.9162	5.10	4.64	29.1	3.309
0.4	0.8861	1402.0	1.242	0.9092	5.74	4.93	33.0	3.688
0.5	0.8639	1351.0	1.167	0.8974	6.33	5.18	37.0	4.094
0.6	0.8485	1309.0	1.110	0.8908	6.87	5.39	41.0	4.486
0.7	0.8317	1264.0	1.051	0.8834	7.52	5.64	45.2	4.888
0.8	0.8188	1232.0	1.008	0.8771	8.04	5.83	49.3	5.289
0.9	0.8064	1206.0	0.972	0.8700	8.52	6.00	53.5	5.702
1.0	0.7934	1169.0	0.927	0.8649	9.21	6.24	58.0	6.107

Table V. Density (ρ), Ultrasonic Velocity (U), Specific Acoustic Impedance (Z), Relative Association ($R.A.$), Adiabatic Compressibility (β), Intermolecular Free Length (L_f), Molar Volume (V_m), and Molar Sound Velocity (R_m) for PrOH + Water Solvent System at 25°C

Mol. Frac. of PrOH	$\rho \times 10^{-3}$ ($kg \cdot m^{-3}$)	U ($m \cdot s^{-1}$)	$Z \times 10^{-6}$ ($kg \cdot m^{-2} \cdot s^{-1}$)	$R.A.$	$\beta \times 10^{5}$ (bar^{-1})	$L_f \times 10^{11}$ (m)	V_m ($cm^3 \cdot mol^{-1}$)	$R_m \times 10^4$ ($(m \cdot s^{-1})^{1/3} \cdot m^3 \cdot mol^{-1}$)
0.0	0.997	1501.0	1.496	1.0000	4.45	4.34	18.0	2.067
0.1	0.9403	1506.0	1.416	0.9420	4.68	4.45	23.6	2.706
0.2	0.9196	1437.0	1.321	0.9358	5.26	4.72	28.7	3.239
0.3	0.8876	1383.0	1.227	0.9149	5.89	4.99	34.4	3.841
0.4	0.8668	1343.0	1.164	0.9024	6.39	5.20	40.1	4.429
0.5	0.8502	1313.0	1.116	0.8916	6.81	5.37	45.8	5.023
0.6	0.8366	1285.0	1.075	0.8837	7.23	5.53	51.6	5.613
0.7	0.8273	1269.0	1.049	0.8775	7.50	5.63	57.2	6.203
0.8	0.8168	1248.0	1.019	0.8712	7.85	5.77	63.1	6.801
0.9	0.8078	1232.0	0.995	0.8653	8.15	5.87	69.0	7.402
1.0	0.8000	1201.0	0.960	0.8643	8.66	6.05	75.0	7.972

Table VI. Density (ρ), Ultrasonic Velocity (U), Specific Acoustic Impedance (Z), Relative Association ($R.A.$), Adiabatic Compressibility (β), Intermolecular Free Length (L_f), Molar Volume (V_m), and Molar Sound Velocity (R_m) for Drug Parvon-spas with Concentration 3.72×10^{-2} mol·dm^{-3} in PrOH + Water Solvent System at 25°C

Mol. Frac. of PrOH	$\rho \times 10^{-3}$ (kg·m^{-3})	U (m·s^{-1})	$Z \times 10^{-6}$ (kg·m^{-2}·s^{-1})	$R.A.$	$\beta \times 10^{5}$ (bar^{-1})	$L_f \times 10^{11}$ (m)	V_m (cm^3·mol^{-1})	$R_m \times 10^4$ ((m·s^{-1})$^{1/3}$·m^3·mol^{-1})
0.0	0.9974	1503.0	1.499	1.0000	4.44	4.33	18.0	2.067
0.1	0.9445	1510.0	1.426	0.9454	4.63	4.43	23.5	2.696
0.2	0.9055	1439.0	1.303	0.9211	5.32	4.75	29.2	3.291
0.3	0.8896	1387.0	1.233	0.9161	5.84	4.97	34.4	3.836
0.4	0.8689	1348.0	1.171	0.9033	6.33	5.17	40.0	4.424
0.5	0.8509	1315.0	1.118	0.8919	6.79	5.36	45.8	5.021
0.6	0.8391	1291.0	1.083	0.8850	7.14	5.50	51.5	5.605
0.7	0.8280	1271.0	1.052	0.8778	7.47	5.62	57.2	6.201
0.8	0.8184	1251.0	1.023	0.8722	7.80	5.75	63.1	6.793
0.9	0.8117	1233.0	1.000	0.8693	8.10	5.85	68.7	7.371
1.0	0.8024	1211.0	0.971	0.8645	8.49	5.99	74.8	7.970

