J. Chem. Thermodynamics 102 (2016) 333–340

Contents lists available at ScienceDirect

J. Chem. Thermodynamics

journal homepage: www.elsevier.com/locate/jct

Determination and correlation thermodynamic models for solid–liquid equilibrium of the Nifedipine in pure and mixture organic solvents

Gang Wu, Yonghong Hu *, Pengfei Gu, Wenge Yang, Chunxiao Wang, Zhiwen Ding, Renlun Deng, Tao Li, Housheng Hong

College of Biotechnology and Pharmaceutical Engineering, The Synergetic Innovation Centre for Advanced Materials, State Key Laboratory of Materials-Oriented Chemical Engineering, Jiangsu National Synergetic Innovation Centre for Advanced Materials, Nanjing Tech University, Nanjing 211816, China

ARTICLE INFO

Article history:
Received 25 May 2016
Received in revised form 19 July 2016
Accepted 21 July 2016
Available online 22 July 2016

Keywords:
Nifedipine
Apelblat model
CNIBS/R-K model
Jouyban-Acree model

ABSTRACT

Knowledge of thermodynamic parameters on corresponding solid-liquid equilibrium of nifedipine in different solvents is essential for a preliminary study of pharmaceutical engineering and industrial applications. In this paper, a gravimetric method was used to correct the solid-liquid equilibrium of nifedipine in methanol, ethanol, 1-butanol, acetone, acetonitrile, ethyl acetate and tetrahydrofuran pure solvents as well as in the (tetrahydrofuran + acetonitrile) mixture solvents at temperatures from 278.15 K to 328.15 K under 0.1 MPa. For the temperature range investigation, the solubility of nifedipine in the solvents increased with increasing temperature. The solubility of nifedipine in tetrahydrofuran is superior to other selected pure solvents. The modified Apelblat model, the Buchowski-Ksiazaczak λh model, and the ideal model were adopted to describe and predict the change tendency of solubility. Computational results showed that the modified Apelblat model stood out to be more suitable with the higher accuracy. The solubility values were fitted using a modified Apelblat model, a variant of the combined nearly ideal binary solvent/Redich-Kister (CNIBS/R-K) model and Jouyban-Acree model in (tetrahydrofuran + acetonitrile) binary solvent mixture. Computational results showed that the CNIBS/R-K model had more advantages than other models.

1. Introduction

Nifedipine (Fig. 1, $C_{17}H_{18}N_2O_6$, FW 346.33, CASRN: 21829-25-4), a yellow crystal powder, is a calcium channel blocker of the dihydropyridine type. Nifedipine is a medication which is used to manage angina, high blood pressure, Raynaud's phenomenon and premature labour [1]. It may be used as the treatment of choice for Prinzmetal angina and the severe high blood pressure in pregnancy [2]. It is one of the most important basic health drugs that included in the WHO Model List of Essential Medicines.

Purity is an important part of a substance used in medicine. The solubility of a solute in the different organic solvents plays the important role in understanding the phase equilibria. With the detailed solubility values, optimal crystallizer configurations and operation conditions with the selection of the solvent for a specific solute can be achieved [3]. For most solid products, solution crystallization is one of the most commonly employed operations for their recovery and purification, where the accurate quantity information of the solute solubility on solvents and temperature is essential. This work is aimed to provide thermodynamic property values for nifedipine. Further, we could explore more separation processes such as the safety of operating and extractive crystallization.

In this study, the solubility of nifedipine in pure and mixture organic solvents was measured within the temperature from 278.15 K to 328.15 K under 0.1 MPa by the gravimetric method, and the results were correlated to the modified Apelblat model, the Buchowski-Ksiazaczak λh model, the ideal model or the combined nearly ideal binary solvent/Redich-Kister (CNIBS/R-K) model and the Jouyban-Acree model. We intended to determine the best pure solvent and the ratio of binary solvent mixtures in the crystallization process of nifedipine based on experimental results. Besides, the analysis of thermodynamic properties would also help to determine the best temperature interval, which provides knowledge of the solubility at different temperatures [4]. Meanwhile,

* Corresponding author at: College of Biotechnology and Pharmaceutical Engineering, The Synergetic Innovation Centre for Advanced Materials, State Key Laboratory of Materials-Oriented Chemical Engineering, Jiangsu National Synergetic Innovation Centre for Advanced Materials, Nanjing Tech University, No. 30, South Puzhu Road, Nanjing 211816, China.

E-mail address: yonghonghu11@126.com (Y. Hu).

http://dx.doi.org/10.1016/j.jct.2016.07.035
0021-9614/

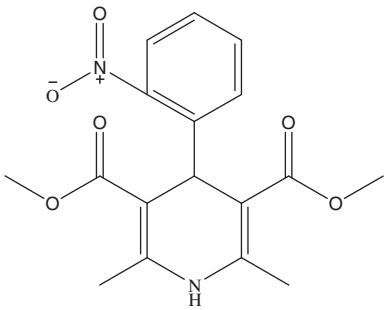

Fig. 1. Chemical structure of nifedipine.

information in the literature is scarce regarding the solubility of nifedipine and therefore this work was conducted.

