# Apparent Specific Volumes of Sucrose in Different Aqueous Cosolvent Mixtures at 298.2 K 

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ArticleInfo
Article History:
Received: 27 July 2018
Revised: 2 September 2018
Accepted: 15 September 2018
ePublished: 30 December 2018
Keywords:
-Sucrose
-Cosolvents
-Density
-Apparent specific volume


#### Abstract

Background: Sucrose is the most widely used sweetener in foods and pharmaceuticals. Apparent specific volumes of this excipient in aqueous cosolvent mixtures are not available. Thus, the main objective of this research was to determine this property by measuring the density of several solutions of sucrose in \{cosolvent + water\} mixtures at 298.2 K.

Methods: Sucrose dissolutions were prepared gravimetrically and a thermostatically controlled digital oscillatory method was used to measure the dissolutions density. Results: From density values of sucrose dissolutions and cosolvent mixtures the apparent specific volumes of sucrose were calculated and analyzed based on the sucrose and cosolvent proportions in the mixtures. Conclusion: Useful density values of sucrose solutions at different concentrations in several aqueous cosolvent mixtures are reported at 298.2 K. Finally, a mean apparent specific volume value of $0.632 \mathrm{~cm}^{3} . \mathrm{g}^{-1}$ for sucrose in different aqueous-cosolvent mixtures could be adequate for practical purposes in pharmaceutical industries.


## Introduction

Sucrose is considered as the most important sweetener ingredient in food and pharmaceutical industries everywhere. In the pharmaceutical industries, this compound is used to develop solid and liquids dosage forms. ${ }^{1}$ Regarding the liquid products intended for peroral administration, sucrose is mainly used as natural sweetener, as volume contributor in vehicles like officinal syrups and elixirs, as water evaporation regulator, and even as an osmotic antimicrobial preservative agent. ${ }^{1}$ In particular, medicinal syrups and elixirs normally contain high proportions of sucrose. ${ }^{2,3}$ For this reason, some physicochemical properties of this natural excipient in aqueous cosolvent mixtures, like equilibrium solubility and volumetric contributions, are very important from a practical point of view to facilitate the duties of pharmaceutical scientists during all the stages related to dosage forms design and development. ${ }^{4,5}$
Although sucrose as additive has been used for centuries in several industries, and some reports about its apparent specific and/or molar volume in water or cosolvent mixtures have been reported in the literature, ${ }^{4-10}$ the information about its volumetric physicochemical behavior in mixed aqueous solutions is still far to be complete. ${ }^{4,5}$ Particularly, up to the best of our knowledge, no apparent specific volumes of sucrose as a function of
sucrose concentration in aqueous cosolvent mixtures have been reported in the literature. In this way, only apparent specific volumes of sucrose at saturation in the most common aqueous cosolvent mixtures have been reported. ${ }^{4,5}$
It is noteworthy that the volumes of components in solution are not additive owing the different intermolecular interactions and/or differences in molar volumes. Therefore, the real volumetric contribution of each component is expressed by the partial molar or specific volumes, which depend on temperature and mixtures compositions, and thus, normally are not known for the vast majority of compounds. This is also valid for drugs and excipients in every liquid pharmaceutical dosage form. Nevertheless, in a good approximation, the use of apparent specific volumes constitutes a good tool in design of liquid products, in contraposition of the wellknown Latin term "Quantum satis", i.e. "the amount which is enough", because it could allow the calculation of the volumetric contribution of each component of the medicinal formulation. ${ }^{2,3}$
With all this in mind, in the present research the apparent specific volumes of sucrose (the solute identified as component 3) as a function of the solute concentration in different $\{$ cosolvent (component 1 ) + water (component 2)\} mixtures were studied at 298.2 K. Cosolvents studied

[^0]were ethanol, propylene glycol, glycerol, and polyethylene glycols 200 and 400 (PEG 200 and PEG 400). Pharmaceutical literature reports a lot of applications and medicinal products were these cosolvents are used as excipients. ${ }^{11,12}$ Thus, this research expands the information reported previously with this pharmaceutical sweetener agent in several \{cosolvent (1) + water (2) \} mixtures. ${ }^{4,5}$

