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Divalent Amino Acid Adsorption on Cation Exchange Resin

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Abstract: Mass transport of divalent amino acids, arginine and histidine, was investigated in an ion exchange system using DIAION SK104, SK1BL, and SK112. Ion exchange equilibrium constants of arginine were 5.0 g/cm^3 for SK104 (4 wt% D.V.B.), 25.0 g/cm^3 for SK1BL (8 wt% D.V.B.) and 25.0 g/cm^3 for SK112 (12 wt% D.V.B.). The ion exchange equilibrium constant of histidine was 8.0 g/cm^3 for SK1BL (8 wt% D.V.B.). Resin phase diffusivities of divalent amino acids are measured by batch uptake experiments. Resin phase diffusivities of divalent arginine were decreased from 9.0×10^{-8} cm^2/s to 1.6×10^{-8} cm^2/s while the D.V.B. content in resin increases from 4 wt% to 12 wt%. Resin phase diffusivity of histidine for 8 wt% D.V.B. resin was 7.0×10^{-8} cm^2/s. The steric hindrance model was able to describe measured resin phase diffusivities.

Keywords: Amino acids, intraparticle diffusivity, ion exchange, mass transfer

INTRODUCTION

Ion exchange plays a central role in the industrial production of amino acids. In most cases, ion exchange is used for the removal of inorganic salt in fermentation medium or undesired counter ion (1). Amino acids are amphoteric and can be positively charged, neutral, or negatively

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charged depending on the solution pH. As a result, amino acids that are bound to a cation exchange resin at low pH and can be desorbed by raising pH to a value where the amino acid becomes negatively charged. Thus, ion exchange processes in the manufacture of amino acids require the complicated column operation and system. Rational design and optimization of such ion exchange processes require the knowledge of both the ion exchange equilibrium, which determines the maximum resin loading capacity, and the ion exchange kinetics, which determines the dynamic binding capacity as a function of the flow rate as well as the time and the amount of the desorbent required for elution. As a result, a quantitative understanding of these two factors is critical.

Many researchers have dealt with this mass transport of amino acids in the system of ion exchange and have reported ion exchange equilibria and kinetics. However, these data are limited to the monovalent amino acids because there are few amino acids having divalent residues in those molecules. In practical application, sometimes we are faced with the necessity of the estimation of divalent impurities. For example, cadaverine can behave as a divalent molecule because of its two amino residues.

For monovalent amino acids, Jones et al. measured ion exchange equilibrium constants and resin phase diffusivities of 4 amino acids and 2 dipeptides with the resins containing various D.V.B. contents (2). For the resin phase diffusivities, they established the steric hindrance model, which is based on the model developed by Kataoka et al. (3) correlating the ratio of the resin phase diffusivity to the solution phase diffusivity for inorganic cations in cross-linked ion exchange resins.

However, for divalent amino acids, there is insufficient data for the estimation of resin phase diffusivities. In our previous work (4), we investigated the ion exchange equilibrium and kinetics for lysine. As a result, the resin phase diffusivity of divalent lysine was $4.0 \times 10^{-8}\,cm^2/s$ while the resin phase diffusivity of monovalent lysine was determined to be $16 \times 10^{-8}\,cm^2/s$. This shows that the relationship of the steric hindrance model for monovalent amio acids cannot be directly used for the divalent amino acids, because the resin phase diffusivity of divalent lysine was extremely small.

The objective for this work is the investigation of ion exchange equilibrium and kinetics for arginine and histidine as representative divalent amino acids. Furthermore, the correlation of those diffusivities will be attempted.

