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Separation and Purification Technologies for Lactic Acid – A Brief Review

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Lactic acid is an important platform chemical with a wide range of applications. Production of lactic acid by fermentation is advantageous because renewable and low cost raw materials can be used as substrates. After fermentation, the broth needs to be purified to obtain pure lactic acid for further uses. Thus, efficient downstream processes are very important because they account for 50% of the production costs. This review discusses different processes that are currently employed for lactic acid recovery, focusing on precipitation, solvent extraction, and separation with membranes. Advances in such recovery processes and drawbacks that limit the application of these technologies at the industrial level are also presented.

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INTRODUCTION

Lactic acid (LA) is an alpha-hydroxy acid with dual functional groups, making it suitable for use in a variety of chemical transformations and products (Biddy *et al.* 2016). LA is used globally for applications in food, pharmaceutical, textiles, cosmetics, and chemical industries. Demand for LA has grown dramatically in recent years due to its potential as a building block for the production of poly-lactic acid (PLA) materials (Abdel-Rahman and Sonomoto 2016) and use as feedstock to produce green solvents. Global LA and PLA demands are expected to reach 1,960.1 and 1,205.3 kilo tons, respectively, by 2020 (Grand View Research 2015).

There are two processes used in LA production: chemical synthesis and carbohydrate fermentation. Chemical synthesis produces only a racemic mixture of LA using acetaldehyde as a starting material. Musashino Chemical Laboratory, Ltd., in Tokyo, Japan, is the sole producer of synthetic LA, producing on the order of approximately 7,000 metric tons per year (Biddy *et al.* 2016; Musashino Chemical Laboratory 2017).

Fermentation is preferred for the production of LA, and about 90% of LA is produced by fermentation (Joglekar *et al*. 2006). In fermentation, the substrates for LA production can be renewable and can utilize low cost raw materials such as starchy materials (Wang *et al.* 2010; Li *et al.* 2012; Nakano *et al.* 2012; Prückler *et al.* 2015), sugarcane (Laopaiboon *et al.* 2010), whey (Tejayadi and Cheryan 1995; Kim *et al.* 2006; Li and Shahbazi 2006), glycerol (Kishida *et al.* 2005; Yin *et al.* 2016), and microalgae (Nguyen *et al.* 2012). Cellulac, Purac, and NatureWorks are researching ways to use lignocellulosic biomass as a carbohydrate source to produce lactic acid (Biddy *et al.* 2016).

Traditionally, several steps of purification are needed after fermentation to produce the final LA product (Biddy *et al.* 2016). Separation and final purification stages account for up to 50% of the production costs (Komesu *et al.* 2015). Besides the high cost of these

steps, it is very difficult to obtain high purity LA, mainly due to its high affinity with water, decomposition at elevated temperatures, and energy-intensive recovery process (Järvinen *et al.* 2000).

A considerable amount of research has been conducted to find an attractive separation technique for the recovery of LA from fermentation broth. Although there are several methods for LA recovery, such as precipitation, distillation, solvent extraction, adsorption, and membrane separation processes (reverse osmosis, electrodialysis, and ultrafiltration), *etc*., many drawbacks still exist for their industrial application. The drawbacks include high equipment costs, solvent recovery, and high energy consumption. Table 1 compares the several methods used for separation and recovery of LA from fermentation broth.

In this work, information about the different technologies and processes that are currently employed for LA recovery such as precipitation, solvent extraction, and separations with membranes are reviewed. Molecular distillation and reactive distillation were reviewed in previous work (Komesu *et al.* 2016).

Table 1. Advantages and Disadvantages of Separation Processes for Lactic Acid Recovery (Komesu *et al.* 2016)

Separation process	Advantages	Disadvantages
Precipitation	- Easy applicable in industrial plants - Simple operation	- High sulfuric acid consumption - Generation of gypsum, which requires landfill disposal - Low product purity
Liquid-liquid extraction	- No generation of gypsum - Reduction in the risk of thermal decomposition	- Extractant needs to be regenerated by distillation or back-extraction (stripping) - Product purity is not high - Conventional extraction agents show very unfavorable distribution coefficients
Membrane processes	- Great flexibility in scale of production - High selectivity - High levels of purification - Possibility of integration with conventional fermenters, reducing the equipment investment cost	- High cost of membranes - Membrane fouling - Polarization problems - Difficult to scale up
Molecular distillation	- Reduction in the risk of thermal decomposition - High levels of purification - No use of solvents - No further purification is needed	- Difficult to scale up - Requires high vacuum conditions
Reactive distillation	- Integration of reaction and separation in the same apparatus - High levels of purification - Lower energy consumption	- Process is complex - Applied specifically to reversible chemical reactions in the liquid phase - Applications are limited to systems in which the reaction rates are fairly high and there is no mismatch of temperatures favorable for reaction and separation - Corrosion and separation problems by the use of homogeneous catalyst