2. Experimental

2.1. Materials and apparatus

Nifedipine with a mass faction purity ⩾ 0.980 was obtained from Aladdin Industrial Corporation. Its purity was measured by high performance liquid chromatography (HPLC type DIONEX P680 DIONEX Technologies). We measured the melting point by the melting point apparatus (HCRD-2C), which is from Chengdu Huacheng Instruments Co., Ltd. The chemical reagents were used without further purification. The purities of the solvents were determined in our laboratory by gas chromatography (GC type Agilent 7820A Agilent Technologies). The detailed information of the materials used in the experiment was listed in Table 1. Analytical balance (model: BSA224S) was bought from Sartorius Scientific Instruments (Beijing) Co., Ltd. with the accuracy of ±0.1 mg. The Smart water-circulator thermostatic bath (model: DC-2006) was bought from Ningbo Scientz Biotechnology Co., Ltd. with the accuracy of ±0.05 K.

Table 1
Properties of the compounds evaluated.

Material	Properties			
	Molar mass /(g·mol^{-1})	Mass fraction purity	Analysis method	Source
Nifedipine	346.33	0.980	HPLC	Aladdin Industrial Corporation
Methanol	32.04	0.995	GC	Shenbo Chemical Industry
Ethanol	46.07	0.997	GC	Shenbo Chemical Industry
1-Butanol	74.12	0.990	GC	Shenbo Chemical Industry
Acetone	58.08	0.995	GC	Shenbo Chemical Industry
Acetonitrile	41.05	0.999	GC	Shenbo Chemical Industry
Ethyl acetate	88.11	0.997	GC	Shenbo Chemical Industry
Tetrahydrofuran	72.11	0.990	GC	Shenbo Chemical Industry

2.2. Methods

The solid (Nifedipine) was put into the melting point apparatus, and then the temperature was raised. The temperature was recorded when the solid had been melted. The melting points were measured by five times. The recorded melting points were 446.15 K, 448.65 K, 445.65 K, 448.15 K and 444.65 K, respectively. So we could calculate the melting point temperature was 446.65 K (u(T) = 0.85 K). Our experimental result and the result of literature were consistent, where the melting point was temperature for 445.15–446.15 K [5].

The solubility of nifedipine was measured, in various solvents, by the analytical stirred-flask method, and we used the gravimetric method to measure the compositions of the saturated solutions. The gravimetric method could achieve solid-liquid equilibrium simply and effectively and was a common method for measuring solubility. Saturated solutions of nifedipine, which were produced by 30 mL solvent mixtures and some excess nifedipine, were prepared in a spherical 50 mL Pyrex glass flask with a bottle stopper (avoid evaporation of solvent during experimental steps). The flask temperature was maintained using jacket glass vessel equipped with circulating water and controlled by thermostat bath. For each measurement, some excess nifedipine was added to a known volume of solvent mixtures. Continuous stirring was achieved for fully mixing the suspension using a magnetic stirrer at the required temperature. The stirring continued for about 24 h to solvents and the solution was allowed to settle for 12 h or more for achieving a static state before sampling in order to ensure that there was no excess of nifedipine in solution and achieve solid-liquid equilibrium [6,7]. The supernatant was taken, filtered, and poured into a warmed flask pre-weighed by using an analytical balance. At last, 5 mL solution supernatant was transferred into 25 mL warmed beaker with a cover and weighted immediately in order to prevent the cooling crystallization. This beaker had been weighted before. All beakers were put into a dryer at room temperature and weighted weekly until reaching constant weight. All determinations were repeated three times to check reproducibility, and then an average value was given. The mole fraction solubility of nifedipine (x) in different solvents was calculated by Eq. (1). The mole fraction solubility of nifedipine (x) and the mole fraction of tetrahydrofuran (x_A) in the binary solvent mixtures were calculated by Eqs. (2), (3).

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

where m_1, m_2 represent the mass of nifedipine and solvent, respectively; and M_1, M_2 represent the molar mass of nifedipine and solvent, respectively.

$$x = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2 + m_3/M_3} \tag{2}$$

$$x_A = \frac{m_2/M_2}{m_2/M_2 + m_3/M_3} \tag{3}$$

where m_1, m_2, m_3 represent the mass of nifedipine, tetrahydrofuran and acetonitrile, respectively; and M_1, M_2, M_3 represent the molar mass of nifedipine, tetrahydrofuran and acetonitrile, respectively.

3. Results and discussion

3.1. In pure solvents

3.1.1. Solubility and correlation models

The saturated mole fraction solubility (x) of nifedipine in methanol, ethanol, 1-butanol, acetone, acetonitrile, ethyl acetate