MATERIALS AND METHODS

The resins used in this work are DIAION SK104, DIAION SK-1BL, and DIAION SK112 (Mitsubishi Chemical Co., Tokyo, Japan). These resins

Table 1. Resin properties of DIAION SK104, DIAION SK1BL and DIAION SK112

	DIAION SK104	DIAION SK1BL	DIAION SK112
D.V.B. content	4%	8%	12%
Mean particle diameter	596 μm	646 μm	654 μm
Capacity	4.8 meq/g-Dry H-form Resin	4.2 meq/g-Dry H-form Resin	4.3 meq/g-Dry H-form Resin
Dry weight of the resin in H-form	42.28%	55.62%	68.33%

are typical gel-type poly (styrene-divinylbenzene) cation exchanger with sulfonic acid functional groups. The characteristics of these resins are summarized in Table 1. The nominal D.V.B. contents of SK104, SK-1BL, and SK112 are 4%, 8%, and 12%, respectively. The mean particle diameters of the hydrogen form resins are determined from microphotographs. The dry weights of the resins in H-form are measured by drying loss method at 120°C. The total ion exchange capacities of the resins are determined by the trial and error method using the measurement of isotherms. L-Arginine HCl, L-Histidine HCl, and L-Lys HCl were obtained from Ajinomoto Co., Inc. (Raleigh, NC).

Ion dissociation constants for arginine and histidine reported by Nagai et al. (5) were used in this study. Ion exchange equilibria were determined by a batch method as described in Nagai and Carta (4). Since we focus on the divalent amino acid equilibrium, solutions containing amino acid were prepared with constant concentrations of chloride ion (0.6 M) using stock solutions of amino acid hydrochloride and hydrochloric acid (HCl). Aliquots of these solutions (10 cm^3) were then added to test tubes containing various amounts of wet H-form resin. The tubes were rotated for 24 hours, which was sufficient to reach equilibrium as indicated by batch experiments where the solution concentrations were monitored as a function of time. Temperatures were set at 25°C with a thermostatic water bath. The amount of divalent amino acid adsorbed by the resin was calculated from the residual composition of the solution phase using a material balance.

HPLC was used to determine the concentrations of ammonia and lysine using a DKK-TOA Co. (Tokyo, Japan) PCI-322 column (4.6 mm I.D. × 250 mm) using a 6 mM aqueous solution of methanesulfonic acid (Wako Junyaku Chemicals, Osaka, Japan) as the mobile phase, and detection with a Model ICA-2000 conductivity detector from DKK-TOA Co. (Tokyo, Japan). The injection sample size was 50 μl.

Ion exchange rates were measured in a 100 cm^3 thermostatted glass vessel at 25°C as discussed in Nagai and Carta (4). The vessel is agitated

at 300 rpm with a magnetically driven Teflon impeller. Samples of amino acid solutions containing hydrochloride were added to the vessel and allowed to reach thermal equilibrium. Resin samples were then quickly added and the course of the exchange process monitored by taking $0.5\,cm^3$ samples and analyzing them by HPLC.

THEORY

Ion Exchange Equilibria and Kinetics

In general, ion exchange equilibria can be described by the mass action law, using empirically determined equilibrium constants (6). For the case of arginine we have:

$$K_{Arg^{2+},H^+} = \frac{q_{Arg^{2+}} C_{H^+}^2}{q_{H^+}^2 C_{Arg^{2+}}} \tag{1}$$

where q_i is the resin concentration of i species and C_i is the solution phase concentration of i species. The kinetics of ion exchange of amino acids is generally controlled by diffusion in the resin phase (6–9). Batch adsorption experiments were used to determine the relevant diffusion coefficients at different temperatures. Diffusional mass transfer within ion exchange particles can be described in terms of the Nernst-Planck equation. The complete set of equations is given in Nagai and Carta (4) and only a brief summary is presented here. The following equations and boundary conditions are written for the case of arginine:

For the resin beads:

$$\frac{\partial q_{Arg^{2+}}}{\partial t} = -\frac{1}{r^2}\frac{\partial}{\partial r}[r^2(J_{Arg^{2+}})] \tag{2}$$

$$r = 0, \quad \frac{\partial q_{Arg^{2+}}}{\partial r} = 0 \tag{3}$$

$$r = r_p, \quad q_{Arg^{2+}} = q^*_{Arg^{2+}} \tag{4}$$

$$t = 0, \quad q_{Arg^{2+}} = q^0_{Arg^{2+}} \tag{5}$$

For the solution:

$$\frac{d\bar{q}_{Arg^{2+}}}{dt} = -\frac{V}{M_r}\frac{dC_{Arg^{2+}}}{dt} = \frac{3}{r_p}(J_{Arg^{2+}})_{|r=r_p} \tag{6}$$

$$t = 0, \quad C_{Arg^{2+}} = C^0_{Arg^{2+}} \tag{7}$$

In these equations, r_p is the particle radius, q_i^* is the equilibrium resin composition, q_i^0 is the initial resin composition, M_r is the mass of resin, V is the solution volume, and C_A^0 is the initial arginine solution concentration. Equations (2–7) are complied with the equation below.

$$q_0 = 2 \times q_{Arg^{2+}} + q_{H^+} \tag{8}$$

where q_0 is the maximum capacity of the resin. The mass transfer fluxes are given by:

$$J_i = -\frac{1}{z_i} \sum_j z_j D_{i,j} \frac{\partial q_j}{\partial r} \tag{9}$$

where z_i is the ion charge and, M is the number of counterions and:

$$D_{i,j} = -\frac{D_i(D_j - D_M) z_i^2 q_i}{\sum_{k=1}^{M} z_k^2 D_k q_k} \quad \text{for } i \neq j \tag{10}$$

$$D_{i,i} = D_i - \frac{D_i(D_i - D_M) z_i^2 q_i}{\sum_{k=1}^{M} z_k^2 D_k q_k} \quad \text{for } i = j \tag{11}$$

The resulting equations were solved numerically as discussed in Nagai and Carta (4).

RESULTS

Ion Exchange Equilibria

Ion exchange equilibrium data were obtained for the binaries Arg^{2+}/H^+ and His^{2+}/H^+ as shown in Figs. 1–4. Figures 1–3 show the results of arginine ion exchange equilibrium on SK104, SK1BL and SK112 resin, respectively. Figure 4 shows the result of histidine equilibrium on SK1BL. The equilibrium constants K_{Arg^{2+},H^+} and K_{His^{2+},H^+} were determined by fitting Eq. (1) to the data. The determined values with lysine equilibrium value reported in Nagai and Carta (4) are summarized in Table 2. For the Arg^{2+}/H^+ and His^{2+}/H^+ exchange equilibria, concentration-independent values of K_{Arg^{2+},H^+} and K_{His^{2+},H^+} provide good fits of the data (see Figs. 1–4).

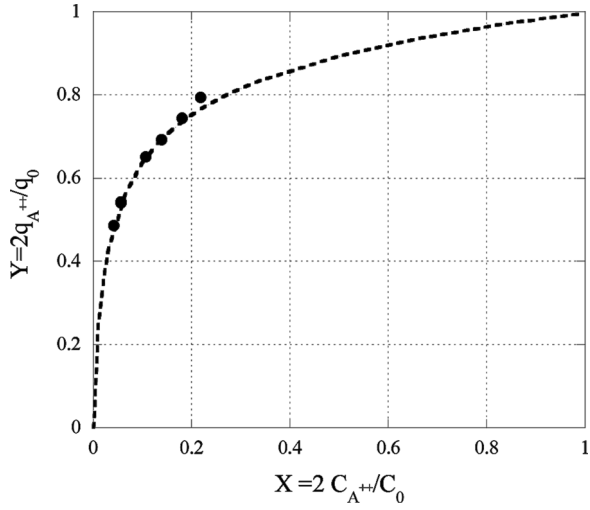

Figure 1. Arg^{2+}/H^{+} ion exchange equilibrium on DIAION SK104 resin at 0.6 M chloride concentrations. Dotted line is calculated by $K_{Arg^{2+}/H^{+}} = 5.0\,g/cm^3$ and $q_0 = 4.8\,meq/g\text{-Dry H-form resin}$.