have been reported in Tables I–VI:

$$Z = U\rho \quad (1)$$

$$\beta = 1/(U^2\rho) \quad (2)$$

$$L_f = K/(U_{\exp}\ \rho^{1/2}{}_{\exp})^{1/2} = K\beta^{1/2} \quad (3)$$

$$R.A. = (\rho/\rho_0)(U/U_0)^{1/3} \quad (4)$$

$$V_m = M/\rho(\text{ in case of pure solvent }) = \overline{M}/\rho(\text{ where } \overline{M} = x_1M_1 + x_2M_2 \quad (5)$$

$$R_m = U^{1/3}V_m \quad (6)$$

where U, ρ and U_0, ρ_0 are the ultrasonic velocities and densities of the studied solution or solvent system and those of the pure solvent system, respectively, K is a temperature-dependent constant [16] ($K = \{93.875 + 0.375T\} \times 10^{-8}$; T is the absolute temperature), and V_m is the molar volume of the solvent, solvent mixture, or solution.

From the tables, it is evident that Z increases with the addition of MeOH up to 20 mol% and then decreases with further addition of alcohol. Similar behavior has been obtained with the addition of drug. However, for the EtOH + water mixture, a maximum is obtained at 10 mol% of EtOH. In the PrOH + water solvent system, a monotonic decrease in Z with the addition of PrOH has been observed. There is practically no change in the behavior of Z values for all studied alcohol systems with a fixed amount of drug indicating that Z values show similar behavior to that of ultrasonic velocity (U) data.

Compressibility (β) is an important parameter as its low value signifies the data of a compact structure characterized by a greater strength of bonding. These β-values have been evaluated as per above given equation and have been presented in Tables I to VI and in Fig. 1a,b,c for different solvent mixtures.

β values show a different behavior in these solvent systems. In the MeOH + H_2O system, β values first decrease up to 20 mol% of MeOH and then increase with further addition of MeOH. A minimum in the β-value has been obtained at 10 mol% of EtOH; however, these values show a regular decrease with the addition of PrOH to water in the PrOH + water system (Fig. 1a,b,c). Anomalous behavior of alcohol–water mixtures has also been reported in the literature [17], whereby small additions of an alcohol to water cause a decrease in compressibility, due to the making and breaking of hydrogen bonds. The general pattern for the compressibility behavior on adding alcohol in the presence of drug remains

