ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Ultrasonic Velocity, Density and Viscosity Studies in the Aqueous Solutions of Hydrate Compounds

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ABSTRACT

Ultrasonic velocity, density and viscosity have been measured in the aqueous solutions of three hydrates levofloxacin hemihydrate, tacrolimus monohydrate and lisinoprildihydrate at two temperatures 30 and 40^{0}C. Apparent molar volumes and apparent molar compressibilities have been computed and the limiting/partial molar volumes and molar compressibilities have been discussed in the light of solute-solvent / solute-solute interactions. Jones Dole constants A and B have also been computed and in turn employed to assess the molecular interactions. Mostly solute-solvent interactions dominate in the aqueous solutions. Also from Jacobson's theory of compressibilities, structure making property of the hydrates has been indicated in their aqueous solutions.

Keywords: Ultrasonic Velocity, apparent molar volume, aqueous solutions, hydrates, Jones Dole constants.

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ISSN: 0975-8585

INTRODUCTION

Ultrasonic studies in aqueous solutions of various drugs yield information about the nature of molecular interactions as observed by several researchers[1-22]. Recently in the aqueous solutions of a homologous series of drugs used for cough [7] and eye diseases to reduce Internal Occular Pressure (IOP) [6] extensive studies have been made at low concentrations by the present authors. In the present investigation, an attempt is made to study the three hydrate drugs – levofloxacin hemihydrate, tacrolimus monohydrate and lisinoprildihydrate in their aqueous solutions at 30 and 40^0C by measuring ultrasonic velocity, density and viscosity. Levofloxacin hemihydrate is a tropical ophthalmic drug for eye diseases whiletacrolimus monohydrate reduces inflammation, suppresses overactivity of immune system and treats eczema. Lisinoprildihydrate is an anti-hypertensive drug for high blood pressure and treats congestive heart failure, diabetic nephropathy or retinopathy. Solute – sovent and solute – solute interactions have been estimated from knowledge of the derived parameters-- apparent molar volumes and apparent molar compressibilities besides the Jones-Dole constants from the viscosity data. Solute-solvent interactions have been reported to be predominant. From a study employing Jacobson's theory of compressibilities in aqueous solutions, all the three solutes are found to be structure makers.

MATERIALS AND METHODS

Experimental

For measuring ultrasonic velocity experimentally, single crystal variable path ultrasonic interferometer (Mittal Enterprises, New Delhi) working at 1MHz has been employed with an uncertainty of ± 0.05%. Double stem capillary type pyknometer and Ostwald Viscometer have been used to measure density and viscosity with uncertainties of 2 parts in 10^5 and ± 0.1% respectively. For standardization, triple distilled water has been taken as reference liquid. A constant temperature water bath whose temperature can be controlled to within ± 0.01% is used for temperature studies. All the three drugs are technically pureand obtained from M/s Bioserve Clinical Research Pvt.Ltd., Hyderabad.

Theoretical

From the data of ultrasonic velocity and density, the following standard relations have been employed to obtain the following parameters

Apparent molar volume $\phi_v = (1000(\rho_0 - \rho)/ C\rho_0) + M_{eff}/\rho_0$ (1)

Apparent molar compressibility $\phi_k = (1000(\beta_0\rho_0 - \beta\rho)/C\rho\rho_0) + M_{eff}\beta/\rho_0$ (2)

Apparent molar volume (ϕ_v) and apparent molar compressibility (ϕ_k) can be fitted to the square root of molarity of the solute through the following equations

$$\Phi_V = \Phi_V^0 + S_V\sqrt{C} \quad (3)$$

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$$\Phi_K = \Phi_K^0 + S_K\sqrt{C} \quad (4)$$

Where Φ_V, Φ_K are apparent molar volume and apparent molar compressibility at infinite dilution , Φ_V^0 and Φ_K^0 are limiting apparent molar volume and apparent molar compressibility, S_v and S_K are the experimental slopes.

The viscosity of bigger molecules in solutions behave interestingly with the molarity of the solution i.e.,

$$\frac{\eta_r - 1}{\sqrt{C}} = A + B\sqrt{C} \quad (5)$$

where η_r is the relative viscosity $= \frac{\eta}{\eta_o}$, A and B are called Jones-Dole constants which reveal the different types of interactions.

To study the structural behavior of the solute in its aqueous solutions, Jacobson's theory of compressibility is also employed at the temperature of study.

