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Molecular Interaction of NSAID in Protic and Aprotic Solvent Mixture- An Acoustical and Viscometric Study

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ABSTRACT

The density (ρ), viscosity (Π) and ultrasonic velocity (U) of non-steroid anti-inflammatory drug was measured in the mixture of DMSO and methanol at 303.15 K. Based on this measurement the values of different volumetric as well as acoustic parameters were calculated. The results are discussed in terms different interactions with protic and aprotic solvent media and structural effect between the solvents over a wide range of concentration.

Keywords: Adiabatic compressibility, Acoustic impedance, Intermolecular free length, Gibbs free energy of activation, Molecular interaction

INTRODUCTION

All types of drugs leads to complex interactions physically or chemically with the living system causing a physiological change. The drug-enzyme mechanism is responsible for activity change through activation and inhibition of enzyme. Ibuprofen is the most important non steroid anti-inflammatory drug (NSAID) employed for rheumatoid arthritis, migrain, pain, fever and inflammation [1]. It also behaves as a photosensitizing agent [2] as compared to other NSAIDs. The drug can also interfere with the anti-platelet on low dose aspirin. Taking excess of Ibuprofen leads to abdominal pain, nausea, vomiting, drowsiness, headache etc. It can also steadily combine with alcohol in human body intensifying the risk of human bleeding [3]. It takes the advantage for the prevention of Alzheimer's disease when given in low dose for a long period [4,5]. So a little amount of Ibuprofen is sufficient to interact with different systems. The knowledge of interaction study is related to physico-chemical behaviour of a system. The density and ultrasonic velocity measurement of sodium ibuprofen have also been reported [6-8]. This present paper reports the effect of ibuprofen in DMSO-methanol system.

MATERIALS AND METHODS

The chemicals used for the present investigation was purchased from Sigma Aldrich company. The purity of DMSO and methanol are confirmed by comparing with literature value as given in Table 1. Ibuprofen used was purchased from Sigma Aldrich Company. All the solution of DMSO and methanol are prepared at different mole fractions of DMSO ranging from 0.027 to 0.281. The other solution with same mole fraction of DMSO is also prepared containing Ibuprofen. The ultrasonic velocity of these solutions was measured by using ultrasonic interferometer (Model, m-81 s, Mittal enterprisers) at frequency of 2 MHz with accuracy of 0.1 ms^{-1}. The densities are also measured using specific gravity bottle (10) ml and electronic balance with accuracy ± 0.01 $mNsm^{-2}$. A thermostat is used to maintain a constant temperature.
Density measurement using apparent molar volume (V_ϕ) with density relation [8],

$$V_\phi = 1000(c\rho_0)^{-1}(\rho_0 - \rho) + M_2\rho_0^{-1}$$

Where, c is the molar concentration of the solution, M_2 is the molecular mass of the solute, ρ_0 and ρ are the densities of pure solvent and solution respectively.

The apparent molar volume thus obtained is found to vary linearly with $\rho^{1/2}$. The (V_ϕ) data were fitted by a method of least squares to Masson's equation [9],

$$V_\phi = V_\phi^{\,0} + S_v c^{1/2}$$

Over the range in which the densities are determined, where (V_ϕ^0) is the limiting apparent molar volume and S_v is the slope of the plot V_ϕ *versus* $c^{1/2}$.

The ultrasonic velocity '*U*' is related to the density '*d*' of the solution and isentropic compressibility ' β ' by the relation [10,11].

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

The adiabatic compressibility (β) is a measure with which a system can be compressed. This parameter determines the physico-chemical properties of mixtures.

