0273-2289/91/2829—0589$03.00

Nondispersive Extraction for Recovering Lactic Acid

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ABSTRACT

A nondispersive extraction process for recovery of lactic acid from fermentation broth is being developed. The criteria for selection of solvent, distribution of lactic acid between the aqueous and solvent phases, and the effect of presence of other compounds in the broth, are discussed. Working with a simulated fermentation broth (without cells), a hydrophobic membrane module has been evaluated for its effectiveness as extractor. Back extraction and its role has been demonstrated. A theoretical comparison of this process with electrodialysis shows membrane extraction to be more desirable.

Index Entries: Lactic acid; hydrophobic membrane; nondispersive extraction; partition coefficient; electrodialysis.

NOMENCLATURE

a_d	Specific surface area of alkali droplets, cm^2/cm^3
A_o	Mass transfer surface area in membrane module, m^2
A_c	Total cross-sectional area of fiber tubes, cm^2
C_1	Concentration of lactic acid in the inlet solvent stream to extractor, g/L
C_2	Concentration of lactic acid in the outlet solvent stream from extractor, g/L
d_o	Outside diameter of membrane fibers, cm
d_p	Average diameter of membrane fibers, cm
F_B	Volumetric flow rate of broth, L/h
F_S	Volumetric flow rate of solvent, L/h

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k_c	Mass transfer coefficient between solvent and alkali phase in the solvent tank, cm/s
k'_c	Mass transfer coefficient between solvent and alkali phase in the fiber tubes, cm/s
k_o	Over-all mass transfer coefficient across the membrane in the extractor, cm/s
m	Distribution coefficient, dimensionless
m'	Distribution coefficient of lactic acid at the pH of alkali solution, dimensionless
m*	Partition coefficient of lactic acid, dimensionless
P_1	Concentration of lactic acid in the inlet aqueous stream to extractor, g/L
P_2	Concentration of lactic acid in the outlet aqueous stream from extractor, g/L
P_a	Concentration of lactic acid in alkali phase, g/L
V_I	Volume of aqueous phase, L
V_{II}	Volume of solvent (TOPO+kerosene) phase, L
V_{III}	Volume of alkali phase emulsified in the solvent, L
ϕ_D	Volume fraction of alkali in the solvent emulsion, L

INTRODUCTION

Lactic acid has found a variety of applications in a number of consumer goods, such as pharmaceuticals, cosmetics, and foods. It is also commonly used in the tanning industry. Since lactic acid contains hydroxyl and carboxyl groups, it has potential for the manufacture of environmentally benign polymers (*1*). Many available carbohydrate-containing resources or hydrocarbons can be used as raw materials in making lactic acid (*1–3*). Its production using microbial fermentation has been successfully done in the past and is receiving increasing attention as the yield is high and substrate sources are regenerable.

However, the problems of inherent product inhibition and purification make the fermentation approach slow and uneconomic (*4,5*). Lactic acid as a fermentation product is strongly inhibitory to cellular activity (*4*). As a consequence, cell growth as well as product formation decrease as lactic acid accumulates. This results in low productivity, low product concentration, and inefficient utilization of substrate. A solution to this problem requires maintenance of a low concentration of lactic acid in the broth. On the other hand, economic considerations demand a high concentration in the product stream. Secondly, lactic acid is very hydrophylic and it is difficult to purify it from broth. Several novel methods based on the electrolytic nature of lactic acid have been explored. Of these, extraction (*6*), electrodialysis (*7–9*), and ion-exchange/adsorption (*10*) appear to have high potential.

Table 1
Comparison of Different Recovery-Coupled Fermentations

	Electrodialysis	Extraction	Ion exchange
pH	high	low	high
product	acid	lactate	lactate
purity of product	low	high	low
electrochemical stimulation of cellular metabolism	possible	none	none
pH control	not required	required	required
microbial fouling	yes	no	yes
water flux across membrane	yes	no	-
loss of product by oxidation	yes	no	no
loss of sugar and anions	yes	no	possible
solvent toxicity to the cells	no	possible	no
energy consumption	high	low	low

One approach to solving these problems is to simultaneously remove product as it is formed. Such *in situ* recovery of desired but toxic product from broth should improve productivity and enhance substrate utilization. The recovery-coupled fermentation may involve any one of a combination of the above mentioned methods.

