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Ion Exchange for Product Recovery in Lactic Acid Fermentation

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ABSTRACT

Lactic acid fermentation is a product-inhibited fermentation, and product recovery costs in downstream processing are considerable. In this paper the feasibility of ion exchange as a technique for product separation is investigated. In initial experiments an indigenously manufactured weak-base resin was found to show promise, and detailed equilibrium and kinetic data required for design and scale-up of the separation process have been obtained for this resin under conditions of relevance to the fermentation. The equilibria show Langmuir-type characteristics. The equilibria have also been established with HCl, which is a possible eluent. Kinetic studies show that the uptake can be described by a shrinking-core mechanism, with diffusion through the particle controlling. The effect of important medium components such as glucose and phosphate on the uptake of lactic acid has been established. Studies of the uptake of these components from fermentation media have been carried out.

INTRODUCTION

Lactic acid is a product of many uses in food, pharmaceutical, and other industries. The preferred route to the production of lactic acid is by the microbial fermentation of sugars such as glucose and lactose. An important feature of this fermentation is the fact that the accumulation of lactic acid in the fermentation broth leads to problems such as end-product inhibition and decrease in pH. Conventional batch processes operate at temperatures of 40–55°C and pH of 5.5–6.5. The economics of the fermen-

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tative process also depends on the downstream processing involved. Esterification, ion exchange, electrodialysis, and solvent extraction are some of the methods used for purification.

A cost-effective method of recovering lactic acid in a pure form from fermentation broths would therefore go a long way in reducing the cost of production. It would be particularly advantageous if the product could be recovered during fermentation. Several strategies have been suggested in the literature for simultaneous recovery of lactic acid from fermentation broth. Prominent among them are solvent extraction (1–3), dialysis/electrodialysis (4–10), adsorption (11), and ion exchange (12–14). Of these techniques, use of ion exchange appears to have several advantages. Problems such as toxicity (in solvent extraction), fouling of membranes (in membrane-based separations), etc. are not of serious concern here. Lactic acid concentrations being small, the requisite capacity may be made available in a reasonable volume of the resin particles. Use of weak base resins, in view of their higher capacities and the possibility of high selectivities, is particularly worthy of attention.

This work is part of an effort toward the development of a fermentative technology for the production of lactic acid from glucose using *L. delbrueckii*, with intensified rates and simultaneous product recovery. In this paper we explore the possibility of using ion exchange for the recovery of lactic acid from fermentation broths either simultaneously or after fermentation.

PREVIOUS WORK

In the following we briefly review the literature on ion exchange, particularly as it pertains to weak acid uptake and separation.

The prediction of ion-exchange equilibria has been extensively studied for strongly basic and acidic resins (15–18). While early work used constant separation factors to characterize the equilibria in the resin systems, more recent work uses the phase equilibrium approach. The phase equilibria in most situations have been observed to follow one of the isotherms used in adsorption studies, such as Freundlich or Langmuir (19, 20). Interpretation of equilibrium data has usually been done by assuming ideality in both the resin and extraparticle solution, or in the resin phase alone (21). Recently, Bhandari et al. (22, 23), in their experimental and theoretical studies on weak base resins with both strong and weak acids, have considered the reversibility of the sorption process and the electrostatic effects within the pores of the resin, and they found that the sorption with weaker base resins was more reversible. Further, they concluded that Donnan exclusion is not effective in the macropores of the resin.

A good amount of work on sorption dynamics using weak base resins has been reported. In ion-exchange phenomena it is usually one or more of the mass transfer processes (such as external mass transfer or diffusion through the pores of the resin) that control the rate, and not the ion-exchange reaction itself (24, 25). Models of the shrinking core type have been proposed for the rate under various controlling regimes, and have been generally found to fit the experimental data quite well (25–27). The controlling regime is usually determined from the goodness of fit of the conversion–time data to the various models. Independent evaluation of the transport parameters is usually not undertaken. It has been found, however, that the diffusivities obtained by fitting pore diffusion-controlled kinetics to experimental data do not remain constant but show a dependence on the concentration of the solute used. The recent work of Bhandari et al. (22, 23) shows that at least a part of such variation can be explained by taking proper account of sorption reversibility and electrostatic phenomena.

On the relative rates of sorption of different acids, it has been observed (26, 28, 29) that strong monobasic acids have higher sorption rates than weak monobasic acids. Rao and Gupta (26) attributed this to the differences in resin swelling when converted from free base to chloride form. Helfferich and Hwang (29) proposed a mechanism of proton transfer via diffusion of HSO_4^- in the resin phase to explain the high rates of sorption observed in the case of sulfuric acid. They further concluded that the diffusion of undissociated acid is rate controlling in the case of weak acids.

Lactic acid is a hydroxy acid with a weak acid group of pK_a of 3.86 at 25°C. Therefore, under the conditions of fermentation, lactic acid is nearly completely dissociated. Not much data are available on the sorption behavior of lactic acid on ion-exchange resins. The interest in this area is, however, evident from the patent literature on the recovery of lactic acid (among other carboxylic acids) from fermentation broths and from some recent papers. Bagoczeck (30) patented an ion-exchange process for the isolation of aliphatic hydroxy or keto-hydroxy carboxylic acid. Dowex-1, a strongly basic resin, was used in carbonate form for the recovery of lactic acid. Yokayama et al. (31) patented a process for purification of calcium lactate solution formed during fermentation in the broth, using an amphoteric exchanger and activated carbon. Hoechst A.G. (32) patented a process for isolation of carboxylic acids produced by fermentation using a column containing a polymer with a tertiary amino group. Methanol was used to elute the acid.

The effect of removing lactic acid during fermentation by ion exchange on the rate of fermentation was studied by Srivastava et al. (12) for *L. delbrueckii* using strong base (IRA 93) in OH form and by Beschkov et al. (14) for *L. casei* using strong and weak base (Wofatit) resins. In both studies an increase in the rate of production and hence of the productivity of lactic acid compared to the case of no pH control was shown. However, a systematic study of the ion-exchange process itself was not reported.

Some aspects of ion-exchange recovery of lactic acid were studied by Zihao and Kefeng (13) from a solution of lactic acid and glucose and fermentation media. They used an initial concentration of lactic acid of 80 g/L during the selection. These authors selected a SBA resin based on the criteria of least glucose adsorption. Equilibria were fitted by a Freundlich-type of equation. Elution of lactic acid was done with sodium hydroxide. Both the exchange capacity and efficiency were observed to decrease in clarified fermentation broths as compared to pure solutions.

