



Solvent effects on polysaccharide conformation

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ARTICLE INFO

Article history:

Received 22 July 2009

Received in revised form 9 August 2009

Accepted 13 August 2009

Available online 19 August 2009

Keywords:

Solution

Viscosity

Solvent

Polysaccharide

Dextran

ABSTRACT

Polymers are widely used in solution to provide structure and function, e.g., colloidal stability, delivery of actives, viscoelasticity, to a variety of products. Underlying these functions are inter- and intra-molecular interactions that depend greatly on the type of solvent used. We consider here the dilute solution viscosity of a common polysaccharide, dextran, in various solvents (water, formamide, dimethylsulfoxide, ethanolamine). The intrinsic viscosity of dextran T500 doubles as the solvent changes from water to ethanolamine. The observed effects on the polymer conformation are discussed in terms of intermolecular interactions and are correlated with a number of solvent properties, including dipole moment, surface tension, empirical parameter of solvent polarity E_T^N , and Hansen solubility parameters. The data discussed here intimate that hydrogen bonding is the most important contributor to the solubility of dextran in the examined solvents. The excellent solvent power of ethanolamine can be ascribed to its capacity to act as both hydrogen bond donor and acceptor.

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1. Introduction

The solubility of polymers is strongly dependent on the solvent in which they are dissolved (Hansen, 2000; Reichardt, 1990). Polymer–solvent interactions also dictate the conformation of the dissolved polymer (Basedow, Ebert, & Feigenbutz, 1980). Polymer solubility is of great interest to products such as coatings, pharmaceuticals, personal care, foods and drinks, which incorporate polymers dissolved in aqueous and/or organic solvents. The dissolution of polymers is also an important step in polymer processing such as blending and separation (Hansen, 2000). The a-priori selection of appropriate solvents for a given polymer can pose a challenge. For this reason various approaches have been proposed to estimate the solvent power and predict polymer solubility. “Like dissolves like” has been a guiding principle for polymer–solvent miscibility. To capture this observation, solubility parameters have been introduced (Hansen, 2000; Reichardt, 1990) that describe the polymer affinity for certain solvents.

Polymers that are soluble in water offer a wide range of functionalities to a variety of applications (cosmetics, detergents, wastewater treatment, oil recovery) and are often used as thickeners, stabilizers, rheology modifiers, and conditioners. The solution properties of water-soluble polymers have been of great interest in our group, with an emphasis on poly(ethylene glycol) (PEG)-containing polymers (Alexandridis, Ivanova, & Lindman, 2000; Alexandridis & Yang, 2000; Holmqvist, Alexandridis, & Lindman, 1997; Ivanova, Lindman, & Alexandridis, 2000, 2002; Lin & Alexan-

dridis, 2002; Sakai & Alexandridis, 2005; Svensson, Olsson, & Alexandridis, 2000; Yang & Alexandridis, 2000; Zipfel et al., 1999). We have recently turned our attention to polymers of biological origin, and, in particular, dextran (Antoniou, Themistou, Tsianou, & Alexandridis, 2007; Antoniou, Tsianou, & Alexandridis, 2008). Among water-soluble polymers, dextran is a well-studied high molecular weight polymer consisting of glucose units (Brant, 1981; De Belder, 2002; Tirtaatmadja, Dunstan, & Boger, 2001). This polysaccharide finds many applications in the food (Glicksman, 1982; McCurdy, Goff, Stanley, & Stone, 1994) and pharmaceutical/biomedical industries (Glicksman, 1982; Heinz, Liebert, Heublein, & Hornig, 2006; Schacht, Vercauteren, & Vansteenkiste, 1988; Sutherland, 1998; Taylor, Tanna, Sahota, & Voermans, 2006).

Having employed dilute solution viscometry as a means of characterizing several dextran fractions in water and formamide (Antoniou et al., 2007), we now extend this research to examine under the same lens dextran of a given molecular weight (T500) in a range of common solvents (water, formamide (Gekko, 1981), dimethylsulfoxide (Basedow et al., 1980; Çatiker & Güner, 1998), and ethanolamine, all good solvents for dextran according to Hansen’s solubility parameters (Hansen, 2000)), with an aim to establish structure–property relationships for polymer–solvent systems. In particular, we want to be able to predict polymer conformation as affected by solution conditions (Graessley, 1980). To this end, we discuss here experimentally observed effects on the dextran intrinsic viscosity, coil radius, and overlap concentration, in terms of solvent quality, following an evaluation of correlations between polymer properties and various solvent properties that are reflective of interactions between the solvent and dextran molecules.

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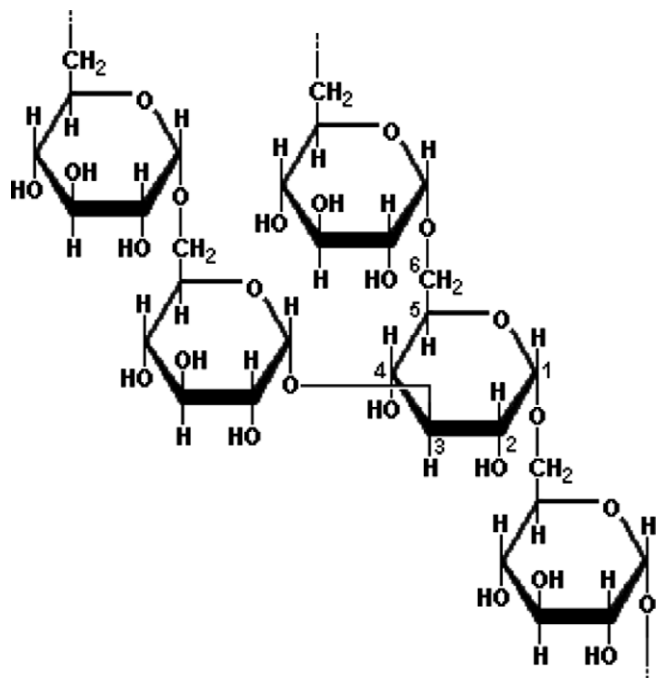


Fig. 1. Chemical structure of a dextran fragment composed of α -(1-6)-linked glucose units, branched by α -(1-3)-linked glucose units.

Despite the practical interest from the side of consumer product applications on effects of polar organic solvents and solutes on water-soluble polymers, and the fundamental aspects underlying the behavior of polymer–solvent–additive systems, the number of relevant published studies remains rather limited. In the case of the relatively well-studied dextran, the effect of aqueous urea, aqueous glycine, aqueous glucose (Mahapatra, Samal, Samal, & Roy, 2001), ethylene glycol, dimethyl sulfoxide (Çatiker & Güner, 2000, 1998), and 40.5% methanol (Wales, Marshall, & Weissberg, 1953) on dextran fractions have been reported. Studies, such as the present, that attempt to correlate polymer solution behavior to solvent properties are also in short supply.

2. Materials and methods

2.1. Materials

We examine the dextran T500 fraction (see Fig. 1 for structure), with weight average (M_w) and number average (M_n) molecular weights 500,000 and 191,500, respectively, purchased from Amersham Biosciences AB (now part of GE Healthcare, Uppsala, Sweden) and Pharmcosmos A/S (Holbaek, Denmark). Several polar organic solvents (Table 1) were used for preparing dextran solutions. Formamide (molecular biology grade) was purchased from VWR International (West Chester, PA). Dimethylsulfoxide (DMSO) and ethanolamine (EA) (purified grade, 99% min) were from Fisher Scientific (Fair Lawn, NJ). The water used was purified with a MilliQ system. We prepared individual dextran solutions for every concentration. The samples remained under stirring for at least one day at room temperature, and then equilibrated at 20 or 40 °C for at least an hour before the measurements were conducted at the same temperature.

