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Vapor–Liquid Equilibrium in Binary and Ternary Aqueous Solutions of Poly(ethylene glycol) and Dextran

Johann Gaube,* Andreas Pfennig, and Matthias Stumpf

Institut für Chemische Technologie, Technische Hochschule Darmstadt, Petersenstrasse 20, W-6100 Darmstadt, Germany

Activities of water for various binary and, in particular, ternary aqueous solutions of poly(ethylene glycol) (PEG) and dextran were measured over the entire homogeneous mixing range up to a polymer weight fraction of 0.3 at 293.15, 313.15, and 333.15 K. The water activities were determined by vapor-pressure osmometry and, additionally, for dilute dextran solutions using membrane osmometry. The experimental data were evaluated using the osmotic virial equation.

Introduction

Aqueous polymer–polymer two-phase systems such as aqueous poly(ethylene glycol)–dextran solutions can be utilized to purify biomolecules (*1,2*). Industrial process design requires knowledge of the liquid–liquid equilibria in these mixtures. However, the liquid–liquid equilibrium in an aqueous polymer–polymer system used for extraction is influenced by a variety of factors, making the experimental investigation of all effects unfeasible in most cases. Thus, a model for the prediction of the phase equilibria has to be applied which is based on a complete and reliable set of experimental data.

One thermodynamic key property in these mixtures is the activity of water which has been extensively studied in binary aqueous PEG and dextran solutions, as reviewed by Haynes et al. (*3*), and in some dilute ternary polymer–polymer systems (*4, 5*). However, the experimental data available in the literature cannot be correlated consistently, since important influencing factors such as the polydispersity (*6*) have not been considered. Thus, for the consistent correlation of water-activity data, measurements have to be performed for accurately and completely characterized polymers and polymer solutions. Also, the ternary solution measurements have to be extended to the entire homogeneous mixing range up to common polymer concentrations encountered in aqueous polymer–polymer two-phase extraction, since the predictability of phase equilibria will be strongly affected by the quality of the experimental water activity data near the two-phase region (*7*).

To fill this gap, this work reports water activities in binary aqueous solutions of PEG (weight-average molecular-weight range 200–6000 g/mol) and dextran (40000–500000 g/mol) and, exemplarily, in ternary aqueous solutions of PEG 3000 and dextran 110000 over the entire homogeneous mixing range up to a polymer weight fraction of 0.3. The polymers and their aqueous solutions have been accurately characterized; e.g., the molecular-weight distributions of the polymers were determined (*8*). The measurements were performed at 293.15, 313.15, and 333.15 K using vapor-pressure osmometry and, additionally, membrane osmometry for dilute dextran solutions. From these measurements, the polymer molecular weights and virial coefficients were calculated on the basis of osmotic virial equation due to McMillan and Mayer (*9*).

Experimental Section

Materials. PEG (weight-average molecular weights 200, 600, 1550, 3000, and 6000 g/mol) was supplied by the Hüls AG, Marl; dextran (weight-average molecular weights 70000, 110000, and 500000 g/mol) was purchased from Pfeifer & Langen, Dormagen, and (weight-average molecular weights 40000 g/mol) from Fluka Chemie AG, Buchs, in the highest purity available and used without further purification. Water used to prepare polymer solutions was triply distilled. For the calibration of the vapor-pressure osmometer sodium chloride (Merck, Darmstadt; pro analysi) and D-(+)-glucose monohydrate (Merck, Darmstadt; pro analysi) were used.

Preparation of Solutions. Initially stock solutions were prepared for each polymer. The polymer concentrations were determined by GPC with an accuracy better than ±0.13 wt % (*8*). For measurements in binary solutions, dilutions were made by weight. For measurements in ternary aqueous polymer–polymer solutions, stock solutions of PEG and dextran were mixed in different ratios over the homogeneous mixing range. The concentrations of the stock solutions were chosen such that each of these mixing series was approximately parallel to the experimental tie lines (*8*) as illustrated in Figure 1. It was observed that the coexistence curve differs slightly from the measured binodal curves (*8*). This effect is caused by the polydispersity of the polymers as pointed out by Rätzsch et al. (*10*). Errors in the preparation of mixtures from the stock solutions were estimated to be well below the instrumental error of the vapor-pressure and membrane osmometer for measurements of binary as well as ternary solutions.