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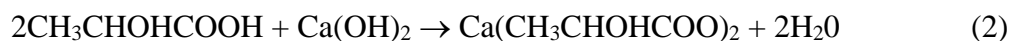## NEUTRALIZATION AND PRECIPITATION OF SALT WITH ACID

Separation by precipitation is the most conventional primary purification step in LA production by fermentation. In this method, excess calcium carbonate or calcium hydroxide is added to the fermenter to neutralize the acid produced, maintaining the pH around 5 to 6, and producing a calcium salt of the acid, the calcium lactate (Datta and Henry 2006; Kumar *et al.* 2010). Neutralization is performed because high concentrations of LA and low pH have inhibitory effects on cellular metabolism through the highly protonated form of LA. LA can traverse the cell membrane and lead to increased intracellular accumulation of LA, which disrupts the cell membrane (Grabar *et al.* 2006; Abdel-Rahman and Sonomoto 2016).

In the process, the fermentation broth is treated with sulfuric acid to precipitate the calcium sulfate or gypsum, which is filtered. The filtrate containing free organic acid is evaporated to obtain the pure LA (Fig. 1). The steps of chemical reactions involved are shown below (Eqs. 1 through 3).
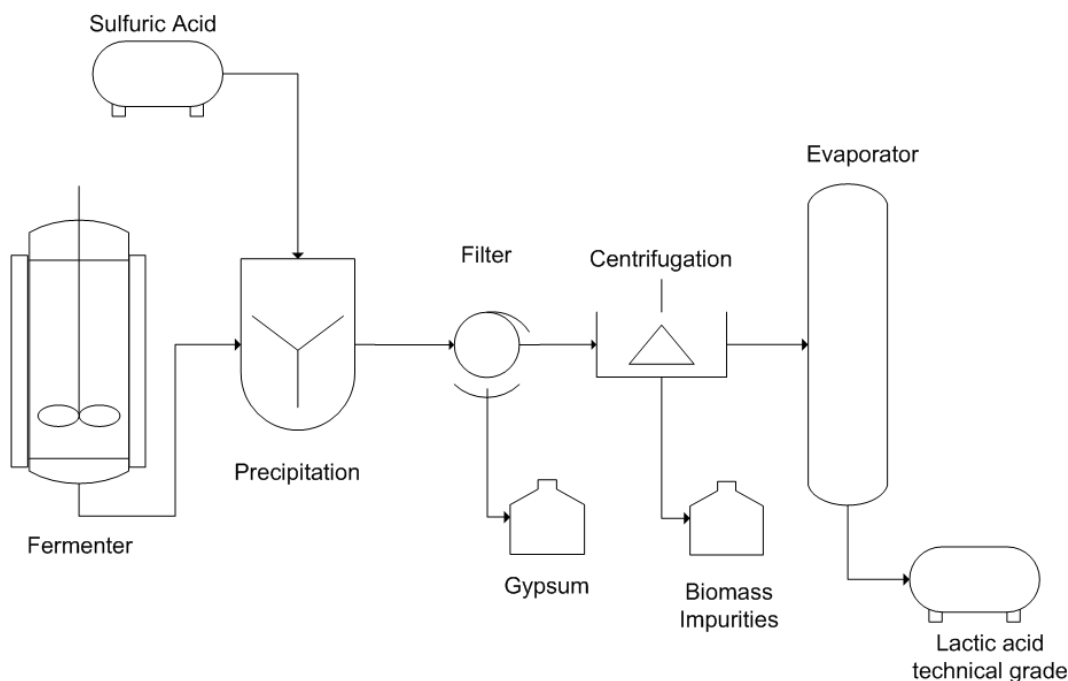
- Production of lactic acid
$$C_6H_{12}O_6 \rightarrow 2CH_3CHOHCOOH \tag{1}$$

- Neutralization
$$2CH_3CHOHCOOH + Ca(OH)_2 \rightarrow Ca(CH_3CHOHCOO)_2 + 2H_2O \tag{2}$$

- Acidification
$$Ca(CH_3CHOHCOO)_2 + H_2SO_4 \rightarrow 2CH_3CHOHCOOH + CaSO_4 \tag{3}$$

Fig. 1. General schematic for lactic acid recovery by precipitation

LA technical grade (22% to 44%) is obtained using precipitation. However, for higher value added applications, LA with high purity and thermal stability are required. For high-purity product, the technical-grade LA is esterified with methanol or ethanol, and

the ester is recovered by distillation, hydrolyzed with water, evaporated, and the alcohol recycled (Datta and Henry 2006). Pure LA can be obtained by conversion of calcium lactate to zinc lactate using sulphate or zinc carbonate, and zinc lactate is recrystallized and dissolved in water. Subsequently, zinc is precipitated as zinc sulfide using a solution of hydrogen sulfide (Trindade 2002). LA solution is clarified with coal, filtered, and vacuum evaporated. Zinc salt is the most suitable for this operation because it crystallizes better than any other lactate (Pereira 1991).

