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Concentration and temperature dependence of the viscosity of polyol aqueous solutions ☆

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ABSTRACT

The concentration and temperature dependence of the viscosity of supercooled polyol (sucrose, trehalose, glucose and glycerol) aqueous solutions was analyzed with the aim of finding simple and accurate correlation equations for the description of this transport property. Three different equations were examined and compared, two empirical equations and an equation derived from the Avramov–Milchev (AM) model. If a description of the viscosity temperature dependence is intended, the AM model gives the best representation of the experimental data with only two adjustable parameters, which have a clear physical meaning. However, if we focus on both, temperature and concentration dependence, the empirical equations are found to be superior to the AM model, except for the glycerol aqueous system. The AM model includes a parameter related to the system fragility, which was obtained for all the aqueous polyol mixtures previously mentioned as a function of concentration, and also for water–trehalose–sodium tetraborate mixtures as a function of the electrolyte content. The results show that the fragility parameter increases with polyol concentration in the series glycerol < glucose ∼ sucrose < trehalose, and that the addition of sodium tetraborate to aqueous trehalose solutions increases the fragility of the mixtures. Our results imply that the hypothesis relating the low fragility of the aqueous mixtures with their high cryo or dehydroprotection capabilities is not valid.

Introduction

Supercooled aqueous solutions are of paramount interest for both academic and technological reasons. In the academic field, these systems have called the attention of many scientists since different behaviors can be observed when aqueous solutions are cooled down to their glass transition temperature (T_g), depending on the nature and the concentration of the second component. In the practical field, aqueous solutions close to and below the glass transition temperature are commonly used as protective media for biomolecules, food and pharmaceuticals. Among these systems, polyol–water mixtures have received special consideration due to the low toxicity of the polyols at high concentrations.

The mechanisms that make some compounds particularly effective for cryo- and dehydro-protection still remain unclear in the literature. Green and Angell [22] have considered that the protection capabilities of cryopreservants are determined by the magnitude of the glass transition temperature of their aqueous solutions. On the contrary, Branca et al. [6] proposed that the fragility of the aqueous solutions is the fundamental magnitude which determines the protection capacity. A different hypothesis was suggested by Crowe et al. [13] who suggested that the effectiveness of the protection media is determined by specific interactions between the biomolecule and the stabilizing agent. This scenario indicates that it is of extreme importance to provide further insight in relation to the effect of polyols on the cryoprotective behavior. Besides, from a practical point of view, it is fundamental to estimate the lifetime of biomolecules in protective media. Thus, for this purpose, and considering that deterioration reactions are determined by the diffusion of the reactants [24], many works dealt with the dependence of the diffusion coefficients of different molecules in protective media as a function of composition and temperature [12,26]. The results show that diffusion coefficients are either proportional to η^{-1} (Stokes–Einstein equation, SE), where η is the viscosity, or to $\eta^{-\delta}$ with $\delta < 1$ (Fractional Stokes–Einstein equation, FSE), depending on the reduced inverse temperature (expressed as T_g/T), and the solute/solvent size relationship [12,26]. Consequently, in order to estimate the mobility of different kind of sol-

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utes in cryoprotective media, it is of fundamental significance to find accurate correlation equations to describe the concentration and temperature dependence of the viscosity of aqueous cryoprotective mixtures in the stable and supercooled liquid regimes, especially close to the glass transition temperature.

The viscosity–temperature behavior close to the glass transition differs markedly between different glass forming liquids. In this context, Angell [1] differentiated glass forming liquids between "strong" and "fragile", according to their viscosity temperature dependence in the supercooled regime above T_g. Strong liquids show a viscosity temperature dependence which can be described by the Arrhenius equation,

$$\eta = \eta_0 \cdot \exp\left(\frac{E_a}{RT}\right) \tag{1}$$

while fragile liquids exhibit a viscosity temperature dependence that deviates markedly from Eq. (1) (super-Arrhenius behavior). The magnitude of this deviation can be quantified by the fragility index, m, given by:

$$m = \left[\frac{d \log \eta}{d(T_g/T)}\right]_{T=Tg} \tag{2}$$

where m increases with increasing fragility.

