

Solubility of D-Aspartic Acid and L-Aspartic Acid in Aqueous Salt Solutions from (293 to 343) K

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The solubility of D-aspartic acid and L-aspartic acid in aqueous solutions of various molalities of sodium chloride and potassium chloride was measured by using a laser technique from (293 to 343) K at atmospheric pressure. Results showed that sodium chloride and potassium chloride have a salting-in effect on the solubility of D-aspartic acid and L-aspartic acid has the same phenomenon in sodium chloride solution. The solubility data were correlated by a semiempirical equation.

Introduction

At the present time, increasing importance has been attached to chiral drug. D-Aspartic acid ($C_4H_7NO_4$, molecular weight 133.1036, CAS Registry No. 1783-96-6) and L-aspartic acid ($C_4H_7NO_4$, molecular weight 133.1036, CAS Registry No. 56-84-8) are white crystalline powder and important chiral compounds. As can be seen from Figures 1 and 2, D-aspartic acid and L-aspartic acid have an amino group and two carboxyl groups in their structure. As an side chain of the β -lactam antibiotic, D-aspartic acid has been widely used in synthesis of aspoxicillin, D-aspartic acid β -hydroxylamine, and other antibiotics for combination drugs. L-Aspartic acid has a slightly acidic taste and is soluble in acid, slightly soluble in water, and difficult to dissolve in ethanol. L-Aspartic acid can be used as a nutritional supplement of cool drinks, can also be used as a biochemical reagent and medium and intermediate in organic synthesis, and is one of the major raw materials for the sweetener aspartame and for the pharmaceutical intermediate L-asparagine monohydrate.

The reported purification of D-aspartic acid includes physical methods, chemical methods, and biological methods. Physical methods are commonly used as the preferential crystallization procedure.¹ The preparation of L-aspartic acid includes the chemosynthesis method, enzymatic synthesis method, extraction method, and zymotechnics method.² During these processes, there are some inorganic salts, acids, and alkali that are present in the system as impurities. To design an optimized crystallization process that is pertinent to be used in a production plant, it is necessary to know their solubilities in such aqueous salt solutions.

Aqueous solubility is an especially important parameter for assessing environmental partitioning of different compounds. Because of the presence of cosolutes, two phenomena can be observed, salting-in and salting-out effects,^{3–7} and the salting-in and salting-out effects are due to a decrease and an increase in the activity coefficient of the nonelectrolyte with increasing electrolyte concentration.⁸ The aim of this paper was to study the effect of electrolytes on the solubility of D-aspartic acid and L-aspartic acid.

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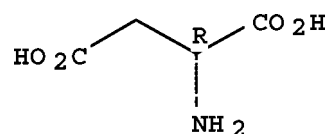


Figure 1. Chemical structure of D-aspartic acid.

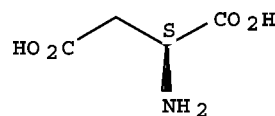


Figure 2. Chemical structure of L-aspartic acid.

Experimental Section

Chemicals. D-Aspartic acid and L-aspartic acid were purchased from the GL Biochem (Shanghai) Co., Ltd. Its purity was determined by high-performance liquid chromatography (HPLC) to be higher than 98.5 % in mass fraction. Distilled deionized water of HPLC grade was obtained from the market. Sodium chloride and potassium chloride which were analytical research grade reagents were purchased from the Beijing Huateng Chemical Co., Ltd., and their mass fraction purity was higher than 99.8 %.

Apparatus and Procedure. The solubilities were measured by a laser technique at atmospheric pressure. A laser generator, a photoelectric transformer, and a light-intensity display comprise the laser monitoring observation system which had been described in the literature.^{9–11} The dissolution of the solute was carried out in a magnetically stirred jacketed glass vessel (300 mL), which was maintained at the constant temperature by continuous forced water circulation from a super thermostat bath (temperature uncertainty of ± 0.05 K) at the required temperature. A calibrated mercury-in-glass thermometer (uncertainty of ± 0.05 K) was inserted into the inner chamber of the vessel to determine the temperature. A condenser was connected with the vessel to prevent the water from evaporating. A laser beam penetrating the vessel was used to monitor the dissolution process. The masses of the samples and water were determined using an analytical balance (Sartorius CP124S, Germany) with an uncertainty of ± 0.1 mg.