## Materials and Methods <br> Reagents

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)ox -olan-2-yl]oxy-6-(hydroxymethyl)oxane-3,4,5-triol; CAS number: 57-50-1; molar mass: $342.30 \mathrm{~g} . \mathrm{mol}^{-1,}{ }^{13}$ mass fraction purity: 0.995; Ingenio Riopaila, Colombia), ethanol (EtOH, CAS number: 64-17-5; molar mass: 46.07 g. $\mathrm{mol}^{-1 .}{ }^{13}$ mass fraction purity: 0.995 ; Merck, Germany), propylene glycol (PG, CAS number: 57-55-6; molar mass: $76.10 \mathrm{~g} . \mathrm{mol}^{-1,13}$ mass fraction purity: 0.992 ; Dow Chemical Co., USA), glycerol (G, CAS number: 56-81-5; molar mass: 92.09 g. $\mathrm{mol}^{-1.13}$ mass fraction purity: 0.990 ; Dow Chemical Co., USA), polyethylene glycol 200 (PEG 200; CAS number: 25322-68-3; mean molar mass: 200 g. $\mathrm{mol}^{-1.13}{ }^{13}$ mass fraction purity: 0.990; Dow Chemical Co., USA), polyethylene glycol 400 (PEG 400; CAS number: 25322-68-3; mean molar mass: $400 \mathrm{~g} . \mathrm{mol}^{-1,13}{ }^{13}$ mass fraction purity: 0.992; Dow Chemical Co., USA), and distilled water with conductivity $<2 \mu \mathrm{~S} . \mathrm{cm}^{-1}$, were used in this research. Molecular sieve (numbers 3 and 4, Merck, Germany) was also used.

## Sucrose cosolvent mixtures preparation

All \{cosolvent (1) + water (2) \} mixtures were prepared by gravimetric method in quantities of 60.00 g by using an analytical balance (Ohaus Pioneer TM PA214, USA, sensitivity $\pm 0.1 \mathrm{mg}$ ). The mass fractions of cosolvent ( $w_{1}^{0}$ ) of the five binary mixtures studied varied by $w_{1}^{0}=0.10$ from $w_{1}^{0}=0.10$ to $w_{1}^{0}=0.50$. After that, six dissolutions of sucrose at different concentrations were gravimetrically prepared in neat water and the \{cosolvent (1) + water (2) \} mixtures. Sucrose concentrations were chosen based on the solubility exhibited by this compound in the respective aqueous cosolvent mixtures to cover a wide range of compositions. ${ }^{4,5}$ Moreover, these are the concentrations commonly used to design liquid dosage forms mainly intended for the oral administration route. ${ }^{2,3}$

## Density determinations

Dissolution density was measured by using a digital density meter (DMA 45 Anton Paar, Austria) directly connected to a recirculating thermostatic bath operating at 298.2 K (Neslab RTE 10 Digital One Thermo Electron Company, USA). Densities were used to calculate the apparent specific volumes of sucrose $\left(\phi_{V}^{\text {sp }}\right)$, according to the following equation: ${ }^{14}$

$$
\begin{equation*}
\phi_{V}^{\mathrm{sp}}=\frac{w_{3}+w_{1+2}\left(1-\rho_{1+2+3} / \rho_{1+2}\right)}{w_{3} \rho_{1+2+3}} \tag{1}
\end{equation*}
$$

Here, $w_{3}$ and $w_{1+2}$ are the mass fractions of sucrose (3) and the cosolvent mixture $(1+2)$ in the respective dissolution, respectively. $\rho_{1+2+3}$ and $\rho_{1+2}$ are the densities of the sucrose dissolution and the cosolvent mixture free of solute, respectively. All density values of the \{cosolvent (1) + water (2) \} cosolvent mixtures free of solute at 298.2 K were taken from the literature. ${ }^{15-19}$

## Results and Discussion

Density of the sucrose dissolutions and apparent specific volumes of sucrose at 298.2 K are reported in Tables 1 to 3 for water, aqueous-alcoholic and aqueous polymeric mixtures, respectively. Besides, for illustration the density of the sucrose dissolutions in neat water and also in $\{$ ethanol (1) + water (2) $\}$ mixtures as a function of the sucrose proportion expressed as mass fraction ( $w_{3}$ ) at 298.2 K is shown in Figure 1. Moreover, just as an example, the density of sucrose dissolutions in the five \{cosolvent (1) + water (2) \} mixtures, with a cosolvent proportion of $0.30\left(w_{1}^{0}=0.30\right)$ in the mixtures free of sucrose, as a function of the sucrose mass fraction ( $w_{3}$ ) at 298.2 K, is shown in Figure 2.

