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# A study of acoustical behaviour of drug colimax in aqueous mixture of methanol at 25$^0$C

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## ABSTRACT

*Ultrasonic velocity and density measurements for binary mixtures of methanol (MeOH) with water have been carried out at 10 mol% interval of the cosolvant at 25$^0$C. The experimental data have been used to estimate the various parameters such as the acoustic impedance (Z), adiabatic compressibility ($\beta$), intermolecular free length ($L_f$), relative association (R.A.), molar volume ($V_m$) and molar sound velocity ($R_m$). In addition, excess functions, i.e., excess adiabatic compressibility ($\beta^E$), excess intermolecular free length ($L_f^E$), excess molar volume ($V^E$), excess ultrasonic velocity ($U^E$) and excess acoustic impedance ($Z^E$) for the solvent mixtures with and without drug have been calculated. The behaviour of these parameters in these alcoholic systems has been discussed in terms of the length of the alcohol molecule, the molecular volume, as well as inter/intramolecular interactions.*

**Key words**: aqueous alcohol mixtures, density, drug, excess functions, ultrasonic velocity.

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## INTRODUCTION

Ultrasonic velocity and its related properties have been extensively used to study the physico-chemical behaviour and intermolecular interaction in a variety of liquid mixtures[1-2]. Ultrasonic velocity and viscosity studies have been made for various salts but these studies are rare for drugs. Therefore, the ultrasonic velocity and density of drug colimax are measured in binary mixture of methanol-water at 1 MHz with 10 mol% interval. From the measured data, various acoustical parameters have been calculated. The results of these studies would be helpful for pharmacological use of the drug.

## MATERIALS AND METHODS

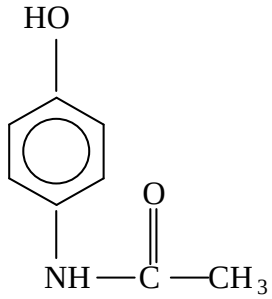
Methanol (extra pure, AR grade, SRL Pvt. Ltd Mumbai) and water were purified as described earlier [3]. The quality and purity of these solvents were checked by measuring density and

ultrasonic velocity. The measured values were compared with literature values and were found in close agreement [4].

Different compositions of the binary mixtures (MeOH-$H_2O$) were prepared at 10 mol% intervals and studied. Solutions containing a fixed amount of drug (0.250 g in 40 ml of a solvent/ solvent system) have also been prepared and studied.

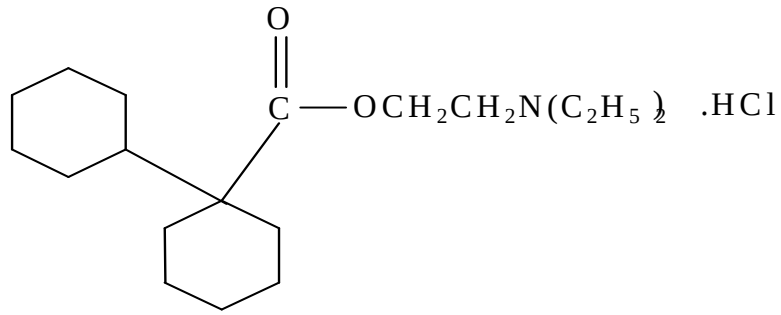
The densities of pure solvent and various mixtures have been measured with specially designed sealable type pycnometer of 20 $cm^3$ capacity, in a water thermostat precise to $25 \pm 0.02^0$C. The ultrasonic velocities in pure solvents as well as various mixtures were measured using Ultrasonic Interferometer (Model-81, supplied by Mittal Enterprises, New Delhi.) operating at a frequency of 1MHz. The temperature was maintained at $25 \pm 0.05^0$C by circulating thermostatic water around the cell with the help of pump. The calibration of the cell was made by measuring ultrasonic velocities of different pure non-aqueous solvents like ethylmethylketone, acetonitrile and acetone at $25^0$C. The drugs Colimax (Wallace Pharmaceuticals Pvt. Ltd., Goa - 403409) have been used as such after drying in the vacuum oven. The various components of drug in a tablet are paracetamol-500mg and dicyclomine hydrochloride-20mg having following structures [5].