The dimensionless parameter μ which speaks of the structural behavior of the solute in aqueous medium is given thus. If the two volume fraction v_a and v_b have slopes Γ_a and Γ_b of the plot $\Delta\beta/\beta$ vs. v, then μ may be evaluated using the formula

$$\mu = \frac{\log \Gamma_a / \Gamma_b}{\log v_a / v_b} + 1 \quad (6)$$

Where v is the volume fraction of the solute given by v = CV/1000 where C is molarity and V is the molar volume. If μ >1, the solute is said to be structure breaker and μ<1 refers to structure making property of the solute in aqueous medium. All the parameters have their usual meaning and explained elsewhere [7].

RESULTS AND DISCUSSION

In the aqueous solutions of levofloxacin hemihydrates, tacrolimus monohydrate and lisinoprildihydrate, ultrasonic velocity, density and viscosity have been measured at two temperatures 30 and 40^{o}C at low concentrations of the three solutes (molarity of the solute) and the measured data are presented in Table 1. In all the aqueous solutions of the solutes, velocity decreases with the increase of the solute concentration (except at very low concentration) at both the temperatures and increases with temperature at any particular concentration as shown in Fig.1. Δu/u vs. c is plotted for all the three solute aqueous systems in Fig.2. It is observed that Δu/udecreases with molarity.

From Fig.2, the limiting slope A is obtained which in turn employed in the plot of $((A - \Delta u/uC)/C)^{1/2}$ vs. $(A - \Delta u/uC)$ to obtain the association constant from the intercept and the slope as Δ, the stacking interaction constant. Apparent molar volume (Φ_v) and apparent molar

ISSN: 0975-8585

compressibility(Φ_k) are also computed and shown in Figs. 3-4 as a fuction of the molarity of the solute. Partial molar volume (Φ_v^0) and partial molar compressibility (Φ_k^0) are also estimated through the linear relationship of Φ_v (and Φ_k) to the square root concentration of the solute and are presented in Table 2. Employing the viscosity data measured, Jones-Dole constants A and B are obtained through the plot of(η/η_0 -1)/√C vs. √C and incorporated in Table 4. Bachem's relations are also fitted to the compressibility data and the constants are presented in Table 3. Δβ/v vs. v (where v is the volume fraction = CV/1000) as shown in Fig.5 is useful in getting a value of the dimensionless parameter μ. Hydration numbers computed are delineated/ portrayed in Fig.6 as a function of molarity of the drug.

Table.1(i). Velocity, density and viscosity in the mixture: Water + Levofloxacin

Molarity	Velocity (ms^{-1})	Density ($kg\ m^{-3}$)	Viscosity (milli.Pa.s)
30^0C			
0.0000	1509.8	0995.67	0.79750
0.00081	1531.6	1006.14	0.72669
0.00155	1529.0	1004.73	0.75601
0.00175	1526.8	1003.24	0.77606
0.00196	1525.6	1002.86	0.74121
0.00270	1524.0	1002.71	0.73782
0.00472	1520.0	1003.34	0.73437
0.00675	1518.0	1.003.28	0.72352
40^0C			
0.0000	1526	0992.27	0.65290
0.00081	1560.0	1008.64	0.62547
0.00155	1558.0	1006.56	0.65593
0.00175	1554.0	1005.21	0.65432
0.00196	1546.0	1008.35	0.64586
0.00270	1541.5	1009.35	0.64111
0.00472	1539.0	1012.34	0.63728
0.00675	1530.0	1014.24	0.61874

Table 1(ii). Velocity, density and viscosity in the mixture: Water + Tacrolimus

Molarity	Velocity (ms^{-1})	Density ($kg\ m^{-3}$)	Viscosity (milliPa.s)
30^0C			
0.00030	1563.6	994.79	0.71975
0.00061	1538.0	994.03	0.70523
0.00122	1534.4	993.32	0.68743
0.00152	1533.5	993.01	0.68106
0.00182	1532.0	992.85	0.68011
0.00243	1531.0	992.81	0.68181
0.00304	1530.0	992.79	0.68623
40^0C			
0.00030	1578.0	990.93	0.60794
0.00061	1556.0	988.34	0.59496
0.00122	1550.8	987.16	0.58851
0.00152	1549.5	987.25	0.59249

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0.00182	1548.0	987.39	0.59679
0.00243	1543.0	988.60	0.60845
0.00304	1540.0	990.71	0.61788