Table 1. Density of water and sucrose solutions ( $\rho$ ) and apparent specific volume of sucrose ( $\phi_{V}^{\text {sp }}$ ) in water at 298.2 K .

| $\boldsymbol{w}_{\mathbf{2}}{ }^{\mathbf{a}}$ | $\rho / \mathbf{g . c m}$ |  |
| :--- | :--- | :--- |
| 0.0000 | 0.9970 | $\phi_{V}^{\text {sp }} / \mathbf{c m}^{\mathbf{3}} \cdot \mathbf{g}^{-\mathbf{1} \mathbf{b}}$ |
| 0.1429 | 1.0555 |  |
| 0.2502 | 1.1019 | 0.614 |
| 0.4000 | 1.1740 | 0.621 |
| 0.501 | 1.2225 | 0.625 |
| 0.5714 | 1.2665 | 0.627 |
| 0.6252 | 1.2974 | 0.630 |
|  | Mean | 0.632 |
|  | Std. dev. | 0.625 |
|  | RSD | 0.006 |
|  | $1.00 \%$ |  |

${ }^{a} w_{2}$ is the mass fraction of sucrose (compound 2) in the binary mixtures with water (compound 1).
${ }^{\mathrm{b}}$ Mean uncertainty in density of dissolutions is $0.0003 \mathrm{g.cm}{ }^{-3}$; mean uncertainty in apparent specific volume of sucrose is 0.002 $\mathrm{cm}^{3} \cdot \mathrm{~g}^{-1}$.

By considering the sucrose behavior in neat water (Table 1), the dissolution density increase with the sucrose proportion by following a parabolic trend. Moreover, the $\phi_{V}^{\mathrm{sp}}$ values also increase with the sucrose proportion following a third degree regular polynomial (Figure 3). Besides, a mean $\phi_{V}^{\mathrm{sp}}$ value of $0.625( \pm 0.006) \mathrm{cm}^{3} . \mathrm{g}^{-1}$, with relative standard deviation (RDS) of $1.00 \%$, is obtained if considering the six individual values. Therefore, despite the sweetener concentration, this mean value could be considered as useful for sucrose in neat water at 298.2 K in development stages of liquid dosage forms, because uncertainties or deviations lower than $1.0 \%$ are normally considered as acceptable in pharmaceutical industries. ${ }^{20}$

Table 2. Density of cosolvent mixtures free of sucrose and sucrose solutions ( $\rho$ ) and apparent specific volume of sucrose ( $\phi_{V}^{\mathrm{sp}}$ ) in different \{cosolvent (1) + water (2)\} mixtures at 298.2 K.