Solutions of dextran are known to contain molecular aggregates (*11*). To dissolve these aggregates, the solutions were treated in a water bath at 80 °C for 30 min. To avoid reaggregation, solutions were stored at 5 °C (*11*).

Vapor-Pressure Osmometry. The vapor-pressure osmometer (Knauer, Berlin) was assembled, calibrated, and equilibrated according to the manufacturer's instructions. The activities of water, a_1, were computed from the detected changes in the resistance of the thermistors, ΔR, which is proportional to the temperature difference, ΔT, between the sample reading and the instrument zero determined with pure solvent. The sample readings were extrapolated after equilibration (15–20 min) to zero time. The measured temperature difference ΔT and the water activity a_1 are related by

$$\ln a_1 = -(\Delta H_1^{\mathrm{vap}}/RT^2\eta)\Delta T \qquad (1)$$

where the efficiency coefficient η corrects the influences of heat losses (*12*). The calibration with various standards showed that the efficiency coefficient is independent of the molecular weight of the solute of the solution.

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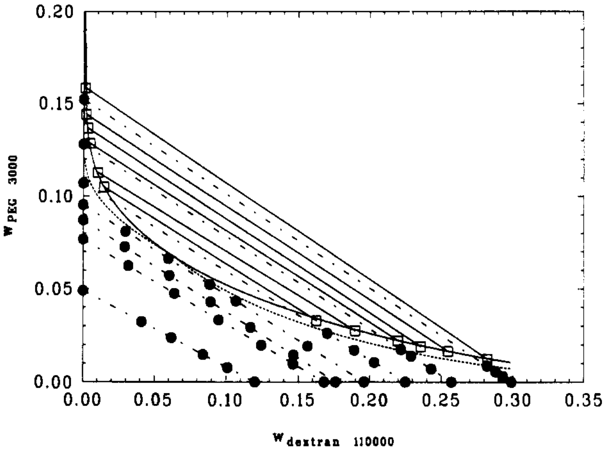

Figure 1. Mixing series with composition investigated for the ternary aqueous solution of PEG 3000 and dextran 110000 at 293.15 K: (●) mixtures investigated; (- – -) mixing series; (- - -) approximate coexistence curve; (□—□) binodal curve, tie lines.

The cell temperature was held constant to within ±10^{-4} K. At least three readings were made for each solution, and the results were averaged. Every fourth or fifth measurement was a reference measurement with solvent on both thermistors to check the reference reading. Under these conditions, the measured temperature differences and thus also the logarithm of the activities of water deviate within ±2% from their mean value.

Membrane Osmometry. The membrane osmometer (Gonotec, Berlin) was fitted with a semipermeable two-layer cellulose acetate membrane, SM 14539 (Sartorius), allowing measurements of substances with molecular weights above 10000 g/mol. Thus, only those dextran fractions with a molecular weight below 10000 g/mol can pass the membrane. For the dextran with the lowest average molecular weight investigated, dextran 40000, this is at most 0.035 weight fraction of the entire sample. This would lead to a measuring value slowly decreasing with time. However, since we have observed stable measuring values and also constant "zero pressures" in our experiments, this effect could be neglected.

Equilibrium was reached after 3–5 min. The temperature was held constant to within ±10^{-3} K. The measurements were repeated two or three times to prove the consistency of the measured value and afterward averaged, resulting in an accuracy of the logarithm of the mean water activities better than ±2%.

Results and Discussion

The measured water activities of the binary PEG and dextran solutions are given in the supplementary material as a function of the polymer weight fraction. The activities of water from vapor-pressure osmometry experiments are given up to the sixth and for membrane osmometry data up to the eighth significant digit.