The values of β calculated for solutions of different concentrations,

$$\beta = d^{-1}U^{-2}$$

Acoustic impedance (*Z*) is defined as the characteristic of the medium offered by infinite media for propagation of sound through it. It is related with velocities

$$Z = Ud$$

Intermolecular free length (L_f) can be determined by using the equation,

$$L_f = K_j \beta^{1/2}$$

Where K_j is Jacobson constant = 2.0965 x 10^{-6}

The excess free energy of activation (ΔG^{*E}) is expressed as

$$\Delta G^{*E} = RT[\ln \eta V - \{X_1 \ln(\eta_1 V_1) + X_2 \ln(\eta_2 V_2)\}]$$

Viscosity deviation ($\Delta\eta$) is given by

$$\Delta\eta = \eta - \{X_1\eta_1 + X_2\eta_2\}$$

Rao's constant and Wada's constant are calculated using the formulae

$$R = [M_{eff} / d_s]V^{1/3}$$

$$W = [M_{eff} / d_s]\beta^{-1/7}$$

The viscosity data of electrolyte solutions both in aqueous and non-aqueous solutions follow the Jone-Dole [12] equation,

$$\eta_r = \frac{\eta}{\eta_0} = 1 + Ac^{1/2} + Bc$$

Where Π_r in the relative viscosity of the solution. Π and Π_0 are the viscosities of solution and solvent respectively. *c* is the molar concentration. *A* and *B* are constants. Falkenhagen [13-16] coefficient A is due to the contributions from interionic forces. The B -coefficient of Jones-Dole equation indicates the ion-solvent interaction in solutions [17].

RESULTS AND DISCUSSIONS

Table 1 indicates the density and viscosity of DMSO and methanol [18-22] in pure form at 303.15 K.

Table 1: Comparison of experimental and literature values of density and viscosity of DMSO and methanol at 303.15 K

Pure solvents	ρ (10^{-3} Kg m^{-3})		Η (mPa.S)	
	Expt.	Lit.	Expt.	Lit.
DMSO	1090.9	1090.5 [18]	1.8401	1.830 [19]
Methanol	782.9	781.8 [20-21]	0.4976	0.510 [22]

The experimental values of density (ρ), ultrasonic velocity (*U*), adiabatic compressibility (β), Intermolecular free length (L_f), acoustic impedance (*Z*) of DMSO-methanol and DMSO-methanol-0.1 M ibuprofen systems are listed in Table 2.

Table 2: The data of density (ρ), ultrasonic velocity (U), adiabatic compressibility (β), Intermolecular free length (L_f), acoustic impedance (Z) of DMSO-methanol and DMSO-methanol- ibuprofen systems at 303.15 K

Mole Fraction (X_{org})	Concentration (c) mol dm^{-3}	Density (d) x 10^3 (kgm^{-3})	Ultrasonic velocity (U) ms^{-1}	Adiabatic compressibility (β) x 10^{-7} m^2N^{-1}	Intermolecular free length (L_f) x 10^{-9} m	Acoustic Impedance (Z) x 10^{-3} kgm^2s^{-1}
DMSO-methanol						
0.027	0.0403	863.92	1161.88	8.5754	1.9413	1.0037
0.059	0.0761	894.65	1204.24	7.7081	1.8406	1.0773
0.097	0.1124	911.87	1214.42	7.0694	1.7627	1.1356
0.144	0.2147	974.73	1245.54	6.2152	1.6528	1.2523
0.224	0.4681	1000.72	1284.88	6.7759	1.7257	1.2153
DMSO-methanol- ibuprofen						
0.027	0.0403	860.91	1145.75	8.8484	1.9221	1.0075
0.059	0.0761	896.43	1200.85	7.7359	1.8139	1.0378
0.097	0.1124	923.33	1231.53	7.1411	1.7216	1.1371
0.144	0.2147	960.51	1271.64	6.4397	1.5924	1.2928
0.224	0.4681	1000.65	1282.57	5.7042	1.4834	1.3244

The experimental value of relative viscosity **(η_r)**, viscosity deviation ($\Delta\eta$), Rao's constant **(R)**, Wada's constant (W) and excess free energy of activation (ΔG^{*E}) are listed in Table 3 of both the systems at 303.15 K.

