Research Article

Volumetric and Viscometric Studies on Aqueous Ibuprofen Solutions at Temperatures

Sulochana Singh*, Upendra Nath Dash
Department Of Chemistry, I.T.E.R, Siksha 'O' Anusandhana University, Bhubaneswar, Odisha, India.
***Corresponding author's E-mail:** ssingh6383@gmail.com

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ABSTRACT

The solubility, density and viscosity values of ibuprofen in aqueous medium were measured at different temperatures ranging from 298.5 to 313.15 K at 5 K interval for different concentrations. Various parameters like apparent molar volume (V_ϕ°), limiting apparent molar volume (V_ϕ°), apparent molar expansibility (E_ϕ), and limiting apparent molar expansibility (E_ϕ°) were evaluated from the density values. From the viscosity data, the values of Falken-Hagen co-efficient (A_F) and the Jole-Dole co-efficient (B_J) were calculated using June-Dole empirical equation. The solubility of ibuprofen in aqueous medium is very very low. The values of V_ϕ°, E_ϕ°, A_F and B_J have been discussed in the light of solute solvent and molecular interactions in aqueous medium.

Keywords: Aqueous ibuprofen solution, Partial molar properties, Viscosity coefficients, Molecular interaction.

INTRODUCTION

Ibuprofen, obtained from isobutyl phenyl propanoic acid, is a weakly acidic, non–steroidal anti-inflammatory drug having high permeability through stomach, but due to its low solubility limitation, it can't enter into systemic circulation and gastric empting time ranging from 30 minutes to 2 hour and after this time ibuprofen goes to small intestine where it is solubilised but cannot permeate through its membrane. Ibuprofen is used to relieve pain from various conditions, such as headache, dental pain, muscle aches or arthritis. It works by blocking our bodies' production of certain natural substances that cause inflammation. This effect helps to decrease swelling, pain or fever.

Aqueous solubility of a therapeutically active substance (poorly water soluble drug) is an essential factor for drug effectiveness. Solubilisation may be defined as the method of preparation of a thermodynamically stable solution of a substance that is normally insoluble or very slightly soluble in a given solvent by the introduction of one or more amphiphilic compounds. Formulation and increasing the dissolution rate of poorly water soluble drugs for oral delivery now present one of the interesting challenges to formulation scientists in the pharmaceutical industry.

Ibuprofen is well known as a NSAIDs, analgesic, antipyretic agent. It is a weakly acidic drug having high permeability through stomach as it remains 99.9 % unionized in stomach (pK_a of ibuprofen =4.43 and pH of gastric juice =1.2). Though ibuprofen is highly permeable through stomach but due to its low solubility limitation it cannot permeate through its membrane. Ibuprofen has some surface active properties. These molecules can insert into membrane which could improve the absorption rate of the drug, but also could damage the gastrointestinal membranes following oral administration. In this respect, it is important to have idea of the drug availability in a highly soluble chemical form or a rapid dissolving solid dosage form.

For this reason, we decided firstly to investigate the solubility of ibuprofen in water. The bulk properties like density and viscosity have been measured which provide insight into the intermolecular arrangement of ibuprofen in water and help understand thermodynamic properties of the solution. Evaluation of partial molar properties is of importance as they provide a lot of information regarding solute-solvent interactions in solution. Since these quantities cannot be determined directly from the experiment, it is difficult to study the molecular interaction in solution. However, these quantities are related to the corresponding apparent molar quantities which are directly determined. Since solubility, dissolution rate and bioavailability of drug is a very challenging task in drug development work, the present investigation aims at determining solubility of ibuprofen and analyzing variations of density (d) and viscosity co-efficient (η) of the solutions of ibuprofen in aqueous medium with different concentrations at four different temperatures ranging from 298.15 K to 313.15 K at an interval of 5K. Attempt has been made to study the possible solute-solvent and solute-solute interactions from the derived volumetric and viscometric parameters in aqueous solutions.

MATERIALS AND METHODS

Chemicals

All chemicals used were of GR, BDH, or AnalaR grades. Conductivity water (Sp.cond.~10^{-6} S cm^{-1}) was used throughout the experiment.

Determination of solubility

The solution was prepared by adding an excess quantity of ibuprofen in 100 ml of conductivity water and heating the solution for 30 minutes maintained at 50°C. Then the

solution was kept with continuous stirring for 8 hours in a water thermostat maintained at the required temperature.