The pros and cons associated with the three separation processes are presented in Table 1. Ion-exchange/adsorption operations require good resins or adsorbents with good selectivity and specificity for lactic acid. The fouling of adsorbents by cells also needs to be addressed. A major drawback of electrodialysis is its high energy consumption and attachment of the cells to the membrane. Compared to these, extraction has been found more suitable in on-line separation of lactic acid owing to its low energy consumption, good solvent selectivity, and no attachment of cells on a membrane.

A schematic diagram for simultaneous ferementation and recovery of lactic acid is presented in Figure 1. The heart of this simultaneous recovery approach is a nondispersive extraction process that utilizes hollow fibers of a hydrophobic membrane as interfacial mass-transfer medium between solvent and aqueous phases. Owing to the hydrophobic nature of the membrane, the microorganisms are excluded from the membrane surface where the two phases contact. As a result, only the molecular toxicity, not the interfacial toxicity, of the solvents plays a role. The proposed process also envisages the use of alkali droplets in solvent phase as reactive

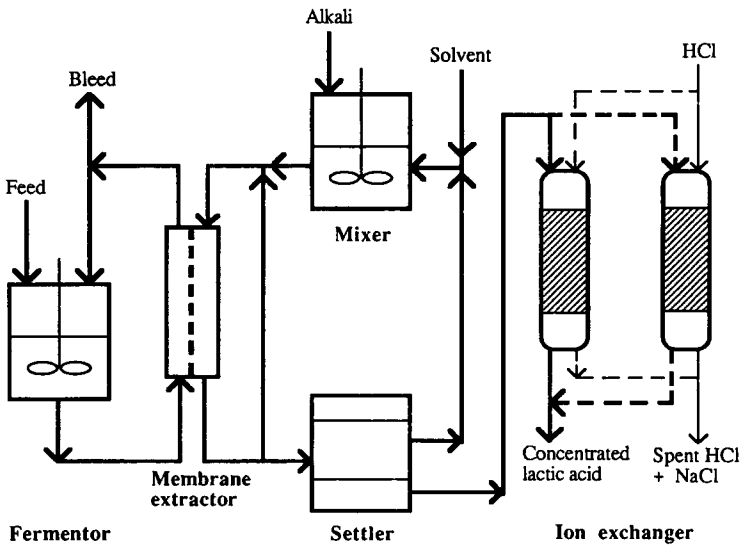

Fig. 1. Process scheme for *in situ* removal of lactic acid in fermentation by membrane-associated-reactive extraction.

agents to enhance the removal of lactic acid. The high back-extractive capability of alkali phase ensures complete removal of lactic acid from solvent, and thus maintains the extractive power of solvent in the system. With the use of solvents having low interfacial tensions (*11,12*), stable emulsions of alkali in solvent can be easily made. Thus, two advantages, concentration of lactic acid in the alkali phase and low solvent inventory, can be combined with the use of alkali-in-solvent emulsion. This emulsion can be easily broken by passage through a bed of glass fibers to separate and recycle the solvent. A final step in the scheme envisages the use of a train of cation-exchangers to recover the acid.

This study has focused on the criteria for solvent selection and characterization of the membrane extraction-module. Only the simulated fermentation broths, without cells, have been used here. The concepts and results will be extended to actual fermentation broths at a later stage.

MATERIALS AND METHODS

Measurement of Partition Coefficient

Six milliliters of lactic acid solution with or without salts and yeast extract and 6 mL of organic solvent were mixed vigorously for 3 min. The mixture was then placed in a water-bath shaker at 37°C for 12 h. The upper solvent phase was carefully removed and 5 mL of it was back-extracted by the same volume of 2 *N* NaOH solution. Back-extraction of the solvent by the alkali solution resulted in a stable emulsion, which was

separated by passing it through a packing of glass fibers. The concentration of lactic acid in aqueous samples was measured by HPLC (a Series 4 Perkin Elmer Unit equipped with a Polypore H 10 μm column and a LC-25 refractive index detector; 0.01 *N* H_2SO_4 solution in double-distilled water as solvent at 0.2 mL/min) at room temperature. The distribution coefficient (m) was calculated as the ratio of total lactic acid concentration in organic phase to that in aqueous phase at equilibrium. The corresponding partition coefficient (m*) was calculated from the pK_a value for lactic acid (3.873 at 37°C) (*3*) and the equilibrium pH as follows

$$m^* = m(1 + 10^{pH-pK})$$

Composition of Salts and Yeast Extract

The concentrations of salts and yeast extract used in studying their effect on the partition coefficient are listed below (*13*):