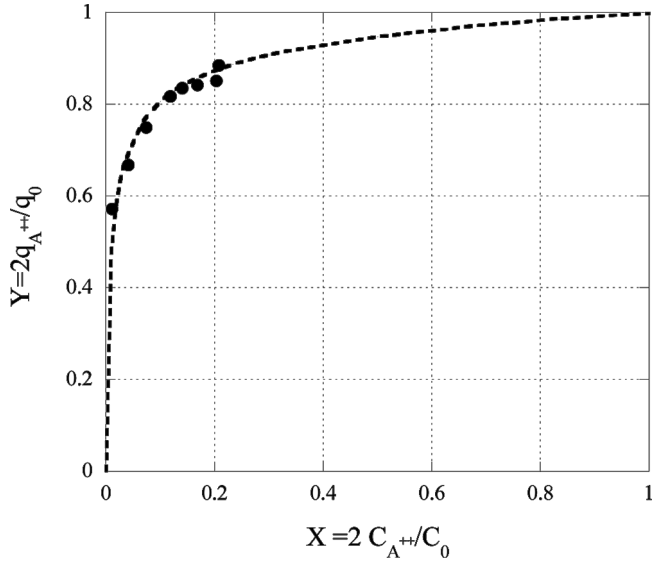

Figure 2. Arg^{2+}/H^{+} ion exchange equilibrium on DIAION SK1BL resin at 0.6 M chloride concentrations. Dotted line is calculated by $K_{Arg^{2+}/H^{+}} = 25.0\,g/cm^3$ and $q_0 = 4.2\,meq/g\text{-Dry H-form resin}$.

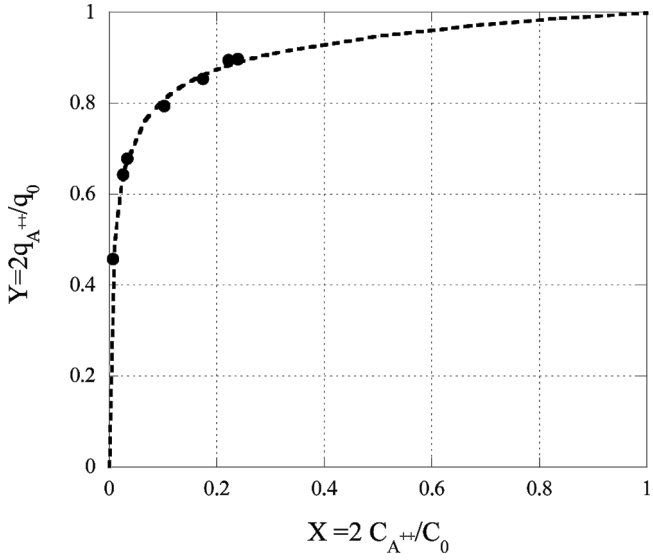

Figure 3. Arg^{2+}/H^{+} ion exchange equilibrium on DIAION SK112 resin at 0.6 M chloride concentrations. Dotted line is calculated by $K_{Arg^{2+}/H^{+}} = 25.0\,g/cm^3$ and $q_0 = 4.3\,meq/g\text{-Dry H-form resin}$.