2.2. Solvent selection

The solvent selection for this work was based in part on information provided by the dextran–solvent χ_{12} interaction parameter and the free energy of interfacial interaction, ΔG_{121} . A polymer is in a good solvent when the χ_{12} value is less than 0.5. We determined χ_{12} following procedures in (Hansen, 2000) (see Appendix A). The calculated dextran–solvent χ_{12} parameters for DMSO, formamide, and ethylene glycol have values close to or lower than 0.5, which suggests that dextran is expected to dissolve in these solvents (Table 2). The free energy of interfacial interaction, ΔG_{121} , obtained according to van Oss (1994) (see Appendix B), offers another approach for predicting interactions between molecules of dextran (1) immersed in a solvent (2). If ΔG_{121} is positive, then molecules of type (1) will repel each other in solvent (2) and will spontaneously dissolve in it. If ΔG_{121} is negative, then molecules (1) will attract each other in solution, and so will tend to precipitate from the solvent (2) (van Oss, 1994). According to the ΔG_{121} values derived from this method (Table 2), dextran is expected to dissolve in DMSO, formamide, ethylene glycol or water (where the ΔG_{121}

Table 1
Physicochemical properties of solvents used in this work.

Solvent	μ^a (25°)	ϵ_T (20/25 °C)	σ^b (20/25 °C)	E_T^N (25°)	logP (25°)	δ^c	δ_D^c	δ_P^c	δ_H^c
Ethanolamine	3.05	37.5	–/49.0	0.679	–1.31	31.3	17.0	15.5	21.2
Dimethylsulfoxide	13.7	46.5	43.5/43	0.444	–1.35	26.7	18.4	16.4	10.2
Formamide	11.2	109	58.5/58.2	0.799	–1.51	36.7	17.2	26.2	19.0
Ethylene glycol	7.7	37/37.7	48.9/–	0.790	–1.36	33.0	17.0	11.0	26.0
Water	5.9	78.5/78.5	70/71.8	1.000	–1.40	47.8	15.5	16.0	42.3

^a 10^{-30} Cm.

^b mN/m.

^c MPa^{1/2}.

Table 2
Surface tension, γ , surface tension apolar component, γ^{LW} , surface tension polar component, γ^{AB} , electron-acceptor parameter of the surface tension, γ^+ , electron-donor parameter of the surface tension γ^- , reported by van Oss (1994) for the various molecules used in this study; free energy of interfacial interaction, ΔG_{121} , estimated with the van Oss (1994) procedure (see Appendix B) for dextran in the single solvents used in this study, and Flory–Huggins dextran–solvent parameter, χ_{12} , estimated (see Appendix A) using the Hansen (2000) procedure and data.

Solvent	γ	γ^{LW}	γ^{AB}	γ^+	γ^-	ΔG_{121}	χ_{12}	RED
Dimethylsulfoxide	44.0	36.0	8.0	0.50	32.0	4.51	0.500	1
Formamide	58.0	39.0	19.0	2.28	39.6	6.67	0.419	0.915
Ethylene glycol	48.0	29.0	19.0	1.92	47.0	0.71	0.503	1.003
Water	72.8	21.8	51.0	25.50	25.5	41.24		
Dextran T150	42.0	42.0	0.0	0.00	55.0			

values are positive). These two different approaches (Hansen (2000) and van Oss (1994)) give predictions that are in agreement.

2.3. Methods

Solution properties of dextran as affected by solvent quality were ascertained by viscosity measurements. The viscosity of dilute polymer solutions was determined using Cannon Fenske Routine type viscometers (Hiemenz & Rajagopalan, 1997) for transparent Newtonian fluids. Aqueous dextran solutions exhibit Newtonian flow characteristics up to 30 wt% (McCurdy et al., 1994; Tirtaatmadja et al., 2001) thus the flow rate is independent of shear stress. Different sizes of viscometers were used depending on the viscosity range of the samples. The viscometer was immersed in a constant temperature bath to ensure that the measurements were taken under constant temperature (controlled to within ± 0.1 °C). The efflux times were measured with an accuracy of ± 0.1 s and were reproducible to $\pm 0.1\%$ (each measurement was repeated three times). The kinematic viscosity η is calculated by multiplying the efflux time with the viscometer calibration constant (supplied by the manufacturer, Cannon Instrument Co., State College, PA). All polymer solutions were examined at two temperatures, 20 and 40 °C.

The viscosity data analysis procedure has been presented previously (Antoniou & Tsianou, submitted for publication). Briefly, the intrinsic viscosity for dextran is obtained from data in the dilute regime, and the coil dimensions are extracted using the Einstein viscosity relation (see below).

2.4. Intrinsic viscosity

The intrinsic viscosity, $[\eta]$, values of dextran in different solvents and at different temperatures are determined using the Huggins (1) and Kramer (2) equations (Flory, 1953; Sperling, 2001) by plotting η_{sp}/C and $\ln(\eta_{rel})/C$, respectively, against the polymer concentration, and subsequent extrapolating to zero polymer concentration (infinite dilution).

$$\eta_{sp}/C = [\eta] + k'[\eta]^2 C \quad (1)$$

$$(\ln \eta_{rel})/C = [\eta] - k''[\eta]^2 C \quad (2)$$

η_{rel} is the relative viscosity ($\eta_{rel} = \eta/\eta_0$, where η and η_0 are the kinematic viscosity of the solution and the pure solvent, respectively, in mPa s or cSt), η_{sp} is the specific viscosity ($\eta_{sp} = \eta_{rel} - 1$), k' and k'' are the Huggins and Kramer constants, respectively, and C is the polymer concentration (g/dl) in the solution. A straight line is typically obtained with $[\eta]$ being the intercept, and $k'[\eta]^2$ or $k''[\eta]^2$, respectively, being the slope (see Fig. 2). The intrinsic viscosity values and the Huggins and Kramer constants extracted from experiments are presented in Table 3.

2.5. Hydrodynamic coil radius

The increase in viscosity of a dilute dispersion of uniform, rigid, non-interacting spheres can be expressed by the Einstein viscosity relation (Eq. 3) (Hiemenz & Rajagopalan, 1997; Sperling, 2001):

$$\eta = \eta_0(1 + 2.5\Phi) \quad (3)$$

where Φ represents the volume fraction of the spheres in the dispersion. Relative viscosity data for dextran in various solvents are plotted versus the (dry) polymer weight fraction in Figs. 3 and 4. The effective volume fraction occupied by the polymer coils in solution is much higher than the dry polymer weight fraction because they are swollen with solvent. This allows the use of Eq. 3 for calculating the radius of

the swollen polymer coils, R_{coil} (for derivation refer to (Antoniou & Tsianou, submitted for publication)):

$$R_{coil} = (3[\eta] \cdot M_w / 10\pi \cdot N_{AV})^{1/3} \text{ (cm)} \quad (4)$$

where N_{AV} is Avogadro's number. The R_{coil} and corresponding hydrodynamic coil volume, $V_{coil} = (4/3)\pi R_{coil}^3$, values for dextran T500 in different solvent systems are reported in Table 3.

2.6. Overlap concentration

The overlap concentration, C^* , marks the crossover between the dilute regime and the concentration regime where polymer coils overlap (De Gennes, 1993). $[\eta]$ can be used to estimate C^* (Evans & Wennerström, 1999):

$$C^* = 2.5/[\eta] \quad (5)$$

C^* can also be estimated from a η_{rel} vs. C plot by identifying the point where the linear fits of the viscosity data in the dilute and the semidilute regime intersect (Antoniou & Tsianou, submitted for publication). The C^* values reported in Table 3 were estimated using Eq. (5) since this is more objective than the intercept method; however both methods give consistent results.

