Measurement and Modeling Process Partitioning of Cephalexin Antibiotic in Aqueous Two-Phase Systems Containing Poly(ethylene glycol) 4000, 10000 and K_2HPO_4, $Na_3Citrate$

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In this work, the partition coefficients of Cephalexin in aqueous two-phase systems containing PEG [poly(ethylene glycol)] 4000, 10000 and K_2HPO_4, $Na_3Citrate$ ($C_6H_5Na_3O_7$ 5, $5H_2O$) have been measured. The experimental data were obtained in a wide range of temperatures, (28.2 to 37.2) °C. The effects of temperature, pH, polymer concentration, polymer molecular weight, and salt concentration on the partitioning of Cephalexin were also studied. The results showed that salt concentration has a large effect on the partition coefficient, and temperature has an almost negligible effect. The Chen−NRTL Gibbs energy model was used to correlate the experimental results.

Introduction

The aqueous two-phase systems containing polymer and salt are widely used in separation and purification of biological compounds such as proteins and enzymes.[1] It should be noted out that aqueous two-phase systems consist of two different polymers such as polyvinyl alcohol (PVA) and dextran (DEX) or one polymer and a salt such as PEG [poly(ethylene glycol)] and sodium sulfate (Na_2SO_4).

In the aqueous two-phase systems, both phases are water rich; densities of both phase are approximately equal; and the interfacial tension between two the phases is very small.[2]

Beijerinck first prepared aqueous two-phase systems containing agar and gelatin in 1896.[3] Albertson used polymer−polymer aqueous two-phase systems for separation and purification of biomolecules.[4] Blazquez measured partitioning of α-amylase enzyme in aqueous two-phase systems of PEG 8000 and $MgSO_4$.[5]

Haghtalab et al. studied partitioning of some biomolecules such as lysozyme, bovine serum albumin, and α-amylase in aqueous two-phase systems of PEG (1500, 4000) and K_2HPO_4 or Na_2SO_4 at 25 °C.[6]

Salabat et al. also measured and correlated partition coefficients of three amino acids such as L-tryptophan, L-phenylalanine, and L-tyrosine in aqueous two-phase systems PEG 6000 and $MgSO_4$, Na_2SO_4, and $(NH_4)_2SO_4$ at 25 °C.[7]

Lee and Sandler studied the effects of pH and concentrations of salt and ligand on partitioning of Vacomycin in aqueous two-phase systems.[8]

Yang et al. measured partition coefficients of Cephalosporin C in various polymer−salt aqueous two-phase systems.[9]

Bora et al. studied the effect of PEG concentration, pH, and salt concentration on the partitioning behavior of certain Cephalosporin antibiotics in an aqueous two-phase system of poly(ethylene glycol) phosphate or sulfate salt solution. The experimental results on partitioning of binary mixture of Cephalexin and 7-amino deacetoxy cephalosporanic acid showed reasonably high selectivity for Cephalexin.[10]

Mokhtarani et al. recently measured and modeled partitioning of Ciprofloxacin in aqueous two-phase systems of PEG 1500, 2000, 4000, and Na_2SO_4.[11]

In this work, partitioning of Cephalexin antibiotic in aqueous two-phase systems containing PEG and K_2HPO_4 or $Na_3Citrate$ has been measured.

The effects of temperature, polymer molecular weight, polymer concentration, and salt concentration on the partition coefficient were investigated. The Chen−NRTL model was used to correlate the partitioning of Cephalexin in polymer−salt aqueous two-phase systems.

Table 1. Parameters of Refractive Index Equation

component	α_0	α_1	α_2
water	1.3324		
$Na_3Citrate$		0.1424	
K_2HPO_4		0.163	
PEG 4000			0.1490
PEG 10000			0.1475

Experimental Section

Materials. PEG with molecular weight of 4000 and 10000, citric acid monohydrate needed for pH control of the systems, $Na_3Citrate$ with the purity of 99 %, and K_2HPO_4 with 99.5 % purity were purchased from Merck. Cephalexin monohydrate with 99.9 % purity was obtained from Jaber-Ebne-Hayyan Company in Iran. The polymer and salts were used without further purification. Double distilled and deionized water was used in all of the experiments.