| $W_{3}{ }^{\text {a }}$ | $\begin{aligned} & \rho / \\ & \mathrm{g} \cdot \mathrm{~cm}^{-3 \mathrm{~b}} \end{aligned}$ | $\begin{aligned} & \phi_{V}^{\mathrm{sp}} / \\ & \mathrm{cm}^{3} \cdot \mathrm{~g}^{-1 \mathrm{~b}} \end{aligned}$ | $W_{3}{ }^{\text {a }}$ | $\begin{aligned} & \rho / \\ & \mathrm{g} \cdot \mathrm{~cm}^{-3 \mathrm{~b}} \end{aligned}$ | $\begin{aligned} & \phi_{V}^{\mathrm{sp}} / \\ & \mathbf{c m}^{3} \cdot \mathbf{g}^{-1 \mathrm{~b}} \end{aligned}$ | $W_{3}{ }^{\text {a }}$ | $\begin{aligned} & \rho / \\ & \mathrm{g} \cdot \mathrm{~cm}^{-3 \mathrm{~b}} \end{aligned}$ | $\begin{aligned} & \phi_{V}^{\mathrm{sp}} / \\ & \mathbf{c m}^{3} \cdot \mathbf{g}^{-1 \mathrm{~b}} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Ethanol (1) + water (2) |  |  | Propylene glycol (1) + water (2) |  |  | Glycerol (1) + water (2) |  |  |
| $w_{1}^{\mathrm{o}}=0.10^{\text {c }}$ |  |  |  |  |  |  |  |  |
| 0.0000 | $0.9802{ }^{\text {d }}$ |  | 0.0000 | $1.0043{ }^{\text {e }}$ |  | 0.0000 | $1.0207^{\text {f }}$ |  |
| 0.2312 | 1.0810 | 0.609 | 0.2309 | 1.1000 | 0.621 | 0.2304 | 1.1067 | 0.649 |
| 0.3755 | 1.1505 | 0.618 | 0.3750 | 1.1660 | 0.628 | 0.3754 | 1.1747 | 0.638 |
| 0.4443 | 1.1846 | 0.624 | 0.4442 | 1.2026 | 0.626 | 0.4448 | 1.2116 | 0.633 |
| 0.4999 | 1.2129 | 0.629 | 0.4998 | 1.2320 | 0.627 | 0.4996 | 1.2385 | 0.635 |
| 0.5428 | 1.2388 | 0.628 | 0.5465 | 1.2559 | 0.631 | 0.5449 | 1.2664 | 0.631 |
| 0.5831 | 1.2629 | 0.629 | 0.5834 | 1.2772 | 0.631 | 0.5831 | 1.2848 | 0.634 |
|  | Mean | 0.623 |  | Mean | 0.627 |  | Mean | 0.637 |
|  | Std. dev. | 0.008 |  | Std. dev. | 0.004 |  | Std. dev. | 0.007 |
|  | RSD | 1.27\% |  | RSD | 0.60\% |  | RSD | 1.04\% |
| $w_{1}^{\text {o }}=0.20^{\text {c }}$ |  |  |  |  |  |  |  |  |
| 0.0000 | $0.9666{ }^{\text {d }}$ |  | 0.0000 | $1.0128^{\text {e }}$ |  | 0.0000 | $1.0453^{\dagger}$ |  |
| 0.1949 | 1.0494 | 0.616 | 0.1939 | 1.0902 | 0.626 | 0.2288 | 1.1332 | 0.632 |
| 0.3246 | 1.1143 | 0.612 | 0.3242 | 1.1474 | 0.630 | 0.3718 | 1.1967 | 0.631 |
| 0.4187 | 1.1593 | 0.624 | 0.4173 | 1.1932 | 0.630 | 0.4739 | 1.2444 | 0.634 |
| 0.4897 | 1.2000 | 0.624 | 0.4896 | 1.2277 | 0.634 | 0.5451 | 1.2818 | 0.633 |
| 0.5451 | 1.2313 | 0.627 | 0.5455 | 1.2614 | 0.631 | 0.5997 | 1.3085 | 0.636 |
| 0.5860 | 1.2516 | 0.633 | 0.5899 | 1.2860 | 0.632 | 0.6356 | 1.3297 | 0.635 |
|  | Mean | 0.622 |  | Mean | 0.630 |  | Mean | 0.633 |
|  | Std. dev. | 0.007 |  | Std. dev. | 0.003 |  | Std. dev. | 0.002 |
|  | RSD | 1.19\% |  | RSD | 0.44\% |  | RSD | 0.27\% |