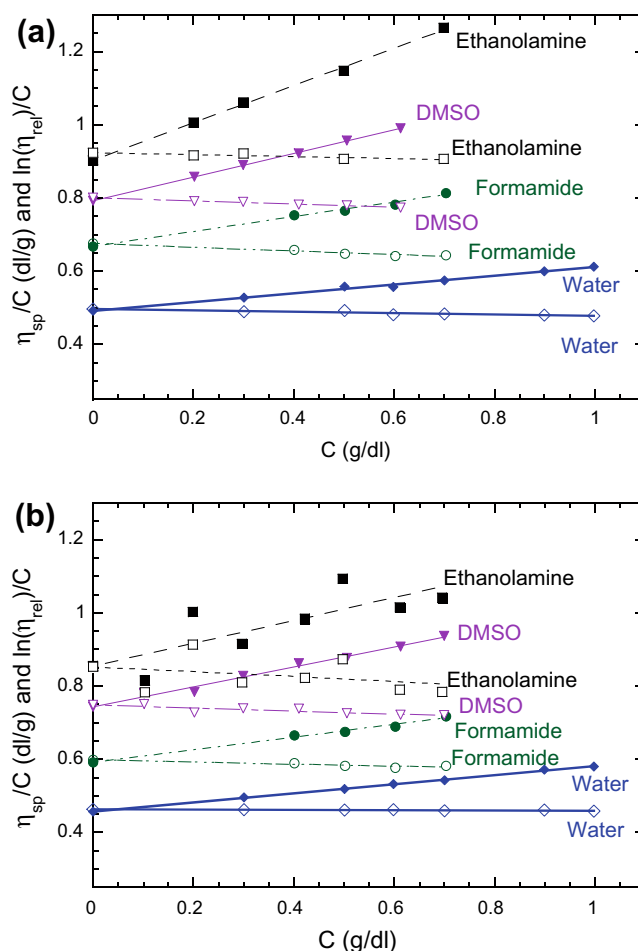


Fig. 2. Specific viscosity (filled symbols) and logarithm of relative viscosity over concentration (open symbols) plotted and linearly fitted vs. dextran T500 concentration in water (\diamond) and in various polar organic solvents (\bullet : formamide, \blacktriangledown : dimethylsulfoxide, \blacksquare : ethanolamine) at (a) 20 °C and (b) 40 °C.

Table 3

Intrinsic viscosity $[\eta]$, Huggins constant k' , Kramer constant k'' , hydrodynamic coil radius R_{coil} , coil volume V_{coil} , and overlap concentration C^* , for dextran T500 in different solvents, calculated using the viscosimetric data obtained in this work at (a) 20 °C and (b) 40 °C. In the case of ethylene glycol we have used $[\eta]$ values reported in [Çatiker and Güner, 2000] and analyzed them with the methods described in this work to obtain the R_{coil} , V_{coil} and C^* values. The ethylene glycol $[\eta]$ value for 20 °C was obtained by linear extrapolation of data at 25° to 40 °C.

Solvent	$[\eta]_{\text{H}}$ (dl/g)	k'	k''	R_{coil} (nm)	V_{coil} ($10^3 \times \text{nm}^3$)	C^* (g/dl)
(a)						
Ethanolamine	0.964	0.471	0.083	19.3	30.0	2.6
Dimethylsulfoxide	0.792	0.515	0.065	18.5	26.3	3.2
Formamide	0.669	0.441	0.110	17.4	22.2	3.7
Ethylene glycol	0.580	–	–	16.6	19.3	4.3
Water	0.491	0.495	0.075	15.7	16.3	5.1
(b)						
Ethanolamine	0.854	0.428	0.092	18.9	28.3	2.9
Dimethylsulfoxide	0.743	0.493	0.074	18.1	24.8	3.4
Formamide	0.591	0.493	0.083	16.7	19.5	4.2
Ethylene glycol	0.347	–	–	14.0	11.5	7.3
Water	0.457	0.597	0.019	15.4	15.3	5.5

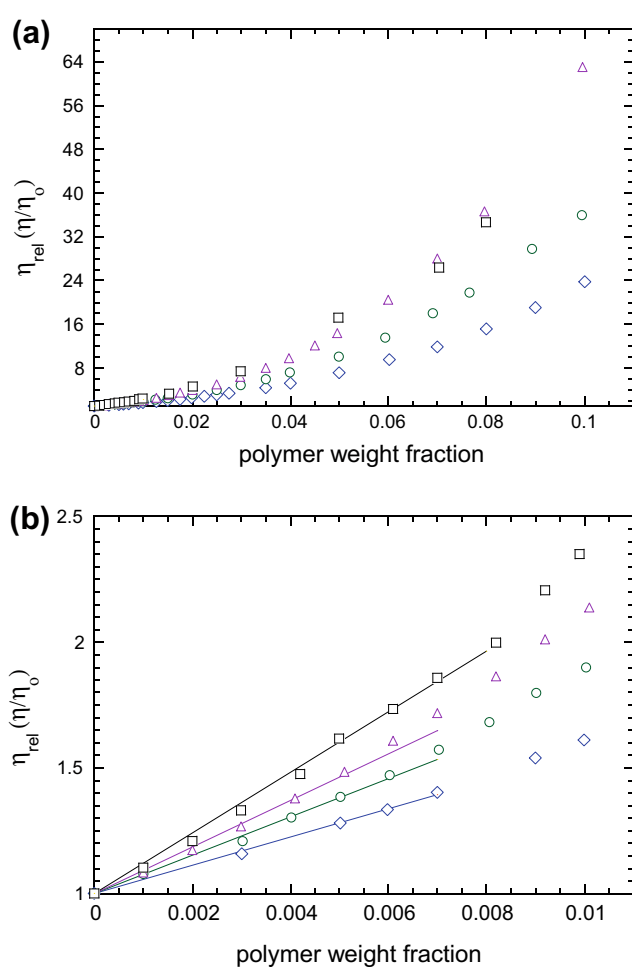


Fig. 3. η_{rel} versus (dry) weight fraction ϕ of dextran T500 in (◇) water, (○) formamide, (Δ) dimethylsulfoxide, and (□) ethanolamine at 20 °C: (a) whole concentration range examined; (b) dilute regime.

3. Results and discussion

3.1. Polymer coil dimensions

The solution structure of dextran as affected by the solvent type and temperature is discussed here. Dextran adopts a random coil conformation in aqueous and formamide solutions as attested by analysis of viscosity and small angle X-ray scattering data reported

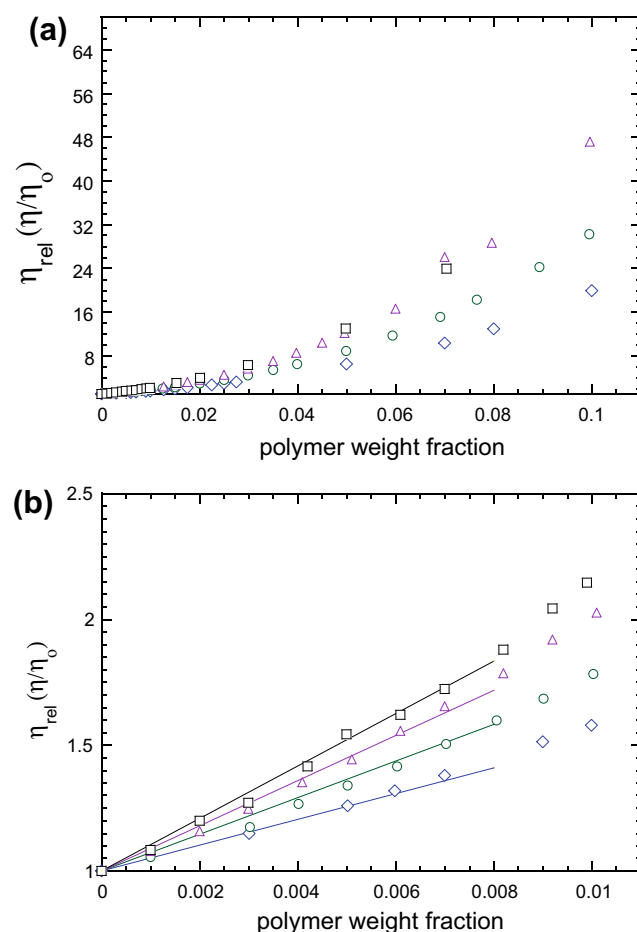


Fig. 4. η_{rel} versus (dry) weight fraction ϕ of dextran T500 in (◇) water, (○) formamide, (Δ) dimethylsulfoxide, and (□) ethanolamine at 40 °C: (a) whole concentration range examined; (b) dilute regime.

elsewhere (Antoniou et al., 2007; Antoniou et al., 2008). Both water and formamide are marginally good solvents for dextran at 20 °C: on the basis of the Mark–Houwink–Sakurada constant α (Sperling, 2001) they are both close to the θ conditions (with water being closer than formamide) (Antoniou & Tsianou, submitted for publication). The intrinsic viscosity, $[\eta]$, that we obtained experimentally is a characteristic property of a polymer molecule in solution. The polymer coil radius, R_{coil} , in the solvents used in this work is calculated through $[\eta]$ using Eq. 4. In the sections that follow we

discuss the solvent quality effects in terms of the dextran coil dimensions. A gradual R_{coil} increase (coil expansion) from 15.7 nm (in water) to 19.7 nm (in ethanolamine) at 20 °C is observed as the solvent changes in the order: water < ethylene glycol < formamide < dimethylsulfoxide < ethanolamine (Table 3). We perceive the higher $[\eta]$ or R_{coil} values as evidence for better solvency, therefore the solvent power (defined as the ability of a solvent to expand the polymer coils) increases in the same order (Flory, 1953). Ethanolamine and dimethylsulfoxide expand the polymer coil significantly, which shows that they are better solvents for dextran than water or formamide. Higher R_{coil} values result in lower C^* (from 5.1 in water to 2.6 g/dl in ethanolamine).