Process improvements have been developed by researchers as described in Table 2. Nakano *et al.* (2012) studied the effects of $Ca(OH)_2$, NH_4OH, and $NaOH$ as neutralizing agents for efficient recovery of LA. The study showed that $Ca(OH)_2$ is an effective neutralizing agent in fermentation of broken rice using *Lactobacillus delbrueckii*. The maximum yields of LA reached with $Ca(OH)_2$, NH_4OH, and $NaOH$ were 3.59 $g \cdot L^{-1} \cdot h^{-1}$, 1.51 $g \cdot L^{-1} \cdot h^{-1}$, and 1.40 $g \cdot L^{-1} \cdot h^{-1}$, respectively. $Ca(OH)_2$ is industrially used in the production of D-(-) lactic acid because calcium hydroxide is easily recovered by precipitation and is relatively cheaper than NaOH and NH_4OH. In addition, the divalent cation (Ca^{2+}) was more effective in neutralizing the cultures compared to monovalent (Na^+ and NH_3^+) cations (Nakano *et al*. 2012). Kwak *et al.* (2012) studied the addition of methanol during the acidification of ammonium lactate with sulfuric acid. Ammonium lactate was formed using ammonia hydroxide to neutralize the fermentation broth. By adding sulfuric acid, ammonium sulfate, and LA were produced. The addition of methanol during the process decreased the solubility of ammonium sulfate in the broth, facilitating their separation by simple filtration, and promoted esterification of LA with methanol to form methyl lactate, at room temperature and yield higher than 80%. The methyl lactate obtained can be easily distilled to obtain LA.

Data from the industrial recovery process are limited in open sources. Ecochem Inc., a Du Pont–Conagra partnership, had developed a recovery and purification process that produced a by-product ammonium salt instead of insoluble gypsum cake, and the company intended to sell this as a low-cost fertilizer (Datta and Henry 2006). The process was unsuccessful and was abandoned due to problems in the separation steps. Cargill developed an alternative process using sodium carbonate as a neutralizing agent and tertiary amine for extraction. The sodium lactate formed with the addition of sodium carbonate was concentrated and extracted with a tertiary amine solvent mixture under CO_2 pressure to produce and precipitate a sodium bicarbonate salt and an amine LA extract. This was back-extracted with hot water at 140 °C and 100 psig to produce a LA solution and a regenerated amine solvent mixture that is recycled. LA was then purified and used for polymer manufacturer (Datta and Henry 2006). ZeaChem, Inc. developed a process which fermentation broth was neutralized with calcium carbonate to produce lactate salt, which was acidified with nitric acid, recovering LA and producing calcium nitrate. LA was recovered from medium and calcium nitrate reacted with ammonium carbonate to produce ammonium nitrate and calcium carbonate. The ammonium nitrate was processed as fertilizer (Verser and Eggeman 2006).

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Table 2. Neutralization/Precipitation of Lactic Acid in Several Studies

