Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. *87* (10) 1171–1184 (2022)
JSCS–5586
Original scientific paper
Published 26 August 2022

Comparison of different types of molar volume equations for the validity and applicability in a ternary carbamazepine + alizarin + methanol solution system and study of the corresponding molecular interactions

TAPAS MALLIK, SRABANTI GHOSH and DEEPAK EKKA*

Department of Chemistry, Cooch Behar Panchanan Barma University, Cooch Behar-736101, West Bengal, India

(Received 29 April, revised 28 June, accepted 28 July 2022)

Abstract: In this work, the molecular interaction between the carbamazepine and alizarin in methanol has been represented in terms of limiting apparent molar volumes and viscosity coefficients. Before further proceeding, the validity and applicability of the calculation of apparent molar volumes have also been checked by considering the available five types of frequently used equations, where the required modifications have proposed by the addition of hypothetical mass and concentration of the solute. After that, the limiting apparent molar volume and viscosity coefficients have been calculated using Masson equation and Jones–Dole equation respectively to predict and cross-check the interactions occurring between the molecules in ternary system. The equation marked with (1) has been found the best-fit equation, and the carbamazepine and alizarin in methanol are strongly bound (ϕ_V^o = 23104 m^3 mol^{-1} and B = = 18.10 kg mol^{-1}) to each other at the concentration 0.003 mol kg^{-1}. The results have been interpreted in favour of the solute–cosolute interactions, which is dominant over the solute–solute and cosolute–cosolute interactions. The interpretations have been discussed with the help of intermolecular forces and non-covalent interactions.

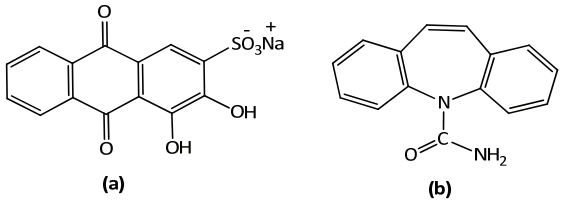
Keywords: dihydroxyanthraquinone; dibenzoazepine-based compound; limiting apparent molar volume; viscosity *B*-coefficient; solute–solvent and solute–solute interactions.

INTRODUCTION

The non-covalent interaction between two drug molecules in alcohol always acts as a driving force of molecular interaction in medicinal industry, academic and research. The information regarding the physical properties of solutions with

* Corresponding author. E-mail: ekadeepak@yahoo.in
https://doi.org/10.2298/JSC220429062M

different solute concentration at room temperature is very important. The interaction which occurs can be interpreted by physicochemical data. Alizarin red S (Scheme 1) is a natural compound known as an anthraquinoic fluorescent dye, having antigenotoxic activity, that can be used as orthotropic drug for the treatment of bone tumours.[1] Carbamazepine (Scheme 1) is a tricycle compound like dibenzoazepine that is carrying a carbamoyl substituent at the azepine nitrogen. Carbamazepine is used in the therapy of epilepsy and trigeminal neuralgia.[2,3] To increase the bio-availability of low solubility drug like carbamazepine, Li and co--workers studied the co-crystal (carbamazepine combine with nicotinamide) formation, and showed an alternative method for reducing the side effects, other than the formation of cyclodextrin inclusion complex.[4] Since carbamazepine is poorly soluble in water, it tends to appears at the surface of water and becomes a harmful agent for the environment.[5] Andreozzi *et.al.* have tried to overcome this situation by a biotic photo degradation at 313 K with 100 days observation in a binary system.[6]



Scheme 1. 2D Molecular structure of: a) alizarin red S and b) carbamazepine.

A binary and ternary systems are common in research and industry. The solute and co-solute interactions in methanol also belongs to the ternary system. This type of molecular interactions in solutions can be determined by physicochemical properties like apparent molar volumes and viscosity coefficient. It has been seen that the molecular interaction of many important drugs like sodium salicylate, L-tryptophan, procaine HCl, ephedrine HCl, amoxicillin also been studied by apparent molar volume.[7] On the other hand, if any patient suffering from diseases above (bone tumours and trigeminal neuralgia) and if he/she is taking both medicinal compounds simultaneously, there is a possibility of interaction between these compounds.

In view of the critical survey of literature from book, journal, article, magazine, *etc*. it is clear that there is no work has done on this ternary system (carbamazepine + alizarin + methanol). The addition of carbamazepine to the solution of alizarine +methanol will perturb the structural influence, which is expected to affect the volumetric and viscometry properties to a high degree. In this work, density and viscosity of the ternary system (0.001, 0.002 and 0.003 mol kg^{-1}) have been measured, by considering carbamazepine and alizarin as a co-solute

and solute, respectively. The result obtained from apparent molar volumes and viscosity coefficients have interpreted in terms of intermolecular forces and non--covalent interactions.

