Apparent Molal Volumes and Viscosity *B*-Coefficients of Acetyl Salicylic Acid (2-Acetoxy Benzoic Acid) Solutions in Higher Alcohols at Different Temperatures

Muhammad J. Iqbal* and Mansoora A. Chaudhry

Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan

Aspirin is used as an analgesic, antipyretic, and anti-inflammatory drug. Density and viscosity of acetyl salicylic acid (2-acetoxy benzoic acid) in propan-1-ol, propan-2-ol, butan-1-ol, and butan-2-ol at temperatures in the range (293.15 to 313.15) K have been measured in a molality range of ($9.5 \cdot 10^{-3}$ to $31.9 \cdot 10^{-3}$) mol·kg^{-1} with the help of a commercially available vibrating-tube densimeter and viscometer. From the density data, apparent molal volume (V_ϕ), partial molal volume (V_m^0), isobaric thermal expansion coefficient (α_2), partial molal expansivity (E_2^0), Hepler's constant ($\delta^2 V_m^0/\delta T^2$), and transfer volume ($\Delta V_m^0$) are calculated. The viscosity data are analyzed by the Jones−Dole equation to determine the values of the viscosity *B*-coefficient.

Introduction

Various biological processes involve volume changes and hydration of molecules, and their complete understanding needs a suitable idea of volumetric and viscometric studies. Drug actions, i.e., drugs reaching the bloodstream, its distribution, binding to receptors, and finally producing the physiological action, all depend on various volumetric and viscometric properties, mostly decided by different interactions, namely, ionic or covalent, charge transfer, hydrogen bonding, or hydrophobic interactions. Both volumetric and viscometric studies provide valuable information about solute−solvent interactions in the solution phase. The characterization of the nonsteroidal anti-inflammatory drug, i.e., 2-acetoxy benzoic acid (acetyl salicylic acid or aspirin), is the subject of interest due to its antipyretic, analgesic, and antiplatelet or anticoagulate properties. It is also used for the prevention of stroke and cardiovascular disease.[1] 2-Acetoxy benzoic acid is a hydrophobic drug with low solubility in water. Therefore, study of its apparent molal volume and viscosity *B*-coefficients in propan-1-ol, propan-2-ol, butan-1-ol, and butan-2-ol is an important task in pharmaceutical technology because it can lead to better bioavailability and more bioefficiency.

Choice of solvents was made due to their wide applications in pharmaceuticals. However, they are not components of living organisms, but they act as a vehicle for pharmaceuticals when introduced into living organisms. Most drugs permeate biological membranes by passive diffusion. The solvents are added to improve solubility and thus allow the permeation of drugs through the membranes more easily. Alcohols have been used as antiseptics, spirits, local anesthetic, and disinfectants for many years. The antibacterial potencies of primary alcohols increase with molecular weight until octanol.[2] The solution structure is of great importance in understanding the nature of action of drugs in the body's system.

The objective of the present study is to provide greater relevance to the drug−macromolecular behavior near physiological temperatures. In continuation of our earlier studies,[3−8] we report here the density, ρ, and viscosity, η, of aspirin solutions in higher alcohols at temperatures in the range (293.15 to 313.15) K. To the best of our knowledge, density and viscosity of aspirin in propan-1-ol, propan-2-ol, butan-1-ol, and butan-2-ol are reported for the first time.

Table 1. Comparison of Physical Properties at 298.15 K of Pure Solvents with Literature Data[17]

	ρ/g·cm^{-3}		η/mPa·s	
component	experimental	literature	experimental	literature
propan-1-ol	0.8007	0.7995	1.968	2.200
propan-2-ol	0.7809	0.7812	2.043	2.044
butan-1-ol	0.8058	0.8059	2.571	2.569
butan-2-ol	0.8031	0.8026	2.998	3.013

