Solution Properties of Dextran in Water and in Formamide

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ABSTRACT: We investigate here solution properties of the common polysaccharide dextran (with various molecular weight fractions: T70, T110, T500, and T2000) in aqueous and in formamide solutions at 20°C and 40°C, as obtained from viscosity measurements. Dextran behaves as a random coil in water and formamide solutions on the basis of the Mark-Houwink-Sakurada constant being in the range $0.5 < \alpha < 0.8$ and the molecular weight dependence of the hydrodynamic coil radius, $R_{coil} \sim M_W^{1/2}$. Dextran segments interact more favorably with the formamide solvent molecules than with water, as attested by higher intrinsic viscosity, R_{coil}, and hydrodynamic expansion factor α_η values in formamide compared to aqueous solutions. This can be attributed to formamide offering more readily available sites ($C=O$ and NH_3) to form hydrogen bonds with dextran. Apparently the stronger cohesive forces (reflected in higher surface tension σ and solubility parameter δ values) between water molecules make it harder for dextran to break them, thus the dextran coils swell less in this medium. As the temperature increases from 20°C to 40°C, dextran is driven toward theta conditions in both water and formamide solutions. Upon heating, the polymer segments interact less with the solvent molecules and adopt a less expanded conformation in the solution; the solvent quality decreases, and the coils contract. © 2012 Wiley Periodicals, Inc. J Appl Polym Sci 125: 1681–1692, 2012

Key words: water-soluble polymers; polysaccharides; viscosity; solution properties

INTRODUCTION

Water soluble polymers have received significant attention due to their use in pharmaceutics, food and drinks, cosmetics, detergents, coatings, and paints.[1,2] Poly(ethylene oxide) and polysaccharides are examples of water soluble polymers.[3–9] The solubility of these polymers in aqueous media has been explained in terms of strong hydrogen bonding between these compounds and water molecules. Polysaccharides are often used as rheology modifiers due to their association behavior. Such association is ascribed to the hydroxyl or amino groups present in these macromolecules, which easily undergo hydrogen bonding.

Dextran is a well-studied polysaccharide[10] that finds several applications in the food,[11,12] cosmetics, pharmaceutical,[13] coatings and paint, photographic, and agricultural industries. Dextran is biocompatible,[14] biodegradable[12] and is safe for human consumption. Therefore, dextran is also suitable for clinical research. Dextran molecules have two types of ether oxygens, one that is located between repeating units and the other in the ring next to the three hydroxyl groups (see Fig. 1). Consequently, dextran molecules have the ability to form hydrogen bonds intramolecularly and with polar solvents.[15] Dextran is soluble in water, methyl sulfoxide, formamide, ethylene glycol, and glycerol.[10] Senti et al.[16] and Ioan et al.[17] have observed that higher molecular weight dextran fractions do not follow the scaling exponents expected for linear polymers and concluded that these fractions are branched.

In this work we investigate the solution behavior of dextran in water and formamide using viscosity measurements. Dextran solutions behave as Newtonian fluids.[12,18] Dilute solution viscometry can provide information about polymer-polymer interactions and polymer solvent interactions.[19] Because of its simplicity, viscometry has proven to be an attractive method for studying polymer structure in connection with solvent properties and has also been used for biopolymers[20] and polymer-surfactant mixtures.[21] Dextran has been relatively well investigated in aqueous solutions.[15,17,18,22–25] Yet, there are only a few studies of different molecular weight dextran fractions in water,[16,22] and even fewer data reported on dextran solutions in formamide. In fact, to the best of our knowledge, this is the first time that data are reported for high molecular weight dextran in formamide.

The presentation of our work is organized as follows. We start from the dilute solution regime and
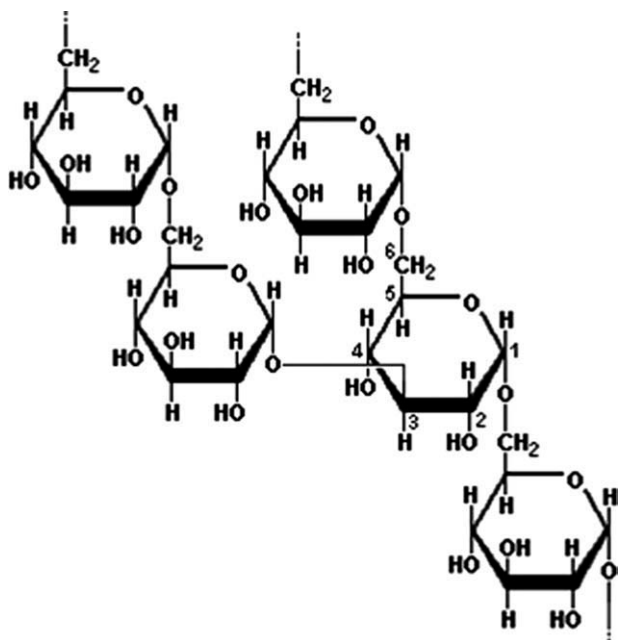
Figure 1 Chemical structure of a dextran fragment composed of α-(1-6)-linked glucose units, branched by α-(1-3)-linked glucose units.

obtain the intrinsic viscosity, $[\eta]$, for dextran of different molecular weights in water and in formamide, at two different temperatures. These results are used to determine the Mark-Houwink characteristic constants and the unperturbed dimensions of dextran. We then proceed to analyze the dilute regime viscosity data in order to extract the hydrodynamic coil radius and the overlap concentration starting from the Einstein viscosity relation. The polymer–solvent interactions are then discussed in terms of solvent molecule structure.

EXPERIMENTAL

Materials

Dextran is a polysaccharide consisting of α-(1-6)-linked glucose units that are branched by α-(1-3)-linked glucose units as shown in Figure 1. The various dextran fractions used in this work were purchased from Amersham Biosciences AB (now part of GE

TABLE I
Molecular Weight of Dextran Fractions Examined in This Study

T70	70,000	46,800
T110	110,000	74,000
T500	500,000	191,500
T2000	2,000,000	360,125

Healthcare, Uppsala, Sweden) and Pharmcosmos A/S (Holbaek, Denmark). Dextran fractions with various molecular weights are derived from the partial acid hydrolysis of native dextran. Here we consider the T70, T110, and T500 dextran fractions, with weight average (M_w) and number average (M_n) molecular weights, reported by the manufacturer, listed in Table I. Also dextran T2000, the M_n of which (Table II) was estimated by using the Mark-Houwink equation and constants determined in this work. Water and formamide were used for preparing dextran solutions. The water was purified with a Milli-Q system. Formamide (molecular biology grade) was purchased from VWR International (West Chester, PA). Dextran samples were prepared individually for every concentration by dissolving appropriate amount of polymer in a given solvent. The samples remained under stirring for at least one day at room temperature and then equilibrated at 20°C or 40°C for at least 1 h before measurements were conducted at the same temperature.

Methods

The solution properties of dextran were assessed by viscosity measurements. The viscosity of dextran T70, T110, T500, and T2000 fractions in water and in formamide was determined using Cannon Fenske Routine type viscometers[26] for transparent Newtonian fluids. Aqueous dextran solutions exhibit Newtonian flow characteristics up to 30 wt %[12,18,25]; 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 placed inside a constant temperature bath to ensure that the measurements were taken under constant temperature (controlled to within ±0.1°C). All polymer solutions were examined at both 20°C and 40°C.

