Kinetics of Reactive Extraction of Penicillin G by Amberlite LA-2 in Kerosene

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Penicillin G was extracted by the carrier, Amberlite LA-2, in a nonpolar organic solvent in a dispersed liquid–liquid extraction system. A mass-transfer model for the system was developed for the purpose of getting a kinetic expression of the reaction between penicillin G and the carrier. The model takes into account the reaction at the interface between continuous aqueous phase and dispersed organic drops, and the diffusion of penicillin G in the dispersed organic drop. The calculated results from the model were in good agreement with the experimental data. Also, the validity of the model was certified by comparing the experimental data with the calculated results from the model at the wide range of Danckwert and Biot numbers used to determine which rate step has a larger effect on the extraction rate. In addition, the rate expression of the interfacial reaction determined here could be satisfactorily used to explain the effect of initial penicillin G concentration on penicillin G extraction by the carrier in previous ELM systems. © 2004 American Institute of Chemical Engineers *AIChE J,* 50: 119–126, 2004
Keywords: penicillin G, reactive extraction, dispersed system, kinetics, nonpolar organic solvent

Introduction

Emulsion liquid membrane (ELM) processes are potentially able to purify or separate biochemical products from fermentation broths because of very high mass-transfer rates, simultaneous extraction/stripping in one stage, and requirement of expensive carrier in small quantities. One of the most important antibiotics, penicillin G ($pK_a = 2.75$), has also been successfully extracted by ELMs with Amberlite LA-2 as the carrier in a batch reactor and a continuous column (Lee and Lee, 1992; Lee et al., 1997; Lee and Yeo, 2002). However, a detailed transport mechanism for the extraction of penicillin G in these ELM systems has not been elucidated yet.

Reschke and Schügerl (1984a) studied the reactive extraction of penicillin G by Amberlite LA-2 in a liquid–liquid extraction system, and suggested the following reaction expression independent of solvent type

$$A + H^+ + P^- \leftrightarrow AHP \tag{1}$$

However, Lee et al. (2002) found that another reaction expression was obtained through liquid–liquid extraction equilibrium experiments in the presence of a highly nonpolar organic solvent, which was used as a diluent of the membrane phase in previous ELM studies (Lee and Lee, 1992; Lee et al., 1997). Although there are a few kinetic works on its reactive extraction (Reschke and Schügerl, 1984b; Wang and Lee, 1995) in a liquid–liquid extraction system with a constant interface, any of the kinetic works does not well explain the experimental results obtained in the works on ELM (Lee and Lee, 1992; Lee et al., 1997). In other words, if a very fast reaction satisfying the equilibrium expression of Eq. 1 had occurred at the external interface between feed and membrane phases, and thus mass transfer in each phase had been a rate-controlling step in the batch and continuous ELM systems, or if the elementary reaction of Eq. 1 at the interface had become a rate-controlling step, the initial degree of extraction in the batch system (Lee and Lee, 1992) or degree of extraction at the inlet of the feed phase in the continuous system (Lee et al., 1997) would have decreased with the initial penicillin G concentration. However,

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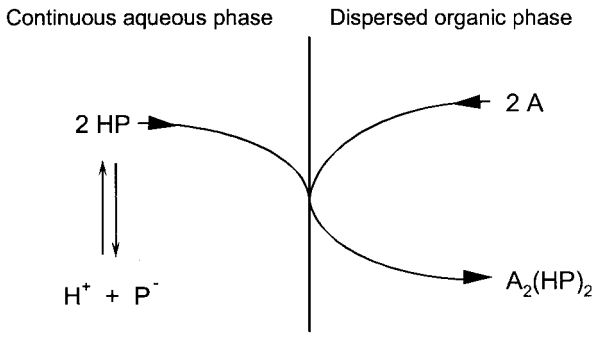

Figure 1. Transport mechanism of penicillin G from aqueous phase to organic phase.

the experimental results of penicillin G extraction by the ELMs in the batch and continuous systems, which imply the possibility that the reaction at the external interface takes part in one of the rate-controlling steps and that the reaction order in penicillin G is larger than one, were contrary to our expectation as stated earlier. Therefore, a kinetic study was required to obtain the rate expression of the reaction of penicillin G with Amberlite LA-2 in a nonpolar organic solvent.

The extraction rate of penicillin G from the aqueous phase to the organic phase is not too high in a Lewis-type stirred cell with a small and constant interfacial area in which stirrer speed is maintained at low to minimize the disturbance of the interface. Thus, it is not easy to accurately measure the concentration of penicillin G in the aqueous phase using the stirred cell at a given time interval during a short extraction period because of the low extraction rate. On the other hand, a long extraction period is not preferred, because it may result in large losses of penicillin G due to its instability at a low pH. Finally, it is inappropriate to obtain a rate expression of the interfacial reaction in the constant-interface extraction system in which aqueous or organic mass-transfer resistance near the interface still may be larger than the interfacial reaction resistance. In this work, we therefore introduced a liquid–liquid dispersion to the present extraction system, in which the organic phase is dispersed in the aqueous phase. The system provides a high mass-transfer rate due to the large interfacial area between the continuous aqueous phase and the dispersed organic drops, and thus brings about a large drop in the concentration of penicillin G with time during a short extraction period. In the extraction system, we will find a kinetic expression of the reaction of penicillin G with Amberlite LA-2 in kerosene, which seems to be helpful to illuminate a transport mechanism of the previous ELM systems in the future.