Methods. Aqueous two-phase systems were prepared by mixing known amounts of polymer and salt in a 350 cm^3 glass cell which was connected to a recycling thermostat. The mass fractions of PEG and salt in the stock solutions were about 0.25 and 0.10, respectively. The mass fraction of Cephalexin in aqueous solution was approximately $2 \cdot 10^{-4}$ in most experiments. However, in some measurements, that mass fraction was decreased to about $1 \cdot 10^{-5}$. A 0.45 mol·L^{-1} aqueous citric acid

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Table 2. Mass Fractions *w* for PEG (1) + $Na_3Citrate$ (2) + Cephalexin (3) in Upper and Lower Phases

	feed			upper phase			lower phase			
t/°C	100 w_1	100 w_2	100 w_3	100 w_1	100 w_2	100 w_3	100 w_1	100 w_2	100 w_3	*K*
				PEG 4000 + $Na_3Citrate$						
28.2	26.47	8.52	0.017	39.38	6.05	0.013	16.04	17.34	0.010	1.498
28.2	26.47	8.52	0.008	36.74	6.14	0.009	16.11	16.14	0.007	1.459
28.2	27.06	7.04	0.018	35.31	5.96	0.018	14.22	16.79	0.008	2.509
28.2	16.61	9.66	0.020	28.68	6.51	0.013	11.65	15.06	0.009	1.532
34.2	26.47	8.52	0.017	41.48	3.85	0.021	14.64	18.61	0.014	1.452
34.2	26.47	8.52	0.008	38.37	4.44	0.015	13.76	18.39	0.011	1.419
34.2	27.06	7.04	0.018	36.37	4.85	0.034	14.01	16.88	0.014	2.464
34.2	16.61	9.66	0.020	28.63	6.56	0.020	11.89	14.67	0.014	1.489
37.2	26.47	8.52	0.017	40.98	4.03	0.027	14.54	17.30	0.018	1.376
37.2	26.47	8.52	0.009	40.05	4.87	0.021	14.79	17.07	0.015	1.331
37.2	27.05	7.04	0.018	35.63	4.58	0.038	14.06	14.88	0.015	2.193
37.2	16.61	9.66	0.020	30.78	5.44	0.026	12.58	13.34	0.017	1.426
				PEG 10000 + $Na_3Citrate$						
28.2	26.46	8.52	0.017	38.66	5.31	0.009	14.67	16.75	0.007	1.427
28.2	26.47	8.52	0.008	39.79	4.84	0.006	15.07	16.06	0.005	1.376
28.2	27.06	7.04	0.018	37.27	5.77	0.011	15.59	15.18	0.006	2.365
28.2	16.61	9.66	0.020	31.08	6.43	0.009	14.01	11.62	0.007	1.462
34.2	26.47	8.52	0.017	17.79	26.93	0.015	14.67	16.75	0.011	1.375
34.2	26.47	8.52	0.008	42.44	2.21	0.011	15.03	16.06	0.008	1.342
34.2	27.06	7.04	0.018	40.25	2.68	0.021	15.60	15.18	0.009	2.312
34.2	16.61	8.89	0.020	33.92	3.47	0.014	14.01	11.63	0.010	1.424
37.2	26.47	8.52	0.017	42.35	3.52	0.022	14.53	17.38	0.016	1.290
37.2	26.47	8.52	0.008	41.83	4.13	0.017	16.39	16.37	0.012	1.256
37.2	27.06	7.04	0.018	39.58	2.89	0.033	12.78	14.28	0.014	2.013
37.2	16.61	9.66	0.020	33.32	4.53	0.022	12.88	13.41	0.015	1.354

Table 3. Mass Fractions *w* for PEG (1) + K_2HPO_4 (2) + Cephalexin (3) in Upper and Lower Phases

