Artículo de investigación científica

Volumetric properties of (PEG 400 + water) and (PEG 400 + ethanol) mixtures at several temperatures and correlation with the Jouyban-Acree model

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SUMMARY

Molar volumes and excess molar volumes were investigated from density values for (PEG 400 + water) and (PEG 400 + ethanol) binary mixtures at temperatures from 283.15 K to 313.15 K. Both systems exhibit negative excess volumes probably due to increased interactions like hydrogen bonding and/or large differences in molar volumes of components. Volume thermal expansion coefficients were also calculated for binary mixtures and pure solvents. The Jouyban-Acree model was used for density and molar volume correlations of the studied mixtures at different temperatures. The mean relative deviations between experimental and calculated density data were 0.1 and 0.5 %, for aqueous and ethanolic mixtures, respectively; whereas, in molar volume data the values were 18.0 and 6.9 %, for aqueous and ethanolic mixtures, respectively. The trained versions of the model for PEG 400 binary solvents could be used to predict the density values of other PEGs with reasonable prediction error employing the density of mono-solvents.

Key words: PEG 400, ethanol, water, binary liquid mixtures, density, excess volume, Jouyban-Acree model.

RESUMEN

Propiedades volumétricas de mezclas binarias (PEG 400 + agua) y (PEG 400 + etanol) a diferentes temperaturas y correlación con el modelo Jouyban-Acree

En este artículo se calcularon los volúmenes molares y molares de exceso a partir de valores de densidad para los sistemas PEG 400 + agua y PEG 400 + etanol, en todo el intervalo de composición, a temperaturas entre 283,15 y 313,15 K. Los sistemas estudiados presentan volúmenes de exceso negativos probablemente debido a las fuertes interacciones por unión de hidrógeno entre las moléculas de los dos compuestos y a la gran diferencia en los volúmenes molares de los dos componentes puros. También se calcularon los coeficientes de expansión térmica-volumétrica en los solventes puros y las respectivas mezclas. Asimismo, se usó el modelo Jouyban-Acree para correlacionar la densidad y el volumen molar de las mezclas a las distintas temperaturas. Las desviaciones medias relativas en densidad fueron 0,1% y 0,5% para las mezclas acuosas y etanólicas, respectivamente, mientras que las desviaciones obtenidas para volumen molar fueron 18% y 6,9% para las mezclas acuosas y etanólicas, respectivamente. Los modelos obtenidos para las mezclas binarias con PEG 400 pueden usarse para predecir los valores con otros PEG, con un adecuado margen de error, utilizando las densidades de los solventes puros.

Palabras clave: PEG 400, etanol, agua, mezclas líquidas binarias, densidad, volumen de exceso, modelo de Jouyban-Acree.

INTRODUCTION

Water-cosolvent mixtures have been used in pharmacy in order to increase the solubility of drugs poorly soluble in water during the design of homogeneous pharmaceutical dosage forms, such as syrups, elixirs, and concentrate drops, among others (1, 2). Ethanol, 1,2-propanediol (propylene glycol), and polyethylene glycol 400 (PEG 400) are the cosolvents most frequently used in duties associated to products design . In particular, these cosolvents are the more indicated for elaboration of peroral and parenteral medications (3). It is important to note that 1,2-propanediol and PEG 400 are also employed as water evaporation regulators. Even more, ethanol and 1,2-propanediol exhibit good properties as controllers of the microorganisms growth in drug formulations (4). Thus, several examples of pharmaceutical formulations using these cosolvents have been presented by Rubino (1) and Yalkowsky (2).

The mixtures obtained using these cosolvents and water, or even among them for non-aqueous liquid formulations such as soft gelatin capsules, show highly non-ideal behavior due to increased interactions between unlike molecules and large differences in molar volumes of the pure components, which leads to non-additive volumes on mixing (5, 6). For this reason it is necessary to characterize the volumetric behavior of these binary homogeneous mixtures as a function of temperature in order to extend the physicochemical information available for liquid mixtures used in pharmacy. This information is useful to understand the intermolecular interactions present in liquid pharmaceutical systems (6). Also, data related to density of solute free mixture of solvents might be useful in prediction of the density of pharmaceutical substances in mixture of solvents (7).

