Pharmaceutical Sciences
June 2018, 24, 163-167
doi: 10.15171/PS.2018.24
http://journals.tbzmed.ac.ir/PHARM

Short communication

Solubility and Apparent Specific Volume of Sucrose in Some Aqueous Polyethylene Glycol Mixtures at 298.2 K

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Article Info

Article History:
Received: 21 December 2017
Revised: 28 January 2018
Accepted: 20 March 2018
ePublished: 20 June 2018

Keywords:
-Sucrose
-PEGs
-Solubility
-Cosolvency
-Apparent specific volume
-Jouyban-Acree model

ABSTRACT

Background: Sucrose is the most widely used sweetener in food and pharmaceuticals. Quantitative solubility values of this excipient in aqueous polyethylene glycol (PEG) mixtures is not abundant. Thus, the main objective of this research was to determine and correlate the equilibrium solubility of sucrose in {PEG 200 (or 400) + water} mixtures at 298.2 K.
Methods: Shaken flask method was used to determine isothermal solubility. Concentration measurements were performed by means of density determinations. Jouyban-Acree model was used to correlate both solubility sets.
Results: Solubility of sucrose decreases non-linearly with the addition of either PEG200 or PEG400 to water. Jouyban-Acree model correlates solubility values with mixtures composition for both cosolvent systems. Moreover, apparent specific volume of sucrose were also calculated from density and compositions.
Conclusion: Useful solubility values of sucrose at equilibrium in aqueous mixtures of PEG200 and PEG400, as well as their volumetric contributions to saturated solutions are reported.

Introduction

Sucrose is the most important sweetener agent in food and pharmaceutical industries. For pharmaceutical purposes this excipient is used in the design and development of both solid and liquids dosage forms.[1] In the case of liquid products, it is mainly used as sweetener, volumetric contributor as vehicle, water evaporation regulator, and even as osmotic antimicrobial preservative agent.[1] Moreover, medicinal syrups and elixirs, as examples of peroral formulations, normally contain high quantities of sucrose.[2,3] In this way, some physicochemical properties of this agent in aqueous cosolvent mixtures, like solubility and volumetric contributions, are very important to facilitate the duties of pharmaceutical scientist during dosage forms design duties.[4]

Although sucrose has been used for centuries in several industries, and several reports about its solubility in solvent mixtures have been presented in the literature,[5-8] the physicochemical information about their mixed aqueous solutions is still far to be complete.[4] In particular, at the best of our knowledge, no solubility values of sucrose in aqueous polyethylene glycol (PEG) mixtures have been reported in the literature. On the other hand, although some volumetric studies about the behavior of sucrose in some aqueous mixtures have been reported,[9-13] none of them involved PEGs in solution. As well-known liquid PEGs are widely used as excipients in pharmaceutics of liquid systems as cosolvents and water evaporation regulators.[1] Thus, several examples of pharmaceutical formulations using this cosolvent have been presented in the literature.[14]

As has already been mentioned, the solubility behavior of excipients in aqueous cosolvent mixtures is relevant in pharmaceutical and chemical fields because several cosolvent blends are frequently employed in purification methods, drug preformulation studies, and design of liquid medicines, among other practical applications.[15-17] Therefore, it is useful to systematically determine the solubility of all pharmaceutical solid compounds such as drugs and excipients.

With this in mind, the present research studied the equilibrium solubility and apparent specific volume at saturation of sucrose (solute identified as component 3) in {PEG200 or 400 (component 1) + water (component 2)} mixtures at 298.2 K. Thus, this research is similar to those developed previously with some drugs in several {cosolvent (1) + water (2)} mixtures.[18-21]