For binary polymer solutions such as aqueous PEG or dextran solutions, the activity of the solvent can be expressed in terms of the osmotic virial equation (*9*):

$$\ln a_1 = -\bar{V}_1 M_1 \left(\frac{c_i}{\bar{M}_{n,i}} + A_{ii} c_i^2 + A_{iii} c_i^3 + \dots \right) \qquad (2)$$

where index i stands for either PEG (index 2) or dextran (index 3) and c_i for the polymer concentration (g of polymer/cm^3 of solution). For the determination of the concentration of the polymers $c_i = w_i/\bar{V}$, we have measured the specific volumes of the solution $\bar{V}$ using an oscillating tube (DSA 48, Heräus-Paar, Graz) for the entire investigated concentration and temperature ranges. The specific volume $\bar{V}$ can be calculated for the investigated binary and ternary concentration ranges as $\bar{V} = \sum_{i=1}^{3} w_i \bar{V}_i$, as proposed by Johansson et al. (*13*), with an accuracy better than 10^{-3} cm^3/g. $\bar{V}_1$ is the specific volume of water (*14*), while $\bar{V}_2$ and $\bar{V}_3$ are the hypothetical specific volumes of the polymers, as extrapolated from the measured specific volumes of the binary solutions. The extrapolated hypothetical specific volumes of the polymers are independent of their molecular weights, but depend on the temperature of the system (Table I). It should be emphasized that the hypothetical specific volumes of the polymers differ significantly from the specific volumes of the polymers because of excess volumes in such aqueous polymer solutions that occur beyond polymer weight fractions of 0.4 (*15*).

Table I. Extrapolated Specific Volumes of PEG (2) and Dextran (3)

T (K)	$\bar{V}_2$ (cm^3/g)	$\bar{V}_3$ (cm^3/g)
293.15	0.8302	0.5959
313.15	0.8573	0.6203
333.15	0.8711	0.6322

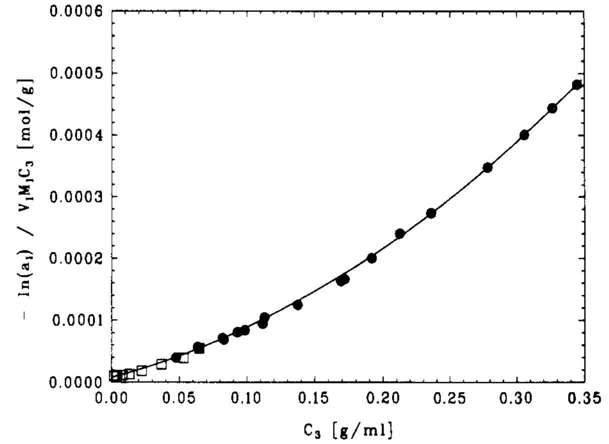

Figure 2. Reduced water activity a_1 as a function of c_3 for the system water (1)–dextran 500000 (3) at 313.15: (●) vapor-pressure osmometry; (□) membrane osmometry; (—) osmotic virial equation.

Using eq 2, the number-average molecular weights of the polymers, $\bar{M}_{n,i}$, and the second and the third virial coefficients, A_{ii} and A_{iii}, were determined from the water-activity data fitted by the least-squares method. Higher order virial coefficients can be neglected, since the description of the experimental data is good. This is exemplarily illustrated in Figure 2 for an aqueous dextran 500000 solution at 313.15 K and in Figure 3 for an aqueous dextran 500000 solution at 293.15 K. Figure 2 also shows the conformity of the data obtained from membrane osmometry and vapor-pressure osmometry. In Figure 3, the measured water activities are compared with literature data. As a result, the water activities are in good agreement with measurements of Zhu (*16*), while the experimental data of Haynes et al. (*3*) differ significantly from our measurements.