The magnitude of the fragility parameter has great influence in the rate of deterioration reactions [6,29]. For instance, above the glass transition, strong liquids reach, at a given T_g/T, higher viscosity values than fragile systems, since in the later case the viscosity changes orders of magnitude very close to T_g. Consequently, in strong liquids chemical reactions become arrested at higher reduced temperatures than in fragile systems.

The analysis of the temperature and composition dependence of the viscosity of aqueous supercooled solutions can be performed using different models. We have addressed this issue for aqueous trehalose and sucrose solutions [27], and recently we have performed a similar analysis for glycerol–water mixtures [52]. In the former case, the viscosity was analyzed using the equation given by Génotelle [20],

$$\log \eta = a_1 + a_2 x + \Phi(b_1 + b_2 x^n) \tag{3}$$

and a polynomial equation which gives the logarithm of the viscosity as a function of T_g/T,

$$\log \eta = a + b\left(\frac{T_g}{T}\right) + c\left(\frac{T_g}{T}\right)^2 + d\left(\frac{T_g}{T}\right)^3 \tag{4}$$

where a_1, a_2, b_1, b_2, n and a, b, c, d are fitting parameters, x is the molar fraction of polyol and Φ is a reduced temperature equal to $(30-t)/(91+t)$, with t the temperature in Celsius.

In the case of glycerol–water mixtures, the viscosity of the aqueous solutions was analyzed using the equation given by Avramov–Milchev (AM) [4,5]:

$$\eta = \eta_0 \cdot \exp\left[(\ln \eta_g - \ln \eta_0) \cdot \left(\frac{T_g}{T}\right)^{\alpha}\right] \tag{5}$$

where η_0 is the limiting viscosity at high temperatures, η_g the viscosity at T_g and α is a model parameter called "fragility index", related to Angell's fragility by,

$$m = \alpha(\ln \eta_g - \ln \eta_0) \tag{6}$$

$\alpha = 1$ means that the liquid is strong, while higher values imply higher fragility. We demonstrated [52] that Eq. (5) describes the viscosity data of glycerol aqueous solutions very precisely, while Eqs. (3) and (4) do not fit properly the experimental data. It is important to notice that an important parameter that characterizes glass forming liquids, as the fragility, is included in Eq. (5), while no physical parameters are included in Eqs. (3) and (4).

In this work, we extended the analysis previously performed for glycerol water mixtures based on the AM model, to other polyol (sucrose, trehalose and glucose) aqueous solutions. We studied the fragility of these solutions, given by the α parameter, as a function of the composition and nature of the polyol compound. In addition, we also examined the fragility of aqueous sodium tetraborate–trehalose solutions as a function of the electrolyte content. The results derived from this work were compared with previous reported data, and implications for cryoprotection were discussed. Moreover, we discussed the accuracy of the AM equation to describe the viscosity of supercooled aqueous solutions as a function of concentration and temperature in comparison to other equations previously studied [27].

The Avramov–Milchev (AM) model

In order to clarify the meaning of α, in this section we will briefly review the main features of the AM model.

This model is based on the idea that disorder in amorphous media leads to some probability distribution function of the activation energy for the elementary jumps of the molecules. The shape of this distribution is not known. Thus, the authors analyzed uniform, truncated Poisson, and truncated Gaussian distributions with activation energy dispersion (width of the distribution), σ. They found that, independently on the type of the distribution, the entropy, S, is related to the dispersion by,

$$S - S_0 = \frac{RZ}{2} \ln\left(\frac{\sigma}{\sigma_0}\right) \tag{7}$$

where S_0 is the entropy for some reference state corresponding to dispersion σ_0, and $Z/2$ is the number of escape channels available for the molecule; that is, the number of directions along which a particle can move out of the cell considering that each channel can be used in two directions. Thus, Z is related to the coordination of the network.

