Adsorption 5, 381–390 (1999)
© 1999 Kluwer Academic Publishers. Manufactured in The Netherlands.

Effect of pH on Adsorption of Cephalosporin C by A Nonionic Polymeric Sorbent

JAE WOOK LEE
Department of Chemical Engineering, Seonam University, Namwon 590-170, Korea
jwlee@tiger.seonam.ac.kr

HEE MOON
Faculty of Applied Chemistry, Chonnam National University, Kwangju 500-757, Korea

Received November 12, 1997; Revised February 23, 1999; Accepted March 12, 1999

Abstract. Adsorption of cephalosporin C in a column charged with a nonionic polymeric sorbent, SP850, was studied at various pH values to assess the effect of pH on the dynamic behavior in column adsorbers. Since cephalosporin C is amphoteric, the fractions of each ionic form were calculated from the pK values at a given solution pH. Single-species isotherm parameters for each ionic form were simultaneously extracted from all sets of adsorption equilibrium data measured at several pH values. The mutual interaction between different ionic forms on SP850 was described by a competitive adsorption, namely the ideal adsorbed solution theory (IAST). This treatment made it possible to simulate the dynamic behavior of cephalosporin C at low pH values properly by a dynamic model which was incorporated with the mutual competitive adsorption.

Keywords: adsorption of cephalosporin C, polymeric sorbent, effect of pH, column operation

Introduction

Cephalosporin C is an important starting material to make medical and pharmaceutical products. Its antibacterial activity was low and similar to that of penicillin N. However, unlike the latter, the former is not hydrolyzed by a penicillinase (Elander and Aoki, 1982). This advantage has been received considerable attention from many researchers because of its potential clinical interest.

Generally, a number of separation steps are normally taken to recover, separate, and purify a pure biochemical from its fermentation broth which contains many byproducts including raw materials. The typical separation techniques are adsorption (Nara et al., 1975; Voser, 1982), ion exchange (Stables and Briggs, 1978), derivatization followed by solvent extraction (Johnson and Smith, 1970; Yang et al., 1994), and enzymatic modification (Arnold et al., 1969). After removing cell mass and higher molecular weight proteins by centrifugation and ultrafiltration, such techniques can be used either separately or in combination for the isolation of a product from the filtrate. The adsorption-based separation technique is one of the promising methods for the separation of cephalosporin C from admixtures since it is a nondenaturing, highly selective, energy efficient, and relatively inexpensive process. A large-scale cyclic operation, which consists of three steps such as adsorption, desorption, and washing, has been generally applied so far.

Design and scale-up of such large-scale separation processes require information to simulate the dynamic behavior both in adsorption and desorption steps (Costa and Rodriques, 1985). Since cephalosporin C is one of amphoteric antibiotics of which ionic form changes with the concentration of hydrogen ion, the adsorption

behavior depends strongly on the solution pH (Chaubal et al., 1995). Irregular pH variations and abnormal breakthrough behaviors with multiple plateaus were often found during adsorption or desorption experiments in batch and column adsorbers, particularly at low pH values. These results could be obtained by the mutual interaction between different ionic forms.

In this study, we deal with the effect of pH on the adsorption of cephalosporin C onto a nonionic polymeric sorbent, SP850. We have introduced a simple method to quantitate the adsorption of cephalosporin C. First, the fractions of different ionic froms are calculated from the pK values of cephalosporin C at a given pH value. Secondly, the single-solute isotherm parameters for each ionic form are obtained simultaneously from all adsorption equilibrium data measured at different pH values. A competitive equilibrium model, namely the IAST (Myers and Prausnitz, 1965), was used to take into account the competition between different ionic forms on the sorbent surface. Furthermore, a dynamic model was constructed by incorporating the solute competition into the mass balance equation. The kinetic parameters such as film mass transfer coefficient and intraparticle diffusion coefficient for the model were estimated separately.

Theoretical Approach

Adsorption Equilibria

Cephalosporin C is characterized by amphoteric behavior and thus can be present in aqueous solution in different ionic forms, depending upon solution pH. As shown in Fig. 1, a structure of cephalosporin C can be generally repersented as $NH_2CHRCOOH$ ($R = C_{14}H_{17}NO_6S$). The values of pK for cephalosporin C are known to be about 2.6, 3.1 and 9.8 from the literature. Cephalosporin C can be classified into three groups: neutral (no functional groups on the side chain or both one carboxylic group and one aminic group on the side chain), acidic (one carboxylic group on the side chain), and basic (one aminic group on the side chain).

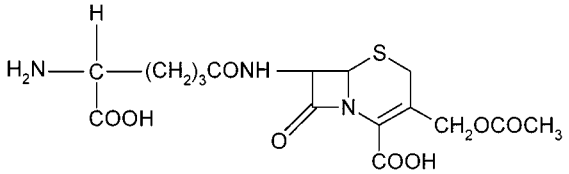

Figure 1. The chemical structure of cephalosporin C.

