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Isopiestic studies of thermodynamic properties of solutions of ampicillin sodium and penicillin sodium in water at $T = 298.15$ K

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ABSTRACT

Osmotic coefficients of the solutions of ampicillin sodium and penicillin sodium in water at $T = 298.15$ K were measured using the isopiestic technique. The experimental osmotic coefficients have been correlated using the ion interaction model of Pitzer, e-NRTL model of Chen, NRF and a fourth-order polynomial in terms of molality. The vapor pressures of the solutions and the solvent activities have been calculated from the osmotic coefficients. Reliability of the models in expression of the osmotic coefficients were compared on the basis of standard deviation of the fittings.

1. Introduction

The process industry is concerned with the modeling and simulation of varieties of chemical products and processes that involve electrolyte systems in aqueous or mixed solvent solutions. Rigorous and accurate representation of the thermodynamic properties of these electrolyte systems is essential for successful modeling and simulation of such chemical products and processes [1]. It is estimated that half of all drug molecules used in medical therapies are administered as salts. Process modeling has not been practiced extensively in the pharmaceutical industry aside from emission reduction and solvent recovery studies, whereas process modeling and molecular thermodynamics could bring significant benefits to the pharmaceutical industry. The industry screens and develops hundreds of new drug candidates each year. Process chemists and engineers are tasked to develop process recipes that involve multiple reaction steps and separation steps such as crystallization or extraction. Formulation chemists are interested in understanding and enhancing drug solubility in therapeutically formulations. They are also interested in the effect of drug solubility of pharmacokinetics. When the molecular parameters are identified for solvent and solute molecules, the model offers a predictive tool for chemists and engineers to qualitatively estimate the activity coefficients and compute the solubility in pharmaceutical process design [2].

In this work, we measured the osmotic coefficients of the solutions of ampicillin sodium and penicillin sodium in water by isopiestic method at 298.15 K. We consider water as solvent in this study, due to its extensive usage in pharmaceutical processes [3]. The measured osmotic coefficient data have been represented by the ion interaction model of Pitzer [4], the local composition (LC) models including e-NRTL of Chen and Evans [5] and the NRF model of Haghtalab and Vera [6]. The data have been also correlated with a fourth-order polynomial equation in terms of molality. Fitted model parameters have been used to predict the osmotic coefficients and vapor pressure of the solutions. In the isopiestic measurements for solutions of ampicillin sodium and penicillin sodium in water, sodium chloride was used as isopiestic reference.

2. Experimental

2.1. Materials

The analytical pure grade reagent (NaCl GR, min. 99.99% by mass) was purchased from Merck. It was dried in an electrical oven at about 423.15 K for 24 h prior to use. Ampicillin sodium and penicillin sodium were obtained from Sigma–Aldrich. Solutions were prepared with deionized water. The sources of the materials used in work are given in Table 1.

2.2. Methods and apparatus

The isopiestic apparatus employed is essentially the same as the one used previously [7–13]. This apparatus consisted of a

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Table 1
provenance of the materials.

Materials	Purity	Provenance
Ampicillin sodium	Minimum 99% by mass	Sigma–Aldrich
Penicillin sodium	Minimum 99% by mass	Sigma–Aldrich
Sodium chloride	Minimum 99.9% by mass	Merck

five-leg manifold attached to round-bottom flasks. The five flasks were typically used as follows. Two flasks contained the standard NaCl solution, two flasks contained investigated solutions, and the central flask was used as water reservoir. The apparatus was held in a constant–temperature bath at least 120 h for equilibration at $T = 298.15$ K. The temperature was adjusted at $T = 298.15 \pm 0.005$ K. After equilibrium had been reached, the manifold assembly was removed from the bath and each flask was weighted with a high precision (10^{-7} kg) analytical balance. It was assumed that the equilibrium condition was reached when the differences between the molalities of each duplicate were less than 1%. The equilibrium was reached in a time interval of 5–7 days depending on the concentration of the solutions. The interval in which the weight of the samples reached a constant value, were determined primarily by continues weighting of a concentrated ($m \approx 7$ mol kg^{-1}) and a dilute sample ($m \approx 0.09$ mol kg^{-1}). In all cases, the mean of the duplicates are reported as final isopiestic molalities.

3. Results and discussion

3.1. Experimental results

The results of the isopiestic experiments including the isopiestic equilibrium molalities, the osmotic coefficients, activities, activity coefficients, and vapor pressures of the solutions have been collected in Tables 2 and 3. The osmotic coefficients of the considered solutions were obtained from the equilibrium molalities via the following relation:

$$\Phi = \frac{m_r}{m} \Phi_r \tag{1}$$

where Φ_r is the osmotic coefficient of the reference NaCl solution at the molality m_r which is in equilibrium with the antibiotic solutions in the molality m. Φ_r was calculated by the Pitzer equation with the help of the parameters reported by Pitzer for water solutions [4]. The Pitzer parameters for reference solution in the case of water are $\beta^{(0)} = 0.07670$, $\beta^{(1)} = 0.26495$, and $C^{(\Phi)} = +0.00122$. In the Pitzer model, the optimum values of α_1 and b parameters for solutions of Ampicillin sodium and Penicillin sodium in water are, respectively, 2 and 1.2. The vapor pressure of the solutions could be easily obtained from the osmotic coefficients using the following set of equations:

$$\ln(a_1) = -\upsilon m M_1 \Phi \tag{2}$$

$$\ln(a_1) = \ln\left(\frac{p}{p^*}\right) + \frac{B - V^*}{RT}(p - p^*) \tag{3}$$

In these equations M_1, B, p^* and V^* are the molar mass, the second virial coefficient, the vapor pressure, and the molar volume of the pure solvent at $T = 298.15$ K, respectively; a_1 and p are activity of the solvent in the solution and vapor pressure of the solution, respectively. R and T are also the universal gas constant and the absolute temperature and ν in Eq. (2) is the total number of ions in one molecule of the solute.