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.*

The uncertainties of the density and ultrasonic velocity measurements were estimated to be ±0.02% 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 velocities are the average values of 4-5 determinations.

## RESULTS AND DISCUSSION

The experimental values of density and ultrasonic velocity for MeOH-$H_2O$, with and without drug are presented in tables (1, 2).

It is clear (from table-1, 2 and fig-1), that density values decrease with the increase in alcohol content for the studied solvent system. However, with the addition of drug these values increases. Similar behavior has been reported by Maity et al. [6] for EtOH-$H_2O$ and MeOH-$H_2O$ solvent systems. It is evident from perusal of these tables and fig.-2, that the ultrasonic velocity increases with the addition of MeOH in MeOH-$H_2O$ mixtures up to 20 mol% of MeOH, and then decreases with further addition of MeOH. At 16 mass% MeOH and 25 mass% EtOH in MeOH-$H_2O$ and EtOH-$H_2O$ mixtures such maxima in the ultrasonic velocity have also been reported [6] which show close agreement between the experimental values of this study and literature results. Syal et al. [7] also reported that, in acetonitrile (AN)-$H_2O$ mixtures 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 as AN acts as a structure breaker. With the addition of drug there is increase in the ultrasonic velocity but the general behavior remains same as for the studied pure solvent system. Syal et al. has reported a similar effect in the case of sucrose in AN-$H_2O$ [7] and DMSO-$H_2O$ [8] solvent mixtures. This shows that solute-solvent interactions, though present, do not alter the solvent-solvent interactions already present in the binary mixtures. However, the addition of a solute is indicative of greater association of molecules due to effective solute-solvent interactions [8], which results in the increase in ultrasonic velocity in any solution.

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 have been reported in tables (1,2):

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

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

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

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

$$V_m = M/\rho \text{ (in case of pure solvent)}$$

$$= \underline{M}/\rho \text{ (where } \underline{M} = x_1M_1 + x_2M_2 \quad (5)$$

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

where U, ρ and $U_0$, $\rho_0$ are velocities and densities of the studied solution or solvent system and those of the pure solvent system, respectively, K is a temperature- dependent constant [9] ( $K = \{93.875 + 0.375T\} \times 10^{-8}$ ;T is absolute temperature) and $V_m$ is the molar volume of the solvent, solvent mixture, or solution.

There is an increase in the Z values with the addition of MeOH up to 20 mol% and then it decreases with further addition of alcohol. Similar behavior has been obtained with the addition of drug as shown in fig.3. It indicates that the Z-values show similar behavior to that of ultrasonic velocity (U) data.

Another important parameter is Compressibility (β), 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 the above given equation and have been presented in tables (1, 2) and in fig.(4) for solvent mixtures.

β values show a different behavior in this solvent system. In the MeOH-$H_2O$ system, β values first decrease upto 10 mole% of MeOH and then increases with further addition of MeOH. Anomalous behavior of alcohol-$H_2O$ mixtures have also been reported in the literature [10], 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 the same in studied solvent system.

As proposed by Eyring and Kincaid [11] that $L_f$ is a predominating factor in determining the variation of the ultrasonic velocity of solutions. The change in 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 (1, 2), it is clear that $L_f$ shows minima at 10 mol% of MeOH. 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 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. It is evident from tables (1, 2) 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 mixture.

The molar sound velocity ($R_m$) (tables1, 2) in general, shows a linear increase with the addition of alcohol in the studied solvent mixtures. No change in $R_m$ has been noted with the addition of drug to solvent systems.

**Excess thermodynamic function:**
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:

$$P_{12(ideal)} = x_1P_1 + x_2P_2$$

where x denotes the mole fraction and the subscripts 1, 2 and 12 denotes the component, the two solvents and their binary mixtures, respectively. Deviation from the additivity rule, often expressed in terms of the excess property [$\Delta P^E = P_{12} - P_{12\ (ideal)}$] contains 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 the excess volume which 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 excess functions ($\beta^E$, $L_f^E$, 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 $\beta^E$, $L_f^E$, 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 $\beta^E$, $L_f^E$, and $V^E$ values.