Study	Fermentation process	Results	Advantages	Reference
Effects of $Ca(OH)_2$, NH_4OH, and NaOH as neutralizing agents for efficient recovery of lactic acid	Substrate: Broken rice. Microorganism: *Lactobacillus delbrueckii*.	● Maximum productivities of lactic acid reached with $Ca(OH)_2$, NH_4OH, and NaOH were 3.59, 1.51, and 1.40 $g \cdot L^{-1} \cdot h^{-1}$, respectively. ● Lactic acid concentrations with $Ca(OH)_2$, NH_4OH, and NaOH were 79.0, 63.3, and 64.1 g l^{-1}, respectively.	● $Ca(OH)_2$ is an effective neutralizing agent. ● $Ca(OH)_2$ is easily recovered by precipitation and is relatively cheaper than NaOH and NH_4OH.	Nakano *et al.* 2012
Addition of methanol during acidification of ammonium lactate	Substrate: Glucose Microorganism: *Lactobacillus paracasei*	● The addition of methanol during the acidification process of ammonium lactate decreased the solubility of ammonium sulfate in the broth, facilitating their separation by simple filtration. ● Methyl lactate was produced at room temperature and yield higher than 80%.	● Simple and cost effective. ● Process can be carried out at room temperature without complicated equipment. ● Ammonium sulfate byproduct can be utilized for production of sulfuric acid and ammonia. ● Methyl lactate obtained can be easily distilled to obtain lactic acid.	Kwak *et al.* 2012
Purification with magnesium lactate	Substrate: crude carbohydrate sources such as molasses Microorganism: not indicated	● Producing cheap lactic acid liquors from molasses. ● Magnesium reagent can be economically recovered and reused. ● Production of high grade lactic acid from the recovered magnesium lactate.	● Magnesium lactate is recovered in high purity. ● Magnesium lactate crystallization results in higher recovery than calcium lactate.	Eli 1969
Effect of operating parameters on precipitation of lactic acid from calcium lactate fermentation broth	Substrate: commercial fermentation broth Microorganism: *Lactobacillus paracasei*	● Mixing of the calcium lactate solution facilitated the precipitation process. ● Activated carbon was found to be the most effective adsorbent for the removal of pigment from the recovered lactic acid after the precipitation process.	● High yield (92%) could be achieved in recovering lactic acid from fermentation broth.	Min *et al.* 2011
Multiple crystallizations in order to obtain high purity lactic acid	Substrate: not indicated Microorganism: not indicated	● Remove the soluble impurities from the fermentation medium. ● Calcium sulfates liberated after treatment with sulfuric acid.	● High purity lactic acid	Ajioka and Suizu 1998
Purification and recovery using base of alkaline and precipitation with sulfuric acid	Substrate: not indicated Microorganism: not indicated	● Fermentation liquid is heated to dissolve all calcium lactate and treated with stoichiometric amounts of sulfuric acid. The resulting calcium sulfate is separated by filtration with through washing of the filter cake.	● Pure lactic acid (food quality) with a concentration of 80 %.	Rauch *et al.* 1960

Separation of LA by precipitation has several disadvantages. There is high cost of reagents, filtration process, and other separation processes, especially when a product of higher purity is required. From an environmental standpoint, large amounts of wastewater are generated. Furthermore, to produce one ton of LA approximately one ton of low-cost calcium sulfate is generated (Pal *et al.* 2009). Neutralizing agents can be avoided if acid-tolerant strains are used in LA fermentation. In this case, gypsum is not produced. Liaud *et al.* (2015) obtained the first *Aspergillus* strains able to produce large amounts of LA by inserting recombinant *ldhA* genes from *R. oryzae* into a wild-type *A. brasiliensis* strain. The strain produced 32.2 g/L of LA, with a yield of 0.44 g/g from glucose in fed-batch fermentation with a final pH of 3.2 (Abdel-Rahman and Sonomoto 2016). The advantages of these strains are they can grow at low pH and utilize cheap abundant carbon sources such as plant biomass (Liaud *et al.* 2015). Another option to overcome the pH inhibition is the *in situ* removal of LA to prevent microorganism inhibition using conventional electrodialysis, solvent extraction, adsorption, and membrane bioreactors (Abdel-Rahman and Sonomoto 2016).

In sum, research to find other methods to avoid the inhibitory effects on cellular metabolism by LA and to avoid production of large amounts of gypsum by using of neutralizing agents is required.

