ORIGINAL RESEARCH

The solubility of sebacic acid in subcritical water using the response surface methodology

Erdal Yabalak · Özkan Görmez · Belgin Gözmen ·
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Abstract The solubility of sebacic acid in subcritical water was investigated. Response surface methodology was used to study the combined effects of the different parameters such as temperature, static and dynamic time to optimize the process conditions for the maximum solubility of sebacic acid. Solubility results of sebacic acid were observed to be highly correlated with quadratic model according to analysis of variance. The solubility of sebacic acid was found as 500 g L^{-1} in the optimum conditions at 400 K temperature, 4 min dynamic time and 28 min static time. Approximation models were employed for determining solubility of sebacic acid at elevated temperatures.

Keywords Dicarboxylic acid · Hot water solubility ·
Box–Behnken design · Sebacic acid · Response surface methodology

Introduction

Subcritical water has been gaining researchers' attention due to its non-toxic, non-flammable, non-explosive properties [1, 2]. Subcritical water has variable physical properties compared to water at ambient conditions such as dielectric constant, which is typically used for measuring polarity and can easily be altered by changing temperature and pressure [3, 4]. Increasing the temperature above 373

and 423 K, the dielectric constant of water can be likened to dimethyl sulfoxide and acetonitrile, respectively [5–7]. The solubility of analytes in subcritical water is reasonably needed which constitutes base date in green subcritical technology, such as subcritical water extraction and chromatography [8]. Subcritical water has been used in various applications such as decomposition and degradation of waste materials [9], extraction of heavy metals [10], dissolve less soluble or insoluble materials and valuable substances [11–15] for the last decades.

Dicarboxylic acids are widely used as a raw material in production process of plasticizers, dyes, inks, adhesive, lubricant, cosmetics, biodegradable polymers, food and pharmaceutical industries [16–21]. Biodegradable polymers have been used as an alternative instead of non-degradable plastics which accumulate in soil and cause pollution [22]. Biodegradable polymers reduce the risk of accumulation of plastic materials in the environment and the cost of waste management of production and usage process [23].

Sebacic acid and its derivatives have been widely applied in biomedical applications for drug delivery devices, wound dressings, orthopedic fixation devices, temporary vascular grafts, different types of tissue-engineered grafts [24–28], etc. Sebacic acid (decanedioic acid, $C_{10}H_{18}O_4$, CAS No: 111-20-6) is one of the most used biodegradable plastics monomer.

There are few quantitative data on the aqueous solubility of sebacic acid in the literature [29]. Aqueous solubility data of the sebacic acid are of increasing interest and significance. There are several conventional studies based on using organic solvents and solvent mixtures to determine the solubility of sebacic acid [30]. These methods may be useful to determine the yield and purity of sebacic acid, but the organic solvents used are often toxic and these methods

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required removal step of solvent. In addition, solvent removal is expensive and time-consuming [6]. There is no difficulty in using subcritical water as a solvent, which is exposed in the traditional methods. Enhancing the solubility of sebacic acid in water is important due to the widespread production of it. The water solubility of sebacic acid at 50 and 60 °C is 2.2 and 4.2 g L^{-1}, respectively [29].

The response surface methodology (RSM) is an advantageous method to evaluate the performance of a system by varying the variables and their interactions effects and carrying out a limited number of experiments [31]. The response of interest is influenced by several variables during RSM and the main goal is to optimize this response [32].

RSM was used for studying the effect of variables such as temperature (K), static and dynamic time (min) on the solubility of sebacic acid (g L^{-1}) to influence the maximum benefit for dissolving more sebacic acid in optimum conditions. The solubility experiment was performed at moderate temperatures ranging from 313 to 433 K with 50 bar pressure to keep water in liquid state under varied static and dynamic extraction time.

We aimed to investigate the solubility of sebacic acid in order that offering a model for removing it from contaminated sites and recover it by further precipitation step.
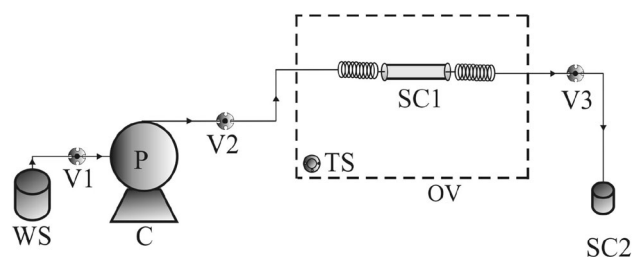
Experimental

Materials

Sebacic acid (purity ≥98 %), HPLC grade methanol (purity ≥99.8 %), triethylamine (purity ≥99 %) and 2-bromoacetophenone (purity ≥98 %) were purchased from Merck (Darmstadt, Germany). Ultra-pure water was prepared in our laboratory using a Millipore Milli-Q Advantage A10.