Chemical contributions include breaking up of the associates present in pure liquids, resulting in positive $\beta^E$, $L_f^E$, 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 $\beta^E$, $L_f^E$, 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 $\beta^E$, $L_f^E$, $V^E$, $U^E$ and $Z^E$ have been evaluated and given in tables (3) using the following relation [12]:

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

where Y represents the respective intensive physico-chemical quantity, namely $\beta_{exp}$ and $Z_{exp}$, which represent the compressibility and specific acoustic impedance of pure component i with $x_i$ being their mole fractions in the mixture.

**Table 1: 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-$H_2O$ Solvent System at $25^0$C.**

| Mol. Frac. of MeOH | $\rho x10^{-3}$ ($kg.m^{-3}$) | U ($m.s^{-1}$) | Z X $10^{-6}$ ($Kg.m^{-2}.s^{-1}$) | R.A. | $\beta$ x$10^5$ ($Bar^{-1}$) | $L_f$ x $10^{11}$ (m) | $V_m$ x $10^5$ ($cm^3.mol^{-1}$) | $R_m$ x $10^4$ ($m.s^{-1}$)$^{1/3}$ $m^3mol^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| 0.0 | 0.9970 | 1501.0 | 1.496 | 1.0000 | 4.45 | 4.34 | 1.80 | 2.067 |
| 0.1 | 0.9750 | 1527.0 | 1.488 | 0.9723 | 4.40 | 4.22 | 1.99 | 2.291 |
| 0.2 | 0.9516 | 1549.0 | 1.474 | 0.9445 | 4.38 | 4.32 | 2.19 | 2.529 |
| 0.3 | 0.9274 | 1535.0 | 1.423 | 0.9232 | 4.57 | 4.40 | 2.39 | 2.761 |
| 0.4 | 0.9052 | 1463.0 | 1.324 | 0.9157 | 5.16 | 4.67 | 2.61 | 2.959 |
| 0.5 | 0.8814 | 1402.0 | 1.235 | 0.9043 | 5.77 | 4.94 | 2.84 | 3.174 |
| 0.6 | 0.8611 | 1330.0 | 1.145 | 0.8992 | 6.56 | 5.27 | 3.06 | 3.371 |
| 0.7 | 0.8415 | 1264.0 | 1.063 | 0.8937 | 7.43 | 5.61 | 3.30 | 3.572 |
| 0.8 | 0.8148 | 1205.0 | 0.981 | 0.8793 | 8.44 | 5.98 | 3.58 | 3.813 |
| 0.9 | 0.8047 | 1154.0 | 0.928 | 0.8810 | 9.32 | 6.28 | 3.80 | 3.988 |
| 1.0 | 0.7848 | 1107.0 | 0.868 | 0.8712 | 10.85 | 6.63 | 4.08 | 4.218 |

The plot of excess properties $U^E$, $Z^E$ for various solvent systems at $25^0$C have been given in fig. (5, 6). From a perusal of tables (1, 2) it is clear that with the increase of alcohol content in water, in general, excess functions $\beta^E$, $L_f^E$, 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 [13], $\beta^E$ 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 [12] and the dimethyl sulphoxide (DMSO)-carbon tetra chloride (CTC) solvent system [15]. In the MeOH-$H_2O$ system, a minimum for $\beta^E$, $L_f^E$ 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 50-60 mol% of $H_2O$-MeOH-drug system.

**Table 2: 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 Colimax with Concentration $4.05 \times 10^{-2}$ mol. $dm^{-3}$ in MeOH-$H_2O$ Solvent System at $25^0$C.**

