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A Study of Acoustical Behaviour of Paracetamol in 70% Methanol at Various Temperature.

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Abstract: Molecular Interaction of antipyretic & analgesic activity having Paracetamol have been investigated using 70% methanol solution. The experimental values of density (ρ), viscosity (η), and ultrasonic velocity (U) of Paracetamol drug in 70% Methanol Solution within the concentration range 0.002M to 0.01M at different temperature i.e. $T = (303.15, 308.15, 313.15, 318.15, 323.15)K$ are reported. From the experimental values different derived parameters such as adiabatic compressibility (β), viscous relaxation time (τ), relative association (R_A), acoustic impedance (Z) and intermolecular free length (L_f) were computed. The result are interpreted in terms of various interaction such as solute – solvent interactions, and structure - making and structure - breaking abilities of the solute in 70% methanol Solvent.

Keywords: Paracetamol, 70% methanol, density, viscosity, ultrasonic velocity.

I. Introduction

Understanding the action of drugs in aqueous 70% methanol solution has been a subject of research. Physico-chemical behavior and intermolecular interaction provide useful information in pharmaceutical and medicinal chemistry. The drug –solvent molecular interaction and their temperature dependence play an important role in the understanding of drug action^[1-4]. Acoustical and Viscometric properties provide valuable clues for solute-solvent interactions in the solution phase which can be helpful in predicting the absorption of drug and transport of drug across the biological membranes. Hence, it may be interesting to study the variation of their properties with temperature for understanding the mechanism of action of drug^[5-6].

In the present paper, we tried to investigate the acoustical properties of pharmacologically significant Paracetamol drug molecules in 70% methanol solvent. Paracetamol (*N*-(4-hydroxyphenyl)acetamide) is a major ingredient in numerous medications due to its analgesic, anti-inflammatory, antipyretic and slightly anti-microbial and anti-fungal activity. It is commonly used for the relief of fever, headaches, and other minor aches and pains, and is a major ingredient in numerous cold and flu remedies^[7-10].

In the present work, we represent the continuation of a systematic investigation of the viscometric and acoustical properties of Paracetamol drug molecules in 70% methanol solution at various temperatures $T = (303.15, 308.15, 313.15, 318.15$ and $323.15)K$ within the concentration range 0.002M to 0.01M. The derived parameters such as adiabatic compressibility (β), viscous relaxation time (τ), relative association (R_A), acoustic impedance (Z) and intermolecular free length (L_f) were computed from the experimental values of density (ρ), viscosity (η), and ultrasonic velocity (U).

II. Experimental

Materials: The drug Paracetamol (CAS No. 103-90-2, minimum assay value 99.74%) used in this study have been procured from Relief Lab Pvt. Ltd., Kalmeshwar which were dried in vacuum oven and were kept in vacuum desiccator over anhydrous fused calcium chloride before use. They were used without any further purification. All the mixtures were prepared in freshly prepared 70% Methanol on a molarity basis by using Digital Balance (Shimadzu AU X 220, UniBloc Ltd.) with an accuracy $\pm 0.1mg$. Methanol of HPLC grade which procured from Merck India Specialities P.Ltd. and double distilled water was used.

Method: The density (ρ) of the solutions were measured at $T = (303.15K, 308.15K, 313.15K, 318.15K, 323.15K)$ by using Digital Densitometer (Model-DDM 2910, Rudolph Research analytical, USA.). The accuracy in density measurement was found to be $\pm 0.0001g/ml$. The viscometric measurements were made by Ostwald's Viscometer with an accuracy $0.001 Ns m^{-2}$. The ultrasonic velocity (U) was measured by using variable path single crystal interferometer (Model F-81S, Mittal Enterprises, India) at fixed frequency of 2MHz with accuracy of 0.03%. The temperature was maintained with an accuracy of $0.1^\circ C$. Electronically digital operated constant temperature bath (Plasto Craft Industries) for low temperature bath model, LTB-10 was used to circulate water

through the double walled measuring cell made up of steel containing the experimental solution at the desired temperature with accuracy in temperature measurement -10°C to 90°C .

