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Thermodynamic properties of laburnine in saline and glucose solutions

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Abstract Laburnine's dissolution behaviors in glucose and saline solution were studied by a micro-calorimetry method. The measured integral and differential heats of solution were utilized to build equations of the solute and the heat, so that dissolution thermodynamic equations and half-time periods, $\Delta_{sol}H_m$, $\Delta_{sol}G_m$, and $\Delta_{sol}S_m$ were obtained. The results show that this study does not only provide a simple method for the determination of the half-life period for a drug but also offer a theoretical reference for the clinical application of laburnine.

Keywords Thermodynamics · Dynamics · Laburnine · Saline · Glucose

Introduction

Laburnine (chemical formula $C_{11}H_{14}N_2O$, molecular weight 190.24, melting point 154–156 °C) is an alkaloid isolated from *Sophora alopecuroides* of leguminous *Sophora* roots. It normally presents as white or whitish crystalline powder without odor and with bitter taste.

Laburnine can increase white blood cells and has functions of enhancing immunity, anti-*Shigella*, skin fungus, hypnosis, anti-asthmatic, anti-arrhythmia effect, etc. [1]. Therefore, it has been widely used in the treatment of diarrhea, lymphadenitis, arrhythmias, leukopenia, and other diseases. It has been utilized as injection medicine and widely used in clinics [2]. However, studies on its half-life are limited in number, which make the preparation and application of this medicine on the empirical or semiempirical level difficult. Although scientists have calculated the half-lives of a few drugs using high performance liquid chromatography to detect its concentration change in human bloods based on pharmacokinetic principles, such a method involves complicated procedures and leads to errors in results because of disparities in individuals' living bodies [3]. Some researchers have studied a few drugs by calorimetry method [4]. However, few studies have been carried out on the dissolution properties of this type of compounds [5], especially in respect of dissolution kinetic equation and kinetic parameter. To address this problem, the calorimetry method was applied to mimic body temperatures, the heats of solution of laburnine were investigated in different solvents, and their half-time periods were further calculated based on thermodynamic treatment. The results are consistent to the ones from pharmacokinetics, but the method is simple. Moreover, the distribution of different systems and thermal stabilities of solutions can be generated from the ΔS during the dissolution process. Therefore, the studies on their thermodynamic functions and determination of its kinetic parameters have significant meanings on improving the quality of medicines and broadening their clinic applications.

Experimental

Materials

Laburnine was purchased from Baoji Fangsheng Biological Development Co., Ltd. (purity: ~99%). Saline (medical), Glucose (medical).

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Equipment and conditions

Thermoanalyzer Systems (American Thermoanalyzer Companies Inc.) were used for determining the DSC–TG curves of laburnine (Fig. 1). The experiment was performed using a RD496-2000 Calvet microcalorimeter (Mianyang CAEP Thermal Analysis Instrument Company, China). The microcalorimeter was calibrated by the Joule effect, and its sensitivity was found to be 64.22 ± 0.04 μV mW^{-1} at 309.65 K. The enthalpy of dissolution of KCl (spectrum purity) in distilled water (about 20 mg/2.000 g) measured at 298.15 K was 17.535 kJ mol^{-1}, which is in excellent accordance with the literature value of 17.545 kJ mol^{-1} [6], proving that the device for measuring the enthalpy used in this study was reliable.

Experimental methods

Laburnine samples of various masses were measured and dissolved in 1.5 mL 0.9% saline and 5% glucose solvent under the atmospheric pressure and certain temperatures. The RD 496–2,000 microcalorimeter was employed to monitor thermodynamic enthalpy changes.

Results and discussion

Thermochemical behaviors of dissolution of laburnine in saline and glucose solution

Based on the experimental methods, the dissolution curve of laburnine in glucose solution and saline under the atmospheric pressure and at 309.65 K are shown in Figs. 2 and 3. For the discussion convenience, the released heats during these dissolution processes are listed in Table 1.

The tables show that the increasing mass of laburnine led to increasing released heats, but kept the molar enthalpy constant. Therefore, the average of molar enthalpies from different masses can be considered as the molar enthalpy in the infinitely diluted glucose solution and saline [7].