SOLVENT EXTRACTION OR LIQUID-LIQUID EXTRACTION

Liquid-liquid extraction or solvent extraction has been proposed as an alternative to the classical precipitation process (Kumar *et al.* 2010). A general schematic is show in Fig. 2.
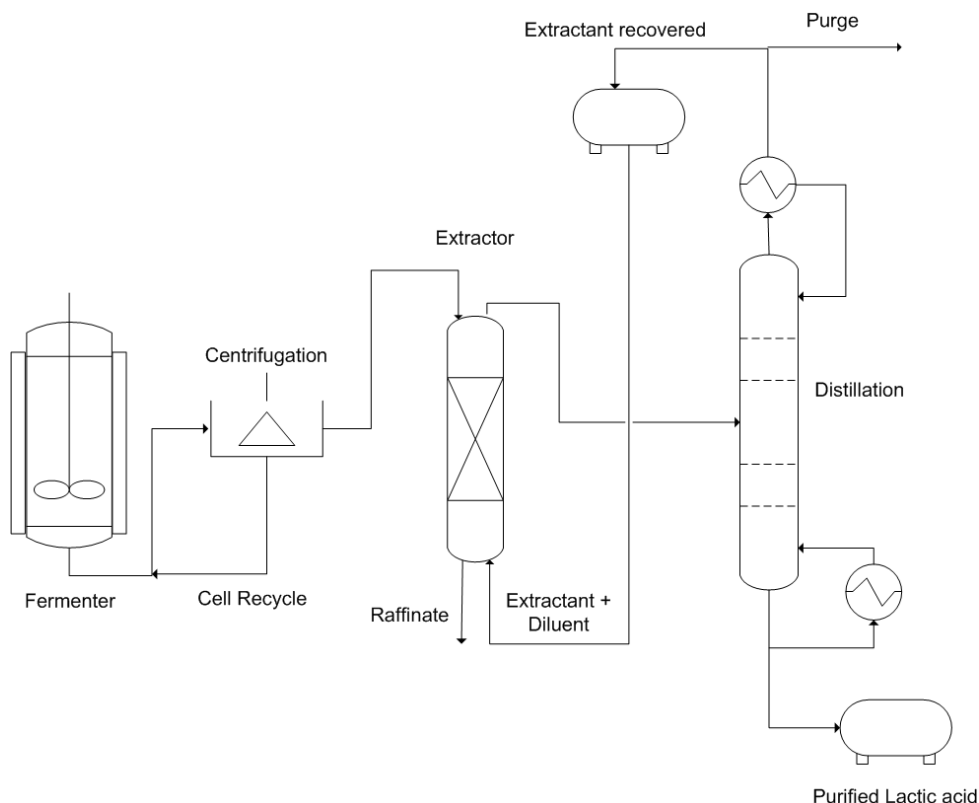
Fig. 2. General schematic for lactic acid recovery by solvent extraction

Solvent extraction is the process in which one or more solutes are removed from a liquid mixture by transferring the solute(s) to a second liquid phase immiscible formed introducing a solvent. Therefore, separation is based on difference in solubility of the solute in the two liquid phases (Wankat 2007). Other important factors are the distribution coefficients (ratio of the LA concentration in solvent phase to aqueous phase), easy separation of the liquid phase, selectivity of the extractant, and choice of solvent extraction. The solvent (or extractant) partially dissolves certain species of the liquid feed, effecting at least a partial separation of the feed components (Seader *et al*. 2011). Characteristics for solvent choice include: selectivity, chemically stable, regenerable, low corrosivity, low toxicity, and low viscosity (King 1980). Diluents are used when the extractants have high viscosity. In addition, they enhance the extracting power of the solvent.

Many studies have been developed over the years to improve solvent extraction. Vaidya *et al*. (2005) classified the types of extractant solvents as:

1. Conventional oxygen-bearing hydrocarbons, such as octanol and methyl isobutyl ketone (MIBK).
2. Phosphorus-bonded oxygen-bearing solvents, such as tributyl phosphate.
3. High molecular weight aliphatic amines, such as dodecyl amine.

The fundamental requirement of a good extractive solvent is a high distribution coefficient (Vaidya *et al*. 2005). Conventional oxygen-bearing hydrocarbons have very low distribution coefficients. In addition, phosphorus-bonded oxygen-bearing solvents have not high enough distribution coefficients to extract LA efficiently. Extractants from the third type, high-molecular-weight amines, are the most effective ones (Vaidya *et al*. 2005). The chemical reactions involved depend on the solvent selected. For example, liquid-liquid extraction of lactic acid (LA) with the tertiary amine Alamine 336 (B) gives a reaction complex (BLA) which remains in the organic phase and may be represented by Eq. 4 (Wasewar *et al.* 2002b):

$$LA_{aq} + B_{org} \leftrightarrow BLA_{org} \tag{4}$$

LA can be separated from the solvent and purified using solvent extraction or distillation (Fig. 2). Table 3 summarizes the reported results for various extractants.

Pereira (1991) studied the LA extraction with the solvents ethyl ether, ethyl acetate, hexanol, isoamyl alcohol, and furfural. Solvents were selected to present higher affinity to LA and little or no affinity to water. Ethyl ether showed the highest selectivity, followed by ethyl acetate, hexanol, isoamyl alcohol, and furfural. Because of risks associated with handling, the ethyl ether was not advisable for use as industrial solvent. Ethyl acetate showed great application potential. The difference in selectivity between hexanol and isoamyl alcohol was not very significant. So, alcohol was chosen as the solvent for LA purification. Malmary *et al.* (2000) studied LA recovery using tributylphosphate as extractant and dodecane as solvent. The high viscosity of tributylphosphate necessitated the use of a low viscosity, water-insoluble solvent. Tributylphosphate was selected because, when compared with other solvents such as ketones, alcohols, and ethers, tributylphosphate had higher partition coefficient of carboxylic acids. The results are promising, but the viscosity of tributylphosphate needs to be reduced to avoid excessive energy consumption (impellers and pump) and to improve the phase settling in continuous

extractors. However, the use of a solvent with low miscibility in aqueous phase (0.039 mass %) minimizes environmental pollution.