TABLE II
Nomenclature Used in This Study

Kinematic viscosity of the solvent	η_o	mPa·s or cSt
Kinematic viscosity of the solution	η	mPa·s or cSt
Relative viscosity	$\eta_{rel} = \eta/\eta_o$	dimensionless
Specific viscosity	$\eta_{sp} = \eta_{rel} - 1 = (\eta - \eta_o)/\eta_o \sim (t - t_o)/t_o$	dimensionless
Reduced viscosity	$\eta_{red} = \eta_{sp}/C$	dL/g
Intrinsic viscosity	$[\eta] = (\eta_{sp}/C)_{C\to 0} = [\ln(\eta_{rel})/C]_{C\to 0}$	dL/g
Solution concentration	C	g/dL
Solvent efflux time	t_o	sec
Solution efflux time	t	sec

The efflux times were reproducible to $\pm$ 0.1% (each measurement was repeated three times) and were measured with an accuracy of $\pm$ 0.1 s. The kinematic viscosity η see Table II for definitions) has been calculated by multiplying the efflux time with the viscometer calibration constant (supplied by the manufacturer, Cannon Instrument Co., State College, PA).

RESULTS

Intrinsic viscosity vs. polymer molecular weight

The intrinsic viscosity, [η], is a characteristic property for a polymer molecule dissolved in a certain solvent.[19] [η] increases with molecular weight, and depends on the polymer structure and conformation as well as on the solvent quality and temperature. The magnitude of [η] is a measure of the effective hydrodynamic volume of the polymer in the solution. It also reflects hydrogen bonding, dipole–dipole, hydrophobic interactions, and complexation ability of the polymer in the presence of different additives.[27]

[η] values of dextran have been determined using the Huggins (1) and Kramer (2) equations[19,28] by plotting η_{sp}/C and $\ln(\eta_{rel})/C$ (only the concentrations that give η_{rel} in the range of 1.1–1.6 are used), respectively, against the polymer concentration, and subsequent extrapolation to zero concentration (infinite dilution). As shown in Figure 2, a straight line is obtained with [η] being the intercept, and $k'[\eta]^2$ or $k''[\eta]^2$, respectively, being the slope.

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

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

k' and k'' are the Huggins and Kramer constants, respectively, and C the concentration (g/dL) of the polymer solution. Definitions and units of the various viscosity terms are given in Table II.

The intrinsic viscosity values for the four dextran homologs in water and formamide at 20°C and 40°C, calculated using the Huggins (1) and Kramer (2) equations, as well as the Huggins and Kramer constants, are presented in Table III. On the basis of the [η] values we can extract the constants of the Mark-Houwink-Sakurada equation, the unperturbed coil dimensions, the hydrodynamic coil radius, and the overlap concentration of dextran. These are discussed below.

The intrinsic viscosity values of dextran in water increase threefold, from 0.236 to 0.681, as the molecular weight increases from T70 to T2000 (Table III). The dependence of intrinsic viscosity on molecular weight for a given polymer series can be described by the Mark-Houwink-Sakurada equation [eq. (3)].[19]
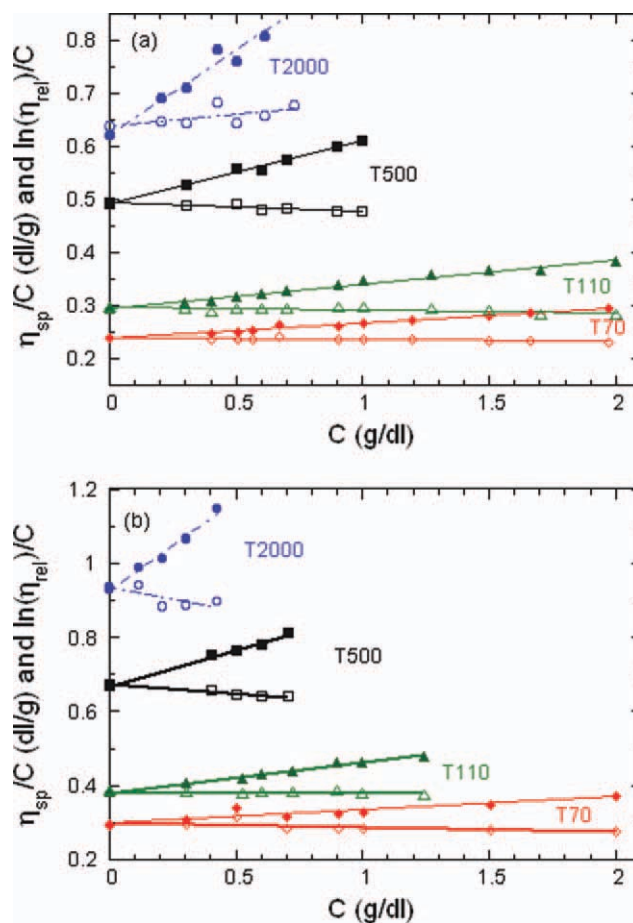

Figure 2 Specific viscosity (filled symbols) and log of relative viscosity over concentration (open symbols) plotted (and linearly fitted) vs. concentration in (a) water and (b) formamide of all dextran molecular weights examined at 20°C (◆: T70, ▲: T110, ■: T500, ●: T2000). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

When the logarithm of the intrinsic viscosities of a series of polymer homologs is plotted versus the logarithm of their molecular weights, linear relationships are typically obtained (see Fig. 3), with the intercept being the logarithm of the constant K and the slope being the value of constant α.[19,28]

$$[\eta] = K\,M^{\alpha} \qquad (3)$$

where M can either be the number average, M_n, or weight average, M_w, molecular weight of the polymer in solution (in this work we use M_n), and K and α are constants for a specific polymer-solvent pair at a particular temperature. α varies from 0 to 2 and is equal to 0.5 for a Flory θ solvent.[28] The values of the Mark-Houwink-Sakurada constants, K and α, for dextran in water and formamide at 20°C and 40°C are reported in Table IV. In both solvents the α values fall in the range $0.5 < \alpha < 0.8$, expected for polymer coils in good solvents.[19,28] Small angle X-ray

TABLE III
Intrinsic Viscosity [η], Huggins Constant k', Kramer Constant k'', Coil Radius R_{coil}, Coil Volume V_{coil}, and Overlap Concentration C^*, Determined by Huggins and Kramer Equations for Various Dextran Molecular Weights in Water and Formamide at 20°C and 40°C

Solvent	Dextran	$[\eta]_H$ (dL/g)		k'		R_{coil} (nm)		V_{coil} ($10^3 \times nm^3$)		C^*	
		20°C	40°C	20°C	40°C	20°C	40°C	20°C	40°C	20°C	40°C
Huggins equation											
Water	T70	0.236	0.222	0.535	0.417	6.4	6.3	1.1	1.0	10.6	11.2
Water	T110	0.295	0.275	0.520	0.606	8.0	7.8	2.2	2.0	8.5	9.1
Water	T500	0.491	0.457	0.495	0.597	15.7	15.4	16.3	15.1	5.1	5.5
Water	T2000	0.681	0.639	0.461	0.576	27.9	27.3	90.5	84.8	3.7	3.9
Formamide	T70	0.292	0.262	0.453	0.537	6.9	6.6	1.4	1.2	8.6	9.5
Formamide	T110	0.382	0.363	0.558	0.457	8.7	8.6	2.8	2.7	6.5	6.9
Formamide	T500	0.669	0.591	0.441	0.493	17.4	16.7	22.2	19.6	3.7	4.2
Formamide	T2000	0.932	0.827	0.421	0.523	30.9	29.7	123.8	109.9	2.7	3.0
Kramer equation											
Water	T70	0.239	0.223	0.057	0.109	6.4	6.3	1.1	1.0	10.4	11.2
Water	T110	0.297	0.278	0.057	0.008	8.0	7.9	2.2	2.0	8.4	9.0
Water	T500	0.496	0.463	0.075	0.019	15.8	15.4	16.5	15.4	5.0	5.4
Water	T2000	0.704	0.618	0.103	0.004	28.0	27.0	91.7	82.0	3.6	4.0
Formamide	T70	0.294	0.265	0.102	0.051	6.9	6.7	1.4	1.2	8.5	9.4
Formamide	T110	0.386	0.366	0.036	0.098	8.8	8.6	2.8	2.7	6.5	6.8
Formamide	T500	0.675	0.598	0.110	0.083	17.5	16.8	22.4	19.9	3.7	4.2
Formamide	T2000	0.939	0.836	0.124	0.066	31.0	29.8	124.7	111.1	2.7	3.0