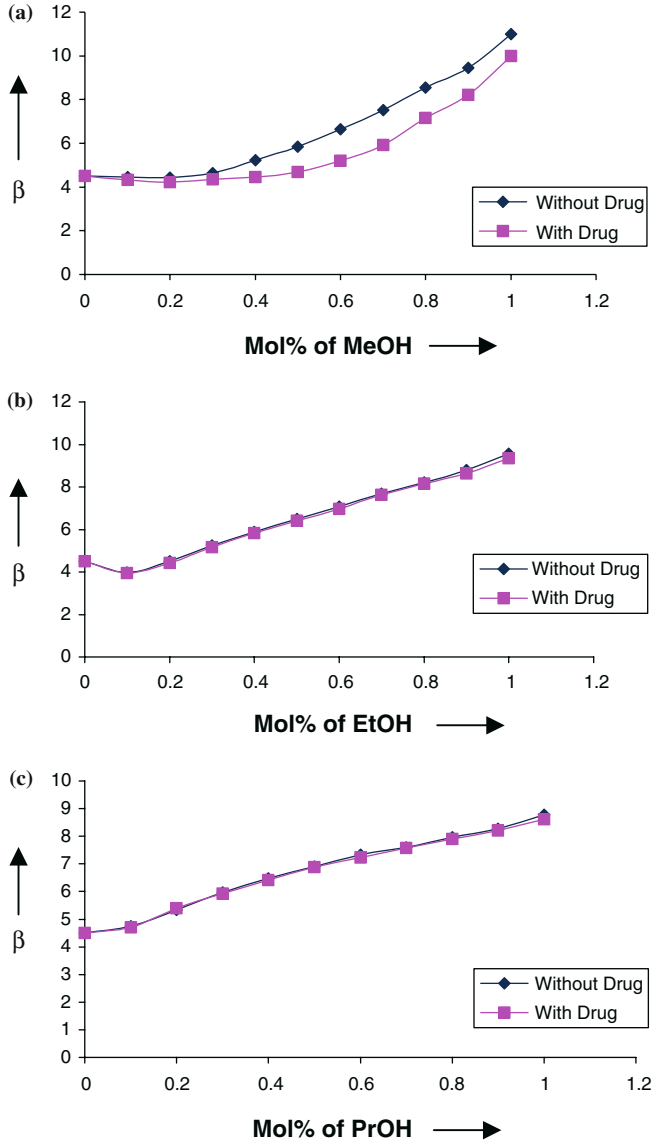


Fig. 1. (a) Plot of adiabatic compressibility versus composition of methanol–water with and without drug, (b) plot of adiabatic compressibility versus composition of ethanol–water with and without drug, and (c) plot of adiabatic compressibility versus composition of propan-1-ol-water with and without drug.

the same in all studied solvent systems. However, the difference in compressibility values of different alcohols in the studied aqueous alcohol mixtures can be attributed to different chain lengths of the alcohol molecule, the molecular volume, as well as inter/intramolecular interactions of these alcohols.

Eyring and Kincaid [18] have proposed that L_f is a predominant factor in determining the variation of the ultrasonic velocity of solutions. The change in the free length also indicates that there is significant interaction between the solute and solvent molecules due to which structural arrangement is also affected. From Tables I to VI, it is clear that L_f shows minima at 20 mol% of MeOH and 10 mol% of EtOH in MeOH + water and EtOH + water systems, respectively. L_f continues to increase with an increase of PrOH in PrOH + water mixtures. Since L_f is directly proportional to compressibility, it shows similar behavior as obtained for β and opposite to that of the ultrasonic velocity (U).

The values of the relative association ($R.A.$) for the studied solvent mixtures, suggest that $R.A.$ decreases with an increase of alcohol content. There is no appreciable variation in relative association ($R.A.$) values with the addition of drug. From Tables I to VI it is evident that the molar volume (V_m) decreases with an increase of water content to the studied aqueous alcohol systems. This shows that it depends upon the molecular mass and density of the studied alcohol as well as on the water content in the solvent mixtures. This also supports the decrease in $R.A.$ reported for all studied systems.

The molar sound velocities (R_m) (Tables I to VI), in general, show a linear increase with the addition of alcohol in all the studied solvent mixtures. No change in R_m has been noted with the addition of drug to solvent systems. Keeping one composition fixed (i.e., 0.6 mol%), the value of R_m shows the following variation for different studied alcohols:

$$\text{MeOH} < \text{EtOH} < \text{PrOH}$$
$$3.37 < 4.50 < 5.61$$

This indicates that R_m depends upon the composition, mass, and nature of the studied solvent system.

4. EXCESS THERMODYNAMIC FUNCTIONS

In an ideal solution, it is assumed that the value of an extensive property (P) obeys a simple additivity rule as given by the following equation:

$$P_{12(\text{ideal})} = x_1 P_1 + x_2 P_2 \tag{7}$$

where x denotes the mole fraction and the subscripts 1,2 and 12 denote the component, the two solvents and their binary mixtures, respectively. Deviations from the additivity rule, often expressed in terms of the excess property $[\Delta P^{E} = P_{12} - P_{12(\text{ideal})}]$ contain information about solute–solvent and solvent–solvent interactions.

The positive and negative deviations in these functions from a rectilinear dependence on composition of the mixture indicate the extent of dissociation or association between unlike molecules of the mixture. These deviations may be attributed to different type of interactions between like and unlike molecules in the mixtures. The excess volume is mainly influenced by two factors: (a) volume expansion due to dipole–dipole interactions of the component molecules and (b) contraction in volume due to hydrogen bonding or self-association between the solvent component molecules.