The potential for ion exchange as a separation technique in lactic acid fermentation is thus clear from the patent and published literature. However, systematic studies on equilibrium and kinetics of uptake are lacking, so there is not enough information on which to base a design. Further, the potential of WBA resins has not been adequately explored.

In this paper we report basic studies on SBA resin and WBA resin for lactic acid uptake. Studies have been carried out in solutions ranging in complexity from pure solutions to fermentation media. Aspects of elution using HCl (to obtain lactic acid and not lactate as the product) have also been carried out.

EXPERIMENTAL

Materials

The resins used in this study were Indion 860, a weak base anion exchange (WBA) resin manufactured by Ion Exchange India Ltd., and Dowex-1, a strong base anion exchange (SBA) resin manufactured by Dow Chemicals, USA. Indion 860 was used in the free base form, and Dowex-1 in the Cl^- form. The resins used were fully swollen by equilibrating them with demineralized water and pretreating according to the procedure given in Helfferich (33). The moisture content of the resin was also measured by the standard procedure (33). Swelling of the resin in the different solutions used in the equilibrium studies was determined by measuring the change in the volume of resin on equilibration. The resin characteristics given by the manufacturers are reproduced in Table 1. Demineralized (DM) water was used for the preparation of all the solutions and for washing the resins. Lactic acid (88–90%), glucose, and other media components used were of analytical grade and were purchased from firms of repute.

TABLE 1
Characteristics of the Ion-Exchange Resins Used

	Indion 860	Dowex 1
Polymer matrix	Styrene–DVB	Styrene–DVB
Type	Macroporous	Macroporous
Form as supplied	Free base	Chloride
Bead size (mm)	0.45–0.55	0.3–1.2
Moisture content (% w/w)	45	50
Capacity (meq/mL dry resin)	1.40	1.25

Determination of the Sorption Equilibria and Kinetics

Pretreated and fully swollen (in water) resin samples of known weight (3 g) were contacted with 200 mL of aqueous solutions of known concentrations of the acid of interest, taken in 500 mL conical flasks. This contacting was done on a continuous orbital shaker (Neolab Instruments, India) at 45°C (which is a typical fermentation temperature) and 180 rpm. Studies were also conducted at the ambient temperature of 30°C, which could be a possible candidate in downstream processing. Samples of extraparticle fluid were taken at intervals and analyzed for the acid concentration by the methods to be described below, to provide information on the kinetics of sorption. The equilibrium sample was taken well after the concentration of the acid in the extraparticle solution had ceased to vary. The pH of the solution was measured initially and at equilibrium. Equilibrium data were obtained in a similar manner with solutions of HCl in 0.1 M NaCl in order to estimate the apparent pK_r of the WBA resin (33). All the equilibrium experiments were repeated at least twice and in some cases thrice or four times.

In the intended application, lactic acid is present in solution along with glucose and salts such as phosphates. It is therefore important to know how the presence of these substances influences lactic acid uptake and equilibria on the one hand, and to what extent these substances are removed from solution by the ion exchanger on the other. Therefore, equilibrium uptake of glucose and phosphate salts was studied in the same manner as described above, both for pure solutions and for solutions containing known concentrations of lactic acid; for glucose solutions, the kinetics of uptake was also determined in such studies. Finally, uptake studies for all three solutes were also carried out with fermentation media optimized for our fermentation studies.

In order to check whether the rates determined in the above manner are influenced by external mass transfer resistance, the solid–liquid mass transfer coefficient was measured under the same experimental conditions of temperature, shaker speed, and vessel geometry as used for the studies described above from the rate of dissolution of benzoic acid pellets.

Analytical Methods

The samples taken from the shake flask experiments were analyzed for glucose, lactic acid, and chloride as required. A colorimetric method based on the *o*-toluidine technique (34) was used to measure glucose concentration. The standard glucose kit made by Chemage Laboratories Ltd. (India) was used. Lactic acid concentration was normally determined by titrating the solution against standardized NaOH solution as described by Fetzer and Jones (35); however, when interfering ions such as phosphates were present, an enzymatic assay based on lactate dehydrogenase (LDH) was

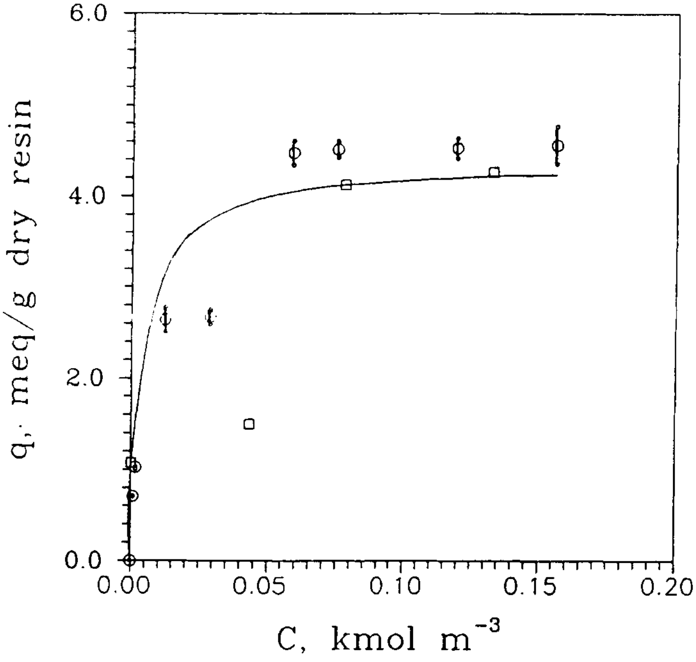

FIG. 1 Sorption equilibria for lactic acid on WBA (Indion 860) resin at 45°C. Line denotes fit of Eq. (1) with data from pure lactic acid solutions. □: data points with fermentation media (not considered in the linear regression).

used (36). Chloride ion (HCl) concentration was measured using a chloride electrode and Orion Ion Analyser-901. The standard phosphorous kit (37) made by Chemage Laboratories Ltd. (India) was used to measure phosphate concentrations.

RESULTS AND DISCUSSION

The moisture content determined experimentally for the two resins were 47% for Indion 860 and 53% for Dowex 1, which are in reasonable agreement with the manufacturers' data (Table 1). The water-swollen resins were found to swell further in acid solutions. For example, in the case of lactic acid solutions, the water-swollen Indion 860 resin increased in volume by a further 18%, while in the case of HCl solutions the increase in volume was 13.8%. In both cases, difference in the concentration of the acid in the range used did not make much difference to the extent of swelling. The pore liquid volumes used in data interpretation were determined from the swollen volumes given above.