The molecular weights and virial coefficients for the examined polymer solutions are given in Table II. The error of the determined molecular weights is approximately ±2% for the smallest PEG and ±25% for the dextran with the highest molecular weight, as indicated by a comparison among the data from the manufacturer, GPC measurements (*8*), and this work. Since the molecular weights of the polymers obtained from GPC measurements are well established, we have based the osmotic virial coefficients given in Table II on these values. The accuracy of the so-obtained second virial coefficients, A_{ii}, is estimated to be 7% for PEG and 20% for

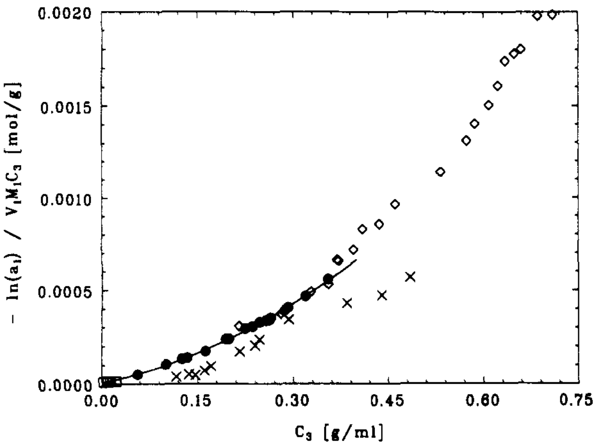

Figure 3. Reduced water activity a_1 as a function of c_3 for the system water (1)–dextran 500000 (3) at 293.15: (●) vapor-pressure osmometry; (□) membrane osmometry; (—) osmotic virial equation; (×) literature data (*3*); (◇) literature data (*16*).

Table II. Average Molecular Weights of the Pure Components and Virial Coefficients

polymer	T (K)	$\bar{M}_n^{\mathrm{manuf}}$ (g/mol)	$\bar{M}_n^{\mathrm{GPC}}$ (g/mol)	$\bar{M}_n^{\mathrm{osm}}$ (g/mol)	A_{ii} (10^{-3} cm^3 mol/g^2)	A_{iii} (10^{-2} cm^6 mol/g^3)
PEG 200	293.15	213	201	201	7.16	1.78
	313.15			197	5.64	1.61
	333.15			203	4.89	1.59
PEG 600	293.15	594	582	593	4.26	1.62
	313.15			603	2.99	1.55
	333.15			588	2.92	0.88
PEG 1550	293.15	1 580	1 440	1 396	3.10	1.54
	313.15			1 454	2.42	1.16
	333.15			1 462	1.46	0.91
PEG 3000	293.15	3 261	2 840	2 756	2.72	1.63
	313.15			2 692	2.37	1.00
	333.15			3 057	1.20	0.81
PEG 6000	293.15	5 744	7 750	5 325	2.60	1.26
	313.15			5 851	2.25	0.97
	333.15			6 280	1.53	0.54
Dex 40000	293.15		23 600	17 000	1.31	0.81
	313.15			20 000	1.24	0.69
	333.15			18 100	0.93	0.67
Dex 70000	293.15	43 201	46 300	41 200	0.99	0.40
	313.15			46 810	0.94	0.30
	333.15			39 400	0.72	0.28
Dex 110000	293.15	59 208	64 800	41 900	0.65	0.26
	313.15			48 000	0.76	0.24
	333.15			53 900	0.45	0.24
Dex 500000	293.15	121 615	101 000	129 000	0.64	0.25
	313.15			89 000	0.57	0.23
	333.15			94 000	0.39	0.18

Table III. Cross Virial Coefficients for the System Water (1)–PEG 3000 (2)–Dextran 110000 (3)

T (K)	A_{23} (10^{-3} cm^3 mol/g^2)	A_{223} (10^{-2} cm^6 mol/g^3)	A_{233} (10^{-2} cm^6 mol/g^3)
293.15	2.30	0.71	0.45
313.15	2.32	0.45	0.36
333.15	1.02	0.77	0.57

dextran and for the third virial coefficients, A_{iii}, to be 5% for PEG and 15% for dextran. The virial coefficients of the binary aqueous solutions of PEG and dextran both decrease with increasing molecular weight of the solute and increasing temperature. The molecular-weight dependence can be explained with the excluded-volume effect caused by the intramolecular interactions of the polymers (*6*), while the temperature dependence is due to specific phenomena in aqueous polymer solutions such as hydrogen bonding and hydrophobic effects (*17*).