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Materials and Methods

Reagents and materials

Sucrose (IUPAC name: (2*R*,3*R*,4*S*,5*S*,6*R*)-2-[(2*S*,3*S*,4*S*,5*R*)-3,4-dihydroxy-2,5-bis(hydroxymethyl)oxolan-2-yl]oxy-6-(hydroxymethyl)oxane-3,4,5-triol; CAS number: 57-50-1; molar mass: 342.30 g.mol^{-1};[22] mass fraction purity: 0.995; Ingenio Riopaila, Colombia), polyethylene glycol 200 (PEG200; CAS number: 25322-68-3; mean molar mass: 200 g.mol^{-1};[22] mass fraction purity: 0.990; Dow Chemical Co., USA), polyethylene glycol 400 (PEG400; CAS number: 25322-68-3; mean molar mass: 400 g.mol^{-1};[22] mass fraction purity: 0.992; Dow Chemical Co., USA), and distilled water with conductivity < 2 μS cm^{-1}, were used in this research. Molecular sieve (numbers 3 and 4, Merck, Germany) and Millipore Corp. Swinnex®-13 (USA) filter units were also used.

Solvent mixtures preparation

All {PEG (1) + water (2)} mixtures were prepared gravimetrically in quantities of 10.00 g by using an analytical balance with sensitivity ± 0.1 mg (Ohaus Pioneer TM PA214, USA). The mass fractions of PEG (w_1^o) of the nine binary mixtures studied varied by w_1^o = 0.10 from w_1^o = 0.10 to w_1^o = 0.90 in order to cover the entire range of compositions.

Solubility determinations

The procedures followed in this research were similar to those used earlier to evaluate the solubility of the analgesic drug acetaminophen in {ethanol (1) + water (2)} mixtures.[23] Briefly, an excess of sucrose was added to 5.00 g of each cosolvent mixture or neat solvent, in stoppered dark glass flasks. The flasks with the solid-liquid mixtures were placed in an ultrasonic bath (Elma® E 60 H Elmasonic, Germany) during 15 min and later they were placed in a thermostatic water bath (Magni Whirl Blue M. Electric Company Burrel, USA) kept at 298.2 ± 0.1 K with sporadic stirring for at least five days to reach the saturation. After this time, the supernatant solutions were filtered in order to remove undissolved particulate matter before sampling for analysis. Sucrose concentrations were determined by measuring the saturated solution density by using a digital density meter (DMA 45 Anton Paar, Austria) connected to a recirculating thermostatic bath at the same temperature (Neslab RTE 10 Digital One Thermo Electron Company, USA) and extrapolation from density calibration curves. Densities were also used to calculate the volumetric contribution of sucrose to the saturated solutions.

Results and discussion

Experimental solubility of sucrose

Table 1 summarizes the experimental solubility of sucrose in all the {PEG (1) + water (2)} mixtures at 298.2 K, expressed in empirical concentration scales (mass/mass and mass/volume percentages), a semiempirical scale (molarity, mol.dm^{-3}), and the rational scale (mole fraction), respectively.

In all concentration scales, the solubility of sucrose decreases continuously from water to PEG in both {PEG200 (or 400) (1) + water (2)} systems to reach the minimum values in neat PEG200 and PEG400. It is noteworthy that the empirical scales do not consider moles of solute or solvents, the semiempirical scales only consider moles of solute but nothing about solvent, whereas, the rational scale consider both moles of solute and solvent.[24] Regarding the sucrose solubility in neat water at 298.2 K, our value (68.79 m/m%, Table 1) is slightly higher than the one reported by Fey et al. (67.89 m/m%).[5] This difference could be attributed mainly to different analytic technique conditions or saturation times, as it is described in the literature for other compounds.[4]

Figure 1 compares the m/m% solubility of sucrose in both {PEG (1) + water (2)} systems. As observed, in water-rich mixtures apparently no significant differences are noted when changing PEG200 and PEG400 but in PEG-rich mixtures a lower solubility is observed when using PEG400. This result could be a consequence of the slightly higher polarity of PEG200 compared with PEG400 because the lower polymer-chain length.