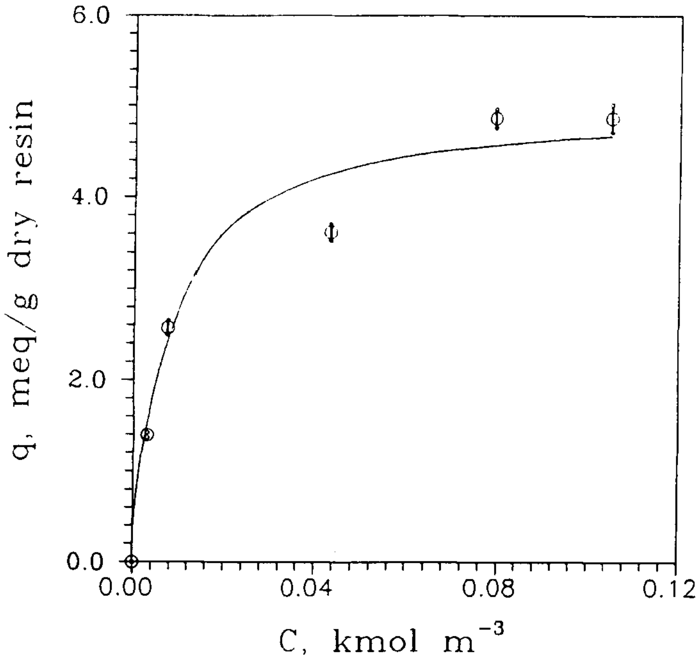

FIG. 2 Sorption equilibria for HCl on WBA (Indion 860) resin at 45°C. Line denotes fit of Eq. (1).

Equilibria

Figures 1 and 2 show, respectively, the equilibrium sorption curves for lactic acid and HCl (a possible eluent) on the WBA resin Indion 860, starting with various initial acid concentrations. The concentration on the resin in units of milliequivalents of acid per gram of dry resin (scientific weight capacity) is plotted against the concentration in solution at equilibrium. It is observed that the isotherms have Langmuir-type characteristics. The corresponding data for Dowex-1 are shown in Fig. 3 (lactic acid) and Fig. 4 (HCl). The data have been fitted to the following equation in accordance with Ref. 19:

$$\frac{q}{q_m} = \frac{KC}{(1 + KC)} \tag{1}$$

The parameters at 45°C, determined from plots of $1/q$ against $1/C$, are tabulated in Table 2. In cases where the saturation part of the curve (i.e., the value of q_m) was well determined (by several data points), the intercept

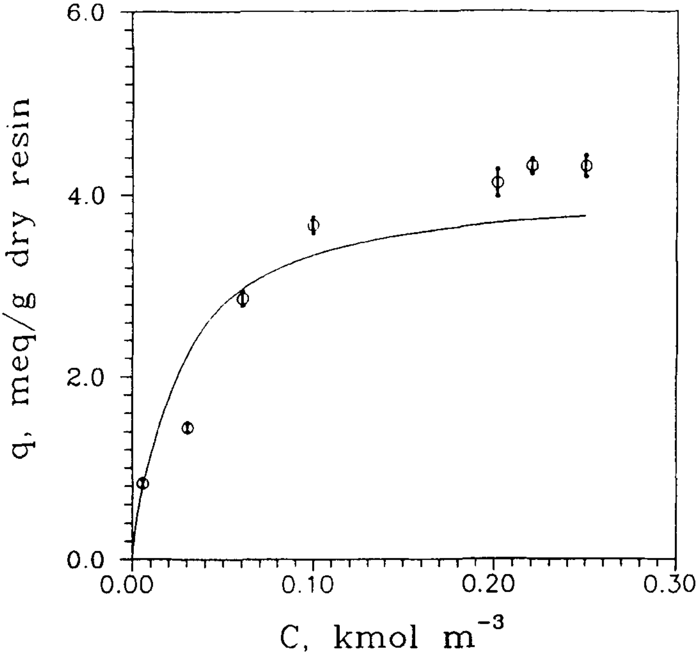

FIG. 3 Sorption equilibria for lactic acid on SBA (Dowex 1) resin at 45°C. Line denotes fit of Eq. (1).

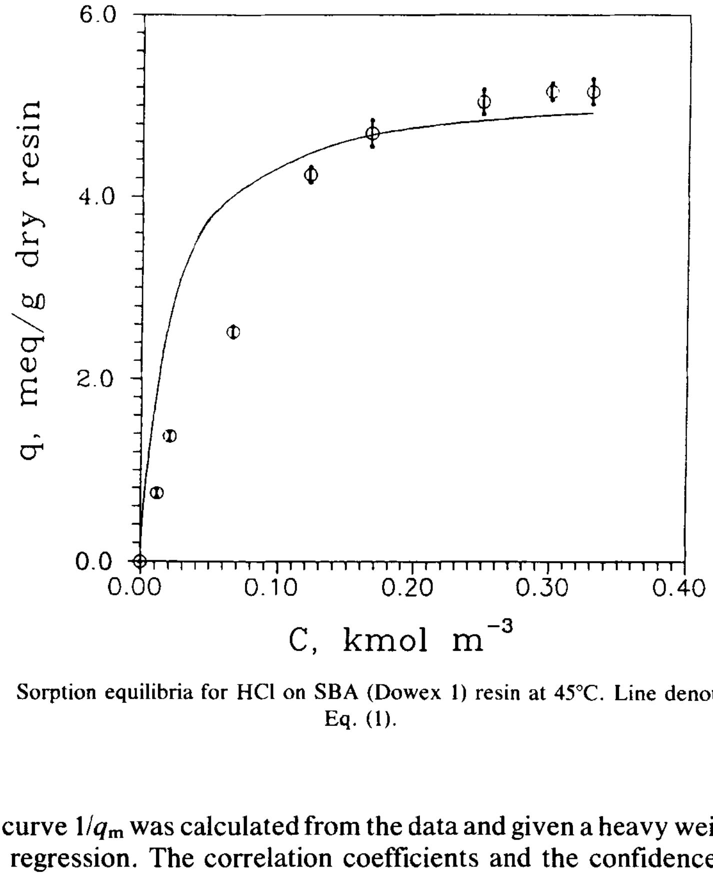

FIG. 4 Sorption equilibria for HCl on SBA (Dowex 1) resin at 45°C. Line denotes fit of Eq. (1).