As shown in Figs. 2 and 3, the dissolution processes in both glucose solution and saline were exothermic. Linear curves (Fig. 4) were generated from the released heats (Q) and sample masses, and the corresponding linear equations

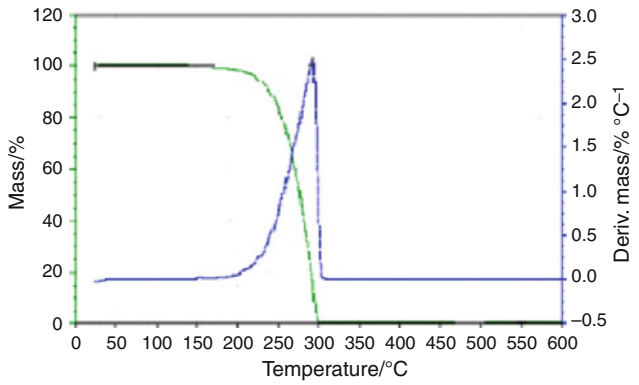

Fig. 1 The DSC–TG curves of laburnine

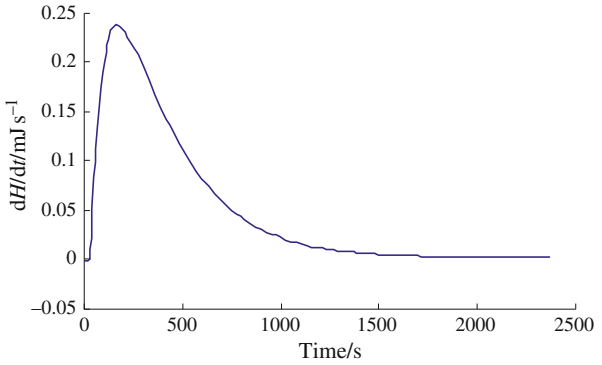

Fig. 2 Heating rate (dH/dt) of the entire dissolution process of laburnine in glucose solution

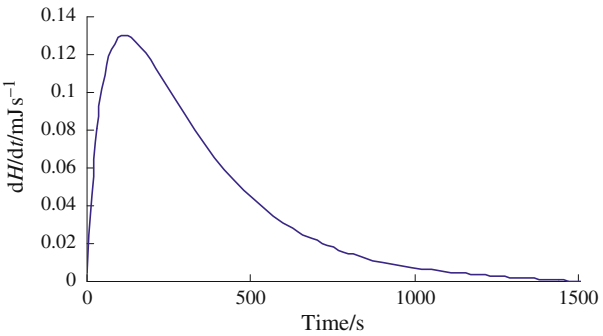

Fig. 3 Heating rate (dH/dt) of the entire dissolution process of laburnine in saline

Table 1 Dissolution enthalpy of laburnine in 1.50 mL saline and glucose solution

	m/mg	$10^3 n$/mol	Q/mJ	$-\Delta H$/kJ mol^{-1}
Glucose solution	12.49	0.07	517.00	7385.71
	28.20	0.15	1139.60	7597.33
	44.16	0.23	1879.20	8170.44
	51.03	0.27	2050.30	7593.71
	62.87	0.33	2487.30	7537.27
	Average			7656.89
Saline	20.54	0.11	897.13	8155.73
	26.19	0.14	1162.00	8300.00
	30.02	0.16	1315.60	8222.50
	36.32	0.19	1507.20	7932.63
	43.35	0.23	1805.60	7850.44
	Average			8092.26

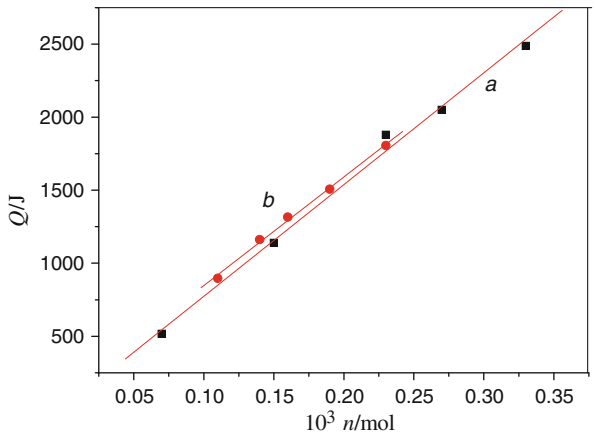

Fig. 4 Linear relationship between the heat effect (Q) and the amount of laburnine (n) (a in glucose solution, b in saline)

for the solvents, glucose solution and saline, are shown as Eq. 1 and 2, respectively.

$$Q = 7652.0n + 7.77 \quad r = 0.9997 \tag{1}$$

$$Q = 7439.7n + 102.5 \quad r = 0.9998 \tag{2}$$

The above equations show that the mass of laburnine and heat Q have very good linear relationships, and so the calculated molar enthalpy changes from Eqs. 1 and 2 are estimated, respectively, as 7659.77 and 7542.2 J mol^{-1}.