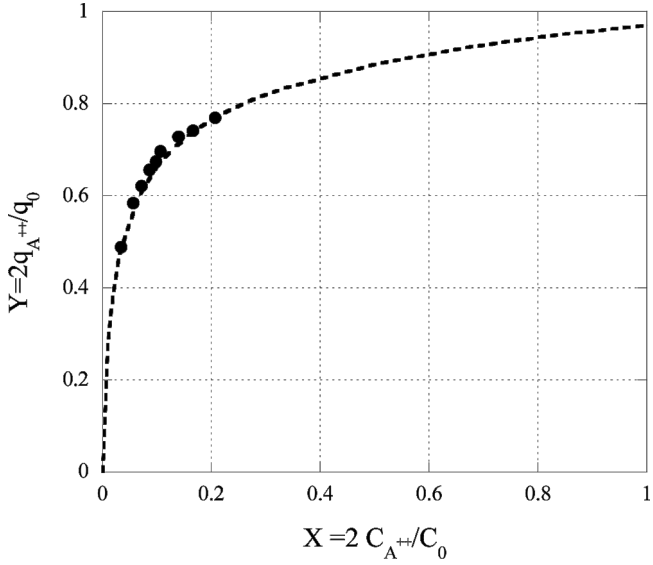

Figure 4. His^{2+}/H^{+} ion exchange equilibrium on DIAION SK1BL resin at 0.6 M chloride concentrations. Dotted line is calculated by $K_{His^{2+}/H^{+}} = 8.0\,g/cm^3$ and $q_0 = 4.2\,meq/g\text{-Dry H-form resin}$.

Table 2. Ion exchange equilibrium constants for arginine, histidine and lysine

	K_{Arg^{2+}/H^+}	K_{His^{2+}/H^+}	K_{Lys^{2+}/H^+}
DIAION SK1104	5.0 g/cm^3		
DIAION SK1BL	25.0 g/cm^3	8.0 g/cm^3	6.0 g/cm^3
DIAION SK112	25.0 g/cm^3		

Resin Phase Diffusivities

Batch ion exchange kinetics data were obtained for the binaries Arg^{2+}/H^+ as shown in Figs. 5–7. Figure 5 is for the case of SK104, Fig. 6 is for the case of SK1BL, and Fig. 7 is for the case of SK112 at 25°C. It can be seen that the kinetics is the fastest for the case of SK104 and the slowest for the case of SK112. As discussed in the Theory section, the mass transfer fluxes are electrically coupled. Thus, individual ion diffusivities were determined by fitting model calculations based on Eqs. (1–10) to the data. The diffusivity of hydrogen ion in 8% crosslinked resins, D_{H^+}, is available at 25°C (10). Thus, $D_{Arg^{2+}}$ can be obtained by fitting the model to the data in Figs. 5–7. For histidine, we conducted batch ion exchange experiments for the case of SK1BL as shown in Fig. 8.

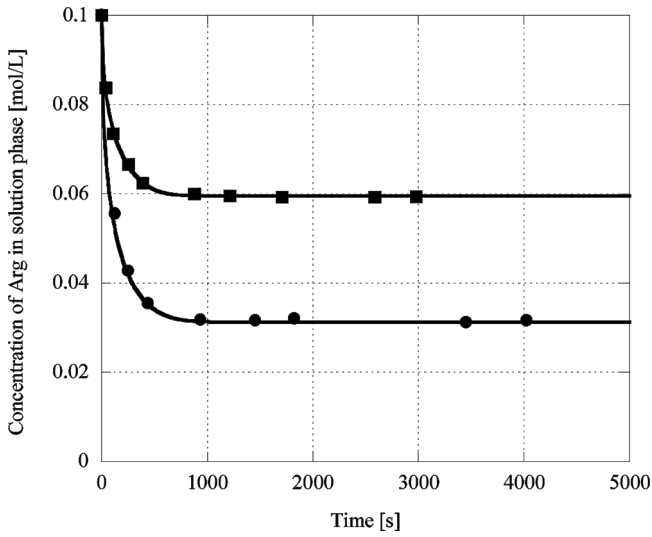

Figure 5. Batch uptake of Arg^{2+} by H^+ form DIAION SK104 with $C_A^0 = 0.10$ M, $C_{Cl^-} = 0.60$ M at 25°C. Lines are calculated by Nernst-Plank model. Symbols: Total arginine (■) at $M_r = 2.1$ g, total arginine (●) at $M_r = 4.0$ g.