The solution was then filtered and its concentration was determined by titration with standard NaOH solution using phenolphthalein indicator.

This solution was then diluted successively to get the next four different concentrations at the corresponding temperature.

Measurement of density

The densities of ibuprofen solutions at the corresponding solubilizing temperatures were determined by using a specific gravity bottle (25 ml capacity) as described elsewhere.

At least five observations were taken and differences in any two readings did not exceed ±0.02%.[1]

Measurement of viscosity

Viscosity measurements on the aqueous solutions of ibuprofen at the respective solubiliizing temperatures were made as described elsewhere using an Ostwald viscometer in a water thermostat whose temperature was controlled to ±0.05K.

The values of viscosity so obtained were accurate to within ± $0.3x10^{-3}$ $kgm^{-1}s^{-1}$.

Viscosity values of water at the required temperatures were obtained from literature.[2,3]

Calculation

From the density data, the apparent molar volume(V_ϕ) was calculated by using the following equation[4]

$$V_\phi = 1000(cd_0)^{-1}(d_0-d)+Md_0^{-1} \quad (1)$$

where d_0 is the density of solvent (water), d is the density of the solution, c is the molar concentration and M is the molecular mass of the solute (ibuprofen).

The apparent molar expansibility, E_ϕ was determined from equation given below,[4]

$$E_\phi = \alpha_0 V_\phi+(\alpha-\alpha_0)1000c^{-1} \quad (2)$$

where α and α_0 are the coefficients of expansion of the solution and solvent, respectively, and were obtained from the following relations.[4]

$$\alpha_0 = \{-1/d_0\}(\delta d_0/\delta t)_P \text{ and}$$

$$\alpha = \{-1/d\}(\delta d/\delta t)_P \quad (3)$$

The relative viscosity of the solution was determined by Jones-Dole empirical equation as follows.

$$\eta_r = \eta/\eta_0 = 1+A_F c^{1/2}+B_J c \quad (4)$$

where η_r is the relative viscosity co-efficient, η is the viscosity coefficient of the solution and η_0 is that of the solvent, A_F is Falken-Hagen co-efficient and B_J is Jones-Dole co-efficient. The constants A_F and B_J are the intercept and slope respectively of the linear plots of $(\eta_r - 1)/c^{1/2}$ vs $c^{1/2}$.

The viscosity data have been analyzed on the basis of transition state theory from the following relation[5]

$$\Delta\mu_2^{0*} = \Delta\mu_1^{0*} + (RT/V_1^0)1000B_J - (V_1^0 - V_2^0) \quad (5)$$

where $\Delta\mu_2^{0*}$ is the contribution per mole of the solute to free energy of activation for viscous flow of the solution and

$$\Delta\mu_1^{0*} = 2.303RT \log(\eta_0 V_1^0/hN) \quad (6)$$

where h and N are Planck's constant and Avogadro number, respectively.

$\Delta\mu_1^{0*}$ is the contribution per mole of the solvent to free energy of activation for viscous flow of the solution.

$$\overline{V}_1^0 = M_{solvent}/d \quad (7)$$

$$\overline{V}_2^0 = V_\phi^0 \quad (8)$$

RESULTS

The relative density values of the solutions of ibuprofen of different concentrations have been determined at four different temperatures varying from 298.15K to 313.15K at 5K intervals. The values of the densities are given in Table -1.

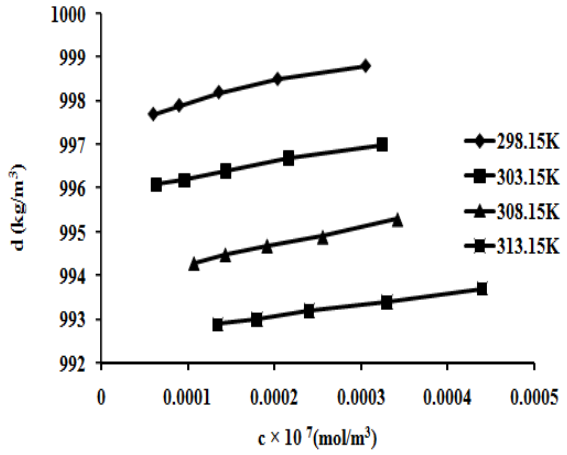

Figure 1: Variation of density of aqueous ibuprofen solutions with concentration at different temperatures