The values of the excess functions (β^{E}, L_f^{E}, and V^{E}) can be quantitatively examined by considering the factors that influence these properties. These excess properties depend upon several physical and/or chemical contributions. The physical contribution consists of dispersion forces or weak dipole–dipole interactions that lead to positive values of β^{E}, L_f^{E}, and V^{E}. Another factor, which involves a physical contribution, is the geometrical effect allowing the fitting of molecules of two different sizes into each other's structure resulting in negative β^{E}, L_f^{E}, and V^{E} values. Chemical contributions include breaking up of the associates present in pure liquids, resulting in positive β^{E}, L_f^{E}, and V^{E}, and specific interactions such as the formation of new hydrogen bonds, formation of charge transfer complexes, and other complex forming interactions between component molecules resulting in negative β^{E}, L_f^{E}, and V^{E} values.

Water and alcohol are hydrogen-bonded associated solvents. In the pure state, all these solvents have a tendency to associate through hydrogen bonding. Hence, the study of excess functions for these systems would be of immense importance for understanding the presence of molecular interactions.

The excess functions β^{E}, L_f^{E}, V^{E}, U^{E}, and Z^{E} have been evaluated and presented in Tables VII to IX using the following relation [19]:

$$Y^{E} = Y_{\text{exp}} - [Y_1 - (1 - x_1) + Y_2 x_2]$$

where Y represents the respective intensive physicochemical quantity, namely, β_{exp} and Z_{exp}, which represent the compressibility and specific acoustic impedance of pure component i with x_i being the mole fractions in the mixture.

The plot of excess properties β^{E}, U^{E}, Z^{E} for various solvent systems at 25°C have been given in Fig. 2a,b,c. From a perusal of Tables VII to IX,

Table VII. Excess Functions, Excess Adiabatic Compressibility (β^E), Excess Intermolecular Free Length (L_f^E), Excess Molar Volume (V^E), Excess Ultrasonic Velocity (U^E), and Excess Specific Acoustic Impedance (Z^E) for Methanol + Water Solvent System (Without and with Drug) at 25°C

Mol. Frac. of MeOH	(1) Without drug					(2) With drug				
	$\beta^E \times 10^6$ (Pa^{-1})	$L_f^E \times 10^{12}$ (m)	$V^E \times 10^7$ ($m^3 \cdot mol^{-1}$)	$U^E \times 10^{-1}$ ($m \cdot s^{-1}$)	$Z^E \times 10^{-4}$ ($kg \cdot m^{-2} \cdot s^{-1}$)	$\beta^E \times 10^6$ (Pa^{-1})	$L_f^E \times 10^{12}$ (m)	$V^E \times 10^7$ ($m^3 \cdot mol^{-1}$)	$U^E \times 10^{-1}$ ($m \cdot s^{-1}$)	$Z^E \times 10^{-4}$ ($kg \cdot m^{-2} \cdot s^{-1}$)
0.0	0.000	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.1	−6.563	−1.16	−4.28	6.54	5.51	−7.39	−3.00	−5.70	7.74	7.91
0.2	−12.78	−2.25	−7.40	12.68	10.31	−14.13	−5.70	−11.20	14.38	14.84
0.3	−16.81	−2.86	−9.32	15.22	11.54	−18.65	−7.30	−13.50	17.92	16.98
0.4	−16.91	−2.66	−10.71	11.96	7.89	−23.42	−9.03	−20.14	20.36	21.18
0.5	−16.74	−2.48	−10.50	9.80	5.30	−26.79	−10.11	−22.58	21.70	22.21
0.6	−14.73	−2.03	−10.28	6.54	2.54	−27.35	−9.93	−23.12	19.44	19.57
0.7	−11.91	−1.53	−9.22	3.88	0.65	−25.93	−9.03	−22.21	15.88	15.89
0.8	−7.66	−0.88	−3.93	1.92	−1.24	−19.22	−6.26	−1.621	9.42	8.81
0.9	−4.77	−0.54	−4.76	7.60	−0.29	−14.48	−4.60	−11.29	6.56	6.23
1.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Table VIII. Excess Functions, Excess Adiabatic Compressibility (β^E), Excess Intermolecular Free Length (L_f^E), Excess Molar Volume (V^E), Excess Ultrasonic Velocity (U^E), and Excess Specific Acoustic Impedance (Z^E) for Ethanol + Water Solvent System (Without and with Drug) at 25°C