The degree of ionization of such an amphoteric antibiotic, which depends strongly on pH, can be represented by the association-dissociation equilibria.

$$NH_3^+CHRCOOH \Leftrightarrow NH_2CHRCOOH + H^+ \quad (1)$$

$$NH_3^+CHRCOOH \Leftrightarrow NH_3^+RCOO^- + H^+ \quad (2)$$

$$NH_2^+CHRCOO^- \Leftrightarrow NH_2CHRCOO^- + H^+ \quad (3)$$

$$NH_2CHRCOO^- \Leftrightarrow NH_2CHRCOO^{2-} + H^+ \quad (4)$$

By assuming ideal behavior for the aqueous phase, the dissociation constants are expressed by

$$K_1 = \frac{[H^+]\left(\left[NH_3^+CHRCOO^-\right] + [NH_2CHRCOOH]\right)}{\left[NH_3^+CHRCOOH\right]} \quad (5)$$

$$K_2 = \frac{[H^+]\left[NH_2CHRCOO^-\right]}{\left(\left[NH_3^+CHRCOO^-\right] + [NH_2CHRCOOH]\right)} \quad (6)$$

$$K_3 = \frac{[H^+]\left[NH_2CHRCOO^{2-}\right]}{\left[NH_2CHRCOO^-\right]} \quad (7)$$

The total analytical concentration of cephalosporin C in solution, C_T, is given by

$$C_T = NH_2CHRCOOH + NH_3^+CHRCOOH + NH_3^+CHRCOO^- + NH_2CHRCOO^- + NH_2CHRCOO^{2-} \quad (8)$$

By combining Eqs. (5)–(8), the following expressions for the concentrations of the different ionic forms can be obtained as a function of the hydrogen ion concentration, $[H^+]$, and of the analytical concentration, C_T:

$$[C^+] = \frac{C_T}{\left(1 + \frac{K_1}{[H^+]} + \frac{K_1K_2}{[H^+]^2} + \frac{K_1K_2K_3}{[H^+]^3}\right)} \quad (9)$$

$$[C^-] = \frac{C_T}{\left(1 + \frac{[H^+]}{K_2} + \frac{[H^+]^2}{K_1K_2} + \frac{K_3}{[H^+]}\right)} \quad (10)$$

$$[C^{2-}] = \frac{C_T}{\left(1 + \frac{[H^+]}{K_3} + \frac{[H^+]^2}{K_2K_3} + \frac{[H^+]^3}{K_1K_2K_3}\right)} \quad (11)$$

Therefore, the neutral concentration can be obtained as follows:

$$[C^\pm] = C_T - [C^+] - [C^-] - [C^{2-}] \quad (12)$$

where C^+, $C^\pm$, C^-, and C^{2-} represent the concentration of cationic, neutral, anioic, and dianionic form, respectively.

Since the relative concentrations of the different ionic forms vary with pH, the apparent affinity of cephalosporin C also varies with the solution pH. Moreover adsorption equilibria of cephalosporin C can not be treated like ion-exchange equilibrium when polymeric sorbents are nonionic. Even a very small fraction of the sorbent can be ionized, the adsorption of ionic forms including a neutral form would be more similar to that of nonionic sorbates rather than ion-exchange equilibria. In this work, the adsorption isotherm of each form was represented by the Langmuir equation and the mutual competitive interaction between different forms of cephalosporin C was expressed by the IAST (Tien, 1994). The governing equations are

$$C_i = C_i^0(\pi, T)x_i \tag{13}$$

$$\Pi_i = \frac{\pi_i A}{RT} = \int_0^{C_i^0} \frac{q_i^0}{C_i^0}\, dC_i^0 \tag{14}$$

$$q_T = \left[\sum_{j=1}^{N} \frac{x_i}{q_i^0} \right]^{-1} \tag{15}$$

$$\sum_{i=1}^{N} x_i = 1.0 \tag{16}$$

When the Langmuir equation is used as a single-species isotherm, Eq. (14) is given by

$$\Pi_i = q_{\mathrm{m}i} \ln\left(1 + b_i C_i^0\right) \tag{17}$$

At equilibrium, the reduced spreading pressures, Π_i, are equal:

$$\Pi_1 = \Pi_2 = \Pi_3 = \cdots \equiv \Pi \tag{18}$$

By combining three Eqs. (13), (16) and (17), the following equation can be drawn

$$F(\Pi) = \sum_{i=1}^{N} \frac{b_i C_i}{\exp(\Pi/q_{\mathrm{m}i}) - 1.0} - 1.0 = 0 \tag{19}$$

If the reduced spreding pressure is determined by trial-and-error procedure, that is, Newton-Raphson method, the total amount adsorbed is evaluated by Eq. (15).