Table 3. Solvents Used in Liquid-Liquid Extraction (Joglekar *et al.* 2006 Adapted)

Extractant	Diluent	LA Initial Concentration	Distribution Coefficient	Reference
Tri-n-octylamine-Tripropylamine (2:8 w/w) 1 mol/kg	1-Octanol/n-heptane (3:7 w/w)	20% w/w	0.8	Hong and Hong 1999
Tri-*n*-butyl phosphate (TBP)	-	20% LA	0.95	Han *et al.* 2000
Tri-n-octylamine (1 M)	Chlorobutane	LA (2.3 mol/L)	1.4	Han and Hong 1998
Alamine 336 0.3 mol/L	MIBK	1.3 mol/L LA	8.13	Tamada *et al.*1990
50 % Alamine 336	Oleyl alcohol	10 g/L LA	13	Inci and Aydin 2003
50 % Alamine 336	Oleyl alcohol	100 g/L LA	4	Inci and Aydin 2003
Alamine 336 (40% v/v)	MIBK	1.6 mol/L LA	4.24	Wasewar *et al.* 2002a
Alamine 336 (30% v/v)	Octanol	0.38 kmol m^{-3}	25.95	Wasewar *et al.* 2003
Alamine 336 (40% v/v)	Decanol	0.76 kmol m^{-3}	23.37	Wasewar *et al.* 2002b

Krzyzaniak *et al.* (2013) studied novel extractants for the recovery of fermentation derived LA. The aim of this study was to develop extractants with a higher affinity for carboxylic acids than trioctylamine. Functionalized silica compounds showed functional groups containing multiple nitrogen-based functionalities, and at least one double bond between nitrogen and carbon displayed higher acid affinity than the single tertiary amine functional group as present in trioctylamine. Highest distribution coefficients of LA were observed for N, N didodecylpyridin-4-amine (27 *versus* 11 for trioctylamine at 25 °C).

Alkylamine extractants are effective for the removal of carboxylic acids from aqueous solutions. The alkylamine most used for LA extraction is alanine 336, which is a mixture of tri-n-octylamine and tri-n-dodecylamine (Trindade 2002). Alanine 336 has high viscosity, requiring the addition of diluents such as methyl isobutyl ketone (MIBK) (Wasewar *et al*. 2002a), hexane (Matsumoto *et al*. 2003), decanol (Wasewar *et al*. 2002b), dodecane (Malmary *et al*. 2000), and kerosene (Alkaya *et al*. 2009).

Solvent extraction requires a high exchange area for efficient separation, resulting in high costs of equipment and solvent recovery in stripping steps. In addition, the high toxicity of the extractant to the microorganisms limits its application to in situ extractive fermentation (Gao *et al.* 2009).

Over the past 30 years, many studies have investigated in the area of separation products based on fermentation. Despite these efforts, liquid-liquid extraction is not generally applied in industrial processes because conventional extraction agents have unfavorable distribution coefficients for organic acids (Kurzrock and Weuster-Botz 2010) and extractant of low toxicity and high extractability is indispensable for an efficient process (Gao *et al.* 2009).

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SEPARATION WITH MEMBRANES

Membrane separation processes are based on the transfer of solutes through a semi-permeable physical barrier that separates two phases, restricting the transport of components from one phase to another. Chemical industry sectors that use membranes in their processes are very diverse: biotechnology, water treatment, food, pharmaceutical, *etc*. The advantage of membranes in these cases refers to the specificity and low power consumption.