Theory

Transport mechanism

Physical extraction of penicillin G can be neglected because of its very low physical solubility into a highly nonpolar organic solvent such as kerosene (Reschke and Schügerl, 1984a). Therefore, Figure 1 shows the transport system for the reactive extraction of penicillin G by the carrier (Amberlite LA-2, A) in the highly nonpolar organic solvent. Two moles of undissociated penicillin acid reacts directly with two moles of carrier at the interface between the continuous aqueous and the dispersed organic phases to form one mole of penicillin–Amberlite LA-2 complex ($A_2(HP)_2$). The complex then diffuses toward the center of the dispersed organic drop. The interfacial reaction between penicillin G and the carrier is expressed as follows:

$$2A + 2HP \leftrightarrow A_2(HP)_2 \tag{2}$$

The reaction expression is known to be effective only when a nonpolar organic solvent is used as the organic phase. The formation of the dimer of AHP, $A_2(HP)_2$ complex in kerosene is regarded as an extreme result of the dipole–dipole interaction of ion pairs (Lee et al., 2002). Also, the reaction equilibrium constant, K'_{eq}, of Eq. 2 is given by

$$K'_{eq} = \frac{C_{A_2(HP)_2}}{C_A^2 C_{HP}^2} \quad \text{or} \quad \frac{C_C}{C_A^2 C_{HP}^2} \tag{3}$$

where C_C denotes the concentration of the penicillin G–Amberlite LA-2 complex.

Mass transfer of penicillin G into the dispersed organic phase

On the basis of the transport mechanism just described, a permeation model has been developed in order to simulate the experimental results. A dispersed drop is assumed to be a rigid sphere of radius R. In order to simplify the model, we have made the following assumptions:

(1) The hydrogen ion concentration in the continuous aqueous phase is constant in space and time because of the high diffusion coefficient of the hydrogen ion and the use of a buffer solution (Lee et al., 1998).

(2) The mass-transfer resistance of undissociated penicillin acid in the continuous phase is negligible because the stirrer speed of the system is quite high.

(3) The sizes of dispersed drops are uniform independent of time (Ho et al., 1982; Lee et al., 1998).

(4) The interfacial reaction cannot be elementary, but it is used as the form of a reversible tetramolecular elementary reaction. Thus, its rate expression is represented by

$$r_i = k'_f(C_A^2 C_{HP}^2 - C_C/K'_{eq}) = k_f(C_A^2 C_H^2 C_P^2 - C_C/K_{eq}) \tag{4}$$

where K_a is the acid dissociation constant of penicillin G, and k'_f/K_a^2 and K'_{eq}/K_a^2 are substituted for k_f and K_{eq}, respectively.

The mass balance of penicillin G in the continuous aqueous phase is expressed by

$$-V_{aq}\frac{dC_p}{dt}(1 + 10^{pK_a - pH}) = k_f S(C_{A,i}^2 C_H^2 C_p^2 - C_{C,i}/K_{eq}) \tag{5}$$

where V_{aq} is the volume of the continuous aqueous phase, and S is the total interfacial area between the continuous aqueous phase and the dispersed drops. Also, the subscript i denotes the interface.

The mass balances of the complex and carrier within a dispersed drop are represented as follows

$$\frac{\partial C_C}{\partial t} = D_C \frac{1}{r^2}\left(\frac{\partial}{\partial r} r^2 \frac{\partial C_C}{\partial r}\right) \quad (6)$$

$$\frac{\partial C_A}{\partial t} = D_A \frac{1}{r^2}\left(\frac{\partial}{\partial r} r^2 \frac{\partial C_A}{\partial r}\right) \quad (7)$$

where D_C and D_A are the molecular diffusivities of complex and carrier in the organic phase, respectively.

The initial and the boundary conditions are as follows

$$\text{I.C. 1:} \quad C_P(1 + 10^{pK_a - pH}) = C_{P0} \quad \text{for} \quad t = 0 \quad (8)$$

$$\text{I.C. 2:} \quad C_A = C_{A0}, C_C = 0 \quad \text{for} \quad t = 0, \quad \text{all} \quad r \quad (9)$$

$$\text{B.C. 1:} \quad \frac{\partial C_A}{\partial r} = 0, \frac{\partial C_C}{\partial r} = 0 \quad \text{for} \quad r = 0, \quad \text{all} \quad t \quad (10)$$

$$\text{B.C. 2:} \quad 2D_C \frac{\partial C_C}{\partial r} = -D_A \frac{\partial C_A}{\partial r} = k_f(C_{A,i}^2 C_H^2 C_P^2 - C_{C,i}/K_{eq}) \quad \text{for} \quad r = R, \quad \text{all} \quad t \quad (11)$$