scattering (SAXS) measurements also confirm that dextran behaves as random coil in water and formamide solutions at room temperature, since the data in both cases have been adequately fitted by the random coil form factor.[29] Mark-Houwink-Sakurada constants for dextran in formamide have been previously reported only by Wales et al.[22] at a single temperature (25°C) for fractions with $M_w < 250,000$. Aqueous dextran solutions have attracted more attention in the literature and K and α values have been reported by Senti et al.[16] and Guner.[15] The K and α constants reported here for the aqueous dex-

tran system compare well with the values reported by Guner.[15] A value of α ≈ 0.5 has been reported by Senti et al.[16] for dextran fractions having molecular weights below 100,000. Above this molecular weight, α was found to decrease,[16] suggesting branching in the dextran fractions, since a branched polymer molecule adopts a reduced spatial extension that consequently decreases its intrinsic viscosity. Once K and α are known for a given polymer-solvent system, the polymer molecular weight can be estimated from viscosity measurements.[30] The M_n value for the dextran T2000 fraction reported in Table I has been estimated from the Mark-Houwink-Sakurada equation that we obtained for dextran in water at 20°C, $[\eta] = 8.525 * 10^{-4} M_n^{0.522}$.

The [η] values for the dextran-formamide solutions are higher (by 24 to 37%) compared to the aqueous solutions. Also the exponent α for dextran in formamide, 0.567, is higher than that in water, 0.522. K values are higher for dextran in water, 8.525×10^4 (dL/g), compared to formamide, 6.605×10^4 (dL/g), at 20°C. The temperature increase from 20°C to 40°C decreases the [η] values up to 12%, with the
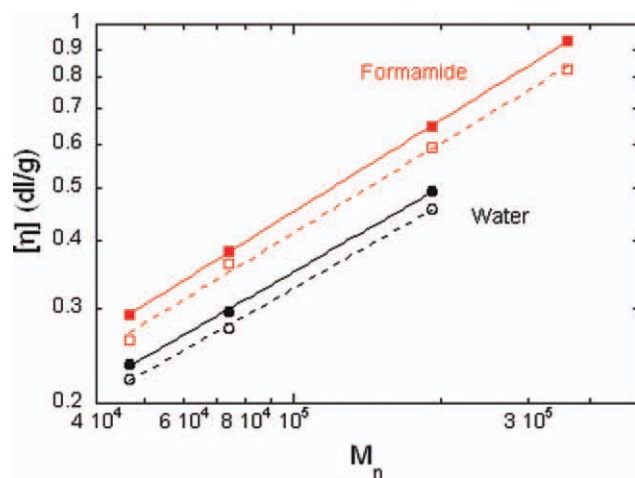

Figure 3 Double logarithmic plot of [η] versus M_n for dextran in water (○) and formamide (□) at 20°C (filled symbols) and 40°C (open symbols). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE IV
Mark-Houwink-Sakurada Constants for Dextran in Water and in Formamide at 20°C and 40°C

Solvent	T (°C)	$K \times 10^4$ (dL/g)	α
Water	20	8.525	0.522
Water	40	8.761	0.514
Formamide	20	6.605	0.567
Formamide	40	7.102	0.553

higher molecular weight dextran fractions affected more considerably than the lower ones. The solvent effect on the dextran $[\eta]$ value is more significant than the temperature effect. The higher temperature causes a decrease in α from 0.522 to 0.514 and from 0.567 to 0.553, for the water–dextran T500 and the formamide–dextran systems, respectively (see Table IV). K values increase with temperature for both solvents.

The Huggins k' and Kramer k'' constants are characteristic for a given polymer-solvent system and can provide information about interactions between polymer molecules.[19] In polymer solutions without strong association, the Huggins constant values typically range from 0.3 to 0.8.[19] In good solvents, the value of Huggins constant for polymer molecules is expected to be about 0.35 (although significant variation is pos-

TABLE V
Short and Long Range Parameters, k_o and B, for Dextran in Water and in Formamide at 20°C and 40°C

Solvent	T (°C)	KSF		Berry	
		$k_o \times 10^4$ (dL/g)	$B \times 10^{30}$	$k_o \times 10^4$ (dL/g)	$B \times 10^{30}$
Water	20	10.60	0.840	10.37	1.097
Water	40	10.00	0.056	9.99	0.033
Formamide	20	15.14	4.669	14.82	2.061
Formamide	40	12.53	1.867	12.42	0.965

sible). In this work, we obtained k' values in the range 0.421–0.558 (Table III). k'' is negative and smaller in magnitude than k'.[19] Theoretically the sum of k' and k'' is 0.5. Subtracting eq. (2) from eq. (1):

$$(\eta_{sp} - \ln \eta_{rel})/[\eta]^2 c^2 = k' + k''$$

and substituting $\ln(\eta_{rel})$ with: $\left. \begin{array}{l} \ln(\eta_{rel}) = \ln(\eta_{sp} + 1) \approx \eta_{sp} - \eta_{sp}^2/2 + \cdots \\ \\ \text{Also } [\eta_{sp}/c]_{C \to 0} = [\eta] \end{array} \right\} k' + k'' = 0.5 \quad (4)$$

The sum $k' + k''$ for each of the different dextran homologs in water is found to be approximately constant and equal to 0.57 at 20°C and to 0.60 at 40°C. In the case of formamide solutions, this sum is 0.55 at 20°C and 0.58 at 40°C.

According to Flory,[19] k' is approximately constant for a series of polymer homologs in a given solvent. Here k' varied by about 20% with molecular weight. The data from the literature concerning the variation of k' with polymer molecular weight are often contradictory. In some cases, the value of k' is reported constant, and in others variable. We note that k' and k'' values are affected more by possible experimental error than the intrinsic viscosity values.[31] A decrease of k' indicates a decrease in the polymer association and is a measure of polymer-solvent interaction[27]; an increase of k' indicates intramolecular association.[32] In this work we did not observe any clear correlation between k' or k'' and coil dimensions that would provide us insight on molecular interactions in the two solvents. We note though that the k' values that we have obtained for dextran (similarly to the k' values reported by Senti et al.[16]) are higher than those found for linear polymers. Senti et al. attributed this to the branched nature of the dextran molecules.