Table 1(iii). Velocity, density and viscosity in the mixture: Water + Lisinopril

Molarity	Velocity (ms^{-1})	Density ($kg\ m^{-3}$)	Viscosity (milliPa.s)
30^0C			
0.00057	1565.0	991.03	0.71259
0.00113	1546.8	991.26	0.72327
0.00226	1538.0	993.05	0.74877
0.00283	1536.0	993.52	0.75919
0.00340	1534.0	993.88	0.77302
0.00453	1531.0	994.14	0.78542
0.00566	1528.0	994.35	0.79599
40^0C			
0.00057	1578.0	990.93	0.60794
0.00113	1556.0	988.34	0.60353
0.00226	1550.8	987.16	0.59497
0.00283	1549.3	987.25	0.59786
0.00340	1548.0	987.39	0.60082
0.00453	1543.0	989.32	0.61296
0.00566	1540.0	990.71	0.61788

Table 2(i). Limiting apparent molar volume, limiting apparent molar compressibility, Jones-Dole constants etc. in the aqueous solutions of levofloxacin

Water + Levofloxacin	Φ_v^0	Φ_k^0	S_v	S_k	A	B	μ
30^0C	-13447	-2.867E-6	173541	3.77E-5	-2.60	21.90	0.3911
40^0C	-20946	-4.30E-6	244911	5.55E-5	-0.577	3.24	0.8705

Table 2.(ii). Limiting apparent molar volume, limiting apparent molar compressibility, Jones-Dole constants etc. in the aqueous solutions of tacrolimus

Water + Tacrolimus	Φ_v^0	Φ_k^0	S_v	S_k	A	B	μ
30^0C	4049	-1.01E-5	-53375	2.095E-4	-6.86	77.57	0.2312
40^0C	8324	-9.32E-6	-131872	1.946E-4	-5.14	76.02	-0.4356

Table 2(iii). Limiting apparent molar volume, limiting apparent molar compressibility, Jones-Dole constants etc. in the aqueous solutions of lisinopril

Water + Lisinopril	Φ_v^0	Φ_k^0	S_v	S_k	A	B	μ
30^0C	9907	8504	-147948	985	-5.822	85.01	-0.1423
40^0C	4472	-5.003E-6	-51921	7.659E-5	-3.795	41.73	-0.170

ISSN: 0975-8585

Table 3(i). Bachem's constants in aqueous solutions of levofloxacin

Temperature	A	B	R
30^0C	-2.28871E-9	3.02557E-8	0.83024
40^0C	-3.42787E-9	4.52826E-8	0.83438

Table.3(ii). Bachem's constants in aqueous solutions of tacrolimus

Temperature	A	B	R
30^0C	-9.96419E-9	2.05487E-7	0.80213
40^0C	-9.3348E-9	1.94066E-7	0.80991

Table 3(iii). Bachem's constants in aqueous solutions of lisinopril

Temperature	A	B	R
30^0C	-5.44523E-9	8.1682E-8	0.83597
40^0C	-5.01158E-9	7.63396E-8	0.80952

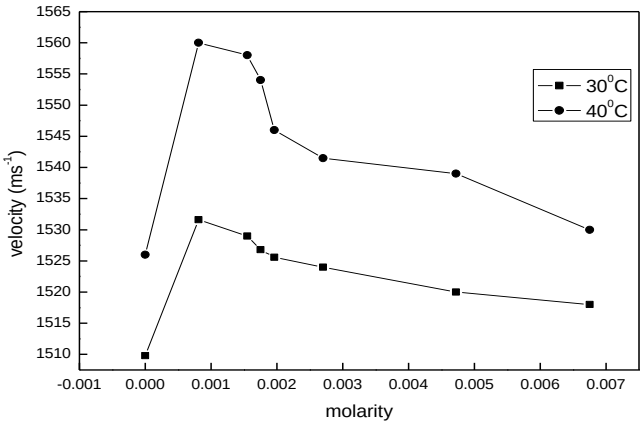

Fig.1(i). Variation of velocity with molarity of levoflxacin in the mixture: Water + levofloxacin

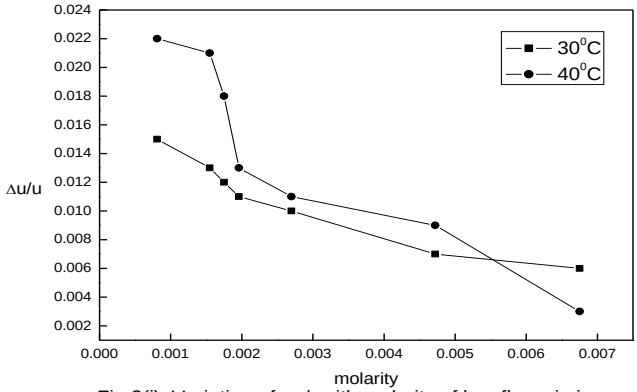

Fig.2(i). Variation of Δu/uwith molarity of levofloxacin in the mixture: Water + levofloxacin