EXPERIMENTAL

Materials

Carbamazepine (molecular weight 236.26 g mol^{-1}) was obtained from medicine tegretol 200 (Novartis contain 0.0002 kg of precursor) tablet. Tegretol was first ground in mortar and dissolved in methanol, the mixture was sonicated for better solubility, then it was filtered by Whatman 41, evaporated by moderate heating, dried, and carbamazepine was obtained in powder form. The melting point of the compound is found to be ~463.15 K[8] and the UV–Vis spectral line measured by Thermo Scientific Evolution 201 UV–Vis spectrometer, which also matches the literature. Alizarin (molecular weight 364.24 kg mol^{-1}) was purchase from Sd. fine-chem Ltd., India, and use as procured. Methanol (mass fraction purity is 0.998) was purchased from Avantor Performance Materials India Ltd. Before performing the experiment all the chemicals have kept in dry and dark desiccators for minimum evaporation.

Apparatus and procedure

The solvent mixture of alizarine in methanol and the stock solutions of carbamazepine of different concentration (0.001, 0.002 and 0.003 mol kg^{-1}) in alizarine + methanol was prepared. Since some of equations the concentration is expressed in molality and some in molarity, therefore to uniform this, the conversion of molality into molarity was carried using experimental density data.[9] Required precautions were taken to trim down losses by evaporation. Density of the solutions was measured with an Ostwald-Sprengel type pycnometer. It was calibrated with doubly distilled water and acetone; equilibrated by experimental liquid in a glass-walled water bath maintained at ±0.01 K of the desired temperature. It was then taken from the bath, dried, and weight by an electronic balance with a precision of 10^{-6} kg. An average three measurements and the required precautions to avoid evaporation losses during measurements were taken. The density values were reproducible to ±0.3 g cm^{-3}. The viscosity was measured by a suspended Ubbelohde-type viscometer, calibrated with doubly distilled water and purified methanol at temperature of 298.15 K. A thoroughly cleaned and perfectly dried viscometer filled with the experimental liquid was filled; placed vertically in the glass-walled thermostat which maintained the temperature ±0.01 K. After the attainment of thermal equilibrium, times of flow were recorded with a stopwatch correct to ±0.1 s. At least three repetitions of each data measurements, reproducible to ±0.1 s, were taken to determine the average flow times. The accuracy of the viscosity measurements was ±0.003 Pa·s. The mixtures were prepared by mixing known volumes of pure liquids in air-tight stoppered bottles. The weights were measured on a Wesner electronic balance (IND/09/08/466) accurate to 10^{-6} kg.

RESULT AND DISCUSSION

Validity and acceptability of apparent molar volume equations

Apparent molar volume is very much important for the elucidation of solute––solvent and solute interactions in ternary solution system. It is usually calculated using molar mass, density and concentration of the solution and solvent. In this work, after a critical survey, only 5 different equations (Eqs. (1)–(5)) were found to appropriately calculate the apparent molar volume.[10–14] From these equations

we have tried to justify the applicability and validity for the chosen ternary system:

$$\phi_V = \frac{m}{\rho} - \frac{(\rho - \rho_0)}{c_m \rho \rho_0} \quad (1)$$

$$\phi_V = \frac{m}{\rho} + \frac{1000(\rho_0 - \rho)}{c_n \rho_0} \quad (2)$$

$$\phi_V = \frac{m}{\rho} + \frac{1000(\rho_0 - \rho)}{\rho \rho_0} \quad (3)$$

$$\phi_V = \frac{m}{\rho} + \frac{1000(\rho_0 - \rho)}{c_m \rho \rho_0} \quad (4)$$

$$\phi_V = \frac{m}{\rho_0} - \frac{1000(\rho - \rho_0)}{c_n \rho_0} \quad (5)$$

where c_n is the molar concentration of ternary mixture in molarity, c_m is the molal concentration of ternary solutions in molality, m is molar mass of the solute, ρ is the solution density and ρ_0 is the solvent density. A confusion was noted on the use of molar mass and concentration of the solution to calculate the apparent molar volume. In some cases, some of the authors have used molar mass of a solute. But in case of ternary solution systems (solute + co-solute + solvent), it is inappropriate to use molar mass of the solute, because of the presence of the co-solute mass in the solution, the interaction with a solute is also involved. As a result, mass of the co-solute also interferes in calculating the apparent molar volume of the ternary solution system. To overcome these problems, we have tried to attempt the calculation and discussion the same using following ways.

Consideration of the molar mass of the solute

Carbamazepine was treated as a solute; therefore, molar mass has been used to calculate ϕ_V in 0.001, 0.002 and 0.003 mol kg^{-1} of alizarin + methanol solvent mixture and the results have been presented in Tables I–III, respectively.