The process of solubility measurement is similar to that in the literature¹² and is unnecessary to be described here.

Table 1. Solubility (x_A) of D-Aspartic Acid (A) in Different Molalities of Aqueous Sodium Chloride Solutions

T/K	$10^3 x_A$	T/K	$10^3 x_A$	T/K	$10^3 x_A$
$b = 0.0000$					
293.50	0.5895	312.65	1.138	332.65	2.159
298.10	0.6835	318.00	1.357	337.55	2.495
303.30	0.8226	322.45	1.571	342.35	2.872
308.00	0.9712	327.95	1.856		
$b = 0.1687$					
292.80	0.6090	313.25	1.269	332.65	2.344
298.60	0.7622	318.15	1.490	338.05	2.749
303.65	0.9135	322.55	1.728	342.85	3.173
308.40	1.082	327.85	2.021		
$b = 0.4957$					
293.45	0.6946	313.10	1.335	332.55	2.453
298.15	0.8066	318.05	1.573	337.45	2.852
303.15	0.9540	322.95	1.843	343.45	3.421
308.40	1.140	327.70	2.130		
$b = 0.9633$					
293.65	0.7280	313.15	1.412	332.95	2.583
298.25	0.8582	318.00	1.645	337.85	3.004
303.15	1.009	322.85	1.936	343.85	3.569
308.45	1.200	328.15	2.224		
$b = 1.4031$					
293.45	0.7645	312.85	1.417	332.95	2.631
298.15	0.8886	318.25	1.681	337.85	3.038
303.50	1.056	323.05	1.955	343.15	3.559
307.85	1.224	328.05	2.263		
$b = 1.8251$					
293.55	0.7685	312.85	1.448	333.25	2.679
298.20	0.9031	318.15	1.720	338.15	3.117
303.60	1.082	322.95	1.995	343.55	3.662
308.05	1.243	328.35	2.309		

The molality of aqueous sodium chloride (or potassium chloride) solutions b ($\text{mol} \cdot \text{kg}^{-1}$) was based on the following equation:

$$b = \frac{m_S/M_S}{(m_W + m_S)/1000} \quad (1)$$

where m_W and m_S represent the masses of the water and sodium chloride (or potassium chloride), respectively, and M_S are the molecular weights of the sodium chloride (or potassium chloride). The mole fraction solubility x_A was based on the following equation:

$$x_A = \frac{m_A/M_A}{m_A/M_A + m_W/M_W + m_S/M_S} \quad (2)$$

where m_A , m_W , and m_S represent the masses of the D-aspartic acid (or L-aspartic acid), water, and sodium chloride (or potassium chloride), respectively, and M_A , M_W , and M_S are the molecular weights of the D-aspartic acid (or L-aspartic acid), water, and sodium chloride (or potassium chloride), respectively. As can be seen in Figure 5, the solubilities of L-aspartic acid in pure water show a satisfactory agreement with the literature values.¹³ The relative uncertainty of the experimental solubility values which comes from temperature measurement and weighing process is about 2%.

Results and Discussion

The experimental solubilities of D-aspartic acid and L-aspartic acid in a series of molalities of aqueous salt solutions are presented in Tables 1 to 3 and graphically plotted in Figures 3 to 5 together with their calculated solubilities. The temperature dependence of D-aspartic acid and L-aspartic acid solubility in

Table 2. Solubility (x_A) of D-Aspartic Acid (A) in Different Molalities of Aqueous Potassium Chloride Solutions