Materials and Methods

2-Acetoxy benzoic acids (acetyl salicylic acid or aspirin) of the best available purity (> 0.99 mass fraction) were purchased from Aldrich. The solvents used were propan-1-ol (0.99 mass fraction, Fluka), propan-2-ol (> 0.99 mass fraction, Lab Scan Asia), butan-1-ol (0.99 mass fraction), and butan-2-ol (0.99 mass fraction) (both supplied by Fluka). The measured values of the viscosity of the solvents were comparable with the literature values (except for 1-propanol) as shown in Table 1; therefore, they were used without further purification. 1-Propanol was, however, subjected to further purification. The main impurities in propan-1-ol are water and 2-propene-1-ol. Water can be removed by refluxing over CaO for several hours followed by distillation and further drying with suitable agents, e.g., NaOH.[9] A sample of maximum purity could not be achieved, and for this reason the data in 1-propanol solutions may not be very reliable. Solutions were prepared in a molality range ($9.5 \cdot 10^{-3}$ to $31.9 \cdot 10^{-3}$) mol·kg^{-1}. The precision of balance was ± 0.001 g. The experiments were carried out at temperature in the range (293.15 to 313.15) K. To avoid a concentration gradient, the solutions were stirred gently before each measurement.

Density and Viscosity Measurement. The density of solutions was measured with an automated vibrating tube densimeter

* Corresponding author. E-mail: mjiqauchem@yahoo.com.

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Table 2. Density (ρ), Apparent Molal Volume (V_ϕ), and Coefficient of Viscosity (η) of 2-Acetoxy Benzoic Acid Dissolved in Propan-1-ol at Temperature in the Range (293.15 to 313.15) K

T	$m \cdot 10^{-3}$	ρ	V_ϕ	η	T	$m \cdot 10^{-3}$	ρ	V_ϕ	η
K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s	K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s
293.15	9.5	0.804657	119.07	2.2571	298.15	9.5	0.801345	130.54	2.2073
	12.7	0.804844	122.76	2.2596		12.7	0.801489	135.95	2.2088
	15.9	0.805025	124.90	2.2609		15.9	0.801595	143.01	2.2099
	19.1	0.805201	126.73	2.2623		19.1	0.801675	150.29	2.2114
	22.3	0.805325	131.73	2.2651		22.3	0.801765	154.42	2.2127
	25.5	0.805485	133.60	2.2655		25.5	0.801855	157.78	2.2148
	31.9	0.805701	140.78	2.2698		31.9	0.801925	167.73	2.2165
303.15	9.5	0.796879	132.08	1.7175	308.15	9.5	0.792851	137.29	1.6221
	12.7	0.796999	140.93	1.7185		12.7	0.792985	142.48	1.6233
	15.9	0.797105	147.09	1.7195		15.9	0.793069	151.17	1.6241
	19.1	0.797195	152.94	1.7207		19.1	0.793171	155.42	1.6248
	22.3	0.797301	155.95	1.7217		22.3	0.793259	159.44	1.6258
	25.5	0.797371	160.18	1.7228		25.5	0.793349	162.06	1.6267
	31.9	0.797405	171.81	1.7255		31.9	0.793365	174.39	1.6281
310.15	9.5	0.791289	138.73	1.4585	313.15	9.5	0.788791	142.11	1.3974
	12.7	0.791425	144.02	1.4589		12.7	0.788899	150.17	1.3976
	15.9	0.791495	153.35	1.4595		15.9	0.788999	155.79	1.3985
	19.1	0.791601	156.93	1.4599		19.1	0.789091	160.19	1.3988
	22.3	0.791691	160.62	1.4604		22.3	0.789165	164.62	1.3992
	25.5	0.791761	164.64	1.4608		25.5	0.789245	167.56	1.3998
	31.9	0.791795	175.60	1.4615		31.9	0.789305	176.71	1.4006

Table 3. Density (ρ), Apparent Molal Volume (V_ϕ), and Coefficient of Viscosity (η) of 2-Acetoxy Benzoic Acid Dissolved in Propan-2-ol at Temperature in the Range (293.15 to 313.15) K