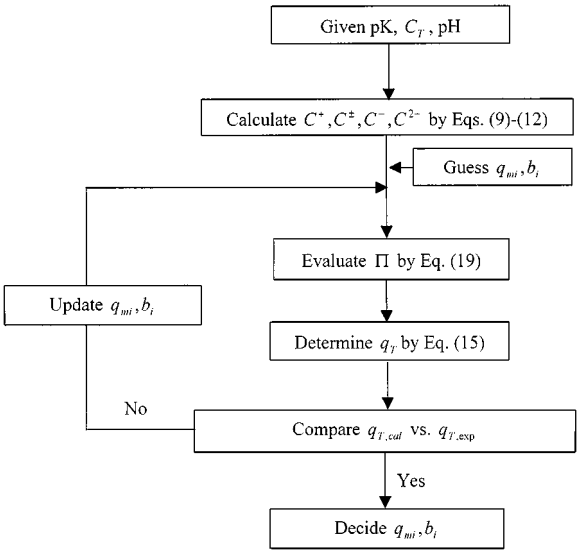

Figure 2. Flow diagram of IAST calculation.

Then, the Langmuir parameters, $q_{\mathrm{m}i}$, and b_i, for each ionic form were simultaneously extracted by comparing all sets of adsorption equilibrium data measured at several pH values with predicted results from Eq. (15) by a nonlinear least-squares fitting routine (DUNLF in the IMSL package). Flow diagram of IAST calculations are shown in Fig. 2.

Model Description

A surface diffusion model with external mass transfer resistance was selected in this study because of its simplicity and adequecy in describing adsorption and desorption of cephalosporin C from aqueous solution on nonionic polymeric sorbents. The model assumes an isothermal adsorption column, packed with porous spherical particles. The flow pattern is described by the axial dispersed plug-flow model. Other assumptions involved in the model include spherical adsorbent particles, isothermal condition and fast intrinsic adsorption kinetics, resulting in local equilibrium between the solid-phase and liquid-phase solute concentrations at the external surface of the particles. The diffusion of a solute inside a spherical adsorbent particle is described by the following equation:

$$\frac{\partial q_i}{\partial t} = D_{si}\left(\frac{\partial^2 q_i}{\partial r^2} + \frac{2}{r}\frac{\partial q_i}{\partial r} \right) \tag{20}$$

with the initial and boundary conditions:

$$q_i(r, t = 0) = 0 \tag{21}$$

$$\left.\frac{\partial q_i}{\partial r}\right|_{r=0} = 0 \tag{22}$$

$$D_{si}\rho_p \left.\frac{\partial q_i}{\partial r}\right|_{r=R} = k_f(C_i - C_{si}) \tag{23}$$

The solute mass balance in the liquid phase and the relevant conditions are:

$$-D_L\frac{\partial^2 C_i}{\partial z^2} + \frac{\partial \nu C_i}{\partial z} + \frac{\partial C_i}{\partial t} + \frac{1-\varepsilon_b}{\varepsilon_b}\frac{\partial q_i}{\partial t} = 0 \tag{24}$$

$$C_i(z, t = 0) = 0 \tag{25}$$

$$D_L\left.\frac{\partial C_i}{\partial z}\right|_{z=0} = -\nu(C_i|_{z=0^-} - C_i|_{z=0^+}) \tag{26}$$

$$\left.\frac{\partial C_i}{\partial z}\right|_{z=L} = 0 \tag{27}$$

The system of partial differential equations were numerically solved. Eqs. (20) and (24) were first discretized using an orthogonal collocation method (Villadsen and Michelson, 1978; Villadsen and Stewart, 1967; Lee et al., 1997). By this method, the second-order partial differential equations are reduced to a set of first-order ordinary differential equations. The resultant equations were simultaneously integrated using an integrating package, DGEAR of the International Mathematics and Science Library (IMSL).

Experimental

The nonionic polymeric sorbent used in this study was SP850, a macroreticular and spherical polystyrene resin cross-linked with DVB (divinylbenzene) which was supplied by Mitzubishi Chemical Co. (Japan). The physical properties of SP850 are summarized in Table 1. The water content of fully swollen resin particles was determined from the weight loss of samples that occurred during drying in a vacuum oven at 80°C for 48 h. The arithmatic average particle diameter was determined by sorting wet resin particles with the aid of an optical microscope. It was about 382 μm.

A zinc form of cephalosporin C used as a standard material was purchased from Sigma (USA) and a sodium form for experimental use was supplied by Cheil Food & Chemicals Inc. (Korea), respectively.

Table 1. Properties of a polymeric sorbent, SP850.

Property	Values	Unit
Particle diameter	382	μm
Particle density	457	kg/m^3
Moisture content[a]	52	%
Surface area[a]	1,000	m^2/s
Average pore diameter[a]	38.1	Å
Pore volume[a]	0.89	ml/g

[a]From the manufacturer's report.

Table 2. Properties of cephalosporin C.

Property	Values
Chemical formula	$C_{16}H_{21}N_3O_8S$
Molecular weight	415.4
Analysis	260
pKa	about 2.6, 3.1, 9.8

Both materials were used without further purification. The properties of cephalosporin C were listed in Table 2.