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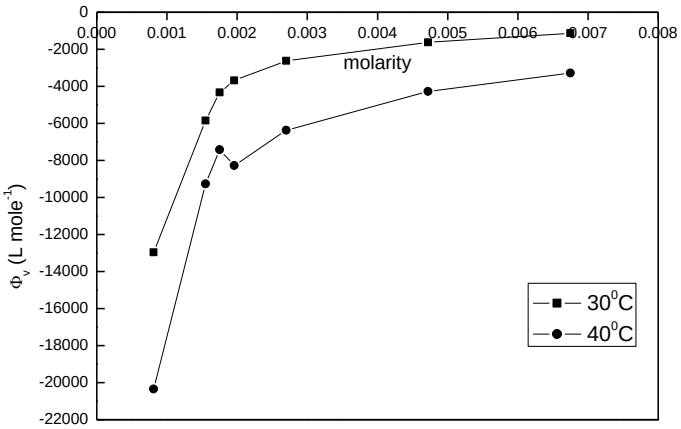

Fig.3(i). Variation ofΦ_v with molarity of levofloxacin in the mixture: Water + levofloxacin

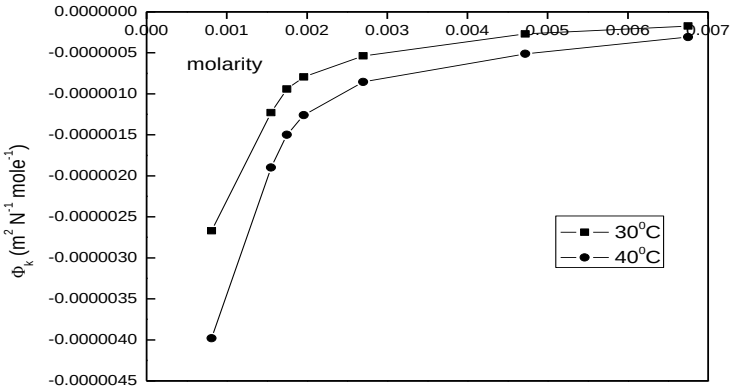

Fig.4(i). Variation of Φ_k with molarity of levofloxacin in the mixture: Water + levofloxacin

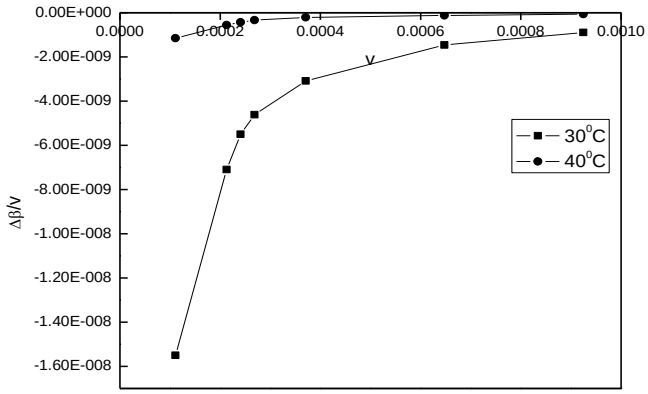

Fig.5(i). Variation of $\Delta\beta/v$ with volume fraction in the mixture: Water + levofloxacin

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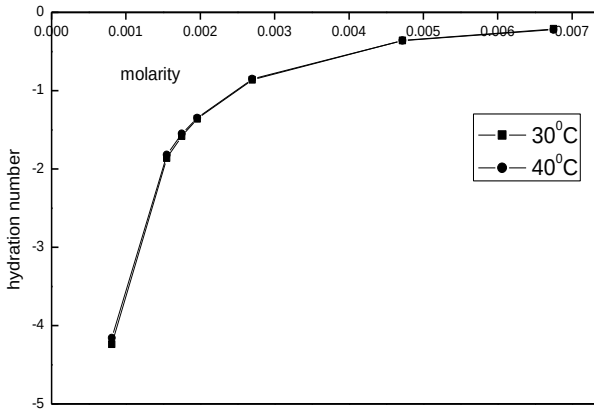

Fig.6(i). Variation of hydration number with molarity of levofloxacin in the mixture: Water + levofloxacin