In this report, the molar volumes and the molar excess molar volumes of the binary systems, a) PEG 400 + water and b) PEG 400 + ethanol, at various temperatures (from 283.15 K to 313.15 K) were calculated according to modified procedures widely exposed in the literature (8-10). This report is a continuation of those presented previously about some volumetric properties for other similar aqueous and non-aqueous binary systems (11-14). It is important to note that in the literature is scarce the volumetric information about these mixtures at low temperatures (below room temperature). Additionally, the Jouyban-Acree model was used to correlate densities and molar volumes with solvent compositions as has been for other binary systems at several temperatures (15-19).

MATERIALS AND METHODS

Reagents

In this investigation dehydrated ethanol (from Merck, Germany) and dehydrated polyethylene glycol 400 (PEG 400 from Dow Chemical Company, U.S.A.) were used and they were in agreement with the quality requirements indicated for medicinal products reported in the American Pharmacopeia USP (18); distilled water with conductivity lower than 2 μS cm^{-1} was also used. The dehydrated ethanol and PEG 400 employed were maintained over molecular sieve 3 Å (from Merck, Germany) to obtain dry solvents prior to prepare the solvent mixtures.

Cosolvent mixtures preparation

All binary mixtures were prepared in quantities of 40.00 g by mass using a Ohaus Pioneer TM PA214 analytical balance with sensitivity ± 0.1 mg, in concentrations from 0.10 to 0.90 varying in 0.10 in mass fraction of solvent 1 (PEG 400), to study nine mixtures and the two pure solvents. This procedure implies an uncertainty of ± 2 x 10^{-5} in mole fraction. The mixtures were allowed to stand in Magni Whirl Blue M or Neslab RTE 10 Digital Plus (Thermo Electron Company) water baths at temperatures from 283.15 K to 313.15 K varying in 5.00 ± 0.05 K for at least 30 minutes prior to density determinations.

Density determination

This property was determined using a DMA 45 Anton Paar digital density meter connected to a Neslab RTE 10 Digital Plus (Thermo Electron Company) recirculating thermostatic water bath according to a procedure previously described (20). The equipment was calibrated according to Instruction Manual using air and water at the different temperatures studied (21). From density values, all volumetric properties were calculated as will be indicate in the next section.

RESULTS AND DISCUSSION

In Table 1 the composition of both binary mixtures, in mass and mole fractions, in addition to density values at several temperatures are presented. Our density values for PEG 400 [1] + water [2] are in good agreement with those reported in the literature at several temperatures and compositions (22-25). On the other hand, up to the best of our knowledge no density values have reported systematically for PEG 400 [1] + ethanol [2] mixtures in the literature, and therefore no comparison is possible. In all cases, density values decrease almost linearly as the temperature increases and they increase as the PEG 400 proportion increases in the mixtures for both cosolvent systems.

Molar volumes and excess molar volumes

Table 2 summarizes the molar volumes (V^0) for the binary mixtures at all temperatures. V^0 values were calculated from Eq. 1.

$$V^0 = \frac{x_1 M_1 + x_2 M_2}{\rho} \qquad \text{(Eq. 1)}$$

where, x_1 and x_2 are the mole fractions and M_1 and M_2 are the molar masses, for both components respectively, and ρ is the mixture density.

Table 1. Densities (g cm^{-3}) for both binary mixtures at various temperatures. *w* and *x* represent mass and mole fraction of the first component, respectively.