With increasing temperature, R_{coil} decreases (and C^* increases), meaning that dextran coils contract. The temperature effect on the dextran T500 coil radius is on the order of 10% (Table 3b) upon a 20 °C increase. The solvent effect that we observe is more significant than the temperature effect on the coil conformation of dextran T500 (in agreement with the literature (Hadjichristidis, 1983)). The temperature change did not affect the solvent quality order observed for 20 °C, except for the relative position of ethylene glycol and water.

The Huggins constant is considered a measure of polymer–solvent interaction (Flory, 1953; Magny, Iliopoulos, & Audibert, 1991). In solutions of polymers without strong association, the Huggins constant values range from 0.3 to 0.8 (Flory, 1953; Magny et al., 1991). In good solvents the expected Huggins constant is about 0.35 (although significant variation is possible). In this work we obtained k' values between 0.441 and 0.515 at 20 °C (Table 3a). No correlation is apparent in our data between k' or k'' and coil dimensions (order of solvency) that could be related to molecular interactions (McCormick, Bock, & Schulz, 1989).

It is important to rationalize the observed changes in the dextran coil dimensions when the solvent or temperature change in terms of interactions between polymer segments and solvent molecules. To this end, we start in Section 4.1 by looking into the molecular structure of each solvent examined in this work, in order to assess possible interactions between dextran and each solvent. We go on in Section 4.2 to examine whether the coil size change of dextran can be correlated to solvent properties such as surface tension, as well as empirical solvent parameters such as the solubility parameter. Finally, in Section 5 we discuss temperature effects on solvent quality and examine if these validate our conclusion from Section 4.

4. Solvent effects

4.1. Solvent structure

The solvents considered in this work are all polar. Water, ethylene glycol, and formamide are protic, hydrogen bonding, strongly associated solvents (Parker, 1969; Reichardt, 1990). Protic solvents are strong hydrogen-bond donors (donor groups: $\text{O}-\text{H}$ or $\text{N}-\text{H}$) and interact with solutes that are strong hydrogen-bond acceptors (acceptor groups: $\text{O}-\text{C}<$, $\text{O}-\text{H}$ or N) (Parker, 1969). Dimethylsulfoxide (DMSO) is an aprotic, highly dipolar, hydrogen bond acceptor solvent. Ethanolamine (EA) is a polar solvent capable of both hydrogen bond donation and acceptance.

Liquid water has been described as a very dense three-dimensional tetrahedral network (Errington & Debenedetti, 2001) of water molecules with local order, where each oxygen atom is hydrogen-bonded to four other oxygen atoms through an $\text{O}-\text{H}-\text{O}$ bridge (Dill, Truskett, Vlachy, & Hribar-Lee, 2000; Hakem, Boussaid, Benchouk-Taleb, & Bockstaller, 2007). Compared to other liquids which have the same molecular size, water is more cohesive, as indicated by its higher boiling and freezing temperatures, dielectric constant, surface tension, and vaporization enthalpies (Dill et al., 2000).

Ethylene glycol (EG) ($\text{C}_2\text{H}_4(\text{OH})_2$) molecules form a three-dimensional, branched hydrogen-bonding network, with the polar groups participating in at least three hydrogen bonds around the O atoms (Gubskaya & Kusalik, 2004). EG may be considered as a water analogue, however, in contrast to water, EG exhibits a competition between intermolecular and intramolecular interactions (hydrogen bonds). In EG, O atoms have a tendency to make, on average, two strong hydrogen bonds, apparently leaving one acceptor and one donor site, respectively, underutilized. Such behavior can be interpreted as a direct consequence of the requirements imposed by hydrogen-bond balance (i.e., the total number of acceptors must equal the total number of donors) (Gubskaya & Kusalik, 2004).

Formamide (HCONH_2) molecules may be linked by hydrogen bonds between the $\text{C}=\text{O}$ and $\text{N}-\text{H}$ groups. Liquid formamide exhibits mainly a three-dimensional $\text{N}-\text{H}-\text{O}$ hydrogen bond network (Puhovski & Rode, 1995), a structuring that is reflected in a relatively high viscosity (3.3 cp at 25 °C) and low self-diffusion coefficient. Electron, neutron, and X-ray diffraction patterns of liquid formamide have suggested that there are, on average, two hydrogen bonds per molecule (Bellissent-Funel, Nasr, & Bosio, 1997). Liquid formamide consists of a continuous H-bond network, like water, with a small number of small clusters (~3% of the molecules not included in the network form clusters of 1–6 molecules) and cyclic dimers (~8%) participating in the H-bond network (Puhovski & Rode, 1995).

Dimethyl sulfoxide ($(\text{CH}_3)_2\text{SO}$) is an aprotic highly dipolar solvent, important in industry and in biology as a cryoprotector and a drug carrier (Luzar & Chandler, 1993; McKim & Strub, 2008). Dipolar aprotic solvents are powerful bases and hydrogen-bond acceptors, so they strongly interact with solutes which are strong hydrogen-bond donors (Parker, 1969; Reichardt, 1990) such as water. Due to two lone electron pairs on its oxygen atom, a single DMSO molecule is thought to form four hydrogen bonds simultaneously with neighboring molecules (Bordallo, Herwig, Luther, & Levinger, 2004).

Ethanolamine (EA) ($\text{NH}_2-(\text{CH}_2)_2-\text{OH}$) is a polar solvent capable of hydrogen bonding by both donation and acceptance of hydrogen bonds (having almost twice the number of H-bonds in water), forming a three-dimensional, branched network (similar to that observed in EG) (Alejandre, Rivera, Mora, & de la Garza, 2000). Both amino and hydroxyl groups are strongly hydrogen-bonded to three neighbors (which is allowed by hydrogen-bond balance of the donation and acceptance abilities) (Gubskaya & Kusalik, 2004; Labban & Marcus, 1997). EA molecules exhibit a competition between intermolecular and intramolecular interactions (hydrogen bonds), a distinctive feature shared by pure molecular liquids like EG. EA molecules often engage in intermolecular bonding in the bulk liquid and are not necessarily readily available to bond with solutes (Labban & Marcus, 1997).

Dextran is a hydrophilic monopolar electron-acceptor molecule that exhibits a strong interaction with water, an electron-donor (van Oss, 1994). Dextran comprises of glucose units. In an attempt to understand the solution behavior of dextran we have looked into literature concerning the structural and dynamical properties of glucose molecules since there are no such data directly available for dextran. The structure of glucose in water and the effect of glucose on the hydrogen bonded network of water have been studied by means of Raman and IR spectroscopy (Paolantoni, Sassi, Morresi, & Santini, 2007; Suzuki & Sota, 2003), deuterium NMR (Moran & Jeffrey, 1999), quasielastic neutron scattering (QENS) (Talon et al., 2004), and molecular dynamics (MD) (Lee, Debenedetti, & Errington, 2005). The glucose molecule is a puckered six-membered ring, composed of five carbon atoms and one oxygen atom, called O5 or ring oxygen. The O5 ring oxygen is single bonded to two carbon atoms: one that carries a hydrogen atom and a hydroxyl group, called C1, and another that carries a hydrogen atom and a hydroxymethyl

group, called C5 (see Fig. 1). Glucose oxygen atoms hydrogen-bond to neighboring water molecules (Suzuki & Sota, 2003). Paolantoni et al. (2007) concluded that: (i) the addition of glucose reduces the number of water free OH groups, not involved in H-bonds; (ii) glucose molecules strongly interact with water and the strength of water–glucose and water–water interactions are of similar extent; (iii) glucose acts as a weak structure breaker on the tetrahedral network of water; and (iv) the action of glucose on the organization of water is rather modest (a destructive effect on the tetrahedral water is partially compensated by the formation of new H-bonds within the glucose hydration shell).