TABLE I. Density, molar mass and apparent molar volume, with corresponding molal and molar concentration of carbamazepine in for different equation at 0.001 mol kg^{-1} alizarin + methanol; m = 236.26 g mol^{-1}

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ / g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.001	0.0012	0.7905	293.25	–4147.63	293.25	4798.66	–4146.30
0.002	0.0025	0.7926	293.57	–3268.39	289.07	3897.65	–3266.26
0.003	0.0037	0.7927	295.01	–2110.47	288.93	2728.70	–2108.31
0.004	0.0050	0.7926	295.82	–1485.15	289.07	2097.86	–1483.03
0.005	0.0062	0.7928	296.12	–1184.17	288.64	1793.51	–1181.96

TABLE I. Continued

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ / g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.006	0.0075	0.7931	296.22	–1006.74	288.00	1613.69	–1004.41
0.007	0.0087	0.7887	299.13	–18.07	296.71	621.66	–17.40
0.008	0.0100	0.7898	298.55	–152.47	294.54	756.51	–151.39
0.009	0.0112	0.7893	298.91	–24.89	295.63	627.94	–24.02
0.010	0.0125	0.7900	298.54	–90.02	294.11	692.99	–88.86
0.011	0.0137	0.7904	298.42	–92.67	293.46	695.25	–91.39
0.012	0.015	0.7908	298.22	–110.40	292.53	712.58	–108.93

TABLE II. Density, molar mass and apparent molar volume, with corresponding molal and molar concentration of carbamazepine in for different equation at 0.002 mol kg^{-1} alizarin + methanol; m = 236.26 g mol^{-1}

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ / g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.001	0.0012	0.7908	296.94	–1507.75	296.48	2126.28	–4146.30
0.002	0.0025	0.7913	297.29	–953.07	295.39	1563.86	–3266.26
0.003	0.0037	0.7918	297.30	–751.83	294.38	1359.35	–2108.31
0.004	0.0050	0.7913	297.93	–324.40	295.41	928.34	–1483.03
0.005	0.0062	0.7920	297.61	–378.18	294.02	981.57	–1181.96
0.006	0.0075	0.7915	298.05	–149.32	295.11	751.13	–1004.41
0.007	0.0087	0.7918	297.91	–151.71	294.38	753.07	–17.40
0.008	0.0100	0.7922	297.77	–153.55	293.66	754.44	–151.39
0.009	0.0112	0.8004	293.62	–1260.03	277.69	1849.55	–24.02
0.010	0.0125	0.8054	291.32	–1739.51	268.10	2312.49	–88.86
0.011	0.0137	0.8096	289.53	–2036.45	260.19	2592.51	–91.39
0.012	0.0150	0.8096	289.72	–1842.74	260.19	2401.09	–108.93

TABLE III. Density, molar mass and apparent molar volume, with corresponding molal and molar concentration of carbamazepine in for different equation at 0.003 mol kg^{-1} alizarin + methanol; m = 236.26 g mol^{-1}

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ / g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.001	0.0012	0.7879	299.53	598.15	299.45	602.70	1.61
0.002	0.0025	0.7877	299.98	265.03	300.03	264.49	334.83
0.003	0.0037	0.7879	299.77	376.86	299.56	378.04	222.91
0.004	0.0050	0.7872	300.28	136.68	300.95	134.03	463.36
0.005	0.0062	0.7881	299.70	387.38	299.24	388.70	212.33
0.006	0.0075	0.7887	299.36	499.50	298.04	502.36	99.99
0.007	0.0087	0.7902	298.51	753.25	294.95	758.84	–154.34
0.008	0.0100	0.7917	297.77	932.33	292.00	938.94	–333.99
0.009	0.0112	0.7895	299.01	545.39	296.45	548.66	53.79
0.010	0.0125	0.7890	299.26	465.09	297.33	467.38	134.26
0.011	0.0137	0.7899	298.82	554.70	295.52	557.94	44.30
0.012	0.0150	0.7901	298.76	552.37	295.17	555.53	46.56

The inspection of the Tables I–III for Eqs. (2), (4) and (5) gives negative ϕ_V values and abnormal trends. Furthermore, it shows 100 to 1000 times higher molar mass, and these vast differences are unusual and not acceptable. They may be explained by the fact that there must be some interaction that occurs between two drugs, and both of drugs with the combination of mass contribute in the calculation. From this result, it is concluded that in this case Eqs. (1) and (3) are the acceptable equations, which are relatively comparable with the molar mass in question.

Consideration of the reduced mass

As usual, here also the reduced mass defined as the product of the two masses divided by their sum of two masses. Since abnormal ϕ_V value have been obtained in case of Eqs. (2), (4) and (5), so the reduced mass (μ) has been used to modify the equation instead of the molar mass of solute. After that, the apparent molar volumes have been calculated and presented in Tables IV–VI. By the observation of the results, it has been inferred the same trend of results as for the molar mass calculation.