| Mol. Frac. of MeOH | $\rho x10^{-3}$ ($kg.m^{-3}$) | U ($m.s^{-1}$) | Z X $10^{-6}$ ($Kg.\ m^{-2}.s^{-1}$) | R.A. | $Bx10^5$ ($Bar^{-1}$) | $L_f$ x $10^{11}$ (m) | $V_m$ x $10^5$ ($cm^3.mol^{-1}$) | $R_m$ x $10^4$ ($m\ .s^{-1})^{.1/3}$ $m^3mol^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| 0.0 | 0.9974 | 1503.0 | 1.499 | 1.0000 | 4.50 | 4.33 | 1.80 | 2.067 |
| 0.1 | 0.9960 | 1572.0 | 1.566 | 0.9838 | 4.12 | 4.14 | 1.95 | 2.265 |
| 0.2 | 0.9679 | 1557.0 | 1.507 | 0.9591 | 4.32 | 4.24 | 2.15 | 2.491 |
| 0.3 | 0.9369 | 1541.0 | 1.444 | 0.9316 | 4.55 | 4.36 | 2.37 | 2.737 |
| 0.4 | 0.9132 | 1500.0 | 1.370 | 0.9162 | 4.93 | 4.54 | 2.58 | 2.958 |
| 0.5 | 0.8896 | 1476.0 | 1.313 | 0.8973 | 5.23 | 4.67 | 2.81 | 3.200 |
| 0.6 | 0.8890 | 1419.0 | 1.233 | 0.8881 | 5.79 | 4.92 | 3.04 | 3.414 |
| 0.7 | 0.8505 | 1350.0 | 1.148 | 0.8838 | 6.54 | 5.22 | 3.27 | 3.613 |
| 0.8 | 0.8319 | 1272.0 | 1.058 | 0.8818 | 7.53 | 5.60 | 3.51 | 3.803 |
| 0.9 | 0.8144 | 1196.0 | 0.974 | 0.8811 | 8.70 | 6.02 | 3.76 | 3.988 |
| 1.0 | 0.7886 | 1111.0 | 0.876 | 0.8745 | 10.4 | 6.59 | 4.06 | 4.203 |

**Table 3: Excess Functions, Excess Adiabatic Compressibility ($\beta^E$), Excess Inter Molecular Free Length ($L_f^E$), Excess Molar Volume ($V^E$), Excess Ultrasonic Velocity ($U^E$) and Excess Specific Acoustic impedance ($Z^E$) for MeOH-$H_2O$ Solvent System (Without and With Drug) at $25^o$C.**

| | 1) Without drug: | | | | | 2) With drug: | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Mol. Frac. of MeOH | $\beta^E x10^6$ ($Pa^{-1}$) | $L_f^E x10^{12}$ (m) | $V^E x10^7$ ($m^3.mol^{-1}$) | $U^E x10^{-1}$ ($m.s^{-1}$) | $Z^E x10^{-4}$ ($kg.m^{-2}.s^{-1}$) | $\beta^E x10^6$ ($pa^{-1}$) | $L_f^E x10^{12}$ (m) | $V^E x10^7$ ($m^3.mol^{-1}$) | $U^E x10^{-1}$ ($m.s^{-1}$) | $Z^E x10^{-4}$ ($Kg.m^{-2}.s^{-1}$) |
| 0.0 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 |
| 0.1 | -6.563 | -1.16 | -4.280 | 6.540 | 5.510 | -0.971 | -4.13 | -8.220 | 10.82 | 12.89 |
| 0.2 | -12.78 | -2.25 | -7.400 | 12.68 | 10.31 | -13.61 | -5.39 | -10.63 | 13.24 | 13.25 |
| 0.3 | -16.81 | -2.86 | -9.320 | 15.22 | 11.54 | -17.16 | -6.50 | -11.11 | 15.56 | 13.16 |
| 0.4 | -16.91 | -2.66 | -10.71 | 11.96 | 7.890 | -19.30 | -6.99 | -12.16 | 15.38 | 11.99 |
| 0.5 | -16.74 | -2.48 | -10.50 | 9.800 | 5.300 | -22.25 | -7.91 | -12.10 | 16.90 | 12.54 |
| 0.6 | -14.73 | -2.03 | -10.28 | 6.540 | 2.540 | -22.53 | -7.71 | -11.86 | 15.12 | 10.78 |
| 0.7 | -11.91 | -1.53 | -9.220 | 3.880 | 0.650 | -20.98 | -6.90 | -11.32 | 12.14 | 8.520 |
| 0.8 | -7.660 | -0.88 | -3.930 | 1.920 | -1.240 | -16.99 | -5.34 | -9.720 | 8.260 | 5.750 |
| 0.9 | -4.770 | -0.54 | -4.760 | 7.600 | -0.290 | -11.20 | -3.40 | -7.510 | 4.580 | 3.560 |
| 1.0 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 |

This behavior in excess parameters can be compared with the AN-PC solvent system [2], 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.