PEG 400 [1] + water [2]

w_{PEG}	x_{PEG}	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	0.0000	0.9997	0.9991	0.9982	0.9970	0.9956	0.9940	0.9922
0.1000	0.0050	1.0166	1.0158	1.0145	1.0131	1.0113	1.0094	1.0070
0.2000	0.0111	1.0348	1.0335	1.0318	1.0298	1.0277	1.0255	1.0231
0.3000	0.0189	1.0538	1.0517	1.0495	1.0471	1.0447	1.0421	1.0392
0.4000	0.0292	1.0731	1.0706	1.0678	1.0650	1.0621	1.0590	1.0558
0.5000	0.0431	1.0918	1.0887	1.0854	1.0821	1.0786	1.0754	1.0719
0.6000	0.0633	1.1080	1.1045	1.1008	1.0971	1.0931	1.0895	1.0857
0.7000	0.0951	1.1208	1.1169	1.1131	1.1090	1.1049	1.1008	1.0970
0.8000	0.1527	1.1287	1.1249	1.1208	1.1164	1.1126	1.1085	1.1042
0.9000	0.2885	1.1328	1.1292	1.1250	1.1204	1.1166	1.1127	1.1085
1.0000	1.0000	1.1348	1.1307	1.1264	1.1224	1.1182	1.1141	1.1100

PEG 400 [1] + ethanol [2]

w_{PEG}	x_{PEG}	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	0.0000	0.7990	0.7946	0.7895	0.7853	0.7811	0.7767	0.7720
0.1000	0.0126	0.8281	0.8229	0.8190	0.8148	0.8110	0.8061	0.8018
0.2000	0.0280	0.8564	0.8520	0.8473	0.8438	0.8393	0.8347	0.8310
0.3000	0.0470	0.8847	0.8817	0.8770	0.8726	0.8681	0.8643	0.8597
0.4000	0.0713	0.9155	0.9128	0.9086	0.9041	0.8992	0.8948	0.8905
0.5000	0.1033	0.9480	0.9449	0.9411	0.9360	0.9320	0.9269	0.9234
0.6000	0.1473	0.9813	0.9785	0.9743	0.9693	0.9653	0.9611	0.9576
0.7000	0.2118	1.0162	1.0136	1.0091	1.0044	1.0002	0.9963	0.9927
0.8000	0.3154	1.0536	1.0505	1.0461	1.0419	1.0377	1.0340	1.0296
0.9000	0.5090	1.0931	1.0898	1.0854	1.0815	1.0769	1.0731	1.0691
1.0000	1.0000	1.1348	1.1307	1.1264	1.1224	1.1182	1.1141	1.1100

Table 2. Molar volumes (cm^3 mol^{-1}) for both binary mixtures at various temperatures.

PEG 400 [1] + water [2]

w_{PEG}	x_{PEG}	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	0.0000	18.03	18.04	18.05	18.07	18.10	18.13	18.16
0.1000	0.0050	19.60	19.61	19.64	19.67	19.70	19.74	19.78
0.2000	0.0111	21.53	21.55	21.59	21.63	21.67	21.72	21.77
0.3000	0.0189	23.97	24.01	24.06	24.12	24.17	24.23	24.30
0.4000	0.0292	27.17	27.24	27.31	27.38	27.45	27.53	27.62
0.5000	0.0431	31.59	31.68	31.77	31.87	31.97	32.07	32.17
0.6000	0.0633	38.09	38.21	38.33	38.46	38.60	38.73	38.87
0.7000	0.0951	48.49	48.67	48.83	49.01	49.19	49.38	49.55
0.8000	0.1527	67.64	67.87	68.11	68.38	68.61	68.87	69.14
0.9000	0.2885	113.18	113.55	113.97	114.44	114.82	115.23	115.66
1.0000	1.0000	352.50	353.77	355.10	356.37	357.73	359.02	360.36

PEG 400 [1] + ethanol [2]

w_{PEG}	x_{PEG}	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	0.0000	57.66	57.98	58.35	58.67	58.98	59.32	59.68
0.1000	0.0126	61.03	61.42	61.71	62.03	62.32	62.70	63.04
0.2000	0.0280	65.36	65.70	66.06	66.34	66.69	67.06	67.36
0.3000	0.0470	70.89	71.13	71.51	71.87	72.25	72.56	72.95
0.4000	0.0713	77.89	78.12	78.48	78.87	79.30	79.69	80.08
0.5000	0.1033	87.16	87.44	87.79	88.27	88.66	89.14	89.47
0.6000	0.1473	100.08	100.37	100.80	101.32	101.74	102.19	102.56
0.7000	0.2118	119.11	119.42	119.95	120.50	121.01	121.49	121.92
0.8000	0.3154	149.67	150.11	150.75	151.36	151.97	152.51	153.17
0.9000	0.5090	206.94	207.57	208.41	209.17	210.06	210.81	211.59
1.0000	1.0000	352.50	353.77	355.10	356.37	357.73	359.02	360.36