Unperturbed coil dimensions

When a polymer chain assumes the so-called random walk conformation, its overall dimensions are

determined solely by bond lengths and angles. This state prevails in theta solvents for a given polymer at a specific temperature. Several parameters that characterize the unperturbed state can be calculated by utilizing the experimentally determined intrinsic viscosity data of different dextran fractions at different temperatures and employing the two extrapolation methods of Kurata-Stockmayer-Fixman (KSF) [eq. (5)] and Berry [eq. (6)].[19]

$$[\eta]M^{-1/2} = k_0 + 0.51 \, B\Phi_0 M^{1/2} \quad (5)$$

$$[\eta]^{1/2}M^{-1/4} = k_0^{1/2} + 0.42 \, k_0^{1/2} B\Phi_0 M[\eta]^{-1} \quad (6)$$

$$k_0 = [\eta]_\Theta/M^{1/2} = \Phi_0(<r^2>_0/M)^{3/2} \quad (7)$$

where k_o is a parameter that describes short-range interactions between units of the polymer chain (very near one another in sequence), depends on properties of the polymer molecule alone (i.e., bond dimensions, angles) and temperature,[33] and represents the value of the Mark-Houwink-Sakurada constant K at the theta temperature[19]; B is a parameter that depicts long-range interactions between pairs of polymer elements (remote from each other in the sequence along the chain) and depends on the polymer molecule chemistry and its environment; $[\eta]_\Theta$ is the intrinsic viscosity at theta temperature; $<r^2>_o^{1/2}$ is the root mean square end-to-end distance of a polymer chain in a solvent; and Φ_o is Flory's universal constant, $\Phi_o = 2.1*10^{23} \, mol^{-1}$.

TABLE VI
Square Root End-to-End Distance, $<r^2>_o^{1/2}$, Intrinsic Viscosity at Theta Temperature, $[\eta]_\Theta$, Hydrodynamic Expansion
Factor, α_η, and Intrinsic Viscosity, $[\eta]_H$, Calculated for Dextran Fractions in Water and Formamide at 20°C and 40°C,
Using the KSF (5) and Berry (6) Equations

		KSF			Berry			
M	T (°C)	$<r^2>_o^{1/2}$ (nm)	$[\eta]_\Theta$	α_η	$<r^2>_o^{1/2}$ (nm)	$[\eta]_\Theta$	α_η	$[\eta]$
Water								
T70	20	3.7	0.231	1.008	3.7	0.231	1.008	0.236
T100	20	4.7	0.290	1.006	4.6	0.290	1.006	0.295
T500	20	7.5	0.467	1.017	7.5	0.467	1.017	0.491
T2000	20	17.8	0.640	1.021	17.7	0.640	1.021	0.681
T70	40	3.6	0.223	0.999	3.6	0.224	0.998	0.222
T110	40	4.6	0.281	0.994	4.6	0.281	0.993	0.275
T500	40	7.4	0.451	1.004	7.4	0.452	1.004	0.457
T2000	40	17.4	0.619	1.011	17.4	0.620	1.010	0.639
Formamide								
T70	20	4.2	0.293	0.998	4.2	0.293	0.999	0.292
T100	20	5.3	0.369	1.012	5.2	0.368	1.013	0.382
T500	20	8.5	0.593	1.031	8.4	0.592	1.031	0.669
T2000	20	20.0	0.814	1.046	19.9	0.812	1.047	0.932
T70	40	3.9	0.269	0.992	3.9	0.269	0.991	0.262
T110	40	4.9	0.338	1.024	4.9	0.339	1.023	0.363
T500	40	7.9	0.543	1.029	7.9	0.545	1.028	0.591
T2000	40	18.8	0.745	1.036	18.8	0.747	1.034	0.827

According to eq. (5), a plot of $[\eta] M_n^{-1/2}$ versus $M_n^{1/2}$ leads to a straight line, with intercept $= k_o$ and a slope that is characteristic of polymer-solvent interactions. Using Berry's eq. (6), a plot of $[\eta]^{1/2} M_n^{-1/4}$ versus $M_n [\eta]^{-1}$ yields a straight line with intercept $= k_o^{1/2}$, and a slope that is also characteristic of polymer-solvent interactions. k_o and B values for dextran in formamide and water at 20°C and 40°C are reported in Table V. Following the calculation of k_o, we can determine the $[\eta]_\Theta$ and $<r^2>_o^{1/2}$ values via eq. (7). Using these $[\eta]_\Theta$ values, the

Figure 4 $<r^2>_o^{1/2}$ increases exponentially with M_W. The scaling exponent is 0.45 and appears independent of solvent type and temperature [dextran in water (○) and formamide (□), at 20°C (filled symbols) and 40°C (empty symbols)]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

hydrodynamic expansion factor, α_η, can be obtained from eq. (8). $[\eta]_\theta$, α_η, and $<r^2>_o^{1/2}$ data for dextran in water and formamide at 20°C and 40°C are reported in Table VI.

$$[\eta] = [\eta]_\Theta \, \alpha_\eta^3 \qquad (8)$$

Knowledge of the parameters that characterize the unperturbed state of a polymer in a solvent can help us evaluate the solvent quality at specific conditions. For example, the closer the polymer coil dimensions are to its unperturbed dimensions, the more the solvent behaves as a theta solvent.

The hydrodynamic expansion factor (α_η) values (Table VI) are close to 1, denoting that both water and formamide are theta rather than good solvents (at theta conditions $\alpha_\eta = 1$). α_η values (Table VI) are bigger for the higher M_w dextran homologs than the low M_w ones, e.g., in water at 20°C, a molecular weight increase from 70,000 to 2×10^6 causes α_η to increase from 1.0075 to 1.0209. So the coil is more expanded from their unperturbed dimensions in the case of higher M_w. $[\eta]_\Theta$ values increase threefold from 0.23 to 0.64 dL/g upon molecular weight increase and $<r^2>_o^{1/2}$ values increase fivefold from 3.7 to 17.8 nm. $<r^2>_o^{1/2}$ increases with M_W exponentially (as shown in Fig. 4) with a 0.45 exponent that is independent of solvent and temperature, similar to the exponent reported by Senti et al.[16] (see further discussion in the "Hydrodynamic coil dimensions" section below). The unperturbed state parameters
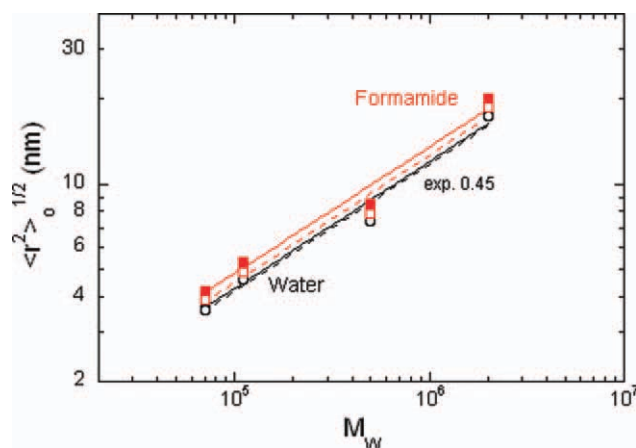
$[\eta]_\Theta$ and $<r^2>_o^{1/2}$ of dextran in water or in formamide are similar for both solvents. A temperature variation from 20° to 40°C did not affect the unperturbed dimensions of the dextran fractions.

