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Density and viscosity studies of aspirin in aqueous ethanol system at 301.5k

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ABSTRACT

Density and Viscosity of drug Aspirin (APN) in various aqueous mixtures of ethanol have been determined. These results are further extended for solutes like electrolyte NaCl and non-electrolyte sucrose in the presence of this drug. The density and viscosity data have been analyzed for the evaluation of partial molar volume, molar excess volume, Gibbs free energy of viscous flow, excess viscosity and A and B viscosity coefficients using Jones-Dole equation. It can be inferred from these studies that this drug acts as a structure-making compound due to hydrophobic hydration of drug molecules. B-coefficients values are found to be positive thereby showing drug solvent interactions. Furthermore these results are correlated to understand the solution behavior of drug.

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KEYWORDS

Aspirin;
Partial molar volume;
Gibbs free energy of
viscous flow;
Excess viscosity.

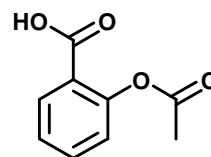
INTRODUCTION

Solute-solvent interactions play an important role in a variety of phenomena. In bio-physical chemistry, drug interaction is a subject of intensive studies, involving complex molecular mechanisms. Despite years of investigations, many important drug actions and their mechanisms are not fully understood. Solute-solvent interaction studies have been a subject of active interest among physical chemists^[1,2] and mostly the inferences regarding these interactions are drawn from molar volume data^[3] & viscosity data^[4] together.

Most of the drugs are organic molecules with both hydrophobic and hydrophilic groups. These molecules often contain certain groups, which are responsible for their acidic, basic or amphoteric properties. Pharma-

logical properties^[5,6] of drugs are highly dependent on the solution behavior. The thermodynamic properties are the convenient parameter for interpreting solute-solvent interactions in the solution phase, which ultimately explain the excess properties using different interaction parameters.

In the present communication an attempt has been made to study density and viscosity measurements of Aspirin in aqueous ethanol to investigate various types of interactions.



Structure of aspirin

TABLE 1 : Density ρ (g cm^{-3}) of APN in binary system at 301.5K

v/v % Et-OH	0.02 M	0.04 M	0.06 M	0.08M	0.10 M
20	0.9968	1.0005	1.0041	1.0075	1.0114
40	0.9723	0.9762	0.9798	0.9833	0.9867
60	0.9461	0.9496	0.9532	0.9568	0.9607
80	0.9069	0.9104	0.9142	0.9178	0.9214
100	0.8148	0.8184	0.8217	0.8256	0.8293
ρ of APN +0.01 M NaCl					
v/v % Et-OH	0.02 M	0.04 M	0.06 M	0.08M	0.10 M
20	0.9974	1.0011	1.0047	1.0082	1.0119
40	0.9730	0.9765	0.9803	0.9838	0.9874
60	0.9468	0.9502	0.9538	0.9576	0.9612
80	0.9073	0.9111	0.9146	0.9181	0.9219
100	0.8153	0.8188	0.8226	0.8261	0.8296
ρ of APN +0.01 M Sucrose					
v/v % Et-OH	0.02 M	0.04 M	0.06 M	0.08M	0.10 M
20	0.9996	1.0038	1.0076	1.0112	1.0146
40	0.9754	0.9796	0.9832	0.9868	0.9904
60	0.9491	0.9532	0.9568	0.9604	0.9638
80	0.9098	0.9139	0.9176	0.9212	0.9248
100	0.8173	0.8217	0.8254	0.8288	0.8324