Salts:	
$MgSO_4 \cdot 7H_2O$	1.225 g/L
$MnSO_4 \cdot H_2O$	0.336 g/L
$FeSO_4 \cdot H_2O$	0.0584 g/L
$CH_3COONa \cdot 3H_2O$	1.658 g/L
K_2HPO_4	0.5 g/L
KH_2PO_4	0.5 g/L
Yeast extract:	30 g/L

RESULTS AND DISCUSSION

Selection of Solvent

Several criteria for solvent selection in an on-line extraction process (*14–17*) are listed in Table 2.

Two levels of solvent toxicity to the cells have been reported: molecular and interfacial or phase toxicity (*18*). Although a number of reports in

Table 2
Criteria for Solvent Selection

Biocompatibility
Distribution coefficient
Selectivity/separation factor
Viscosity
Personnel safety
Solubility of water in solvent and solubility of solvent in water
Interfacial tension, density, boiling and melting points, polarity
Thermodynamic and chemical stability
Cost Environmental risks Availability

literature have discussed solvent toxicity, few have made a distinction between these two forms. As suggested earlier, the hydrophobic nature of the membrane module keeps the cells away from the solvent interface. As a result, mainly the molecular form of toxicity needs to be considered in nondispersive extraction.

Several solvents were selected on the basis of the criteria in Table 2, mainly the reported toxicities, solubility of solvent in aqueous phase, solubility of water in the solvent, selectivity of solute distribution, cost, and so on. Generally, the solvents with high distribution coefficients also exhibit strong toxicity to the cells. These solvents, with the measured partition coefficient of lactic acid at 37°C, are listed in Table 3. From these, kerosene saturated with TOPO (trioctyl phosphine oxide) emerges as the solvent of choice.

A number of factors (temperature, pH of solution, concentrations of lactic acid, salts, sugars, proteins) govern the distribution coefficient of lactic acid between fermentation broth and a solvent. Partition coefficient (ratio of the concentrations of undissociated solute in the two phases) is, however, independent of pH (*19*). The effect of some other factors is shown in Fig. 2. The concentration of total lactic acid in aqueous phase strongly influences the partition coefficient. This is mainly a result of the tendency of lactic acid to form a dimer (*5*). For carboxylic acids, presence of salts in aqueous phase has been reported to affect the partitioning of solute (*20–22*). This however, was not found to be the case for the salt concentrations (*13*) used in this work. Similarly, the presence of yeast extract was also found to have no effect on the partition coefficient of lactic acid between aqueous phase and kerosene saturated with TOPO.

For nondispersive extraction, the viscosity of solvent phase plays an important role (*19*). Distribution coefficient for lactic acid in Alamine (a

Table 3
Partition Coefficients of Selected Solvents at 37°C

Solvent	Equilibrium Lactic acid Concentration (g/L)		Partition coefficient
	Aqueous phase	Solvent phase	
21% TOPO + kerosene	96.9	18.0	0.51
	72.7	14.8	0.56
	50.4	11.1	0.61
	23.0	6.2	0.75
10% TOPO + kerosene	66.6	7.7	0.34
	50.0	6.1	0.34
5% TOPO + kerosene	69.6	4.0	0.16
	51.8	3.2	0.16
Kerosene	52.3	0.02	<0.001
15% Alamine +kerosene	76.8	2.5	0.10
	60.5	2.1	0.09
15% Alamine + oleyl alcohol	65.3	15.2	1.39
	49.5	14.4	1.55
Oleyl alcohol	60.5	0.07	<0.001
Cumene	67.5	0.08	<0.001
	76.2	0.09	<0.001
Methyl crotonate	64.8	4.8	0.19
	46.2	2.9	0.16
Hexanoic acid	78.5	5.8	0.17
	61.9	4.4	0.15
Tributyl phosphate	53.0	14.6	1.10

tertiary amine)-in-oleyl alcohol is higher than that in TOPO-in-kerosene. Yet, the rate of extraction of lactic acid with alamine is significantly lower because of the high viscosity of oleyl alcohol.