Prior to experiments, the sorbent was leached with isopropyl alcohol for 24 h to wet internal pores. Sorbent particles were loaded in a 0.02 m ID glass column and a ten-bed volume of sodium hydroxide (0.1N) and HCl (0.1N) were passed through the column successively at a flow rate of 1.0×10^{-4} m^3/min in order to remove impurities. Finally, a twenty bed-volume of distilled and deionized water was passed at the same flow rate to rinse off HCl.

Equilibrium experiments were carried out by contacting a given amount of sorbent with cephalosporin C solution of 1–80 mol/m^3 and keeping in a constant temperature shaking incubator. The weight of sorbent particles was measured after drying for 48 h in a vacuum oven maintained at 80°C. After equilibrium was reached, the excess cephalosporin C left in the solution was analyzed using a ultraviolet spectrometry (Varian DMS 100S) and then the adsorption capacity of resin was evaluated from the material balance.

Dynamic adsorption experiments were carried out in a glass column of 0.02 m diameter and 0.145 m length, which was packed with resin particles. The column was lined with a water jacket to maintain a uniform column temperature. The flow rate was regulated by a precision pump (Fluid Metering Inc., QSY). The solution was introduced downward into the column. To prevent channeling and to enhance the flow distribution

through the column, two layers of small glass beads were packed in the top and bottom regions of the column. Breakthrough experiments were carried out under various experimental conditions. Samples were withdrawn from the effluent line and were analyzed to get breakthrough curves.

Results and Discussion

Adsorption isotherms play a crucial role in predicting modeling procedures for analysis and designing of adsorption systems. Adsorption onto synthetic adsorbents is generally driven by the dispersed force between the adsorbate and the resin. Thus, the adsorption capacity depends on the property of the sorbate. Besides, the adsorption capacity is also influenced by other factors such as temperature and pH of the solution to be treated, and the amount of impurities contained in the solution. Equilibrium data for cephalosporin C on SP850 are shown in Fig. 3 and listed in Table 3 for pH values in the range of 2–8, which are typical for the recovery of cephalosporin C in industrial separation processes. The adsorption amount greatly decreases with pH. The difference in amount adsorbed might be due to the change of its ionic form which strongly depends on the solution pH. Fig. 4 shows the fractions of various ionic form of cephalosporin C as a function of pH which were calculated from the association-dissociation equilibria with pK values. In the pH range from 5 to 8, the negatively charged cephalosporin C is obviously predominant while, under pH values of 2–5, either posiviely or negatively charged forms coexist with its zwitterionic (neutral) form. Generally a low pH value around 2–3 has been used in the industrial recovery process for cephalosporin C based on a cyclic operation since the working capacity is large and a byproduct, namely penicillin N, can be destructed at low pH

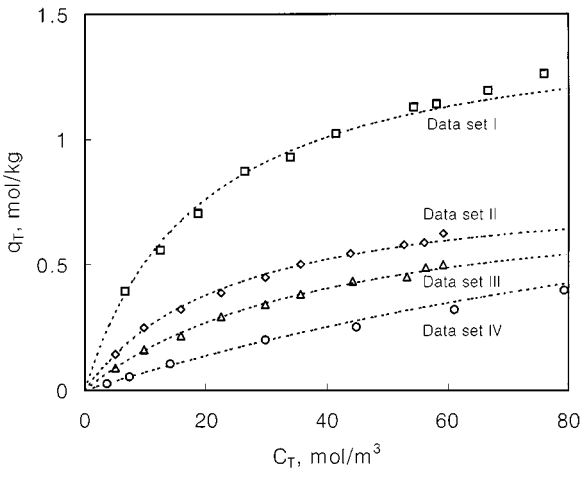

Figure 3. Adsorption equilibrium of cephalosporin C on SP850 at 25°C.

Table 3. Adsorption equilibrium data of cephalosporin C in terms of solution pH.

Data set	Final pH	C_T	q_T
I	2.65	6.587	0.393
	2.73	12.421	0.558
	2.73	18.631	0.706
	2.70	26.346	0.873
	2.70	33.937	0.928
	2.67	41.486	1.022
	2.69	54.395	1.128
	2.68	58.155	1.141
	2.67	67.678	1.194
	2.70	75.952	1.260
II	3.92	5.018	0.143
	4.01	9.723	0.248
	3.87	15.809	0.321
	3.76	22.457	0.387
	3.63	29.797	0.448
	3.60	35.595	0.502
	3.48	43.867	0.545
	3.44	52.766	0.580
	3.43	56.150	0.588
	3.50	59.283	0.625
III	4.89	5.016	0.089
	4.91	9.724	0.162
	4.91	15.803	0.215
	4.81	22.452	0.292
	4.83	29.799	0.340
	4.81	35.597	0.381
	4.83	43.867	0.434
	4.71	52.766	0.450
	4.64	56.151	0.488
	4.62	59.285	0.500
IV	7.50	3.655	0.027
	7.50	7.337	0.054
	7.50	14.062	0.106
	7.50	29.835	0.200
	7.50	44.886	0.251
	7.50	61.204	0.340
	7.50	79.259	0.418