Apparatus and procedures

A special stainless steel cylindrical HPLC column (100 mm × 5 mm i.d.) was used as equilibration cell for solubility experiments. The column was filled with 1.25 g sebacic acid. Both ends of the column covered with 0.45 μm mesh size frits and cell were tightened to prevent leakage of particulates. A preheating coil was placed in front of the equilibration cell. Thus, required subcritical water which passed through the cell along the experiment provided (Fig. 1). The loaded cell was placed in the Teknosem TF R 400 model oven to provide precise temperature control (0.1 K) during the solubility determination (Fig. 1). A Teledyne ISCO 260 D series syringe pump system (Lincoln, NE, USA) was used to deliver water and supply pressure at 50 bars in the constant pressure mode.

Fig. 1 Diagram of the solubility apparatus. *P* isco 260 D syringe pump, *C* control unit, *WS* water supply, *TS* temperature sensor, *SC1* solubility equilibrium cell, *V1–V3* valves, *SC2* solution collector, *OV* teknosem TF R 400 oven

Pre-experiments were performed to select the maximum temperature. It was obtained that 1.45 ± 0.18 % of initial amount of sebacic acid was degraded at 453 K. Thus, experiments were performed at three different temperatures ranging from 313 to 433 K, three dynamic time modes (2, 4 and 6 min) and three static time modes (10, 20 and 30 min) using RSM to ensure the reliability of the experimental solubility data. To achieve set temperature inside equilibration cell, oven was heated slowly to the beginning of the static time. After the static time at which the solute (sebacic acid) and solvent (subcritical water) reach to equilibrium in the equilibration cell, dynamic mode was started and fractions were collected during this mode in each experiment. To diminish the carryover effect (such as repulsion of solute–solvent), valve 2 was closed after every experiment (Fig. 1). Fractions (approximately 2.5 mL) of the heated water–acid solution were collected and 2.5 mL of methanol was added to the solution to dissolve obtained sebacic acid at room temperature. The mixtures were then analyzed by high-performance liquid chromatography.

Experimental design

In the present study, the Box–Behnken design (BBD) was employed for the optimization of solubility of sebacic acid by subcritical water. Three main operating parameters (the three factors with three levels) were chosen as independent variables: temperature (K) x_1; static x_2 and dynamic time (min) x_3 also solubility (g L^{-1}) (Y) was assumed as the dependent variable (response). Each independent variable was coded at three levels −1, 0 and +1. The three-factor Box–Behnken design has 17 runs and is presented in Table 1. Each solubility experiment was done in triplicates; average and standard deviation of each experimental value are presented in Table 1.

Derivatization procedure and HPLC analysis

One milli liter of analyte solution (maximum containment: 0.0125 g mL^{-1} of sebacic acid), 75 μL of

Table 1 The three-factor Box–Behnken design and the value of the response function

Experiment number	Temperature (K)	Static time (min)	Dynamic time (min)	Solubility (g L^{-1} water)
1	313 (−1)	10 (−1)	4 (0)	6.9 ± 0.2
2	433 (+1)	10 (−1)	4 (0)	296.3 ± 7.1
3	313 (−1)	30 (+1)	4 (0)	8.5 ± 0.4
4	433 (+1)	30 (+1)	4 (0)	456.8 ± 8.3
5	313 (−1)	20 (0)	2 (−1)	7.1 ± 0.3
6	433 (+1)	20 (0)	2 (−1)	314.2 ± 5.5
7	313(−1)	20 (0)	6 (+1)	7.3 ± 0.3
8	433 (+1)	20 (0)	6 (+1)	373.5 ± 10.1
9	373 (0)	10 (−1)	2 (−1)	188.2 ± 5.2
10	373 (0)	30 (+1)	2 (−1)	464.2 ± 7.7
11	373 (0)	10 (−1)	6 (+1)	252.4 ± 5.2
12	373 (0)	30 (+1)	6 (+1)	484.3 ± 9.6
13	373 (0)	20 (0)	4 (0)	429.3 ± 13.1
14	373 (0)	20 (0)	4 (0)	468.3 ± 8.8
15	373 (0)	20 (0)	4 (0)	402.6 ± 20.7
16	373 (0)	20 (0)	4 (0)	470.2 ± 6.9
17	373 (0)	20 (0)	4 (0)	487.5 ± 12.1