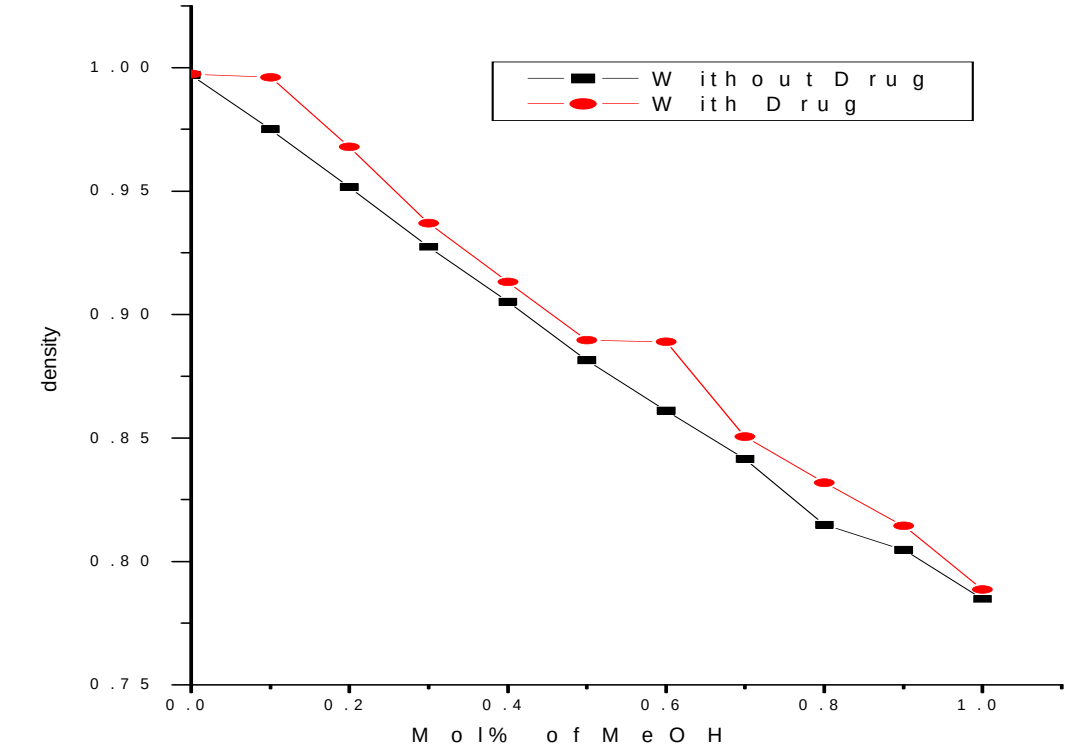



**Fig.1 Plot of Density vs composition of MeOH-$H_2O$ with and without drug.**

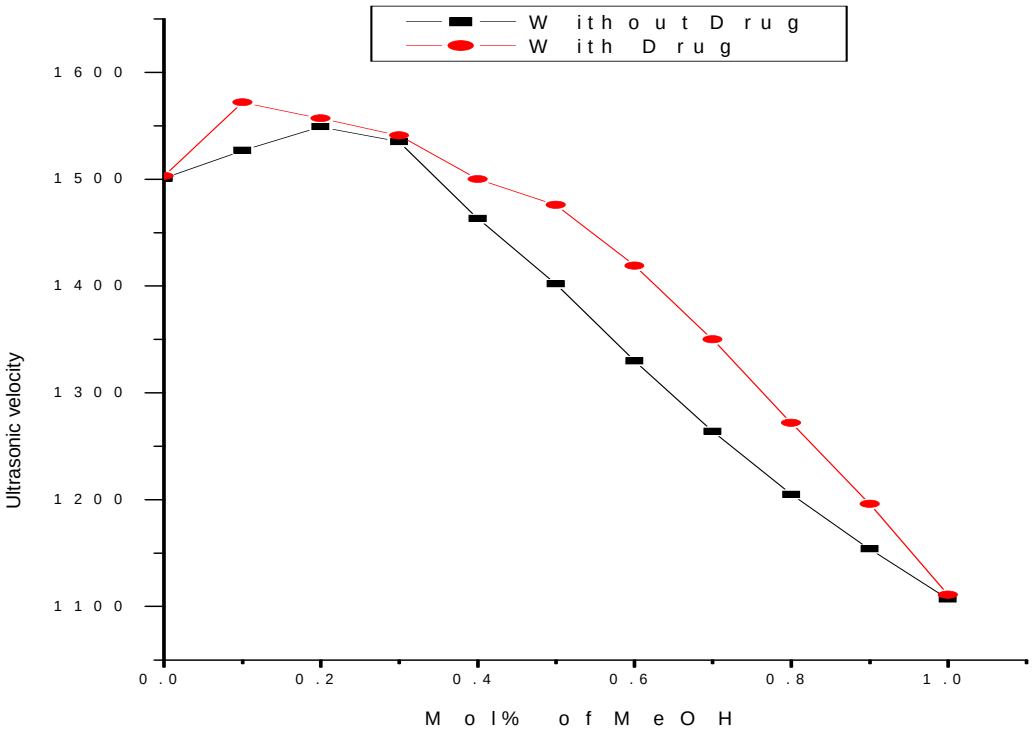



**Fig.2 Plot of Ultrasonic velocity vs composition of MeOH-$H_2O$ with and without drug.**

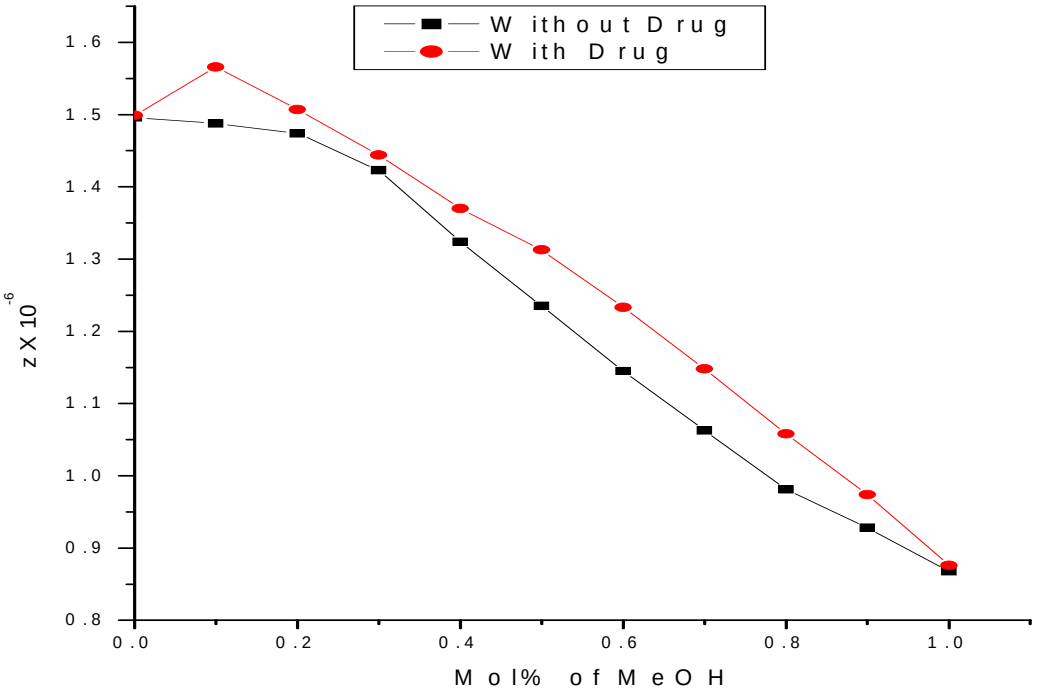