The dextran-water system at 20°C has a short range interaction parameter k_o value of 10.60×10^{-4} (dL/g) and the dextran-formamide system 15.14×10^{-4} (dL/g) (Table V). The higher k_o value in formamide could be related to the influence of this solvent on the short range interactions and the flexibility of the dextran chains. The temperature increase from 20°C to 40°C does not change the k_o value for water, indicating that water is a proper theta solvent, while in formamide k_o decreases from 15.14×10^{-4} to 12.53×10^{-4}, indicating a solvent effect that is influenced by temperature. It is worth comparing the Mark-Houwink-Sakurada constants, K, for these systems to k_o that represents the same quantity at θ-conditions [compare eq. (4) with eq. (7)]. K for water at 20°C, 8.53×10^{-4} (dL/g), has a value relatively close to the k_o value, 10.60×10^{-4} (dL/g), whereas
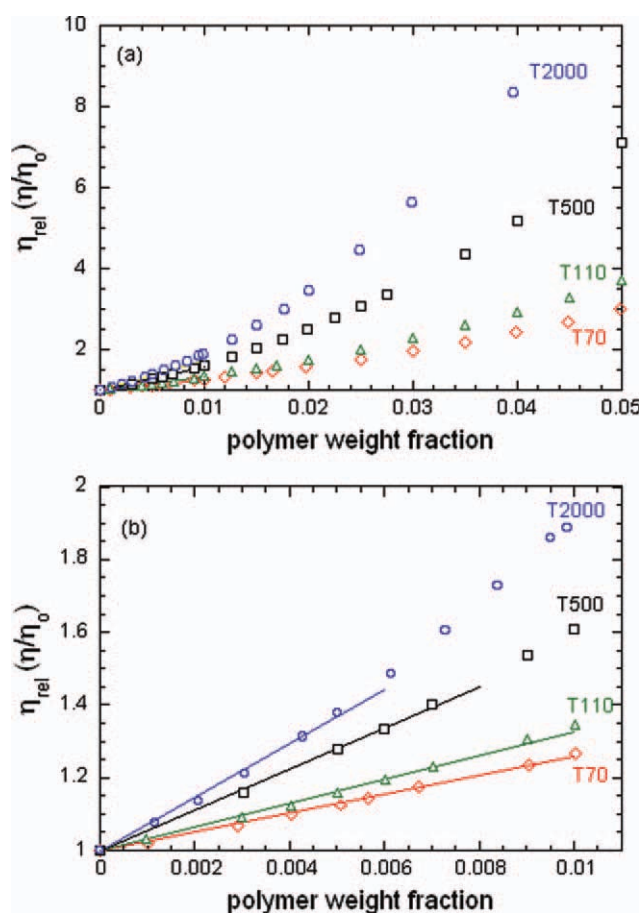

Figure 5 Relative viscosity, η_{rel}, plotted against the (dry) weight fraction of dextran T70 ($\diamond$), T110 ($\triangle$), T500 ($\square$), and T2000 ($\bigcirc$) in water at 20°C: (a) whole concentration range examined; (b) dilute regime. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 6 Relative viscosity, η_{rel}, plotted against the (dry) weight fraction of dextran T70 ($\diamond$), T110 ($\triangle$), T500 ($\square$), and T2000 ($\bigcirc$) in formamide at 20°C: (a) whole concentration range examined; (b) dilute regime. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
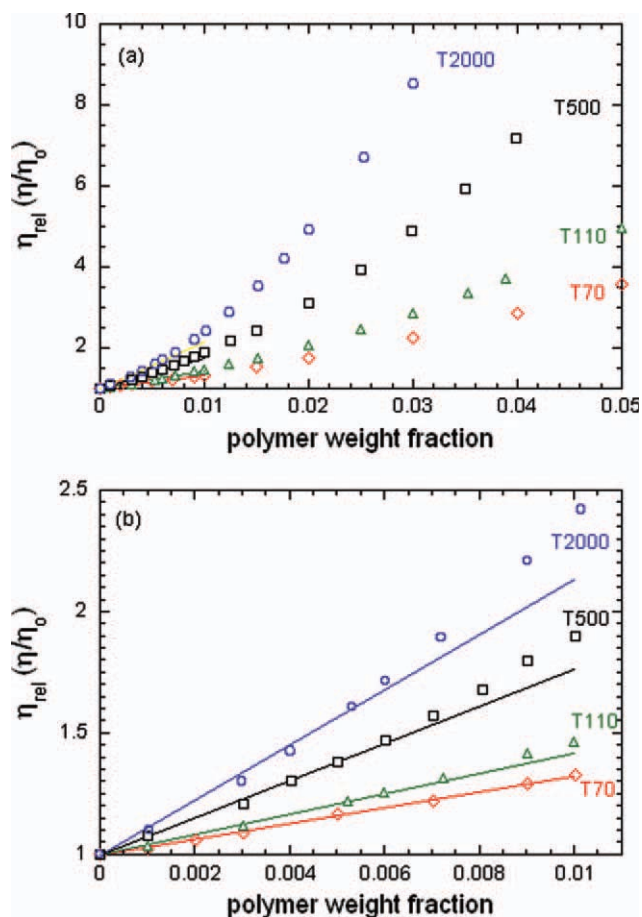
the K for formamide solutions at the same temperature, 6.61×10^{-4} (dL/g), is much lower than k_o, 15.14×10^{-4} (dL/g). The Mark-Houwink-Sakurada constant K for dextran in water increases with temperature from 8.53×10^{-4} to 8.76×10^{-4} (dL/g), approaching the short range interaction parameter k_o value 10.60×10^{-4} (dL/g).[23]

Hydrodynamic coil dimensions

The increase in viscosity caused by a dilute dispersion of uniform, rigid non-interacting spheres having volume fraction Φ, can be expressed by the Einstein viscosity relation:[26,28]

$$\eta = \eta_0 \, (1 + 2.5\Phi) \tag{9}$$

Equation 9 is applicable when the density and the viscosity of the fluid are constant and the flow velocity is low, with no slippage of the liquid at the surface of the spheres. The spheres should to be
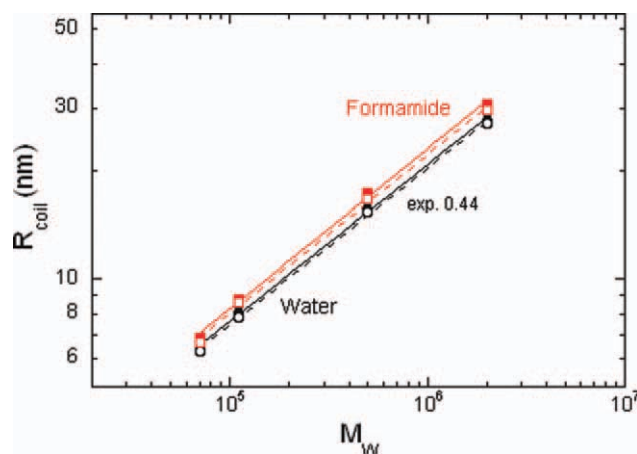
Figure 7 R_{coil} increases exponentially with M_W. The scaling exponent is 0.44 and appears independent of solvent type and temperature [dextran in water (○) and formamide (□), at 20°C (filled symbols) and 40°C (empty symbols)]. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

large enough compared to the solvent molecules to permit us to treat the solvent as a continuum, but small enough compared to the dimensions of the viscometer so as to ignore wall effects. These size restrictions make the Einstein equation very applicable to particles in the colloidal size range, which include polymer coils.[26,28] Relative viscosity data for dextran solutions in water and formamide are plotted in Figures 5 and 6, respectively, versus the (dry) polymer weight fraction. As expected, the η_{rel} values of dextran solutions of a given polymer concentration increase as the molecular weight of dextran increases (i.e., for the 0.04 weight fraction samples of the dextran T70, T110, T500 and T2000 fractions in water at 20°C, the relative viscosity increases from 2.5 to 8.5).