	feed			upper phase			lower phase			
t/°C	100 w_1	100 w_2	100 w_3	100 w_1	100 w_2	100 w_3	100 w_1	100 w_2	100 w_3	*K*
				PEG 4000 + K_2HPO_4						
28.2	26.47	11.40	0.017	48.39	1.71	0.019	7.09	24.85	0.021	0.986
28.2	26.47	11.39	0.009	47.42	1.67	0.014	7.10	25.11	0.018	0.854
28.2	27.06	9.42	0.018	35.51	9.01	0.011	1.78	22.16	0.027	0.569
28.2	16.61	12.92	0.020	40.66	1.85	0.017	7.08	18.15	0.030	0.852
34.2	26.47	11.40	0.017	41.74	7.78	0.033	0.35	29.49	0.033	0.983
34.2	26.47	11.40	0.009	42.31	6.35	0.021	0	29.20	0.027	0.826
34.2	27.06	9.42	0.018	44.37	0.91	0.024	7.50	20.96	0.038	0.525
34.2	16.61	12.92	0.020	33.91	8.02	0.032	0	25.99	0.041	0.781
37.2	26.47	11.40	0.017	44.74	7.32	0.040	7.52	25.69	0.041	0.903
37.2	26.47	11.40	0.009	42.97	6.30	0.026	2.05	25.85	0.031	0.769
37.2	27.05	9.42	0.018	48.60	6.55	0.024	3.48	26.32	0.042	0.403
37.2	16.61	12.92	0.020	38.81	6.91	0.038	0	25.74	0.045	0.584
				PEG 10000 + K_2HPO_4						
28.2	26.47	11.3992	0.017	48.51	0.64	0.019	7.37	21.14	0.026	0.967
28.2	26.47	10.18	0.007	48.01	1.09	0.015	7.68	20.79	0.022	0.830
28.2	27.06	9.29	0.018	44.52	1.91	0.012	7.22	20.22	0.033	0.546
28.2	16.61	8.89	0.020	40.30	1.76	0.016	4.91	19.73	0.036	0.786
34.2	26.47	11.40	0.017	43.30	5.35	0.027	1.75	29.45	0.031	0.889
34.2	26.47	11.40	0.007	42.89	5.72	0.019	0	27.17	0.026	0.761
34.2	27.06	9.42	0.018	40.10	5.91	0.017	7.80	30.50	0.035	0.476
34.2	16.61	8.89	0.020	34.56	6.94	0.026	0	29.37	0.037	0.702
37.2	26.47	11.40	0.017	42.31	6.86	0.033	0	28.08	0.034	0.739
37.2	26.47	11.40	0.008	41.41	6.75	0.024	0.50	26.59	0.030	0.667
37.2	27.06	9.42	0.018	42.45	6.49	0.020	0	27.83	0.037	0.365
37.2	16.61	8.89	0.020	37.50	7.41	0.033	0	28.01	0.042	0.455

solution was used to adjust the pH to about 4.8. The mixture was mixed using a magnetic stirrer for about 20 min. To achieve final phase equilibrium, the thermostat connecting to the cell was set to the temperature of the solution for 24 h, and then samples of the top and bottom phases were removed by a plastic syringe.

Quantitative Analysis. Flame photometry (Corning 410, from Jenway, England) was used to determine the concentration of salt. The relative experimental uncertainty in the salt mass fraction measurement was less than 3 %. Mass fractions of PEG were determined by refractive index measurements using an Erma optical refractometer (model 17101, from Erma optical, Japan). The refractive index of an aqueous phase depends on the mass fractions of PEG and salt in the aqueous two-phase systems. In this study, it is assumed that the refractive index depends linearly on the mass fractions both of the polymer and of the salts at least in the small range of salt concentrations investigated. This relation is as follows

$$n_D = \alpha_0 + \alpha_1 w_s + \alpha_2 w_p \quad (1)$$

The parameters of eq 1 are reported in Table 1 for different polymer−salt systems.

The relative experimental uncertainty for the PEG mass fraction is < 3.5 %. The mass fraction of Cephalexin was

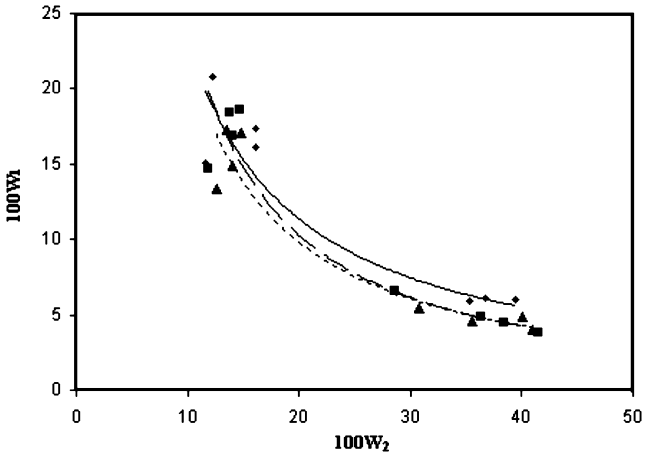

Figure 1. Effect of temperature on two-phase separation in PEG 4000 (1) + $Na_3Citrate$ (2) aqueous two-phase systems. _, $t = 28.2$ °C; ----, $t = 34.2$ °C; ••••, $t = 37.2$ °C.

determined by a UV/vis spectrophotometer at 291 nm using a spectrometer (M501, from Comspec, England). This wavelength was measured by scanning a solution of Cephalexin.