On the other hand, the excess volumes ($V^{0\text{-Exc}}$) calculated from Eq. 2 (where, ρ_1 and ρ_2 are the densities of pure components) at all temperatures studied are presented in Table 3. This behavior is shown graphically in Figure 1 for both systems at 298.15 K.

$$V^{0\text{-Exc}} = \frac{x_1M_1 + x_2M_2}{\rho} - \left(\frac{x_1M_1}{\rho_1} + \frac{x_2M_2}{\rho_2}\right) \qquad \text{(Eq. 2)}$$

Table 3. Excess molar volumes ($cm^3\ mol^{-1}$) for both binary mixtures at various temperatures.

PEG 400 [1] + water [2]

w_{PEG}	x_{PEG}	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
0.1000	0.0050	−0.094	−0.096	−0.093	−0.094	−0.091	−0.090	−0.083
0.2000	0.0111	−0.225	−0.223	−0.218	−0.213	−0.208	−0.206	−0.202
0.3000	0.0189	−0.394	−0.381	−0.373	−0.363	−0.359	−0.351	−0.342
0.4000	0.0292	−0.606	−0.590	−0.575	−0.560	−0.550	−0.536	−0.523
0.5000	0.0431	−0.856	−0.832	−0.810	−0.788	−0.768	−0.756	−0.740
0.6000	0.0633	−1.110	−1.081	−1.054	−1.023	−0.994	−0.973	−0.953
0.7000	0.0951	−1.346	−1.305	−1.280	−1.241	−1.210	−1.176	−1.164
0.8000	0.1527	−1.458	−1.430	−1.401	−1.346	−1.342	−1.306	−1.272
0.9000	0.2885	−1.330	−1.346	−1.317	−1.230	−1.254	−1.239	−1.219
1.0000	1.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

PEG 400 [1] + ethanol [2]

w_{PEG}	x_{PEG}	283.15 K	288.15 K	293.15 K	298.15 K	303.15 K	308.15 K	313.15 K
0.0000	0.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
0.1000	0.0126	−0.351	−0.297	−0.389	−0.397	−0.435	−0.402	−0.440
0.2000	0.0280	−0.550	−0.556	−0.595	−0.657	−0.652	−0.645	−0.735
0.3000	0.0470	−0.636	−0.759	−0.797	−0.796	−0.783	−0.850	−0.866
0.4000	0.0713	−0.794	−0.951	−1.030	−1.022	−0.982	−0.992	−1.041
0.5000	0.1033	−0.951	−1.087	−1.210	−1.142	−1.180	−1.132	−1.256
0.6000	0.1473	−1.009	−1.184	−1.269	−1.206	−1.252	−1.279	−1.414
0.7000	0.2118	−1.002	−1.215	−1.263	−1.220	−1.247	−1.311	−1.442
0.8000	0.3154	−0.979	−1.159	−1.194	−1.204	−1.231	−1.334	−1.341
0.9000	0.5090	−0.785	−0.966	−0.985	−1.024	−0.978	−1.051	−1.133
1.0000	1.0000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Analogous to the behavior obtained for other aqueous and non-aqueous mixtures (11-18), in all cases the excess volumes are negative indicating contraction in volume. Maximum volume contractions were obtained in the mixtures with compositions near to 0.15 or 0.20 in mole fraction of PEG 400 being these values slightly greater for the PEG 400 [1] + water [2] cosolvent system. In this way, according to Fort and Moore