T	$m \cdot 10^{-3}$	ρ	V_ϕ	η	T	$m \cdot 10^{-3}$	ρ	V_ϕ	η
K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s	K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s
293.15	9.5	0.785805	126.67	2.3851	298.15	9.5	0.781589	129.02	2.0475
	12.7	0.785969	131.54	2.3859		12.7	0.781745	134.41	2.0484
	15.9	0.786119	135.87	2.3869		15.9	0.781895	138.25	2.0496
	19.1	0.786295	136.55	2.3879		19.1	0.782045	141.26	2.0509
	22.3	0.786405	141.81	2.3895		22.3	0.782155	145.92	2.0516
	25.5	0.786545	143.84	2.3904		25.5	0.782265	149.41	2.0525
	31.9	0.786679	154.09	2.3917		31.9	0.782399	158.91	2.0541
303.15	9.5	0.777301	132.70	1.7659	308.15	9.5	0.772925	136.78	1.5275
	12.7	0.777465	136.14	1.7669		12.7	0.773071	142.40	1.5287
	15.9	0.777595	141.76	1.7675		15.9	0.773205	146.44	1.5297
	19.1	0.777725	145.94	1.7686		19.1	0.773349	148.70	1.5308
	22.3	0.777855	148.54	1.7694		22.3	0.773465	152.01	1.5316
	25.5	0.777985	150.48	1.7705		25.5	0.773595	153.89	1.5328
	31.9	0.778079	162.19	1.7715		31.9	0.773705	164.01	1.5344
310.15	9.5	0.771109	143.29	1.4418	313.15	9.5	0.768415	147.69	1.3245
	12.7	0.771271	145.24	1.4425		12.7	0.768545	152.09	1.3256
	15.9	0.771405	149.28	1.4432		15.9	0.768685	154.19	1.3266
	19.1	0.771525	152.74	1.4439		19.1	0.768785	159.03	1.3275
	22.3	0.771635	156.30	1.4447		22.3	0.768891	162.03	1.3284
	25.5	0.771725	160.24	1.4453		25.5	0.768975	165.69	1.3291
	31.9	0.771849	168.43	1.4466		31.9	0.769069	174.44	1.3305

(Anton Paar DMA 5000) with an uncertainty of $\pm 10^{-5}$ g·cm^{-3} which was calibrated with deionized and doubly distilled water for the temperature range investigated. The density measurements were performed at temperature in the range (293.15 to 313.15) K with an uncertainty of $\pm$ 0.01 K in temperature.

The solution viscosity was measured at the desired temperatures by means of an Anton Paar SVM 3000 viscometer which was calibrated with both the deionized and doubly distilled water. The viscosity was measured with an uncertainty of measurements of $\pm$ 0.003 mPa·s at different temperatures in the range (293.15 to 313.15) K. The uncertainty of temperature measurement was $\pm$ 0.01 K. All experiments were repeated thrice.

Results

The experimental values of densities and viscosities of 2-acetoxy benzoic acid in higher alcohols as functions of concentration and temperature are listed in Tables 2 to 5.

The apparent molal volume V_ϕ is calculated by using the relation[3]

$$V_\phi = \frac{1000(\rho_o - \rho)}{m\rho\rho_o} + \frac{M_2}{\rho} \quad (1)$$

where m is the molal concentration of acetyl salicylic acid; ρ and ρ_0 are the densities of the drug and the solvent, respectively; and M_2 is the molar mass. The values of V_ϕ are given in Tables 2 to 5. Variations of ρ of 2-acetoxy benzoic acid solutions in propan-1-ol with molarity (m) at different temperatures are depicted in Figure 1.

The value of partial molal volume, V_m^0, of acetyl salicylic acid is obtained using the equation

$$V_\phi = V_m^0 + S_v m \quad (2)$$

Table 4. Density (ρ), Apparent Molal Volume (V_ϕ), and Coefficient of Viscosity (η) of 2-Acetoxy Benzoic Acid Dissolved in Butan-1-ol at Temperature in the Range (293.15 to 313.15) K