Table 2
Isopiestic equilibrium molalities, osmotic coefficient, activity, activity coefficient and vapor pressure solution of ampicillin sodium in water at 298.15 K.[a]

m_r (mol kg^{-1})	m (mol kg^{-1})	Φ_A	$\ln a_1$	$\ln \gamma_1$	p (kPa)
0.0000	0.0000	1.000	0.0000	0.0000	3.170
0.0712	0.0754	0.885	−0.0024	0.0003	3.162
0.1454	0.1575	0.856	−0.0049	0.0008	3.155
0.2358	0.3044	0.714	−0.0078	0.0031	3.145
0.2468	0.3032	0.750	−0.0082	0.0027	3.144
0.2967	0.3871	0.705	−0.0098	0.0040	3.139
0.3541	0.4627	0.704	−0.0117	0.0048	3.133
0.3679	0.4700	0.720	−0.0122	0.0046	3.132
0.3730	0.5250	0.654	−0.0124	0.0064	3.131
0.3749	0.5325	0.648	−0.0124	0.0066	3.131
0.3810	0.5215	0.672	−0.0126	0.0060	3.130
0.4864	0.7507	0.597	−0.0161	0.0105	3.119
0.4893	0.6922	0.651	−0.0162	0.0084	3.119
0.4901	0.7007	0.644	−0.0163	0.0087	3.119
0.4923	0.6767	0.670	−0.0163	0.0078	3.119
0.4936	0.7369	0.617	−0.0164	0.0098	3.118
0.5455	0.8511	0.591	−0.0181	0.0121	3.113
0.5497	0.8284	0.612	−0.0183	0.0111	3.113
0.5686	0.8951	0.586	−0.0189	0.0128	3.111
0.6327	1.0150	0.576	−0.0211	0.0149	3.104
0.6433	1.0293	0.578	−0.0214	0.0150	3.103
0.6439	0.9725	0.612	−0.0214	0.0130	3.103
0.6515	0.9835	0.612	−0.0217	0.0131	3.102
0.6804	1.0932	0.576	−0.0227	0.0160	3.099
0.6918	1.1342	0.564	−0.0231	0.0170	3.098
0.8463	1.3690	0.575	−0.0284	0.0198	3.081
0.8640	1.3919	0.578	−0.0290	0.0200	3.079
0.8920	1.4758	0.563	−0.0299	0.0219	3.076
0.9909	1.6992	0.546	−0.0334	0.0260	3.066
1.1136	1.9122	0.548	−0.0377	0.0289	3.052
1.2994	2.3980	0.514	−0.0444	0.0385	3.032
1.3109	2.3965	0.519	−0.0448	0.0380	3.031
1.4856	2.8554	0.498	−0.0512	0.0467	3.011
1.5126	2.8671	0.506	−0.0522	0.0461	3.008
1.5366	2.9582	0.499	−0.0531	0.0481	3.006
1.5383	2.9319	0.504	−0.0532	0.0472	3.005
1.7437	3.3011	0.513	−0.0610	0.0514	2.982
2.0876	3.8392	0.538	−0.0744	0.0552	2.942
2.2218	4.1030	0.540	−0.0798	0.0581	2.926
2.3803	4.2610	0.562	−0.0863	0.0565	2.908
2.4306	4.4394	0.553	−0.0884	0.0600	2.901
3.6415	5.6988	0.696	−0.1430	0.0438	2.747
4.3216	5.9914	0.822	−0.1774	0.0181	2.654
4.9481	6.7731	0.867	−0.2117	0.0067	2.565
5.6021	7.4678	0.930	−0.2502	−0.0120	2.467

[a] m_r, molality of isopiestic reference; m, molality of studied solution; Φ_A, osmotic coefficient; $\ln \gamma_1$, logarithm of activity coefficient of solvent; $\ln a_1$, logarithm activity of solvent; p, vapor pressure; uncertainty for molality $\delta(m) = \pm 0.0001$ mol kg^{-1}, uncertainty for osmotic coefficient $\delta(\Phi) = \pm 0.025$, and uncertainty for vapor pressure $\delta(p) = \pm 0.001$ kPa.

3.2. Correlation of data

3.2.1. Pitzer model

The Pitzer's equation for a binary solution of a 1:1 electrolyte in a solvent has the following form:

$$\Phi = 1 + f^{\Phi} + mB^{\Phi} + m^2 C^{\Phi} \tag{4}$$

in which

$$f^{\Phi} = \frac{-A_{\Phi}\sqrt{I}}{1 + b\sqrt{I}} \tag{5}$$

and

$$B^{\Phi} = \beta^{(0)} + \beta^{(1)} \exp(-\alpha_1 \sqrt{I}) + \beta^{(2)} \exp(-\alpha_2 \sqrt{I}) \tag{6}$$

In the above equations A_{Φ} and I are Debye–Hückel constants for the osmotic coefficients and ionic strength on a molal basis ($I = (1/2)\sum_{i=\text{ions}} m_i z_i^2$); b, α_1 and α_2 are constant parameters of the model; $\beta^{(0)}$, $\beta^{(1)}$, $\beta^{(2)}$ and C^{Φ} are adjustable parameters fitted to the experimental osmotic coefficient data.