Dimensionless variables are now introduced to reduce the preceding equations to dimensionless forms

$$Y_P = \frac{C_P(1 + 10^{pK_a - pH})}{C_{P0}}; Y_C = \frac{C_C}{C_{P0}}; Y_A = \frac{C_A}{C_{P0}}; Y_H = \frac{C_H}{C_{P0}}$$

$$\eta = \frac{r}{R}; \tau = \frac{D_C t}{R^2}; N_{Da} = \frac{k_f R}{D_C}; z = 1 + 10^{pK_a - pH};$$

$$\phi = \frac{V_{org}}{V_{aq}}$$

$$C_1 = \frac{C_{P0}^5}{z^2}; C_2 = \frac{z^2}{K_{eq} C_{P0}^5}; C_3 = \frac{D_A}{D_C} \quad (12)$$

The dimensionless equations for the model are as follows:

- Continuous aqueous phase

$$\frac{dY_P}{d\tau} = -3C_1 \phi N_{Da}(Y_{A,i}^2 Y_H^2 Y_P^2 - C_2 Y_{C,i}) \quad (13)$$

- Dispersed drops

$$\frac{\partial Y_C}{\partial \tau} = \frac{1}{\eta^2}\frac{\partial}{\partial \eta}\left(\eta^2 \frac{\partial Y_C}{\partial \eta}\right) \quad (14)$$

$$\frac{\partial Y_A}{\partial \tau} = C_3 \frac{1}{\eta^2}\frac{\partial}{\partial \eta}\left(\eta^2 \frac{\partial Y_A}{\partial \eta}\right) \quad (15)$$

$$\text{I.C. 1:} \quad Y_P = 1 \quad \text{for} \quad \tau = 0 \quad (16)$$

$$\text{I.C. 2:} \quad Y_A = C_{A0}/C_{P0}, Y_C = 0 \quad \text{for} \quad \tau = 0, \quad \text{all} \quad \eta \quad (17)$$

$$\text{B.C. 1:} \quad \frac{\partial Y_A}{\partial \eta} = 0, \frac{\partial Y_C}{\partial \eta} = 0 \quad \text{for} \quad \eta = 0, \quad \text{all} \quad \tau \quad (18)$$

$$\text{B.C. 2:} \quad \frac{\partial Y_C}{\partial \eta} = \frac{C_3}{2}\frac{\partial Y_A}{\partial \eta} = \frac{C_1}{2} N_{Da}(Y_{A,i}^2 Y_H^2 Y_P^2 - C_2 Y_{C,i}) \quad \text{for} \quad \eta = 1, \quad \text{all} \quad \tau \quad (19)$$

The preceding partial differential equations were transformed to ordinary differential equations using the orthogonal collocation method (Finalyson, 1980). The ordinary differential equations were solved with the initial and the boundary conditions by the Fortran subroutine IVPAG and NEQNF, which are available from the IMSL Math/Library.

Experimental Section

The investigations conducted were of extraction equilibrium in a shaker. The organic and the aqueous solutions were prepared by dissolving Amberlite LA-2 (secondary amine, Sigma-Aldrich Co.) in kerosene (Junsei Chemical, viscosity and density at 25°C: 1.3 cP and 0.8 g/cm^3) and dissolving penicillin G potassium salt (Sigma-Aldrich Co.) in a citrate buffer solution, respectively. The citrate buffer solution was composed of a mixture of citric acid and trisodium citrate (EP grade, Junsei Chemical), and its concentration was 0.408 mol/dm^3. Equal volumes (30 mL) of the prepared organic and aqueous solutions in a 250-mL flask were vigorously shaken for about one hour, and the concentration of penicillin G in the aqueous phase was measured by a UV spectrophotometer (UV2-100, ATI Unicam) at 258 nm after separation of the two immiscible phases.

The experimental apparatus for kinetics measurements was a batch-type stirred-glass cell 15 cm deep with an ID of 10 cm. The vessel was fitted with stainless steel baffles and set up in a water bath maintained at 25°C. Stirring was carried out using a turbine impeller with six flat blades, each of 5.5 cm diameter, connected with a speed controller. First of all, we added penicillin G to 140 mL of the aqueous buffer solution in the vessel and stirred the solution at 250 rev/min. We continued to take samples at known time intervals after pouring 35 mL of the organic solution into the aqueous solution in an instant. Since the samples were not viscous, we could take them from the vessel by a pipette at the intervals without any delay. The samples were spontaneously separated into two phases in the pipette because of their immiscible property. The separated aqueous phase was further purified with a centrifuge (Universal 32, Hettich). In order to minimize experimental errors, however, we did each experiment five times for each run, and used the average experimental data when comparing them with the calculated results from the model. On the other hand, penicillin G concentration in the aqueous phase was analyzed in the same way as just described.

