

수소결합 수용체 용매계에서 페니실린 G의 추출평형 모델 연구

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**A study on equilibrium model for physical and reactive extraction of penicillin G
 in hydrogen-bond acceptor solvent system**

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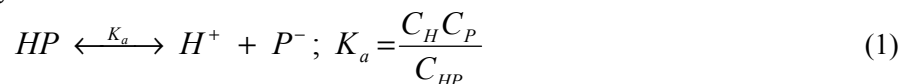
서론

For all that the amount of physically extracted penicillin G may stand comparison with that of reactively extracted penicillin G in the reactive extraction systems, its physical equilibrium has been simply expressed by partition of undissociated penicillin acid from aqueous phase to organic phase. The partition principle represents that the degree of extraction of penicillin G in physical extraction systems depends only on the partition coefficient between the two phases and pH of the aqueous phase [1,2]. Reschke and Schügerl [1] used the partition principle to explain their physical extraction system with n-butyl acetate where a few physical extraction equilibrium data were obtained. Lee and Lee [2] investigated physical extraction of penicillin G using n-butyl acetate at various volume ratios between aqueous and organic phases. The simple partition principle seemed to effectively explain their physical equilibrium data only within a low and narrow concentration range of penicillin G.

In this work, therefore, we will not only investigate justification of the partition principle which has been used to explain physical extraction of penicillin G by the hydrogen-bond acceptor solvent, but also find a physical equilibrium expression which is useful in physical and reactive extraction systems with the wide ranges of aqueous pH, extractant concentration, and penicillin G concentration. For this, we will present several equilibrium models for physical extraction of penicillin G using the hydrogen-bond donor solvent, and finally analyze a reactive extraction system of penicillin G with the hydrogen-bond acceptor solvent experimentally and theoretically.

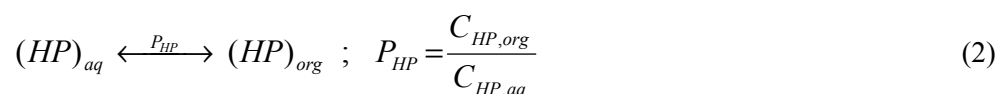
이론

Penicillin G (HP) is a monocarboxylic and weak acid ($pK_a=2.75$). Its dissociation in an aqueous solution is expressed by



In this work, the undissociated penicillin acid was physically transported into the organic phase of n-butyl acetate. Here we suggested two equilibrium models for the physical extraction of penicillin G.

Model 1: Reschke and Schügerl [3] introduced the following equilibrium model for physical extraction of penicillin G:



where P_{HP} is the partition coefficient. The overall material balance of penicillin G is written by

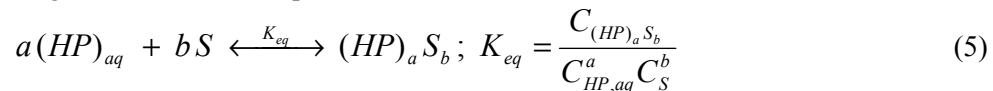
$$C_{PG} = C_P + C_{HP,aq} + C_{HP,org} \quad (3)$$

where C_{PG} is the overall penicillin G concentration. The degree of extraction (E) is written as follows:

$$E = \left(\frac{C_{PG} - \beta C_{HP, aq}}{C_{PG}} \right) \times 100 = \frac{100}{1 + \beta / P_{HP}} \quad (4)$$

with $\beta = 1 + 10^{pH - pK_a}$. As in their previous works [1,3], P_{HP} was considered as a constant value, independent of overall penicillin concentration and pH.

Model 2: Actually, the degree of extraction depended on overall penicillin concentration as well as pH in the current physical extraction system. Thus we could present a more general equilibrium expression including solute-solvent complexation as follows:



The overall material balance of penicillin G is given by

$$C_{PG} = C_P + C_{HP, aq} + a C_{(HP)_a S_b} \quad (6)$$

Also, the degree of extraction is represented by

$$E = \frac{K_{eq} a C_{HP, aq}^a C_S^b}{C_{PG}} \times 100 \quad (7)$$

실험

The investigations conducted were of extraction equilibrium in a shaker. Pure n-butyl acetate was used as the organic solution for the physical extraction of penicillin G. For an examination of the effect of n-butyl acetate concentration on the physical extraction, an organic solvent mixture at a wide concentration range was prepared using kerosene as an inert organic solvent.

The organic solution in the reactive extraction experiments was also prepared by dissolving 2~20 mmol/dm³ of Amberlite LA-2 in n-butyl acetate. 0.408 mol/dm³ of citrate buffer solution was prepared at pH 4.8~6.2, and 5~110 mmol/dm³ of penicillin G potassium salt was dissolved in the buffer solutions. Equal volumes (30cm³) of the prepared organic and aqueous solutions in a 250-mL flask were vigorously shaken at 25°C for about one hour, and the concentration of penicillin G in the aqueous phase was measured by UV spectrophotometer at 258nm after separation of the two immiscible phases.