In this model, the viscosity is a function of σ, and therefore of the entropy, where a reference state defined at T_g is used,

$$\ln\left(\frac{\eta}{\eta_0}\right) = \ln\left(\frac{\eta_g}{\eta_o}\right) \exp\left[-\frac{2(S - S_g)}{ZR}\right] \tag{8}$$

where S_g is the equilibrium entropy at T_g. According to Eq. (8), the viscosity is a double exponential function on the entropy, but this little inconvenience can be solved taking into account that the entropy is a logarithmic function of the temperature. Therefore, Eq. (8) can be converted into Eq. (5), with α, the "fragility parameter" given by,

$$\alpha = \frac{2C_p}{ZR} \tag{9}$$

where C_p is the average heat capacity between T and T_g, and R is the gas constant. As a result, α increases with the heat capacity, which is proportional to the number of vibrational degrees of freedom, and decreases with the coordination of the network, proportional to Z.

In this work, T_g of the polyol aqueous solutions were taken from data determined using differential scanning calorimetry (DSC) and fitted as a function of composition with the Gordon and Taylor equation [21]:

$$T_g = \frac{w_1 T_{g1} + k_{GT} w_2 T_{g2}}{w_1 + k_{GT} w_2} \tag{10}$$

where T_g is the glass transition temperature of the water–polyol mixture, w_1 and w_2 the mass fractions of polyol and water, respectively, and T_{g1} and T_{g2} the glass transition temperatures of the polyol and water, respectively.

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The value of η_g was fixed at $10^{12.5}$ mPa s, which corresponds to the value obtained from extrapolating the viscosity of pure glycerol to the glass transition temperature [52]. Thus, viscosity data at fixed compositions were analyzed with Eq. (5) with only two, η_0 and α, fitting parameters.

Viscosities and glass transition temperatures of the aqueous solutions

In this section we will summarize the available information on the viscosity of aqueous solutions in the stable and supercooled regimes to be analyzed with Eqs. (3)–(5). Considering that the glass transition temperatures of the aqueous solutions as a function of composition in Eqs. (4) and (5) are taken as input values in our analysis, a description of the sources of T_g values is also included.

Viscosity data for aqueous glycerol, glucose, sucrose and trehalose were published in a T_g/T range between 0.4–1.0, 0.4–1.0, 0.4–0.9, and 0.4–0.9, respectively. Data for ternary mixtures trehalose–borate–water were reported for T_g/T between 0.6 and 0.9.

Sucrose and trehalose–water mixtures

These systems have been analyzed in detail in a previous work [27], where the literature on the viscosity and glass transition temperature of both disaccharide–water mixtures was reviewed. The glass transition temperature data available in the literature as a function of composition were adjusted with the Gordon–Taylor equation and the best-fit parameters are reported in Table 1. The glass transition temperatures of the pure saccharides, T_{g1}, were fixed at the experimental values determined by DSC, while T_{g2} was fixed at 135 K [23].

Viscosity data sources for pure water and their analysis as a function of temperature with the AM model were described in a previous work [52].

Glucose–water mixtures

Several authors have reported the viscosity of aqueous glucose solutions as a function of composition and temperature [9,10,14,18,31,40,51,55,57]. The glass transition temperatures of these mixtures, reported in the literature [8,22,30,32,34,37,38,41,43,45,46], were fitted as a function of composition using the Gordon–Taylor equation and the best-fit parameters are summarized in Table 1. In this case, T_{g1}, T_{g2}, and k_{GT} were adjustable parameters since the calculation gave T_g values for the pure components within the error of the results obtained by DSC.

Glycerol–water mixtures

The glass transition temperature data of aqueous glycerol solutions as a function of composition, previously reviewed [52], were analyzed with Eq. (10). T_{g1}, T_{g2} and k_{GT} were adjustable parameters and the best-fit parameters are summarized in Table 1. It should be noticed that in this case the glass transition temperature value predicted for pure water (T_{g2}) differs from the T_g value commonly accepted for this liquid (135 K) [23]. This could be explained considering that the determination of the glass transition temperatures of aqueous solutions with high water contents have large errors due to the high tendency of water to crystallize in these samples. Therefore, we decided to fit T_g of aqueous glycerol mixtures leaving T_{g1} and T_{g2} as adjustable parameters [52] since, if T_{g2} was fixed at 135 K, T_g calculations for water rich solutions would differ significantly from the experimental data.