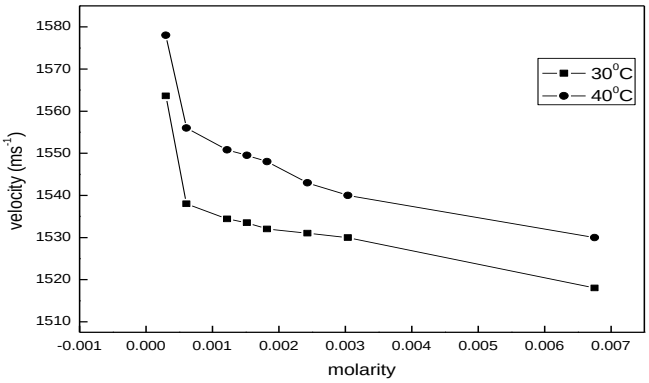

Fig.1(ii). Variation of velocity with molarity of tacrolimus in the mixture: Water + tacrolimus

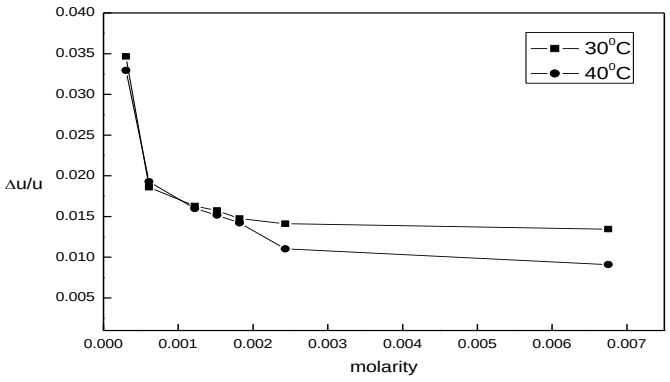

Fig.2(ii). Variation of Δu/u with molarity of tacrolimus in the mixture: Water + tacrolimus

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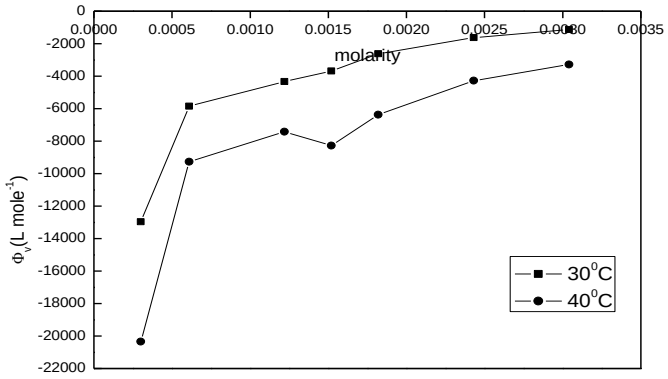

Fig.3(ii). Variation of Φ_v with molarity of tacrolimus in the mixture: Water + tacrolimus

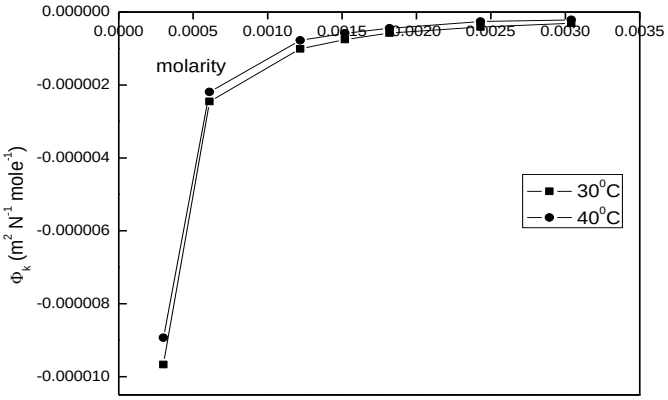

Fig.4(ii). Variation of Φ_k with molarity of tacrolimus in the mixture: Water + tacrolimus

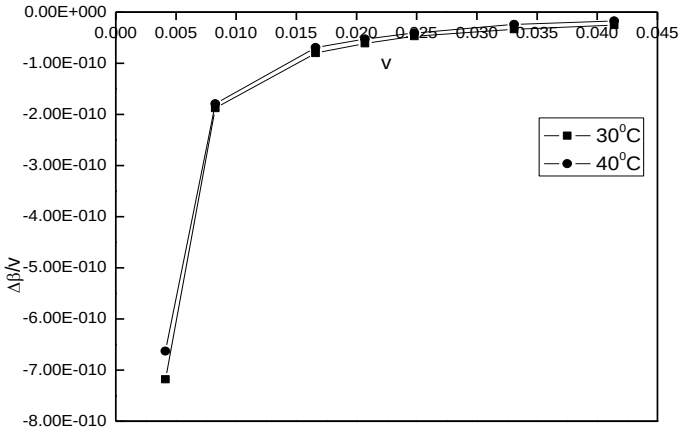

Fig. 5(ii). Variation of $\Delta\beta/v$ with volume fraction in the mixture: Water + tacrolimus