of the curve $1/q_m$ was calculated from the data and given a heavy weightage in the regression. The correlation coefficients and the confidence limits from the regression analysis are also given in Table 2. The limits for q_m have been directly calculated from those for the intercept, while the limits

TABLE 2

Parameters of Eq. (1) for the Various Equilibria Studied. 95% Confidence Limits for the Slope and Intercept Are Also Shown

System	Correlation coefficient	95% Confidence limits		q_m		K	
		Slope × 10^3	Intercept	Value	Limits	Value	Limits
Lactic acid–Indion 860	0.977	(0.966, 1.148)	(0.204, 0.254)	4.36	(3.94, 4.90)	217	(178, 263)
HCl–Indion 860	0.990	(1.231, 1.775)	(0.155, 0.245)	5.01	(4.10, 6.45)	133	(87, 198)
Lactic acid–Dowex 1	0.940	(4.826, 6.458)	(0.206, 0.278)	4.13	(3.60, 4.86)	43	(32, 58)
HCl–Dowex 1	0.720	(0.820, 6.266)	(0.184, 0.200)	5.21	(5.01, 5.43)	52	(29, 244)

for K have been calculated from those for the slope and q_m. Equilibrium studies at 30°C showed no significant change from the behavior at 45°C.

For lactic acid, while the capacities of the WBA resin (Indion 860) and the SBA resin (Dowex-1) are not far different (the former shows a marginally higher capacity), the isotherms saturate at a much smaller liquid concentration in the case of Indion 860. This is also reflected in the higher value of K for the WBA–lactic acid system as compared to the SBA–lactic acid system. This should lead to sharper breakthrough curves in column operation. Further discussion refers only to Indion 860.

The shape of the equilibrium isotherms shows the possible influence of reaction reversibility, as pointed out by Bhandari et al. (22, 23). For the weak base resin, reaction of the acid involves protonation of the ionogenic sites of the resin by the acid. The high value of K in the present results can therefore be interpreted as indicating that the reversibility of the sorption process is small in the concentration range considered.

In the case of the WBA resins, it is expected that the capacity of the resin will depend on the pH of the medium. It is therefore of interest to know how the observed capacities compare with those calculated accounting for such pH dependence. We need to estimate the pK_r of the ionogenic groups in the resin for this purpose. This value is also useful for optimizing the fermentation conditions if simultaneous recovery is contemplated. The apparant pK_r value for the WBA resin, i.e., the equilibrium constant for the reaction

$$R_1R_2N^+H_2 \rightleftharpoons R_1R_2NH + H^+$$

was determined (33), using the equation

$$pK_r = pH - \log[Cl^-] + \log\frac{x}{2} \tag{2}$$

where pH and the chloride ion concentration ([Cl$^-$)] are the values at half the maximum capacity. The concentration on the resin, as a function of solution pH at equilibrium, for solutions with and without NaCl is shown in Fig. 5, and the values required for Eq. (2) are conveniently obtained from this plot, taken together with Fig. 2. Calculations with both curves in Fig. 5 (with and without NaCl) give similar values for pK_r. The value from the equilibria in NaCl solution (which is probably more accurate) is pK_r = 6.49. Since apparent pK values thus obtained are usually lower than the intrinsic pK value of the ionogenic groups (33), this value shows that the resin has reasonable useful capacities in the pH range of fermentation (5–6.5). This point is further emphasized later, when uptake data for lactic acid from fermentation media are discussed. It may be noted that the value of pK_r found is in the expected range (33) for WBA resins.

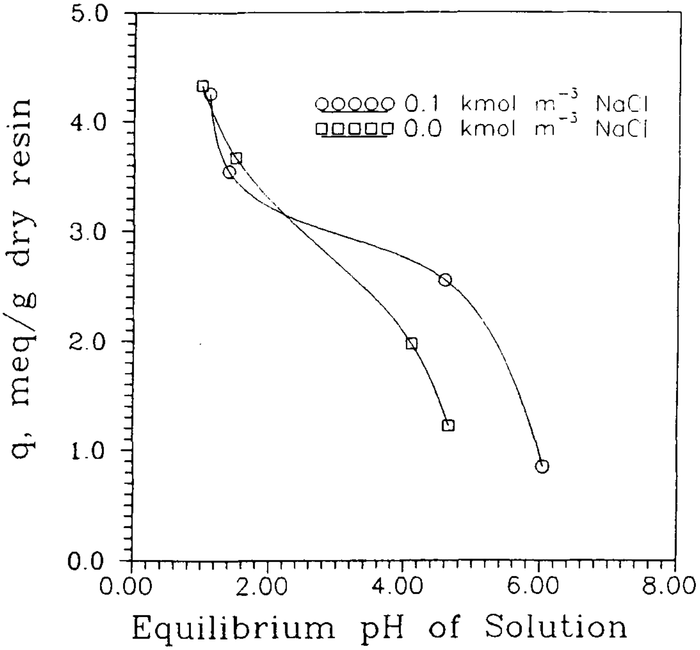

FIG. 5 pH titration curves of WBA (Indion 860) with HCl (with and without added NaCl).

The phenomenon of Donnan exclusion can result in the H-ion concentration inside the resin particle being much lower from that in the extraparticle environment, and is therefore of relevance in calculating available capacities. Bhandari et al. (22, 23) theorized that Donnan exclusion is not of importance in macroporous resins because of the presence of an electrical double layer at the pore walls, and obtained good agreement with their experimental results. In order to obtain an appreciation of the severity of Donnan exclusion, the value of pK_r obtained above was used to calculate the available capacity (i.e., the concentration of protonated amino groups in the resin) at different pH values. These calculated values are compared with the experimentally observed values in Table 3. The two match only at very low pH, when the resin is almost totally protonated. Thus, ideal Donnan exclusion is incompatible with the high values of available capacity observed at pH values higher than 1.5.

It may thus be concluded that, while some exclusion possibly occurs, it is well short of what is predicted by the Donnan principle, as concluded by Bhandari et al. (23). This implies that significant ion-exchange capacity would be available in the pH range of interest.

TABLE 3
Comparison of Observed Capacities as a Function of pH with Calculation Based on Donnan Exclusion (pK_r = 6.49)

	q (meq/g dry resin)	
pH	Experimental	Calculated
4.65	1.394	0.09
4.10	2.573	0.30
1.5	3.623	4.86
1.1	4.867	4.86
1.0	4.867	4.86

Kinetics of Acid Uptake

Decrease in bulk solution concentration with time during sorption of lactic acid on the WBA resin at 45°C could be fitted well by the following first-order uptake equation:

$$\ln \frac{C - C_{\mathrm{eq}}}{C_0 - C_{\mathrm{eq}}} = kt \tag{3}$$

Values of the constant k, obtained from semilog plots of the data, are shown in Table 4.