| $w_{1}^{\text {o }}=0.30^{\text {c }}$ |  |  |  |  |  |  |  |  |
| 0.0000 | $0.9509^{\text {d }}$ |  | 0.0000 | $1.0213^{\text {e }}$ |  | 0.0000 | $1.0707^{\text {f }}$ |  |
| 0.1803 | 1.0244 | 0.633 | 0.1661 | 1.0840 | 0.638 | 0.1807 | 1.1325 | 0.652 |
| 0.3060 | 1.0815 | 0.637 | 0.2859 | 1.1340 | 0.639 | 0.3055 | 1.1855 | 0.638 |
| 0.3975 | 1.1298 | 0.633 | 0.3750 | 1.1761 | 0.635 | 0.3988 | 1.2231 | 0.642 |
| 0.4684 | 1.1690 | 0.633 | 0.4444 | 1.2111 | 0.634 | 0.4527 | 1.2494 | 0.639 |
| 0.5239 | 1.2029 | 0.631 | 0.5005 | 1.2417 | 0.632 | 0.5238 | 1.2848 | 0.637 |
| 0.5687 | 1.2359 | 0.625 | 0.5657 | 1.2757 | 0.634 | 0.5690 | 1.3070 | 0.637 |
|  | Mean | 0.632 |  | Mean | 0.635 |  | Mean | 0.641 |
|  | Std. dev. | 0.004 |  | Std. dev. | 0.003 |  | Std. dev. | 0.006 |
|  | RSD | 0.60\% |  | RSD | 0.42\% |  | RSD | 0.90\% |
| $w_{1}^{\text {o }}=0.40^{\text {c }}$ |  |  |  |  |  |  |  |  |
| 0.0000 | $0.9321^{\text {d }}$ |  | 0.0000 | $1.0290^{\text {e }}$ |  | 0.0000 | $1.0971{ }^{\text {f }}$ |  |
| 0.1304 | 0.9874 | 0.612 | 0.1523 | 1.0856 | 0.639 | 0.1525 | 1.1491 | 0.641 |
| 0.2307 | 1.0307 | 0.628 | 0.2646 | 1.1288 | 0.647 | 0.2644 | 1.1970 | 0.624 |
| 0.3104 | 1.0711 | 0.624 | 0.3504 | 1.1657 | 0.647 | 0.3415 | 1.2269 | 0.629 |
| 0.3750 | 1.1031 | 0.629 | 0.4187 | 1.2001 | 0.641 | 0.4171 | 1.2547 | 0.637 |
| 0.4285 | 1.1331 | 0.629 | 0.4739 | 1.2248 | 0.644 | 0.4738 | 1.2812 | 0.635 |
| 0.4737 | 1.1627 | 0.624 | 0.5188 | 1.2511 | 0.639 | 0.5192 | 1.3043 | 0.633 |
|  | Mean | 0.624 |  | Mean | 0.643 |  | Mean | 0.633 |
|  | Std. dev. | 0.007 |  | Std. dev. | 0.004 |  | Std. dev. | 0.006 |
|  | RSD | 1.05\% |  | RSD | 0.55\% |  | RSD | 0.96\% |
| $w_{1}^{\mathrm{o}}=0.50^{\mathrm{c}}$ |  |  |  |  |  |  |  |  |
| 0.0000 | $0.9100^{\text {d }}$ |  | 0.0000 | $1.0348^{e}$ |  | 0.0000 | $1.1238{ }^{\text {f }}$ |  |
| 0.1151 | 0.9584 | 0.617 | 0.1253 | 1.0798 | 0.645 | 0.1151 | 1.1592 | 0.653 |
| 0.2064 | 0.9997 | 0.621 | 0.2187 | 1.1176 | 0.639 | 0.2059 | 1.1904 | 0.648 |
| 0.2806 | 1.0388 | 0.613 | 0.2959 | 1.1519 | 0.634 | 0.2809 | 1.2184 | 0.644 |
| 0.3411 | 1.0676 | 0.623 | 0.3594 | 1.1778 | 0.640 | 0.3367 | 1.2402 | 0.642 |
| 0.3938 | 1.0948 | 0.628 | 0.3907 | 1.1937 | 0.637 | 0.3939 | 1.2634 | 0.640 |
| 0.4382 | 1.1212 | 0.626 | 0.4505 | 1.2221 | 0.638 | 0.4381 | 1.2807 | 0.641 |
|  | Mean | 0.621 |  | Mean | 0.639 |  | Mean | 0.645 |
|  | Std. dev. | 0.006 |  | Std. dev. | 0.004 |  | Std. dev. | 0.005 |
|  | RSD | 0.91\% |  | RSD | 0.55\% |  | RSD | 0.79\% |