T	$m \cdot 10^{-3}$	ρ	V_ϕ	η	T	$m \cdot 10^{-3}$	ρ	V_ϕ	η
K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s	K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s
293.15	9.5	0.810254	121.27	2.9323	298.15	9.5	0.806421	123.84	2.5759
	12.7	0.810441	123.53	2.9332		12.7	0.806601	126.38	2.5773
	15.9	0.810619	125.76	2.9345		15.9	0.806785	127.49	2.5785
	19.1	0.810791	127.74	2.9355		19.1	0.806935	131.53	2.5795
	22.3	0.810901	133.50	2.9374		22.3	0.807089	133.69	2.5808
	25.5	0.811075	133.88	2.9387		25.5	0.807245	135.18	2.5831
	31.9	0.811305	140.19	2.9415		31.9	0.807489	140.90	2.5865
303.15	9.5	0.802560	125.19	2.2635	308.15	9.5	0.798651	129.82	2.0031
	12.7	0.802731	128.55	2.2651		12.7	0.798829	131.96	2.0049
	15.9	0.802911	129.66	2.2661		15.9	0.799001	133.23	2.0055
	19.1	0.803056	133.78	2.2677		19.1	0.799151	135.91	2.0064
	22.3	0.803209	135.73	2.2687		22.3	0.799329	136.22	2.0085
	25.5	0.803361	137.26	2.2695		25.5	0.799481	138.07	2.0091
	31.9	0.803636	141.09	2.2715		31.9	0.799745	142.35	2.0121
310.15	9.5	0.797079	131.57	1.8999	313.15	9.5	0.794711	135.20	1.7691
	12.7	0.797253	133.79	1.9006		12.7	0.794881	136.33	1.7699
	15.9	0.797425	134.72	1.9013		15.9	0.795049	137.76	1.7709
	19.1	0.797591	136.31	1.9019		19.1	0.795208	138.99	1.7716
	22.3	0.797741	138.19	1.9027		22.3	0.795361	141.41	1.7725
	25.5	0.797869	141.30	1.9033		25.5	0.795509	142.27	1.7735
	31.9	0.798145	144.37	1.9047		31.9	0.795799	144.49	1.7745

Table 5. Density (ρ), Apparent Molal Volume (V_ϕ), and Coefficient of Viscosity (η) of 2-Acetoxy Benzoic Acid Dissolved in Butan-2-ol at Temperature in the Range (293.15 to 313.15) K

T	$m \cdot 10^{-3}$	ρ	V_ϕ	η	T	$m \cdot 10^{-3}$	ρ	V_ϕ	η
K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s	K	mol·kg^{-1}	g·cm^{-3}	cm^3·mol^{-1}	mPa·s
293.15	9.5	0.807809	133.86	3.6231	298.15	9.5	0.803661	135.45	3.0171
	12.7	0.807969	136.35	3.6241		12.7	0.803799	141.05	3.0181
	15.9	0.808035	147.14	3.6256		15.9	0.803885	149.02	3.0196
	19.1	0.808139	151.20	3.6272		19.1	0.803985	153.18	3.0206
	22.3	0.808245	153.94	3.6284		22.3	0.804095	155.44	3.0211
	25.5	0.808375	154.78	3.6307		25.5	0.804175	159.26	3.0229
	31.9	0.808405	166.88	3.6326		31.9	0.804221	170.02	3.0249
303.15	9.5	0.799521	139.48	2.5285	308.15	9.5	0.795185	146.98	2.1221
	12.7	0.799639	145.99	2.5297		12.7	0.795325	154.08	2.1229
	15.9	0.799735	152.58	2.5305		15.9	0.795415	158.42	2.1238
	19.1	0.799835	156.23	2.5316		19.1	0.795505	162.11	2.1249
	22.3	0.799945	158.44	2.5325		22.3	0.795591	164.99	2.1255
	25.5	0.799999	163.32	2.5332		25.5	0.795675	172.72	2.1269
	31.9	0.800103	170.72	2.5347		31.9	0.795765	144.35	2.1275
310.15	9.5	0.793418	146.97	1.9752	313.15	9.5	0.790852	151.74	1.7923
	12.7	0.793555	149.38	1.9758		12.7	0.790985	154.14	1.7933
	15.9	0.793651	155.44	1.9763		15.9	0.791108	156.56	1.7943
	19.1	0.793731	160.79	1.9769		19.1	0.791185	161.69	1.7953
	22.3	0.793815	164.31	1.9781		22.3	0.791261	165.72	1.7962
	25.5	0.793911	165.94	1.9787		25.5	0.791355	167.60	1.7971
	31.9	0.794014	173.08	1.9799		31.9	0.791454	174.69	1.7984

where S_v is the semiempirical solute−solute interaction parameter and m is the molality of the drug. The value of V_m^0 has been estimated by the least−square fitting of the plot of V_ϕ versus molality of the drug solution method. The values are given in Table 6. Since S_v values for large organic molecules are not of much significance, they have not been reported here.

The variation of V_m^0 with temperature[10] can be expressed as

$$V_m^0 = a + bT + cT^2 \quad (3)$$

The coefficients a, b, and c have been estimated by the least-squares fitting method of partial molal volume in equation. Since the density has been measured at six temperatures only, the reliability of Hepler's model may be a little doubtful. To obtain the qualitative information on solvation of drugs, the value of $(\delta^2 V_m^0/\delta T^2)$, i.e., Hepler's constant, has been calculated. The $(\delta^2 V_m^0/\delta T^2)$ values are included in Table 6.