Table 2 ANOVA results of quadratic model

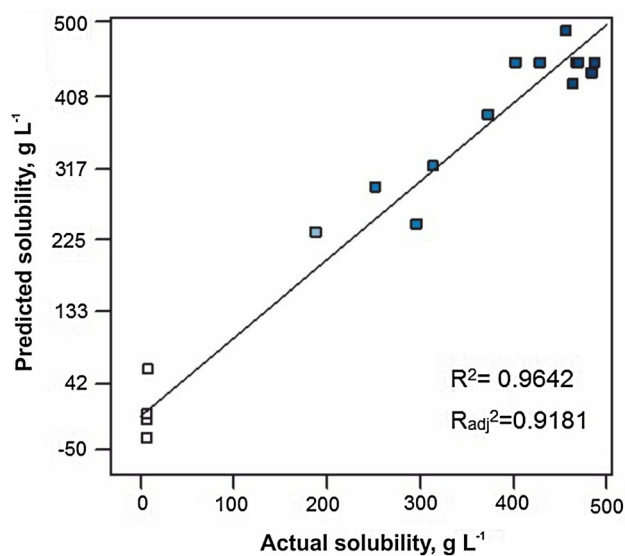| Source	Sum of squares	Degrees of freedom	Mean square	F value	P value prob > F
Model	5.476 × 10^5	9	6,0841.60	20.92	0.0003
Residual	2,0355.50	7	2,907.93	–	–
Lack of fit	1,5538.90	3	5,179.62	4.30	0.0963
Pure error	4,816.64	4	1,204.16	–	–

2-bromoacetophenone solution (200 mM in acetonitrile) and 75 μL of triethylamine solution (60 mM in acetonitrile) were combined. Final volume of this solution was completed at 10 mL and heated up to 60 °C and allowed to stand over 1 h before detection by HPLC.

HPLC analyses were carried out using an Agilent 1200 model liquid chromatography system. Separation was performed on ACE 5 C18 column (250 × 4.6 mm, ACE, Scotland) at 30 °C. Sebacic acid was eluted by a mixture of 70 % (v/v) MeOH, 29 % (v/v) H$_2$O, 1 % (v/v) HOAc at a flow rate of 0.8 mL min^{-1} and was detected at 254 nm.

Fig. 2 The actual and predicted plot of the solubility of sebacic acid

Results and discussion

Optimization of solubility using RSM approach

The three factors with three-level BBD matrix and results of solubility experiments are presented in Table 1. Using RSM approach, the responses can be simply related to the chosen factors by linear or quadratic models in the optimization process. A quadratic model, which also includes the linear model, is given below as Eq. (1).

$$Y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_{12} x_1 x_2 + \beta_{13} x_1 x_3 + \beta_{23} x_2 x_3 + \beta_{11} x_1^2 + \beta_{22} x_2^2 + \beta_{33} x_3^2 + e_i \quad (1)$$

where Y is the response, x_i and x_j are the coded variables, β_0 is the constant coefficient, β_j, β_{jj} and β_{ij} the first-order,

Fig. 3 **a** The effects of static time and temperature on the solubility ▶
of sebacic acid in subcritical water at constant dynamic time. **b** The
effects of dynamic time and temperature on the solubility of sebacic
acid in subcritical water at constant static time. **c** The effects of
dynamic time and static time on the solubility of sebacic acid in
subcritical water at constant temperature

quadratic and interaction effects, respectively, i and j are
the index numbers for factor, and e_i is the residual error
[33, 34].

The approximating function of solubility obtained by
Design-Expert software [35] is given in Eq. (2).

$$Y = +451.58 + 176.38x_1 + 83.75x_2 + 17.95x_3 \\ + 39.75x_1x_2 + 14.77x_1x_3 - 11.02x_2x_3 \qquad (2) \\ - 215.61x_1^2 - 43.85x_2^2 - 60.45x_3^2$$

In Eq. (2), Y corresponds to the response of solubility of
sebacic acid by subcritical water system; x_1, x_2, x_3 corre-
spond to independent variable of temperature, static and
dynamic time, respectively. For solubility of sebacic acid
coefficients of all the factors showed positive correlation
and the temperature (x_1) is the most effective factor for the
solubility. This factor (x_1) is followed by static (x_2) and
dynamic time (x_3). Also, two-variable interaction temper-
ature-static time (x_1x_2) has been demonstrated to be the
crucial factors for solubility of sebacic acid. Dynamic time
remains low when compared with other positive effects.