Table 3: Calculated value of relative viscosity (η_r), viscosity deviation ($\Delta\eta$), Rao's constant (R), Wada's constant (W) and excess free energy of activation (ΔG^{*E}) in DMSO-methanol and DMSO-methanol- ibuprofen systems at 303.15 K

Mole Fraction (X_{org})	Concentration (c) mol dm^{-3}	Relative viscosity (η_r) x10^3	Viscosity deviation mPa.s	Rao's constant (R) x 10^{-2}	Wada's constant (W) x 10^{-4}	Excess free energy Of activation (ΔG^{*E}) x 10^{-3} $Jmol^{-1}$
DMSO-methanol						
0.027	0.0403	1.1453	0.5839	5.9101	0.3563	2.2994
0.059	0.0761	1.2191	0.6217	5.7073	0.7641	2.7213
0.097	0.1124	1.2809	0.6338	5.5996	1.3671	3.0631
0.144	0.2147	1.4612	0.7543	5.2383	3.1501	3.578
0.224	0.4681	1.5632	0.7524	5.1022	1.6762	3.8457
DMSO-methanol-ibuprofen						
0.027	0.0403	1.1009	0.5448	5.9307	0.3008	2.2114
0.059	0.0761	1.1557	0.5584	5.6958	0.7401	2.5869
0.097	0.1124	1.2355	0.5893	5.5299	1.258	2.9739
0.144	0.2147	1.3354	0.6287	5.3168	3.7193	3.3515
0.224	0.4681	1.5314	0.7218	5.1892	5.594	3.7959

Table 4 includes the values of apparent molar volume (V_ϕ), limiting molar volume (V_ϕ^0), ion-ion interaction parameter (S_v), Falkenhagen coefficient (A) and Jones-Dole coefficient (B).

Table 4: Values of apparent molar volume (V_ϕ), limiting molar volume (V_ϕ^0), ion-ion interaction parameter (S_v), Falkenhagen coefficient (A) and Jones-Dole coefficient (B) of DMSO-methanol and DMSO-methanol- ibuprofen systems at 303.15 K

Mole Fraction (X_{org})	Concentration (c) mol dm^{-3}	apparent molar volume (V_ϕ) x 10^{-3} (m^3mol^{-1})	limiting molar volume (V_ϕ^0) (m^3mol^{-1})	(S_v) x10^{-7} $m^3kg^{1/2}mol^{-3/2}$	(A) x 10^{-9} $dm^{3/2}mol^{-1/2}$	(B) x 10^{-3} dm^3mol^{-1}
DMSO-methanol						
0.027	0.0403	-0.9518				1.0037
0.059	0.0761	-0.4358				1.0773
0.097	0.1124	-0.2439	1.1863	-0.9521	1.8662	1.6419
0.144	0.2147	-0.1986				1.2523
0.224	0.4681	-0.1387				1.2153

DMSO-methanol- ibuprofen						
0.027	0.0403	-1.4389				1.0075
0.059	0.0761	-0.8538				1.0378
0.097	0.1124	-0.6869	1.1963	-0.4221	1.6419	1.6419
0.144	0.2147	-0.6164				1.2928
0.224	0.4681	-0.5775				1.3244

The values of ρ for both the system increase with mole fraction of DMSO. The increase in ρ values may be explained in terms of ion-ion interaction attributed to an increase in vanderWaal's interaction [23] with increase in mole fraction of DMSO the Π_r values slowly increase. It may be argued that the intermolecular interaction is strong enough to increase in Π_r values. The dependence of viscosity deviation $\Delta\Pi$ on mole fraction of DMSO is shown in Figure 1.

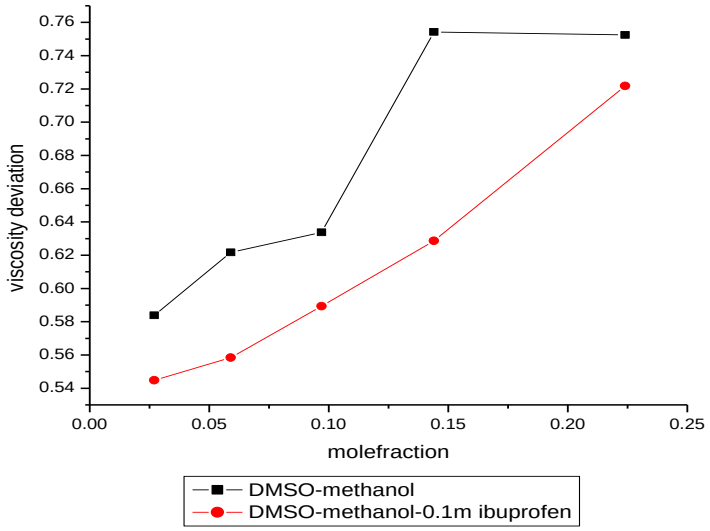

Figure 1: Variation of viscosity deviation with mole fraction of DMSO-methanol and DMSO-methanol- ibuprofen at 303.15 K