Mol. Frac. of MeOH	(1) Without drug					(2) With drug				
	$\beta^E \times 10^6$ (pa^{-1})	$L_f^E \times 10^{12}$ (m)	$V^E \times 10^7$ ($m \cdot s^{-1}$)	$U^E \times 10^{-1}$ ($m^3 \cdot mol^{-1}$)	$Z^E \times 10^{-4}$ ($kg \cdot m^{-2} \cdot s^{-1}$)	$\beta^E \times 10^6$ (Pa^{-1})	$L_f^E \times 10^{12}$ (m)	$V^E \times 10^7$ ($m \cdot s^{-1}$)	$U^E \times 10^{-1}$ ($m^3 \cdot mol^{-1}$)	$Z^E \times 10^{-4}$ ($kg \cdot m^{-2} \cdot s^{-1}$)
0.0	0.00	0.00	0.00	0.000	0.00	0.000	0.00	0.00	0.000	0.00
0.1	−10.47	−4.66	−5.21	15.94	13.15	−10.27	−4.61	−4.99	15.94	13.10
0.2	−10.17	−3.98	−8.94	11.68	7.15	−10.48	−4.20	−8.57	12.78	8.13
0.3	−7.92	−2.58	−10.05	6.220	0.33	−7.82	−2.61	−9.22	6.72	0.58
0.4	−6.85	−1.90	−10.58	3.660	−2.66	−6.18	−1.70	−10.66	3.26	−2.81
0.5	−5.44	−1.22	−10.49	1.500	−4.52	−4.95	−1.10	−9.71	1.50	−4.61
0.6	−4.87	−0.99	−8.96	0.94	−4.68	−4.36	−0.86	−9.92	0.64	−4.54
0.7	−3.84	−0.68	−8.82	0.80	−4.16	−2.65	−0.30	−7.90	0.52	−4.77
0.8	−3.38	−0.66	−6.36	0.32	−2.83	−2.22	−0.29	−6.51	0.38	−3.30
0.9	−2.75	−0.65	−3.72	0.66	−1.08	−2.21	−0.49	−4.13	0.36	−1.21
1.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Table IX. Excess Functions, Excess Adiabatic Compressibility (β^E), Excess Intermolecular Free Length(L_f^E), Excess Molar Volume (V^E), Excess Ultrasonic Velocity (U^E), and Excess Specific Acoustic Impedance (Z^E) for Propanol + Water Solvent System (Without and With Drug) at 25°C

Mol. Frac. of MeOH	(1) Without drug					(2) With drug				
	$\beta^E \times 10^6$ (pa^{-1})	$L_f^E \times 10^{12}$ (m)	$V^E \times 10^7$ ($m^3 \cdot mol^{-1}$)	$U^E \times 10^{-1}$ ($m \cdot s^{-1}$)	$Z^E \times 10^{-4}$ ($kg \cdot m^{-2} \cdot s^{-1}$)	$\beta^E \times 10^6$ (Pa^{-1})	$L_f^E \times 10^{12}$ (m)	$V^E \times 10^7$ ($m^3 \cdot mol^{-1}$)	$U^E \times 10^{-1}$ ($m \cdot s^{-1}$)	$Z^E \times 10^{-4}$ ($kg \cdot m^{-2} \cdot s^{-1}$)
0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.000
0.1	−1.86	−0.57	−1.39	3.50	−2.68	−2.03	−0.67	−2.15	3.62	−2.016
0.2	−0.29	0.37	−7.35	−0.40	−6.78	8.40	8.42	−2.37	−56.0	−9.060
0.3	1.76	1.37	−6.62	−2.80	−10.82	1.89	1.39	−6.68	−2.84	−10.70
0.4	2.62	1.76	−6.84	−3.80	−11.81	2.74	1.78	−6.87	−3.82	−11.69
0.5	2.67	1.75	−6.55	−3.80	−11.23	3.32	1.97	−5.77	−4.20	−11.65
0.6	2.61	1.65	−5.84	−3.60	−10.00	2.79	1.69	−6.00	−3.68	−9.938
0.7	1.05	9.47	−6.21	−2.20	−7.16	1.98	1.26	−5.10	−2.76	−7.753
0.8	0.37	0.54	−4.37	−1.30	−4.85	1.23	0.83	−3.80	−18.4	−5.337
0.9	−0.89	−0.94	−2.28	0.10	−1.91	0.11	0.25	−3.58	−72.0	−2.362
1.0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.000