Table 1. Equilibrium solubility of sucrose (3) in {PEG200 (or 400 (1) + water (2)} mixtures at 298.2 K expressed in several concentration scales.

w_1^o [a]	PEG200 (1) + water (2) [b]				PEG400 (1) + water (2) [b]			
	m/m %	m/v %	mol.dm^{-3}	x_3	m/m %	m/v %	mol.dm^{-3}	x_3
0.00	68.79	92.00	2.688	0.1040	68.79	92.00	2.688	0.1040
0.10	66.31	87.76	2.564	0.1023	66.69	88.13	2.575	0.1044
0.20	60.79	79.25	2.315	9.07 x 10^{-2}	61.40	80.41	2.349	9.38 x 10^{-2}
0.30	54.85	70.72	2.066	8.09 x 10^{-2}	55.15	70.85	2.070	8.32 x 10^{-2}
0.40	49.39	62.26	1.819	7.47 x 10^{-2}	48.60	61.33	1.792	7.46 x 10^{-2}
0.50	40.67	50.24	1.468	6.21 x 10^{-2}	38.24	47.02	1.374	5.87 x 10^{-2}
0.60	31.70	38.17	1.115	5.11 x 10^{-2}	27.00	32.26	0.942	4.36 x 10^{-2}
0.70	19.85	23.21	0.678	3.47 x 10^{-2}	15.41	17.88	0.522	2.81 x 10^{-2}
0.80	10.65	12.19	0.356	2.25 x 10^{-2}	6.66	7.57	0.221	1.57 x 10^{-2}
0.90	4.72	5.33	0.156	1.42 x 10^{-2}	1.98	2.24	6.53 x 10^{-2}	7.52 x 10^{-3}
1.00	1.08	1.22	3.55 x 10^{-2}	6.36 x 10^{-3}	0.148	0.166	4.85 x 10^{-3}	1.73 x 10^{-3}

[a] w_1^o is the mass fraction of PEG (1) in {PEG (1) + water (2)} mixtures free of sucrose (3).

[b] Mean relative uncertainty in solubility is 0.018 or 1.8%.

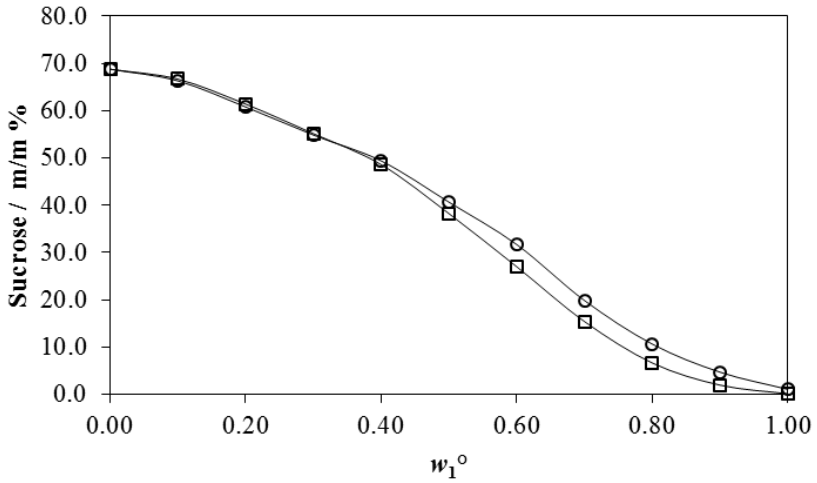

Figure 1. Solubility of sucrose in aqueous PEG mixtures at 298.2 K expressed in mass/mass percentage. ○: PEG200 (1) + water (2); □: PEG400 (1) + water (2).

Solubility correlation with the Jouyban-Acree model

The Jouyban-Acree model was the first used cosolvency model to calculate the solute solubility in the binary solvent mixtures in relation to both solvent composition and temperature. The general form of the Jouyban-Acree model, as an accurate linear mathematical model both from correlative and predictive capabilities viewpoints, for calculation of the solubility of drugs in the binary solvent mixtures is:[25]

$$\ln x_{m,t}^{Sat} = \ln x_{1,t}^{Sat} + \ln x_{2,t}^{Sat} + \frac{w_1 w_2}{T}\sum_{i=0}^{2} J_i (w_1 - w_2)^i \qquad \text{Eq. (1)}$$

where $x_{m,t}^{Sat}$, $x_{1,t}^{Sat}$ and $x_{2,t}^{Sat}$ are the mole fraction solubility of the solute in the solvent mixtures, mono-solvents 1 and 2 at temperature T, w_1 and w_2 denote the mass fractions of mono solvents 1 and 2, and J_i is the constant computed by regressing $\ln x_{m,t}^{Sat} - \ln x_{1,t}^{Sat} - \ln x_{2,t}^{Sat}$ against $\frac{w_1 w_2}{T}$, $\frac{w_1 w_2 (w_1 - w_2)}{T}$, and $\frac{w_1 w_2 (w_1 - w_2)^2}{T}$.