The Π_r values are positive for both systems. For DMSO+CH_3OH mixture, the maximum value of $\Delta\Pi$ occurs at x DMSO=0.144 whereas in the presence of Ibuprofen, $\Delta\Pi$ steadily increase with mole fraction of DMSO which indicate the interaction of ibuprofen with the system.

After a detailed analysis of values of Table 2 it is suggested that *U* values are increasing over the entire range of mole fraction of DMSO. The increase may be due to self-association between DMSO and methanol. The increase in *U* value leads to decrease in β values. The β values decrease up to X_{DMSO}=0.144 then suddenly increase with mole fraction. The variation of β values with mole fraction is shown in Figure 2.

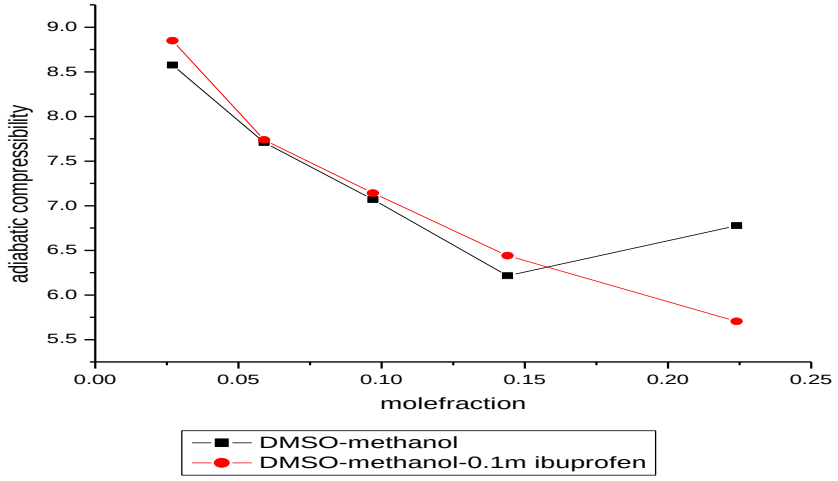

Figure 2: Variation of adiabatic compressibility with mole fraction of DMSO-methanol and DMSO-methanol-0.1 m ibuprofen at 303.15 K

The decrease in β values indicates the existence of attractive force between the DMSO and methanol in solution but the decrease in β values is

more prominent in System-II in the presence of ibuprofen.

The acoustic impedance increases regularly in system-II but the increase is not regular in the system-I. The increase in *Z* value explains the dipole-dipole interaction through hydrogen bonding between solute and solvent [24]. The variation of intermolecular free length in solution is based on sound propagation model [25]. It was found that the intermolecular free length values increase in both the systems due to greater attractive influence of one component over another. But the lower value of L_f in system-II suggests that the interaction get weakened due to the addition of ibuprofen. Values of *R* and *W* decrease with mole fraction of DMSO which is shown in Table 3. The graphical representation of ΔG^{*E} is shown in Figure 3.