${ }^{a} w_{3}$ is the mass fraction of sucrose (compound 3 ) in the \{cosolvent (compound 1 ) + water (compound 2 ) \} mixtures.
${ }^{\mathrm{b}}$ Mean uncertainty in density of dissolutions is $0.0003 \mathrm{~g} . \mathrm{cm}^{-3}$; mean uncertainty in apparent specific volume of sucrose is $0.002 \mathrm{~cm}^{3} . \mathrm{g}^{-1}$.
${ }^{c} w_{1}^{0}$ is the mass fraction of cosolvent (1) in the \{cosolvent (1) + water (2) \} mixtures free of sucrose (3).
${ }^{d}$ Data from Ref. [15].
${ }^{e}$ Data from Ref. [16]. ${ }^{\dagger}$ Data from Ref. [17].

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Table 3. Density of cosolvent mixtures free of sucrose and sucrose solutions ( $\rho$ ) and apparent specific volume of sucrose ( $\phi_{V}^{\mathrm{sp}}$ ) in $\{\mathrm{PEG} 200$ (or 400) (1) + water (2)\} mixtures at 298.2 K.

| $W_{3}{ }^{\text {a }}$ | $\begin{aligned} & \rho / \\ & \mathrm{g} \cdot \mathrm{~cm}^{-3 \mathrm{~b}} \end{aligned}$ | $\begin{aligned} & \phi_{V}^{\mathrm{sp}} / \\ & \mathbf{c m}^{3} \cdot \mathbf{g}^{-1 \mathrm{~b}} \\ & \hline \end{aligned}$ | $W_{3}{ }^{\text {a }}$ | $\begin{aligned} & \rho / \\ & \text { g.cm } \end{aligned}$ | $\begin{aligned} & \phi_{V}^{\mathrm{sp}} / \\ & \mathbf{c m}^{3} \cdot \mathbf{g}^{-1 \mathrm{~b}} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| PEG 200 (1) + water (2) |  |  | PEG 400 (1) + water (2) |  |  |
| $w_{1}^{\mathrm{o}}=0.10^{\mathrm{c}}$ |  |  |  |  |  |
| 0.0000 | $1.0116^{\text {d }}$ |  | 0.0000 | $1.0131^{\text {e }}$ |  |
| 0.1663 | 1.0728 | 0.649 | 0.1672 | 1.0764 | 0.640 |
| 0.2859 | 1.1249 | 0.640 | 0.2855 | 1.1281 | 0.635 |
| 0.4083 | 1.1870 | 0.631 | 0.4119 | 1.1910 | 0.629 |
| 0.4735 | 1.2198 | 0.632 | 0.4740 | 1.2255 | 0.626 |
| 0.5238 | 1.2486 | 0.630 | 0.5242 | 1.2492 | 0.631 |
| 0.5625 | 1.2707 | 0.630 | 0.5655 | 1.2747 | 0.629 |
|  | Mean | 0.636 |  | Mean | 0.632 |
|  | Std. dev. | 0.008 |  | Std. dev. | 0.005 |
|  | RSD | 1.23\% |  | RSD | 0.77\% |
| $w_{1}^{\mathrm{o}}=0.20^{\mathrm{c}}$ |  |  |  |  |  |
| 0.0000 | $1.0272^{\text {d }}$ |  | 0.0000 | $1.0298{ }^{\text {e }}$ |  |
| 0.2194 | 1.1156 | 0.622 | 0.1936 | 1.1061 | 0.625 |
| 0.3595 | 1.1767 | 0.629 | 0.3217 | 1.1634 | 0.624 |
| 0.4568 | 1.2215 | 0.635 | 0.4185 | 1.2087 | 0.628 |
| 0.5283 | 1.2622 | 0.630 | 0.4896 | 1.2439 | 0.630 |
| 0.5833 | 1.2910 | 0.632 | 0.5448 | 1.2721 | 0.632 |
| 0.6002 | 1.2965 | 0.637 | 0.5871 | 1.2953 | 0.632 |
|  | Mean | 0.631 |  | Mean | 0.628 |
|  | Std. dev. | 0.005 |  | Std. dev. | 0.003 |
|  | RSD | 0.81\% |  | RSD | 0.52\% |
| $w_{1}^{\mathrm{o}}=0.30^{\mathrm{c}}$ |  |  |  |  |  |
| 0.0000 | $1.0432{ }^{\text {d }}$ |  | 0.0000 | $1.0471^{\text {e }}$ |  |
| 0.1526 | 1.1017 | 0.625 | 0.1536 | 1.1044 | 0.632 |
| 0.2648 | 1.1460 | 0.634 | 0.2646 | 1.1506 | 0.630 |
| 0.3506 | 1.1824 | 0.637 | 0.3506 | 1.1876 | 0.633 |
| 0.4184 | 1.2152 | 0.634 | 0.3974 | 1.2118 | 0.628 |
| 0.4737 | 1.2443 | 0.632 | 0.4736 | 1.2456 | 0.634 |
| 0.5237 | 1.2674 | 0.635 | 0.5193 | 1.2674 | 0.635 |
|  | Mean | 0.633 |  | Mean | 0.632 |
|  | Std. dev. | 0.004 |  | Std. dev. | 0.002 |
|  | RSD | 0.65\% |  | RSD | 0.39\% |
| $w_{1}^{\mathrm{o}}=0.40^{\mathrm{c}}$ |  |  |  |  |  |
| 0.0000 | $1.0591{ }^{\text {d }}$ |  | 0.0000 | $1.0650{ }^{\text {e }}$ |  |
| 0.1303 | 1.1075 | 0.628 | 0.1303 | 1.1123 | 0.633 |
| 0.2248 | 1.1465 | 0.624 | 0.2309 | 1.1483 | 0.644 |
| 0.3103 | 1.1786 | 0.636 | 0.3105 | 1.1844 | 0.634 |
| 0.3750 | 1.2066 | 0.636 | 0.3754 | 1.2124 | 0.635 |
| 0.4286 | 1.2285 | 0.640 | 0.4286 | 1.2350 | 0.637 |
| 0.4736 | 1.2525 | 0.636 | 0.4739 | 1.2555 | 0.638 |
|  | Mean | 0.633 |  | Mean | 0.637 |
|  | Std. dev. | 0.006 |  | Std. dev. | 0.004 |
|  | RSD | 0.98\% |  | RSD | 0.64\% |
| $w_{1}^{\text {o }}=0.50^{\text {c }}$ |  |  |  |  |  |
| 0.0000 | $1.0750{ }^{\text {d }}$ |  | 0.0000 | $1.0821^{e}$ |  |
| 0.0977 | 1.1111 | 0.621 | 0.0909 | 1.1148 | 0.626 |
| 0.1778 | 1.1412 | 0.627 | 0.1665 | 1.1425 | 0.631 |
| 0.2449 | 1.1669 | 0.631 | 0.2307 | 1.1667 | 0.634 |
| 0.3016 | 1.1891 | 0.634 | 0.2857 | 1.1880 | 0.636 |
| 0.3506 | 1.2098 | 0.635 | 0.3335 | 1.2087 | 0.634 |
| 0.3926 | 1.2293 | 0.633 | 0.3742 | 1.2259 | 0.634 |
|  | Mean | 0.630 |  | Mean | 0.632 |
|  | Std. dev. | 0.005 |  | Std. dev. | 0.004 |
|  | RSD | 0.84\% |  | RSD | 0.56\% |