TABLE IV. Density, reduced mass, and apparent molar volume, with corresponding molal and molar concentration of carbamazepine for different equation at 0.001 mol kg^{-1} alizarin + methanol; μ = 143.30 g mol^{-1}

c_n /mol L^{-1}	c_m /mol kg^{-1}	ρ / g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.001	0.0012	0.7905	175.65	-4265.22	175.65	4681.06	-4264.41
0.002	0.0025	0.7926	176.30	-3385.66	171.80	3780.37	-3384.37
0.003	0.0037	0.7927	177.74	-2227.74	171.66	2611.44	-2226.43
0.004	0.0050	0.7926	178.55	-1602.43	171.80	1980.58	-1601.14
0.005	0.0062	0.7928	178.88	-1301.41	171.40	1676.26	-1300.07
0.006	0.0075	0.7931	179.03	-1123.94	170.80	1496.49	-1122.52
0.007	0.0087	0.7887	181.28	-135.92	178.86	503.81	-135.51
0.008	0.0100	0.7898	180.86	-270.16	176.86	638.82	-269.50
0.009	0.0112	0.7893	181.14	-142.66	177.86	510.16	-142.13
0.010	0.0125	0.7900	180.89	-207.68	176.45	575.33	-206.97
0.011	0.0137	0.7904	180.81	-210.28	175.85	577.65	-209.50
0.012	0.0150	0.7908	180.68	-227.94	174.99	595.05	-227.05

TABLE V. Density, reduced mass, and apparent molar volume, with corresponding molal and molar concentration of carbamazepine for different equation at 0.002 mol kg^{-1} alizarin + methanol; μ = 143.30 g mol^{-1}

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ /g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.001	0.0012	0.7908	179.39	–1625.30	178.93	2008.73	–1624.97
0.002	0.0025	0.7913	179.82	–1070.54	177.92	1446.39	–1070.08
0.003	0.0037	0.7918	179.91	–869.22	176.99	1241.96	–868.65

TABLE V. Continued

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ /g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.004	0.0050	0.7913	180.46	–441.87	177.94	810.87	–441.42
0.005	0.0062	0.7920	180.25	–495.55	176.66	864.20	–494.94
0.006	0.0075	0.7915	180.60	–266.76	177.66	633.69	–266.28
0.007	0.0087	0.7918	180.52	–269.11	176.99	635.68	–268.54
0.008	0.0100	0.7922	180.43	–270.89	176.33	637.10	–270.23
0.009	0.0112	0.8004	177.48	–1376.17	161.55	1733.41	–1373.66
0.010	0.0125	0.8054	175.90	–1854.92	152.68	2197.08	–1851.31
0.011	0.0137	0.8096	174.71	–2151.27	145.37	2477.69	–2146.74
0.012	0.0150	0.8096	174.90	–1957.57	145.37	2286.27	–1953.03

TABLE VI. Density, reduced mass, and apparent molar volume, with corresponding molal and molar concentration of carbamazepine for different equation at 0.003 mol kg^{-1} alizarin + methanol; μ = 143.30 g mol^{-1}

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ / g m^{-3}	ϕ_V / 10^{-3} m^3 mol^{-1}				
			Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.001	0.0012	0.7879	181.56	480.18	181.48	484.72	–116.39
0.002	0.0025	0.7877	181.96	147.02	182.02	146.47	216.83
0.003	0.0037	0.7879	181.80	258.89	181.58	260.07	104.90
0.004	0.0050	0.7872	182.20	18.60	182.87	15.95	345.36
0.005	0.0062	0.7881	181.75	269.43	181.28	270.75	94.33
0.006	0.0075	0.7887	181.50	381.63	180.18	384.50	–18.01
0.007	0.0087	0.7902	180.88	635.61	177.32	641.21	–272.35
0.008	0.0100	0.7917	180.36	814.92	174.59	821.53	–452.00
0.009	0.0112	0.7895	181.26	427.64	178.71	430.92	–64.207
0.010	0.0125	0.7890	181.45	347.28	179.52	349.57	16.26
0.011	0.0137	0.7899	181.15	437.02	177.85	440.27	–73.69
0.012	0.0150	0.7901	181.11	434.72	177.52	437.88	–71.43

For further clarification of the equations in order to make them applicable, we have modified them by adding two type of correction factors: *i*) hypothetical mass and *ii*) solution concentration including both the solute and cosolute. The brief discussion of these sub-units is given below.

Modification by adding hypothetical mass

This issue has been overcome using hypothetical mass, which can be calculated as:

$$m_1 = \frac{(m_2 V_2 c_2 + m_3 V_3 c_3)}{V_1 c_1} \tag{6}$$

where, m_1, m_2 and m_3 are respectively the hypothetical mass of the solution, the molar mass of solute (CBZ) and the molar mass of co-solute (alizarin). c is the concentration in molality/molarity, V is the volume of solution and the subscripts 1, 2 are 3 are standing for the ternary solution, the binary solution of carbamaz-

epine and the binary solution of alizarin, respectively. Applying the hypothetical mass on the above five equations, the calculated M_1 values and shown in Tables VII–IX.