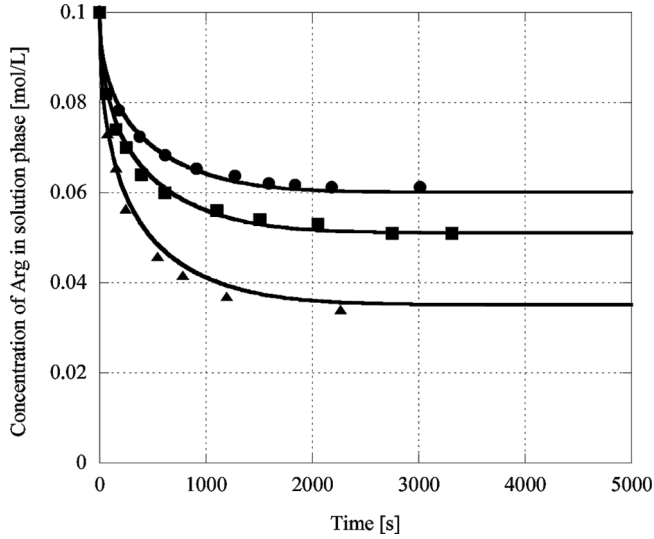

Figure 6. Batch uptake of Arg^{2+} by H^+ form DIAION SK1BL with $C_A^0 = 0.10\,M$, $C_{Cl^-} = 0.60\,M$ at 25°C. Lines are calculated by Nernst-Plank model. Symbols: Total arginine (●) at $M_r = 2.9\,g$, total arginine (■) at $M_r = 3.6\,g$ and total arginine (▲) at $M_r = 5.4\,g$.

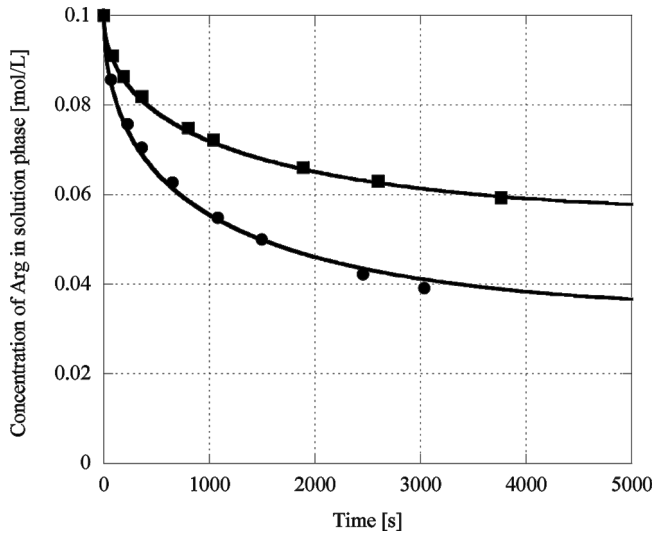

Figure 7. Batch uptake of Arg^{2+} by H^+ form DIAION SK112 with $C_A^0 = 0.10\,M$, $C_{Cl^-} = 0.60\,M$ at 25°C. Lines are calculated by Nernst-Plank model. Symbols: Total arginine (■) at $M_r = 3.1\,g$, total arginine (●) at $M_r = 5.1\,g$.