T/K	$10^3 x_A$	T/K	$10^3 x_A$	T/K	$10^3 x_A$
$b = 0.0000$					
293.50	0.5895	312.65	1.138	332.65	2.159
298.10	0.6835	318.00	1.357	337.55	2.495
303.30	0.8226	322.45	1.571	342.35	2.872
308.00	0.9712	327.95	1.856		
$b = 0.1324$					
292.95	0.6168	313.25	1.277	333.05	2.362
298.55	0.7572	318.10	1.496	338.35	2.781
303.62	0.9101	322.45	1.725	343.25	3.217
308.50	1.084	328.15	2.041		
$b = 0.3982$					
293.63	0.7104	313.05	1.361	333.20	2.512
298.25	0.8383	318.35	1.632	338.20	2.938
303.15	0.9803	323.10	1.869	343.15	3.374
307.95	1.160	328.50	2.188		
$b = 0.7744$					
293.55	0.7517	313.10	1.448	333.60	2.713
298.02	0.9044	318.05	1.735	338.55	3.140
303.25	1.080	323.15	2.009	343.50	3.634
307.95	1.245	328.75	2.349		
$b = 1.1047$					
293.50	0.8052	312.80	1.521	332.50	2.754
298.20	0.9229	318.05	1.779	337.60	3.187
303.15	1.107	323.00	2.058	342.90	3.692
307.60	1.282	328.00	2.381		
$b = 1.4360$					
293.65	0.8550	313.00	1.602	333.50	2.928
298.25	0.9982	318.05	1.884	338.90	3.402
303.00	1.167	323.20	2.178	344.10	3.938
308.20	1.355	328.75	2.524		

Table 3. Solubility (x_A) of L-Aspartic Acid (A) in Different Molalities of Aqueous Sodium Chloride Solutions

T/K	$10^3 x_A$	T/K	$10^3 x_A$	T/K	$10^3 x_A$
$b = 0.0000$					
292.96	0.5588	313.75	1.206	333.25	2.216
298.44	0.7081	318.25	1.398	338.08	2.557
303.58	0.8619	323.56	1.646		
308.56	1.032	328.47	1.922		
$b = 0.1646$					
293.86	0.6314	313.24	1.251	332.95	2.288
298.36	0.7606	317.68	1.452	337.85	2.669
303.24	0.9131	323.05	1.716		
308.17	1.076	327.84	1.997		
$b = 0.4581$					
294.03	0.6943	312.98	1.341	333.33	2.438
298.65	0.8249	317.98	1.577	338.06	2.821
303.35	0.9738	323.05	1.834		
308.07	1.138	328.04	2.108		
$b = 0.8956$					
292.90	0.7202	313.54	1.450	333.35	2.580
298.64	0.8772	318.30	1.667	338.19	2.942
303.83	1.052	323.46	1.929		
308.70	1.238	328.37	2.242		
$b = 2.4036$					
293.34	0.8032	313.45	1.483	333.27	2.660
298.10	0.9320	318.44	1.728	338.08	3.048
304.04	1.105	323.44	1.995		
308.26	1.271	328.46	2.301		
$b = 3.0446$					
293.70	0.8414	312.93	1.499	333.03	2.691
298.13	0.9523	317.90	1.742	337.76	3.087
302.80	1.107	323.00	2.032		
307.86	1.278	328.24	2.348		

aqueous solutions was described by the modified empirical equation proposed by Heidman et al.¹⁴

$$\ln x_A = A + \frac{B}{T/K} + C \ln(T/K) \quad (3)$$

In eq 3, x_A is the mole fraction solubility of D-aspartic acid (or L-aspartic acid) in aqueous solutions, and T is the absolute