Although Eq. (3) is similar to what one would expect if external mass transfer were to be controlling, a number of factors point otherwise. For one thing, the k values are different for different initial concentrations. Rates of uptake with HCl were much higher than for lactic acid (compare Figs. 6 and 7). Again, experiments for lactic acid uptake rates, repeated

TABLE 4
Parameter k of Eq. (3) for Various Initial Lactic Acid Concentrations in the Kinetic Studies with WBA Resin

Initial concentration ($\mathrm{kmol \cdot m^{-3}}$)	$k \times 10^4\ \mathrm{s^{-1}}$
0.0065	7.75
0.0100	4.71
0.0520	4.70
0.0950	3.69
0.1920	3.93

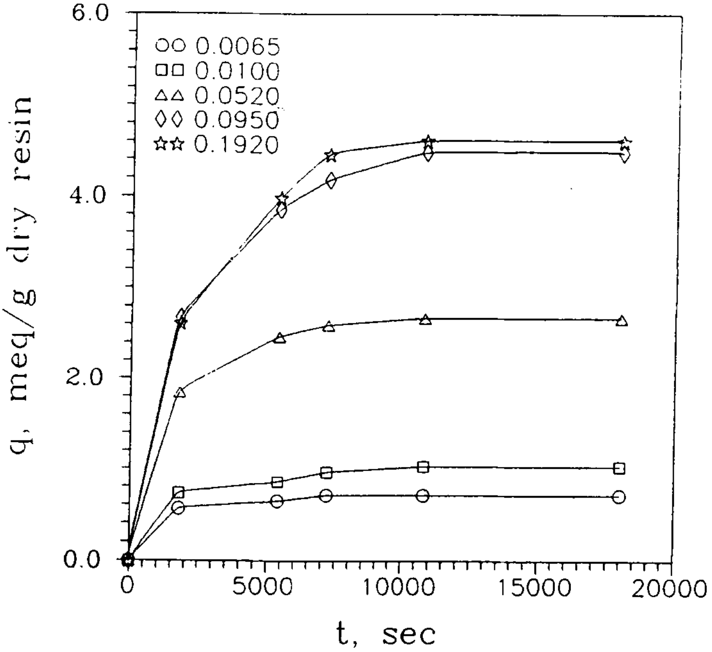

FIG. 6 Sorption kinetics of lactic acid on WBA (Indion 860) resin at 45°C. Legend shows initial concentrations of lactic acid in kmol·m^{-3}.

at two different shaker speeds, 180 and 240 rpm, gave identical results. Experiments were conducted on benzoic acid dissolution to determine the liquid side mass transfer coefficients under identical hydrodynamic conditions as used in the resin experiments. After correcting for particle size (assuming Sh to be proportional to $Re^{1/2}$) and diffusivity of lactic acid, the values of mass transfer coefficients obtained were, in all cases, much higher than the k values shown in Table 4. All the above indicate that external mass transfer is unimportant and Eq. (3) should only be regarded as a fitting equation.

Thus, having eliminated the possibility of external mass transfer control, we may now test for the possibility of diffusion through the controlling particle. The relevant equation (26) is

$$[1 - 3(1 - \overline{X})^{2/3} + 2(1 - \overline{X})] = \frac{6\overline{D}_e}{Q_m R^2} \int_0^t C\, dt \tag{4}$$

where $\overline{X}$ = fraction of equilibrium conversion reached in time t

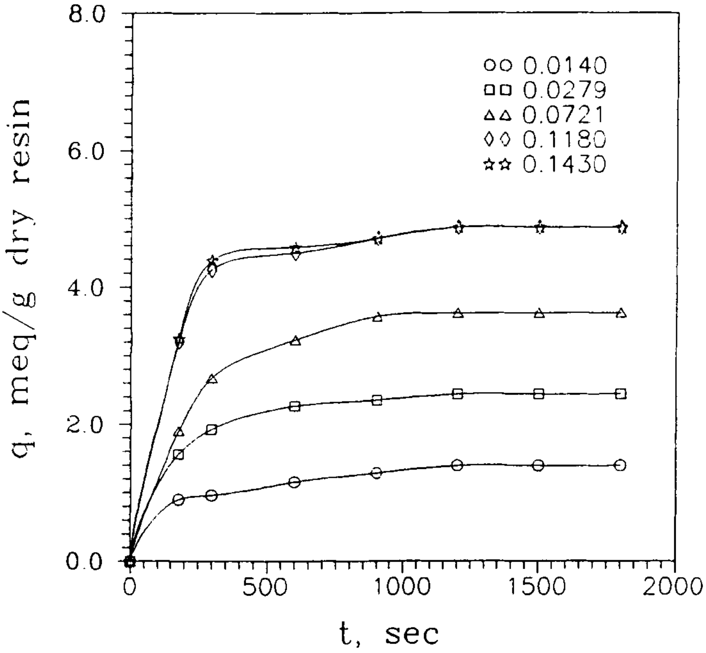

FIG. 7 Sorption kinetics of HCl on WBA (Indion 860) resin at 45°C. Legend shows initial concentrations of HCl in kmol·m^{-3}.

C = solute concentration in the bulk (kmol/m^3)
$\overline{D}_e$ = effective diffusivity (m^2/s)
R = radius of the resin particle (m)
Q_m = capacity of the resin (kmol/m^3)

The left side of Eq. (4) was calculated from the experimental data and plotted against the integral on the right side of Eq. (4), which was calculated using Eq. (3). Figures 8 and 9 show the plots. The data plot linearly as predicted by Eq. (4). While the data from low initial concentration experiments (Fig. 8) show small nonzero intercepts, those from higher initial concentration experiments (Fig. 9) pass through the origin. This behavior is similar to that observed by Rao and Gupta (26), and has been explained by these authors as resulting from possible external mass transfer limitations in the very early part of these runs. Since the intercepts are small, further refinement of the model was not attempted. The diffusivities calculated from the slopes of these plots are tabulated as the ratio D_e/Q_m