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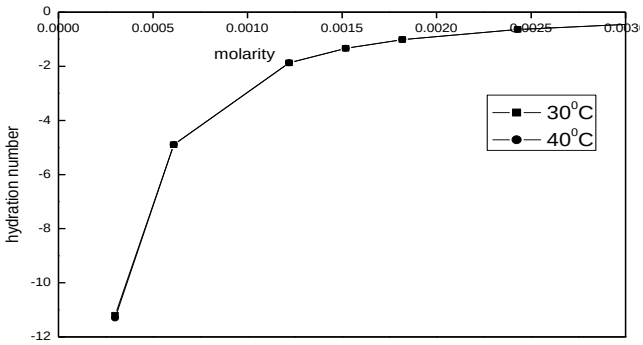

Fig.6(ii). Variation of hydration number with molarity of tacrolimus in the mixture: Water + Tacrolimus

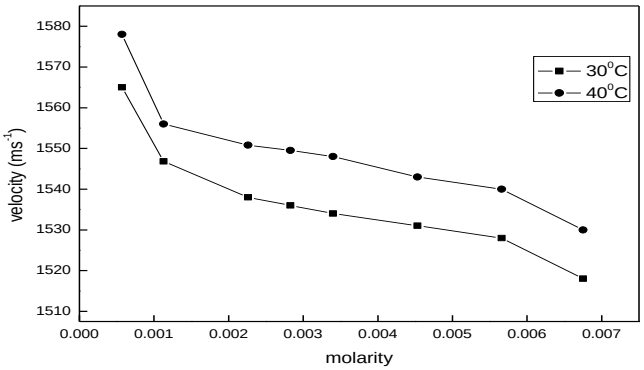

Fig.1(iii). Variation of velocity with molarity of lisinopril in the mixture: Water + lisinopiril

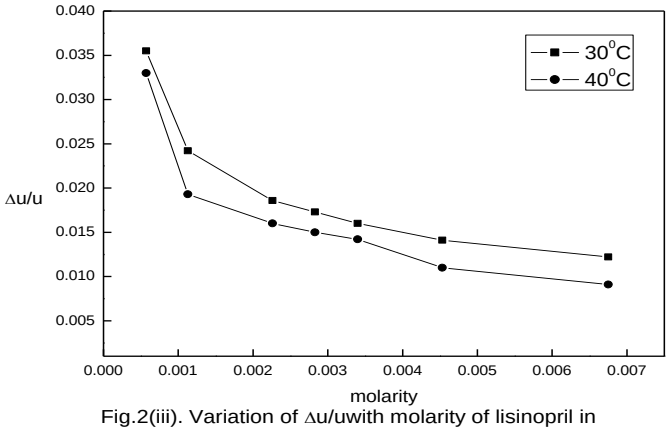

Fig.2(iii). Variation of Δu/uwith molarity of lisinopril in the mixture: Water + lisinopril

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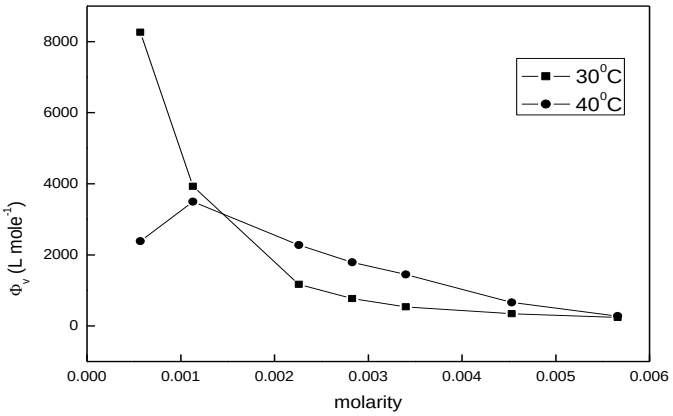

Fig.3(iii). Variation ofΦ_v with molarity of lisinopril in the mixture: Water + lisinopril