The densities of the organic solutions were measured over a carrier concentration range of 0–140 mol/m^3 at 25°C. The density measurements were performed by using a 25-mL Gay-Lussac pycnometer that was submerged in a thermostated water bath. The viscosity measurements were made using the UL adapter of the Brookfield Digital Viscometer Model DV-II+ manufactured by Brookfield Engineering Laboratories,

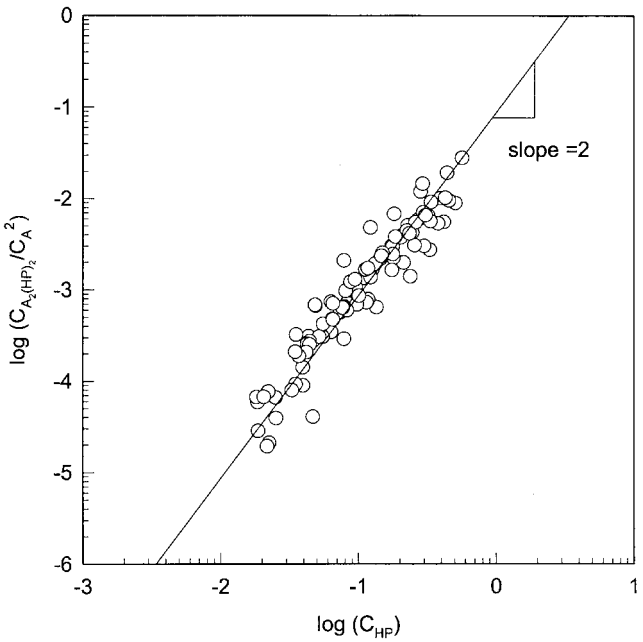

Figure 2. Reaction equilibrium between penicillin G and Amberlite LA-2 in a liquid–liquid extraction system.

Inc. The interfacial tension between the aqueous and the organic solutions was obtained using the Fisher Surface Tensiomat Model 21. The force necessary to pull a platinum-iridium du Nuoy ring through the liquid–liquid interface was measured.

Estimation of Parameters

The reaction between penicillin G and Amberlite LA-2 in a nonpolar organic solvent and its equilibrium constant are expressed in Eqs. 2 and 3, respectively, which has been considered already in our previous work (Lee et al., 2002b). Figure 2 shows the equilibrium relationship between $C_{A_2(HP)_2}/C_A^2$ and C_{HP}, and the slope of the straight line is 2, which confirms that Eq. 2 is valid. The value of K'_{eq} is listed in Table 1.

The experimentally measured density and viscosity data for the organic solution are given in Table 2. Both density and viscosity increased with the increase in carrier concentration. The experimental values of the density and the viscosity were used to estimate the size of the dispersed drops and the diffusivities of the carrier and the complex in the organic solution, respectively.

Figure 3 shows that the interfacial tension between the organic and the aqueous solutions decreases with an increase in carrier concentration, suggesting that the carrier is interface-active, with interfacial saturation adsorption concentration evaluated as 129.5 mol/m^3. The adsorption equilibrium of

Table 1. Values of Parameters Under the Typical Experimental Condition

K'_{eq}: 8.655×10^{-2} m^9/mol^3	K_{ad}: 6.515×10^{-1} m^2/mol
S_i: 4.766×10^5 m^2/mol	γ_0: 3.020×10^{-2} N/m
D_A: 8.412×10^{-10} m^2/s	D_C: 4.112×10^{-10} m^2/s
R: 2.783×10^{-4} m	

Note: (C_{P0}: 80 mol/m^3; C_{A0}: 50 mol/m^3; pH: 5.0)

Table 2. Density and Viscosity Data for the Organic Solution as a Function of Amberlite LA-2 Concentration

Amberlite LA-2 Conc. (mol/m^3)	30	50	80	110	140
Density (kg/m^3)	787.8	788.2	788.8	789.1	789.6
Viscosity ($10^3 \times$ kg/m · s)	1.28	1.29	1.31	1.34	1.38

carrier at the interface between the organic and the aqueous solutions is expressed by

$$A_{\text{org}} \overset{K_{ad}}{\longleftrightarrow} A_i \tag{20}$$

where K_{ad} is the adsorption equilibrium constant. Assuming the Langmuir adsorption isotherm between the amount of carrier adsorbed and its bulk concentration, the relation between the interfacial tension and the bulk concentration is given as follows (Wang et al., 1991; Yoshizuka et al., 1985)

$$\gamma = \gamma_0 - (R_g T/S_i)\ln(1 + K_{ad}C_A) \tag{21}$$

where γ_0 is the interfacial tension between pure kerosene and the aqueous solution, and S_i is the interfacial area occupied by a unit mole of carrier. The values of K_{ad} and S_i were obtained by fitting the experimental data for the interfacial tension to Eq. 21 by a nonlinear regression method. Actually, we could not directly measure the interfacial tension through the kinetic experiments. For the sake of convenience, the interfacial tension used to calculate the mean radius of the dispersed drops was considered to depend on both carrier and complex interfacial concentrations, which were calculated from the mass-transfer model. For this, we assumed that one complex molecule functioned as interface-actively as the two carrier molecules did, because the interface-active part in the complex