Analysis of variance (ANOVA) result of this quadratic
model is presented in Table 2. The coefficient of variation
(CV) and adequate precision were 17.9 and 12.6, respec-
tively. If adequate precision value in other word signal to
noise ratio is greater than four, then adequate precision
would be obtained [36].

The predicted values for the solubility of sebacic acid
versus experimental ones showed that experimental values
were distributed near to the straight line in Fig. 2. This
distribution is supported by the values obtained, R^2 and
R^2_{adj}, in Table 2. The R^2 value was 0.9642 and adjusted R^2
was 0.9181. The high R^2 values indicate that the model is
significant (Fig. 2).

Figure 3 shows the effects of independent variable on
the solubility of sebacic acid with subcritical water.
When dynamic time was kept constant at 4.0 min, the
effects both static time and temperature are tested in
Fig. 3a. Effective dissolution occurred at temperatures
above 373 K, but began to decline above 410 K due to
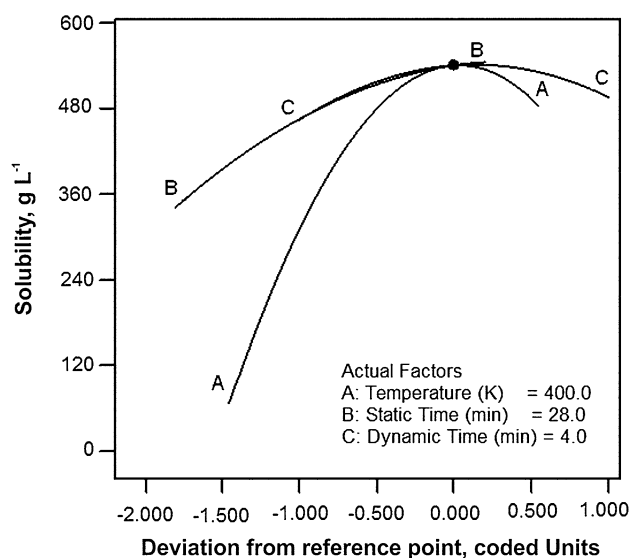degradation of sebacic acid. Also, static time of
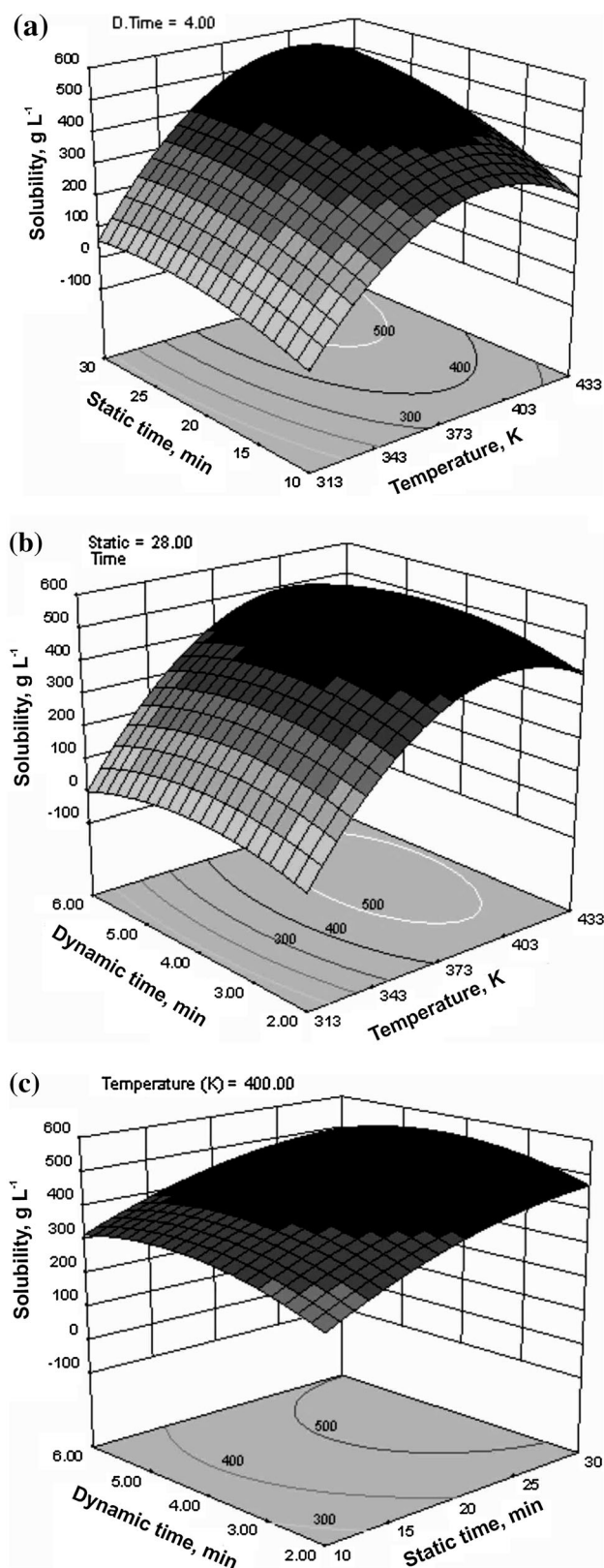
extraction must be kept for at least 20 min for effective solubility. The influence of temperature and dynamic time investigated when the static time is kept constant at 28 min as shown in Fig. 3b. It can be seen from Fig. 3b that dynamic time was not very effective variable in the range of 2–6 min for solubility experiments. The maximum solubility of sebacic acid with subcritical water was observed at 400 K, which increased the solubility to 500 g L^{-1} (Fig. 3c).