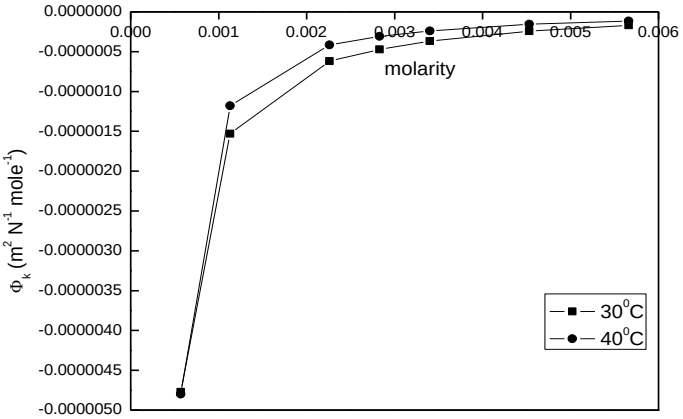

Fig.4(iii). Variation of Φ_k with molarity of lisinopril in the mixture: Water + lisinopril

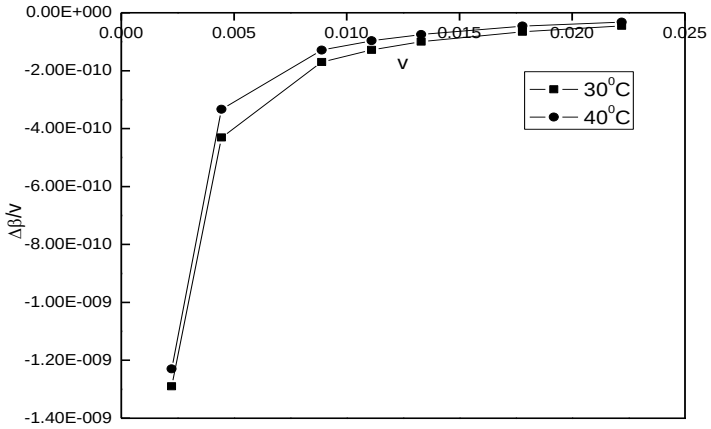

Fig. 5.(iii). Variation of $\Delta\beta/v$ with volume fraction in the mixture: Water + lisinopril

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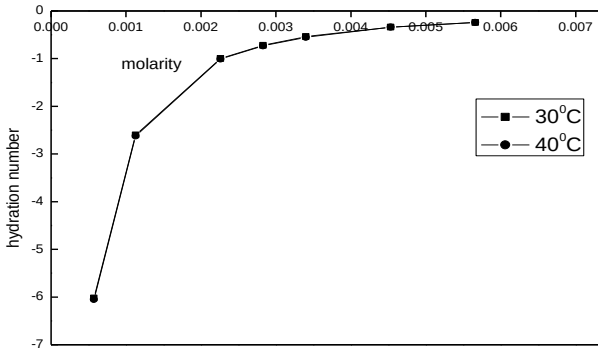

Fig.6(iii). Variation of hydration number with molarity of lisinopril in the mixture: Water + lisinopril

The nonlinearity of Δu/u vs. c suggests strong solute-solute interactions. Limiting slope A is negative at 30 and 40°C. The value of K confirms the presence of stacking phenomena in the aqueous solutions of levofloxacin. Compressibility of the stack is less than the corresponding monomers in this case. Δ, the stacking constant is positive at both 30 and 40°C and Φ_v and Φ_k are all negative and these negative values increase with molarity. $\Phi_k^0$are negative indicating strong solute-solvent interactions due to electrostrictive solvation of ions. Negative Φ_v^0 also indicate similar interactions. S_v, positive refers to strong interaction while B positive refers to strong alignment of the solvent molecules with the ions. The Jones-Dole constant A, negative, indicates strong solute-solvent interactions.

The values of (β water/ β) >1 suggests the presence of structure change of water in the levofloxacin solutions. Hydration numbers are negative at both the temperatures. From Jacobson's theory of compressibilities, the dimensionless parameter μ<1 suggests structure making property of levofloxacin in water medium.

For the aqueous solutions of the second hydrate i.e. tacrolimus monohydrate also similar interactions are estimated from nonlinearity of Δu/u vs. c, negative ϕ_k , the stacking interaction constant Δ , negative Φ_k^0, negative limiting slope A, negative Jones-Dole constant A. Here also($_{water}$/β)>1. Hydration numbers are negative. In the aqueous solutions of tacrolimus monohydrate also, μ<1 exhibiting the structure making property.In the third system.i.e.aqueous solutions of lisinopril dehydrate also, limiting slope A is negative, Δu/u is nonlinear. Φ_k^0 are negative indicating the existence of electrostrictive and hydrophobic interaction in the solution. Positive ϕ_v^0refers to strong solute-solvent interactions. From μ<1, structure promoting /building nature of the solute lisinopril is confirmed. Observed values of (β water/ β) >1 suggest the presence of structure change of water in the solutions.