Since 1960, membrane separation processes have been suggested as an alternative for LA extraction (Prado-Rubio 2010). Advances in separation and purification based on membranes, particularly microfiltration, ultrafiltration, and electrodialysis technology allowed the creation of new production processes, which do not produce a salt residue (Datta and Henry 2006), instead of the traditional precipitation process of LA. Various studies of LA recovery using membranes are shown in Table 4. A general schematic diagram for LA separation by membranes is shown in Fig. 3.
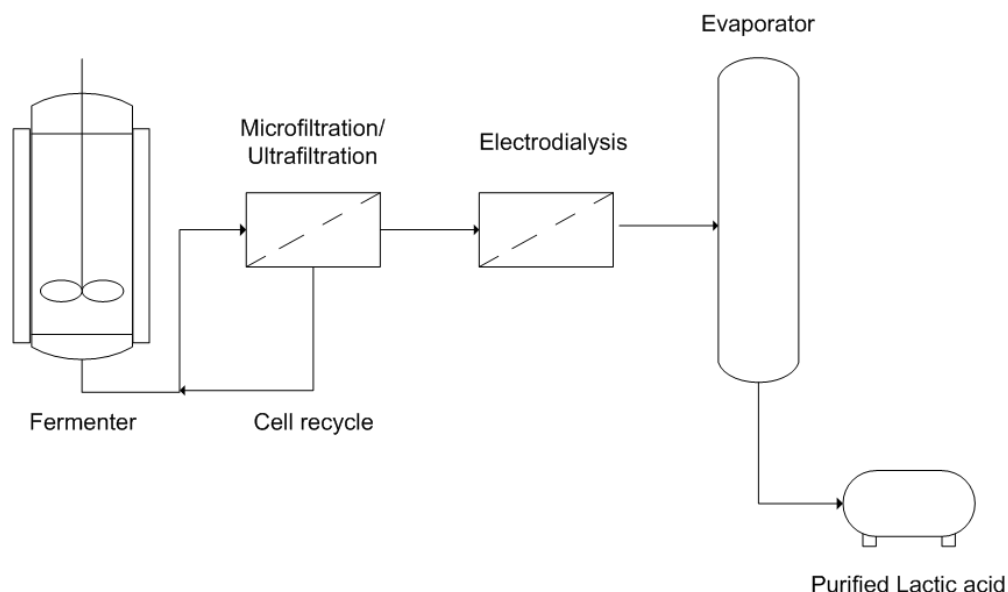
Fig. 3. General schematic for lactic acid recovery by membranes

Electrodialysis is a separation method employing selectively permeable cationic and anionic exchange membranes. These membranes are alternately arranged between the cathode and the anode; by applying an electric potential between the electrodes, cations migrate to cathode and anions to the anode. Membranes used in electrodialysis are polymeric, non-porous, and have a thickness between 10 and 500 µm (Porciúncula 2007). Electrodialysis is applied to remove salts from solutions or to concentrate ionic substances (Hábová *et al*. 2004). A special type of configuration is electrodialysis with bipolar membranes. These membranes can dissociate the water molecule into protons (H^+) and hydroxyl ions (OH^-). Membranes can operate at approximately 80% of theoretical thermodynamic efficiency (Datta and Henry 2006).

Michigan Biotechnology Institute (MBI) and Argonne National Laboratory (ANL) developed a process that employs double electrodialysis, obtaining very promising results. This process uses electrodialysis desalting to remove the multivalent cations and to

concentrate the lactate salt. The electrodialysis unit with bipolar membranes is used for water separation, producing concentrated LA, and ammonia is recycled to process.

The electrodialysis desalination stage is very important because it provides an efficient and economical process operation. In this step, lactate salt is twice or more concentrated (8% to 10% in the broth to about 20% by weight). The product is purified, and the divalent ions are rejected with an efficiency of 98% to 99%. The recovery yield is high, and the energy consumption is low (0.33 kWh·kg^{-1}). This configuration with double electrodialysis showed great potential to promote an efficient and economical process for LA recovery and purification derived from fermentation without salt generation as a residue (Datta and Henry 2006).

Membrane separation processes offer great flexibility in scale of production depending on market demand. Because of high selectivity, membranes can ensure high levels of purification and separation. In addition, membranes can be integrated with conventional fermenters, allowing simultaneous production and purification, eliminating the need of additional separation units, and reducing the equipment investment cost (Pal *et al.* 2009). Despite its advantages, the high cost of membranes, polarization, and fouling problems limit the use of the electrodialysis processes in large scale. Therefore, more research should be done to optimize this process.

Table 4. Contribution to the Development of Lactic Acid Recovery using Separations with Membranes

Process	Contribution	Reference
One-stage electrodialysis with two-and there-compartment water-splitting	● High volumetric productivity (71.7 g·dm^{-3}·h^{-1}) of lactic acid. Viable alternative in terms of the improved effectiveness of the separation processes by reduction in capital and operating costs.	Kim and Moon 2001
Mono- and bi-polar electrodialysis	● Lactate was concentrated by mono-polar electrodialysis to a maximum of 150 g·L^{-1}. Current efficiency for bi-polar electrodialysis was in excess of 90%. Free lactic acid concentration reached a moderate of 160 g·L^{-1} while colour and other chemical impurities were significantly reduced.	Madzingaidzo *et al.* 2002
Conventional electrodialysis (CED) and ion substitution electrodialysis (ISED)	● Both electrodialysis operations removed over 95% of sodium ions from the feed solution. ISED operation is more efficient than the CED in the production of lactic acid from sodium lactate, due to the prevention of lactic acid loss. There is potential advantage of ISED over CED in a wide range of industrial application.	Choi *et al.* 2002
Ultrafiltration and nanofiltration membranes combined	● Nanofiltration membrane system has successfully separated lactic acid from lactose in cheese whey fermentation broth. When lactose retention reached 99% to 100%, as much as 64% of the lactic acid could be recovered in the permeate.	Li and Shahbazi 2006
Nanofiltration using two kinds of polyamide membranes	● Strong influence of pH on lactic acid transport through membranes was observed. pH value affected both rejection and permeate flux.	González *et al.* 2008
Bioreactor and ceramic microfiltration equipment	● Maximum yield and productivity of l(+)-lactic acid production reached 157.22 ± 3.42 g·L^{-1} and 8.77 ± 0.15 g·L^{-1}·h^{-1}, which were 4.23% and 315.64% higher than those of batch fermentation, respectively, when equal amount of sugar was consumed. Cost of l(+)-lactic acid production was successfully reduced	Lu *et al.* 2012