III. Results and Discussion

The data of density, viscosity and velocity at different temperatures are listed in table 1. The relative association (R_A), acoustic impedance (Z) and viscous relaxation time (τ) have been calculated by using the density (ρ), viscosity (η) and ultrasonic velocity (U) in 70% Methanol solutions of Paracetamol drugs at $T = (303.15\text{K}, 308.15\text{K}, 313.15\text{K}, 318.15\text{K}, 323.15\text{K})$ using following equations and are listed in Table 1.:

$$R_A = \left(\rho_s / \rho_o \right) \left(U_o / U_s \right)^{1/3} \quad Z = U_s \cdot \rho_s \quad \tau = 4\eta_s / 3\rho_s U_s^2$$

The adiabatic compressibility (β_s) of the solution has been calculated using the well-known Newton-Laplace equation, assuming that the absorption of wave is negligible and from the computed values of adiabatic compressibility (β_s), intermolecular free length (L_f) has been calculated by using following equation and are listed in Table 1:

$$\beta_s = 1/U_s^2 \rho_s \quad L_f = K \sqrt{\beta_s}$$

where K is temperature dependant Jacobson Constant.

ρ_s , η_s and U_s are the density, viscosity and ultrasonic velocity of solution.

Table I: Density (ρ), viscosity (η), ultrasonic velocity (U), relative association (R_A), acoustic impedance (Z), viscous relaxation time (τ), adiabatic compressibility (β) and intermolecular free length(L_f) of solutions at $T = (303.15, 308.15, 313.15, 318.15, 323.15)\text{K}$.

Temp., K	c, M	ρ , kg m ⁻³	η , N s m ⁻²	U , m s ⁻¹	R_A	$Z \times 10^6$, Nm ⁻²	$\tau \times 10^{-10}$, s	$\beta \times 10^{-10}$, m ² N ⁻¹	L_f , Å
303.15	0.002	876.1	1.135875	1386.267	0.996614	1.2145	8.99543	5.93954	0.5057
	0.004	876.3	1.146802	1368.267	1.003377	1.1990	9.32036	6.09545	0.5123
	0.006	876.4	1.146933	1379.867	0.999265	1.2093	9.16432	5.99271	0.5080
	0.008	876.6	1.152531	1381.6	0.998866	1.2111	9.18386	5.97632	0.5073
	0.01	876.8	1.163468	1381.867	0.998997	1.2116	9.26531	5.97265	0.5071
308.15	0.002	871.8	1.034782	1371.867	0.996951	1.1960	8.409044	6.094795	0.5172
	0.004	872.0	1.040327	1357.067	1.002602	1.1834	8.63753	6.22703	0.5228
	0.006	872.2	1.045755	1354.533	1.003654	1.1813	8.71411	6.24963	0.5237
	0.008	872.3	1.051304	1357.467	1.002799	1.1841	8.72053	6.22122	0.5225
	0.01	872.4	1.056735	1358.533	1.002521	1.1852	8.75082	6.21075	0.5221
313.15	0.002	867.3	0.923857	1357.867	0.997214	1.1777	7.703	6.2534	0.5289
	0.004	867.5	0.92935	1350.8	1.00005	1.1718	7.82828	6.31755	0.5316
	0.006	867.7	0.934846	1352	0.999836	1.1731	7.85879	6.30488	0.5311
	0.008	867.9	0.940345	1345.867	1.002343	1.1681	7.97539	6.36101	0.5334
	0.01	868.0	0.945736	1356.4	0.998558	1.1774	7.89612	6.26188	0.5293
318.15	0.002	862.7	0.84544	1348.933	0.995955	1.1637	7.18094	6.37029	0.5389
	0.004	862.9	0.850889	1333.733	1.001847	1.1509	7.39117	6.51481	0.5449
	0.006	863.0	0.850987	1352	0.995171	1.1668	7.19279	6.33922	0.5375
	0.008	863.2	0.861693	1336.8	1.001045	1.1539	7.44813	6.4827	0.5436
	0.01	863.3	0.867048	1346.533	0.997536	1.1625	7.3856	6.38858	0.5396
323.15	0.002	857.9	0.778073	1321.6	1.003038	1.1338	6.92345	6.67365	0.5567
	0.004	858.1	0.783477	1328.533	1.000651	1.1400	6.89736	6.60264	0.5537
	0.006	858.2	0.794016	1316.933	1.005165	1.1302	7.11299	6.71868	0.5586
	0.008	858.4	0.794201	1331.2	0.999997	1.1427	6.96134	6.57391	0.5525
	0.01	858.6	0.799613	1324.133	1.002896	1.1369	7.08214	6.64272	0.5554