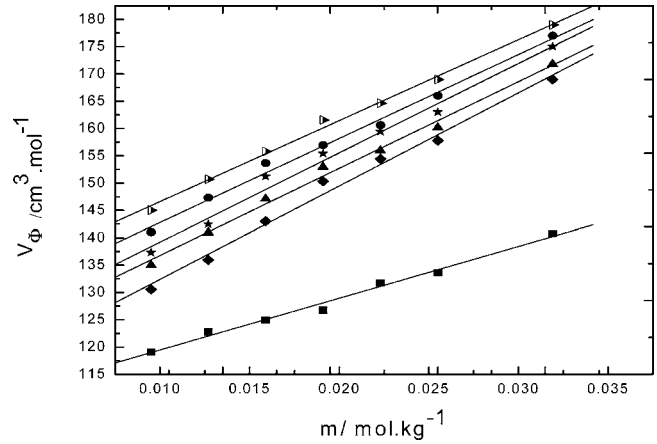

Figure 1. Plot of apparent molal volumes, V_ϕ, as a function of molality, m, of 2-acetoxy benzoic acid solutions in propan-1-ol at ■, 293.15 K; ◆, 298.15 K; ▲, 303.15 K; ★, 308.15 K; ●, 310.15 K; half-filled triangle pointing right, 313.15 K.

Table 6. Partial Molal Volumes at Infinite Dilution (V_m^0), Isobaric Thermal Expansion Coefficient (α_2), Partial Molar Expansivity (E_2^0), and Hepler's Constant ($\delta^2V_m^0/\delta T^2$) of 2-Acetoxy Benzoic Acid Solutions in Higher Alcohols at Temperature in the Range (293.15 to 313.15) K

T	V_m^0		α_2	E_2^0	$\delta^2V_m^0/\delta T^2$
K	$cm^3.mol^{-1}$	st. dev.	$K\cdot10^{-3}$	$cm^3\cdot mol^{-1}\cdot K^{-1}$	$cm^6\cdot mol^{-2}\cdot K^{-2}$
			Propan-1-ol		
293.15	111.01	0.12	7.47	0.83	0.007
298.15	114.10	0.20	7.27		
303.15	118.84	0.10	6.98		
308.15	123.25	0.16	6.73		
310.15	124.96	0.12	6.66		
313.15	127.11	0.20	6.53		
			Propan-2-ol		
293.15	116.02	0.15	8.10	0.94	0.08
298.15	117.26	0.10	8.02		
303.15	120.66	0.20	7.79		
308.15	127.19	0.12	7.39		
310.15	131.33	0.15	7.16		
313.15	133.50	0.16	7.04		
			Butan-1-ol		
293.15	112.49	0.20	7.11	0.80	0.01
298.15	116.46	0.10	6.87		
303.15	119.07	0.15	6.72		
308.15	124.87	0.16	6.40		
310.15	125.91	0.12	6.35		
313.15	128.36	0.14	6.23		
			Butan-2-ol		
293.15	121.01	0.12	8.09	0.98	0.06
298.15	123.05	0.13	7.96		
303.15	129.02	0.15	7.59		
308.15	132.20	0.20	7.41		
310.15	135.85	0.10	7.21		
313.15	141.00	0.10	6.95		

The isobaric thermal expansion coefficient α_2 is calculated by the relation

$$\alpha_2 = \frac{1}{V_m^0}\left[\frac{\partial V_m^0}{\partial T}\right] \tag{4}$$

ΔV_m^0 is the transfer volume of solute from solvent I to solvent II and is defined by the following equation[4]

$$\Delta V_m^0(\mathrm{I, II}) = V_m^0(\mathrm{II}) - V_m^0(\mathrm{I}) \tag{5}$$

where V_m^0(II) is the partial molal volume of a solute in water and V_m^0(I) is its partial molal volume at infinite dilution in an alcohol. The values are given in Table 7. Figure 2 shows the dependence of ΔV_m^0 on temperature.