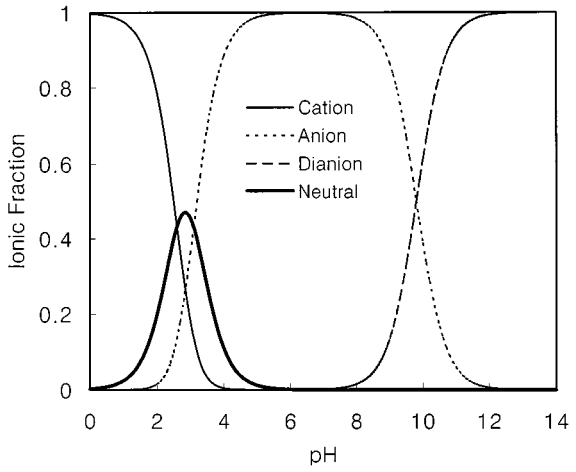

Figure 4. Ionic fractions in terms of solution pH at $C_T = 30\,\text{mol/m}^3$.

values. Therefore, the information on adsorption and desorption of cephalosporin C under low pH values is necessary to simulate the dynamic behavior and to design an optimum separation unit for this purpose. However, adsorption equilibria can not be represented easily by a simple isotherm since there are different ionic forms. The adsorption equilibrium for cephalosporin C at low pH values should be encountered by a competitive model. From experimental results, adsorption occurs physically and the positive and neutral forms of cephalosporin C significantly contributed to the adsorption capacity. Though there are several reports on the ion-exchane equilibria for amphoteric chemicals on ion-exchangers, the adsorption of charged forms on nonionic sorbents is poorly defined. Hence, a competitive multicomponent adsorption model seems to be more suitable rather than the ion-exchange model.

In order to use a conventional approach for analyzing the adsorption of different ionic forms, single-species isotherms for each form should be known. However it is not possible to define them directly from equilibrium data since no single form exists independently as shown in Fig. 4. Therefore, an alternative method was deviced. A single-species isotherm was assumed for an ionic form and a competitive adsorption model was utilized to deal with their mutual interaction. Isotherm parameters for all ionic forms were extracted simultaneously from all sets of equilibrium data obtained at different pH values. In this work, a single-species isotherm were assumed to be the Langmuir equation and the mutual competition between ionic forms is represented by the IAST. IAST was chosen as a matter of conveneience. It is quite possible for someone to use the other competitive theory instead of the IAST. The isotherm parameters for each ionic form, which are obtained by the optimization procedure using all experimental data listed in Table 3, are listed in Table 4. To justify the present apporoach, two different results with experiemntal data at pH = 7.5 are shown in Fig. 4. The possiblity of this comparison is that the solution pH before and after adsorption is constant and only negative form is existed at pH = 7.50. The solid line represents the Langmuir isotherm parameter fitted with experimental data, that is, considering as a single component while the dashed line indicates the result predicted by the IAST using the isotherm parameters of all ionic forms. There are some discrepancies from experimental data when using the IAST. However, such a difference may not be so critical, considering the experimental error encountered.

Table 4. Langmuir isotherm parameters of cephalosporin C on SP850 at 25°C.

Ions	q_m	b
Positive	2.699	0.048
Neutral	0.584	0.382
Negative	0.965	0.011
Langmuir from pH = 7.50 data	1.414	0.005

In a column packed with porous adsorbents, the major kinetic parameters are the axial dispersion coefficient, the film mass transfer coefficient and the intraparticle diffusion coefficient. Axial dispersion contributes to the broadening of the adsorption front due to flow in the void space between particles. The axial dispersion coefficient was estimated from a correlation proposed by Wakao and Funazkri (1978). The values are in the range of $1.0–2.0 \times 10^{-6}$ m^2/s.

For spherical particles, the film mass transfer coefficient can also be estimated from a correlation reported in literature. In this work, the Ranz and Marshall equation (Ruthven, 1984) was employed.

$$\frac{2k_f R}{D_m} = 2.0 + 0.6Sc^{1/3}Re^{1/2} \tag{28}$$

where *Sc* and *Re* denote Schmidt and Reynolds numbers, respectively and D_m is the molecular diffusion coefficient which was estimated by Wilke-Chang equation (Reid et al., 1994). Under experimental conditions used here, the estimated film mass transfer coefficient for cephalosporin C is in the range of $1.05–1.30 \times 10^{-5}$ m/s.

Rate of adsorption in porous adsorbents are generally controlled by transport within the pore network, rather

Table 5. Mass transfer coefficients for cephalosporin C at 25°C and pH = 5.30.

Concentration (mol/m^3)	Flow rate (m/s)	$D_L \times 10^6$ (m^2/s)	$k_f \times 10^5$ (m/s)	$D_s \times 10^{12}$ (m^2/s)
12.039	0.503	1.00	1.05	3.00
21.543	0.530	1.06	1.07	4.10
31.281	0.503	1.00	1.05	5.00
38.741	0.848	2.00	1.30	6.30
51.438	0.654	1.37	1.17	8.00

than by the intrinsic kinetics of sorption at the surface. Although various methods are available for determining the diffusion coefficient, it was determined by comparing the experimental elution curve and the predicted one based on a diffusion model. As shown in Table 5, the values of D_s for negative form of cephalosporin C at pH = 5.30 are approximately 0.30–0.80 $\times 10^{-11}$ m^2/s. It is very difficult to determine the diffusivity of each ionic form of cephalosprin C coexisted in the low range of solution pH. We assumed that the diffusion coefficient for each ionic form is identical with negative form of cephalosporin C.