In our attempt to rationalize the dextran R_{coil} increase in the order water < EG < formamide < DMSO < EA using the literature information that we highlighted above, we can argue that dextran coils (having three hydroxyl (–OH) and one ether oxygen (C–O–C) groups per glucose unit, Fig. 1) would: (i) swell more in EG than in water, since the chances to form hydrogen bonds increase in EG (two –OH groups), (ii) dissolve better in formamide than in EG since –NH and =O groups are stronger than –OH groups in forming hydrogen bonds, (iii) interact strongly in DMSO with the readily available hydrogen bond acceptors (S=O group) forming strong O–H \cdots O hydrogen bonds, whereas in the protic solvents water, EG or formamide dextran would have to first break the usually dense hydrogen bonded network, and (iv) dissolve in EA to a similar or greater extent than in DMSO, since EA has both donor (N–H) and acceptor (–OH) hydrogen bond groups. In EA solution dextran coils will have to face competition between intermolecular and intramolecular hydrogen bonding. According to Gubskaya and Kusalik (2004), EA molecules prefer to interact through N–H \cdots O (weak) hydrogen bonds instead of the O–H \cdots N (strong) bonds, so dextran would probably dissolve more readily in EA (breaking the weak N–H \cdots O bonds) and to a higher extent compared to DMSO.

4.2. Solvent properties

The solvation capability of a solvent depends on the action of all possible, specific and nonspecific, intermolecular forces between solvent and solute molecules, including Coulomb interactions between ions, directional interactions between dipoles, inductive, dispersion, hydrogen-bonding, and charge transfer forces, as well as solvophobic interactions (Reichardt, 1990). Therefore we examine here whether the coil size changes of dextran can be correlated to a variety of solvent properties that may be reflective of the above interactions, as well as to empirical solvent parameters such as octanol/water partition coefficient, $\log P$, empirical parameter of solvent polarity, E_T^N , and solubility parameter, δ .

The dielectric constant (or relative permittivity), ϵ_r , and the dipole moment, μ , are important complementary solvent properties and are often used in the quantitative characterization of solvent polarity (Parker, 1969; Reichardt, 1990). The dielectric constant reflects the solvent molecular symmetry. The effect is produced by the orientation of dipoles along an externally applied electric field and from the separation of charges in apolar molecules. This orientation causes polarization of the molecules and a drop in electric field strength (Wypych, 2001, chap. 2.3). Non-charged polar molecules with an unsymmetrical charge distribution possess a permanent dipole moment μ , defined as $\mu = ql$, where l is the distance between two charges $+q$ and $-q$ (Evans & Wennerström, 1999). ϵ_r and μ can be related through: $\mu = (\epsilon_r - 1) V_M / (\epsilon_r - 2)$, where V_M is the molar volume. The product of dipole moment and dielectric constant, called the electrostatic factor, can serve as another means of classifying solvents according to their polarity (Wypych, 2001).

The surface tension, σ , expresses the energy per unit area of the surface of a liquid relative to vacuum, in principle, or relative to air saturated with the vapors, in practice (Reichardt, 1990). Cohesive

forces between the liquid molecules are responsible for surface tension. The molecules at the surface do not have other like molecules on all sides of them, and consequently they cohere more strongly to those directly associated with them on the surface.

The octanol–water partition coefficient, $\log P$, is a hydrophobicity parameter that can serve as a measure of solvent polarity and has proven valuable in the fields of pharmacology, toxicology, and environmental science (Reichardt, 1990). The octanol–water partition coefficient represents the ratio of the concentration of a certain molecule in octanol and in water at equilibrium and at a specified temperature.

Dimroth and Reichardt's $E_T(30)$ is a measure of the “general polarity” of a solvent, mainly involving its hydrogen bond donation ability (Marcus, 2002) in addition to its polarity and polarizability. $E_T(30)$ is generally expressed in kcal mol $^{-1}$ and is obtained from $E_T(30) = 28590 / (\lambda_{\text{max}}/\text{nm})$, where λ_{max} is the wavelength of the lowest energy peak in the spectrum of the particular 4-(2,4,6-triphenylpyridinium)-2,4-diphenylphenolate betaine used to measure λ_{max} . This polarity index is often used (also in this work) in its normalized, dimensionless form, the so-called empirical parameter of solvent polarity, E_T^N (Marcus, 2002; Reichardt, 1990):

$$E_T^N = [E_T(30) - 30.7] / 32.4 \quad (6)$$

where 30.7 is the $E_T(30)$ value of tetramethylsilane, the lowest measured, and 32.4 is the difference between $E_T(30)$ of water, 63.1, the highest measured, and that of tetramethylsilane.

The Hildebrand solubility parameter δ is defined as the square root of the cohesive energy density, and is an important quantity for predicting the solubility of a polymer in a given solvent (Sperling, 2001). For example, δ is used in the coatings industry to aid in solvent selection (Hansen, 2000). Still, as a single number, δ cannot capture the various interactions (donor–acceptor, electron pair, and hydrogen bonding) between solvents and solutes. We thus employed the Hansen Solubility Parameters (HSPs). In a framework proposed by Hansen (2000), the cohesive energy described by δ is attributed to three different interactions (forces): dispersion (atomic), polar dipole–dipole forces (molecular), and hydrogen bonding (electron exchange, molecular), quantified by δ_D , δ_P , and δ_H , respectively. The HSPs [δ_D , δ_P , δ_H] are used to interpret-predict solubility behavior of solvents and polymers (Hansen, 2000). Solvents will dissolve polymers with similar HSPs (e.g., compare the [δ_D , δ_P , δ_H] values of dextran [24.3, 19.9, 22.5] to such data for various solvents listed in Table 1) (Hansen, 2000). The total solubility parameter, δ , is connected to the three contributors through Eq. 7:

$$\delta^2 = \delta_D^2 + \delta_P^2 + \delta_H^2 \quad (7)$$

Data for the dipole moment μ , dielectric constant ϵ_r , surface tension σ , empirical parameter of solvent polarity E_T^N , octanol/water partition coefficient $\log P$, Hildebrand and Hansen solubility parameters of the various solvents used in this work are presented in Table 1 (Hansen, 2000; Reichardt, 1990).

The experimentally determined dextran T500 coil radius (R_{coil}) data are plotted against the fundamental solvent properties μ , ϵ_r , and σ , in Fig. 5(a)–(c), and against the empirical solvent parameters E_T^N , $\log P$, and δ , in Fig. 5(d)–(f). Our motivation in examining such possible correlation between the dextran solution structure (R_{coil}) and solvent properties emanated from previous work in our group that investigated polar organic solvent effects on the micellization of an amphiphilic siloxane-graft-polyether copolymer (Lin & Alexandridis, 2002) and the phase behavior of a polyether block copolymer (Ivanova et al., 2000; Ivanova, Lindman, & Alexandridis, 2002). For example, we found that the critical micellization concentration (CMC) values in mixed aqueous-organic solvents correlated well to the solubility parameters and to the $\log P$ of the organic solvent component (Lin & Alexandridis, 2002). Güner