The viscosity data given in Tables 2 to 5 are analyzed by using the Jones−Dole equation.

$$\frac{\eta_r - 1}{m^{1/2}} = \psi = A + Bm^{1/2} \tag{6}$$

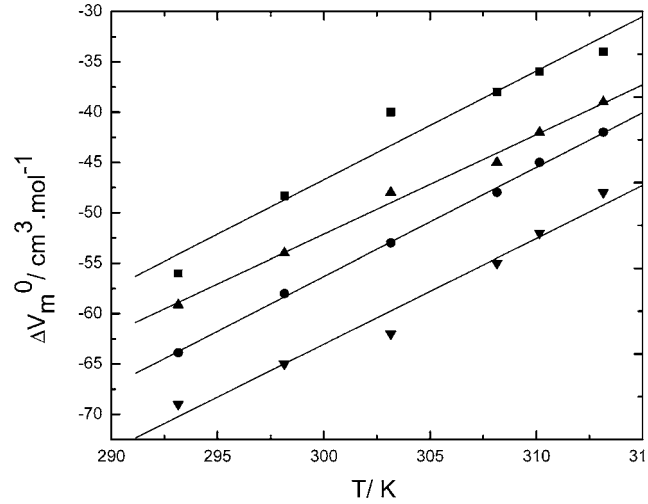

Figure 2. Plot of the transfer volume, ΔV_m^0, for 2-acetoxy benzoic acid solutions in ■, propan-1-ol; ▲, propan-2-ol; ●, butan-1-ol; and ▼, butan-2-ol at the temperature range (293.15 to 313.15) K.

where η_r is the relative viscosity of the solution, $\eta_r = \eta/\eta_o$, with and η and η_o being the viscosities of solution and the solvent, respectively; and m is the molality of the drug. Linear plots for $[(\eta_r - 1)/m^{1/2}]$ versus $m^{1/2}$ were obtained from where the A- and B-coefficients have been evaluated by the least-squares method. The A-coefficient is independent of concentration, and B is related to solute−solvent interactions. Figure 3 shows a plot of $\eta_r - 1/m^{1/2}$ versus $m^{1/2}$ for 2-acetoxy benzoic acid in propan-1-ol over the temperature range analyzed in this study.

The hydration[7] of a solute molecule dissolved in higher alcohols can be judged from the value of the hydration number (H_n) as given below

$$H_n = \frac{B}{V_m^0} \tag{7}$$

Discussion

The density of 2-acetoxy benzoic acid solution increases with an increase in its concentration as shown in Tables 2 to 5. Figure 1 shows a plot of the apparent molal volume V_ϕ in propan-1-ol over the temperature range (293.15 to 313.15) K. A similar trend is observed in all the solvents used in this study.

Table 6 shows that the calculated values of V_m^0 are positive for 2-acetoxy benzoic acid in alcohol solutions at all the investigated temperatures, suggesting strong solute−solvent interactions that promote the structure-making effect. Values of the V_m^0 of the solutions in propan-2-ol are larger than in propan-1-ol as shown in Table 6. This behavior is due to favorable packing of propan-1-ol solvent molecules into the spaces created by aspirin, whereas propan-2-ol experiences more steric hindrance by the bulky $(CH_3)_2CH$ group. The difference in V_m^0 values of 2-acetoxy benzoic acid in butan-1-ol and butan-

Table 7. Partial Molal Volumes of Transfer (ΔV_m^0) for 2-Acetoxy Benzoic Acid in Higher Alcohols at Temperature in the Range (293.15 to 313.15) K

	$\Delta V_m^0/(cm^3\cdot mol^{-1})$					
solvents	T/K = 293.15	T/K = 298.15	T/K = 303.15	T/K = 308.15	T/K = 310.15	T/K = 313.15
propan-1-ol	−56.06	−48.33	−40.09	−38.07	−36.00	−34.00
propan-2-ol	−63.87	−51.49	−49.53	−48.01	−45.09	−42.18
butan-1-ol	−59.13	−54.09	−48.00	−45.09	−42.00	−39.04
butan-2-ol	−69.00	−65.20	−62.00	−55.02	−52.21	−48.06