The effects of all the independent variables on the solubility of sebacic acid at the optimal run conditions in the design space are compared in the perturbation plot (Fig. 4). When this perturbation plot is analyzed it was seen that to provide an effective resolution of sebacic acid, temperature, static and dynamic time were kept constant at 400 K, 28 and 4 min, respectively.

Approximation models

There are a few approximation models to predict solubility of organic molecules reported in the literature. One of these models which offered by Miller et al. [37] was used to

Fig. 4 Perturbation plot for solubility of sebacic acid with subcritical water

predict mole fraction of solubility of polycyclic aromatic hydrocarbons in high-temperature water. As indicated in Eq. (3), the mole fraction of solubility at ambient temperature (T_0) can be predicted with the knowledge of the mole fraction of solubility at higher temperatures.

$$\ln x_2(T) \approx \left(\frac{T_0}{T}\right) \ln x_2(T_0) \tag{3}$$

Miller et al. [36] modified Eq. (3) and obtained Eq. (4) for the mole fraction solubility at T as follows:

$$\ln x_2(T) = \left(\frac{T_0}{T}\right) \ln x_2(T_0) + 15\left(\frac{T_0}{T} - 1\right)^3 \tag{4}$$

To predict the solubility of liquid nonpolar organic compounds in subcritical water, Mathis et al. [37] modified Eq. (3) using the following equation:

$$\ln x_2(T) = \left(\frac{T_0}{T}\right) \ln x_2(T_0) + 2\left(\frac{T - T_0}{T_0} - 1\right)^3 \tag{5}$$

Kayan et al. [38] achieved a better approximation model for the solubility prediction of the organic acids in subcritical water using Eq. (6).

$$\ln x_2(T) = \left(1.85\frac{T_0}{T} - 1\right) \ln x_2(T_0) \tag{6}$$

The experimental data in comparison with the predicted values obtained by Eqs. (3)–(6) were summarized in Table 3. Although, Eqs. (3)–(5) failed to predict the correct values, Eq. (6) which was previously modified by Kayan et al. [39] showed better prediction for the solubility of sebacic acid.

Conclusions

The results of this study demonstrate that the Box–Behnken design methodology could efficiently optimize solubility of the sebacic acid with subcritical water, using a homemade system. It was found that temperature and static time are effective parameters on the solubility of the sebacic acid. The solubility of sebacic acid was found as 500 g L^{-1} at optimum values of temperature, static time and dynamic time such as 400 K, 28 and 4 min, respectively. Experimental results show a good consistency with

Table 3 Comparison of experimental mole fraction of solubility x_2 for sebacic acid (2) in water (1) with predict values using Eqs. (3)–(6)

	$10^3 x_2$				
T/K	Experimental	Equation (3)	Equation (4)	Equation (5)	Equation (6)
298	0.02225 ± 0.00814	0.022250	0.02225	0.003011	0.1110
313	0.61360 ± 0.01317	0.037170	0.03724	0.006702	0.2868
373	16.47000 ± 0.38850	0.191600	0.24330	0.082850	5.9600
433	25.69000 ± 0.41500	0.627200	2.52500	0.452000	53.4000

approximation model developed for the organic acids (Eq. 6), which is based on simplifying assumptions in relation with previously reported works.

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