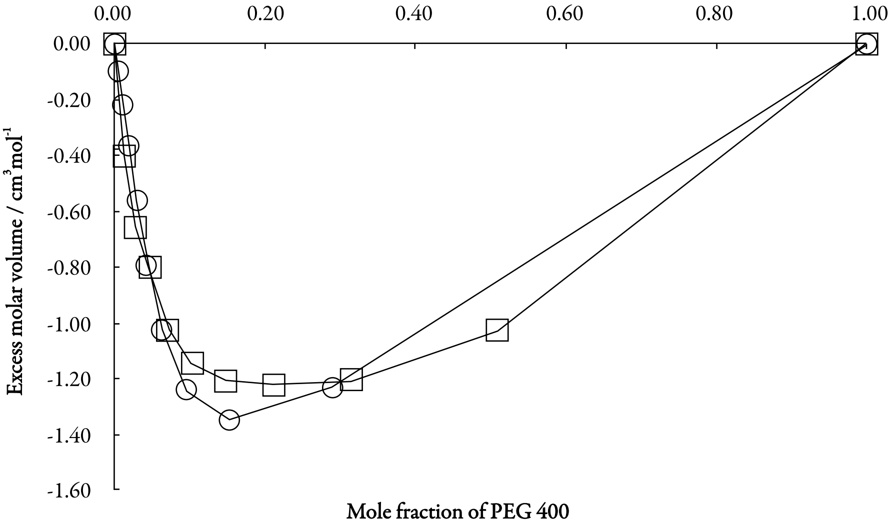

Figure 1. Excess molar volumes for both binary mixtures at 298.15 K. (○): PEG 400 [1] + water [2] system; (□): PEG 400 [1] + ethanol [2] system.

(26), a negative excess volume is an indication of strong hetero-molecular interactions in the liquid mixtures and is attributed to charge transfer, dipole-dipole, dipole-induced dipole interactions, and hydrogen bonding between the unlike components, while a positive sign indicates a weak interaction and is attributed to dispersion forces (London interactions), which are operative in all cases.

In the aqueous systems, just as PEG 400 [1] + water [2] is, where the hydrogen bonding predominates, the contraction in volume has been interpreted basically in qualitative terms considering the following events, first: expansion due to depolymerization of water by addition of cosolvent; second: contraction due to free volume difference of unlike molecules; and third: contraction due to hydrogen bond formation between cosolvent and water through –OH---OH bonding (26).

Thus, the large negative values of $V^{0\text{-Exc}}$ over the free volume contribution indicate the presence of strong specific interactions with predominance of formation of hydrogen bonds between cosolvent and water over the rupture of hydrogen bonding in water-water. The molecular behavior of PEG 400 [1] + ethanol [2] mixtures could be similar because ethanol is also self-connected although no in the same extent as water is.

For PEG 400 [1] + water [2] mixtures the excess molar volumes becomes less negative as the temperature is raised indicating volume expansion which points out the decrease in the interactions between cosolvent and water molecules with increase in temperature. In contrast, the behavior is opposite for PEG 400 [1] + ethanol [2], i.e. it increases as temperature arises, although the reasons for this result are unclear because of the lack of knowledge about the structure of organic solvents.

Volume thermal expansion

On the other hand, in pharmaceutical and chemical pre-formulation studies, it is very important to predict the variation of physicochemical properties related to pharmaceutical dosage forms, with respect to temperature changes; especially those properties which affect the concentration of active ingredients in the formulations developed. For this reason, the volume thermal expansion coefficients (α) were calculated by means of Eq. 3 (27) using the variation of molar volumes with temperature (Table 2).

$$\alpha = \frac{1}{V^0}\left(\frac{\partial V^0}{\partial T}\right)_{P,x} \qquad \text{(Eq. 3)}$$

Table 4 summarizes the ($\partial V^0/\partial T$) and α values for pure solvents and binary mixtures. Figure 2 shows the α values at 298.15 K for both cosolvent systems. For all mixtures and pure solvents, linear models were used, in which obtained determination coefficients are greater than 0.999, except for water where quadratic model has been obtained. The α values varied from 2.53×10^{-4} K^{-1} in water up to 7.36×10^{-4} K^{-1} in pure PEG 400 and from this value to 1.139×10^{-3} K^{-1} in neat ethanol. From 0 to 0.030 in mole fraction of PEG 400 the α values increase readily. In a first approach this fact would be explained in terms of water-structure losing by addition of PEG 400. It should be kept in mind that over 0.030 in mole fraction of PEG 400 the most contributing component in mass to all mixtures is just PEG 400, which is also the less polar solvent in these mixtures (1, 2, 28). On the other side, for PEG 400 [1] + ethanol [2] mixtures the behavior is just opposite being α greater for ethanol, although this solvent is more polar than PEG 400.

