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Study of molecular interactions of Loperamide drug in different solvents at 308.15 K

Nilesh Godvani, Jagdish Movaliya, Ravi Gajera, Shipra Baluja*

Physical Chemical Laboratory, Department of Chemistry, Saurashtra University, Rajkot-360005, Gujarat, India.

ABSTRACT

Density, viscosities and speed of sound of Loperamide drug were measured as a function of concentrations in different solvents at 308.15K. From the experimental data, various acoustical parameters have been evaluated. The results are interpreted in terms of molecular interactions occurring in these solutions.

*Corresponding author
E-mail: shipra_baluja@rediffmail.com

INTRODUCTION

Ultrasonic waves provide valuable information about the structure of solids [1,2]). By ultrasonic velocity measurements, the molecular interactions in pure liquids [3-6], aqueous solutions [7-9] and liquid mixtures [10-13] have also been studied. It provides a powerful, effective and reliable tool to investigate properties of solutions of polymers [14-16], carbohydrates [17-19], amino acid [20-21] etc. However, little work has been done for the solutions of drugs [22-24].

In present paper, Loperamide drug is selected for the study. It is effective against diarrhea resulting from gastroenteritis or inflammatory bowel disease. It also decreases colonic mass movements and suppresses the gastro colic reflex [25].

The acoustical properties of Loperamide drug have been studied in methanol (MeOH), ethanol (EtOH), isopropyl alcohol (IPA) and N, N- dimethyl formamide (DMF) solutions at 308.15 K.

EXPERIMENTAL

All the solvents used in the present work were of AR grade and were purified according to the standard procedures described in the literature [26]. The compound was recrystalized before use.

The computation of ultrasonic and thermodynamic properties require the measurements of ultrasonic velocity (U), viscosity (η) and density (ρ).

The densities of pure solvents and their solutions were measured by using a single capillary pycnometer, made of borosil glass having a bulb capacity of 10 ml. The ultrasonic velocity of pure solvents and their solutions were measured by using single crystal variable path ultrasonic interferometer operating at 2 MHz. The accuracy of density and velocity are $\pm$ 0.0001 g/cm^3 and $\pm$ 0.1% cm/sec respectively. Viscosity of pure solvents and solutions were measured by an Ubbelohde viscometer with an accuracy of 0.05%. All the measurements were carried out at 308.15 K. The uncertainty of temperature is $\pm$ 0.1 K and that of concentration is 0.0001 moles /dm^3.

The experimental data of ultrasonic velocity, density and viscosity are given in Table 1.

Theory

From the experimental data of density, viscosity and ultrasound velocity of pure solvent and solutions, various acoustical parameters were calculated using following standard equations:

Isentropic compressibility (κ_S): $= 1/ (U^2\rho)$

Intermolecular length (L_f): $L_f = K_J \kappa_S^{1/2}$

where K_J is Jacobson constant (= 2.0965 x 10^{-6}).

Relaxation Strength (r): $r = 1- (U/U_\infty)^2$ where $U_\infty = 1.6 \times 10^5$ cm/s.

Rao's molar sound function (R_m): $R_m = (M/\rho)U^{1/3}$

where M is the molecular weight of solution.

Van der Waal's Constant (b): $b = (M/\rho) (1-RT/MU^2 (\sqrt{(1+MU^2/3RT)}-1))$

Where R is gas constant and T is absolute temperature.

Molar Compressibility (W): $W = (M/\rho)\ \kappa_S^{-1/7}$

Solvation number (S_n) : $S_n = M_2/M_1\ [1- \kappa_S / \kappa_{S1}]\ [(100- X) /X]$

Where X is the number of grams of solute in 100 gm of the solution. M_1 and M_2 are the molecular weights and κ_{S1} and κ_S are isentropic compressibility of solvent and solute respectively.

Apparent Molar Volume (ϕ_V): $\phi_V = [M/\rho]-[(1000\{\rho-\rho_o\})/(\rho C)]$

Where ρ and ρ_o are the densities of solutions and solvent respectively and C is the concentration of the solution in molarity.

Apparent Molar Compressibility (ϕ_k):

$\phi_k = [(\rho_o\kappa_S - \rho\kappa_{S1})\ (1000/C\rho_o)] + [\kappa_{S1}\ M_2/\rho_o]$

Where M_2 is the molecular weight of the drug.

Some of these acoustical parameters are given in Table 2.

RESULTS AND DISCUSSION

Table 1 shows that for all the four systems density (ρ), ultrasonic velocity (U) and viscosity (η) increase with concentration. The variation of ultrasonic velocity with concentration in all the four solvents is shown in Figure 1. The increase in ultrasonic velocity is due to decrease in intermolecular free length (L_f), as shown in Table 2. This suggests that there is a strong interaction between Loperamide and solvent molecules.