**Fig.3 Plot of Specific acoustic impedance (Z) vs composition of methanol-water with and without drug.**

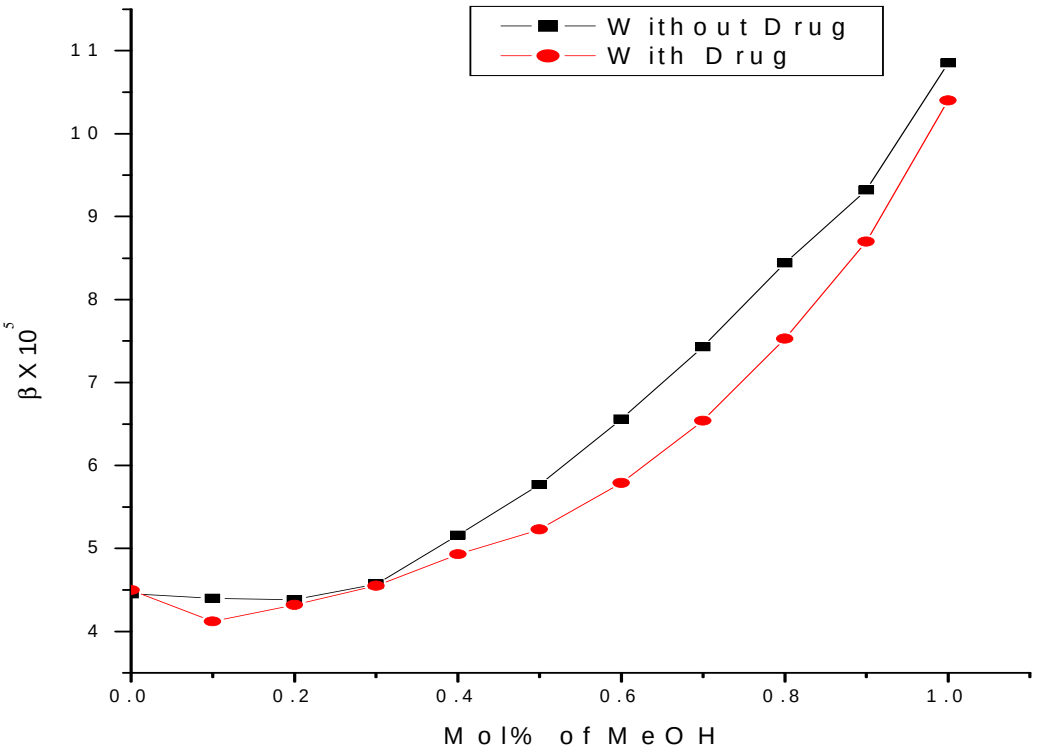



**Fig.4 Plot of Adiabatic compressibility (β) vs composition of methanol-water with and without drug.**

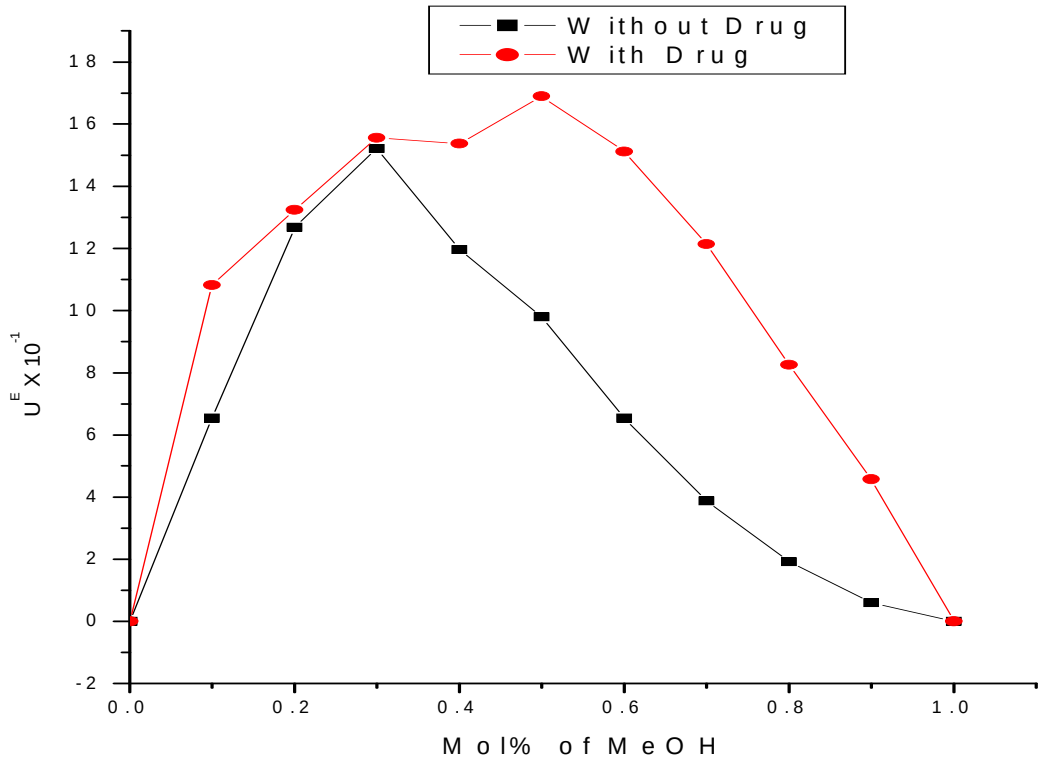



**Fig.5 Plot of Excess Ultrasonic Velocity ($U^E$) vs