${ }^{a} w_{3}$ is the mass fraction of sucrose (compound 3 ) in the $\{P E G$ (compound 1) + water (compound 2)\} mixtures.
${ }^{\mathrm{b}}$ Mean uncertainty in density of dissolutions is $0.0003 \mathrm{~g} . \mathrm{cm}^{-3}$; mean uncertainty in apparent specific volume of sucrose is $0.002 \mathrm{~cm}^{3} . \mathrm{g}^{-1}$.
${ }^{c} w_{1}^{0}$ is the mass fraction of PEG (1) in the $\{$ PEG (1) + water (2) \} mixtures free of sucrose (3).
${ }^{\mathrm{d}}$ Data from Ref. [18].
${ }^{e}$ Data from Ref. [19].

It is important to note that reported $\phi_{V}^{\mathrm{sp}}$ value at saturation in neat water is $0.632 \mathrm{~cm}^{3} . \mathrm{g}^{-1}$ (equilibrium solubility is $\left.w_{3}=0.6879\right)^{4,5}$ which is just coincident with that obtained in the mixture of $w_{3}=0.6252$ (Table 1 ).
Table 2 summarizes the sucrose behavior in aqueous cosolvent mixtures of ethanol, propylene glycol and glycerol, which are the non-polymeric cosolvents more used in pharmaceutics of liquid medicines. As observable, in all cases the dissolution densities increase with the sucrose proportion as expected because this compound is the densest agent among all the studied compounds. In contrast to aqueous systems, in these systems no regular behavior is observed with $\phi_{V}^{\mathrm{sp}}$ values as the sucrose concentration increases. This is shown in Figure 3 for all the $\{$ ethanol (1) + water (2) $\}$ mixtures and also in Figure 4 for the five different $\{\operatorname{cosolvent}(1)+$ water (2) $\}$ systems with $w_{1}^{0}=0.30$ as a function of the sucrose mass fraction. Apparent specific and molar volume magnitudes depend on solute-solute and solvent-solute interactions and normally follow regular trends with the solute concentration in the mixtures. Nevertheless, this is not observed in Figures 3 and 4, except for water. This could be a consequence of the use of only four decimal places in our density measurements, which propagates high uncertainties in $\phi_{V}^{\mathrm{sp}}$ values, as compared with some other studies reported in the literature, where six decimal places have been reported for density in ternary mixtures finding regular trends. ${ }^{20,21}$ Nevertheless, it is important to keep in mind that our main objective is to know the apparent volumetric contribution of sucrose, rather than deepen in the respective intermolecular interactions. In this way, in similar way to aqueous dissolutions, in these mixtures the RDS is lower than $1.0 \%$ in almost all cases, except in $\{$ ethanol (1) + water (2) $\}$ mixtures of $w_{1}^{0}=0.10,0.20$ and 0.40 . Moreover, Table 4 shows that the general RDS in
each aqueous cosolvent mixtures is lower than $1.3 \%$ despite the sucrose or cosolvent proportion. Otherwise, it is interesting to note that the $\phi_{V}^{\text {sp }}$ values increase with the polarity of every non-polymeric cosolvent as described by the Hildebrand solubility parameter, i.e. 26.5, 30.2 and $36.1 \mathrm{MPa}^{1 / 2}$ for ethanol, propylene glycol and glycerol, respectively. ${ }^{22}$
Table 3 shows the sucrose behavior in aqueous cosolvent mixtures of PEG 200 and PEG 400, which are the polymeric cosolvents more used in design and development of peroral and parenteral drug products. As expected, in all cases the density values also increase with the sucrose concentration in the mixtures. In these mixtures the RDS is also lower than $1.0 \%$ in almost all cases, with the only exception of the \{PEG 200 (1) + water (2) \} mixture of $w_{1}^{0}=0.10$.
Besides, Table 4 shows that the general RDS in each one of the aqueous PEG mixtures is almost lower than $1.0 \%$ despite the sucrose or PEG proportion in the mixtures.
Finally, if all the $\phi_{V}^{\mathrm{sp}}$ values reported in Tables 1 to 3 are considered a mean value of $0.632( \pm 0.008) \mathrm{cm}^{3} \cdot \mathrm{~g}^{-1}$, with RDS $=1.20 \%$, is obtained. Although this RDS value is slightly higher than $1.0 \%$, within a good approximation, for practical purposes at room temperature an apparent volumetric contribution of $0.632 \mathrm{~cm}^{3} \cdot \mathrm{~g}^{-1}$ could be considered as adequate for sucrose in those liquid mixtures that involve these cosolvents and water. Moreover, this value is close to those reported at saturation for sucrose in the same mixtures ( 0.636 and $\left.0.637 \mathrm{~cm}^{3} . \mathrm{g}^{-1}\right){ }^{4,5}$ This is very important because the pharmaceutical formulations involves several components including active ingredients and excipients, which makes them real multicomponent systems. Therefore, an exhaustive study about the individual contribution of every agent during preparation of liquid mixtures would be expensive in time and economic resources at industrial level.