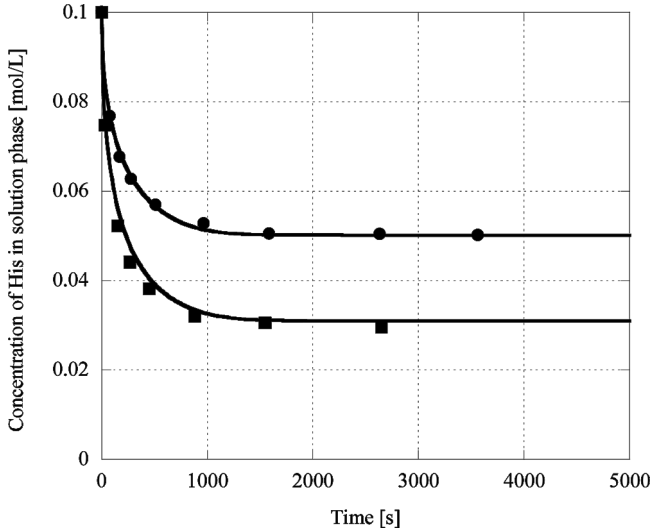

Figure 8. Batch uptake of His^{2+} by H^+ form DIAION SK1BL with $C_A^0 = 0.10\,M$, $C_{Cl^-} = 0.60\,M$ at 25°C. Lines are calculated by Nernst-Plank model. Symbols: Total arginine (■) at $M_r = 3.2\,g$, total arginine (●) at $M_r = 5.0\,g$.

A summary of the diffusivities of divalent amino acids is given in Table 3. Also, we included the ratio of measured intraparticle diffusivities to solution phase diffusivities estimated by the Wilke-Chang equation (11). For the estimation of solution phase diffusivities, Le Bas Volume was picked as Molar Volume. Le Bas volume of divalent arginine, histidine, and lysine are calculated as 221, 180, and 193, respectively.

For the resin phase dffusivities of inorganic ions, Kataoka et al. (3) developed the experimental model as the following:

$$\frac{D_i}{D_i^0} = a_i \exp(-k_i x_i') \tag{12}$$

where a_i and k_i are constants characteristics of solute. x_i' is a modified degree of cross-linking defined as:

$$x_i' = \frac{\overline{V}_{\mathrm{H}}^W}{\overline{V}_{\mathrm{i}}} x \tag{13}$$

where x is the degree of cross-linking of the resin (wt% D.V.B.), $\overline{V}_H^W$ is the specific volume of the hydrogen form of the resin in water, and $\overline{V}_i$ is the specific volume of the i form of the resin in a given solution.

Table 3. Resin phase diffusivities for divalent arginine, histidine and lysine. D_i: Resin phase diffusivities, D_i^0: Solution phase diffusivities estimated from Wilke-Chang equation. D_{H^+}: Resin phase diffusivities for hydrogen ion estimated by the method of Kataoka et al. (1995)

Resin Degree of cross-linking		SK104 4%	DIAION SK1BL 8%	DIAION SK112 12%
D_{H^+}	[cm^2/s]	2.4×10^{-5}	1.2×10^{-5}	0.6×10^{-5}
$D_{Arg^{2+}}$	[cm^2/s]	9.0×10^{-8}	5.0×10^{-8}	1.6×10^{-8}
$D_{Arg^{2+}}/D^0_{Arg^{2+}}$	[–]	0.016	0.0085	0.0028
$D_{His^{2+}}$	[cm^2/s]	–	7.0×10^{-8}	–
$D_{His^{2+}}/D^0_{His^{2+}}$	[–]	–	0.010	–
$D_{Lys^{2+}}$	[cm^2/s]	–	4.0×10^{-8}	–
$D_{Lys^{2+}}/D^0_{Lys^{2+}}$	[–]	–	0.0062	–

The coefficient a_i shows the deviation of the diffusivity ratio D_i/D_i^0 when the crosslinking degree is zero. k_i is the proportionality constant.

For monovalent amino acids, Carta et al. organized resin-phase diffusivities by using the steric hindrance model (12). This model is based on the model developed by Kataoka et al. They assumed that the size of the solvated species should not be very different from that of the unhydrated ones. Further, if steric hindrance in the cross-linked resin mesh is the dominant factor, it is reasonable to assume that the proportionality constant is dependent on the cube root of the molar volume of the diffusing counterion. However, their model is based on the sodium ion because they used sodium ion as a reference ion. We plotted their equation on the plane of $(V_i)^{0.33}x$ vs. D_i/D_i^0 in order to compare with our equation as shown in Fig. 9. The steric hindrance model reported by Carta et al. (12) can be converted into:

$$\frac{Di}{D_i^0} = \exp[-0.0916(V_i)^{0.33}x] \tag{14}$$

where V_i is the Le Bas volume of the amino acid.

