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Solubility and dissolution thermodynamic properties of lansoprazole in pure solvents

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ABSTRACT

In this work, solubility data of lansoprazole in twelve pure solvents (methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetone, acetonitrile, methyl acetate, ethyl acetate, propyl acetate, butyl acetate) was measured by using a static gravimetric method at temperatures ranging from 278.15 K to 318.15 K under atmospheric pressure. The results showed that the solubility of lansoprazole increased with the increasing of temperature in the investigated temperature range. The modified Apelblat equation, the λ*h* equation and the NRTL model were used to correlate the experimental solubility data of lansoprazole in selected solvents and the computational data showed that the Apelblat equation gave the best correlation result. Furthermore, the apparent dissolution thermodynamic properties, including Gibbs energy, entropy and enthalpy, of lansoprazole in different solvents were calculated based on the experimental solubility data and the NRTL model.

1. Introduction

Lansoprazole (Fig. 1, $C_{16}H_{14}F_3N_3O_2S$, CAS registry NO:103577-45-3), 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl] methyl]-sulfinyl]-1H-benzimidazole, which is an effective acid pump inhibitor acting at the acid secretory pathway of the parietal cell decreasing gastric acid secretion [1]. Clinically, it can be used for treatment of gastric ulcer, reflux esophagitis, duodenal ulcer, Zollinger-Ellison syndrome (gastrinoma), especially for the inhibition of Helicobacter pylori [2].

In pharmaceutics, crystallization is of vital importance for separation and purification of crystalline compound. Thermodynamic data of pharmaceuticals can provide basic data for the development and design of crystallization process [3,4]. Lansoprazole is poor soluble in water. Therefore, the solubility data and dissolution thermodynamic properties of lansoprazole in other organic solvents are vital in order to precisely design and optimize the crystallization of lansoprazole. From literature review, no reports about the thermodynamics of lansoprazole was found.

In this work, the solubility of lansoprazole in twelve pure solvents (methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetone, acetonitrile, methyl acetate, ethyl acetate, propyl acetate, butyl acetate) was measured at temperature ranging from 278.15 K to 318.15 K by a gravimetric method. The experimental solubility data was correlated by three models including the modified Apelblat equation, the λ*h* equation and the NRTL model. Lansoprazole crystals used in all experiments were identified by powder X-ray diffraction (PXRD) to make sure that the form of lansoprazole crystal didn't change during the dissolution process. In addition, the apparent dissolution thermodynamic properties of lansoprazole in the tested solvents, such as the Gibbs energy, enthalpy and entropy, were also derived.

2. Experimental section

2.1. Materials

The white crystalline powder of lansoprazole was obtained from Jiangsu Aokang Chemical Co. Ltd. of China with the mass fraction purity higher than 0.995. All of the selected solvents (methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, acetone, acetonitrile, methyl acetate, ethyl acetate, propyl acetate, butyl acetate) are analytical reagent grade and were obtained from Tianjin Jiangtian Chemical Technology Co. Ltd. of China. All chemicals were used without any further purification and more details are listed in Table 1.

2.2. X-ray powder diffraction

The polymorphic form of lansoprazole was identified by powder X-ray diffraction (PXRD) which was carried out on D/max-2500 diffractometer (Rigaku, Japan). The experimental samples were measured over the

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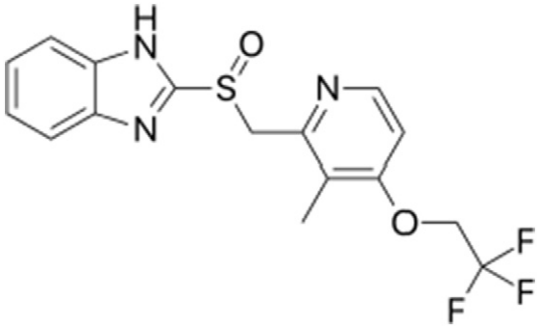

Fig. 1. Chemical structure of lansoprazole.

2-theta degree range from 2 to 50° with a scanning rate of 8°/min, a voltage of 40 kV, a current of 100 mA.