Viscosity data include that reviewed in our recent work [52], and our recent data measured in the supercooled region [53].

Table 1
Parameters of the Gordon–Taylor equation (Eq. (10)) for the aqueous solutions analyzed in this work.

Compound	T_{g1} (K)	T_{g2} (K)	k_{GT}
Sucrose	336[a]	135[a]	4.74 ± 0.07
Trehalose	388[a]	135[a]	5.04 ± 0.04
Glucose	307 ± 1	135 ± 5	4.1 ± 0.3
Glycerol	195.4 ± 0.5	141 ± 1	1.96 ± 0.10

[a] Fixed values.

Trehalose–sodium tetraborate–water mixtures

Miller et al. [33] studied the effect of the addition of sodium tetraborate on the viscosity of aqueous trehalose mixtures. The data restrict to solutions with trehalose mole fraction $x_T = 0.075$, and borate mole fractions $x_B = 0.0224$, 0.0597, 0.0748, 0.1123, and 0.1515. Considering that these solutions are ternary mixtures, their glass transition temperatures dependence on composition could not be analyzed with Eq. (10). Thus, the glass transition temperatures of these mixtures were used as already reported [33].

Results and discussion

In Section "Viscosity of Polyol–Water Mixtures" the viscosity of polyol and polyol–salt aqueous solutions is analyzed using the AM model, with emphasis in the fragility parameter of these systems. In Section "Viscosity of Aqueous Sodium Borate–Trehalose Solutions" the same analysis is performed for ternary mixtures trehalose–sodium tetraborate–water. Finally, in Section "Comparative Viscosity Analysis as a Function of Concentration and Temperature" the accuracy of the AM model to describe the viscosity temperature and composition dependence is compared with that obtained with empirical equations.

Viscosity of polyol–water mixtures

The viscosity of aqueous solutions of sucrose, trehalose, glucose and glycerol were analyzed at fixed compositions with the AM model (Eq. (5)) using T_g data calculated as previously described. The obtained results for η_0 and α are reported in Table 2, where the compositions for which this analysis was performed are listed. In this case not all the available data were fitted since for some composition values the viscosity was determined over a narrow temperature range.

Fig. 1a and b shows the composition dependence of α and $-\ln \eta_0$, respectively, for aqueous solutions of sucrose, trehalose, glucose and glycerol. It can be observed that the fragility of sucrose aqueous mixtures increases moderately up to $w_1 = 0.7$ and more steeply above that limit, while trehalose aqueous solutions exhibit a similar behavior, although fragility increases dramatically above $w_1 = 0.6$. Fragility data for glucose aqueous solutions are restricted to mixtures with $w_1 \leqslant 0.6$ and pure glucose. For $w_1 < 0.6$ the fragility seems to be almost invariant with composition with an α value bigger for pure glucose. The fragility for pure glucose is larger than that observed for the aqueous solutions, even considering that the experimental error is the largest. The large error bar for the α parameter for pure glucose is probably due to the scattering in the viscosity data, caused by the browning reactions that occur during the melting prior the viscosity determinations. In the case of glycerol aqueous solutions, the fragility seems to increase slightly with the glycerol content below the eutectic concentration, while an opposite behavior is observed above this concentration. However, the α concentration dependence for low glycerol con-

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Table 2
η_0 and α of the AM equation for aqueous polyol solutions.