In our case, the determined resin phase diffusivities were plotted on the same plane and we could obtain the similar relationship for divalent amino acids:

$$\frac{Di}{D_i^0} = 0.042 \times \exp[-0.037(V_i)^{0.33}x] \tag{15}$$

Interestingly, the value of a_i is not unity. Therefore, the resin phase diffusivities for divalent amino acid might be strongly affected by the

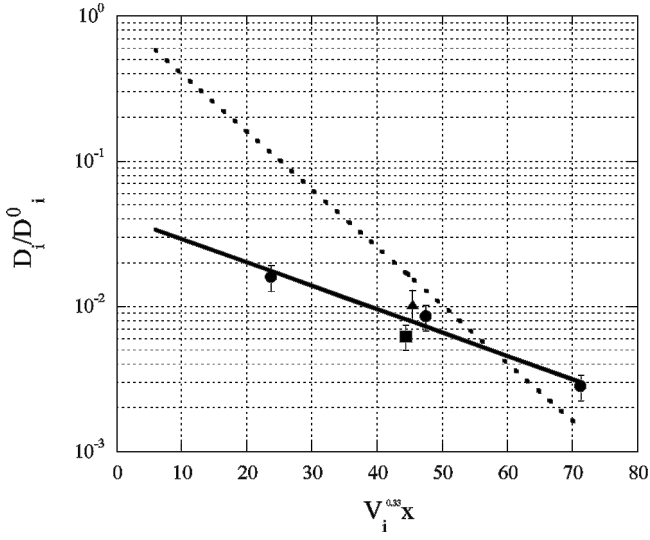

Figure 9. Comparison of experimental reduced diffusivity values for divalent amino acids, arginine, histidine and lysine with the steric hindrance model. Symbols are ratios of resin phase diffusivities to solution phase diffusivities, arginine (●), lysine (■) and histidine (▲). Dotted line shows the equation reported by Carta et al.

electrostatic effect. Also, the steric hindrance index was −0.037, which is larger than the slope of the monovalent amino acid equation. Kataoka et al. mentioned that the proportionality constant is proportional to the net charge of the diffusing species. On the contrary, divalent amino acids showed half the proportionality of the monovalent amino acids.

CONCLUSIONS

Mass transport of divalent amino acids, arginine and histidine, was investigated in ion exchange system using DIAION SK104, SK1BL, and SK112. The ion exchange equilibrium constants of arginine were 5.0 g/cm^3 for SK104 (4 wt% D.V.B.), 25.0 g/cm^3 for SK1BL (8 wt% D.V.B.), and 25.0 g/cm^3 for SK112 (12 wt% D.V.B.). The ion exchange equilibrium constant of histidine was 8.0 g/cm^3 for SK1BL (8 wt% D.V.B.). Resin phase diffusivities of divalent amino acids are measured by batch uptake experiments. Resin phase diffusivities of divalent arginine were decreased from 8.5×10^{-8} cm/s to 1.5×10^{-8} cm/s while the D.V.B. content in resin increases from 4 wt% to 12 wt%. Resin phase diffusivity of histidine for 8 wt% D.V.B. resin was 7.5×10^{-8} cm/s. The

steric hindrance model was able to describe the measured resin phase diffusivities for divalent amino acids. However, the obtained equation has the large deviation of the diffusivity ratio D_i/D_i^0 when the crosslinking degree is zero. Also, the proportionality constant of the divalent lysine was larger than that of the monovalent amino acids.

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