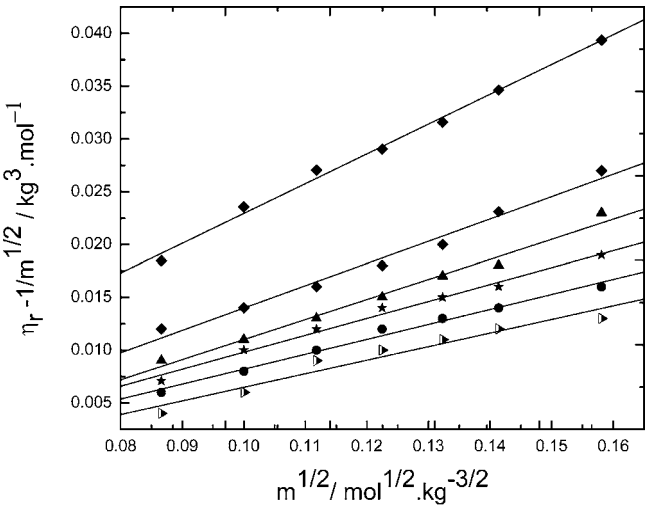

Figure 3. Plot of $\eta_r - 1/m^{1/2}$ versus $m^{1/2}$ for 2-acetoxy benzoic acid solutions in propan-1-ol at $T =$ ◆, 293.15 K; ◆, 298.15 K; ▲, 303.15 K; ★, 308.15 K; ●, 310.15 K; half-filled triangle pointing right, 313.15 K.

2-ol is due to a difference in the structure and "solvation" pattern of the two solvents. Butan-1-ol with a linear chain shows self-association to a greater extent than butan-2-ol. The number of drug molecules that shows favorable packing of butan-1-ol molecules into the spaces created by the solute is greater than that of butan-2-ol because of the extent to which the drug molecules are bonded to one another in butan-1-ol as compared to that in butan-2-ol.[11] It results in greater V_m^0 for 2-acetoxy benzoic acid in butan-2-ol than in butan-1-ol. Similar trends have also been reported by Ali et al.[12] for amino acids in (water + propan-1-ol) solutions and Banipal et al.[13] for glycine and alanine in (water + propan-1-2-diol) solutions. The standard deviation (σ) for the quantity x is given as

$$\sigma = \sqrt{\frac{1}{(N-1)}\sum_{i=1}^{N}(x_i - \mu)^2}$$

where μ is the mean value of data.

It can be seen from Table 6 that the partial molal volume increases with increasing temperature. The reduction of electrostriction occurs, and release of some solvent molecules from the loose solvation layers of the solute in the solution results in an increase in V_m^0. Positive values of the partial molal expansivity ($\delta V_m^0/\delta T$) suggest that 2-acetoxy benzoic acid (aspirin) is a structure maker in alcoholic solvents. To obtain the qualitative information on the hydration of drug solutes,[10] the Hepler's constant ($\delta^2 V_m^0/\delta T^2$) has been calculated using eq 3, and the values are listed in Table 2. It is suggested that the structure-breaking solutes have negative ($\delta^2 V_m^0/\delta T^2$) values. Correspondingly, the positive values of ($\delta^2 V_m^0/\delta T^2$) are associated with the structure-making solutes. In the present investigation, the positive values of ($\delta^2 V_m^0/\delta T^2$) suggest that 2-acetoxy benzoic acid is a structure maker in all the alcohols investigated here. Similar results were also obtained by Khrat.[14]

The values of the transfer volumes ΔV_m^0 of 2-acetoxy benzoic acid (aspirin) from water to alcohols are listed in Table 7. The value of ΔV_m^0 is negative at all the temperatures investigated here. The observed negative values for ΔV_m^0 are a result of the dominance of solvophobic−solvophilic interactions. Similar trends have also been reported by Sinha et al.[15] for L-valine in (water + tetramethyl ammonium iodide) solutions. Figure 2 shows the dependence of ΔV_m^0 on temperature. The observed increase in the value of ΔV_m^0 with temperature increment is indicative of the release of solvent molecules from the secondary solvation layer into the bulk of alcoholic solvent. Similar results have also been obtained by Nain et al.[16] for amino acids in (aqueous butan-1-4-diol) solutions. Figure 2 shows the transfer volume to be dependent on temperature.