TABLE VII. Density, hypothetical mass and apparent molar volume; with corresponding molal and molar concentration of carbamazepine for different equation at 0.001 mol kg^{-1} alizarin + methanol

c_n	c_m	ρ	m_1	ϕ_V / 10^{-3} m^3 mol^{-1}				
mol L^{-1}	mol kg^{-1}	g m^{-3}	g mol^{-1}	Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.0010	0.0012	0.7905	277.59	345.52	–4095.35	345.52	4850.93	–4093.79
0.0016	0.0025	0.7926	261.06	323.95	–3950.40	320.35	4648.84	–3948.05
0.0023	0.0037	0.7927	253.97	316.48	–2776.28	311.27	3445.52	–2773.96
0.0030	0.0050	0.7926	250.04	312.45	–2062.18	306.45	2715.17	–2059.93
0.0036	0.0062	0.7928	247.53	309.66	–1708.92	302.86	2351.54	–1706.61
0.0043	0.0075	0.7931	245.80	307.61	–1496.49	300.02	2131.79	–1494.07
0.0050	0.0087	0.7887	244.53	309.45	–134.63	307.19	760.99	–133.94
0.0056	0.0100	0.7898	243.56	307.54	–329.19	303.78	954.08	–328.08
0.0063	0.0112	0.7893	242.79	307.01	–153.14	303.90	774.56	–152.24
0.0070	0.0125	0.7900	242.17	305.80	–249.30	301.58	869.29	–248.10
0.0076	0.0137	0.7904	241.65	305.02	–256.11	300.28	874.40	–254.80
0.0083	0.0150	0.7908	241.22	304.26	–284.15	298.79	900.95	–282.65

TABLE VIII. Density, hypothetical mass and apparent molar volume; with corresponding molal and molar concentration of carbamazepine for different equation at 0.002 mol kg^{-1} alizarin + methanol

c_n	c_m	ρ	m_1	ϕ_V / 10^{-3} m^3 mol^{-1}				
mol L^{-1}	mol kg^{-1}	g m^{-3}	g mol^{-1}	Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.0014	0.0012	0.7908	284.05	357.88	–931.18	356.90	1664.56	–930.53
0.002	0.0025	0.7914	277.59	349.51	–900.85	347.61	1616.08	–899.97
0.0026	0.00375	0.7919	274.11	344.93	–865.61	342.18	1570.37	–864.52
0.0032	0.0050	0.7914	271.94	342.85	–435.06	340.49	1130.86	–434.21
0.0038	0.0062	0.7921	270.45	340.55	–548.65	337.18	1240.50	–547.50
0.0044	0.0075	0.7915	269.37	339.71	–270.34	336.93	957.55	–269.42
0.005	0.0087	0.7919	268.54	338.49	–290.98	335.15	975.72	–289.92
0.0056	0.0100	0.7922	267.90	337.50	–307.24	333.59	989.89	–306.02
0.0062	0.0112	0.8004	267.38	331.79	–1923.52	316.56	2590.39	–1918.84
0.0068	0.0125	0.8054	266.95	328.47	–2658.05	306.20	3300.78	–2651.31
0.0074	0.0137	0.8096	266.59	325.87	–3131.68	297.65	3749.22	–3123.24
0.008	0.0150	0.8096	266.28	325.74	–2872.96	297.27	3492.80	–2864.53

From Tables VII–IX it can be seen that among the five equations only Eqs. (1) and (3) gives a reliable value, where other equations give negative and/or large deviation values. By the inspections of the Tables, Eqs. (1) and (3) were considered as the most correct form of equation for calculating apparent molar volume. Between these two, the equation containing molality is the more appro-

priate equation, because molality is independent on temperature. So, the Eq. (1) is considering as an acceptable equation.

TABLE IX. Density, hypothetical mass, and apparent molar volume, with corresponding molal and molar concentration of carbamazepine for different equation at 0.003 mol kg^{-1} alizarin + methanol

c_n / mol L^{-1}	c_m / mol kg^{-1}	ρ / g m^{-3}	m_l / g mol^{-1}	ϕ_V /10^{-3} m^3 mol^{-1}				
				Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)	Eq. (5)
0.0017	0.0012	0.7908	310.65	391.73	–691.08	390.54	1489.34	–690.37
0.0023	0.0025	0.7913	289.39	364.61	–707.13	362.53	1450.24	–706.21
0.0030	0.0037	0.7918	277.59	349.49	–699.65	346.57	1411.53	–698.54
0.0037	0.005	0.7913	270.07	340.60	–338.31	338.14	1028.31	–337.46
0.0043	0.0062	0.7920	264.87	333.63	–446.14	330.14	1122.81	–445.01
0.0050	0.0075	0.7915	261.06	329.28	–207.56	326.43	872.99	–206.67
0.0057	0.0087	0.7918	258.14	325.43	–229.99	322.01	887.69	–228.96
0.0063	0.0100	0.7922	255.84	322.36	–247.73	318.37	899.20	–246.56
0.0070	0.0112	0.8004	253.97	315.30	–1682.25	299.81	2315.78	–1677.87
0.0077	0.0125	0.8054	252.43	310.78	–2338.13	288.18	2947.10	–2331.768
0.0083	0.0137	0.8096	251.14	307.17	–2763.13	278.57	3347.10	–2755.18
0.0090	0.0150	0.8096	250.04	306.03	–2537.26	277.20	3121.19	–2529.35