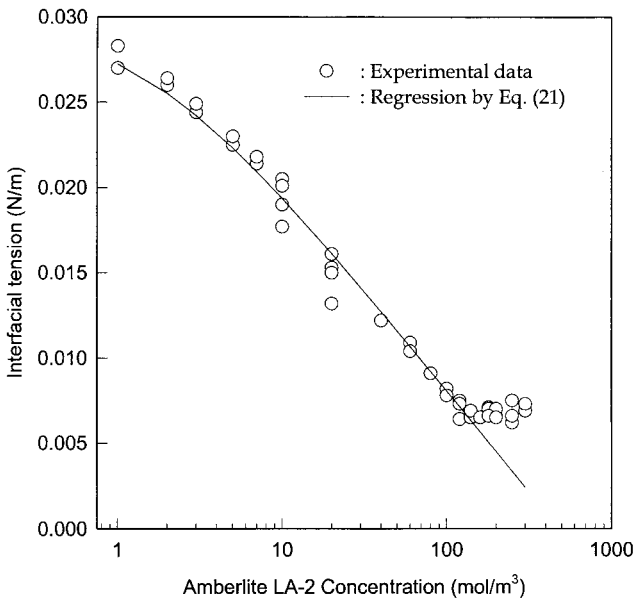

Figure 3. Relationship between interfacial tension and carrier concentration.

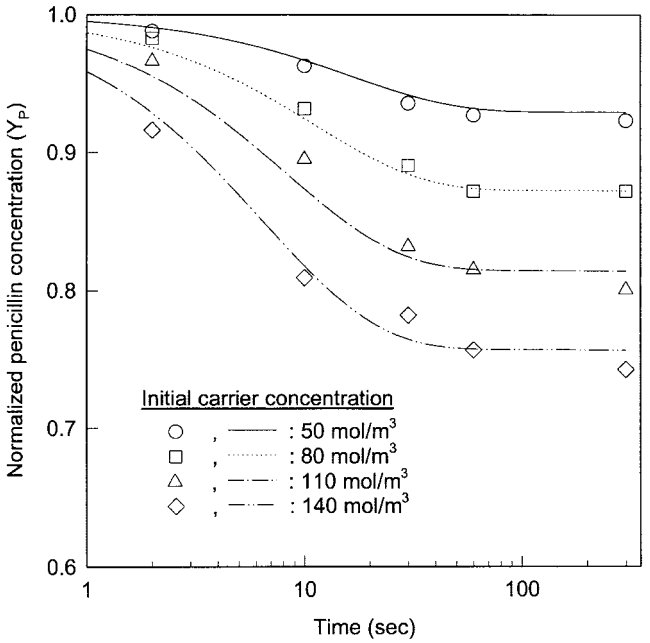

Figure 4. Comparison of the experimental data with the calculated results for penicillin G extraction as a function of initial concentration of carrier in the dispersed organic phase (C_{P0} = 80 mol/m^3; pH = 5.0).

corresponded to only two carrier molecules. This assumption is effective only for the present extraction system with low degrees of penicillin G extraction.

The molecular diffusivities of the carrier and the complex in the organic solution were estimated from the Wilke-Chang method which was an empirical modification of the Stokes-Einstein relation (Reid et al., 1977). The calculated value for each component is listed in Table 1.

To obtain the steady-state Sauter–mean drop diameter, d^*_{32}, Lee and Soong (1985) developed a correlation with the correction factor for surfactants, C_s, equivalent to 0.63, independent of surfactant type. The correlation is applicable to the carrier, Amberlite LA-2, which is surface-active

$$\frac{d^*_{32}}{d_I} = 0.05C_s\left(1 + 2.316\,\frac{\phi}{1+\phi}\right)\left(\frac{d_I}{d_T}\right)^{-0.75} N_{Fr}^{-0.13}N_{We}^{-0.6} \tag{22}$$

Also, a general correlation for a change in the Sauter–mean drop diameter with respect to time during the initial period of liquid–liquid dispersions in agitated vessels was developed by Hong and Lee (1985) as follows

$$\frac{d_{32} - d^*_{32}}{d^*_{32}} = 29.70\left(\frac{d_I}{d_T}\right)^{-2.015}\left(\frac{N_{We}}{N_{Re}}\right)^{0.5508}(Nt)^{-0.7} \tag{23}$$

The average value of the Sauter–mean drop diameter ($\bar{d}_{32}$) over the total extraction time (t_f) is expressed by

$$\bar{d}_{32} = \frac{1}{t_f}\int_0^{t_f} d_{32}\,dt \tag{24}$$

For simplicity, the average radius of the dispersed drops (R) was assumed to be $\bar{d}_{32}/2$, regardless of time.

Results and Discussion

The experimental data from 12 runs were obtained through the kinetics experiments, and the absolute mean deviation f was introduced so as to optimize the forward reaction rate constant (k_f) of the interfacial reaction

$$f = \frac{1}{n}\sum_{i=1}^{n}\left|\frac{E_{\text{exp},i} - E_{\text{cal},i}}{E_{\text{exp},i}}\right| \times 100 \tag{25}$$

where $E_{\text{exp},i}$ is the experimental data for the degree of extraction at any time, and $E_{\text{cal},i}$ is the calculated results predicted from the mass-transfer model. The optimal value of k_f, 5.188×10^{-8}, gave an excellent fit to the experimental data with an absolute mean deviation of 0.96%. Such a small deviation justifies the mass-transfer model.