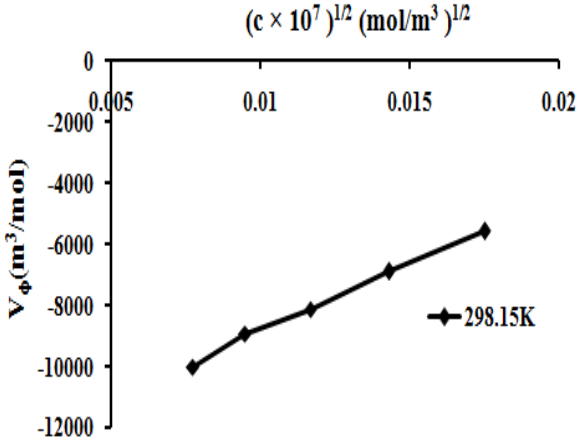

Figure 2: Plot of apparent molar volume (V_ϕ) vs $c^{1/2}$ of aqueous ibuprofen solution at 298.15K

The values of limiting apparent molar volumes (V^0_ϕ), limiting apparent molar expansibility (E^0_ϕ), the slope(S_v) of the plot of $V_\phi$vs $c^{1/2}$ and the slope (S_E) of the plot E_ϕ vs $c^{1/2}$ are given in Table 2 for the aqueous ibuprofen solutions at the experimental temperatures.

The experimentally determined values of viscosity (η) for ibuprofen solutions at 298.15 K to 313.15 K at an interval of 5K are presented in Table-3. The relative values of viscosities (η_r), viscosity coefficients A_F and B_J ,$\Delta\mu_1^{0*}$ and $\Delta\mu_2^{0*}$ have been evaluated by means of equations (6), (7) and (8), respectively and are also presented in Table 3.

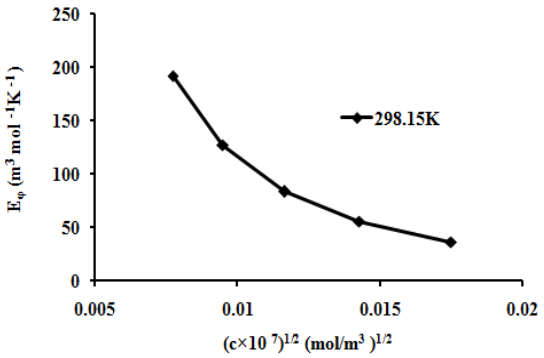

Figure 3: Plot of apparent molar expansibility(E_ϕ) vs $c^{1/2}$ of aqueous ibuprofen solution at 298.15K.

Table 1: Density values, d_0 of water and d, of aqueous ibuprofen solutions at different temperatures

Temp (K)	$c \times 10^7$ (mol/m^3)	d_0 (kg/m^3)	d (kg/m^3)
298.15	3.06	997.1	998.8
	2.04		998.5
	1.36		998.2
	0.9		997.9
	0.6		997.7
303.15	3.24	995.7	997
	2.16		996.7
	1.44		996.4
	0.96		996.2
	0.64		995.9
308.15	3.42	994.1	995.3
	2.56		994.9
	1.92		994.7
	1.44		994.5
	1.08		994.3
313.15	4.4	992.3	993.7
	3.3		993.4
	2.4		993.2
	1.8		993.0
	1.35		992.9

The density values of water at the required temperatures were obtained from literature.

Table 2: Values of V_ϕ^0 ,S_v ,E_ϕ^0 and S_E for aqueous ibuprofen solutions at different temperatures

Temperature (K)	$V_\phi^0 \times 10^{-3}$ (m^3mol^{-1})	$S_v \times 10^{-4}$ ($m^{9/2}mol^{3/2}$)	$E_\phi^0 \times 10^{-2}$ ($m^3mol^{-1}K^{-1}$)	$S_E \times 10^{-4}$ ($m^{9/2}mol^{-3/2}K^{-1}$)
298.15	-13.34	4.48	2.80	-1.51
303.15	-7.48	1.98	2.67	-1.39
308.15	-0.56	-0.17	1.92	-0.90
313.15	-5.81	1.30	1.50	-0.62