TABLE 2: Viscosity η (mPa.s) of APN in binary system at 301.5K

v/v % Et-OH	0.02 M	0.04 M	0.06 M	0.08M	0.10 M
20	1.7063	1.7135	1.7251	1.7286	1.7498
40	2.3374	2.3513	2.3748	2.3873	1.7395
60	2.4182	2.4376	2.4543	2.4654	2.3979
80	1.9863	1.9906	2.0867	2.1880	2.4818
100	1.3691	1.3745	1.3911	1.4131	2.3048
η of APN +0.01 M NaCl					
v/v % Et-OH	0.02 M	0.04 M	0.06 M	0.08M	0.10 M
20	1.7158	1.7233	1.7389	1.7428	1.7471
40	2.3458	2.3692	2.3885	2.4064	2.4274
60	2.4466	2.3827	2.4717	2.4896	2.5182
80	1.9906	1.9627	2.1464	2.2848	2.3317
100	1.3717	1.3986	1.4023	1.4447	1.4544
η of APN +0.01 M Sucrose					
v/v % Et-OH	0.02 M	0.04 M	0.06 M	0.08M	0.10 M
20	1.7318	1.7582	1.7613	1.7844	1.8093
40	2.3815	2.3908	2.4018	2.4650	2.5064
60	2.5614	2.5864	2.5984	2.6171	2.6390
80	2.1196	2.1321	2.3589	2.4502	2.4708
100	1.4009	1.4255	1.4367	1.5584	1.6478

EXPERIMENTAL

Materials

The binary solvent selected for the study was ethanol + water. Commercial ethyl alcohol is refluxed with CaO for six to eight hours and distilled^[7]. Double distilled water is used for preparation of solution mixture. The distillation of water was carried out using a pinch of KMnO₄ & KOH in glass quick fit apparatus. The density and viscosity of water and ethanol are measured at 298.15 K and 303.15 K and compared with literature values.

Apparatus and procedure

Densities of liquids and various solutions were measured at 301.5K by using specific gravity bottle of 10 cm³ capacity. A single pan electronic balance [Sansui; model KD-UBED of capacity 120 gm and with a precision of 0.0001 gm] was used for weighing purpose. The weighing was repeated thrice to ensure the accuracy in weights with a little interval of time. The reproducibility of the result was close to hundred percent.

Viscosity measurements were carried out using Ostwald's viscometer with precision $\pm 0.1\%$. The viscometer was clamped vertically in a thermostatically controlled water-bath, whose temperature was maintained constant at 301.5K ($\pm 0.02^\circ\text{C}$). A fixed volume (10ml) of the solution was delivered into the viscometer.

The viscometer was kept for 30 minutes in the thermostatically controlled water-bath to achieve constant temperature. The experiments of measurements of flow time of the solution between the two points on the viscometer were performed at least three times for each solution and the average results were noted.

RESULTS AND DISCUSSION

Aspirin is chemically 2-acetoxybenzoic acid. It is white crystals, commonly tabular or needle-like, or a white, crystalline powder; odorless or a faint odor; stable in dry air.

The densities and viscosities of ethanol- water binary mix from 20 % to 100 % range are measured

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TABLE 3a : Φ_v in $\text{cm}^3 \text{mol}^{-1}$ and V^E in $\text{cm}^3 \text{mol}^{-1}$ of APN in binary mixture at 301.5 K

V/V % Et- OH	0.02 M (APN)		0.04 M (APN)		0.06 M (APN)	
	Φ_v	V^E	Φ_v	V^E	Φ_v	V^E
20	180.0856	-0.9168	179.2601	-0.9910	177.5838	-1.0627
40	184.6256	-1.5869	183.7961	-1.6804	181.9038	-1.7661
60	189.6993	-2.5552	188.9828	-2.6598	186.9829	-2.7665
80	197.8443	-3.6481	197.0650	-3.7899	194.8266	-3.9426
100	220.0783	-2.3229	218.9802	-2.5712	216.5845	-2.7969
V/V % Et- OH	0.08 M (APN)		0.10 M (APN)			
	Φ_v	V^E	Φ_v	V^E		
20	176.7778	-1.1299	176.0159	-1.2064		
40	181.1329	-1.8488	180.3863	-1.9286		
60	186.1099	-2.8725	185.1875	-2.9864		
80	193.7931	-4.0861	192.9396	-4.2285		
100	215.2039	-3.0614	214.0213	-3.3100		