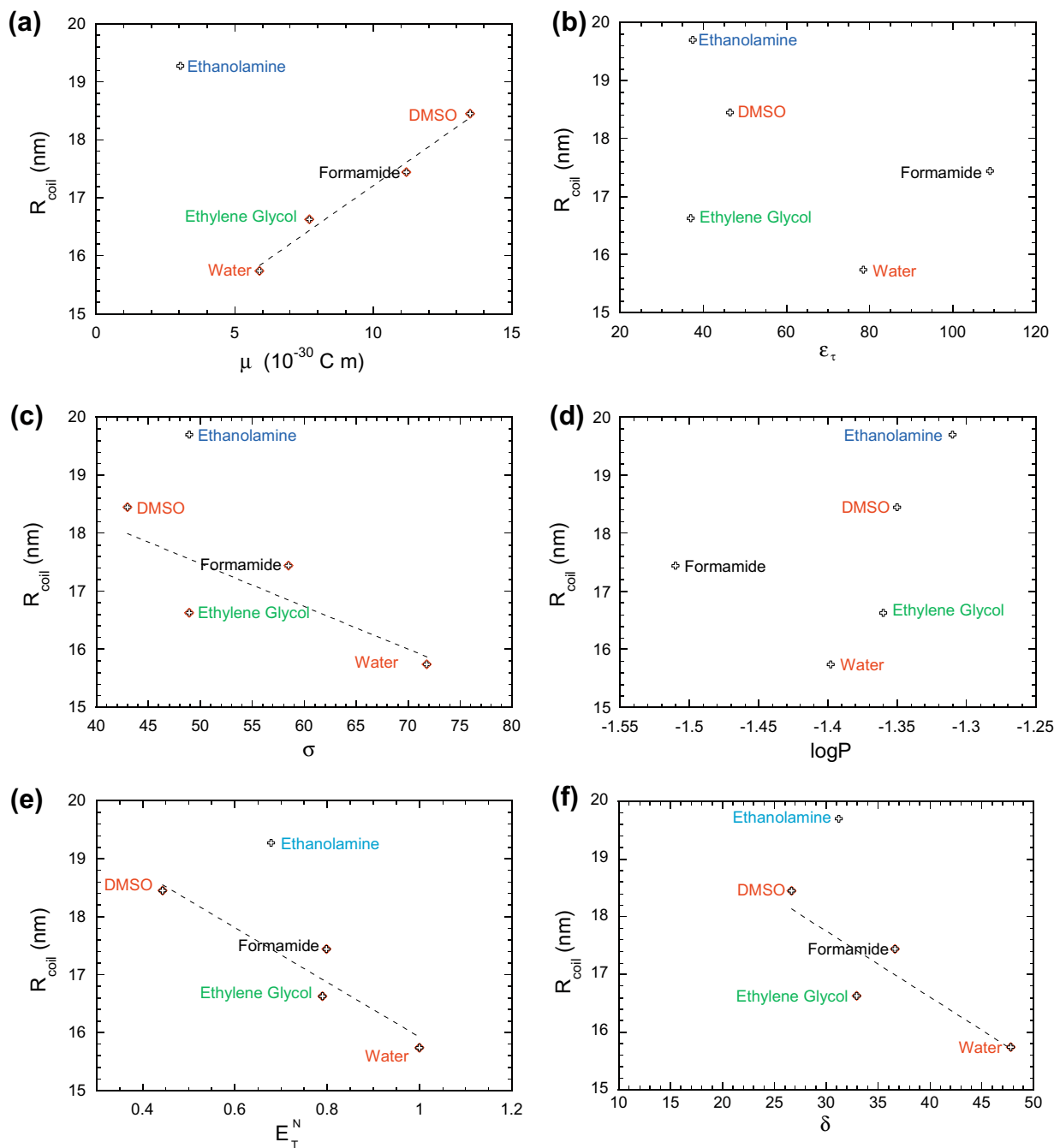


Fig. 5. Coil radius, R_{coil} , for dextran T500 at 20 °C plotted vs the solvent (a) dipole moment, μ , (b) dielectric constant, ϵ_r (c) surface tension, σ , (d) octanol/water partition coefficient, $\log P$, (e) empirical parameter of solvent polarity, E_T^N , and (f) Hildebrand solubility parameter, δ . The dotted lines are linear fits (ethanolamine was excluded).

(2004) has previously used solubility parameters to evaluate the solubility of dextran in various solvents: in a δ_H vs. δ_P or vs. δ plot, the dextran solubility parameter component defined the center of a circle; solvents with solubility parameter components falling within this circle and closer to the solubility component of dextran were considered good solvents, whereas the ones remaining outside the circle either swelled dextran slightly or had no effect at all.

Fig. 5 reveals that the dextran coil radius data correlate linearly with the dipole moment, surface tension, empirical parameter of solvent polarity E_T^N , and Hildebrand solubility parameter δ in the case of the protic (water, ethylene glycol, formamide) and the aprotic (DMSO) solvents considered here. More specifically, R_{coil} increases as σ , E_T^N , and δ decrease, while R_{coil} increases with increas-

ing dipole moment. In the following we attempt to rationalize the R_{coil} dependence on the solvent properties.

The dextran coils expand with an increase in dipole moment (Fig. 5(a)). Recall that the dipole moment originates from the degree of charge separation in a molecule. At the same time, the term hydrogen bond denotes strong short-range highly directional electrostatic interactions. The higher the dipole moment of the solvent molecules, the stronger the electrostatic interactions in the solution, so hydrogen bonding interactions increase and become stronger. Consequently the dextran coil can expand when interacting with high dipole moment solvent molecules. The dextran coils also expand with E_T^N decrease. E_T^N represents the hydrogen bond donation ability of a solvent. As E_T^N values increase, the H-bond donicity

of a solvent increases. Dextran being a H-bond donor, it interacts better with (and expands in) H-bond acceptor solvents (such as DMSO that has a low E_T^N value). Thus as the solvent H-bond donicity decreases (lower E_T^N values) the dextran R_{coil} increases. The increase of the dextran R_{coil} while σ and δ decrease can be related to a weakening of cohesive forces between the solvent molecules, which makes it is easier for dextran to break them and form hydrogen bonds with the solvent. We note that the σ and δ values for the solvents considered here exhibit some cross-correlation.

EA appears to be an outlier in Fig. 5(a), (c), and (e), since the R_{coil} data for this solvent do not fall on the same line that the other properties do, as discussed above. This can be attributed to the difference of EA from the rest of the solvents considered here: EA is both hydrogen bonding acceptor and donor, as opposed to water, EG, and formamide which are all protic solvents (H-bond donors), and DMSO that is an aprotic solvent (H-bond acceptor). Amine solvents like ethylenediamine, *N*-methylmorpholine-*N*-oxide (NMMO) (Fink, Weigel, Purz, & Ganster, 2001), and tertiary amine oxides are known to dissolve the generally insoluble (due to considerable inter- and intramolecular hydrogen bonding) polysaccharide cellulose (that consists of $\beta(1 \rightarrow 4)$ linked D-glucose units). This effectiveness of amines on cellulose dissolution has been attributed mainly to the strong hydrogen bonding interactions between the cellulose and the amine solvent, which could explain why ethanolamine appears to be such a good solvent also for the polysaccharide dextran.

The dextran coil radius for different solvents does not exhibit a dependence on ϵ_r (Fig. 5(b)) and $\log P$ (Fig. 5(d)), or on the product of $\mu \times \epsilon_r$ (data not presented here). Recall that ϵ_r and μ are connected through the $\mu = (\epsilon_r - 1) V_M / (\epsilon_r - 2)$ relationship. The lack of R_{coil} correlation with ϵ_r (at a time that there is a correlation with μ) may be because the dipole moment describes the interaction between two specific molecules (dipoles) whereas the dielectric constant represents more complex (collective) interactions among the solvent molecules. The lack of R_{coil} correlation to the solvent $\log P$ may simply be due to the $\log P$ capturing mostly hydrophobic interactions that are not operating in our case.

It appears from the above that hydrogen bonding is an important interaction behind the solvation capability of a given solvent for dextran. In order to test this we examined how the dextran R_{coil} correlates with the Hansen solubility parameters that represent dispersion, polar or hydrogen bonding interactions (Fig. 6). The R_{coil} variation among solvents is not connected to any significant change in the solvent dispersion solubility parameter (see Fig. 6(a)), and there is no clear relation between R_{coil} and the polar HSP (Fig. 6(b)). In the case of the hydrogen bonding HSP, however, R_{coil} increases with decreasing δ_H , i.e., a similar correlation is observed to the one identified for the E_T^N , σ , and δ parameters. We can thus conclude that the increase in the R_{coil} values with decreasing δ (Fig. 5(f)) can be attributed to the δ_H component that captures the cohesive energy due to hydrogen bonding (Fig. 6(c)).