The connection between the weight fraction of the (dry) polymer and the volume fraction occupied by the solvent-swollen polymer coils (assuming them to be spherical and non-interacting, below the overlap concentration) allows us to apply the Einstein viscosity relation [reorganized into eq. (10)] to estimate the radius of the dextran coils.

$$[\eta_{sp}/C]_{C \to 0} = 2.5 \Phi / C \qquad (10)$$

We first need to introduce the volume of the spherical particles (polymer coils) in eq. (10) in order to determine their radius. This is done by substituting $\Phi = V_p/V_{tot}$, where V_p is the volume of all the (solvated) polymer molecules and V_{tot} is the total volume of the solution. $V_p = N_{AV} \cdot n_p \cdot V_{coil}$, where n_p = number of polymer moles, N_{AV} = Avogadro's number, and V_{coil} = volume per polymer coil. Finally $n_p = m_p/M_w$ and $C = m_p/V_{tot}$, where m_p =

polymer mass (g) and M_w = polymer molecular weight (g/mol). Rearranging eq. (10) we obtain:

$$[\eta] = 2.5 N_{AV} \cdot V_{coil}/M_w \text{ (dL/g)} \qquad (11)$$

$V_{coil} = (4/3)\pi R_{coil}^3$, so the effective radius of a polymer coil, R_{coil}, called hydrodynamic coil radius in this work, equals:

$$R_{coil} = [3[\eta] \cdot M_w/10\pi \cdot N_{AV}]^{1/3} \text{ (cm)} \qquad (12)$$

The calculated R_{coil} and V_{coil} values for all dextran fractions in water and in formamide are reported in Table III. The coil radius increases significantly with dextran molecular weight, from 6.4 to 27.9 nm in water and from 6.9 to 30.9 nm in formamide. In fact, the dependence of R_{coil} on polymer molecular weight is exponential, $R_{coil} \sim M_W^{0.44}$ independently of the solvent type and temperature considered here (see Fig. 7). The same dependence is obtained by R_{coil} data provided by the dextran supplier Amersham Biosciences and data reported by Ioan et al.[17] The Flory theory leads to a universal power law dependence of the polymer coil size R on the number of monomers N: $R \sim N^v$. An $R \sim M^{1/2}$ relationship (M is proportional to N for linear polymers) denotes polymer coils in theta solvents, while $R \sim M^{3/5}$ describes swollen polymer coils in good solvents.[34] In both water and formamide solutions, the dextran coils obey the $R_{coil} \sim M_W^{1/2}$ equation indicative of theta solvent, but with a somewhat smaller exponent, 0.44, which can be attributed to the branching of the dextran molecules. Note that the exponent in the relationship $<r^2>_o^{1/2} \sim M_W^{0.45}$ (Fig. 4) is the same as that followed by the R_{coil} dependence on molecular weight; this is reassuring since these two coil dimensions have been calculated by different methods. The root mean square end-to-end distance dependence on molecular weight $<r^2>_o^{1/2} \sim M_W^{0.43}$ reported by Senti et al.[16] for dextran in water is also consistent with our findings. The R_{coil} of a specific dextran fraction is greater in formamide than in water. A 20 degree increase in temperature decreased slightly the dextran R_{coil} for both solvents (Table III).

Overlap concentration

In θ-solvent systems polymer coils retain their unperturbed dimensions. For dilute solutions in good solvents the coils are expanded, with the coil dimensions varying from one solvent to another depending on the thermodynamics of mixing. As the polymer concentration increases the coils come to contact and contract. At high polymer concentrations the coil dimensions approach their unperturbed values, and the effects of chain entanglement become important. Three distinct concentration regimes of a
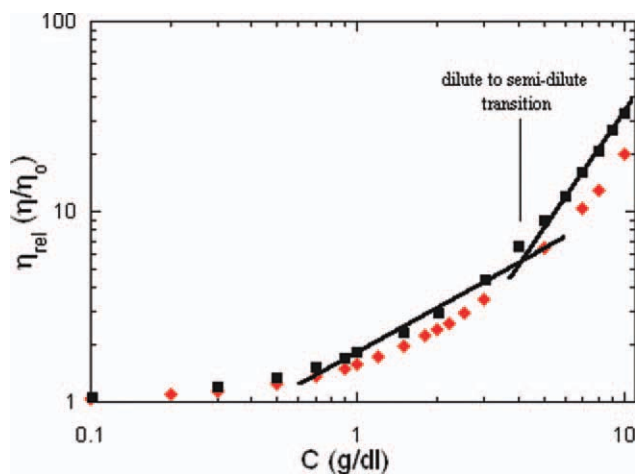
Figure 8 Relative viscosity plotted against concentration for dextran T500 solutions in water (◆) and formamide (■) at 20°C. The arrow indicates the C^*. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
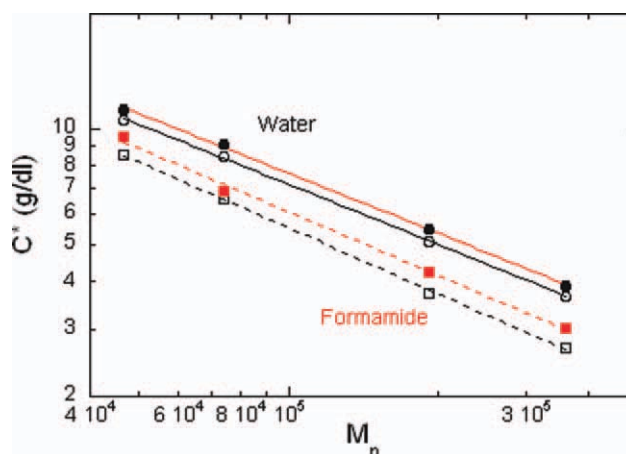

Figure 9 C^* decreases exponentially with M_n for dextran dissolved in water (○) and formamide (□), respectively, at 20°C (empty symbols) and 40°C (filled symbols). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

polymer solution have been suggested[35,36]; dilute (individual polymer molecules in a bath of solvent), semidilute, and concentrated. The crossover from the dilute to the semidilute regime, where the coils begin to overlap and become entangled with each other resulting in a more rapid rise in viscosity (see Fig. 8), defines the overlap concentration C^*.[35–37] The crossover is not sharp; it is rather a transition region between regimes. According to de Gennes,[35] C^* is comparable with the local concentration of polymer inside a single coil. At the polymer concentration where coils overlap, they fill the whole volume of the solution, so the volume fraction of (swollen) coils approaches 1. The overlap concentration is given by eq. 13, considering that at the point of coil overlap $V_{tot} = V_p = n_p N_{AV} V_{coil}$ and substituting $n_p = m_p/M_w$.

$$C^* = m_p/V_{tot} = n_p M_w/n_p N_{AV} V_{coil} = M_w/N_{AV} V_{coil} \tag{13}$$

$$C^* = M_w/(N_{AV}(4\pi/3)R_{coil}^3) \tag{14}$$

The overlap concentration C^* can be related to the intrinsic viscosity, by assuming that each polymer

coil in the dilute solution contributes to the zero-shear viscosity in a manner similar to that of a hard sphere with radius equal to the radius of gyration of the coil.[37] Substituting eq. (11) in eq. (13) we obtain:

$$C^* = 2.5/[\eta] \tag{15}$$

C^* can also be estimated by plotting η_{rel} vs. C and calculating the point at which the linear fits of the η_{rel} data in the dilute and the semidilute regimes intersect, as shown in Fig. 8. In this work, we estimate C^* (reported in Table III) using eq. (15) since this is less subjective than the intercept method; however both methods give consistent results.

Using the Mark-Houwink-Sakurada equation and substituting with $[\eta] \approx 2.5/C^*$, we can obtain a relationship (eq. 16) that describes the C^* dependence on M_n[36]:

$$C^* \sim M_n^a \tag{16}$$

The exponent a of eq. (16) equals -0.8 for good solvents and -0.5 for theta solvents.[36] In this work we found -0.52 for the dextran-water and -0.57 for the dextran-formamide systems (see Fig. 9). The exponent a has the same absolute value as the

TABLE VII
Physicochemical Properties of Solvents Used in This Work

Solvent	μ^a(25°)	ε_T (20°C)	σ^b(20°C)	E_T^N (25°)	log P (25°)	δ^c	δ_D^c	δ_P^c	δ_H^c
Formamide	11.2	109	58.5	0.799	−1.51	36.7	17.2	26.2	19.0
Water	5.9	78.5	70	1.000	−1.40	47.8	15.5	16.0	42.3

$^a 10^{-30}$C m.
^{b} mN/m.
^{c} MPa$^{1/2}$.