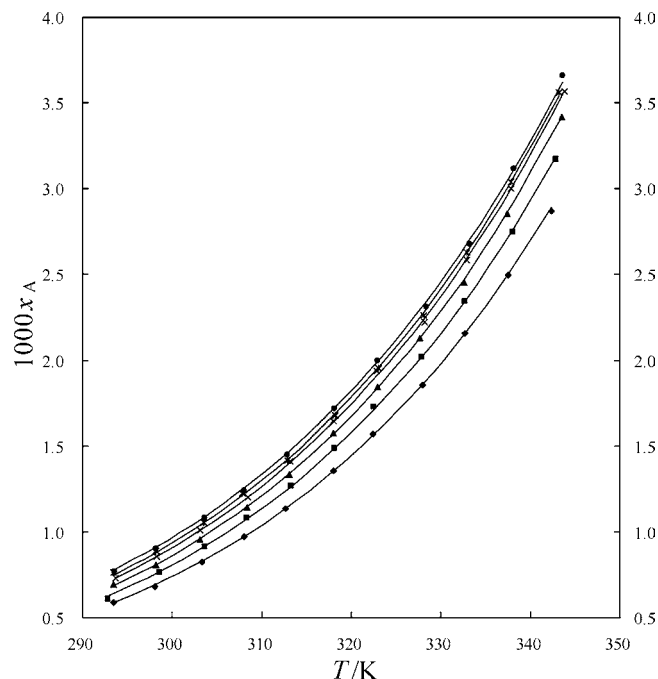


Figure 3. Experimental solubility of D-aspartic acid in aqueous sodium chloride solution: \blacklozenge , $b = 0.0000$; \blacksquare , $b = 0.1687$; \blacktriangle , $b = 0.4957$; \times , $b = 0.9633$; $*$, $b = 1.4031$; \bullet , $b = 1.8251$; solid line, calculated from eq 3.

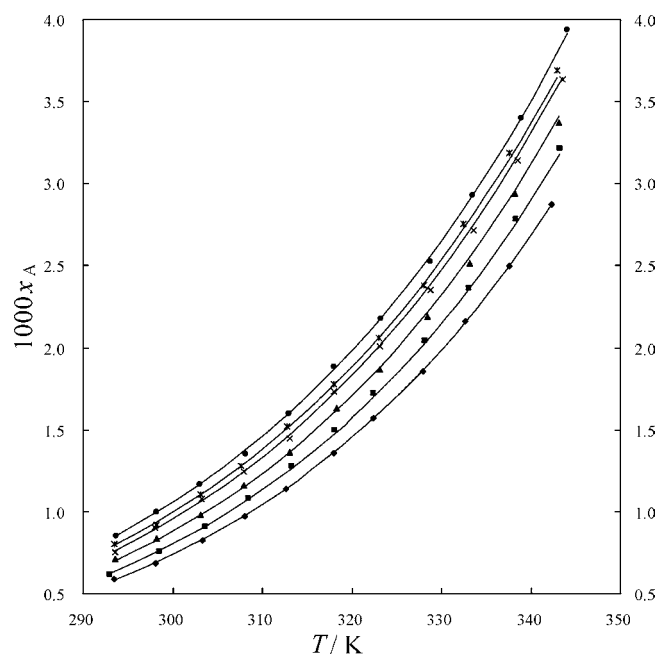


Figure 4. Experimental solubility of D-aspartic acid in aqueous potassium chloride solution: \blacklozenge , $b = 0.0000$; \blacksquare , $b = 0.1324$; \blacktriangle , $b = 0.3982$; \times , $b = 0.7744$; $*$, $b = 1.1047$; \bullet , $b = 1.4360$; solid line, calculated from eq 3.

temperature. A , B , and C are the empirical parameters which are given in Table 4 together with the root-mean-square deviations (rmsd's) calculated according to the formula:

$$\text{rmsd} = \left[\sum_{i=1}^n \frac{(x_A - x_A^{\text{cal},2})^2}{N} \right]^{1/2} \quad (4)$$

where N is the number of experimental points and x_A^{cal} and x_A represent the solubilities calculated from eq 3 and the experimental values, respectively.