Since at that wavelength the salts and the polymer also absorb, the absorbance coefficients of the salts and of PEG were measured in a free antibiotic solution. Furthermore, the Cephalexin absorbance was measured based on the blank solutions of salts and PEG. The relative experimental uncertainty for the Cephalexin mass fraction was less than 7.5 %. The pH of an aqueous solution was measured with a precision pH meter (type 744 from Deutsche Metrohm, Filderstadt, Germany).

Results and Discussion

Experimental results. The mass fraction of PEG, salt and Cephalexin in upper and lower phases at (301 to 310) °C are reported in Tables 2 and 3.

The partition coefficient of Cephalexin showed that, in PEG + $Na_3Citrate$ aqueous two-phase systems, Cephalexin prefers to stay in the PEG-rich phase, and in PEG + K_2HPO_4 aqueous two-phase systems it prefers to stay in the salt-rich phase.

The reported results indicate that with decreasing salt or polymer concentration in feed, the mass fraction of Cephalexin in the upper phase increases in PEG + $Na_3Citrate$ aqueous two-phase systems and decreases in PEG + K_2HPO_4 aqueous two-phase systems. Also, the Cephalexin partitioning is higher depending on salt mass fraction than the polymer. In all aqueous two-phase systems, the partition coefficient of Cephalexin increases with an increase in temperature.

Figure 1 shows the effect of temperature on the two-phase separation in PEG 4000 + $Na_3Citrate$ aqueous two-phase systems. The effect of PEG molecular weight on the two-phase separation in PEG + $Na_3Citrate$ is also presented in Figure 2.

These figures show that the two phases separate faster with increasing temperature and decreasing molecular weight of PEG.

Figure 3 shows the phase diagram and tie lines of the PEG 4000 + $Na_3Citrate$ aqueous two-phase system at 34.2 °C.

Finally, it is concluded that the aqueous two-phase system containing PEG 4000 and $Na_3Citrate$ is the best system for partitioning of Cephalexin.

Thermodynamic Modeling. According to the thermodynamic relations, the excess Gibbs energy is expressed as long-range, short-range, and combinatorial terms

$$\frac{G^E}{RT} = \frac{G^E_{LR}}{RT} + \frac{G^E_{Comb}}{RT} + \frac{G^E_{SR}}{RT} \quad (2)$$

where in eq 2 subscripts "LR", "Comb", and "SR" stand for the long-range, the combinatorial, and the short-range effects, respectively. It should be noted that the long-range term must be omitted for nonelectrolyte solutions.

The activity coefficient of each component can be obtained as below

$$\ln \gamma_i = \ln \gamma_{i,LR} + \ln \gamma_{i,Comb} + \ln \gamma_{i,SR} \quad (3)$$

The mean ionic activity coefficient of electrolyte reported by Debye−Huckel is considered for the long-range term as below[12]

$$\ln \gamma_{i,LR} = \frac{A|Z_A Z_C| I^{1/2}}{1 + bI^{1/2}} \quad (4)$$

where Z_A and Z_C are absolute charge number of the anion and cation. A and b are Debye−Huckel parameters and are calculated from these relations

$$A = 1.327757 \cdot 10^5 \cdot \frac{d^{0.5}}{(\varepsilon T)^{1.5}} \quad (5)$$

I is the ionic strength of solution on the molality scale, given as

$$I = \frac{1}{2} \sum Z_i^2 m_i \quad (6)$$

In the above equation, m_i is molality of ion i.