This is further supported by isentropic compressibility (κ_s) and relaxation strength (r) values (as shown in Figure 2 and Table 2 respectively), which are also observed to decrease with concentration for all the four systems. The decrease of κ_s with concentration might be due to aggregation of solvent molecules around solute molecules indicating thereby the presence of solute-solvent interactions.

Properties like molar sound function (R_m), molar compressibility (W), and Vander Waal's constant (b) are observed to increase linearly with concentration in all the four systems. Figure 3 shows the variation of Vander Waals constant for the four solvents. The linear variation of these acoustical properties indicates the absence of complex formation.

The interactions occurring in different solutions can also be confirmed by the solvation number (S_n), which is measure of structure tendency of solute in solutions. Figure 4 shows the variation of solvation number with concentration in all the four solvents. The solvation number increases continuously with concentration in methanol, ethanol and DMF solutions. The increase in S_n suggests the structure forming tendency of this drug in these solvents. Where as in isopropyl alcohol, S_n values decreases continuously with concentration indicating thereby structure breaking tendency of the drug in this solvent.

The decrease of S_n in isopropyl alcohol (IPA) may be due to side group of IPA which may cause steric hindrance. This may cause structure breaking tendency of drug in IPA.

Further, isentropic compressibility values for all the solutions are fitted to Bachem's relation [27].

$$\kappa_S = \kappa^o_S + AC + BC^{3/2}$$

Where C is the concentration. The constants A and B are evaluated and are given in Table 3.

The apparent molar compressibilities (ϕ_k) of the solutions are fitted to Gucker's relation [28].

$$\phi_k = \phi^o_k + S_k C^{1/2}$$

From the plot of ϕ_k verses $C^{1/2}$, ϕ^o_k and S_k are evaluated from the intercept and slope respectively.

The apparent molar volume (ϕ_v) is also related to concentration by Masson's equation [29]

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$$\phi_v = \phi^o_v + S_v C^{1/2}$$

The intercept ϕ^o_v and slope S_v values were also calculated from the plot of apparent molar volume (ϕ_v) verses concentration. All these values of intercept and slopes are given in Table 3.

Table 1: Experimental data of density, ultrasonic velocity and viscosity of Loperamide in different solvents at 308.15K.

Conc. (M)	Density, $g.cm^{-3}$	Velocity $\times 10^{-5}$ $cm.s^{-1}$	Viscosity $\times 10^{3}$ poise
METHANOL			
0.00	0.7749	1.0792	4.4700
0.01	0.7829	1.0848	4.5975
0.02	0.7849	1.0892	4.7181
0.04	0.7879	1.0968	4.7515
0.06	0.7883	1.1032	4.8428
0.08	0.7893	1.1060	4.8669
0.10	0.7903	1.1108	4.9622
ETHANOL			
0.00	0.7771	1.1216	8.2070
0.01	0.7779	1.1292	8.3732
0.02	0.7787	1.1312	8.5284
0.04	0.779	1.1340	8.6865
0.06	0.7832	1.1348	8.9227
0.08	0.7855	1.1372	9.1210
0.10	0.789	1.1392	9.4894
ISOPROPYL ALCOHOL			
0.00	0.7715	1.1136	14.3872
0.01	0.7717	1.1144	16.0345
0.02	0.7722	1.1172	16.4389
0.04	0.7747	1.1204	17.0151
0.06	0.7793	1.1240	17.5031
0.08	0.7828	1.1276	18.8106
0.10	0.7901	1.1316	19.7335
DIMETHYL FORMAMIDE			
0.00	0.9285	1.4400	7.0330
0.01	0.9297	1.4524	7.6221
0.02	0.9307	1.4536	7.7625

0.04	0.9315	1.4556	7.9180
0.06	0.9325	1.4568	8.0408
0.08	0.9347	1.4584	8.2789
0.10	0.938	1.4612	8.4885

Table 2: Variation of some acoustical parameters with concentration of Loperamide in different solvents at 308.15K.