- The values of V_ϕ calculated by means of Eqn (1) were fitted by a method of least-sqaures to Massion equation to obtain V_ϕ^0 (limiting apparent molar volume) and the slope, S_v [4]

$$V_\phi = V_\phi^0 + S_v c^{1/2} \quad (9)$$

- The values of E_ϕ were fitted to Massion equation to get the limiting apparent expansibility, E_ϕ^0, and the slope S_E.[4]

$$E_\phi = E_\phi^0 + S_E c^{1/2} \quad (10)$$

Table 3: Values of viscosity η, relative viscosity (η_r), A_F ,B_J ,$\Delta\mu_1^{0*}$ and $\Delta\mu_2^{0*}$ for aqueous ibuprofen solutions at different temperatures.

Temp (K)	Solvent η ($kgm^{-1}s^{-1}$)	c×10^7 (mol m^{-3})	η ($kgm^{-1}s^{-1}$)	η_r	A_F ($10^{7/2}$ ×$mol^{-1/2}$ $m^{3/2}$)	B_J (10^7 m^3 mol^{-1})	$\overline{V_1}°$×10^4 (m^3mol^{-1})	$\overline{V_2}°$×10^{-3} (m^3 mol^1)	$\Delta\mu_1{}^{o*}$×10^{-3} (kJ mol^{-1})	$\Delta\mu_2{}^{o*}$×10^{-9} (kJ mol^{-1})
298.15	8.94	3.06	9.48	1.06	-0.644	243.7	2.07	-13.33	3.06	28.90
		2.04	9.33	1.04						
		1.36	9.17	1.03						
		0.9	9.09	1.02						
		0.6	9.01	1.01						
303.15	8.01	3.24	8.44	1.05	0.051	188.8	2.07	-7.48	3.11	22.70
		2.16	8.37	1.05						
		1.44	8.30	1.04						
		0.96	8.15	1.02						
		0.64	8.08	1.01						
308.15	7.23	3.42	7.80	1.08	-0.172	267.5	2.07	-0.56	3.15	32.63
		2.56	7.73	1.07						
		1.92	7.67	1.06						
		1.44	7.52	1.04						
		1.08	7.37	1.02						
313.15	6.56	4.4	6.96	1.06	-0.687	187.0	2.07	-5.81	3.20	23.15
		3.3	6.89	1.05						
		2.4	6.83	1.04						
		1.8	6.76	1.03						
		1.35	6.62	1.01						

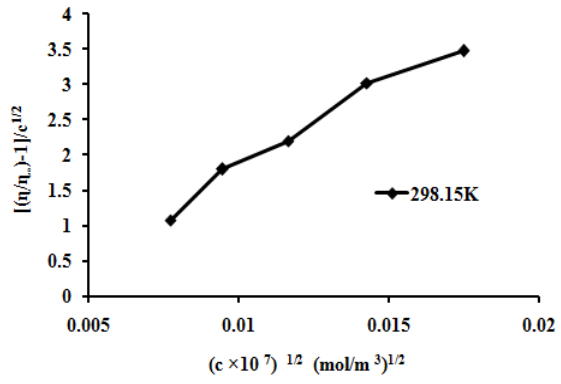

Figure 4: Plots of $[(\eta/\eta_0) - 1)]/c^{1/2}$ vs. $c^{1/2}$ of aqueous ibuprofen solution.

DISCUSSION

It was found that the V_ϕ varied linearly with concentration $c^{1/2}$. From Table-1, it is evident that the densities of solutions are greater than that of the solvent and the density values decrease with decrease in concentrations and decrease with increase in temperature (shown in Figure-1).

A typical plots of V_ϕ vs $c^{1/2}$ and E_ϕ vs $c^{1/2}$ are shown in Figure-2 and 3, respectively.

As observed from Table-2, the values of limiting apparent molar volume V_ϕ^0 are negative at the experimental temperatures.

Since V_ϕ^0 is a measure of solute-solvent interaction, the negative values suggest that there is weaker solute-solvent interaction and also provides for the evidence of electrostriction varying irregularly with temperature.