While choosing an appropriate solvent, recovery of solute from the solvent must also be considered (*5,19*). Recovery of lactic acid from a solution of TOPO-in-kerosene was investigated by repeatedly contacting a 2*N* aqueous solution of NaOH with equal volumes of the solvent, which

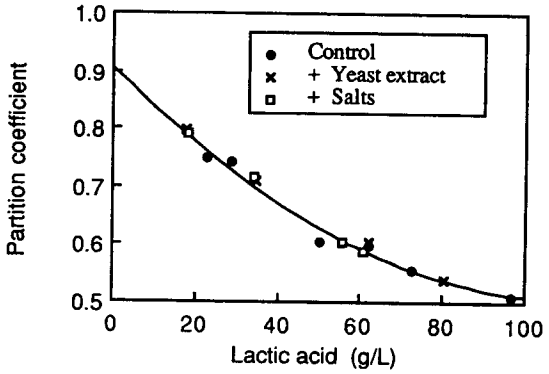

Fig. 2. Effects of aqueous phase concentration on the partition coefficient of lactic acid.

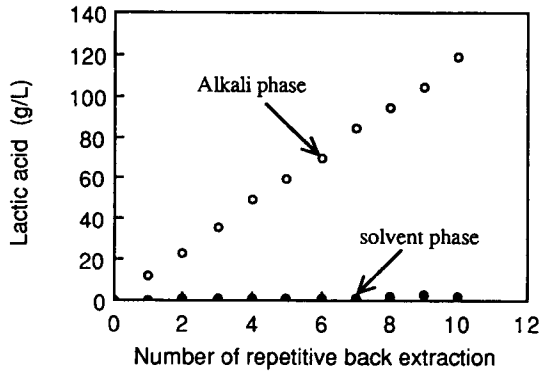

Fig. 3. Back extractive capacity of 2*N* NaOH in 10 repetitive extractions.

contains about 12 g/L lactic acid. Such solvent was prepared by saturating 200 mL of 21% TOPO-in-kerosene with equal volume of 88 g/L lactic acid solution at around pH 4.0. Figure 3 shows the result of such an experiment in which the concentrations of lactic acid in the alkali and in the spent solvent phases are plotted as a function of the number of repeated back-extractions. With each repetition, the concentration of lactic acid in alkali increased linearly until it reached 119 g/L after 10 extractions. Lactic acid concentration in spent solvent remained low until ninth extraction when it rose to 1.8 g/L. This essentially suggests that lactic acid can be efficiently back-extracted from TOPO-in-kerosene. In addition, the partition coefficient of glucose between the aqueous and solvent phases was found to be only 0.002, implying a high selectivity for lactic acid.

Extraction Performance

A shell and tube type of membrane-module was constructed using polypropylene hollow fibers obtained from Hoechst-Celanese, Charlotte, NC. These fibers had an internal diameter of 400 μm, wall thickness of 25 μm, and pore size of 0.03 μm. The diameter of shell was 2.54 cm, and

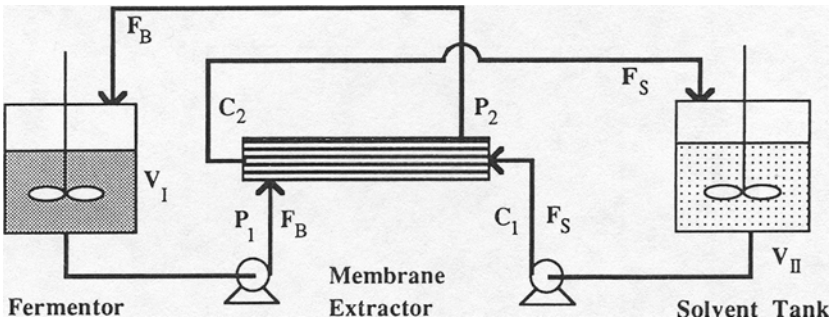

Fig. 4. Schematics of an experimental set-up for membrane characterization.