In summary, we note that the dextran coil dimensions exhibit dependence on solvent properties that are related to cohesive forces like μ , σ , and δ , and to hydrogen bonding such as the empirical solvent parameters E_T^N and δ_H . Hydrogen bonding thus emerges as the main interaction between dextran and the solvent molecules. Consequently, we may explain (and predict) the solubility of dextran according to the hydrogen bonding donor or acceptor sites of the solvents. The solvent quality order established here, water < EG < formamide < DMSO < EA, agrees with the water < -EG ~ DMSO order that would be expected according to the Mark–Houwink–Sakurada constant α data reported by Güner (2004). Our experimental results on the relative quality of the various solvents confirm the expectations generated by the χ_{12} and ΔG_{121} values (Table 2), a fact that adds confidence to the use of the Hansen and van Oss methods to predict polymer solubility.

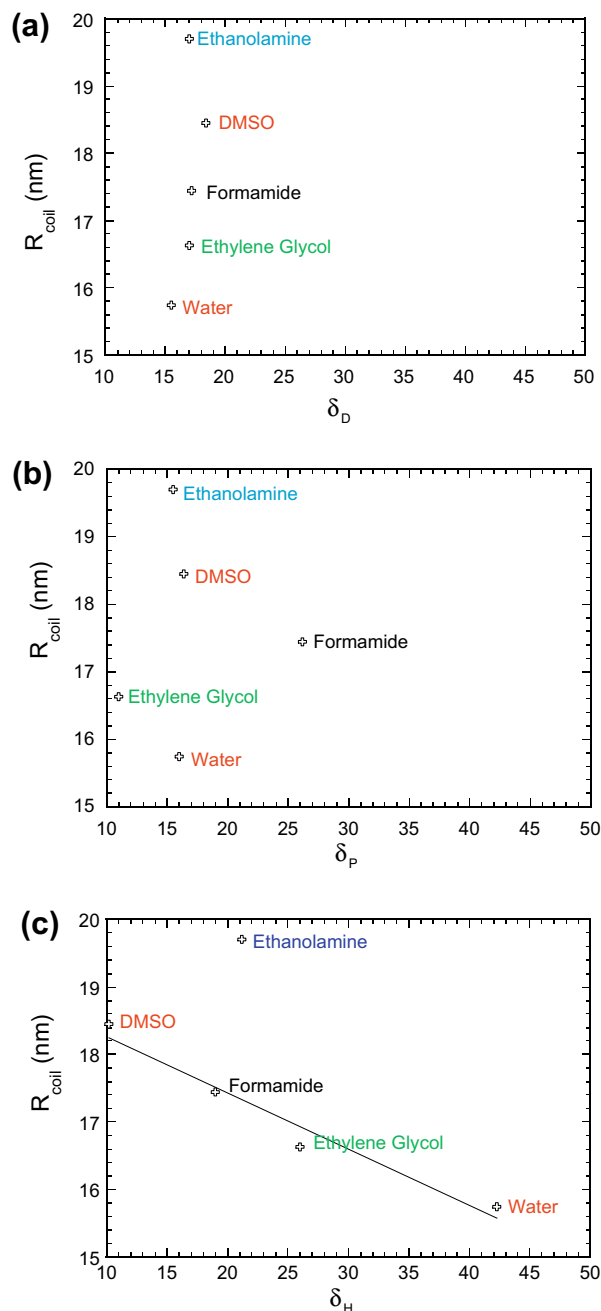


Fig. 6. Coil radius, R_{coil} , for dextran T500 at 20 °C plotted vs the solvent (a) dispersion, δ_D , (b) polar, δ_P , and (c) hydrogen bonding, δ_H , Hansen solubility parameters.

5. Temperature effects

The effect of temperature perturbation away from ambient conditions is of general interest in colloidal systems. In this work, we are also interested on the temperature effect in the dextran–solvent systems in order to validate the conclusion from the previous section that hydrogen bonding is the main interaction. In what follows we discuss the general temperature effects on polymer solubility and, more specifically, on hydrogen bonding interactions in the systems of interest, as they relate to our experimental findings.

Polymers dissolve in aqueous and organic solvents forming homogeneous one-phase solutions. It is common for polymers solutions to phase separate by increasing temperature, exhibiting

a lower critical solution temperature (LCST) behavior (Sperling, 2001; Tsianou, Thuresson, & Piculell, 2001). The θ -point, characterized by the θ temperature, θ is the threshold where phase separation begins. As the temperature increases, polymer coils contract approaching their unperturbed dimensions. At the θ -temperature the polymer coil volume or intrinsic viscosity are at a minimum because the polymer coil is not swollen by the presence of a solvent (solvent quality drops), and the polymer conformation depends only on its own molecular conformational constraints; the Mark–Houwink constant α equals to 1/2, and the hydrodynamic expansion factor α_{η} to 1 ($\alpha > 1/2$ and $\alpha_{\eta} > 1$ in good solvents (Flory, 1953)). Poly(ethylene glycol) is a well-known polymer that exhibits LCST behavior. It is well-soluble in water at room temperature but its solubility decreases dramatically with an increase in temperature of the order of only 30 °C. Güner (2004) reported that dextran solutions move towards θ conditions upon heating. The θ -temperature of dextran in DMSO, ethylene glycol, and water was estimated to be 57 °C (Çatiker & Güner, 2000), 54 °C (Çatiker & Güner, 1998), and 43 °C (Güner, 1995), respectively, on the basis of the decrease of the Mark–Houwink constant α to the value of 0.5 with increasing temperature. In this study the decrease of R_{coil} (V_{coil}) with increasing temperature that is observed for the different solvent systems (Table 3), indicates that the solvent power of water, formamide, DMSO, and ethanolamine for dextran decreases as the temperature is raised from 20 to 40 °C. This shows that the dextran–solvent systems moved towards θ conditions with increasing temperature, something that can be related to LCST behavior. Considering the discussion from the previous section, hydrogen bonding of dextran with solvent molecules will likely be affected by the temperature increase, and the interactions between the polymer segments will become more dominant.

Studies on temperature effects on water and organic solvents like formamide, ethanolamine or glycerol (Alejandre et al., 2000; Bellissent-Funel et al., 1997; Champeney, Joarder, & Dore, 1986; Hakem et al., 2007) reveal that the structure of the solvent is not affected significantly, but rather the hydrogen bonding stability is influenced (i.e., it decreases with temperature increase). More specifically, in the case of water the stability of the hydrogen bonds decreases with increasing temperature from 0 to 400 °C (at 300–400 °C they have disappeared completely) due to the increasing influence of the entropy loss associated with the formation of bonds (Hakem et al., 2007; Postorino, Tromp, Ricci, Soper, & Neilson, 1993). In liquid formamide the number of hydrogen bonds is not significantly affected when temperature changes from –10 to 64 °C. The N...O distance decreases with increasing temperature; at low temperature (–10 °C), the N, H, and O atoms of the hydrogen bond (N–H...O) are lined up, but as the temperature increases the hydrogen (N–H...O) bonds bend, causing a stronger and more dense H-bonded network (Bellissent-Funel et al., 1997). In the case of ethanolamine, intramolecular associations increase with temperature (in the range 25–277 °C) while intermolecular associations decrease (Alejandre et al., 2000), since the hydrogen bonds weaken. At the same time that the intermolecular association between solvent molecules decreases with increasing temperature, the intermolecular association among the solvent and polymer molecules is also affected (H-bonding stability decreases) (Hakem et al., 2007, causing the intramolecular association of dextran to increase and the coils to contract.

In the case of glucose (of interest as a dextran analogue) the extent of hydrogen bonding among molecules in the glassy state, both at –10 and 35 °C (1.3–1.6 H-bonds per OH group), is comparable to that in the glucose crystal state (1.6 H-bonds per OH group) (Tromp, Parker, & Ring, 1997). A temperature rise causes a restructuring of the hydrogen bonded network, since the stability of hydrogen bonds decreases, accompanied by a drop (of about 20%) in the number of OH groups that are closely associated (Ha-

kem et al., 2007). A consequence of HB weakening is the viscosity reduction of the glassy glucose by a factor of 10^8 .