Dissolution dynamics of laburnine in saline and glucose solution

The dissolution speeds of laburnine in glucose solution and saline are described by the Eqs. 3 and 4 [7], which can be further solved to obtain Eq. 5 by replacing α by H_t/H_0.

The reaction speed constant k and the reaction order n could be achieved from the measured the heat H_t at time t and the whole dissolution heat H_0.

The slopes (n) and intercepts (ln k) of different concentrations were achieved from the figures and listed in Table 3.

$$\frac{\mathrm{d}\alpha}{\mathrm{d}t} = kf(\alpha) \tag{3}$$

$$f(\alpha) = (1-\alpha)^n \tag{4}$$

$$\ln\left[\frac{1}{H_0}\left(\frac{\mathrm{d}H}{\mathrm{d}t}\right)_i\right] = \ln k + n\ln\left[1-\left(\frac{H_t}{H_0}\right)_i\right] \quad i = 1, 2, \ldots, L \tag{5}$$

In the above equations, α is the conversion degree; $f(\alpha)$ is the kinetic function; H_t represents the heat at time t; H_0 is the heat of the whole process; k is the rate constant; n is the reaction order; and L is the counting index. The values of n and ln k obtained by substituting the original data taken from Table 2, $(\mathrm{d}H/\mathrm{d}t)_i$, $(H_t/H_0)_i$, H_0, $i = 1, 2, \ldots, L$, into the kinetic Eq. 5 are listed in Table 3. Substituting the values of n and k from Table 3 into Eq. 2, we can derive the kinetics equations for the solvents. Glucose solution and saline of the dissolution process, respectively, which are as follows:

$$\frac{\mathrm{d}\alpha}{\mathrm{d}t} = 10^{-3.86}(1-\alpha)^{1.00} \tag{6}$$

$$\frac{\mathrm{d}\alpha}{\mathrm{d}t} = 10^{-3.87}(1-\alpha)^{1.05} \tag{7}$$

The Eqs. 6 and 7 show that the reaction is close to a quasi-first-order reactions of the dissolution process. Therefore, the half-life periods using Eq. 8, can be calculated as 82.19 and 86.41 min, respectively, for the glucose solution and saline.

$$t_{\frac{1}{2}} = \frac{\ln 2}{k} \tag{8}$$

Thermodynamics of laburnine in saline and glucose solution

Thermodynamic relations are shown as [8]

$$\Delta G_{\neq} = -RT\ln k^{\neq} \tag{9}$$

$$\Delta G^{\theta}_{\neq} = \Delta H^{\theta}_{\neq} - T\Delta S^{\theta}_{\neq} \tag{10}$$

$$k = \frac{RT}{Nh}k^{\neq} \tag{11}$$

Then, we obtain Eq. 12:

$$\ln\frac{k}{T} = \left(\frac{\Delta S^{\theta}_{\mathrm{m}}}{R} + \ln\frac{k_{\mathrm{B}}}{h}\right) - \frac{\Delta H^{\theta}_{\mathrm{m}}}{RT} \tag{12}$$

Equation 12 can be changed into the following expression:

$$\ln\frac{kh}{k_{\mathrm{B}}T} = \frac{\Delta_{\mathrm{sol}}S_{\mathrm{m}}}{R} - \frac{\Delta_{\mathrm{sol}}H_{\mathrm{m}}}{RT} \tag{13}$$

By substituting $k_{\mathrm{B}} = 1.38 \times 10^{-23}$ J K^{-1}, $h = 6.626 \times 10^{-34}$ J s^{-1}, $R = 8.314$ J mol^{-1} K^{-1}, $T = 309.65$ K, and the corresponding values of k and $\Delta_{\mathrm{sol}}H$ of laburnine in saline and glucose solution into Eq. 13, we can obtain the values of $\Delta_{\mathrm{sol}}S_{\mathrm{m}}$, which are found to be −362.78 and −345.52 J mol^{-1} K^{-1}.