it is clear that with the increase of alcohol content in water, in general, excess functions β^E, L_f^E, and V^E are negative in magnitude, approach minima, and then increase with further addition of alcohol content. In ethyl–methyl ketone (EMK) and dimethyl formamide (DMF) solvent systems [20], β^E values are negative over the entire solvent composition range with a minimum at 70 mol% EMK. Similar behavior has also been shown for binary mixtures of MeOH in DMF [21] and the dimethyl sulphoxide (DMSO)–carbon tetrachloride (CTC) solvent system [22]. In the MeOH–water system, a minimum for β^E, L_f^E, and V^E lies at nearly 40 mol% of MeOH. This minimum shifts to around 60 mol% of MeOH with the addition of drug. However, U^E and Z^E being positive in magnitude, show a maximum at around 30 mol% of MeOH, which on addition of drug shifts to 50 mol% of MeOH. This shows that maximum structural changes lie around 30 to 40 mol% of MeOH and maximum solute-solvent interactions are present around 50 to 60 mol% of water + MeOH + drug system.

For the case of EtOH + water, β^E and Z^E attain minima at 10 mol% and V^E has a minimum around 40 mol% of EtOH with and without drug. U^E has a maximum around 10 mol% in the absence/presence of drug. However, Z^E has a maximum at 10 mol%, and becomes negative at 40 mol% showing a minimum at around 60 to 70 mol% of EtOH with and without drug.

In PrOH + water, β^E and L_f^E show maxima at around 40 to 50 mol% of PrOH, and V^E, U^E, and Z^E show minima at around 40 to 50 mol% with and without the addition of drug to the solvent system. This behavior in excess parameters can be compared with the AN–PC solvent system [1], where the dipole–dipole type of interactions exists between these molecules. The system shows positive deviations for Z^E whereas L_f^E and V_f^E show negative deviations from a rectilinear dependence.

On analyzing the above observations, it can be said that, although MeOH, EtOH, and PrOH all belong to the alcohol class, they have different solution behavior with water showing minima and maxima at different compositions of MeOH, EtOH, and PrOH. It can be further stated that a drug acting as a solute, in general, shows similar behavior to that of a solvent system but only increases the magnitude of a property, viz., density and velocity, and changes the magnitude of derived parameters, namely Z, $R.A.$, L_f, etc. and excess functions β^E, L_f^E, V^E, U^E, etc. due to solute–solvent interactions.

As these systems are characterized by hydrogen bonding, the solute–solvent interactions can be interpreted in terms of structural changes that arise due to hydrogen-bond interactions between various components of the solvent and solution systems.

