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Thermodynamics Properties of Oxymatrine in NaCl Solution

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The enthalpies of dissolution of oxymatrine in 0.9%NaCl solution were measured using a RD496-2000 Calvet Microcalorimeter at 309.65 K under atmospheric pressure. The differential enthalpy and molar enthalpy of oxymatrine dissolution in the 0.9%NaCl solution of were determined. The corresponding kinetic equation that described the dissolution process was elucidated. Moreover, the half-life, molar entropy, molar enthaply, and Gibbs free energy of the dissolution process were also obtained.

Key words: Oxymatrine, Thermodynamic, Kinetics, 0.9%NaCl solution

I. INTRODUCTION

Oxymatrine is one of the quinolizidine alkaloids extracted from the root of traditional Chinese herbal medicine *Sophora japonica* (*Sophora Flavescesn Ait*) [1]. The chemical structure of oxymatrine is shown in Fig.1. As we can see, there are two nitrogen atoms in the molecule, one as an amide and another binding with an oxygen atom to form a coordination bond. This mode of the bond resulted in its electron supplying capacity weakened, so its alkaline weakened, but its hydrophilicity increased. As a result, oxymatrine would dissolve well in water, solution of citric acid, and carbonate, chloroform, and ethanol; but poor in ether, petroleum ether and ethyl acetate *etc.* [2].

In the clinical researches of the past few years, oxymatrine played important roles in anti-virus, protecting hepatocytes, anti-hepatic fibrosis, and immune regulation [3−6]. However, few studies have been done on its dissolution properties, especially in the aspect of dissolution kinetic equation and kinetic parameter. Wang *et al.* detected the change of oxymatrine concentration in blood by the pharmacokinetic principle using high performance liquid chromatography (HPLC) and calculated its half-life period in blood, which was 1.5 h [7]. This method was accurate and effective for living system but the operating procedure was complex and its results produced a great deviation.

In this work, the enthalpy of oxymatrine in 0.9% NaCl solution which is isotonic to human plasma was measured by microcalorimetry, which is simple and easy. On the basis of these experimental data and calculated results, the kinetic equation, half-life period, molar entropy $\Delta_{\rm sol}H_{\rm m}$, Gibbs free energy $\Delta_{\rm sol}G_{\rm m}$, and molar enthaply $\Delta_{\rm sol}S_{\rm m}$ of the dissolution process were obtained. This work may provide a potential reference for the clinical application of oxymatrine.

II. EXPERIMENTS

Oxymatrine was purchased from Baoji Fangsheng Biological Development Co., Ltd. (purity: >98%). NaCl was analytical grade, and the solution of NaCl was prepared with deionized water.

The experiment was performed using a RD496-2000 Calvet Microcalorimeter (Mianyang CAEP Thermal Analysis Instrument Company, China). The microcalorimeter was calibrated by Joule effect and its sensitivity was 64.22±0.04 mV/W at 309.65 K. The enthalpy of dissolution of KCl (spectrum purity) in distilled water (about 20 mg/2.0 g) measured at 298.15 K was 17.535 kJ/mol, which was in an excellent accordance with the literature value of 17.545 kJ/mol [8], showing that the device of measuring the enthalpy used in this work was reliable.

The proper amounts of oxymatrine (119.4, 167.4, 240.3, 305.1, 382.1 mg) were dissolved in 2.00 mL of 0.9%NaCl solution, respectively, at 309.65 K under the atmospheric pressure. The enthalpy change of the process was detected by the RD496-2000 Calvet Microcalorimeter.

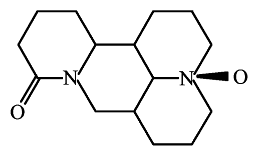

FIG. 1 The chemical structure of oxymatrine.

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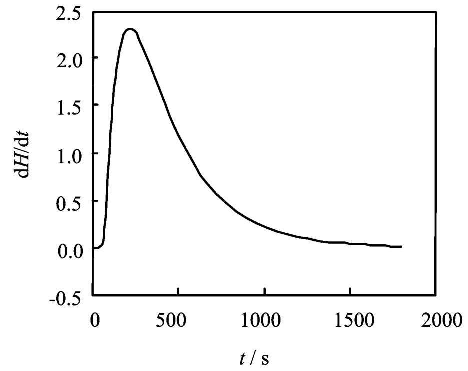

FIG. 2 Heating rate ($\mathrm{d}H/\mathrm{d}t$) of the entire dissolution process of oxymatrine in 2.00 mL 0.9%NaCl.

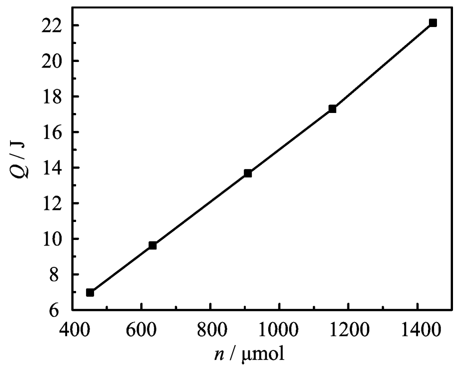

FIG. 3 The liner relationship between the heat effect Q and the amount of the oxymatrine n.