From Tables 1 to 4 and Figures 3 to 5, we can draw the following conclusions: (1) The solubility of D-aspartic acid and

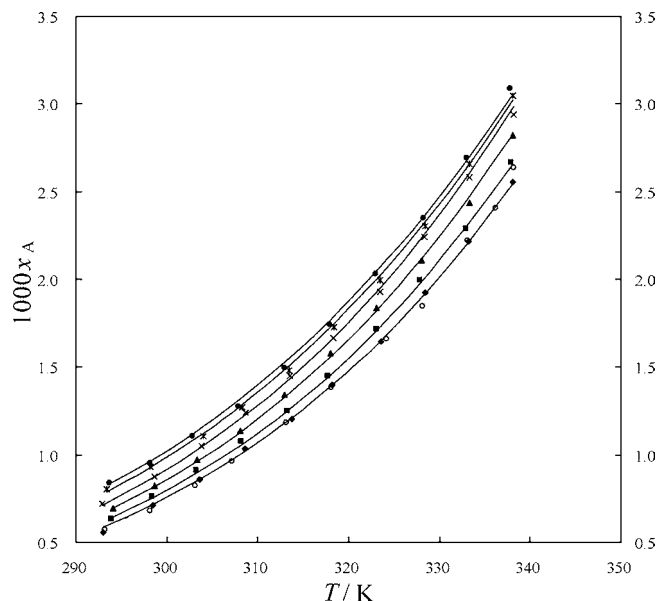


Figure 5. Experimental solubility of L-aspartic acid in aqueous sodium chloride solution: \blacklozenge , $b = 0.0000$; \blacksquare , $b = 0.1646$; \blacktriangle , $b = 0.4581$; \times , $b = 0.8956$; $*$, $b = 2.4036$; \bullet , $b = 3.0446$; \circ , ref 12; solid line, calculated from eq 3.

Table 4. Parameters of Equation 3 for D-Aspartic Acid and L-Aspartic Acid in Aqueous Sodium Chloride and Potassium Chloride Solutions

	$b/\text{mol}\cdot\text{kg}^{-1}$	A	B	C	10^5 rmsd
D-aspartic acid	Water + Sodium Chloride				
	0.0000	-48.6458	-830.615	7.74965	0.72
	0.1687	-48.2665	-830.608	7.69882	0.97
	0.4957	-47.6292	-830.604	7.59866	0.80
	0.9633	-46.7255	-830.601	7.44939	1.17
	1.4031	-45.8721	-830.597	7.30510	1.08
	1.8251	-45.0171	-830.593	7.16081	1.88
	Water + Potassium Chloride				
	0.0000	-32.8269	-1561.25	5.40376	0.52
	0.1324	-32.3899	-1561.13	5.34165	1.81
0.3982	-31.5764	-1561.09	5.21484	2.16	
0.7744	-30.4172	-1561.07	5.02591	2.08	
1.1047	-29.4024	-1561.04	4.85511	2.10	
1.4360	-28.3068	-1561.01	4.67395	1.54	
L-aspartic acid	Water + Sodium Chloride				
	0.0000	-10.7399	-2549.96	2.11348	1.19
	0.1646	-10.4227	-2549.92	2.06692	1.53
	0.4581	-9.87353	-2549.89	1.98310	1.53
	0.8956	-9.06699	-2549.82	1.85332	1.97
	2.4036	-6.23409	-2549.75	1.36946	2.04
	3.0446	-4.91051	-2549.61	1.14392	2.46

L-aspartic acid in aqueous solutions increases with temperature. (2) Sodium chloride and potassium chloride have a salting-in effect on the solubility of D-aspartic acid. With the molalities of sodium chloride or potassium chloride increasing, the solubility of D-aspartic acid increases in aqueous solution. The solubility of L-aspartic acid has the same phenomenon in sodium chloride solution. The potassium chloride has a stronger salting-in effect than sodium chloride on the solubility of D-aspartic acid. When the molalities of solutions of the two salts approach saturated molalities, the solubility of the two aspartic acids increases slightly. (3) The solubilities of D-aspartic acid in pure water are similar to the solubilities of L-aspartic acid in pure water. (4) The calculated solubilities of D-aspartic acid and L-aspartic acid in aqueous solutions show good agreement with the experimental values, and the experimental solubility and correlation equation in this work can be used as essential data and models in the practical purification process of D-aspartic acid and L-aspartic acid.

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