The positive and large values of S_v (except at 303.15K) of solutions of ibuprofen indicates the presence of strong solute-solute interaction (a weak solute-solvent interaction) varying with change of temperatures.[5,6]

A perusal of Table-2 shows that the E_ϕ^0 values are positive in all cases and decrease with increase in temperature.

Since E_ϕ^0 gives an indication of caging or packing effect the positive values of E_ϕ^0 suggest that the structure making (hydrophilic) effect of ibuprofen is favoured in aqueous medium. As observed, the values of S_E are negative in all cases.

The results are again in agreement with the above contention that the structure making effect is favoured in aqueous solution.[5]

A perusal of Table-3 reveals that the viscosity values decrease with decrease in concentration, and with

increase in temperature. A typical plot of $[(\eta/\eta_0) - 1)]/c^{1/2}$ vs $c^{1/2}$ at 298.15 K is shown in Figure-4.

The values of A_F are very small and negative in most cases (except at 303.15K).

Since A_F is considered to be a measure of solute-solute interaction, the very small negative values of A_F may indicate that the interactions are dependent on the nature of the solute and also the structure of the solvent.

The co-efficient B_J is a measure of the effective solvodynamic volume of solvated ions and is governed by solute-solvent interactions, i.e. the structural effect of the solvent in solution.

It is a fact that when a solute is dissolved in solvent, some of the solvent molecules are wrenched out of the solvent structure because of solute-solvent interactions and this causes an increase in viscosity of solution (a positive contribution to the B_J co-efficient). On the other hand, the solvent molecules have to be wrenched out of the bulk solvent and this breaking of this solvent structure cause a decrease in viscosity of the solution (a negative contribution to B_J). Thus, the value of BJ are positive but very small indicating that the interactions are also dependent on the nature of the solute and the structure of the solvent.[7,8]

The values of $\Delta\mu_1^{0*}$ are found to be positive at all temperatures showing positive contribution per mole of the solvent to free energy of activation for viscous flow of solution.

The positive values of $\Delta\mu_2^{0*}$ show greater contribution per mole of solute to free energy of activation for viscous flow of the solution and are in good agreement with the values of B_J-coefficient. Again positive and large values of $\Delta\mu_2^{0*}$ indicate the formation of the transition state accompanied by the rupture and distortion of the intermolecular forces in solvent structure.[9]

CONCLUSION

The density and viscosity values were found to decrease with decrease in concentration and increase in temperature. The negative value of limiting apparent molar volume (V_ϕ^0) is the indicative of the weak solute-solvent interaction. The positive values of E_ϕ^0 suggest that the structure making effect of ibuprofen is favoured in aqueous medium. The viscosity value decreases with decrease in concentration of the solution. The positive and large values of $\Delta\mu_2^{0*}$ indicate the formation of the transition state accompanied by the rupture and distortion of the intermolecular forces in solvent structure.

REFERENCES

1. Dash UN, Supkar S, Acoustic behaviour of glycine and its salts in aqueous organic solvent system. Acoust Letters, 16, 1992, 135.
2. Dash UN, Supkar S, Ion association and salvation of octahedral Co(III) complexes in water + mannitol and water + surbitol mixtures Proc Indian Acad Sci (Chem Sci) 107(5), 1995, 541.
3. Robinson RA, Stokes RH, Electrolyte Solutions, Butterworths Scientific Publication, London, 1955, p.30.
4. Harned HS, Owen BB, The Physical Chemistry Of Electrolytic Solutions,3rd edn, Reinhold, NewYork, 1958.
5. Feakins D, Freemantle J D, Lawrence KG, Transition state treatment of the relative viscosity of electrolytic solutions, application to aqueous and non aqueous and methanol + water systems. J. Chem. Soc. Faraday Trans. I, 70, 1974, 795.
6. Thirumanar S, JobSaba K, Ultrasonic investigation of amino acids in aqueous sodium acetate medium. Indian J. Pure and Appl.Physics, 47, 2009, 87.
7. Palani R, Jayachitra K, Ultrasonic study of ternary electrolytic mixtures at 303, 308 and 313K. Indian J. Pure and Appl.Physics, 46, 2008, 251.
8. Stokes RH Mills R, International Encyclopedia of Physical Chemistry and Chemical Physics, Pergamon, New York; 1965.
9. Gurney R W, Ionic Processes in Solutions, Dover, New York, 1962, Ch 9.

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