결과 및 토론

We found some equilibrium values by fitting the experimental data for the physical extraction into each equilibrium model. The mean deviation (φ) between experimental data ($E_{exp,i}$) and calculated results ($E_{cal,i}$) for the degree of physical extraction is defined by

$$\varphi = \sum_1^N \sqrt{(1 - E_{cal,i} / E_{exp,i})^2} / N \quad (8)$$

IMSL subroutine BCLSF was used to minimize the mean deviation, and the optimized equilibrium values of each model are described in Table 1.

Figure 1 shows the effect of overall penicillin G concentration on the degree of physical extraction at several pH values. The calculated results from Model 1 were plotted on the figure for comparison with the experimental data. While the calculated degree of extraction from the model was dependent only on pH, the measured degree of extraction decreased with an increase in the overall penicillin concentration at a given pH. Although several researchers [1,2,4] introduced Model 1 to analysis of reactive extraction using n-butyl acetate, the large deviation in Table 1 and the overall penicillin concentration-dependent extraction behavior did not support justification of Model 1.

Table 1. Mean deviation between experimental data and calculated results for degree of physical extraction and optimized equilibrium constants.

Model No.	deviation(%)	Equilibrium constant
Model 1	34.7	$P_{HP} = 86.6$
Model 4	16.5	$K_{eq} = 1.860 \times 10^{-2} (\text{dm}^3/\text{mol})^{2.24}$, $a = 0.61$, $b = 2.63$

The calculated degrees of extraction from Model 2 were compared with the experimental data from the physical extraction of penicillin using the FORTRAN subroutine BCLSF in order to find the most reasonable stoichiometric coefficients a and b . The optimized values are described in Table 1. The lowest mean deviation was obtained with Model 2, and a change in degree of extraction with the overall penicillin concentration was well reflected on eq. 7. As shown in Figure 2, the solid lines calculated from Model 2 also represent the dependence of overall penicillin concentration on degree of physical extraction.

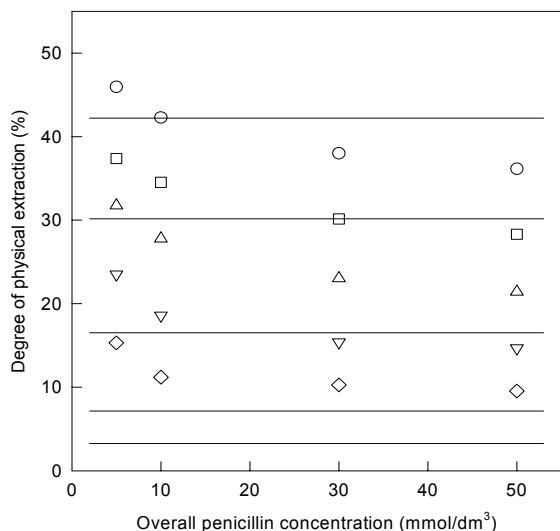


Fig. 1. Comparison of experimental data with calculated results from Model 1 for degree of physical extraction as a function of overall penicillin G concentration at different pH values. (O: 4.8, □: 5.1, Δ: 5.4, ▽: 5.8, ◇: 6.2; —: calculated results)

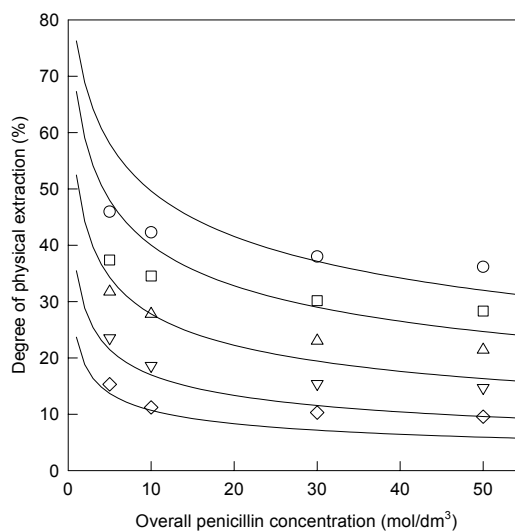
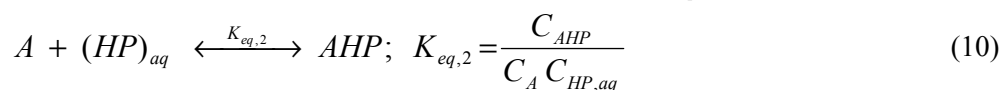
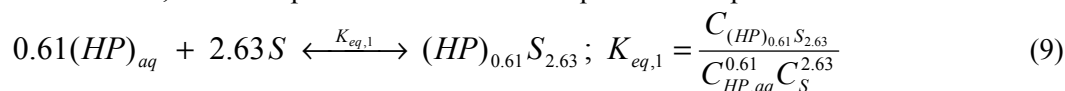