Then by substituting the values of $\Delta_{\mathrm{sol}}H_{\mathrm{m}}$ and $\Delta_{\mathrm{sol}}S_{\mathrm{m}}$ into the following formula

$$\Delta_{\mathrm{sol}}G_{\mathrm{m}} = \Delta_{\mathrm{sol}}H_{\mathrm{m}} - T\cdot\Delta_{\mathrm{sol}}S_{\mathrm{m}}, \tag{14}$$

Table 2 Original data of laburnine in 1.50 mL saline (left) and glucose solution (right) at 309.65 K

m/mg	t/s	dH/dt/mJ s^{-1}	H_t/H_o	H_∞/kJ mol^{-1}	m/mg	t/s	dH/dt/mJ s^{-1}	H_t/H_o	H_∞/kJ mol^{-1}
12.49	0	0.079	0.291	7.83	20.54	0	0.127	0.275	8.31
	30	0.074	0.362			60	0.113	0.402	
	60	0.068	0.427			120	0.096	0.512	
	90	0.062	0.487			180	0.080	0.605	
	120	0.056	0.541			240	0.066	0.682	
	150	0.051	0.590			300	0.054	0.745	
	180	0.046	0.634			360	0.043	0.796	
	210	0.041	0.673			420	0.035	0.837	
	240	0.036	0.709			480	0.028	0.870	
	270	0.032	0.740			540	0.022	0.897	
	300	0.029	0.768			600	0.018	0.918	
	330	0.026	0.793			660	0.014	0.935	
	360	0.027	0.815			720	0.011	0.948	
	390	0.020	0.834			780	0.009	0.959	
	420	0.018	0.851			840	0.007	0.967	
	450	0.016	0.867			900	0.006	0.974	
	480	0.014	0.880			960	0.005	0.980	
28.2	0	0.059	0.787	7.70	26.19	0	0.144	0.242	8.44
	30	0.053	0.810			40	0.137	0.319	
	60	0.047	0.831			80	0.126	0.390	
	90	0.042	0.850			120	0.115	0.456	
	120	0.038	0.866			160	0.103	0.515	
	150	0.034	0.881			200	0.092	0.568	
	180	0.030	0.895			240	0.082	0.615	
	210	0.027	0.906			280	0.074	0.658	
	240	0.024	0.917			320	0.066	0.696	
	270	0.022	0.927			360	0.059	0.730	
	300	0.020	0.935			400	0.052	0.760	
	330	0.018	0.943			440	0.045	0.787	
	360	0.016	0.950			480	0.040	0.810	
	390	0.014	0.956			520	0.035	0.830	
	420	0.012	0.961			560	0.032	0.848	
	450	0.011	0.966			600	0.028	0.864	
	480	0.009	0.970			640	0.026	0.878	
	510	0.008	0.974			680	0.023	0.892	
44.16	0	0.154	0.574	8.10	30.02	0	0.197	0.213	8.34
	30	0.142	0.611			60	0.183	0.351	
	60	0.130	0.645			120	0.158	0.474	
	90	0.119	0.677			180	0.132	0.578	
	120	0.108	0.705			240	0.108	0.664	
	150	0.099	0.731			300	0.087	0.734	
	180	0.090	0.755			360	0.070	0.790	
	210	0.082	0.776			420	0.056	0.835	
	240	0.074	0.796			480	0.044	0.871	
	270	0.067	0.814			540	0.035	0.899	
	300	0.061	0.830			600	0.028	0.922	
	330	0.055	0.844			660	0.022	0.940	