the fibers were uniformly spaced over a core of 0.7 cm. A total of 96 fibers were used in the module and effective fiber length was 23 cm. The total mass transfer area was about 0.03 m^2 and it was confirmed by the measurements of water flux and comparing it with the standard curves provided by Hoechst-Celanese. This membrane-module was tested using an experimental setup, schematically shown in Fig. 4. The shell-side was connected to the lactic acid tank and solvent was pumped from the tube side. Owing to the hydrophobic nature of the membrane, solvent wets the pores and easily leaks into the aqueous phase. This, however, can be avoided by having a positive pressure differential (1–2 psi in this work) between the aqueous phase and solvent phases. Excessive pressure differential leads to reversal of leakage. The exit streams from the module were recycled to their respective reservoirs and the concentrations of lactic acid in these were measured at regular intervals. The results of these experiments are presented in Figs. 5–7.

In the first experiment, a solution of 21% (w/v) TOPO-in-kerosene was used as solvent. The experimental conditions and the measured concentrations are presented in Fig. 5 as points. Since a recycle system was used, the results showed a saturation type of behavior that was consistent with the experimentally measured distribution coefficients for the conditions of the experiment. The solid curves in Fig. 5 were obtained by numerical simulations of the governing equations for the system. The general governing equations are presented in Table 4. The notations are identified in Fig. 4; F represents the flow rates; P and C, the concentrations of total lactic acid in aqueous phase and solvent phase, respectively; and V, the volumes. The equations for P_2 and C_2 were derived based on a plug flow mass transfer model (not shown here) between solvent and broth in the extraction module. The mass transfer coefficients (K_o, k_C, k'_c) are defined in Table 5. For the experiment shown in Fig. 5 (no alkali in the solvent), $P_a = k_c = \phi_D = k'_c = 0$. The simulation results with $\beta = 1.0$ are in good agreement with the experimental observations. The discrepancies between the two after 5 h of operation can be explained by the physical observations of the loss of some fibers as a result of particulate matter present in the unfiltered kerosene used in this experiment.

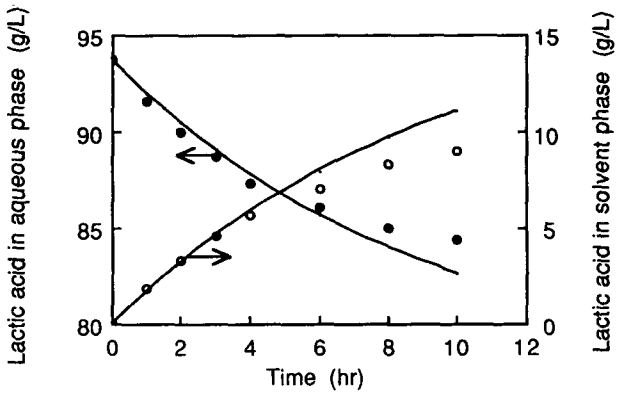

Fig. 5. Batch extraction of lactic acid by 21% (w/v) TOPO-in-kerosene in a membrane extractor without back extraction (F_B=1.665 L/h; F_S=0.792 L/h; T=40°C; pH=4.0; 96 fiber tubes).

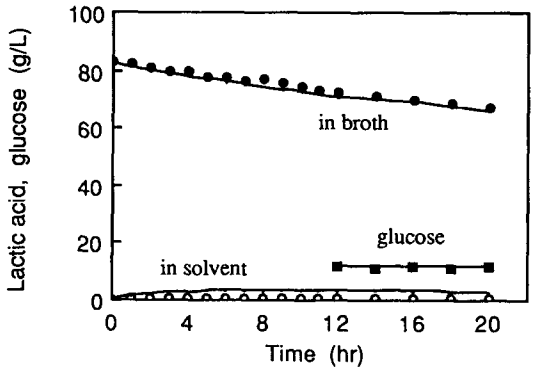

Fig. 6. Batch extraction of lactic acid by 21% (w/v) TOPO-in-kerosene in a membrane extractor with back extraction (F_B=2.30 L/h; F_S=0.206 L/h; T=40°C; pH=4.0; 64 fiber tubes; d_p=600 μm).