In commercial equipments for adsorption separation, a column has been used since it gives a sharp breakthrough curve by means of the difference in affinity to the sorbent. The breakthrough curve depends on adsorption equilibrium, interparticle mass transfer, and hydrodynamic conditions in the column. Thus, it is important to consider the adsorption equilibrium and kinetic information simultaneously in simulating the adsorption behavior. To examine the effect of pH on the breakthrough curve of cephalosporin C, all the operating conditions except pH were fixed and at various pH values breakthrough curves were simulated as described in Fig. 6. At high pH values, the breakthrough curve shows a common sigmoid shape which is typical for single-species systems. However, those simulated at low pH values are very unusual with multiple plateaus which is normally represented by a multicomponent system with competitive effects. On the other hand, it is known that removal of a byproduct, penicillin N is one of the serious problems for the separation of cephalosporin C in the broth. This is achieved by lowering the working pH down to 3.0. Moreover the broth is often acidified to about pH 3.0 to precipitate proteins from the culture medium and to improve the adsorption capacity onto the sorbent as shown in Fig. 2. Therefore, it is essential to separate cephalosporin C at a low pH of 3.

Figure 7 shows an experimental breakthrough curve at a pH value of 3.40 with and without introducing the

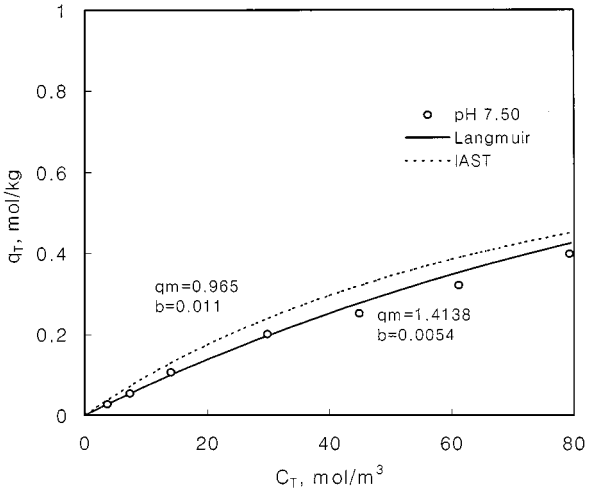

Figure 5. Comparison of isotherm parameters at pH = 7.50.

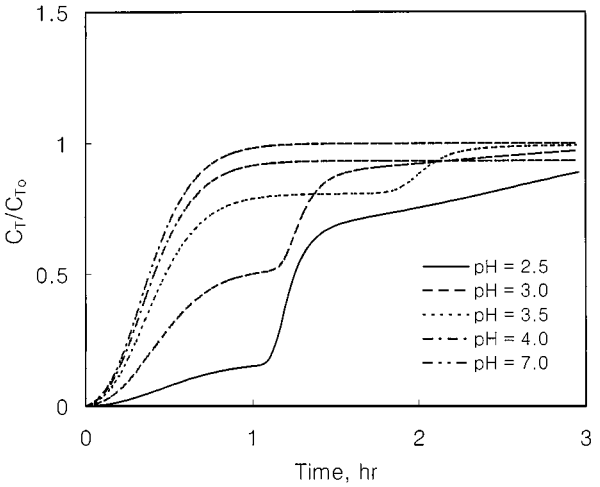

Figure 6. Effect of pH on adsorption breakthrough curves. (T = 25°C, C_{T0} = 40 mol/m^3, $\nu = 2.124 \times 10^{-4}$ m/s, and L = 0.145 m).

competitive effect. By correlating adsorption equilibrium data, C_T versus q_T, with the Langmuir equation, the determined Langmuir parameters, q_m and b, are 1.093 and 0.021, respectively. The predicted curve with

Table 6. Experimental conditions for fixed-bed adsorption.

Variables	Range	Unit
Bed length (L)	0.145	m
Bed diameter (D)	0.02	m
Flow rate (ν)	$0.50–2.12 \times 10^{-4}$	m/s
Bed porosity (ε_b)	0.37	—
Packing density (ρ_b)	290	kg/m^3
Temperature (T)	25	°C
pH	2.5–8.0	—
Cephalosporin C conc.	1–80	mol/m^3