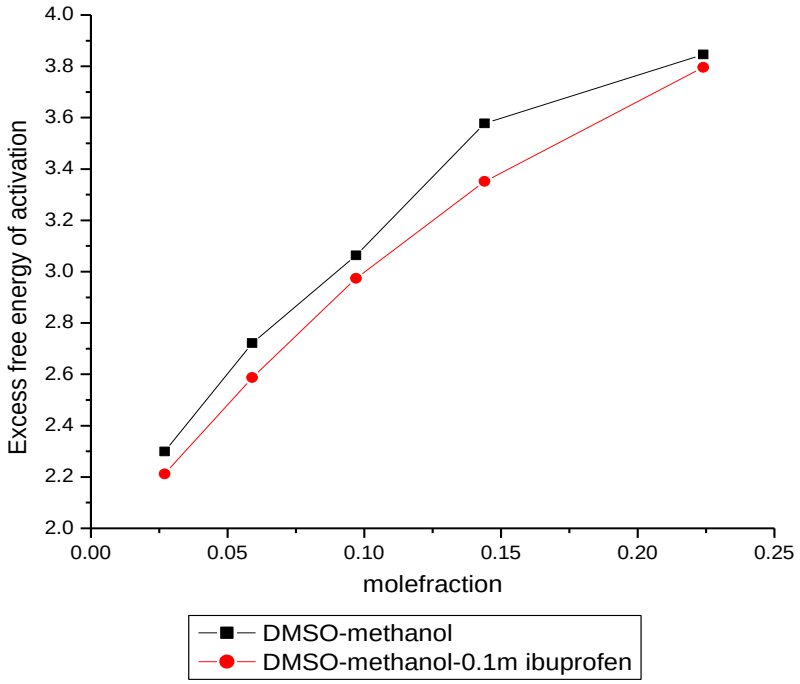

Figure 3: Variation of excess free energy of activation with mole fraction of DMSO-methanol and DMSO-methanol- ibuprofen at 303.15 K

It shows the values of (ΔG^{*E}) are positive for both the systems. But it increases linearly in the presence of Ibuprofen. The regular increase is due to association of molecules forming Hydrogen bond between -OH of methanol and –COOH of Ibuprofen. The V_ϕ values are all negative for both the systems. The negative values of V_ϕ indicate electrostrictive solvation of ions [26]. From Table 4 it is observed that V_ϕ values increase for both the system with mole fraction. The increase in V_ϕ value may be due to dipole-dipole interaction in DMSO and intermolecular Hydrogen bonding in methanol system. The values of V_ϕ^0 which are determined by least square fitting method are positive for both the system and is represented in Figures 4 and 5.

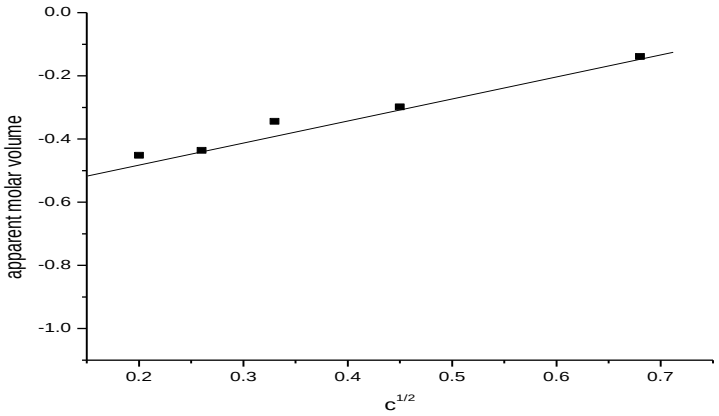

Figure 4: Variation of apparent molar volume with $c^{1/2}$ of DMSO-methanol at 303.15 K

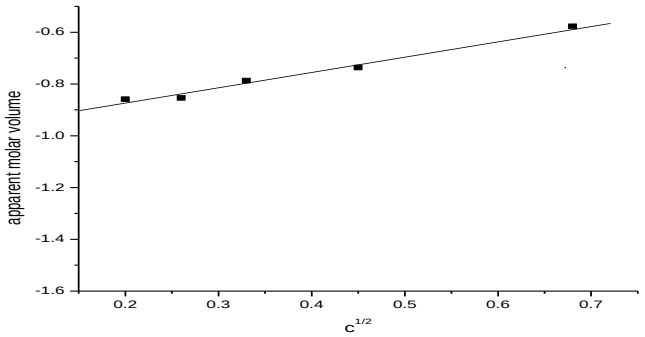

Figure 5: Variation of apparent molar volume with $c^{1/2}$ of DMSO-methanol- ibuprofen at 303.15 K