Mark-Houwink-Sakurada constant α [eq.(4)], since C^* and $[\eta]$ are connected through the $C^* \approx 2.5/[\eta]$ relationship.

DISCUSSION

Solvent effects

Both water and formamide are protic, hydrogen bonded, strongly associated polar solvents. Relevant solvent properties such as dipole moment μ surface tension σ, and Hildebrand solubility parameters are presented in Table VII.[38,39] Protic solvents are strong hydrogen-bond donors (donor groups: $-O-H$ or $>N-H$) and interact favorably with solutes like dextran which are strong hydrogen-bond acceptors.[40]

The solvent effects on dextran aqueous or formamide solutions are manifested in dextran solution properties such as intrinsic viscosity, $[\eta]$, and coil radius, R_{coil}. We perceive the $[\eta]$ magnitude as evidence for better solvency[19]: the higher the $[\eta]$, the better the solvent. In the presence of formamide, dextran coils swell more than in aqueous solutions at a given temperature. Higher $[\eta]$ values translate in more expanded coils (Table III). For example, the dextran T500 R_{coil} increases from 15.7 nm in water to 17.4 nm in formamide at 20°C, and V_{coil} expands from 16.3×10^3 nm^3 in water to 22.2×10^3 nm^3 in formamide. The Mark-Houwink-Sakurada constant α value of the aqueous dextran solutions, 0.522, is closer to the 0.5 value (denoting theta solvent) than the value of the formamide dextran solutions, 0.567. Similarly, the Mark-Houwink-Sakurada constant K for dextran in water has a higher value, 8.53×10^{-4} (dL/g) than that for dextran in formamide, 6.61×10^{-4} (dL/g). The K value for water is closer to the k_o parameter value describing short range interactions 10.60×10^{-4} (dL/g) at theta conditions. The difference between the K (6.61×10^{-4} (dL/g)) and k_o (15.14×10^{-4} (dL/g)) values of the formamide-dextran system is greater than the difference for the water-dextran system, denoting that formamide is further away from theta conditions than water. The long range interaction parameter B that expresses the magnitude of polymer solvent interactions[15] is larger for the formamide than the water systems. Also the root mean square end-to-end distance, $<r^2>_0^{1/2}$, and hydrodynamic expansion factor, α_η, values are higher for dextran fractions in formamide than in water ($<r^2>_0^{1/2}$ = 8.5 nm and 7.5 nm, and α_η = 1.031 and 1.017 in formamide and water, respectively) (Table VI). In summary, both formamide and water behave more as theta than good solvents, with formamide being somewhat better solvent for dextran than water.

We note that water has higher σ and δ values (both reflecting cohesive forces) than formamide.

Apparently, the stronger the cohesive forces (the bigger the σ and δ values) between the solvent molecules, the harder it becomes for dextran to break them and form hydrogen bonds with the solvent. Thus, dextran segments interact more favorably with formamide molecules than with water.[41–43]

We can further rationalize the R_{coil} difference between the two solvents considering the solvent structure. Liquid water has been described in the literature as a very dense three-dimensional tetrahedral network[44] of water molecules with local order, where each oxygen atom forms hydrogen bonds with four other oxygen atoms through $O-H-O$ bridges.[45] Formamide molecules are linked together by hydrogen bonds formed between the $C=O$ and $N-H$ groups; two hydrogen bonds per molecule form, on average.[46] Liquid formamide consists of a continuous three-dimensional $N-H-O$ hydrogen-bond network.[47] Dextran, when in solution, interacts mainly through hydrogen bonding with the solvent molecules or its own polymer segments.[48,49] The solvent molecules can form hydrogen bonds with the three hydroxyl groups and the ring or bridge-oxygen atoms of dextran. Polymer-solvent interactions and interactions between the polymer segments (hydrogen bonding) happen simultaneously and they compete with each other.[49] In the case of aqueous dextran solutions, the active sites of dextran prefer to interact with each other, given that the H-bonded network that water molecules form is very dense, characterized as the perfect example of hydrogen bonding.[50] As a result, dextran dissolves better in formamide that has additional and more readily available active sites ($C=O$ and NH_3 groups) to form hydrogen bonds, since the H-bonds formed between formamide molecules have sorter lifetime than those among water molecules.[51]

Temperature effects

Homogeneous one-phase polymer solutions often phase separate at a lower temperature (low critical solution temperature, LCST).[28] The theta-point, characterized by the theta temperature, θ, is the threshold where phase separation commences. As the temperature increases, polymer coils contract approaching their unperturbed dimensions. At the theta temperature, the polymer coil volume or intrinsic viscosity is at a minimum because the polymer coil is not swollen by the presence of a solvent (solvent quality drops), and the polymer conformation is only due to its own molecular conformational constraints; the Mark-Houwink constant α equals to 1/2, and the hydrodynamic expansion factor α_η to 1 (in good solvents $\alpha > 1/2$ and $\alpha_\eta > 1$[19]). In dextran solutions, upon a temperature increase from 20 to 40°C, the Mark-Houwink-Sakurada constant, α, decreases

toward the 0.5 value, and the hydrodynamic expansion factor, α_η, also decreases toward the 1 value expected at theta conditions (see Table IV). The α_η decrease is reflected on the R_{coil} and $<r^2>^{1/2}$ values that also decrease (coils contract by 5–10%) as the temperature increases. The drive of both aqueous and formamide dextran systems toward theta conditions can be related to LCST behavior (Güner[15] reported the theta temperature for dextran in water to be 43°C). The Mark-Houwink-Sakurada constant K for dextran in water increases with temperature from 8.53×10^{-4} to 8.76×10^{-4} (dL/g), approaching the short range interaction parameter k_o value 10.60×10^{-4} (dL/g) at 20°C. This is an indication that dextran coils attain a more contracted conformation while temperature increases in both water and formamide solvents.[23] Also the long range interaction parameter B decreased upon temperature increase, indicating that the interactions among dextran and solvent molecules decreased.[15] So upon heating, the intramolecular interactions among dextran segments predominate over the intermolecular interactions between dextran and solvent molecules. Heating has a greater effect on dextran in formamide (for example, the dextran T500 coil volume changed by 12%) than in water (6% coil volume change).

Temperature changes have no significant effects on the structure of water and formamide, rather the hydrogen bonding stability decreases with temperature increase.[45,46] So the contraction of the dextran coils upon heating, from 20 to 40°C, can be attributed to a decrease in the hydrogen bonding interactions between the dextran and solvent molecules.[48,49,52,53] The polymer segments interact less with the solvent molecules, and dextran coils adopt a less expanded conformation in the solution; the solvent quality decreases with temperature increase and the coils contract.

CONCLUSIONS

Dextran is a common polysaccharide that finds many applications and is commercially available in several molecular weights. The solution properties of four dextran fractions (T70, T110, T500, and T2000) in aqueous or formamide solutions at 20°C and 40°C were obtained form viscosity measurements. This is the first time that viscosity data are reported in formamide for this wide range of dextran molecular weights and at different temperatures.

Dextran behaves as random coil in both water and formamide solutions, as attested by the experimentally determined Mark-Houwink-Sakurada constant that is found in the range $0.5 < \alpha < 0.8$, and the unperturbed coil dimensions $<r^2>_o^{1/2}$ and the hydrodynamic coil radius which both scale with the molecular weight as $R \sim M_W^{1/2}$, with an exponent

that is independent of temperature and solvent. The hydrodynamic expansion factor, α_η values are close to 1, which is evidence that formamide and water are theta rather than good solvents ($\alpha_\eta = 1$ at theta conditions), with formamide being a somewhat better solvent than water for the dextran coils.