At this juncture, it is appropriate to refer to some of the findings of earlier workers in aqueous and non aqueous solutions of some drugs.

In the aqueous solutions of seven ophthalmic solutions which reduce the intra-occular pressure (IOP) having the major component as pilocarpine nitrate/ pilocarpine hydrochloride /

timolol maleate, the effect of the solutes on the structure of water has been studied[6]. As the dimensionless parameter from Jacobson's theory of compressibility i.e., $\mu < 1$ in all the systems, structure making property of the drugs is established. In the aqueous solutions of some organic liquids generally used as solvents/ medicine/ drugs, also structure breaking/structure making property from μ values has been studied[2-3]. From apparent molar volumes and apparent molar compressibility studies of aqueous solutions of some drugs (sodium salicylate, methyl orange, L tryptophane, phenol and hydrochloride salts of propanol, procains, pilocarpene and ephydrine), solute-solute and solute-solvent interactions are suggested qualitatively[8].

From the Φ_v, Φ_k, n_h studies in the aqueous media of three drugs-Phenylpherine hydrochloride, pseudoephedrine hydrochloride and salbutanolsulphate, the hydrophobic and electrostatic hydrations are obtained. Low values of hydration numbers indicated the hydrophobic nature of drug molecules[9]. In the methanol studies of four drugs, it is observed that Φ_v^0 and B show differential solute-solute interactions while Φ_k^0 show that the drugs compress the solvent to some extent[10]. In the aqueous solutions of antibiotic doxy cyclinehyclate[11], from the association and stacking parameters and ultrasonic velocity deviation slope, solute-solute interactions at 313K and solute-solvent interactions at high temperatures have been observed. From the calculated parameters β, Z, L_f etc. in the aqueous solutions of phloroglucinol, strong association between solute and solvent molecules is recorded[12]. In the aqueous solutions of guicol[13], L-Alanine[14] and DSHP[15], molecular interactions between the solute and solvent molecules have been studied from the thermodynamic parameters and also hydration numbers. In the binary mixtures of alcohol + water with the drugs tramacip and parvodex[16], in the aqueous solutions of some amino acids like alanine, cysteine, methionine, glycine and pyroline (strong solute solvent interactions from Φ_v , Φ_k, S_v etc.,)[17], and in the aqueous solutions of cefadroxil[18] (solute-solvent interactions from β, β_{water}/β, Δ, k, Δu etc.,), various molecular interactions like solute-solvent, solute-solute interactions have been suggested. In the aqueous solutions of the two drugs digoxin and thiabenzadole in 1,4dioxane and acetone recently at 303.15K, weak solute-solvent interactions in the former drug solutions and strong solute-solvent interactions in thiabenzadole system are indicated[19]. The work of Rajkotia et al.[20], Paliwar and Tabhane[21] and ShipraBaluja and Anjana Shah[22] also deserve a mention here for comparison.

In the solutions of four esters in 1,4 dioxane at 30^{o}C, Rajkotia et al.[20] have observed more structure forming tendency in esters 1 and 3 to 2 and 4 and predominant solute – solute interactions in 1 and 3 ester solutions. From the behavior of some antimicrobials viz., amoxicillin (trihydr), ciprofloxacin (HCl), cephalaxin by studying the ultrasonic velocity, adiabatic compressibility, free length and internal pressure, the presence of molecular interactions, complex formation, formation of hydrogen bonds, solute – solvent interactions are observed. The nonlinearity confirms the presence of complex formation, solute – solvent interaction and weak association solute – solvent interaction and weak association due to hydration[21]. Acoustical / thermodynamic parameters have been determined in the solution of benzotriazole and diloxamide base in methanol, 1, 4 dioxane, dmf and tetra hydrofuran at 308.15 K. In both the systems ShipraBaluja and Anjana Shah[22] have observed from Φ_k^o , Φ_v^o,

S_v and Sk and other parameters that though both types of interactions exist, solute – solvent interactions are predominant.

Referring to the above workers' contributions and findings our results and discussion are found to be in conformity. The application of the apparent molar volumes, apparent molar compressibilities and some other thermodynamic parameters play a vital role in estimating the molecular interactions in the aqueous and non aqueous solutions of the drugs/organic liquids (in general solutes).

ACKNOWLEDGEMENTS

The authors are thankful to the authorities of the university and one of the authors (JG) acknowledges the UGC for RGNF (Senior).

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