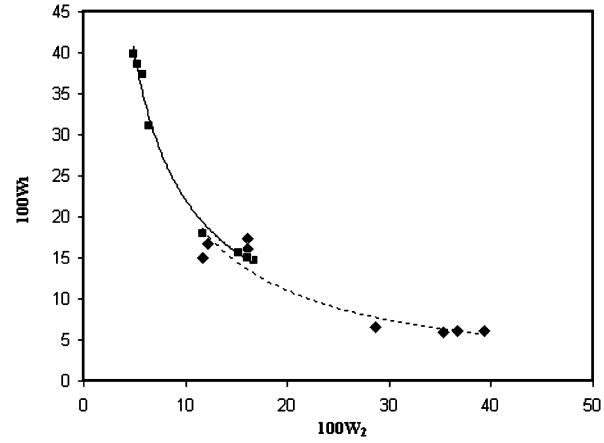

Figure 2. Effect of PEG molecular weight on two-phase separation in PEG (1) + $Na_3Citrate$ (2) aqueous two-phase systems. _, PEG 10000; ••••, PEG 4000.

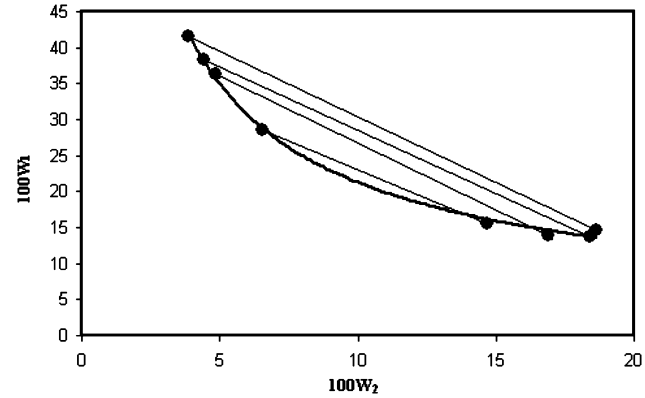

Figure 3. Phase diagram and tie lines of the PEG 4000 + $Na_3Citrate$ aqueous two-phase system at 34.2 °C.

$$b = 6.359696 \cdot \frac{d^{0.5}}{(\varepsilon T)^{0.5}} \tag{7}$$

where d and ε are density and dielectric constant and are calculated from these relations

$$d = \sum \varphi'_j d_j \tag{8}$$

$$\varepsilon = \sum \varphi'_j \varepsilon_j \tag{9}$$

$$\varphi'_j = \frac{n_j V_j}{n_1 V_1 + n_3 V_3} \tag{10}$$

where φ'_j is salt-free volume fraction; V_j is molar volume of species j; and n_i is mole number of molecular species (water and polymer).

Also, the activity coefficient of molecular species (water and polymer) is calculated by the following equation[13]

$$\ln \gamma_{j,\mathrm{LR}} = \left(\frac{2AV_j d}{b^3}\right)\left[1 + bI^{1/2} - \frac{1}{(1 + bI^{1/2})} - 2\ln(1 + bI^{1/2})\right] \tag{11}$$

The Flory−Huggins equation is used in obtaining the combinatorial activity coefficient term as

$$\ln \gamma_{i,\mathrm{Comb}} = \ln\left(\frac{\varphi_i}{x_i}\right) + 1 - r_i \sum_j \left(\frac{\varphi_j}{r_j}\right) \tag{12}$$

where x_i and φ_i are mole fraction and volume fraction of component i, respectively. The volume fraction of component i in a mixture can be defined as

$$\varphi_i = \frac{r_i x_i}{\sum_j r_j x_j} \tag{13}$$

where r_i is the number of segments of pure component i.

The Chen−NRTL local composition model is used for short-range effects in multicomponent mixtures.[13]

Table 4. Regressed Values of the Chen−NRTL Model Parameters in Binary Systems[a]

binary system	τ_{EW}	τ_{WE}	Ω	100 AAD
$K_2HPO_4 + H_2O$	−2.2541	4.787	0.049	2.970
$Na_3Citrate + H_2O$	−1.890	2.190	0.930	1.030
PEG 4000 + H_2O	28.24	−25.17	0.006	0.350
PEG 10000 + H_2O	−11.98	12.87	0.001	0.132

[a] AAD = $\sum_{i=1}^{N} |(\ln \gamma^{\mathrm{calcd}} - \ln \gamma)/\ln \gamma| / N$.