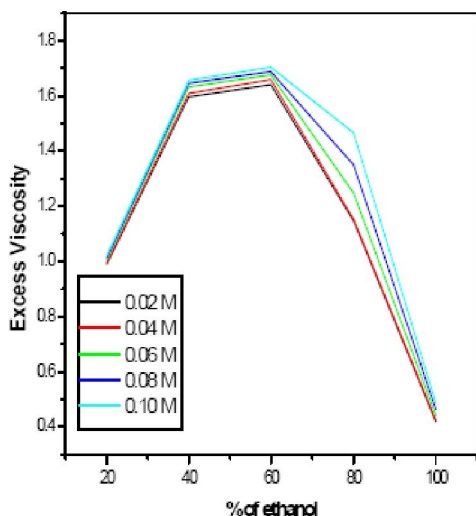


Figure 1 : Variation of η^E with % ethanol

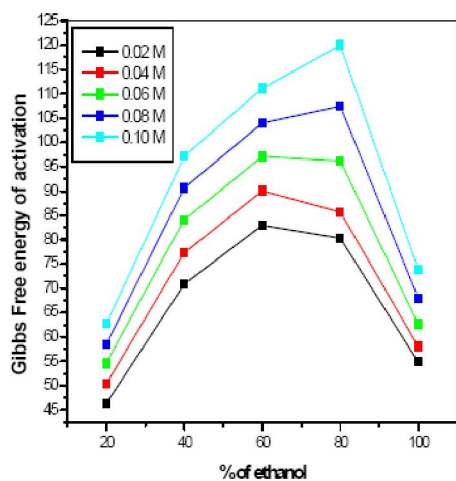


Figure 2 : Variation of ΔG^{*E} with % ethanol

TABLE 3b : Φ_v in $\text{cm}^3 \text{mol}^{-1}$ and V^E in $\text{cm}^3 \text{mol}^{-1}$ of (APN) +0.01 M NaCl in binary mixture at 301.5 K

V/V % Et- OH	0.02 M (APN)		0.04 M (APN)		0.06 M (APN)	
	Φ_v	Φ_v	Φ_v	Φ_v	Φ_v	Φ_v
20	58.5571	58.5571	58.3408	58.3408	58.1319	58.1319
40	60.0185	60.0185	59.8280	59.8280	59.5840	59.5840
60	61.6781	61.6781	61.4640	61.4640	61.2322	61.2322
80	64.3825	64.3825	64.0930	64.0930	63.8688	63.8688
100	71.6352	71.6352	71.3379	71.3379	70.9653	70.9653
V/V % Et- OH	0.08 M (APN)		0.10 M (APN)			
	Φ_v	V^E	Φ_v	V^E		
57.9244	-1.1457	57.7242	-1.1457	57.7242		
59.3721	-1.8621	59.1438	-1.8621	59.1438		
60.9766	-2.8985	60.7674	-2.8985	60.7674		
63.6324	-4.0990	63.3564	-4.0990	63.3564		
70.6992	-3.0973	70.4181	-3.0973	70.4181		

TABLE 3c : Φ_v in $\text{cm}^3 \text{mol}^{-1}$ and V^E in $\text{cm}^3 \text{mol}^{-1}$ of (APN) +0.01 M sucrose in binary mixture at 301.5 K

V/V % Et- OH	0.02 M (APN)		0.04 M (APN)		0.06 M (APN)	
	Φ_v	V^E	Φ_v	V^E	Φ_v	V^E
20	341.1785	-0.9751	339.5852	-1.0616	338.2414	-1.1396
40	349.5110	-1.6638	347.9104	-1.7667	346.6409	-1.8543
60	359.2024	-2.6474	357.4364	-2.7725	356.0966	-2.8813
80	374.7086	-3.7683	372.7872	-3.9369	371.3304	-4.0872
100	417.1710	-2.4984	414.5388	-2.8043	412.4872	-3.0601
V/V % Et- OH	0.08 M (APN)		0.08 M (APN)			
	Φ_v	V^E	Φ_v	V^E		
20	336.9745	-1.2133	336.9745	-1.2133		
40	345.3455	-1.9416	345.3455	-1.9416		
60	354.7668	-2.9893	354.7668	-2.9893		
80	369.8846	-4.2325	369.8846	-4.2325		
100	411.0516	-3.2904	411.0516	-3.2904		

(TABLE 1 and 2) and used for determination of partial molar volume. The partial molar volume Φ_v was obtained from density results using eq. 1

$$\phi_v = \frac{1000}{C} \left(\frac{d_0 d}{d} \right) + \frac{M}{d} \quad (1)$$

where d_0 is the density of pure solvent & d is the density of solution, c is molar concentration, M is molar mass of drug.