Now, considered the variation of ϕ_V with $\sqrt{c_m}$, there is a linearly growing trend with increase of carbamazepaine concentration. Thereafter, ϕ_V values used in Masson equation were calculated by the important parameters limiting apparent molar volume ϕ_V^o and related coefficients S_V and $S_{VV}^{\neq}$ by least square method:[15]

$$\phi_V = \phi_V^0 + S_V\sqrt{c_m} + S_{VV}^{\neq}c_m \quad (7)$$

where S_V and $S_{VV}^{\neq}$ are the apparent molar volume coefficient and calculated values are shown in Table X. It has found that ϕ_V values gradually increase with higher alizarin solution concentration given in the Table XI and Fig. 1. This indicates there is more alizarin interaction with their functional groups towards carbamazepine molecule. The coefficient S_V implies that there is a possibility of interaction between carbamazepine itself and/or alizarin itself. From Table X, it is observed that the coefficient S_V has some positive values, but they are very much lower (for 0.001 mol kg^{-1}, ϕ_V^o = 16504 m^3 mol^{-1}, S_V = –14527 m^3 mol$^{-3/2}$ kg$^{1/2}$, *i.e.*, $\phi_V^o >> S_V$). The coefficient S_V reveals that there must be some self--interaction between the drug molecules. However, it is negligible in comparison to solute and co-solute interaction.

Another coefficient S_V implies that there is a higher order interaction between solute and co-solute. From Table XI, it is observed that the coefficient S_V has negative values and $S_{VV}^{\neq}$ have positive values but the magnitude is very low. S_V values are very much lower than $S_{VV}^{\neq}$, *i.e.*, $S_{VV}^{\neq} >> S_V$, which can be interpreted as solute–solute or co-solute–co-solute self-interaction being neglig-

ible when compared to solute and co-solute interaction. The possible solute and co-solute interaction in molecular level (2D) are presented in Scheme 2.

Table X. Apparent molar volume at room temperature and atmospheric pressure on a particular Eq. (1) with variation of carbamazepine

Alizarin concentration, mol kg^{-1}								
0.001			0.002			0.003		
c_m mol L^{-1}	ρ g m^{-3}	$\phi_V\times10^3$ m^3 mol^{-1}	c_m mol L^{-1}	ρ g m^{-3}	$\phi_V\times10^3$ m^3 mol^{-1}	c_m mol L^{-1}	ρ g m^{-3}	$\phi_V\times10^3$ m^3 mol^{-1}
0.0010	0.7905	345.52	0.0014	0.7908	357.88	0.0016	0.7908	391.73
0.0016	0.7926	323.95	0.002	0.7914	349.51	0.0023	0.7913	364.61
0.0023	0.7927	316.48	0.0026	0.7919	344.93	0.003	0.7918	349.49
0.0030	0.7926	312.45	0.0032	0.7914	342.85	0.0036	0.7913	340.60
0.0036	0.7928	309.66	0.0038	0.7921	340.55	0.0043	0.7920	333.63
0.0043	0.7931	307.61	0.0044	0.7915	339.71	0.005	0.7915	329.28
0.0050	0.7887	309.45	0.005	0.7919	338.49	0.0056	0.7918	325.43
0.0056	0.7898	307.54	0.0056	0.7922	337.50	0.0063	0.7922	322.36
0.0063	0.7893	307.01	0.0062	0.8004	331.79	0.007	0.8004	315.30
0.0070	0.7900	305.80	0.0068	0.8054	328.47	0.0076	0.8054	310.78
0.0076	0.7904	305.02	0.0074	0.8096	325.87	0.0083	0.8096	307.17
0.0083	0.7908	304.26	0.0080	0.8096	325.74	0.009	0.8096	306.03

TABLE XI. Apparent molar volume coefficient S_V and $S_{VV}^{\neq}$, limiting apparent molar volume (ϕ_V^0), Falkenhagen coefficient (A), viscosity coefficient B and D values with corresponding co-solute concentration in three different alizarin solutions at room temperature

c_m mol kg^{-1}	A kg$^{1/2}$ mol$^{-1/2}$	B kg mol^{-1}	D kg$^{3/2}$ mol$^{-3/2}$	$\phi_V^0\times10^3$ m^3 mol^{-1}	S_V m^3 mol$^{-3/2}$ kg$^{1/2}$	$S_{VV}^{\neq}$ m^3 mol^{-2} kg
0.001	–0.338	20.30	–126.47	100.00	–14527.0	349.33
0.002	0.7868	26.27	–250.61	199.57	–6230.2	362.62
0.003	–5.095	92.22	–513.74	200.00	–26112.0	420.37