Figure 1: Variation of Density with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.

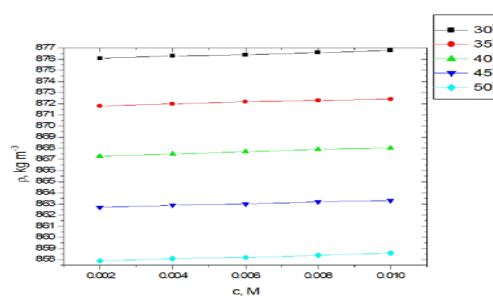


Figure 2: Variation of Viscosity with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.

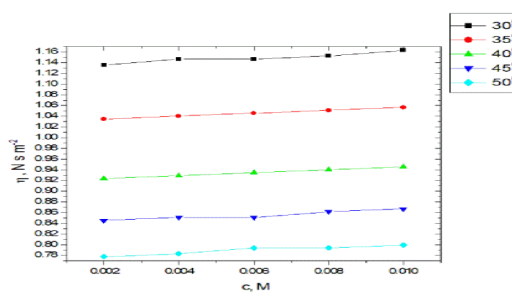


Figure 3: Variation of Ultrasonic Velocity with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.

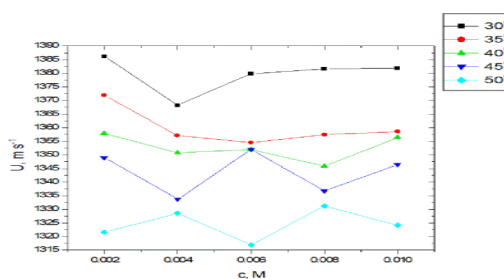


Figure 4: Variation of Relative Association with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.

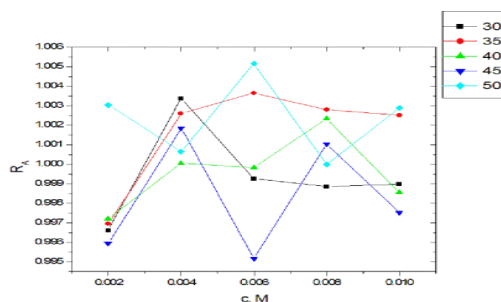


Figure 4: Variation of Acoustic Impedance with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.

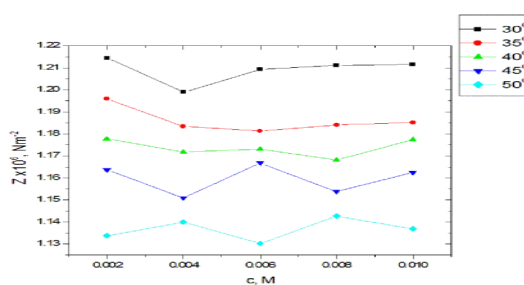


Figure 7: : Variation of Viscous Relaxation Time with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.

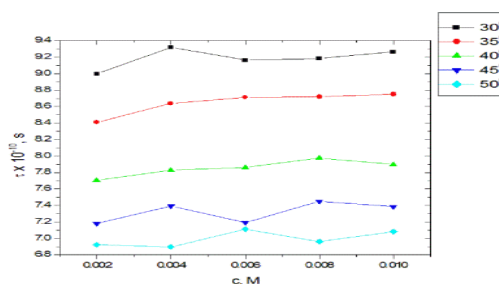


Figure 7: : Variation of Adiabatic Compressibility with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.