Effects of various experimental conditions on penicillin G extraction

Figures 4 and 5 show the effects of the initial concentration of the carrier in the dispersed organic phase and the pH of the continuous aqueous phase, respectively, on the extraction of penicillin G. The calculated results from the mass-transfer model, represented by four different lines, agreed well with the

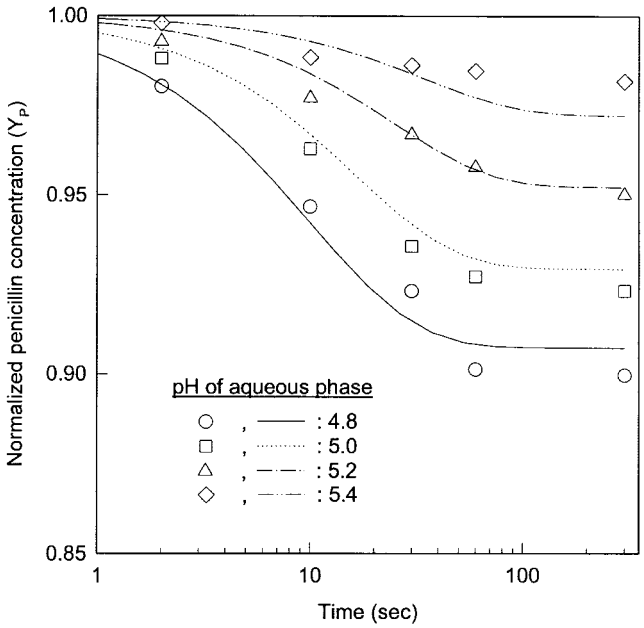

Figure 5. Comparison of the experimental data with the calculated results for penicillin G extraction as a function of pH of the continuous aqueous phase (C_{P0} = 80 mol/dm^3; C_{A0} = 50 mol/m^3).

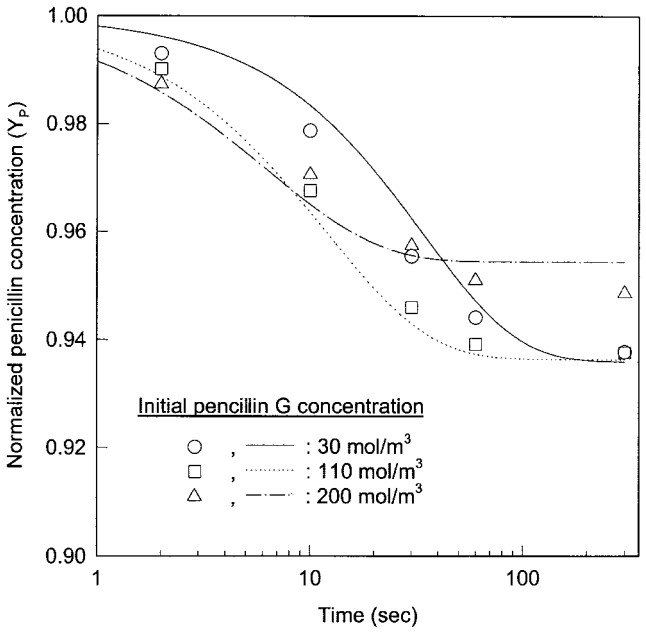

Figure 6. Comparison of the experimental data with the calculated results for penicillin G extraction as a function of initial concentration of penicillin G in the continuous aqueous phase (C_{A0} = 50 mol/m^3; pH = 5.0).

experimental data, represented by four different symbols. The initial extraction rates based on the normalized concentration of penicillin G (Y_P) increased with the decrease in the pH or the increase in the carrier concentration, because the forward reaction orders in hydrogen ion and carrier were positive values. Also, the degree of extraction in each figure was higher at a lower pH or a higher carrier concentration. This is because a higher carrier concentration gives a higher reaction capacity of the carrier with penicillin G, and a lower pH shifts the reaction equilibrium to the right side of Eq. 2.

The effect of the initial concentration of penicillin G in the continuous aqueous phase on the extraction of penicillin G is shown in Figure 6. The initial extraction rate based on the normalized concentration of penicillin G in the aqueous phase was higher at a higher initial penicillin G concentration. The extraction behavior justifies the fact that the initial extraction rate for batch extraction and the concentration gradient at the inlet of the feed phase for continuous extraction increased with an increase in the initial concentration of penicillin G in the feed solution in the previous ELM systems (Lee and Lee, 1992; Lee et al., 1997). In the case of 200 mol/m^3 of the initial penicillin G concentration, the degree of extraction decreased more rapidly with time because the carrier in the dispersed organic drops was saturated with undissociated penicillin acid earlier.