Table 8. Viscosity *B*-Coefficients and Hydration Numbers (H_n) of 2-Acetoxy Benzoic Acid in Higher Alcohols at Temperature in the Range (293.15 to 313.15) K

T	B			B	
K	dm^3·mol^{-1}	st. dev.	H_n	dm^3·mol^{-1}	H_n
	Propan-1-ol			Propan-2-ol	
293.15	0.295	0.01	2.66	0.251	2.16
298.15	0.273	0.01	2.39	0.205	1.75
303.15	0.215	0.01	1.81	0.192	1.59
308.15	0.143	0.01	1.16	0.126	1.00
310.15	0.109	0.01	0.87	0.099	0.75
313.15	0.103	0.01	0.81	0.091	0.67
	Butan-1-ol			Butan-2-ol	
293.15	0.215	0.02	1.91	0.179	1.48
298.15	0.185	0.02	1.59	0.161	1.31
303.15	0.175	0.02	1.47	0.150	1.16
308.15	0.119	0.02	0.95	0.093	0.70
310 0.15	0.093	0.02	0.74	0.088	0.65
313.15	0.090	0.02	0.69	0.086	0.61

The calculated values of isobaric thermal expansion coefficient (α_2) for 2-acetoxy benzoic acid are given in Table 6. The highest value of α_2 is obtained in propan-2-ol and the lowest in butan-1-ol. The isobaric thermal expansion coefficient (α_2) decreases with an increase in temperature indicating that drug−solvent binding is weakened.

Figure 3 shows a representative plot of $\eta_r - 1/m^{1/2}$ versus $m^{1/2}$ for 2-acetoxy benzoic acid in propan-1-ol over the temperature range analyzed in this study. Similar plots have been obtained in other alcohols. Similar conclusions were also reported by Ali et al.[12] Positive values of viscosity *B*-coefficient as given in Table 8 also support the behavior of the partial molal volume of acetyl salicylic acid which suggests stronger solute−solvent interactions. The value of *B*-coefficient for acetyl salicylic in propan-1-ol is the highest and the smallest in butan-2-ol. The temperature derivative of the *B*-coefficient is shown in Figure 4. The sign of d*B*/d*T* provides information regarding structure-making or -breaking ability of the drug in solvent

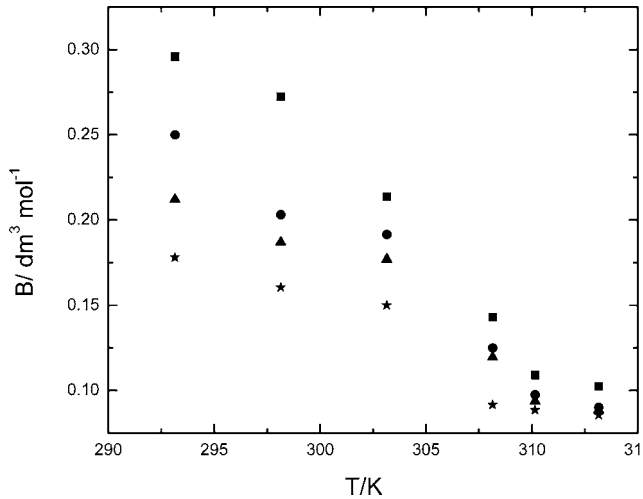

Figure 4. Plot of viscosity *B*-coefficients versus temperature for 2-acetoxy benzoic acid solutions in ■, propan-1-ol; ●, propan-2-ol; ▲, butan-1-ol; and ★, butan-2-ol at the temperature range (293.15 to 313.15) K.

media. A negative value of dB/dT represents the structure maker and a positive value the structure breaker drug in the particular solvent. In the case of 2-acetoxy benzoic acid in higher alcohols, the calculated value of dB/dT is negative as shown in Figure 4. This shows that 2-acetoxy benzoic acid is a structure maker drug in higher alcohols. This conclusion is in excellent agreement with the conclusions drawn from Hepler's constant ($\delta^2 V_m^0/\delta T^2$) discussed earlier.

The value of hydration number, H_n, for the unsolvated molecules lies between 0 and 2.5, but its value is higher for the solvated drug molecules. The values of hydration number are given in Table 8. $H_n < 2.5$ at low temperatures show lesser solvation of 2-acetoxy benzoic acid at low temperatures in higher alcohols because a value higher than $H_n = 2.5$ shows solvated spherical species.

Conclusions

In this work, partial molal volume and viscosity B-coefficient of 2-acetoxy benzoic acid (acetyl salicylic acid or aspirin) in propan-1-ol, propan-2-ol, butan-1-ol, and butan-2-ol have been determined. The values of partial molal volume and viscosity B-coefficient are positive indicating strong solute−solvent interactions and its structure-promoting tendency.

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