Water activities of the ternary polymer solutions of PEG 3000 and dextran 110000 were measured over the entire homogeneous mixing range up to a polymer weight fraction of 0.3, as illustrated in Figure 1. For this polymer combination, the determined activity data are reported in the supplementary material as a function of the polymer weight fractions at 293.15, 313.15, and 333.15 K. These ternary activity data can also be expressed in terms of the osmotic virial equation

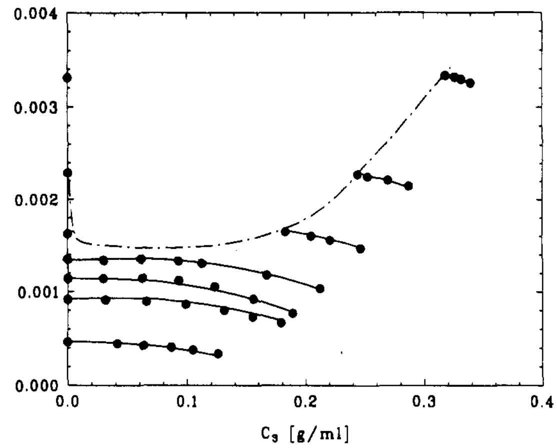

Figure 4. Water activity as a function of c_3 for the ternary system water (1)–PEG 3000 (2)–dextran 110000 (3) at 293.15 K for the mixing series given in Figure 1: (●) experimental data; (—) osmotic virial equation; (- - -) approximate coexistence curve.

$$\ln a_1 = -\bar{V}_1 M_1 \left(\frac{c_2}{\bar{M}_{n,2}} + \frac{c_3}{\bar{M}_{n,3}} + A_{22}c_2^{\,2} + 2A_{23}c_2c_3 + A_{33}c_3^{\,2} + A_{222}c_2^{\,3} + 3A_{223}c_2^{\,2}c_3 + 3A_{233}c_2c_3^{\,2} + A_{333}c_3^{\,3} + \ldots \right) \quad (3)$$

where all virial coefficients have been determined from binary polymer solution measurements except the cross virial coefficients A_{23}, A_{223}, and A_{233}. On the basis of the results of the binary solution measurements, the cross virial coefficients were fitted simultaneously to the water activity data of the ternary solution by the least-squares method. The results are listed in Table III. The accuracy of the so-obtained second cross virial coefficients was estimated to be 20% and of the third osmotic cross virial coefficients to be 30%. Exemplarily, the measured and fitted ternary water activities for the system water–PEG 3000–dextran 110000 at 293.15 K are illustrated in Figure 4. Figure 4 shows the consistency of the experimental data and the good model description. Using the osmotic virial equation, the logarithms of the measured water activities can be calculated with an accuracy better than ±2%. It can also be seen that the water activities or equivalently the chemical potentials of water are equal on both sides of the experimentally determined phase boundaries, being a necessary condition for phase equilibria. This further confirms the accuracy of the data.

Glossary

a_i	activity coefficient
A_{ii}, A_{iii}	virial coefficients
c_i	concentration
M_1	molecular weight of water
$\bar{M}_{n,i}$	number-average molecular weight
R	gas constant
T	cell temperature
$\bar{V}_i$	specific volume
w_i	weight fraction
$\Delta H_i^{\mathrm{vap}}$	heat of vaporization
ΔR	change of resistance between thermistors

ΔT	temperature difference between thermistors
η	efficiency coefficient

Subscripts

i	component index
1	water
2	PEG
3	dextran

Registry Numbers Supplied by Author. Poly(ethylene glycol), 25322-68-3; dextran, 9004-54-0.

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Supplementary Material Available:

Tables of the measured water activities as a function of the polymer concentrations at 293.15, 313.15, and 333.15 K for water (1)–PEG (2), water (1)–dextran (3), and water (1)–PEG (2)–dextran (3), with data obtained by vapor-pressure osmometry given to the sixth significant digit and those measured with the membrane osmometer to the eighth significant digit (8 pages). Ordering information is given on any current masthead page.