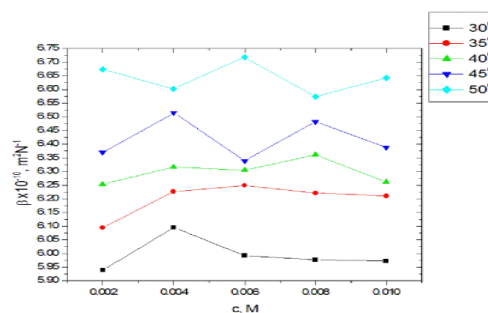
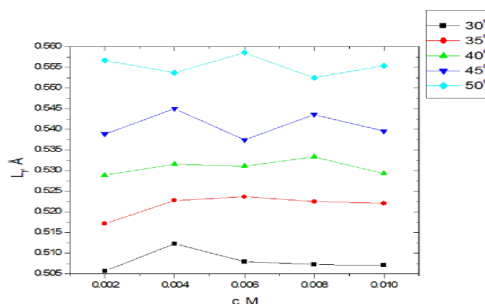


Figure 8: Variation of Intermolecular Free Length with Concentration of solutions at T = (303.15, 308.15, 313.15, 318.15, 323.15)K.



The figures represents the variation of concentration with density, viscosity, ultrasonic velocity, adiabatic compressibility, acoustic impedance, relative association, intermolecular free length and viscous relaxation time of solutions T = (303.15K, 308.15K, 313.15K, 318.15K, 323.15K) where X - axis represents concentration change and Y – axis represents the change in viscometric and acoustical properties.

It is evident from Fig. 1, that the density of solution increases continuously with the increase in molarity and decrease in temperature of solution for all the systems of Paracetamol within the concentration and temperature range studied^[11]. Variation in viscosity indicates the presence of intermolecular interactions between the Paracetamol molecules and solvent molecules. It is observed from Fig. 2, that viscosity of solution increases with the increase in concentration and decrease in temperature. The increasing concentration of drug supports non rupturing of molecules hence there is increase in viscosity but when there is a increase in temperature of solution rupturing of molecules takes place hence viscosity decreases^[12].

Fig. 3, shows that ultrasonic velocity of solution increases with the increase in molarity and the decrease in temperature of solution for all the systems. As density of solution increases the number of particles in a given region increases and this leads to quick transfer of sound energy and thus velocity also increases but when temperature is increases the density of solution is decrease so that number of particles in a given region decreases hence there is not quick transfer of sound energy and thus velocity also decreases. This suggests the disruption of solvent structure with the addition of drug molecules and effect of temperature^[13]. Fig. 4, shows that the relative association increases with increase in temperature and the increase of concentration of solution. This is due to the solute-solvent interaction dominates over solvent-solvent interactions. It depends on either the

breaking up of the solvent molecules on addition of drug molecules in solvent at certain temperature or the solvation of ions that are present^[14].

Fig. 5, indicates that the acoustic impedance increases with decrease in temperature and increase in concentration of solution. The increase of acoustic impedance with concentration is due to the effective solute-solvent interactions^[15]. Fig. 6, shows that the relaxation time increases with increase in concentration and decrease in temperature of solution. The variation of relaxation time is a cumulative effect of the density, viscosity and ultrasonic velocity^[16].

It is observed from Fig. 7, that adiabatic compressibility decreases with decreasing temperature and increase of solute concentration for all the drug systems. The decrease of adiabatic compressibility with increasing concentration clearly indicate the presence of solute-solvent interactions due to aggregation of solvent molecules around solute molecules^[17]. Fig. 8 shows L_f increases with increase in temperature and decrease in concentration of solution which suggest that there is strong interaction between solvent and drug molecules^[18].

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