But highest V_ϕ in system-I indicates that the interaction get diminished due to presence of Ibuprofen. Ibuprofen also forms hydrogen bond with methanol. It is due to the fact that DMSO contain highly polar S=O group. The S_v known as ion-ion interaction parameter is negative in both the cases. The high negative value of S_v in system-II reflects on the interaction between DMSO and methanol which get decreased due to the presence of ibuprofen. The Ibuprofen containing -COOH group is responsible for the formation of hydrogen bonding with methanol. The value of Falkenhagen coefficient (*A*) and Jone- Dole coefficient (*B*) are determined from the graphical representation of η_r -1/$c^{1/2}$ with $c^{1/2}$ (Figures 6 and 7).

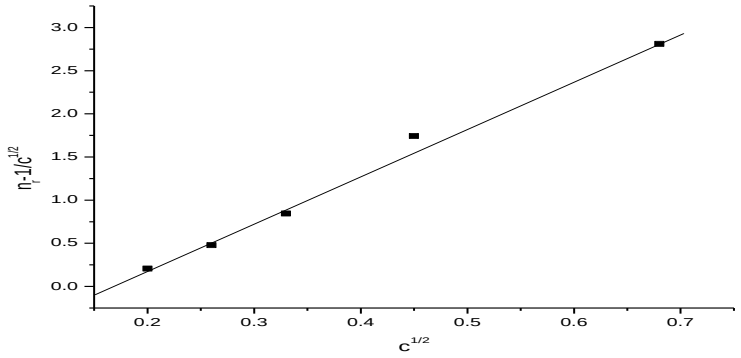

Figure 6: Variation of η_r -1/$c^{1/2}$ with $c^{1/2}$ for DMSO-methanol

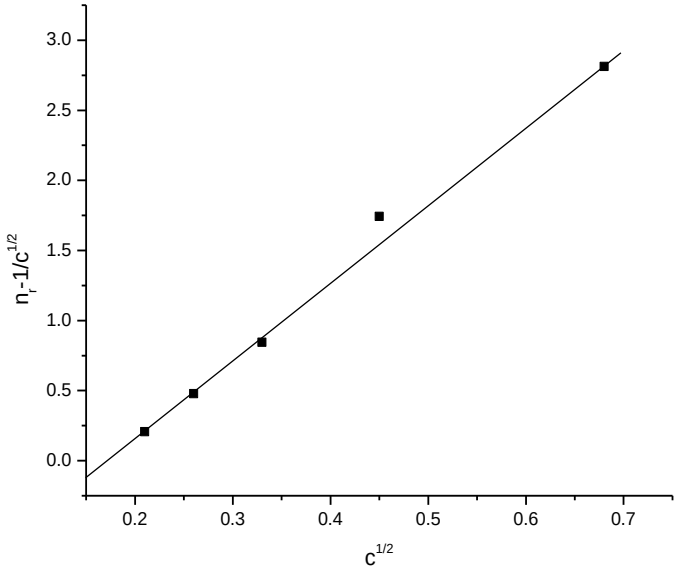

Figure 7: Variation of η_r -1/$c^{1/2}$ with $c^{1/2}$ for DMSO-methanol- ibuprofen at 303.15 K

The values of *A* are negative in both the systems. The higher value of *A* indicates the interaction between DMSO and methanol but its value lowers in system-II which suggests that ibuprofen may lower the interaction between DMSO and methanol. The values of *B* are positive in both the systems indicating interaction of ibuprofen and methanol.

CONCLUSION

The calculation of volumetric and acoustic parameters reveals the existence of molecular interaction between the components. The molecular interactions become stronger due to the presence of ibuprofen containing-COOH group forming hydrogen bond. It becomes weaker in DMSO - methanol mixture. The dispersion force and dipolar interaction are responsible for weak molecular interaction. It can be concluded that the interaction between DMSO and methanol is weakening because of the presence low quantity of ibuprofen. Ibuprofen interacts more strongly with protic solvent as compared to aprotic solvent. This study determines the physico-chemical behaviour of ibuprofen in different solvent media.

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