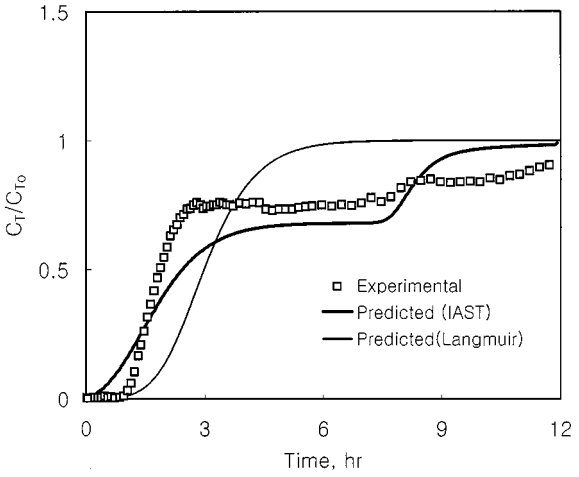

Figure 7. Adsorption breakthrough curves on SP850 at pH = 3.40. ($T = 25$°C, $C_{T0} = 30$ mol/m^3, $\nu = 0.531 \times 10^{-4}$ m/s, and $L = 0.145$ m).

a corresponding isotherm without introducing the competitive effect is in poor agreement with the experimental result. However, more precise prediction can be achieved with introducing the competitive effect, that is, IAST. This result implies that peculiar behavior can not simulated without considering competitive effect proposed in this work.

Various experimental conditions are listed in Table 6. The parameters for the negatively charged form determined from the previous section were used in these calculations without further adjustment. Figures 8 and 9 show that the theoretical curves are in good agreement with experimental results except at low pH by introducing the competitive adsorption effect. In particular, the deviation between experimental and predicted elution curves may be due to the use of kinetic parameters for negatively charged cephalosporin C at pH of around 5.0 regardless of its ionic from. The kinetic parameters of positively charged and neutral forms can not be obtained independently because they exist as an admixture shown in Fig. 4. If we determine the kinetic parameters for each ionic form, the experimental breakthrough curve can be predicted very accurately. Further works on determination of mass transfer coefficient in terms of solution pH will be continued systematically.

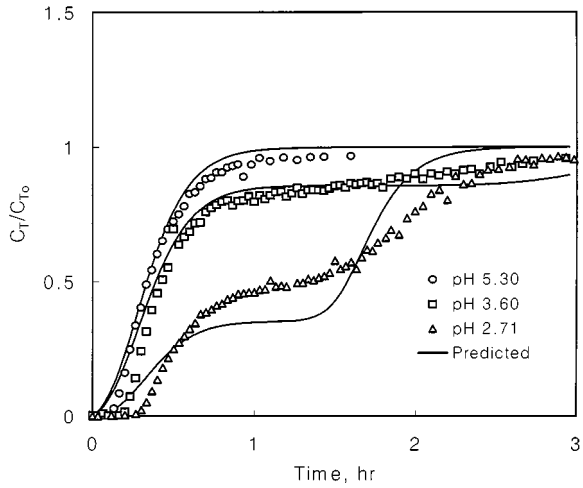

Figure 8. Effect of pH on breakthrough curves of cephalosporin C on SP850. ($T = 25$°C, $C_{T0} = 40$ mol/m^3, $\nu = 2.124 \times 10^{-4}$ m/s, and $L = 0.145$ m).

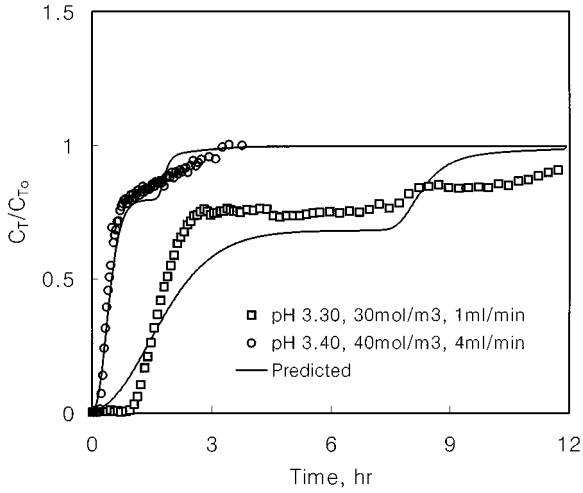

Figure 9. Effect of pH on breakthrough curve of cephalosporin C on SP850. ($T = 25$°C and $L = 0.145$ m).

Concluding Remarks

For the recovery of cephalosporin C from aqueous solutions, the effect of pH on the adsorption of

cephalosporin C was studied in a column charged with a nonionic polymeric sorbent, SP850. Since cephalosporin C can exist as cationic, neutral, or anionic forms depending on the solution pH, the single-solute isotherms of each form were obtained simultaneously from all equilibrium data measured at different values of pH. The fractions of each ionic form were calculated from the association-dissociation equilibrium relation with pK values of cephalosporin C. It was also assumed that the mutual interaction between ionic forms can be expressed by a competitive adsorption model, namely IAST. Single-species isotherms for each ionic form were simply expressed by the Langmuir equation.