Dextran coils swell more (higher $[\eta]$, R_{coil}, hydrodynamic expansion factor α_η) in the presence of formamide than in aqueous solutions. This shows that dextran segments interact more favorably with the formamide solvent molecules than with water. Apparently, dextran dissolves better in formamide because formamide has additional and more readily available active sites (C=O and NH_3 groups) to form hydrogen bonds compared to water; also the H-bonds formed between formamide molecules have sorter lifetime than those among water molecules.[51] Hydrogen bonding appears to be the main type of interaction in the systems examined here. The stronger the cohesive forces (the larger the σ and δ values) between the solvent molecules, the harder it is for dextran to break them and swell with the solvent.

As temperature increases both dextran in water and in formamide systems are driven toward theta conditions. Upon heating, the polymer segments interact less with the solvent molecules, adopt a less expanded conformation in the solution, and the intermolecular association with other polymer segments is enhanced; the coils contract and the solvent quality decreases. The decrease in the hydrogen bonding interactions appears to be the reason for dextran coils to contract.

References

1. Glass, E., ed. Polymers in Aqueous Media "Performance Through Association"; ACS: Washington, DC, 1989.
2. Dickinson, E.; Walstra, P. Food Colloids and Polymers: Stability and Mechanical Properties; The Royal Society of Chemistry, 1993.
3. Brant, D. A., ed. Solution Properties of Polysaccharides; ACS Symposium Series: Washington, DC, 1981; Vol.150.
4. Sutherland, I. W. TibTech 1998, 16, 41.
5. Tsianou, M.; Alexandridis, P. Langmuir 1999, 15, 8105.
6. Chronakis, I. S.; Alexandridis, P. Macromolecules 2001, 34, 5005.
7. Bokias, G.; Mylonas, Y.; Staikos, G.; Bumbu, G. G.; Vasile, C. Macromolecules 2001, 34, 4958.
8. Ivanova, R.; Lindman, B.; Alexandridis, P. Adv Colloid Interface Sci 2001, 89, 351.
9. Ivanova, R.; Lindman, B.; Alexandridis, P. J Colloid Interface Sci 2002, 252, 226.
10. De Belder, A. N. Ullmann's Encyclopedia of Industrial Chemistry; Wiley-VCH Verlag: Germany, 2002.
11. Glicksman, M. Food Hydrocolloids; CRC Press: Boca Raton, FL, 1982; p 157.
12. McCurdy, R. D.; Goff, H. D.; Stanley, D. W.; Stone, A. P. Food Hydrocolloid 1994, 8, 609.
13. Schacht, E. H.; Vercauteren, R.; Vansteenkiste, S. J Bioactive Compatible Polym 1988, 3, 72.

14. Armstrong, J. K.; Wendy, R. B.; Meiselman, H. J.; Fisher, T. C. Biophys J 2004, 87, 4259.
15. Güner, A. J Appl Polym Sci 1999, 72, 871.
16. Senti, F. R.; Hellman, N. N.; Ludwig, N. H.; Babcock, G. E.; Tobin, R.; Glass, C. A.; Lamberts, B. L. J Polym Sci 1955, 17, 527.
17. Ioan, C. E.; Aberle, T.; Burchard, W. Macromolecules 2000, 33, 5730.
18. Carrasco, F.; Chornet, E.; Overend, R. P.; Costa, J. J Appl Polym Sci 1989, 37, 2087.
19. Flory, P. J. Principles of Polymer Chemistry; Cornell University Press: Ithaca, 1953.
20. Lee, J.; Tripathi, A. Anal Chem 2005, 77, 7137.
21. Chari, K.; Antalek, B.; Lin, M. Y.; Sinha, S. K. J Chem Phys 1994, 100, 5294.
22. Wales, M.; Marshall, P. A.; Weissberg, S. G. J Polym Sci 1953, 10, 229.
23. Güner, A.; Kibarer, G. Eur Polym J 2001, 37, 619.
24. Morris, E. R.; Cutler, A. N.; Ross-Murphy, S. B.; Rees, D. A. Carbohydr Polym 1981, 1, 5.
25. Tirtaatmadja, V.; Dunstan, D. E.; Boger, D. V. J Non-Newtonian Fluid Mech 2001, 97, 295.
26. Hiemenz, P. C.; Rajagopalan, R. Principles of Colloid and Surface Chemistry, 3rd ed.; Marcel Dekker: New York, 1997.
27. Mazi, H.; Zü Mreog Lu-Karan, B.; Güner, A. J Appl Polym Sci 2001, 82, 323.
28. Sperling, L. H. Introduction to Physical Polymer Science, 3rd ed.; Wiley–Interscience: New York, 2001.
29. Antoniou, E.; Themistou, E.; Sarkar, B.; Tsianou, M.; Alexandridis, P. Colloid Polym Sci 2010, 288, 1301.
30. Chee, K. K. J Appl Polym Sci 1985, 30, 1359.
31. Filiatrault, D.; Delmas, G. Macromolecules 1979, 12, 65.
32. McCormick, C. L.; Bock, J.; Schulz, D. N. Encyclopedia of Polymer Science and Engineering, 2nd ed.; John Wiley: New York, 1989; p 730–784.
33. Hadjichristidis, N. Makromol Chem 1983, 184, 1043.
34. Rubinstein, M.; Colby, R. Polymer Physics; Oxford University Press: New York, 2003.
35. de Gennes, P.-G. Scaling Concepts in Polymer Physics; Cornell University Press: Ithaca, 1993.
36. Evans, D. F.; Wennerström, H. The Colloidal Domain Where Physics, Chemistry, Biology, and Technology Meet, 2nd ed.; Wiley-VCH: New York, 1999.
37. Larson, G. R. The Structure and Rheology of Complex Fluids; Oxford University Press: New York, 1999.
38. Hansen, C. M. Hansen Solubility Parameters: A Users Handbook; CRC Press LLC: Boca Raton, FL, 2000.
39. Reichardt.C. Solvents and Solvent Effect in Organic Chemistry, 2nd ed.; VCH: New York, 1990.
40. van Oss, C. J. Interfacial Forces in Aqueous Media; Marcel Dekker: New York, 1994.
41. Alexandridis, P. Macromolecules 1998, 31, 6935.
42. Alexandridis, P.; Yang, L. Macromolecules 2000, 33, 3382.
43. Yang, L.; Alexandridis, P. Langmuir 2000, 16, 4819.
44. Errington, J. R.; Debenedetti, P. G. Nature 2001, 409, 318.
45. Hakem, I. F.; Boussaid, A.; Benchouk-Taleb, H.; Bockstaller, M. R. J Chem Phys 2007, 127, 224106.
46. Bellissent-Funel, M.-C.; Nasr, S.; Bosio, L. J Chem Phys 1997, 106, 7913.
47. Puhovski, Y. P.; Rode, B. M. Chem Phys 1995, 190, 61.
48. Basedow, A. M.; Ebert, K. H.; Feigenbutz, W. Macromol Chem 1980, 181, 1071.
49. Güner, A. J Appl Polym Sci 1995, 56, 1561.
50. Engberts, J. B. F. N.; Blandamer, M. J. Chem Commun 2001,1701.
51. Elola, M. D.; Ladanyi, B. M. J Chem Phys 2006, 125, 184506.
52. Antoniou, E.; Buitrago, C. F.; Tsianou, M.; Alexandridis, P. Carbohydr Polym 2010, 79, 380.
53. Antoniou, E.; Alexandridis, P. Eur Polym J 2010, 46, 324.