With derivation of the Gibbs energy equation, the short-range activity coefficient of molecule and ion species can be written as[13]

$$\frac{1}{q_m} \ln \gamma_m^{\mathrm{SR}} = \frac{\sum_j X_j G_{jm} \tau_{jm}}{\sum_k X_k G_{km}} + \sum_{m'} \frac{X_{m'} G_{mm'}}{\sum_k X_k G_{km'}} \left(\tau_{mm'} - \frac{\sum_k X_k G_{km'} \tau_{km'}}{\sum_k X_k G_{km'}}\right) + \sum_c \sum_{a'} \frac{X_{a'}}{\sum_{a''} X_{a''}} \frac{X_c G_{mc,a'c}}{\sum_k X_k G_{kc,a'c}} \left(\tau_{mc,a'c} - \frac{\sum_k X_k G_{kc,a'c} \tau_{kc,a'c}}{\sum_k X_k G_{kc,a'c}}\right) + \sum_a \sum_{c'} \frac{X_{c'}}{\sum_{c''} X_{c''}} \frac{X_a G_{ma,c'a}}{\sum_k X_k G_{ka,c'a}} \left(\tau_{ma,c'a} - \frac{\sum_k X_k G_{ka,c'a} \tau_{ka,c'a}}{\sum_k X_k G_{ka,c'a}}\right) \tag{14}$$

$$\frac{1}{Z_c} \ln \gamma_c^{\mathrm{SR}} = \sum_{a'} \frac{X_{a'}}{\sum_{a''} X_{a''}} \frac{\sum_k X_k G_{kc,a'c} \tau_{kc,a'c}}{\sum_k X_k G_{kc,a'c}} + \sum_m \frac{X_m G_{cm}}{\sum_k X_k G_{km}} \times \left(\tau_{cm} - \frac{\sum_k X_k G_{km} \tau_{km}}{\sum_k X_k G_{km}}\right) + \sum_a \sum_{c'} \frac{X_{c'}}{\sum_{c''} X_{c''}} \frac{X_a G_{ca,c'a}}{\sum_k X_k G_{ka,c'a}} \times \left(\tau_{ca,c'a} - \frac{\sum_k X_k G_{ka,c'a}}{\sum_k X_k G_{ka,c'a}}\right) \tag{15}$$

The activity coefficient of an anion can be expressed in the same forms as the activity coefficient of a cation in eq 15, by replacing the subscript of $c(c', c'')$ with that of $a(a', a'')$ and a with c.

The partition coefficient of Cephalexin in aqueous two-phase systems containing salt and polymer is obtained by the Chen−NRTL thermodynamic equation.

The partition coefficient of Cephalexin in aqueous two-phase systems (K_C) can be defined as[14]

$$K_C = \frac{w'_C}{w''_C} \tag{16}$$

where in eq 16 w'_C and w''_C are Cephalexin mass fractions in the top and bottom phases, respectively. The partitioning of Cephalexin in aqueous two-phase systems is determined by isoactivity criterion for Cephalexin in the top and bottom phases as[15]

$$(w_C \gamma_C)' = (w_C \gamma_C)'' \tag{17}$$

Table 5. Regressed Values of the Chen−NRTL Model Parameters in $Na_3Citrate$ Quaternary Systems[a,b]

t/°C	τ_{wb}	τ_{bw}	τ_{PE}	τ_{EP}	τ_{Pb}	τ_{bP}	τ_{bE}	τ_{Eb}	100 AAD^{top}	Ω_3	100 AAD^{bot}
						PEG 4000					
28.2	−3.33	−0.060	4.03	−0.405	−0.696	−3.11	7.41	7.02	1.25	3.22	1.53
34.2	3.85	−1.96	7.41	−5.41	−2.18	−3.87	−2.17	−1.55	3.40	2.76	1.09
37.2	5.32	−1.65	16.3	−11.0	−3.22	3.68	−3.00	−2.08	1.42	4.17	1.95
						PEG 10000					
28.2	0.871	−71.5	9.5	−4.37	−58.4	14.2	61.3	57.7	1.51	4.01	1.32
34.2	1.89	−0.53	26.1	−19.7	−1.8	1.11	−0.39	−0.108	1.43	4.27	1.86
37.2	−2.64	24.2	29.9	−23.3	17.1	−10.5	−13.3	−14.9	9.32	4.08	9.40

[a] AAD = $\sum_{i=1}^{N} |(\ln \gamma^{\mathrm{calcd}} - \ln \gamma)/\ln \gamma| / N$. [b] $\Omega_3 = \sum_{i=1}^{N} \sum_j \left[(x_i \gamma_i)'_j - (x_i \gamma_i)''_j / (x_i \gamma_i)''_j\right]^2$.