TABLE I The dissolution enthalphy of oxymatrine with different mass in 2.00 mL 0.9%NaCl solution.

m/mg	n/μmol	c/(mol/L)	Q/J	$\Delta_{\mathrm{sol}}H_{\mathrm{m}}$[a]/(kJ/mol)
119.4	451.66	0.2258	6.9711	15.43
167.4	633.15	0.3166	9.61710	15.18
240.0	908.99	0.4545	13.6715	15.04
305.1	1154.26	0.5771	17.2943	14.98
382.1	1445.49	0.7237	22.1394	15.31

[a] Average is 15.19±0.18.

III. RESULTS AND DISCUSSION

A. Thermochemical behaviors of the dissolution of oxymatrine in 0.9%NaCl solution

Five different mass of oxymatrine was dissolved in 2 mL 0.9%NaCl at 309.65 K, and there are five concentration of oxymatrine to be carried out in this experiment. The entire dissolution process of oxymatrine in 0.9%NaCl was studied and repeated three times. The results are shown in Fig.2. The dissolution is an exothermic process. The heat flow curves obtained under the same conditions overlap with each other, indicating that the reproducibility of test is satisfactory.

Table I shows the experimental data obtained from the typical thermogram curve of the dissolution with different mass of oxymatrine in 2.00 mL 0.9%NaCl solution. As we can see in Table I, the concentration of the solution almost has little influence on the values of the molar enthalpy ($\Delta_{\mathrm{sol}}H_{\mathrm{m}}$) at 309.65 K. So the average value of $\Delta_{\mathrm{sol}}H_{\mathrm{m}}$ can represent the molar enthalpy of the infinite diluted 0.9% NaCl solution at 309.65 K [9].

The relationship between heat effect and the amount of the substance of oxymatrine in 0.9%NaCl solution is shown in Fig.3. The according linear equation for the 0.9%NaCl solution is as follow:

$$Q = 1.5173n, \quad r = 0.9996 \tag{1}$$

where r is correlation coefficient. The differential enthalpy ($\Delta_{\mathrm{dif}}H_{\mathrm{m}}$) is obtained from Eq.(1). So the differential enthalpy of oxymatrine in the 0.9%NaCl solution is about 15.17 kJ/mol.

B. Kinetic of dissolution process of oxymatrine in the 0.9%NaCl solution

Table II shows the original data in dissolution process of oxymatrine in the 0.9%NaCl solution, the kinetic equation Eq.(2) describing the dissolution of oxymatrine in 0.9%NaCl is chosen as the model function to describe the dissolution rate,

$$\frac{\mathrm{d}\alpha}{\mathrm{d}t} = kf(\alpha) = k\,(1-\alpha)^n \tag{2}$$

where α is the conversion degree, $f(\alpha)$ is the kinetic function. And then substituting $\alpha = H_t/H_0$ into the Eq.(2) and then get a logarithmic converter:

$$\ln\left[\frac{1}{H_0}\left(\frac{\mathrm{d}H}{\mathrm{d}t}\right)_i\right] = \ln k + N\ln\left[1-\left(\frac{H_t}{H_0}\right)_i\right] \tag{3}$$
$$i = 1, 2, \ldots, L$$

H_t represents the heat at time of t, H_0 is the heat of the whole process, k is the rate of oxymatrine dissolved in the 0.9%NaCl solution, N is the reaction order and L is the counting number. By substituting the data taken from Table II, $(\mathrm{d}H/\mathrm{d}t)_i$, $(H/H_\infty)_i$, H_∞, i=1, 2, ..., L, into the kinetic Eq.(3), the obtained values of N and ln$k$ are listed in Table III. Substituting the values of N and ln$k$ in Table III into Eq.(2), we can get that the kinetic equation of the dissolution process is

$$\frac{\mathrm{d}\alpha}{\mathrm{d}t} = 10^{-3.68}(1-\alpha)^{1.01} \tag{4}$$

The kinetic equation is similar to quasi-first order reaction of the dissolution process. So the half-life period can be calculated with Eq.(6), which was 55.29 min.

$$t_{1/2} = \frac{\ln 2}{k} \tag{5}$$

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TABLE II The original data of oxymatrine in 2.00 mL 0.9%NaCl solution.