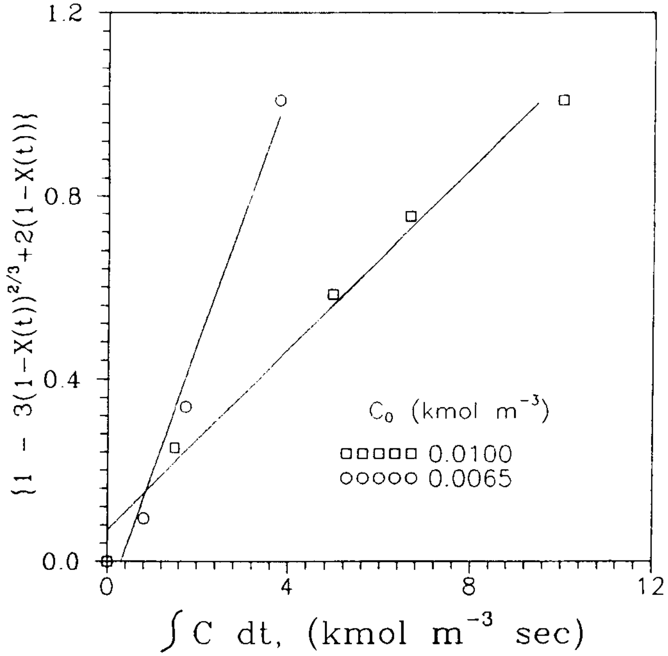

FIG. 8 Modeling of kinetics of sorption of lactic acid on WBA (Indion 860) resin with pore diffusion controlling mechanism (Eq. 4).

for the different experiments in Table 5. The diffusivities are of the same order of magnitude as obtained by other workers, for example Rao and Gupta (26). It can be seen from the table that the higher the initial concentration used, the lower the diffusivity estimated. In dilute solutions the pH in the external solution is high and the solute is considerably dissociated, while in concentrated solutions it is possible for a reasonable concentration of the undissociated acid to prevail. Since it is likely to be the diffusion of H^+ that controls the rate of acid uptake in the presence of some degree of co-ion exclusion, these differences in the degree of dissociation can explain the observed trends in the diffusivities.

No significant effect of temperature was observed on the kinetics of uptake, at least in the temperature interval 30–45°C.

Effect of Medium Components on Kinetics and Equilibria

Figure 10 shows sorption kinetics for lactic acid from solution containing 1, 5, and 10% (w/v) glucose. The initial lactic acid concentration in

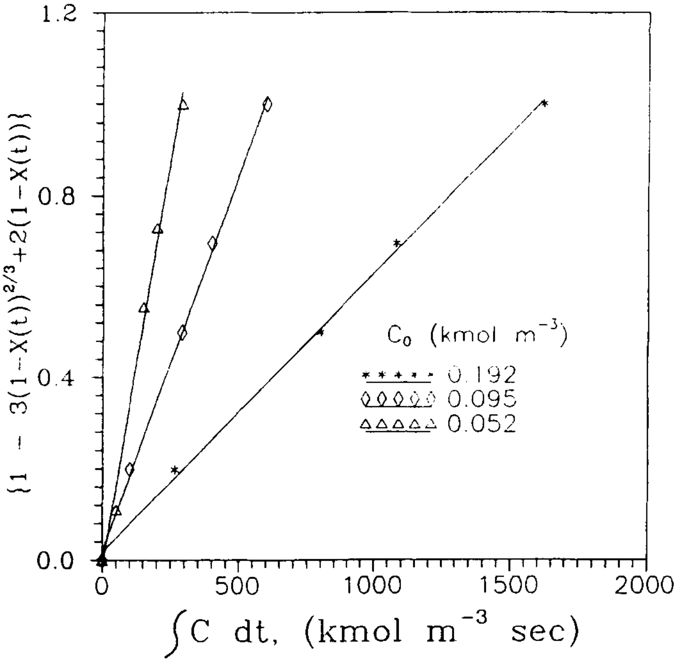

FIG. 9 Modeling of kinetics of sorption of lactic acid on WBA (Indion 860) resin with pore diffusion controlling mechanism (Eq. 4).

these experiments was 0.1 kmol/m^3. The glucose concentrations used are typical of fermentation media. While 10% w/v is typical of batch fermentation, there are certain advantages in using a lower concentration in the fed batch and continuous operations. Figure 10 shows that the rate as

TABLE 5
Diffusivity Values Estimated from Eq. (4) for Experiments with Different Initial Concentrations of Lactic Acid

Initial bulk concentration (kmol·m^{-3})	$\overline{D}_e/Q_m \times 10^{10}$ [(m^2·s^{-1})/(kmol·m^{-3})]
0.0056	5.360
0.0100	1.930
0.0525	0.682
0.0950	0.339
0.1900	0.124

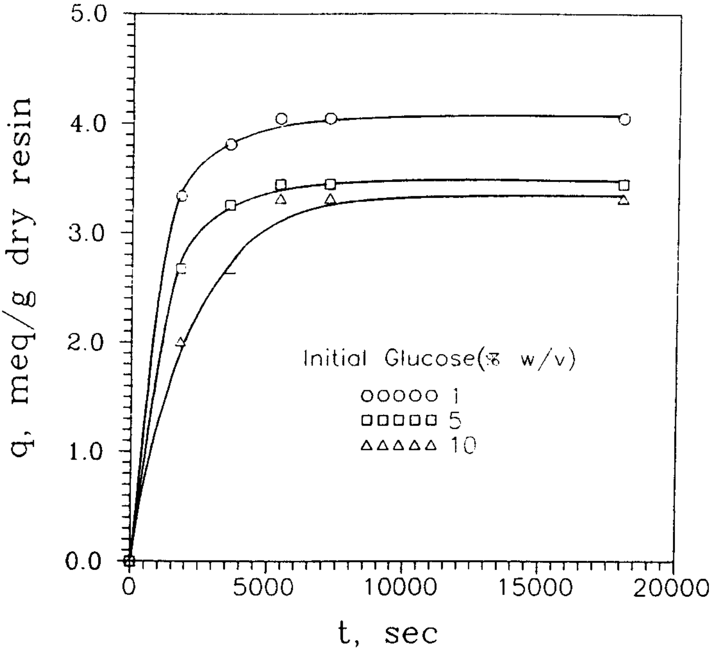

FIG. 10 Sorption kinetics of lactic acid (C_0 = 0.1 kmol·m^{-3}) on WBA (Indion 860) resin in the presence of various glucose concentrations at 45°C.

well as the capacity decreases as the initial glucose concentration increases. The reduction in capacity is likely to be due to the uptake of glucose, as has been observed in other such studies (13, 20).