Aspirin consist of bulkier carboxylic and acetate group. It is observed that the Φ_v values decreases with concentration of APN and increases with increase in percentage of alcohol (TABLE 3).

TABLE 4 : Excess viscosities (η^E) : - (mPas)

V/V % Et- OH	0.02 M	0.04 M	0.06 M	0.08 M	0.10 M
Ethanol-water + (APN)					
20	0.9890	0.9962	1.0078	1.0113	1.0222
40	1.5954	1.6093	1.6328	1.6453	1.6559
60	1.6398	1.6592	1.6759	1.6870	1.7034
80	1.1489	1.1532	1.2493	1.3506	1.4674
100	0.4195	0.4249	0.4415	0.4635	0.4881
Ethanol-water + (APN) + 0.01 M Sucrose					
20	1.0145	1.0409	1.0440	1.0671	1.0920
40	1.6395	1.6488	1.6598	1.7230	1.7644
60	1.7830	1.8080	1.8200	1.8387	1.8606
80	1.2822	1.2947	1.5215	1.6128	1.6334
100	0.4513	0.4759	0.4871	0.6088	0.6982
Ethanol-water + (APN) + 0.01 M NaCl					
20	0.9985	1.0060	1.0216	1.0255	1.0298
40	1.6038	1.6272	1.6465	1.6644	1.6854
60	1.6682	1.6043	1.6933	1.7112	1.7398
80	1.1532	1.1253	1.3090	1.4474	1.4943
100	0.4221	0.4490	0.4527	0.4951	0.5048

The density data was also used to evaluate excess molar volumes (TABLE 3) calculated by using the relation (eq. 2).

$$V^E = \left(\frac{x_1 M_1 + x_2 M_2}{\rho} \right) - \frac{x_1 M_1}{\rho_1} - \frac{x_2 M_2}{\rho_2} \quad (2)$$

where, ρ is the density of mixture, M_1 , X_1 , V_1 and M_2 , X_2 & V_2 are the molecular weight, mole fraction and molar volumes of ethanol & water respectively.

The excess molar volumes calculated for APN in absence and in presence of additives are negative. We observed that V^E changes parabolically in negative direction with % of ethanol. Over all range of concentration it was observed that V^E values are less in absence of additives and slightly high when NaCl is used. But in presence of sucrose these values are higher in negative direction. This indicates more solubility of it in the mixture. The parabolic shape of V^E against % ethanol is characterized by well defined minima which indicate the presence of complex form between mixing components of solution.

The excess volume of mixture containing APN with and without additives is shown in TABLE 3. These values are positive and changes in parabolic way with the % of ethanol. The higher values of excess viscosities of

TABLE 5 : Gibbs free energy of viscous flow ΔG^{*E} (kJ mole⁻¹)

V/V% Et-OH	0.02 M	0.04 M	0.06 M	0.08 M	0.10 M
Ethanol-water + APN					
20	46.3301	50.3194	54.5241	58.4344	62.7108
40	70.8388	77.2882	84.1162	90.6377	97.1606
60	82.9775	90.0794	97.1325	104.0027	111.1286
80	80.3369	85.7136	96.2390	107.4665	119.9832
100	54.8506	58.0204	62.5937	67.9387	73.8263
Ethanol-water + APN + 0.01 M Sucrose					
20	50.8367	55.7521	59.7715	64.8481	70.1958
40	77.9417	84.3584	90.8573	99.5563	107.6675
60	94.0835	101.8277	109.1786	116.8446	124.7641
80	92.3301	98.6808	117.0594	128.4104	135.8726
100	60.9882	66.6451	70.8725	89.1992	103.9187
Ethanol-water + APN + 0.01 M NaCl					
20	47.2662	51.3144	55.7482	59.7389	63.7331
40	72.0542	78.8728	85.5990	92.3827	99.4007
60	84.9585	89.0395	98.8725	106.0773	113.8874
80	81.4046	84.9315	100.5868	114.1301	122.6052
100	55.5588	61.3000	64.3946	72.4694	76.5569

non-electrolyte in binary system may be due to the presence of larger and bulkier groups.