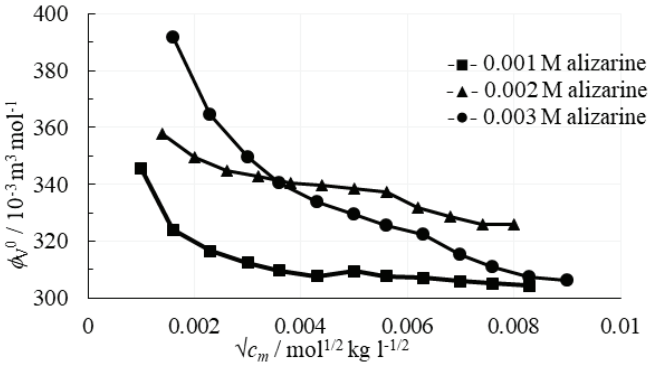
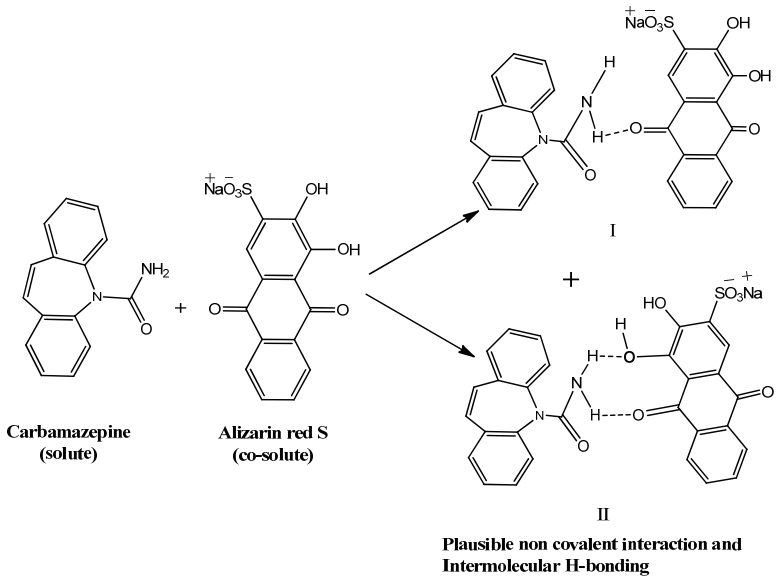


Fig. 1. Plot of apparent molar volume *vs.* different square root of concentration of carbamazepine for 0.001, 0.002, 0.003 mol kg^{-1} alizarin.



Scheme 2. Plausible non-covalent interaction between the two drug molecules.

Viscosity

Viscosity coefficient has been measured with the help of extended Jones–Dole equation for non-electrolytes:[17]

$$\frac{(\eta_r - 1)}{\sqrt{c_m}} = A + B\sqrt{c_m} + D\left(\sqrt{c_m}\right)^2 \quad (8)$$

where $\eta_r = \eta/\eta_o$ is the relative viscosity, η and η_o are the viscosities of ternary solutions (carbamazepine+alizarin+methanol) and solvent (methanol), respectively, and c_m is the molality of carbamazepine in ternary solutions. Their values are given in Table XII.

A is the Falkenhagen coefficient and it is determined by the ionic attraction theory of Falkenhagen–Vernon. Another constant, B is an empirical constant known as viscosity B-coefficient, that indicates interaction of the solute with co-solute molecules, respectively.[16] The values of $(\eta_r - 1)/\sqrt{c_m}$ and $\sqrt{c_m}$ are given in Table X. After plotting $(\eta_r - 1)/\sqrt{c_m}$ against $\sqrt{c_m}$ in Fig. 2 the coefficients A, B, and D are estimated by the least-square polynomial method. The valuable information about their effects on the structure of the co-solute (carbamazepine) in the local vicinity of the solute (alizarin) molecules, in ternary solutions, have been obtained from viscosity B coefficient. It is found from Table X the values of B coefficient are positive and higher than A coefficient.

This signifies that the solute-co-solute interaction is dominant over the solute–solute and the co-solute–co-solute interaction. It is also observed that the positive magnitude of viscosity B coefficient increases with solute concentration.

Another co-efficient *D*, also measures the solute–co-solute interaction, presented in Table XI. The values indicate that the solute–co-solute interactions are much weaker compared to the solute–solvent interactions. The molecular interactions occurring between the drug molecules are due to the dipole–dipole interactions or van der Waals forces or non-covalent interactions.[18] These results are in good agreement with those obtained from limiting apparent molar volume ϕ_V values.

TABLE XII. $((\eta/\eta_0) - 1)/\sqrt{c_m}$ and $\sqrt{c_m}$ of carbamazepine at different concentration of alizarin (0.001, 0.002 and 0.003 mol kg^{-1}) variation with carbamazepine