w_1	$-\ln(\eta_0/\text{mPa s})$	α	w_1	$-\ln(\eta_0/\text{mPa s})$	α
Sucrose			*Trehalose*		
0.10	1.47 ± 0.04	3.77 ± 0.02	0.100	1.4 ± 0.1	3.88 ± 0.08
0.20	1.73 ± 0.03	3.62 ± 0.02	0.188	1.75 ± 0.05	3.67 ± 0.03
0.30	1.21 ± 0.02	3.85 ± 0.01	0.300	0.94 ± 0.08	4.07 ± 0.05
0.40	1.13 ± 0.03	3.82 ± 0.01	0.383	0.35 ± 0.02	4.33 ± 0.01
0.50	0.59 ± 0.07	4.02 ± 0.03	0.481	0.08 ± 0.05	4.44 ± 0.03
0.60	0.30 ± 0.05	4.05 ± 0.02	0.549	−0.46 ± 0.04	4.67 ± 0.03
0.65	0.05 ± 0.10	4.10 ± 0.04	0.606	−0.5 ± 0.1	4.61 ± 0.07
0.70	−0.02 ± 0.05	4.11 ± 0.02	0.650	−3.2 ± 0.2	6.1 ± 0.1
0.75	−0.21 ± 0.03	4.16 ± 0.01	0.725	−9.0 ± 0.3	12.3 ± 0.5
0.80	−0.60 ± 0.07	4.31 ± 0.03	0.746	−8.5 ± 0.2	11.9 ± 0.4
0.85	−1.5 ± 0.2	4.65 ± 0.07			
Glucose			*Glycerol*		
0.10	2.3 ± 0.2	3.38 ± 0.09	0.0	2.19 ± 0.15	3.62 ± 0.07
0.20	1.79 ± 0.05	3.57 ± 0.03	0.1	1.84 ± 0.02	3.78 ± 0.02
0.30	2.1 ± 0.1	3.43 ± 0.05	0.2	1.67 ± 0.02	3.82 ± 0.01
0.4	1.5 ± 0.1	3.68 ± 0.06	0.3	1.53 ± 0.03	3.82 ± 0.02
0.5	2.0 ± 0.3	3.5 ± 0.1	0.4	1.43 ± 0.04	3.80 ± 0.02
0.6	1.6 ± 0.4	3.6 ± 0.1	0.5	1.18 ± 0.05	3.84 ± 0.03
1.0	−3 ± 1	6.7 ± 0.6	0.6	0.92 ± 0.09	3.86 ± 0.04
			0.7	1.2 ± 0.1	3.57 ± 0.04
			0.8	1.4 ± 0.1	3.41 ± 0.04
			0.9	1.27 ± 0.06	3.29 ± 0.02
			1.0	0.9 ± 0.1	3.26 ± 0.03

tents is doubtful considering the high tendency of water to crystallize from these mixtures.

The fragility of aqueous polyol solutions were also analyzed by other authors using viscosity data in a more restricted concentration and temperature range [2,7,15,28]. Thus, it is worthwhile to compare those results with the reported in this work on the basis of an extended viscosity database.

Elias and Elias [15] estimated the fragility of aqueous trehalose solutions in a concentration range $0.051 < w_1 < 0.537$, by analyzing the viscosity of these mixtures with the equation of Vogel–Fulcher–Tamman [19,50,56].