2.3. Thermogravimetric analysis

Thermogravimetry (Mettler Toledo TGA/DSC/SF, Greifensee, Switzerland) was used to estimate whether lansoprazole will decompose or not at the melting point. The measurement was operated within the temperature ranging from 303.15 K to 473.15 K protected by nitrogen. Samples ($5–10 \cdot 10^{-6}$ kg) of lansoprazole were treated with a heating rate of 0.02 K/s.

2.4. Solubility measurement

The solubility data of lansoprazole in different pure solvents was obtained by gravimetric method which has been described in literature [5–7]. To begin with, an excess amount of solid state lansoprazole was added into different known amount of pure solvent in a 100 ml jacketed glass vessel. The obtained solution was agitated by a magnetic stirrer for 10 h to make sure that the solid-liquid equilibrium could be reached. An thermostat (Julabo CF41,Germany) was used to control the systematic temperature with accuracy of ±0.05 K. After the mixture was agitated for 10 h, the agitation was stopped and the mixture was kept static for another 5 h at the same temperature to allow the undissolved particles to settle down. After that the pre-heated or pre-cooled 0.2 μm organic membranes were used to filter the upper clear saturated solution and collect the solution in pre-weighted beakers. Then, the total weight of the beaker and solution was measured immediately. Finally, the corresponding samples together with the beakers were put into a vacuum oven at 313.15 K to evaporate the solvents until the weight didn't change any more. All samples were weighed by an electronic analytic balance (Mettler Toledo ML204, Switzerland) whose accuracy is ±0.0001 g. To verify the accuracy of the measurement, the experimental process was repeated for three times and the average values were used to calculate the mole fraction solubility. The relative standard uncertainty of the solubility measurement is about 0.05.

The mole fraction solubility (x_1) of lansoprazole can be calculated according to the following equation [8].

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2} \tag{1}$$

where m_1 and m_2 are the masses (g) of lansoprazole and solvent, respectively; M_1 and M_2 are the molecular weight (g/mol) of lansoprazole and solvent, respectively.

3. Thermodynamic models

3.1. Modified Apelblat equation

The modified Apelblat equation deduced from the Clausius-Clapeyron equation is a semi-empirical equation which can predict and correlate the solubility of materials [9–11].The equation is shown as follows.

$$\ln x_1 = A + \frac{B}{T(K)} + C\ \ln(T(K)) \tag{2}$$

where x_1 is the mole fraction solubility of solute; T represent the absolute temperature; A, B, C are empirical parameters. The values of A and B are relative to the variation in the solution activity coefficients. The value of C refers to temperature effect on the fusion enthalpy [12].

3.2. λh equation

The λh equation was presented firstly by Buchowski et al. [13]. It can also correlate the liquid-solid phase equilibrium for many systems. The relationship between the mole fraction of solute and temperature is shown as follows [14].

$$\ln\left(1 + \lambda\frac{1-x_1}{x_1}\right) = \lambda h\left(\frac{1}{T} - \frac{1}{T_m}\right) \tag{3}$$

where x_1 is the solute mole fraction in saturated solution; T refers to the solution temperature; T_m is the melting temperature of solute. λ and h are the equation parameters. The value of λ indicates the nonideality of the solution system. The value of h indicates the excess mixing enthalpy of the solution.

Table 1
The sources and mass fraction purity of the materials used in this work.[a,b]

Substance	Source	Mass fraction purity	Purification method	Analysis method
Lansoprazole	Jiangsu Aokang Chemical Co. Ltd.	≥0.995	None	HPLC[a]
Methanol	Tianjin Jiangtian Chemical Co. Ltd	>0.997	None	GC[b]
Ethanol	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
N-propanol	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Isopropanol	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
N-butanol	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Isobutanol	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Acetone	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Acetonitrile	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Methyl acetate	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Ethyl acetate	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Propyl acetate	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]
Butyl acetate	Tianjin Jiangtian Chemical Co. Ltd.	>0.997	None	GC[b]

[a] High-performance liquid chromatography.
[b] Gas chromatography.