Table 2 continued

m/mg	*t*/s	d*H*/d*t*/mJ s^{-1}	H_t/H_o	H_∞/kJ mol^{-1}	*m*/mg	*t*/s	d*H*/d*t*/mJ s^{-1}	H_t/H_o	H_∞/kJ mol^{-1}
	360	0.050	0.858			720	0.017	0.954	
	390	0.046	0.870			780	0.014	0.965	
	420	0.041	0.881			840	0.011	0.974	
	450	0.037	0.890			900	0.008	0.981	
	480	0.034	0.899			930	0.007	0.983	
	510	0.031	0.907			960	0.007	0.986	
	540	0.028	0.915			990	0.006	0.988	
51.03	0	0.070	0.564	7.65	36.23	0	0.240	0.250	7.89
	50	0.067	0.590			60	0.214	0.393	
	100	0.064	0.615			90	0.197	0.458	
	150	0.061	0.639			150	0.162	0.571	
	200	0.058	0.662			210	0.132	0.663	
	250	0.054	0.684			270	0.106	0.737	
	300	0.050	0.704			330	0.084	0.797	
	350	0.047	0.722			390	0.066	0.844	
	400	0.044	0.740			450	0.052	0.881	
	450	0.040	0.756			510	0.040	0.909	
	500	0.038	0.771			570	0.030	0.931	
	550	0.035	0.785			630	0.023	0.948	
	600	0.033	0.798			690	0.018	0.961	
	650	0.032	0.811			750	0.014	0.971	
	700	0.030	0.822			810	0.010	0.978	
	750	0.027	0.833			870	0.008	0.984	
	800	0.027	0.844			930	0.005	0.988	
	850	0.025	0.854			960	0.004	0.990	
62.87	0	0.256	0.090	7.54	43.65	0	0.215	0.222	7.92
	40	0.269	0.157			60	0.204	0.333	
	80	0.263	0.225			120	0.183	0.434	
	120	0.248	0.290			180	0.161	0.524	
	160	0.229	0.350			240	0.138	0.603	
	200	0.209	0.406			300	0.117	0.670	
	240	0.190	0.456			360	0.098	0.726	
	280	0.172	0.502			420	0.082	0.773	
	320	0.157	0.544			480	0.068	0.812	
	360	0.143	0.582			540	0.056	0.845	
	400	0.131	0.617			600	0.047	0.872	
	440	0.119	0.648			660	0.039	0.894	
	480	0.108	0.677			720	0.032	0.912	
	520	0.099	0.703			780	0.026	0.928	
	560	0.091	0.727			840	0.022	0.940	
	600	0.083	0.749			900	0.018	0.950	
	640	0.077	0.769			930	0.016	0.955	
	680	0.071	0.788			960	0.014	0.959	
	720	0.065	0.805			990	0.013	0.962	

Table 3 n and $\ln k$ of laburnine in 1.50 mL saline and glucose solution at 309.65 K

	m/mg	n	$\ln k/s^{-1}$	r
Glucose	12.49	0.90	−8.51	0.9957
solution	28.20	0.98	−8.32	0.9989
	44.16	1.18	−8.28	0.9991
	51.03	1.01	−10.26	0.9995
	62.87	0.95	−8.96	0.9986
	Average	1.00	−8.87	
Saline	20.54	1.05	−8.84	0.9991
	26.19	1.00	−8.65	0.9980
	30.02	1.19	−10.15	0.9975
	36.32	1.07	−8.98	0.9974
	43.35	0.94	−7.97	0.9968
	Average	1.05	−8.92	

we can get the corresponding values of $\Delta_{sol}G_m$ of laburnine in saline and glucose solution as 104.68 and 98.90 kJ mol^{-1}, respectively.

Conclusions

1. The calorimetric method has been successfully employed to achieve laburnine's half-life, $\Delta_{sol}H$, $\Delta_{sol}S_m$, and $\Delta_{sol}G$ values and the thermal dynamic equations of the dissolution process. All the obtained information provides evidence for clinical applications of this medicine.
2. The RD 496–2000 micro calorimeter was utilized to measure molar dissolution enthalpy of laburnine in saline or glucose solution at atmospheric pressure and certain temperatures. The results show that concentration changes have limited effect on measured enthalpies, and so the average of $\Delta_{sol}H$ values can be used for obtaining molar dissolution enthalpy.
3. The dissolution enthalpies are found to be 7656.89 and 8092.26 J mol^{-1} in glucose and saline solutions, respectively. The closeness between the two values indicates that laburnine can be used in both solvents.
4. The molar Gibbs free energy is positive but small during the laburnine dissolution process. At the same time, the entropy value is negative, which indicates that the dissolution of laburnine in saline or glucose solutions results in stable systems.

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