m/mg	t/s	dH/dt	H_t/mJ	H_0/mJ	m/mg	t/s	dH/dt	H_t/mJ	H_0/mJ
119.4	60	0.7391	2890.27	6971.1	240.3	420	0.3294	12397.87	
	120	0.5480	4095.29			480	0.2664	12676.43	
	180	0.3808	4957.90			540	0.2153	12902.01	
	240	0.2573	5548.59			600	0.1724	13082.16	
	300	0.1723	5945.34			660	0.1832	13226.62	
	360	0.1157	6211.08			720	0.1078	13340.84	
	420	0.0788	6390.63		305.1	60	1.2672	11457.97	17293.4
	480	0.0540	6513.28			120	1.0456	12537.70	
	540	0.0384	6598.68			180	0.8570	13425.35	
	600	0.0285	6660.63			240	0.6993	14151.80	
	660	0.0222	6707.67			300	0.5693	14743.41	
	720	0.0182	6745.15			360	0.4636	15224.89	
167.4	60	0.9730	4921.94	9617.1		420	0.3773	15616.70	
	120	0.6795	6549.04			480	0.3086	15936.07	
	180	0.4561	7509.85			540	0.2510	16196.51	
	240	0.3009	8208.65			600	0.2051	16409.51	
	300	0.1975	8668.01			660	0.1669	16583.01	
	360	0.1288	8968.01			720	0.1366	16724.64	
	420	0.0841	9164.38		382.1	60	1.5453	15120.64	22139.4
	480	0.0553	9293.08			120	1.2746	16333.91	
	540	0.0378	9378.83			180	1.0513	17419.70	
	600	0.0267	9438.24			240	0.8632	18313.01	
	660	0.0201	9481.26			300	0.7061	19044.81	
	720	0.0151	9514.06			360	0.5758	19642.85	
240.3	60	1.0606	8835.61	13671.5		420	0.4699	20130.55	
	120	0.8858	9744.20			480	0.3830	20528.49	
	180	0.7337	10500.06			540	0.3119	20852.66	
	240	0.6028	11124.67			600	0.2539	21116.40	
	300	0.4937	11636.90			660	0.2059	21330.73	
	360	0.4041	12055.67				720	0.1673	21504.80

TABLE III N and ln$k$ of oxymatrine in the solution of NaCl (0.9%) at 309.65 K.

m/mg	N	ln$k$	r
119.4	1.2660	−8.38	0.9941
167.4	1.0827	−8.39	0.9986
240.0	0.8549	−8.59	0.9999
305.1	0.9546	−8.49	0.9999
382.1	0.9151	−8.55	0.9998
Average	1.0147	−8.48	0.9985

C. Thermodynamic of oxymatrine in the 0.9%NaCl solution

On the basis of these experimental data and calculated results, the kinetic parameters of the dissolution process can be obtained from Eq.(6) [10].

$$\ln\frac{k}{T}=\left(\frac{\Delta S_{\mathrm{m}}^{\ominus}}{R}+\ln\frac{k_{\mathrm{B}}}{\hbar}\right)-\frac{\Delta H_{\mathrm{m}}^{\ominus}}{RT} \tag{6}$$

Eq.(6) can be changed into the following expression,

$$\ln\frac{kh}{k_{\mathrm{B}}T}=\frac{\Delta_{\mathrm{sol}}S_{\mathrm{m}}}{R}-\frac{\Delta_{\mathrm{sol}}H_{\mathrm{m}}}{RT} \tag{7}$$

substituting k=$10^{-3.68}$ s^{-1}, k_B=1.38×10^{-23} J/K, $\hbar$=6.626×10^{-234} J/s, $\Delta_{\mathrm{sol}}H_{\mathrm{m}}$=15.19 kJ/mol, R=8.314 J/(mol K), T=309.65 K into Eq.(6), so $\Delta_{\mathrm{sol}}S_{\mathrm{m}}$=−266.62 J/(mol K). And then putting $\Delta_{\mathrm{sol}}H_{\mathrm{m}}$ and $\Delta_{\mathrm{sol}}S_{\mathrm{m}}$ into the following formula

$$\Delta_{\mathrm{sol}}G_{\mathrm{m}}=\Delta_{\mathrm{sol}}H_{\mathrm{m}}-T\Delta_{\mathrm{sol}}S_{\mathrm{m}} \tag{8}$$

we can obtain $\Delta_{\mathrm{sol}}G_{\mathrm{m}}$=97.75 kJ/mol.

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IV. CONCLUSION

The molar enthalpy of oxymatrine in the 0.9%NaCl solution was measured with the RD496-2000 type Calvet Microcalorimeter at 309.65 K under the atmospheric pressure. From the results it can be observed that the concentration of oxymatrine have little impact on the enthalpies. Thus, the average value of $\Delta_{\rm sol}H_{\rm m}$ can represent the molar enthalpy which is 15.19 kJ/mol.

The kinetic equation of the dissolution process of oxymatrine in the 0.9%NaCl solution at 309.65 K is $d\alpha/dt=10^{-3.68}(1-\alpha)^{1.01}$. It is a quasi-first order reaction, and its half-life is $t_{1/2}$=55.29 min, the rate constant is $k=10^{-3.68}$ s^{-1}.

The dissolution of oxymatrine in the 0.9%NaCl solution is an exothermic process. The $\Delta_{\rm sol}H_{\rm m}$ is 15.19 kJ/mol, and $\Delta_{\rm sol}S_{\rm m}$ is −266.62 J/(mol K). The negative value of entropy of activation indicates that the dissolution of oxymatrine in the 0.9%NaCl solution get a more ordered system.

V. ACKNOWLEDGMENTS

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