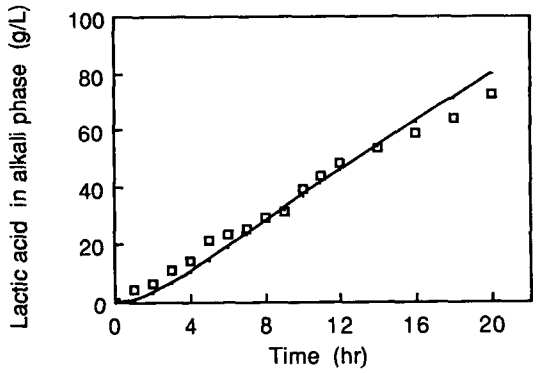

Fig. 7. Lactic acid concentration in alkali phase in a back extraction equipment (d_p=600 μm).

Table 4
Governing Equations for Batch Cocurrent Extraction
of Lactic Acid in a Recycle Membrane Extractor

$$\frac{dP_1}{dt} = -\frac{F_B}{V_I}(P_1 - P_2)$$

$$\frac{dC_1}{dt} = \frac{F_S(C_2 - C_1)}{V_{II}} - \frac{k_c a_d C_1 (V_{II} + V_{III})}{V_{II}}$$

$$\frac{dP_a}{dt} = \frac{k_c a_d (V_{II} + V_{III}) C_1}{V_{III}}$$

$$P_2 = B_1 e^{\lambda_1 L} + B_2 e^{\lambda_2 L}$$

$$C_2 = \frac{F_B\left(B_1 \lambda_1 e^{\lambda_1 L} + B_2 \lambda_2 e^{\lambda_2 L}\right)}{K_o n \pi d_o} + m P_2$$

$$\lambda_1 = \frac{-a + \sqrt{a^2 - 4b}}{2}; \qquad \lambda_2 = \frac{-a - \sqrt{a^2 - 4b}}{2}$$

$$a = \frac{K_o n \pi d_o}{(1 - \phi_D) F_S} + \frac{K_o n \pi d_o m}{F_B} + \frac{k_c' a_d A_c}{(1 - \phi_D) F_S}; \qquad b = \frac{K_o n \pi d_o k_c' a_d A_c m}{(1 - \phi_D) F_S F_B}$$

$$B_1 = -\frac{(F_B \lambda_2 + K_o n \pi d_o m)}{F_B(\lambda_1 - \lambda_2)} P_1 + \frac{K_o n \pi d_o}{F_B(\lambda_1 - \lambda_2)} C_1$$

$$B_2 = \frac{(F_B \lambda_1 + K_o n \pi d_o m)}{F_B(\lambda_1 - \lambda_2)} P_1 - \frac{K_o n \pi d_o}{F_B(\lambda_1 - \lambda_2)} C_1$$

$$A_c = \frac{\pi}{4} d_i^2 n$$

A second experiment was conducted with an emulsion of 2*N* NaOH in 21% TOPO-in-kerosene. The volume fraction of alkali in the solvent phase was 0.2. The kerosene used in this experiment was prefiltered through a 0.2 μm filter. The results of this experiment are presented in Figs. 6 and 7. Figure 6 shows the concentrations of lactic acid in the aqueous phase and the solvent phases. Solid lines show the results of numerical simulation. The simulations assume no alkali droplets in the membrane module ($k_c'=0$). The diameter of alkali droplets in the solvent reservoir was assumed to be 600 μm. Alkali droplets in the solvent phase effectively strip lactic acid from the solvent; as a result, the concentration of lactic acid in the solvent

Table 5
Correlations for Mass Transfer Coefficients

Overall mass transfer coefficient:
(based on the external surface area of tubes)

$$\frac{1}{K_o} = \frac{m}{k_s} + \frac{d_o}{d_{lm}\, k_m} + \frac{d_o}{d_i\, k_t}$$

Shell-side mass transfer coefficient [23]:

$$k_s = \beta\ (1-\phi)\ D^{0.67}\ d_H^{0.6}\ \nu^{0.66}\ L^{-1}\ \eta^{-0.33}$$

Membrane-side mass transfer coefficient [24]:

$$k_m = D\ \frac{\varepsilon}{\tau_m\, w}$$

Tube-side mass transfer coefficient [25]:

$$k_t = 1.62\ D^{0.67}\ \nu^{0.33}\ d_i^{-0.34}\ L^{-0.33}$$

Mass transfer coefficient between solvent and aqueous phase in the tank [26]:

$$\frac{k_c\, d_p}{D} = 2 + 0.31\left(\frac{\mu_c}{\rho_c\, D}\right)^{1/3}\left(\frac{d_p^3\ \rho_c\ g\ \Delta\rho}{\mu_c^2}\right)^{1/3}$$

Mass transfer coefficient between solvent and aqueous drops in the tubes:

$$\frac{k_c\, d_p}{D} = 2$$

stayed negligible. After 12 h of operation, glucose was added to the membrane assembly to detect any leakage through membrane. This concentration in broth stayed unchanged. Glucose was also not found in alkali phase, confirming the integrity of the membrane module.