Data correlation using the Jouyban-Acree model

For binary data analyses, the Jouyban-Acree model was used to correlate the experimental density data of mixed solvents (29):

$$\ln \rho_{m,T} = m_1 \ln \rho_{1,T} + m_2 \ln \rho_{2,T} + \frac{m_1 m_2}{T} \cdot \sum_{i=0}^{2} J_i \left(m_1 - m_2\right)^i \qquad \text{(Eq. 4)}$$

where m_1 and m_2 are the mass fractions of solvents [1] and [2], $\rho_{m,T}$, $\rho_{1,T}$, $\rho_{2,T}$ are densities of mixed solvents, and solvents [1] and [2], at different temperatures (T), respectively. The methodology to find the J_i terms was described in previous works (29). The

Table 4. Volume thermal expansion coefficients of both binary mixtures at 298.15 K

PEG 400 [1] + water [2]

w_{PEG}	x_{PEG}	100 ($\partial V/\partial T$) / cm^3 mol^{-1} K^{-1}	10,000 α / K^{-1}
0.0000	0.0000	0.458	2.53
0.1000	0.0050	0.620	3.15
0.2000	0.0111	0.826	3.82
0.3000	0.0189	1.11	4.61
0.4000	0.0292	1.48	5.41
0.5000	0.0431	1.96	6.15
0.6000	0.0633	2.62	6.81
0.7000	0.0951	3.53	7.20
0.8000	0.1527	5.01	7.33
0.9000	0.2885	8.33	7.28
1.0000	1.0000	26.23	7.36

PEG 400 [1] + ethanol [2]

w_{PEG}	x_{PEG}	100 ($\partial V/\partial T$) / cm^3 mol^{-1} K^{-1}	10,000 α / K^{-1}
0.0000	0.0000	6.68	11.39
0.1000	0.0126	6.55	10.56
0.2000	0.0280	6.66	10.04
0.3000	0.0470	6.99	9.73
0.4000	0.0713	7.52	9.53
0.5000	0.1033	8.00	9.06
0.6000	0.1473	8.57	8.46
0.7000	0.2118	9.71	8.06
0.8000	0.3154	11.45	7.56
0.9000	0.5090	15.84	7.57
1.0000	1.0000	26.23	7.36

main advantage of the Jouyban-Acree model over other correlation methods such as the one developed by Redlich and Kister (30) is that it includes the effects of temperature in the model constants and provides the possibility of density predictions at other temperatures using interpolation technique, whereas the constants of the Redlich-Kister equation is only valid for one temperature. The interactions between water and/or ethanol with different PEGs are similar and the trained versions of Eq. 4 (for the model constants see Table 5), the densities of their mixtures could be predicted using the den-