Table 6. Regressed Values of the Chen−NRTL Model Parameters in K_2HPO_4 Quaternary Systems[a]

t/°C	τ_{wb}	τ_{bw}	τ_{PE}	τ_{EP}	τ_{Pb}	τ_{bP}	τ_{bE}	τ_{Eb}	100 AAD^{top}	100 AAD^{bot}	Ω_3
						PEG 4000					
28.2	−12.4	16.7	−10.4	19.1	14.3	−10.8	−1.02	−1.77	1.36	1.42	4.34
34.2	−198	33.8	−18.5	30.0	−139	−18.9	−47	36.2	2.90	4.70	5.25
37.2	−17.8	3.14	8.40	−3.88	6.86	−11.7	13.1	10.9	0.80	0.83	4.01
						PEG 10000					
28.2	−24.9	21	1.40	5.73	13	−6.10	46.5	49.2	2.60	2.90	4.40
34.2	7.45	4.76	1.45	3.85	0.858	3.15	−9.43	−8.31	1.56	1.73	4.13
37.2	27.4	1.15	3.21	1.79	−7.18	22.3	−15.4	−20.9	1.28	1.57	4.11

[a] $\Omega_3 = \sum_{i=1}^{N} \sum_j \left[(x_i\gamma_i)'_j - (x_i\gamma_i)''_j / (x_i\gamma_i)''_j\right]^2$.

Therefore, the partition coefficient is obtained in terms of the activity coefficient as

$$K_C = \frac{\gamma''_C}{\gamma'_C} \tag{18}$$

The adjustable parameters between PEG 4000, PEG 10000, and water are obtained from the activity data of water in polymer solutions and optimization of the following objective function:[16]

$$\Omega_1 = \left[\frac{\sum_{i=1}^{N} (a_w - a_w^{calcd})^2}{N}\right]^{1/2} \tag{19}$$

In the above equation, N is the number of experimental data points.

Also, adjustable parameters between ion and water are obtained from the mean activity coefficient of salt data and optimization of the following objective function[17]

$$\Omega_2 = \left[\frac{\sum_{i=1}^{N} (\ln \gamma_\pm - \ln \gamma_\pm^{calcd})^2}{N}\right]^{1/2} \tag{20}$$

In this work, the adjustable parameters between ionic component−polymer and also Cephalexin−other components are obtained from the results of activity coefficients in aqueous-phase systems containing PEG 4000, PEG 10000, $Na_3Citrate$, and K_2HPo_4 and optimization of the following objective function

$$\Omega_3 = \sum_i \sum_j \sum_k \left(\frac{x_{ijk} - x_{ijk}^{calcd}}{x_{ijk}}\right)^2 \tag{21}$$

In the above equation, i, j, and k are the number of components, phases, and tie lines, respectively.

Tables 4 to 6 present the regressed values of the parameters for the Chen−NRTL model and the average absolute deviation between the experimental data and result of the Chen−NRTL model.

Using the binary interactions, the partition coefficients of Cephalexin antibiotic in polymer-salt aqueous two-phase systems can be calculated from eq 18.

The results indicated that the Chen−NRTL model can accurately correlate the partition coefficient of Cephalexin in aqueous two-phase systems.

Conclusion

New experimental data for partitioning of Cephalexin within aqueous two-phase systems of PEG + $Na_3Citrate$ + water and PEG + K_2HPO_4 + water have been presented. The experimental data show that the partitioning of antibiotic is dependent on the temperature, the polymer molecular weight, as well as the salt and polymer concentration in feed. The Chen−NRTL model was applied to fit the partition coefficients. The proposed model has a good agreement with the experimental data. The results of the model show that the salt concentration in feed is the most important factor in antibiotic partitioning. This factor decreases the partitioning coefficient of antibiotic in PEG + $Na_3Citrate$ systems and increases it in PEG + K_2HPO_4 systems significantly. The PEG concentration in feed decreased the Ciprofloxacin partitioning coefficient. The effect of temperature on antibiotic partitioning is increasing the partition coefficient. Also, it is observed that with increasing the PEG molecular weight, the Ciprofloxacin partition coefficient decreases.

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