Conc. (M)	L_f (A^o)	r	$R_m.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	b $cm^3.mol^{-1}$	$W.10^{-3}$ $cm^{-1}.dyn^{-1}$
METHANOL					
0.00	0.2207	0.5450	1.9661	41.2937	1.0917
0.01	0.2184	0.5403	2.1414	44.8974	1.1905
0.02	0.2173	0.5366	2.3296	48.7780	1.2954
0.04	0.2153	0.5301	2.7052	56.5114	1.5045
0.06	0.2140	0.5246	3.0896	64.4162	1.7180
0.08	0.2134	0.5222	3.4670	72.2258	1.9280
0.10	0.2123	0.5180	3.8456	79.9957	2.1384
ETHANOL					
0.00	0.2120	0.5086	2.8547	59.1922	1.5829
0.01	0.2105	0.5019	3.0495	63.0902	1.6906
0.02	0.2100	0.5002	3.2391	66.9722	1.7958
0.04	0.2095	0.4977	3.6225	74.8389	2.0083
0.06	0.2088	0.4970	3.9781	82.1644	2.2070
0.08	0.2080	0.4948	4.3421	89.6209	2.4097
0.10	0.2072	0.4931	4.6919	96.7828	2.6053
IPA					
0.00	0.2143	0.5156	3.7416	77.7679	2.0732
0.01	0.2142	0.5149	3.9293	81.6500	2.1772
0.02	0.2135	0.5124	4.1176	85.4918	2.2815
0.04	0.2126	0.5096	4.4804	92.9349	2.4833
0.06	0.2113	0.5065	4.8237	99.9485	2.6754
0.08	0.2101	0.5033	5.1687	106.9841	2.8682
0.10	0.2084	0.4998	5.4737	113.1631	3.0410
DMF					
0.00	0.1511	0.1900	4.1260	78.7165	2.3189
0.01	0.1497	0.1760	4.2697	81.2258	2.3992
0.02	0.1495	0.1746	4.4031	83.7410	2.4744
0.04	0.1492	0.1724	4.6748	88.8663	2.6272
0.06	0.1490	0.1710	4.9436	93.9503	2.7786
0.08	0.1487	0.1692	5.2037	98.8587	2.9257
0.10	0.1481	0.1660	5.4551	103.5683	3.0683

Table 3 : Bachem's constants A and B and ϕ^{o}_{v}, S_v, ϕ^{o}_{k} and S_k of Loperamide drug in different solvents 308.15K.

Solvent	A X 10^{11} $dyn^{-1}.cm^{3}.mol^{-1}$	B X 10^{11} $dyn^{-1}.cm^{-1/2}.mol^{-3/2}$	ϕ^{o}_{k} X 10^{8} $dyn^{-1}.mol^{-1}$	S_k X 10^{8} $dyn^{-1}.cm^{-3/2}.mol^{-3/2}$	ϕ^{o}_{v} $cm^{3}.mol^{-1}$	S_v $cm^{3}.mol^{-1}$
Methanol	-26.10	58.00	-23.60	65.00	-470.00	3500.00
Ethanol	-8.70	-13.60	-1.60	7.00	-30.00	1966.66
IPA	-2.10	10.28	5.45	20.00	75.00	191.66
DMF	-5.10	10.00	-2.45	8.75	-62.00	1400.00

Figure 1: Variation of Ultrasonic velocity (U) with concentration of Loperamide in different solvents at 308.15K.

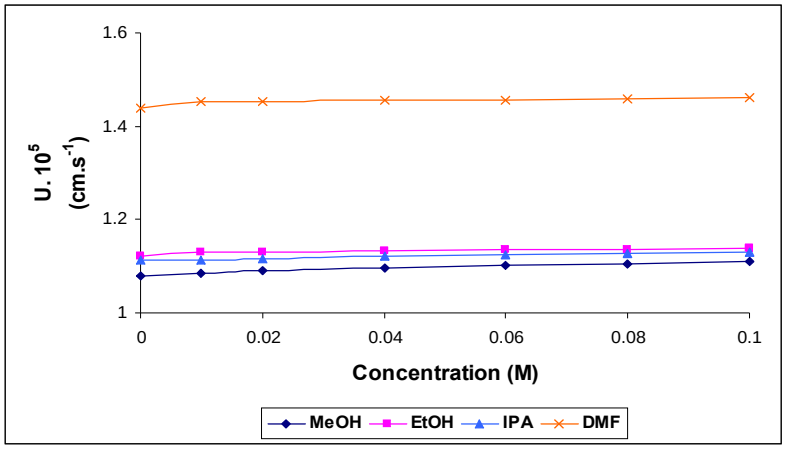


Figure 2: Variation of Isentropic compressibility (κ_s) with concentration of Loperamide in different solvent at 308.15K.