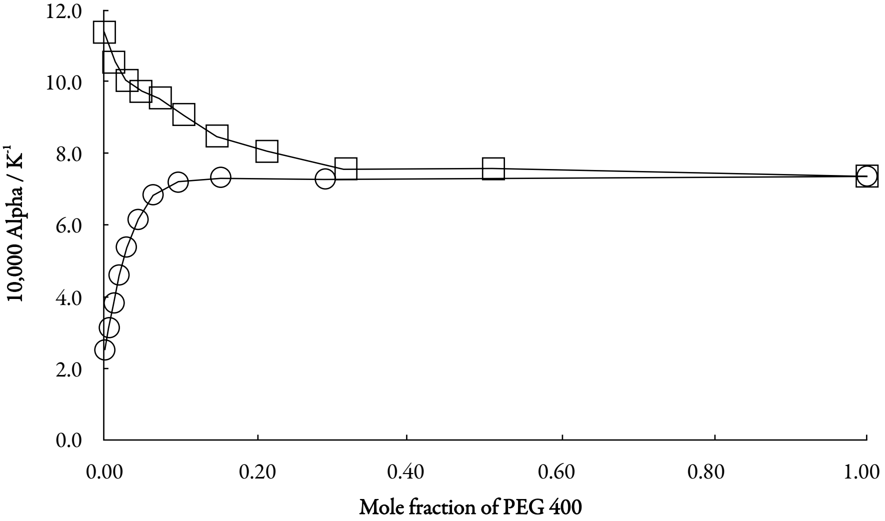

Figure 2. Volume thermal expansion coefficients for both binary mixtures at 298.15 K. (○): PEG 400 [1] + water [2] system; (□): PEG 400 [1] + ethanol [2] system.

sity values of the mono-solvents. As examples, the densities of PEG 200 + water, and PEG 600 + water mixtures at 298.2 K taken from earlier works (7, 31) were predicted with the MRDs of 1.0 and 1.1 %, respectively by using the model constants of PEG 400 + water system from this work. The MRDs for the predicted densities of PEG 200 + ethanol and PEG 600 + ethanol were 1.8 and 0.6 %.

An adopted version of Eq. 4 could be used for representing the molar volume data of mixed solvents. The trained version of the model for glycerol + water mixtures at various temperatures is:

$$\ln V_{m,T}^{0} = x_1 \ln V_{1,T}^{0} + x_2 \ln V_{2,T}^{0} + \frac{x_1 x_2}{T} \cdot \sum_{i=0}^{2} A_i \left(x_1 - x_2\right)^i \qquad \text{(Eq. 5)}$$

where x_1, x_2 are the mole fractions of solvents 1 and 2, $V^0_{m,T}$, $V^0_{1,T}$, $V^0_{2,T}$ are molar volumes of mixed solvents, and solvents [1] and [2], at different temperatures and A_j are the model constants.

The mean relative deviation (MRD) between experimental and calculated data was calculated using:

$$MRD = \frac{100}{N} \sum \left(\frac{\left| Calculated - Experimental \right|}{Experimental} \right) \qquad \text{(Eq. 6)}$$

where N in is the number of data points in the data set.

The computed model constants of the Jouyban-Acree model, the coefficients of determinations and MRD values for density and molar volume data of the investigated solvent systems are listed in Table 5. Careful examinations of the results reveal that the model describes the densities and molar volumes of the investigated solvent systems and could be recommended for practical applications where the simulation of such data is required in process design.

Table 5. The model constants of the Jouyban-Acree model, the coefficient of determinations and mean relative deviations for the density and molar volumes of the investigated binary mixtures.

Density					
Solvent system	J_0	J_1	J_2	r^2	*MRD*
PEG 400 [1] + water [2]	1.480	0.895	NS	0.835	0.5
PEG 400 [1] + ethanol [2]	-0.237	-0.227	0.169	0.866	0.1
Molar volume					
Solvent system	A_0	A_1	A_2	r^2	*MRD*
PEG 400 [1] + water [2]	90.095	NS	NS	0.732	18.0
PEG 400 [1] + ethanol [2]	22.850	-18.884	NS	0.804	6.9

NS: Not significant ($p > 0.05$).

CONCLUSIONS

This work reports new density values of PEG 400 [1] + ethanol [2] at several temperatures and compositions, whereas it expands widely the experimental volumetric information about PEG 400 [1] + water [2] cosolvent binary systems available nowadays because it includes the behavior at low temperatures commonly found in technological and storage conditions. The reported constants of the Jouyban-Acree model for PEG 400 + water and PEG 400 + ethanol mixtures could be used to predict the densities of other PEGs + water or PEGs + ethanol mixtures employing the density values of the mono-solvents. As mentioned earlier (11-18), this information could be employed in several chemical engineering processes and for the theoretical understanding of the behavior of cosolvent mixtures used in the pharmaceutical industries. Based on the results presented here and those reported in the literature (22-25), it can be concluded that these mixtures clearly show non-ideal behavior. These observations demonstrate clearly that it is necessary to characterize systematically all possible pharmaceutical binary system in order to have complete experimental information about the physical and chemical properties useful in the understanding of all kind of homogeneous liquid pharmaceutical dosage systems.

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