Viscosity is found to maximum at around 50% (V/V) in aqueous mixtures of alcohol. It seems that some kind of structural organization of water surrounding the hydrocarbon chain of alcohol is the most likely explanation of the observed dependence of viscosity on solvent composition.

The measured values of viscosities of liquid mixtures and those of pure components were used to calculate the excess viscosity η^E (TABLE 4) in the liquid mixtures using the formula (eq. 3),

$$\eta^E = \eta_{\text{mix}} - (x_1 \eta_1 + x_2 \eta_2) \quad (3)$$

where, η_{mix} , η_1 & η_2 are the viscosities of liquid mixtures, component (1) & (2) respectively and x_1 & x_2 are the mole fractions of component (1) & (2) respectively.

The hydrocarbon residue of APN in alcohol results in a considerable amount of hydrophobic hydration. However the further decrease of excess viscosity with increase in percentage alcohol may result because these hydrophobic groups exerts there effect predominantly with increase in alcohol percent (Figure 1). It appears that above 60 % v/v alcohol concentration a loss of

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TABLE 6 : A and B coefficient values

V/V% Et-OH	(APN)		(APN) +0.01 Sucrose		(APN) +0.01 NaCl	
	A	B	A	B	A	B
20	2.1994	0.0641	2.6456	0.0976	2.1639	0.0698
40	2.1894	0.0695	2.7082	0.1090	2.1985	0.0693
60	2.4844	0.0839	3.4030	0.1284	2.6351	0.0948
80	2.9165	0.0958	4.4502	0.1581	3.3395	0.1121
100	3.3706	0.1106	5.0488	0.1785	3.4954	0.1217

hydrophobic hydration takes place which leads to decrease in excess viscosity^[8].

On the basis of the theory of absolute reaction rates, the excess Gibb's free energy of activation for viscous flow, $\Delta G^{E[9,10]}$ were calculated (TABLE 5) for all the system under study using the equation:

$$\Delta G^{*E} = RT \{ \ln(\eta V/\eta_2 V_2) - x_1 \ln(\eta_1 V_1/\eta_2 V_2) \} \quad (4)$$

where, η , η_1 & η_2 are the viscosities of liquid mixtures, components (1) & (2) respectively, V_1 & V_2 are the molar volumes of components (1) & (2) respectively, x_1 is the mole fraction of first component, R is the gas constant & T is the absolute temperature.

The values are positive and changes parabolically with percentage of ethanol (Figure 2). The maximum Gibbs free energy of viscous flow for ethanol-water is 75.4598 KJ mole⁻¹. The trend in maxima shows that ΔG^{*E} for NaCl is less than ΔG^{*E} for sucrose. This excess free energy increases with increase in concentration of APN keeping concentration of additive const.

The values of ΔG^{*E} is much higher when APN and additives are present together. The positive values of ΔG^{*E} represent the size effect of mixing components. It is considered that if ΔG^{*E} is positive there are specific interactions like hydrogen bonding which exists between molecules of mixture^[11].

B coefficient values are calculated using Jones-Dole equation.

$$\eta_r = 1 + A\sqrt{c} + B \quad (5)$$

The values of A & B are determined (TABLE 6) from the intercept & slope of the lines of plots of $(\eta/\eta_0 - 1)$ verses \sqrt{c} . We observed positive values for all the systems. The B coefficient for APN in absence of additives is less and in presence of non-electrolyte sucrose is more. This increases with increase in percentage of alcohol which indicates the structural increases of solution from water to alcohol. The B coefficient of APN solution reflects the net structural effects of polar groups and hydrophobic benzene ring.

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