$$\eta = A.\exp\left(\frac{DT_0}{T - T_0}\right) \qquad (11)$$

where A and T_0 are constants, and D is a parameter related to Angell's fragility by $m = 16 + 590/D$ [15]. The authors observed that the fragility of the mixtures increases with trehalose concentration, as observed in the present work. Based on the analysis of the viscosity *vs.* T_g/T for water–sucrose mixtures of varying concentration, Angell [2] observed the same tendency; an increase in the solution fragility with increasing sugar content, in agreement with our results reported in Table 2 and Fig. 1a. However, other authors have reported a different behavior, that is, a reduction in the fragility of the aqueous solutions with increasing polyol concentration. By analyzing viscosity and Raman scattering data of aqueous trehalose, Magazú and coworkers [7] concluded that the fragility m increases with the water content. The viscosity of the mixtures were studied in a concentration range $0.1 \leqslant w_1 \leqslant 0.5$, and T_g/T between 0.4 and 0.6, that is, very far from the glass transition temperature. They studied the Raman spectra of two aqueous solutions: trehalose + 2 H_2O at 276.15 K and trehalose + 20 H_2O at 249.15 K, assuming that both experiments were performed at the same inverse reduced temperatures. They observed the presence of a trace of the boson peak in the more concentrated sugar solution while this peak was absent in the diluted mixture. Since it is well known [16,35,36,47–49] that the intensity of the Boson peak increases with decreasing fragility, they assigned a composition dependence of the mixture fragility that is opposite to that found in the present work and in previous studies [2,15]. However, by comparing the T_g values of the trehalose–water mixtures used by Magazú and coworkers [7] with those calculated with Eq. (10) and the parameters reported in Table 1, we found differences in the T_g of the mixtures. T_g values calculated with Eq. (10) with the parameters reported in Table 1, gave $T_g/T = 1.09$ for trehalose + 2 H_2O and $T_g/T = 0.70$ for trehalose + 20 H_2O, meaning that the Raman spectra were performed in the glassy state for the concentrated mixture and well above the glass transition for the diluted one. Therefore, the fragility of both systems could not be compared using Magazú's experimental data. Probably, the same inconsistencies found in the T_g values of the trehalose aqueous solutions, whose Raman spectra were determined, were also present in the viscosity analysis and in the study of the neutron scattering spectra of trehalose and sucrose [28].

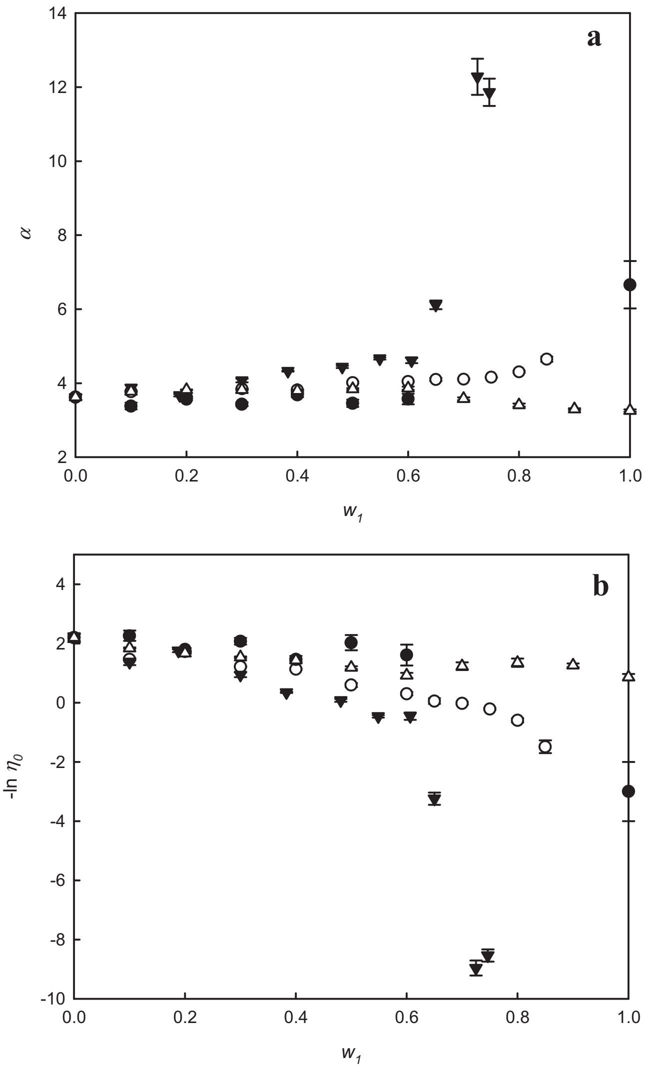

Fig. 1. α (a) and $-\ln\eta_0$ (b) as a function of polyol weight fraction (w_1) for sucrose (○), trehalose (▼), glucose (●) and glycerol (△).

In order to analyze the fragility parameter α of the pure polyol components, we compared the data for glycerol and glucose in Table 2, with the data for sucrose and trehalose determined by linear extrapolation of the behavior observed for $w_1 > 0.6$ towards $w_1 = 1$. The obtained results are α (sucrose) = 5.4 ± 1.9 and α (trehalose) 27 ± 15. Thus, these results show that the fragility of the pure polyols seems to increase in the following manner: glycerol < glucose ~ sucrose < trehalose.