Equilibrium uptake experiments were also conducted to see if phosphate ions (HPO_4^{2-} and $H_2PO_4^-$), usually present in the fermentation broth, had any effect on lactic acid uptake. Two levels of phosphate ($H_2PO_4^-$) and two levels of lactic acid were used in these experiments. The results are shown in Table 6. While some uptake of phosphates is seen, it is noteworthy that the uptake at the higher level of lactic acid is less than at the lower level, indicating a higher selectivity for lactic acid. This can be explained by the principle of site-sharing (33), since it is likely to be the un-ionized form of the lactic acid that diffuses into the resin particles. Column studies, to be reported separately, confirm these conclusions, with lactic acid being able to displace completely the phosphate from the resin.

Finally, an experiment was carried out with the following medium composition (glucose = 10 g/L; KH_2PO_4, K_2HPO_4, diammonium phosphate,

TABLE 6
Equilibrium Uptake of Phosphate in the WBA (Indion 860) Resin

Lactic acid concentration (kmol·m^{-3})	Bulk phosphate concentration × 10^3 Initial (kmol·m^{-3})	Bulk phosphate concentration × 10^3 Equilibrium (kmol·m^{-3})	Capacity (meq/g dry resin)
0.056	18.56	13.61	0.622
0.056	95.88	77.32	2.330
0.110	17.32	14.84	0.311
0.110	92.78	77.32	1.944

= 1 g/L each; yeast extract = 3 g/L) with different lactic acid concentrations. Results on equilibrium compositions in the liquid and resin phases are reported in Table 7. It is observed that there is a marginal decrease in the capacity for lactic acid. The equilibrium pH in these cases was higher than with the pure system (data for which were discussed earlier) due to buffering action of the medium components. Hence the decrease in capacity could be due to the presence of the medium components as well as higher equilibrium pH. In any case, the decrease is small and this substantiates the conclusion made earlier on the availability of significant sorption capacity in fermentation media. The data are also plotted in Fig. 1 for comparison with the results on the pure system. A general agreement with the earlier curve is seen except in the case of one point at $C = 0.0436$ kmol/m^3. This experiment was repeated with the same result. The reason for the low available capacity for this case is not clear.

The available capacity at a pH value of 5.1 was checked by neutralizing a solution of lactic acid with lime to this pH, filtering off the solids, and

TABLE 7
Uptake of Solutes at Equilibrium from Fermentation Media

Equilibrium pH	Lactic acid $C \times 10^2$	Lactic acid q	Glucose $C \times 10^3$	Glucose q	Phosphate $C \times 10^3$	Phosphate q
6.32	0.02556	1.076	50.55	0.629	12.7	0.969
4.07	4.36000	1.500	50.55	0.629	12.1	1.051
3.52	7.80000	4.120	51.11	0.559	12.2	1.037
3.31	13.3000	4.260	52.22	0.419	12.2	1.027

recirculating the solution through a column of resin continuously. As the pH increased due to uptake, it was adjusted from time to time by addition of lactic acid. The experiment was continued till constant pH, indicating no further uptake of the acid. The final liquid concentration (total lactate + lactic acid) at this point was 0.064 kmol/m^3, and the concentration in the resin phase (q) was 1.8 meq/g dry resin. While this q is less than what was observed for pure lactic acid solutions at lower pH, it does indicate that a significant sorption capacity exists at the pH values of interest to the fermentation, as anticipated from earlier pK_r information.

Minor differences in the equilibrium uptake of glucose and phosphate are also observed when data on fermentation media are compared with those from lactic acid solutions.

CONCLUSIONS

The ion-exchange method has been studied with a view to assessing its suitability for product recovery in lactic acid fermentation and obtaining basic data necessary for designing the system. Data have been obtained at the temperatures known to be best suited for fermentation, but the influence of temperature on both equilibria and kinetics in the range 30–45°C has been shown to be unimportant. The weak base resin examined in this work, Indion-860, shows promise, with reasonably high capacities and sharp equilibria. The kinetics can be explained by the shrinking core concept, with diffusion through the particle controlling. The equilibria with lactic acid as well as hydrochloric acid have been correlated by a Langmuir-type expression. While some uptake of glucose is seen, this can be minimized in a fed-batch operation, and is in any case not a problem in recovery from fermented broth. The phosphate ions usually present in fermentation media have been seen not to interfere to any significant extent with lactic acid uptake. Equilibrium data obtained on made-up fermentation media, with all the components present, show no significant differences in the capacity for lactic acid.

Therefore, on the basis of these studies, ion exchange using a weak base resin emerges as a feasible option in lactic acid recovery and purification, both as a downstream process and in simultaneous recovery. While the option exists in downstream processing to adjust the pH of the broth (freed of biomass) before subjecting it to ion exchange so that conditions best suited to the latter process can be chosen, some optimization of conditions is necessary in a simultaneous fermentation–recovery process. This is because the optimum conditions for fermentation may be different from those for ion exchange. Based on the data presented in this paper, a first choice of conditions can be theoretically derived for a combined process if data on the rates of fermentation over a range of conditions (mainly pH) are available. A number of options exist for the experimental realization of such a system. An attractive option is to circulate the contents of a batch fermenter continuously through a column packed with the ion exchanger and placed in a recycle loop, thereby achieving the twin objectives of pH maintenance and product removal. These issues will be addressed in forthcoming publications.

NOMENCLATURE

C	bulk solute concentration (kmol/m^3)
C_{eq}	solute equilibrium concentration in solution (kmol/m^3)
C_0	initial solute concentration (kmol/m^3)
$\overline{D}_e$	effective diffusivity (m^2/s)
k	rate constant (s^{-1})
K	equilibrium constant (m^3/kmol)
q	concentration on resin (meq/g dry resin)
q_m	maximum sorption capacity (meg/g dry resin)
Q_m	maximum sorption capacity (kmol/m^3 resin)
R	radius of the resin particle (m)
t	time (s)
x	sorption capacity (meq/m^3 resin pore volume)
$\overline{X}$	fraction of equilibrium reacted in time t