Fig. 2. Comparison of experimental data with calculated results from Model 4 for degree of physical extraction as a function of overall penicillin G concentration at different pH values. (O: 4.8, □: 5.1, Δ: 5.4, ▽: 5.8, ◇: 6.2; —: calculated results)

In many reactive extraction systems [1,2,4] where the organic solution was n-butyl acetate containing Amberlite LA-2 as a secondary amine, it has been known that one mole of undissociated penicillin acid reacts with one mole of Amberlite LA-2 to form one mole of penicillin-Amberlite LA-2 complex (AHP). Figure 3 shows the transport mechanism of penicillin G in the current reactive extraction system with Amberlite LA-2 in n-butyl acetate, where we introduced the chemical equilibrium. Therefore, we could present two extraction equilibrium expressions as follows:



The overall material balances of penicillin G and amine are written by

$$C_{PG} = C_P + C_{HP,aq} + 0.61C_{(HP)_{0.61S_{2.63}}} + C_{AHP} \quad (11)$$

$$C_{AG} = C_A + C_{AHP} \quad (12)$$

where C_{AG} is the overall amine concentration. The two equations for $C_{HP,aq}$ and C_A , i.e. eqs 11 and 12, were solved with the help of IMSL subroutine BCLSF, and the degree of extraction is given by

$$E = \frac{0.61K_{eq,1}C_{HP,aq}^{0.61}C_S^{2.63} + K_{eq,2}C_A C_{HP,aq}}{C_{PG}} \times 100 \quad (13)$$

The calculated results from eq 13 were compared with the experimental data for the degree of reactive extraction of penicillin G so as to optimize a sole unknown variable ($K_{eq,2}$). The optimized value of $K_{eq,2}$ ($2.325 \times 10^5 \text{ dm}^3/\text{mol}$) gave a good fit to the experimental data with an absolute mean deviation of 11.2%. Figure 4 shows the effect of pH of the aqueous phase on the reactive extraction of penicillin G. The degree of extraction was higher at lower pH of the aqueous phase under the same overall penicillin G concentration. This is because the position of equilibria moves to the right of eqs 9 and 10 according to Le Chatelier's principle when the concentration of undissociated penicillin acid increases with the decrease in pH.

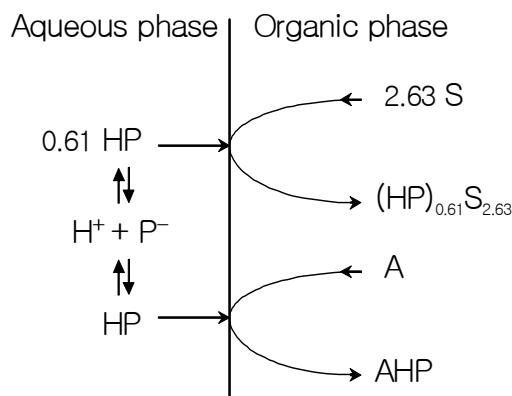


Fig. 3. Schematic diagram of reactive extraction system of penicillin G.

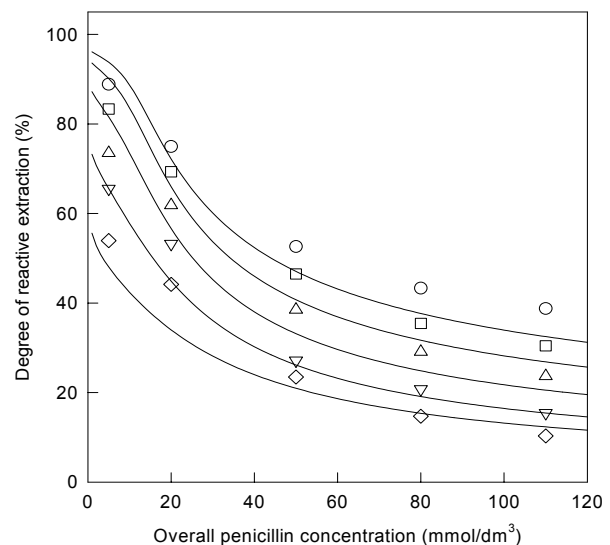


Fig. 4. Comparison of experimental data with calculated results for degree of reactive extraction as a function of overall penicillin G concentration at different pH values. (C_{AG} : 10 mmol/dm³; O: 4.8, □: 5.1, Δ: 5.4, ▽: 5.8, ◇: 6.2; —: calculated results)

참고문헌

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