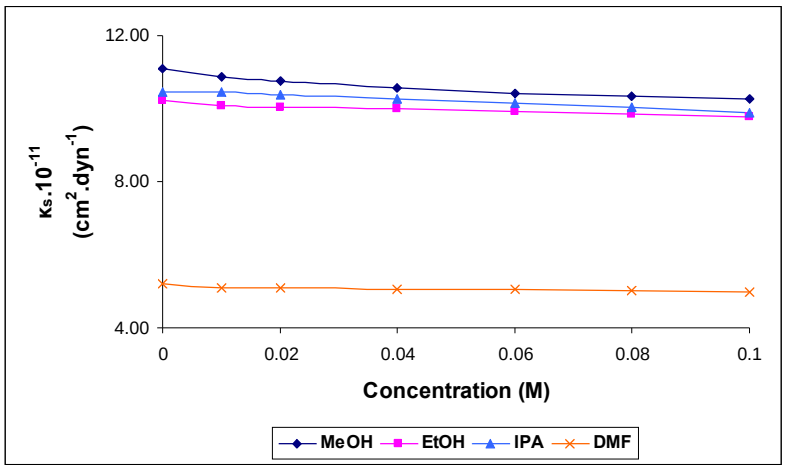


Figure 3: Variation of Vander Waal's constant (b) with concentration of drug in different solvent at 308.15K.

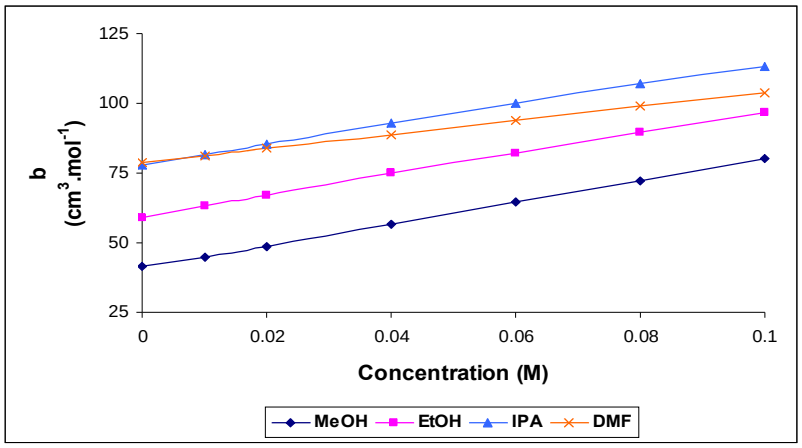
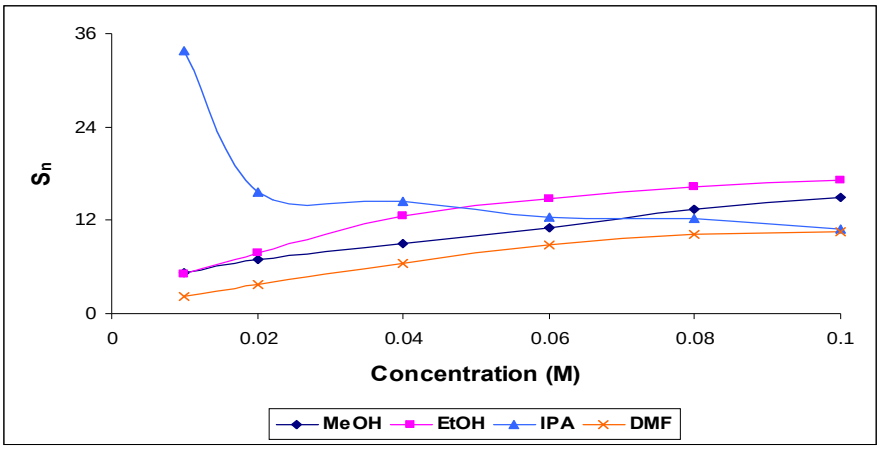


Figure 4: Variation of Solvation number (S_n) with concentration of drug in different solvent at 308.15K.



It is evident from Table 3 that A and ϕ^{o}_{k} values are negative for methanol, ethanol and DMF solutions of the drug whereas in IPA solution, A values are less negative and ϕ^{o}_{k} values are positive. The negative A and ϕ^{o}_{k} suggest solute-solvent interactions whereas positive values are due to solute-solute interactions. This is further confirmed by ϕ^{o}_{v} values which are positive for IPA and negative for other three solutions of the drug. This type of behavior was observed by Semwal et al., who reported that the negative values of ϕ^{o}_{v} indicate electrostrictive solvation of ions [30-32]. Thus, in methanol, ethanol and DMF solutions, predominance of solute-solvent interaction is again proved by negative A, ϕ^{o}_{k} and ϕ^{o}_{v} values. However, in IPA solutions, positive ϕ^{o}_{k} and ϕ^{o}_{v} values and low negative A values suggest that solute-solute interactions predominate. S_v is a measure of solute-solvent interaction. It is observed from Table 3 that again S_v values are higher in all the solutions except isopropyl alcohol. This further confirms that in IPA solute-solute interactions and in other three solvents, solute-solvent interactions predominate.

Thus, it is concluded that Loperamide exhibits structure forming tendency in methanol, ethanol and DMF solutions where as in isopropyl alcohol, structure breaking tendency of drug is observed.

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