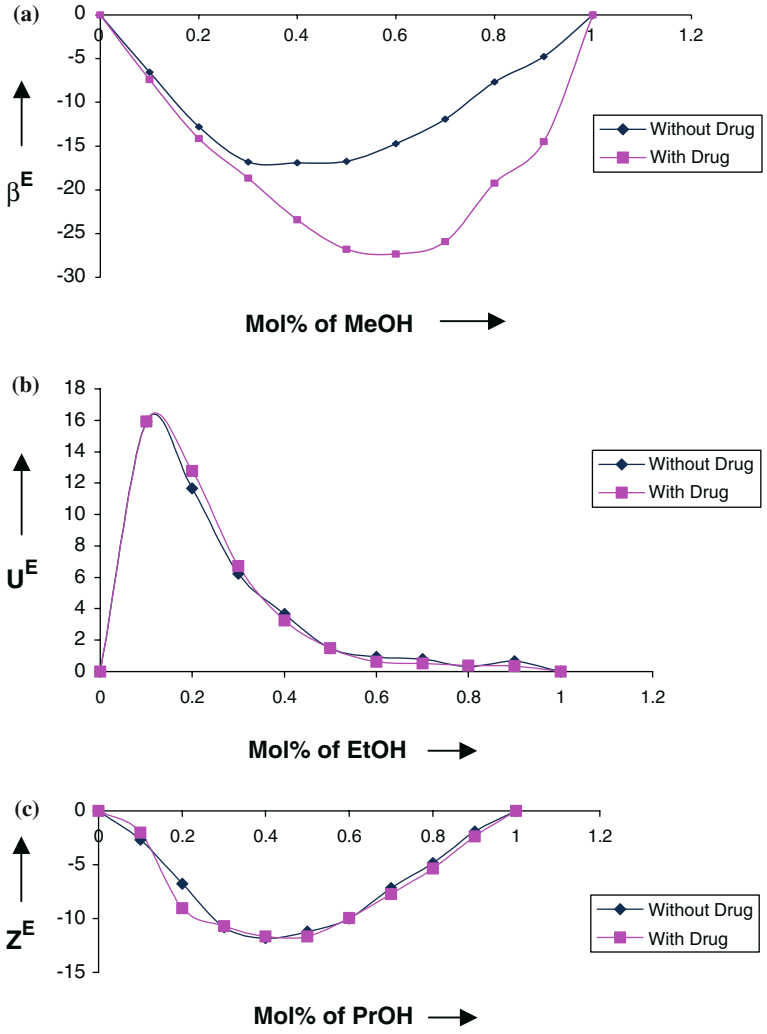


Fig. 2. (a) Plot of excess β versus composition of methanol–water with and without drug; (b) plot of excess U versus composition of ethanol–water with and without drug; and (c) plot of excess Z versus composition of propan-1-ol-water with and without drug.

ACKNOWLEDGMENT

Authors VKS, SC, and PS thank UGC, New Delhi for the sanction of research project F.12-145/2001 (SR-I) and award of project fellow under the project.

REFERENCES

1. S. Chauhan, V. K. Syal, and M. S. Chauhan, *Indian J. Pure Appl. Phys.* **32**:186 (1994); **33**:92 (1995).
2. V. K. Syal, G. Lal, P. Bisht, and S. Chauhan, *J. Mol. Liquids* **63**:317 (1995).
3. A. Korol Kovas, *Essentials of Medicinal Chemistry*, 2nd Ed. (Wiley, New York, 1988), Chap. 3.
4. J. B. Stenlake, *Foundations of Molecular Pharmacology* (Athlone Press, London, 1975).
5. M. Rowland and T. N. Tozer, *Clinical Pharmokinetics, Concepts and Applications* (Lea and Febiger, Malvern, Pennsylvania, 1989).
6. M. Gibaldi, *Biopharmaceuits and Clinical Pharmokinetics*, 4th Ed. (Lea and Febiger, Malvern, Pennsylvania, 1991).
7. M. S. Bakshi and G. Kumar, *J. Chem. Eng. Data* **42**:298 (1997).
8. A. Pal and G. Dass, *Zeitschrift fur Physikalische chemie* **215**:943 (2001).
9. P. Venkatesu and M. V. Prabhakar Rao, *Ind. J. Pure Appl. Phys*. **37**:59 (1999).
10. R. C. Weast, *CRC Handbook of Chemistry and Physics*, 69th Ed. (CRC Press Inc, Boca Raton, Florida, 1988–1989).
11. J. D. Pandey and Ashok Kumar, *J. Pure Appl. Ultrasonics* **16**:63 (1994).
12. Ashotosh Kar, *Medicinal Chemistry* (Wiley Eastern Ltd., New Delhi, 1993).
13. S. K. Maity, A. K. Chattopadhyay, and S. C. Lahari, *Electro Chimica Acta* **25**:148 (1980).
14. V. K. Syal, R. Gautam, and S. Chauhan, *Indian J. Pure Appl. Phys.* **36**:108 (1998).
15. V. K. Syal, R. Gautam, and S. Chauhan, *Ultrasonics* **36**:619 (1998).
16. V. Rajendran, *J. Pure Appl. Ultrasonics* **17**:65 (1995).
17. F. Franks and D. J. G. Ives, *Quart. Rev*. **20**:1 (1966).
18. B. Eyring and J. F. Kincaid, *J. Chem. Phys*. **6**:620 (1938).
19. M. S. Chauhan, K. C. Sharma, S. Gupta, M. Sharma, and S. Chauhan, *Acoustic Lett.* **18**:233 (1995).
20. V. K. Syal, B. S. Patial, and S. Chauhan, *Indian J. Pure Appl. Phys*. **37**:366 (1999).
21. M. S. Chauhan, K. C. Sharma, and S. Gupta, *Acoustic Lett.* **18**:233 (1995).
22. V. K. Syal, M. S. Chauhan, B. K. Chandra, and S. Chauhan, *J. Pure Appl. Ultrasonics* **18**:104 (1996).