As it has been pointed out in Section "the Avramov–Milchev (AM) model", the α parameter is proportional to the heat capacity and inversely proportional to Z, which is related to the

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coordination of the network. Thus, knowing the value of C_p of the supercooled liquid above T_g, and considering that it is almost constant between ambient temperature and T_g, the coordination of the network can be deduced using Eq. (9) [39]. Considering Avramov's [4] claim that for most molecular glass formers $Z = 10$, Paluch et al. [39] hypothesize that the smaller value observed for PMPS is a natural consequence of the constrains imposed by the connectivity of the chain units in the polymer. Senkov and Miracle [42] have also determined the value of Z for different oxide glass formers, all with varying SiO_2 content, using the procedure mentioned previously. The authors found $Z = 10.5$ for SiO_2 with not a well defined trend in Z composition dependence.

Using the α values determined for pure glucose and pure glycerol and the extrapolated values for pure sucrose and trehalose we calculated the connectivity of the network, given by Z. For this purpose heat capacities determined at T_g for glucose ($C_p = 382$ J K^{-1} mol^{-1}) [17], sucrose ($C_p = 765$ J K^{-1} mol^{-1}) [17], and trehalose ($C_p = 907.1$ J K^{-1} mol^{-1}) [44] were used. In the case of glycerol, the heat capacity increases almost linearly from 175 J K^{-1} mol^{-1} at T_g, to 219 J K^{-1} mol^{-1} at 298 K [59]. Therefore, an averaged value $C_p = 197$ J K^{-1} mol^{-1} was used to calculate Z. The obtained results are summarized in Table 3.

The same calculation for pure water is not so direct because of the lack of data in the "no man's land" region and the anomalous heat capacity behavior observed in the supercooled region. However, Z could be estimated considering a mean value $C_p = 90$ J K^{-1} mol^{-1} within the range between the homogeneous nucleation temperature and room temperature [3]. The resulting value, $Z \sim 6$, is consistent with a relatively ordered hydrogen bonded structure.

From the results reported in Table 3, it can be noticed that the coordination of the network, given by Z, is very different for the two disaccharides analyzed in this work, being smaller for the more efficient cryoprotector trehalose. Considering the high error in the calculation of Z, it is difficult to make a comparison between the values obtained for trehalose, glucose and glycerol. However, it could be noticed that, within the error, the Z value for trehalose is similar to that estimated for water, indicating that trehalose has a highly ordered structure, at least more ordered than sucrose.

Viscosity of aqueous sodium borate–trehalose solutions

Table 4 shows the values of ln η_0 and α obtained for the analysis of the viscosity of trehalose–sodium borate–water mixtures with the AM model. It can be observed that the addition of sodium borate increases the α parameter, indicating an increase in the fragility of the aqueous mixtures, as already concluded by Miller et al. [33] using the Williams–Landel and Ferry equation [58].

In a previous study [25], we have shown that trehalose forms an ester with borate, whose formation constant equals 11 kg mol^{-1} at 298.15 K. From RMN results [54], it was concluded that the ester is formed between the OH groups of borate and the pyranose rings of trehalose. Thus, it can be hypothesized that the ester formation could increase the C_p of the system and probably also reduce Z, accounting for the increment of the α parameter with increasing borate content in the ternary mixture.

Table 3
Z values obtained using Eq. (9) with α values for the pure components calculated or extrapolated from Fig. 1a.

Compound	Z
Sucrose	34 ± 12
Trehalose	8 ± 4
Glucose	14 ± 1
Glycerol	14 ± 2

Table 4
η_0 and α in Eq. (5) for trehalose + sodium tetraborate aqueous solutions with $x_T = 0.075$.

x_B	$-\ln(\eta_0/\text{mPa s})$	α
0.0224	−1.6 ± 0.2	5.6 ± 0.1
0.0597	−2.5 ± 0.2	6.3 ± 0.2
0.0748	−2.5 ± 0.2	5.9 ± 0.2
0.1123	−3.2 ± 0.3	6.6 ± 0.2
0.1515	−4.4 ± 0.4	7.7 ± 0.4

Table 5
Standard deviations of the fits performed for the viscosity of aqueous polyol solutions as a function of composition and temperature.