composition of methanol-water with and without drug.**

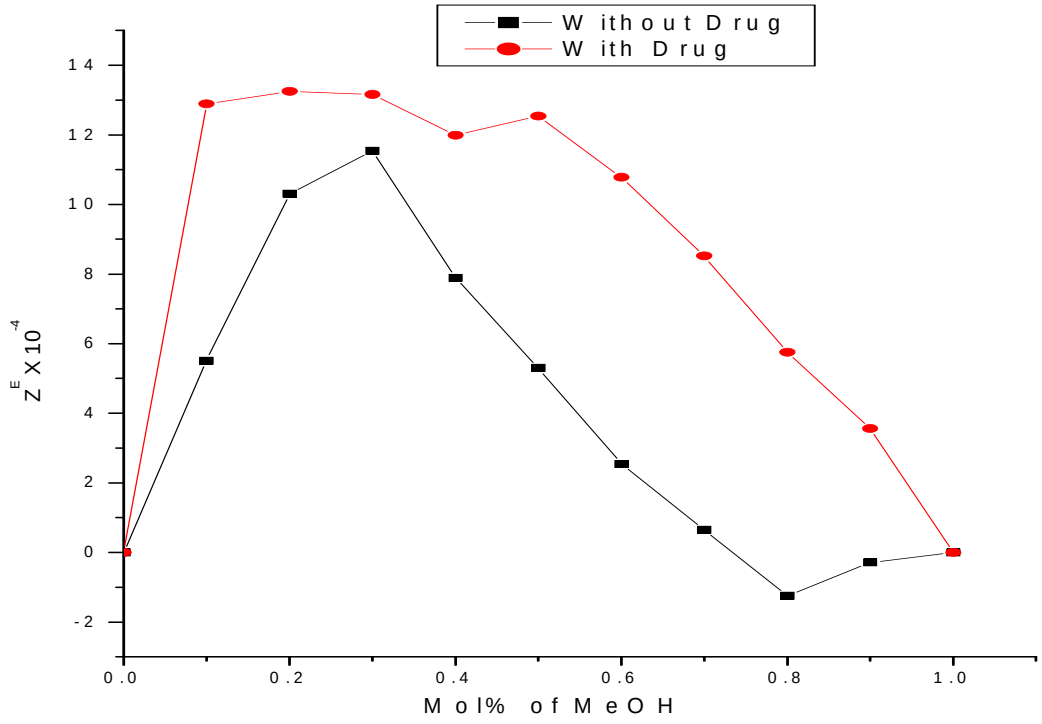



**Fig.6 Plot of Excess Specific Acoustic Impedance ($Z^E$) vs composition of methanol-water with and without drug.**

On analysing the above observations, it can be stated that drug acting as a solute, in general shows similar behaviour to that of 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 $\beta^E$, $L_f^E$, $V^E$, $U^E$ 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, which arise due to hydrogen-bond interactions between various components of the solvent and solution systems.

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