Table 2. Parameters of the Jouyban-Acree model for the mole fraction solubility of sucrose (3) in {PEG 200 (or 400 (1) + water (2)} mixtures at 298.2 K.

	Jouyban-Acree constants			
PEG 200 (1) + water (2)	J_0	1045.367	R^2	0.998
	J_1	485.037	F	1084
	J_2	0*	*MRD*%	2.5
			p-value	<0.05
PEG 400 (1) + water (2)	J_0	1736.144	R^2	0.998
	J_1	1072.320	F	1485
	J_2	820.694	*MRD*%	3.2
			p-value	<0.05

* Not statistically significant (p > 0.05).

The experimental solubility results for sucrose (3) in the {PEG (1) + water (2)} mixture solutions are correlated and re-calculated with Eq. (2) by using a no intercept least square analysis.[26] For the binary mixtures of {PEG 200 (1) + water (2)} and {PEG 400 (1) + water (2)}, the parameters of the Jouyban–Acree model along with overall *MRD*% of predicted data are presented in Table 2. Using these computations, the solubility of sucrose (3) could be calculated with the *MRD*% of 2.5 and 3.2% for mixtures of {PEG 200 (1) + water (2)} and {PEG 400 (1) + water (2)}, respectively.

Apparent specific volumes of sucrose at saturation

The volumetric contribution of drugs and excipients in aqueous cosolvent mixtures is important from several practical and theoretical viewpoints.[23] In this way, a very well-considered property of solutes in saturated solutions is the apparent specific volume (ϕ_V^{sp}), which is calculated by means of Eq. (2):[23]

$$\phi_V^{SP} = \frac{w_3 + w_{1+2}(1 - \rho_{1+2+3}/\rho_{1+2})}{w_3 \rho_{1+2+3}} \qquad \text{Eq. (2)}$$

Here, w_3 and w_{1+2} are the mass fractions of the solute and the cosolvent mixture in the saturated solution, respectively. ρ_{1+2+3} and ρ_{1+2} are the densities of the saturated solution and the cosolvent mixture free of solute, respectively. The density of the {PEG (1) + water (2)} cosolvent mixtures at 298.2 K was taken from the literature.[27,28] The density of both saturated solutions and cosolvent mixtures as well as the apparent specific volumes of sucrose at 298.2 K are presented in Table 3. Figure 2 allows the visual comparison of densities for all the saturated solutions and the cosolvent mixtures free of solute. All the saturated solutions exhibit density values higher than those of the cosolvent mixtures free of sucrose, in both systems, indicating that this solute is more dense than the respective solvents. However, in despite of the density of the cosolvent mixtures increases with a greater proportion of PEG (1), the density values of the saturated solutions decrease as a result of the solubility of sucrose is lower in PEG-rich mixtures.

Table 3. Density of saturated solutions (ρ_{1+2+3}) and cosolvent mixtures free of sucrose (ρ_{1+2}) and apparent specific volume of sucrose (ϕ_V^{sp}) in {PEG200 (or 400 (1) + water (2)} mixtures at 298.2 K.