REFERENCES

1. V. M. Yabannawar and D. I. C. Wang, "Bioreactor Systems with Solvent Extraction for Organic Acid Production," *Ann. N. Y. Acad. Sci., Biochem. Eng.*, *506*, 523 (1987).
2. V. M. Yabannawar and D. I. C. Wang, "Analysis of Mass Transfer for Immobilized Cells in an Extractive Lactic Acid Fermentation," *Biotech. Bioeng.*, *37*, 544 (1987).
3. K. V. Venkatesh, M. Okos, and P. Wankat, "Kinetic Model of Growth and Lactic Acid Production from Lactose by *L. bulgaricus*," *Process Biochem.*, *28*, 231 (1993).
4. P. Gerhart and S. D. M. Gally, "Dialysis Flask for Concentrated Culture of Microorganisms," *J. Bacteriol.*, *86*, 919 (1970).
5. M. Friedman and E. L. Gaden, "Growth and Acid Production by *Lactobacillus delbrueckii* in a Dialysis Culture System," *Biotech. Bioeng.*, *12*, 961 (1970).
6. R. W. Steiber, G. A. Coulman, and P. Gerhardt, "Dialysis Continuous Process for Ammonium Lactate Fermentation of Whey," *Appl. Environ. Microbiol.*, *34*, 733 (1977).
7. R. W. Steiber and P. Gerhardt, "Dialysis Continuous Process for Ammonium Lactate Fermentation, Improved Mathematical Model and Use of Deprotinized Whey," *J. Dairy Sci.*, *62*, 1558 (1979).
8. M. Hongo, Y. Nomura, and N. Iwahara, "Novel Method of Lactic Acid Production by Electrodialysis Fermentation," *Appl. Environ. Microbiol.*, *52*, 314 (1986).

9. Y. Nomura, "Lactic Acid Production by Electradialysis Fermentation Using Immobilized Growing Cell," *Biotech. Bioeng.*, *30*, 788 (1987).
10. M. Czytks, "Continuous Glucose Fermentation for Lactic Acid Production: Recovery of Acids by Electrodialysis," *Chem. Eng. Tech.*, *59*, 952 (1987).
11. B. H. Davison and C. D. Scott, "A Proposed Biparticle Fluidized Bed for Lactic Acid Fermentation and Simultaneous Adsorption," *Biotech. Bioeng.*, *39*, 365 (1992).
12. D. Srivastava, P. K. Roychaudhary, and P. Sahay, "Extraction of Lactic Acid from Fermentation Using Ion Exchange Resins," *Ibid.*, *39*, 607 (1992).
13. W. Zihao and Z. Kefeng, "Kinetics and Mass Transfer for Lactic Acid Recovered with Anion Exchange Method in Fermentation Solution," *Ibid.*, *47*, 1 (1995).
14. V. Beschkov, L. Peeva, and B. Valchanova, "Ion Exchange Separation of Lactic Acid from Fermentation Broth," *Hung. J. Ind. Chem.*, *23*, 135 (1995).
15. H. P. Gregor, "Gibbs–Donnan Equilibrium in Ion Exchange Resin System," *J. Am. Chem. Soc.*, *73*, 642 (1951).
16. G. Klein, D. Tondeur, and T. Vermeulen "Multicomponent Ion Exchange in Fixed Beds," *Ind. Eng. Chem., Fundam.*, *6*, 339 (1967).
17. G. Klein and D. Tondeur, "Multicomponent Ion Exchange in Fixed Bed Constant Separation Factor Equilibrium," *Ibid.*, *6*, 351 (1967).
18. G. Klein, "Calculation of Ideal or Empirically Modified Mass Action Equilibria in Heterovalent, Multicomponent Ion Exchange," *Comput. Chem. Eng.*, *6*, 171 (1984).
19. A. A. Garcia and J. C. King, "The Use of Polymer Sorbents for the Recovery of Acetic Acid from Dilute Aqueous Solution," *Ind. Eng. Chem. Res.*, *8*(2), 205 (1989).
20. W. Takatsuji and H. Yoshida, "Removal of Organic Acids from Wine by Adsorption on Weakly Basic Ion Exchangers: Equilibria for Single and Binary Systems," *Sep. Sci. Technol.*, *29*(11), 1473 (1994).
21. T. Kataoka and H. Yoshida, "Ion Exchange Equilibria in Ternary Systems," *J. Chem. Eng. Jpn.*, *13*, 328 (1980).
22. V. M. Bhandari, V. A. Juvekar, and S. R. Patwardhan, "Sorption Studies on Ion Exchange Resins. I. Sorption of Strong Acids on Weak Base Resins," *Ind. Eng. Chem. Res.*, *1*(4), 1061 (1992).
23. V. M. Bhandari, V. A. Juvekar, and S. R. Patwardhan, "Sorption Studies on Ion Exchange Resins. II. Sorption of Weak Acids on Weak Base Resins," *Ibid.*, *1*(4), 1073 (1992).
24. R. Kunin, *Ion Exchange Resins*, Wiley, London, 1958.
25. F. G. Helfferich, "Ion Exchange Kinetics, V. Ion Exchange Accompanied by Reactions," *J. Phys. Chem.*, *9*, 1178 (1965).
26. M. G. Rao and A. K. Gupta, "Kinetics of Ion Exchange in Weak Base Anion Exchange Resins," *AIChE Symp. Ser.*, *219*(7), 96 (1982).
27. M. G. Rao and A. K. Gupta, "Ion Exchange Processes Accompanied by Ionic Reactions," *Chem. Eng. J.*, *24*, 181 (1982).
28. G. Adams, P. M. Jones, and J. R. Miller, "Kinetics of Acid Uptake by Weak Base Anion Exchangers," *J. Chem. Soc., Sec. A*, p. 2543 (1969).
29. F. G. Helfferich and Y. L. Hwang, "Kinetics of Acid Uptake by Weak Base Anion Exchangers. Mechanisms of Proton Transfer," *AIChE Symp. Ser.*, *242*(1), 17 (1985).
30. R. Bagoczeck, "Aliphatic Hydroxy or Ketohydroxy Carboxylic Acid," Polish Patent 64,835 (1972).
31. M. Yokayama, "Lactic Acid Production," Japanese Patent 7,688,691 (1976).
32. A. G. Hoechst, "Isolation of Carboxylic Acids Produced by Fermentation," German Patent 3,328,094 (1985).

33. F. Helfferich, *Ion Exchange*, McGraw-Hill, New York, NY, 1962, p. 260.
34. G. R. Cooper and V. McDaniell, *Standard Methods of Clinical Chemistry, Vol. 6*, Academic Press, New York, NY, 1970, p. 159.
35. W. R. Fetzer and R. C. Jones, "Determination of Free and Total Acidity in Commercial Lactic Acid," *Anal. Chem.*, *24*, 835 (1952).
36. R. J. Henry, N. Chiamori, O. J. Golup, and S. Berkman, *Am. J. Clin. Pathol.*, *34*, 381 (1960).
37. G. Gomarri, *J. Lab. Clin. Med.*, *27*, 955 (1942).

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