Validity of the mass-transfer model

The mass-transfer model did not take a mass-transfer resistance in the continuous aqueous film into consideration. If the mass-transfer resistance is significant in the dispersed liquid–liquid extraction system, the mass balance of penicillin G in the continuous phase for the mass-transfer model can be rewritten as follows

$$-V_{aq}\frac{dC_P}{dt}(1+10^{pK_a-pH}) = k_{HP}S(C_{HP}-C_{HP,i}) \qquad (26)$$

where k_{HP} is the mass-transfer coefficient of undissociated penicillin acid in the continuous aqueous film. At the same time, the second boundary condition given in Eq. 11 should be replaced by

$$\text{B.C. 2:}\quad k_{HP}(C_{HP}-C_{HP,i}) = 2D_C\frac{\partial C_C}{\partial r} = -D_A\frac{\partial C_A}{\partial r}$$
$$= k_f(C_{A,i}^2C_H^2C_P^2 - C_{C,i}/K_{eq}) \quad \text{for} \quad r=R, \quad \text{all} \quad t \qquad (27)$$

Equations 26 and 27 can be reduced to the following dimensionless forms using Biot number, N_{Bi}

- Continuous aqueous phase

$$\frac{dY_P}{d\tau} = -3N_{Bi}\phi(Y_{HP}-Y_{HP,i}) \qquad (28)$$

$$\text{B.C. 2:}\quad \frac{N_{Bi}}{2}(Y_{HP}-Y_{HP,i}) = \frac{\partial Y_C}{\partial \eta} = \frac{C_3}{2}\frac{\partial Y_A}{\partial \eta}$$
$$= \frac{C_1}{2}N_{Da}(Y_{A,i}^2Y_H^2Y_P^2 - C_2Y_{C,i}) \quad \text{for} \quad \eta=1, \quad \text{all} \quad \tau \qquad (29)$$

The continuous-phase mass-transfer coefficient of undissociated penicillin acid in agitated vessels was estimated from the

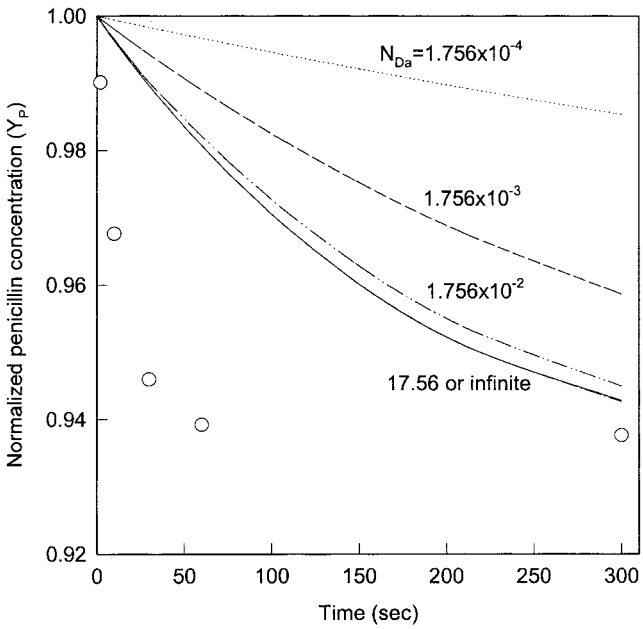

Figure 7. Change in the normalized penicillin concentration in the continuous phase with time at different Danckwert numbers (C_{P0} = 110 mol/m^3; C_{A0} = 50 mol/m^3; pH = 5.0; k_{HP} = 1.327 × 10^{-5}).

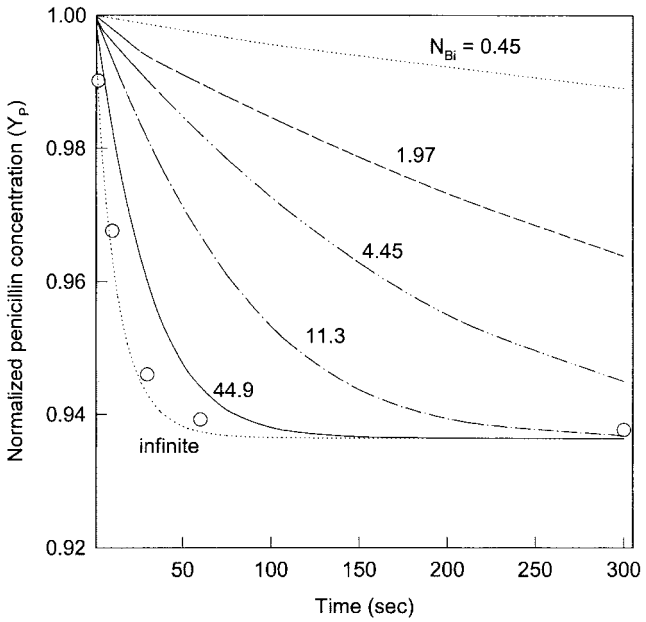

Figure 8. Change in the normalized penicillin concentration in the continuous phase with time at different Biot numbers (C_{P0} = 110 mol/m^3; C_{A0} = 50 mol/m^3; pH = 5.0; $k_t = 5.188 \times 10^{-8}$).

correlation for the low interfacial tension systems below (Skelland and Lee, 1981)

$$\frac{k_{HP}}{\sqrt{ND_{HP}}} = 1.864 \times 10^{-6}\left(\frac{\phi}{1+\phi}\right)^{-0.287}\left(\frac{d_I}{d_T}\right)^{0.548} N_{Re}^{1.371} N_{We}^{-0.095} \tag{30}$$