Polyol	σ (Eq. (5))	σ (Eq. (3))	σ (Eq. (4))
Glycerol	0.074	0.80	0.26
Glucose	0.12	1.48	0.11
Sucrose	0.038	0.029	0.059
Trehalose	0.35	0.10	0.10

Comparative viscosity analysis as a function of concentration and temperature

Eq. (5) gives an excellent description of the viscosity temperature dependence of aqueous solutions at fixed compositions. For instance, the standard deviations of the fits performed for aqueous trehalose and sucrose with Eq. (5) with η_0 and α reported in Table 2, gave standard deviations smaller than those obtained with Eqs. (3) and (4) [27]. Besides, it is important to notice that Eqs. (3) and (4) have five and four fitting parameters, respectively while the expression from the AM model has only two.

However, if the AM model is intended to be used to fit the viscosity of aqueous polyol solutions as a function of concentration and temperature, η_0 and α should be fitted as a function of concentration. For this purpose we used cubic equations, and the resultant AM equations have eight fitting parameters. In order to compare the accuracy of these fits with those obtained by using Eqs. (3) and (4) for all the aqueous systems studied, Table 5 presents the standard deviations obtained for all the fits performed. The standard deviations given in Table 5 correspond to the logarithmic difference between the experimental and calculated viscosity data.

It can be observed that for aqueous glycerol the best fit is obtained with the AM model. For aqueous glucose, Eq. (4) gives a similar standard deviation as the AM model, while the equation given by Génotelle (Eq. (3)) does not fit properly the experimental viscosity data. On the other hand, for aqueous sucrose and trehalose mixtures the equation given by Génotelle gives a better description of the experimental viscosity data as a function of concentration and temperature than the AM model. This is probably due to the strong concentration dependence of α and η_0 which cannot be properly described with simple cubic equations.

Conclusions and implications for cryoprotection

In this work we have analyzed the viscosity of aqueous sucrose, trehalose, glucose and glycerol solutions with the Avramov–Milchev model. We obtained a fragility parameter, α, related to Angell's fragility, as a function of composition, for aqueous sucrose, trehalose, glucose and glycerol solutions. The results show that α increases with the polyol content in the series glycerol < glucose ~ sucrose < trehalose. These results contradict previous conclusions derived by Magazú and collaborators [7,28], who

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suggested that trehalose and trehalose aqueous solutions have less fragile character than other pure or aqueous cryoprotectans, such as sucrose. These authors hypothesize that trehalose less fragile character is the cause of the higher protection capabilities of this sugar and its aqueous solutions. In this work we have demonstrated that trehalose is more fragile while exhibits a better cryoprotection capacity than sucrose. This enables us to conclude that smaller fragilities do not imply higher protection capacities, as stated by Magazú and coworkers.

Additionally, we studied the effect of the addition of sodium tetraborate on the fragility of aqueous trehalose mixtures, and observed that borate increases the fragility of the mixtures. Again, this observation reinforces our remark that, in contradiction to previous conclusions, an increment in the fragility does not imply smaller protection capabilities, since the addition of sodium tetraborate to aqueous trehalose solutions increases their ability to protect biomolecules [11], while increases the fragility character of the aqueous mixtures.

Finally, we analyzed the accuracy of the AM model to describe the concentration and temperature dependence of the viscosity of aqueous polyol mixtures. We conclude that this model gives a good description for aqueous glycerol and glucose solutions, while the Génotelle equation renders a better representation of the viscosity data of aqueous trehalose and sucrose. It should be remarked that if we focus on the temperature dependence of the viscosity of polyol aqueous solutions at a given concentration, the AM model leads to the best description of the experimental data with only two adjustable parameters which, in addition, have a clear physical meaning.

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