Alizarin concentration, mol kg^{-1}					
0.001		0.002		0.003	
$\sqrt{c_m}$ mol$^{1/2}$ kg$^{-1/2}$	$((\eta/\eta_0) - 1)/\sqrt{c_m})$ kg$^{1/2}$ mol$^{-1/2}$	$\sqrt{c_m}$ mol$^{1/2}$ kg$^{-1/2}$	$((\eta/\eta_0) - 1)/\sqrt{c_m})$ kg$^{1/2}$ mol$^{-1/2}$	$\sqrt{c_m}$ mol$^{1/2}$ kg$^{-1/2}$	$((\eta/\eta_0) - 1)/\sqrt{c_m})$ kg$^{1/2}$ mol$^{-1/2}$
0.0316	0.3506	0.0316	0.1280	0.0316	–3.0575
0.0447	0.1338	0.0447	0.2100	0.0447	–1.8272
0.0547	0.2011	0.0548	0.1830	0.0547	–0.9566
0.0632	0.2347	0.0632	0.0730	0.0632	–1.2923
0.0707	1.0944	0.0707	0.2120	0.0707	–1.1519
0.0774	0.1545	0.0775	0.3070	0.0775	–1.1006
0.0836	0.5638	0.0837	0.1770	0.0837	–1.3279
0.0894	0.7616	0.0894	0.1700	0.0894	–1.1819
0.0948	0.1359	0.0949	0.7770	0.0949	–1.1651
0.1000	0.5967	0.1000	0.8040	0.1000	–1.0141
0.1048	0.2195	0.1049	0.8200	0.1049	–0.9227

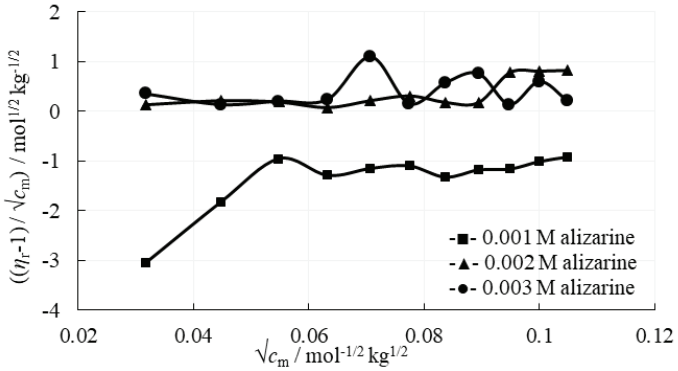


Fig. 2. Plot of $(\eta_r - 1)/\sqrt{c_m}$ against carbamazepine concentration ($\sqrt{c_m}$ at 0.001, 0.002 and 0.003 mol kg^{-1} alizarin concentration.

CONCLUSION

From the experimental results and the derived parameters of the studied ternary system *viz*. carbamazepine + alizarin + methanol, we conclude that Eq. (1), with some modification, is the most suitable equation for the calculation of apparent molar volume. We also derived the conclusion that the interaction sig-

nifying parameters, *e.g.*, limiting apparent molar volume and viscosity *B*-coefficient are increasing with alizarin concentration. The study also proved that the solute–co-solute interaction is dominant over the solute–solute and the co-solute and co-solute.

Acknowledgment. The authors are grateful to the institution Cooch Behar Panchanan Barma University, for providing a space, and supporting the financial aids to carry out this work.

ИЗВОД

ПОРЕЂЕЊЕ РАЗЛИЧИТИХ ТИПОВА ЈЕДНАЧИНА ЗА МОЛАРНУ ЗАПРЕМИНУ ЗА ПРОВЕРУ И ПРИМЕНУ КОД ТЕРНАРНОГ КАРБАМАЗЕПИН + АЛИЗАРИН + МЕТАНОЛ СИСТЕМА И ИСПИТИВАЊЕ ОДГОВАРАЈУЋИХ МОЛЕКУЛСКИХ ИНТЕРАКЦИЈА

TAPAS MALLIK, SRABANTI GHOSH и DEEPAK EKKA

Department of Chemistry, Cooch Behar Panchanan Barma University, Cooch Behar-736101, West Bengal, India

У овом раду, молекулске интеракције карбамазепина и ализарина у метанолу су представљене ограничавајућим привидним моларним запреминама и коефицијентима вискозности. Пре даљег рада, извршена је и провера и примена прорачуна привидне моларне запремине узимајући у обзир доступних пет типова често коришћених једначина, при чему су потребне модификације извршене додатком хипотетичне масе и концентрације растворка. Након тога, ограничавајућа привидна моларна запремина и коефицијенти вискозности су израчунати применом Масон (Masson) једначине и Џонс–Долове (Jones–Dole) једначине, редом, да би предвидели и додатно проверили интеракције које се јављају између молекула у тернарном систему. Показало се да једначина означена бројем 1 представља најбољи аналитичи израз којим су фитовани резултати, а да постоје јаке интеракције између карбамазепина и ализарина у метанолу (ϕ_V^o = 23104 m^3 mol^{-1} и B = 18,10 kg mol^{-1}) при концентрацији 0,003 mol kg^{-1}. Резултати су интерпретирани у корист растворак–ко-растворак интеракција, који су доминантније у односу на растворак–растворак и ко-растворак–ко-растворак интеракције. Добијени резултати су дискутовани уз помоћ интермолекуларних сила и нековалентних интеракција.

(Примљено 29. априла, ревидирано 28. јуна, прихваћено 28. јула 2022)

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