The experimental and simulated concentrations of lactic acid in the alkali phase are presented in Fig. 7. The discrepancy between these two may be related to poor mixing in the solvent reservoir and a lack of accurate knowledge of droplet diameter. This is being investigated. The comparisons between theoretical calculations and experimental results suggest the validity of mass transfer correlations. The relatively small amounts of total lactic acid removal observed in these experiments was a consequence of the small area of mass transfer (0.03 m^2) used in this study.

Table 6
Comparison of the Electrodialysis Performance
[8] with the Simulation Results of Extraction Processes#

	Electrodialysis@ (immobilized)	Extraction* back[a]	Extraction* back/drops[b]
Total lactic acid produced	42.1 g	44.7 g	45.1 g
Concentration of lactic acid			
in Broth (g/L)	12.1 (330 ml)	11.4 (500 ml)	3.6 (500 ml)
Dialysate (g/L)	55.4 (670 ml)	-	-
Alkali (g/L)	-	97.5 (400 ml)	108.3 (400 ml)
Beads (g/L)	9.0 (100ml)	-	-
Concentration of Residual (g/L) glucose	18.2 (330 ml)	0.0 (500ml)	0.0 (500ml)
Time of fermentation (hrs)	120	85	90
Productivity (g/L/hr)	0.35	0.41	0.42

#: mass transfer area = 0.03 m^2,
circulating flow rates for broth and solvent = 0.51 L/hr.
@: *Lactobacillus delbrueckii* IFO 3534
*: solvent contains 10% (v/v) alkali phase (*Lactobacillus delbrueckii* NRRL-B445).
a: back extraction without alkali droplets in membrane fiber tubes (pH=4.6).
b: back extraction with alkali droplets in membrane fiber tubes (pH=4.4).

The theoretical computations suggest that increasing the area of mass transfer to 0.2 m^2 would be desirable.

A Comparison with Electrodialysis

Nomura et al. (*8*) have recently published a study of an electrodialytic process for recovery of lactic acid from fermentation broths. These results have been used in a simulative study to compare the performance of extractive and electrodialytic processes. The simulations of the extractive processes were conducted by coupling the governing equations of the membrane extractor (Table 4) with the appropriate equations for growth and product formation in a fermentor. The kinetics of the fermentation were simulated using a model (*27*) developed from the data of Luedeking and Piret (*28*). As in the experiment of Nomura et al. (*8*), a batch operation was considered. In order to compare the two processes on the same basis, except the operating pH and microorganisms, it was decided to use a membrane assembly having the same area of mass transfer as the one used by Nomura and coworkers. The initial concentration of carbohydrates was also considered the same. The results of such an exercise are presented in Table 6. Electrodialysis data are those presented

by Nomura et al. The concentrations are reported after 120 h of operation. The productivities are also calculated on the basis of 120 h of operation, even though the extractive fermentation was over in 85 h. This comparison clearly demonstrates the desirability of nondispersive extraction, which provides a more concentrated product stream in the form of lactate solution at a higher productivity, and a better utilization of substrates. The predictions of the extraction system, however, need to be demonstrated through experimentation.

CONCLUSIONS

Extraction through membrane fibers appears to be a viable process for recovering lactic acid from fermentation broths. Its success, however, depends on the right choice of solvent and the membrane assemblies. In our experiments, no damage to the membrane material was observed. However, postexperiment handling did result in some clogging of the membrane pores owing to formation of TOPO crystals whenever the membrane was exposed to air. Both TOPO/kerosene as well as lacticacid adversely affected the epoxy used for potting the membrane assembly. Attempts are underway to improve their performance. The existing correlations of mass transfer across the membrane appear to hold for membrane extraction too. Membrane fouling by proteins remains to be investigated.

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