The adsorption capacity of SP850 for cephalosporin C decreased considerably with the solution pH. This implies that the affinity to SP850 depends strongly on the type of ionic form. At low values of pH, the adsorption behavior was quite different from that of a usual single-component system, showing the breakthrough curve with multiple plateaus which has been considered as a typical for multicomponent systems. That peculiar behavior was simulated by the method proposed in this work. Though there are somewhat deviations between experimental and simulated breakthrough curves, it was proven that the method for the treatment of different ionic forms will be very useful in predicting the adsorption behavior, especially at low values of pH which is a typical condition for separating of cephalosporin C from aqueous solutions or broths. It is also noted that the adsorption characteristics in a cyclic operation was also strongly dependent on the kinetic parameters. Therefore, more accurate values of the kinetic parameters should be required to simulate the dynamic behavior well.

At present, further works to separate cephalosporin C directly from its fermentation broths are being carried out continuously, based on a cyclic operation. The method used in this work will be assessed also for practical problems in near future.

Nomenclature

A Adsorption surface area per unit mass of adsorbent, m^2
b Langmuir constant, m^3/mol
C Concentration in the fluid phase, mol/m^3
C_T Total concentration in the fluid phase, mol/m^3
D_L Axial dispersion coefficient, m^2/s
D_m Molecular diffusion coefficient, m^2/s
D_s Surface diffusion coefficient, m^2/s
E Percent error, %
k_f Film mass transfer coefficient, m/s
K Dissociation constant
L Bed length, m
N Number of data point
q Concentration in particle phase, mol/kg
q_m Langmuir constant, mol/kg
q_T Total concentration in particle phase, mol/kg
r Radial distance, m
R Particle radius, m
Re Reynolds number
Sc Schmidt number
t Time, s or h
T Temperature or total, °C
x Mole fraction in adsorbed phase
z Axial distance or mole fraction, m

Greek Letters

ε_b Bed porosity
Π Reduced spreading pressure
ρ_p Particle density, kg/m^3
ν Interstitial velocity, m/s

Acknowledgments

This research was supported by Korean Science and Engineering Foundation under Grant No. 941-1100-027-2. The authors gratefully acknowledge the effort of Cheil Food & Chemicals Inc. for supplying cephalosporin C.

References

Arnold, B.H., R.A. Fildes, and D.A. Gilbert, Ger. Pat. 1, 939, 341 (1969).

Chaubal, M.V., G.F. Payne, C.H. Reynolds, and R.L. Albright, "Equilibria for the Adsorption of Antibiotics onto Neutral Polymeric Sorbents: Experimental and Modeling Studies," *Biotech. and Bioeng.*, **47**, 215–226 (1995).

Costa, C. and A.E. Rodriques, "Design of Cyclic Fixed-Bed Adsorption Processes," *AIChE J.*, **31**(10), 1645–1654 (1985).

Elander, R.P. and H. Aoki, *β-Lactam-Producing Microorganisms*: *Their Biology and Fermentation Behavior, in Chemistry and Biology of β-Lactam Antibiotics*, Vol. 3, pp. 83–153, Academic Press, 1982.

Lee, J.W., H.C. Park, and H. Moon, "Adsorption and Desorption of Cephalosporin C on Nonionic Polymeric Sorbents," *Sep. & Purif. Technol.*, **12**(1), 1–11 (1997).

Myers, A.L. and J.M. Prausnitz, "Thermodynamics of Mixed-Gas Adsorption," *AIChE J.*, **11**(1), 121–127 (1965).

Nara, K., K. Ohta, K. Katamoto, N. Mizokami, and H. Fukuda, Method for Separating Cephalosporin C. US Pat. 3, 926, 973 (1975).

Reid, R.C., J.M. Prausnitz, and B.E. Poling, *The Properties of Gases and Liquids*, 4th edition, MaGraw-Hill Co., New York, 1994.

Ruthven, D.M., *Principles of Adsorption and Adsorption Precesses*, John Wiley and Sons, New York, 1984.

Stables, H.C. and K. Briggs, Ger. Pat. 2, 852, 596 (1978).

Tien, C., *Adsorption Calculations and Modeling*, Butterworth-Heinemann, Boston, 1994.

Villadsen, J.V. and W.E. Stewart, "Solution of Boundary-Value Problems by Orthogonal Collocation," *Chem. Eng. Sci.*, **22**, 1483 (1967).

Villadsen, J. and M.L. Michelsen, *Solution of Differential Equation Models by Polynomial Approximation*, Prentice-Hall, Englewood Cliffs, 1978.

Voser, W., "Isolation of Hydrophilic Fermentation Products by Adsorption Chromatography," *J. Chem. Technol. Biotechnol.*, **32**, 109 (1982).

Wakao, N. and T. Funazkri, "Effect of Fluid Dispersion Coefficients on Particle to Fluid Mass Transfer Coefficients in Packed Beds," *Chem. Eng. Sci.*, **33**, 1375–1384 (1978).

Yang, W.Y., C.D. Lin, I.M. Chu, and C.J. Lee, "Extraction of Cephalosporin C from Whole Broth and Separation of Desacetyl Cephalosporin C by Aqueous Two-Phase Partition," *Biotech. and Bioeng.*, **43**, 439–445 (1994).