The value of k_{HP} was 1.327×10^{-5} m/s under the given experimental condition. Figure 7 shows the results of the normalized penicillin concentration in the continuous phase vs. time at different Danckwert numbers (N_{Da}) in the dispersed liquid–liquid extraction system with a fixed value of k_{HP}. The Danckwert number is the ratio of the diffusional resistance in the organic drops to the interfacial reaction resistance. As the Danckwert number increased, the extraction rate increased. However, the calculated results for the normalized penicillin concentration was still larger than the experimental data, even when the Danckwert number was infinite, that is, the interfacial reaction was at an equilibrium state. Therefore, it would be impossible to obtain these experimental data if the mass transfer in the continuous aqueous film controlled the extraction rate. Figure 8 shows the change in the normalized penicillin concentration in the continuous phase with time at different Biot numbers (N_{Bi}) in the extraction system, with the value of k_f obtained from the mass-transfer model, which was described in Eqs. 5–11. The Biot number stands for the ratio of the diffusional resistance in the organic drops to the mass transfer resistance in the continuous aqueous film. The larger the Biot number was, the higher the extraction rate was. Especially, the experimental data agreed well with the calculated results at the infinite value of the Biot number, which means that the mass-transfer resistance in the aqueous film is negligible. Therefore, it could be certified that the mass-transfer model, which was developed without consideration of the mass-transfer resistance in the continuous aqueous film, was suitable to describe the dispersed liquid–liquid extraction system.

Conclusions

Reactive extraction of penicillin G was carried out in an agitated liquid–liquid extraction system, and a mass-transfer model was developed to obtain a kinetic expression of the reaction of penicillin G with Amberlite LA-2 in kerosene. For the purpose of the kinetic study, the dispersed extraction system was preferable to a constant interface stirred cell, which requires a long extraction period because of the low extraction rate of penicillin G, and thus may result in large losses of penicillin G due to its instability.

The mass-transfer model, where the interfacial reaction and the diffusion in an organic drop control the extraction rate, was not only seen to be effective because the calculated results were in good agreement with the experimental data, but also its validity was proved using Danckwert and Biot numbers. In addition, the interfacial reaction expression could be used to satisfactorily explain the effect of the initial penicillin G concentration on the degree of extraction in our previous ELM systems.

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Notation

A = Amberlite LA-2 or carrier
HP = undissociated penicillin acid
AHP = penicillin–Amberlite LA-2 complex given by Eq. 1
$A_2(HP)_2$ = penicillin–Amberlite LA-2 complex given by Eq. 2
C = concentration, mol/m^3
C_s = correction factor given by Eq. 22
D = diffusivity, m^2/s
d_{32} = Sauter mean diameter at any time, m
d_{32}^* = steady-state Sauter mean diameter, m
$\bar{d}_{32}$ = average value of Sauter mean diameter given by Eq. 24, m
d_I = impeller diameter, m
d_T = vessel diameter, m
E = degree of extraction, %
f = absolute mean deviation given by Eq. 25, %
H = height of liquid in the vessel, m
K_a = acid dissociation constant of penicillin G, mol/m^3
K_{ad} = adsorption equilibrium constant, m^3/mol
K_{eq} = equilibrium constant given by Eq. 4, m^{15}/mol^5
K'_{eq} = equilibrium constant defined by Eq. 3, m^9/mol^3
k_f = forward reaction rate constant given by Eq. 4, m^{16}/mol$^5 \cdot$ s^2
k'_f = forward reaction rate constant given by Eq. 4, m^{10}/mol$^3 \cdot$ s^2
k_{HP} = mass-transfer coefficient of undissociated penicillin acid in the continuous aqueous film, m/s
n = number of data
N = impeller speed, rev/s
N_{Da} = Danckwert number, defined by $k_f R/D_C$
N_{Fr} = impeller Froude number, defined by $\rho_c N^2 d_I^2/\Delta\rho Hg$
N_{Re} = impeller Reynolds number, defined by $\rho_c N d_I^2/\mu_c$
N_{Bi} = Biot number, defined by $k_{HP}R/D_C$
N_{We} = impeller Weber number, defined by $\rho_c N^2 d_I^3/\sigma$
P^- = penicillin acid anion
R = average radius of dispersed drops, m
R_g = gas constant, J/mol $\cdot$ K
r = radius, m
r_i = reaction rate per unit interfacial area, mol/s $\cdot$ m^2

S = interfacial area between continuous phase and dispersed drops, m^2
S_i = interfacial area occupied by unit mole of carrier given by Eq. 21, m^2
T = temperature, K
t = time, s
t_f = total extraction time, s
V = volume, m^3

Greek letters

γ = interfacial tension, N/m
γ_o = interfacial tension between kerosene and aqueous solution, N/m
ϕ = volume ratio of organic phase to aqueous phase, dimensionless
ρ_c = density of continuous phase, kg/m^3
ρ_d = density of dispersed phase, kg/m^3
$\Delta\rho$ = $\rho_c - \rho_d$, kg/m^3
σ = interfacial tension, N/m
μ_c = viscosity of continuous phase, kg/m · s

Subscripts

A = Amberlite LA-2
$A_2(HP)_2$ = penicillin–Amberlite LA-2 complex
aq = aqueous phase
C = penicillin–Amberlite LA-2 complex, $A_2(HP)_2$
cal = calculated value
exp = experimental value
HP = undissociated penicillin acid
i = interface
org = organic phase
P = penicillin acid anion
0 = initial value

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