The dextran coil volume decreases (by 5–12%) when temperature increases from 20 to 40 °C, with the formamide and ethanolamine systems being more affected (11–12%), and water and DMSO less (7 and 6%, respectively) (see Table 3). Note that V_{coil} is mostly affected by temperature in the case of EG (~40% change), but since the $[\eta]$ data for EG were extracted from the literature (Çatiker & Güner, 2000), we do not comment on these further here. As discussed above, hydrogen bonds weaken when temperature increases. So the contraction of the dextran coils upon heating from 20 to 40 °C can be attributed to a decrease of the hydrogen bonds between the dextran and solvent molecules (Antoniou & Tsianou, submitted for publication; Basedow et al., 1980; Güner, 1995). The polymer segments adopt a less expanded conformation in the solution and the intermolecular association within polymer segments is enhanced at higher temperatures; the coils contract. The solvent property correlations in the previous section and the temperature effects discussed above intimate that the main interaction between dextran and solvent molecules is hydrogen bonding.

6. Conclusions

We investigated here the conformation of a common polysaccharide, dextran T500, in aqueous, formamide, dimethylsulfoxide, and ethanolamine solutions, as affected by the solvent type and temperature change, using viscosity measurements that have been analyzed to obtain intrinsic viscosity, $[\eta]$, and hydrodynamic coil radius, R_{coil} , values.

The ability of a solvent to increase $[\eta]$ and expand the dextran coils increases in the order: water < ethylene glycol < formamide < dimethylsulfoxide < ethanolamine. Ethanolamine, dimethylsulfoxide, and formamide are thus better solvents for dextran than water. The dextran R_{coil} increase in this order (from 15 to 19 nm) can be rationalized in terms of the molecular structure and interactions of each solvent. Dextran coils would: (i) swell more in EG than in water, since the chances to form hydrogen bonds increase in EG (two –OH groups), (ii) dissolve better in formamide than in EG since –NH and =O groups are stronger in forming hydrogen bonds than –OH groups, (iii) interact strongly (as H-bond donors) in DMSO with the readily available hydrogen bond acceptors (S=O group), and (iv) dissolve in EA to a similar or greater extent than in DMSO, since EA has both donor (N–H) and acceptor (–OH) hydrogen bond groups.

The dextran coil dimensions exhibited dependence on solvent properties that are related to cohesive forces like μ and σ , and to hydrogen bonding such as the empirical solvent parameters E_{T}^{N} , δ , and δ_{H} , in the case of protic solvents water, ethylene glycol, and formamide, and the aprotic solvent DMSO. In particular, R_{coil} increased with solvent dipole moment increase (increasing directional electrostatic interactions between solvent and dextran) and with E_{T}^{N} decrease (decreasing solvent H-bond donation to dextran that is a donor itself). The dextran R_{coil} increased while σ and δ decrease. The lower the σ and δ values, the weaker the cohesive forces between the solvent molecules, and the easier for dextran to break them and form hydrogen bonds with the solvent. R_{coil} for EA does not follow the monotonic relationships that the other properties do, probably because EA differs by being both hydrogen bonding acceptor and donor.

All the dextran–solvent binary systems studied here are at good (or marginally good) solvent conditions at 20 °C, but moved towards the θ conditions with increasing temperature. The dextran coil volume decreased when temperature increased from 20 to 40 °C, with the formamide and ethanolamine systems being more affected (11–12% V_{coil} increase), and water and DMSO less affected

(7 and 6%, respectively). The contraction of the dextran coils upon heating can be attributed to some rupture of the hydrogen bonds among the dextran and solvent molecules. The polymer segments interact less with the solvent molecules and adopt a less expanded conformation in the solution, since the intra-polymer association is enhanced at higher temperatures. Overall, the solvent effects that we have observed on the coil conformation are more significant than the effects of temperature.

On the basis of the solvent property correlations and the temperature effects summarized above we can conclude that the main interaction between dextran and solvent molecules is hydrogen bonding. Evaluation of solvents is possible through solvent-polymer property correlations. These findings can facilitate the selection of solvents for systems containing dextran and the interpretation of the behavior of such systems. They can also be generalized to address the solution behavior of other polysaccharides.

Acknowledgements

We thank NSF (grant CBET 0124848/TSE) for supporting this research. The undergraduate research of Mr. C.F. Buitrago has been supported by the SUNY Louis Stokes Alliance for Minority Participation (LSAMP) program.

Appendix A. χ_{12} estimation procedure

We calculate χ_{12} using the equations below:

Solubility parameter distance: $(Ra)^2 = 4(\delta_{D2} - \delta_{D1})^2 + (\delta_{P2} - \delta_{P1})^2 + (\delta_{H2} - \delta_{H1})^2$ (Table 1)

Relative energy difference: $RED = Ra/Ro$

Radius of interaction sphere in Hansen space: $Ro = Ra/RED$

Distance in Hansen space: $RA = Ra/2$

Maximum distance in Hansen space allowing solubility: $R_M = Ro/2$

Hydrogen bonding cohesion (solubility) parameter: $H = (RA/R_M)^2$

$\chi_{12} = H/2$

The Hansen solubility parameters, δ_D , δ_P , δ_H , and the parameter called RED that describes polymer miscibility in solvents are available in Hansen (2000).

The δ_D , δ_P , and δ_H values of different solvents are reported in Table 1. The RED and χ_{12} values of different dextran-solvent pairs are reported in Table 2.

Appendix B. ΔG_{121} estimation procedure

The surface tension (or surface free energy per unit area), γ_i , of a liquid or solid is defined as half of the free energy change due to cohesion of the material in vacuo, ΔG_{ii} .

$$\gamma_i = -1/2\Delta G_{ii}$$

Since the free energy of cohesion is contributed by a number of more or less independent forces, the surface tension can also be broken down into its separate components, i.e.:

$$\gamma_i = \sum \gamma_i^j$$

where j stands for dispersion, dipolar, induction, H-bonding and metallic interactions, and γ_i^j stands for the component of the surface tension arising from the j 'th type of interaction.

The free energy of interfacial interaction, ΔG_{121} , between molecules or particles of substance 1, immersed in liquid 2, comprises of the additive apolar, ΔG^{LW} , and polar, ΔG^{AB} , free energy components. The apolar component describes the Lifshitz-van der Waals

(LW) interactions and the polar component the electron-acceptor-electron-donor interactions (AB) (van Oss, 1994).

$$\Delta G = \Delta G^{LW} + \Delta G^{AB}$$

Given that:

$$\Delta G_{ii} = -2\gamma_i$$

and

$$\gamma_i = \gamma_i^{LW} + \gamma_i^{AB}$$

Then:

$$\Delta G_{121} = -2\gamma_{12}$$

$$\gamma_{12} = \gamma_{12}^{LW} + \gamma_{12}^{AB}$$

$$\gamma_{12}^{LW} = (\sqrt{\gamma_1^{LW}} - \sqrt{\gamma_2^{LW}})^2$$

$$\gamma_{12}^{AB} = 2(\sqrt{\gamma_1^+} - \sqrt{\gamma_2^+})(\sqrt{\gamma_1^-} - \sqrt{\gamma_2^-})$$

So:

$$\Delta G_{121} = -2(\sqrt{\gamma_1^{LW}} - \sqrt{\gamma_2^{LW}})^2 - 4(\sqrt{\gamma_1^+} \cdot \sqrt{\gamma_1^-} + \sqrt{\gamma_2^+} \cdot \sqrt{\gamma_2^-} - \sqrt{\gamma_1^+} \cdot \sqrt{\gamma_2^-} - \sqrt{\gamma_1^-} \cdot \sqrt{\gamma_2^+})$$

where γ^+ and γ^- are electron-acceptor and electron-donor parameters of the surface tension of substances 1 and 2.

The γ_{12} , γ_{12}^{LW} , γ_{12}^{AB} , γ^+ , γ^- , and ΔG_{121} values for different dextran-solvent pairs are reported in Table 2.

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