Figure 1. Density of sucrose dissolutions in neat water and in \{ethanol (1) + water (2)\} mixtures as a function of the sucrose mass fraction at 298.2 K. ○: Neat water; ם: $w_{1}^{0}=0.10 ; \Delta: w_{1}^{0}=0.20 ; ~ \wedge: w_{1}^{0}=0.30 ; \times: w_{1}^{0}=0.40 ;+: w_{1}^{0}=0.50$.


Figure 2. Density of sucrose dissolutions in different $\left\{\operatorname{cosolvent}(1)+\right.$ water (2)\} mixtures with $w_{1}^{0}=0.30$ as a function of the sucrose mass fraction at 298.2 K. ○: Ethanol (1) + water (2); ם: propylene glycol (1) + water (2); $\Delta$ : glycerol (1) + water (2); 仓: PEG 200 (1) + water (2); $\times$ : PEG 400 (1) + water (2).


Figure 3. Apparent specific volume of sucrose in neat water and in \{ethanol (1) + water (2) \} mixtures as a function of the sucrose mass fraction at 298.2 K. ○: Neat water; $\square: w_{1}^{\mathrm{o}}=0.10 ; \Delta: w_{1}^{\mathrm{o}}=0.20 ; \diamond: w_{1}^{\mathrm{o}}=0.30 ; \times: w_{1}^{\mathrm{o}}=0.40 ;+: w_{1}^{\mathrm{o}}=0.50$.


Figure 4. Apparent specific volume of sucrose in different \{cosolvent (1) + water (2)\} mixtures with $w_{1}^{0}=0.30$ as a function of the sucrose mass fraction at $298.2 \mathrm{~K} . \circ$ : Ethanol (1) + water (2); $\square$ : propylene glycol (1) + water (2); $\Delta$ : glycerol (1) + water (2); $\Delta$ : PEG 200 (1) + water (2); $x$ : PEG 400 (1) + water (2).

Table 4. Mean apparent specific volume of sucrose ( $\phi_{V}^{\text {sp }}$ ) in different \{cosolvent (1) + water (2)\} mixtures at 298.2 K. ${ }^{\text {a }}$

| Parameter | EtOH + W | PG + W | $\mathbf{G}+\mathbf{W}$ | PEG 200 + W | PEG 400 + W |
| :--- | :--- | :--- | :--- | :--- | :--- |
| Mean $\phi_{V}^{\text {sp }}$ value $/ \mathrm{cm}^{3} . \mathrm{g}^{-1}$ | 0.625 | 0.633 | 0.636 | 0.631 | 0.631 |
| Std. dev. $/ \mathrm{cm}^{3} \cdot \mathrm{~g}^{-1}$ | 0.007 | 0.007 | 0.008 | 0.006 | 0.005 |
| RSD | $1.10 \%$ | $1.17 \%$ | $1.29 \%$ | $1.02 \%$ | $0.87 \%$ |

${ }^{2} \mathrm{EtOH}$ is ethanol, PG is propylene glycol, G is glycerol and PEG is polyethylene glycol.

## Conclusion

In this research, useful apparent specific volumes of sucrose at different concentrations in several aqueous cosolvent mixtures are reported at 298.2 K involving polymeric and non-polymeric cosolvents. Moreover, a mean $\phi_{V}^{\text {sp }}$ value of $0.632 \mathrm{~cm}^{3} . \mathrm{g}^{-1}$ for sucrose in aqueouscosolvent mixtures could be considered as adequate for practical purposes in pharmaceutical industries.

## Acknowledgements

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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