	PEG200 (1) + water (2) [b]			PEG400 (1) + water (2) [b]		
w_1^o [a]	ρ_{1+2+3} / g.cm^{-3}	ρ_{1+2} / g.cm^{-3} [c]	ϕ_V^{sp} / cm^3.g^{-1}	ρ_{1+2+3} / g.cm^{-3}	ρ_{1+2} / g.cm^{-3} [d]	ϕ_V^{sp} / cm^3.g^{-1}
0.00	1.3373	0.9970	0.632	1.3373	0.9970	0.632
0.10	1.3234	1.0116	0.637	1.3215	1.0131	0.642
0.20	1.3036	1.0272	0.634	1.3097	1.0298	0.633
0.30	1.2892	1.0432	0.625	1.2845	1.0471	0.635
0.40	1.2607	1.0591	0.638	1.2619	1.0650	0.638
0.50	1.2352	1.0750	0.634	1.2296	1.0821	0.634
0.60	1.2041	1.0890	0.641	1.1946	1.0971	0.636
0.70	1.1691	1.1010	0.642	1.1598	1.1090	0.645
0.80	1.1444	1.1101	0.647	1.1376	1.1164	0.645
0.90	1.1294	1.1162	0.674	1.1273	1.1204	0.617
1.00	1.1230	1.1196	0.644	1.1225	1.1224	0.855

[a] w_1^o is the mass fraction of PEG (1) in {PEG (1) + water (2)} mixtures free of sucrose (3).

[b] Mean uncertainty in density of saturated solutions is 0.0008 g.cm^{-3}; mean uncertainty in apparent specific volume of sucrose is 0.003 cm^3.g^{-1}.

[c] From Ref. 27.

[d] From Ref. 28.

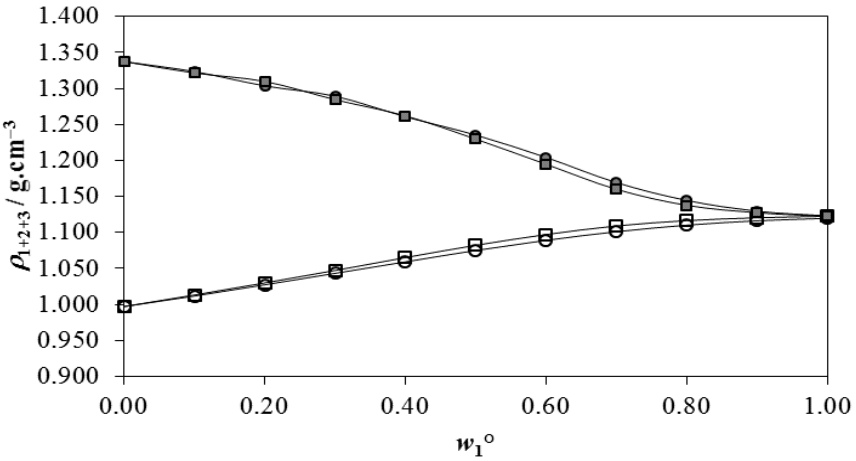

Figure 2. Density of the saturated solutions of sucrose in aqueous PEG mixtures (filled symbols) and density of the {PEG200 or 400 (1) + water (2)} mixtures free of sucrose (3) (empty symbols) at 298.2 K. ● and ○: PEG200 (1) + water (2); ■ and □: PEG400 (1) + water (2).

If the ϕ_V^{sp} values of sucrose in mixtures of $0.00 \leq w_1^o \leq 0.80$ in both cosolvent systems are contemplated, the obtained average value is: 0.637 (±0.006) cm^3.g^{-1} (RSD: 0.89%). No PEG-rich mixtures are considered because the ϕ_V^{sp} values calculated in w_1^o = 0.90 and neat PEGs involve high uncertainty as a consequence of the low solubility of sucrose in these systems. This small uncertainty, lower than 1.0%, is normally accepted during all the stages of design and development of liquid pharmaceutical dosage forms [24]. Thus, a specific volumetric contribution of 0.637 cm^3.g^{-1} could be considered as adequate for sucrose in liquid mixtures involving PEG and water for practical purposes at room temperature.

Conclusion

The sucrose solubility values presented in this report expand the physicochemical information about pharmaceutical excipients in aqueous cosolvent mixtures. As observed, Jouyban-Acree model correlates adequately these solubility values. Finally, a mean ϕ_V^{sp} value of 0.637 cm^3.g^{-1} for sucrose in aqueous-PEG mixtures is adequate for practical purposes.

Acknowledgement

We thank the Department of Pharmacy of the Universidad Nacional de Colombia for facilitating the equipment and laboratories used.

Conflict of interests

The authors claim that there is no conflict of interest.

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