Process	Contribution	Reference
	about two-thirds by the increase of yield and productivity. Twelve rounds of cell-recycle fermentations were successfully achieved in the pilot system. The membrane filtration productivity reached to 61.27 ± 2.74 $L \cdot m^{-2} \cdot h^{-1}$ which increased 172.80%, while the cell damaging rate dropped to 3.88 ± 0.18%, which decreased 85.77% when compared with ultrafiltration. The ceramic membrane showed advantages compared to the tolerance temperature, pressure, and acid compared with the organic membrane ultrafiltration.	
Nanofiltration	● Nanofiltration unit did not produce products of high purity, and further treatment technology of lactic acid and the amino acid should be performed.	Ecker *et al.* 2012
Membrane-integrated bioreactor system	● Recycle membrane bioreactor operating with a cell concentration of 22 $g \cdot L^{-1}$ resulted in a productivity of 53 $g \cdot L^{-1} \cdot h^{-1}$, with a lactic acid concentration of 106 $g \cdot L^{-1}$, and a yield of 0.96 $g \cdot g^{-1}$. Operating cost could be reduced further by using a cheaper nitrogen source such as silk worm larvae or yeast autolysate and installing the lactic acid plant in the sugarcane-growing areas or by optimizing the recycle of nanofiltration retentate to the fermenter.	Sikder *et al.* 2012
Submerged membrane fermentation process	● Replacement of fermented medium using submerged hollow fibre membranes more than doubled the lactic acid production and cell growth.	Ramchandran *et al.* 2012
Three-stage membrane-integrated hybrid reactor system	● This modular design ensured high yield (0.96 $g \cdot g^{-1}$), productivity (12.4 $g \cdot L^{-1} \cdot h^{-1}$), concentration (250 $g \cdot L^{-1}$), and purity (95 %) in a very simple, environmentally friendly, compact, and flexible plant configuration reflecting all the major characteristics of high process intensification.	Pal and Dey 2013
Two-stage membrane-integrated hybrid reactor system	● The highest lactic acid concentration achieved after the final stage of nanofiltration was 66.97 $g \cdot L^{-1}$ at 13 $kg \cdot cm^{-2}$ operating pressure when the overall productivity reached 12.40 $g \cdot L^{-1} \cdot h^{-1}$. Developed model could successfully predict production, purification, and transport of lactic acid through two-stage membrane modules.	Dey and Pal 2013
Fermentation and separation integration system	● This novel approach overcame the problem of product inhibition and extended the cell growth period from 41 h to 120 h. Production of lactic acid was improved by 23% to 183.4 $g \cdot L^{-1}$. Overall yield and productivity for glucose were 0.97 $g \cdot g^{-1}$ and 1.53 $g \cdot L^{-1} h^{-1}$, respectively. These experimental results indicate that the integrated system could benefit continuous production of lactic acid at high levels.	Wang *et al.* 2014

CONCLUSIONS

1. The literature reports many lactic acid (LA) separation and purification technologies, but some drawbacks still limit the application of these technologies at industrial level.

2. Precipitation is the conventional method for LA recovery, but it is unattractive for economic and environmental viewpoint because it generates LA with low purity and solid waste residue.

3. Solvent extraction has the advantage of not generating a lot of waste as the precipitation method. However, it requires high exchange area, high cost with solvent recovery, and high toxicity of extractants, which limits the large-scale potential. Advances in solvent extraction, particularly with the novel extractants, have given promising results.

4. Membrane-based separation technologies have reported high selectivity, high levels of purification and separation. Despite its advantages, high cost of membranes, polarization, and fouling problems preclude the use of these processes.

5. LA produced by fermentation process has not been more profitable because of the high cost in separation process. To address this problem, the development of more efficient and viable separation technologies is needed.

ACKNOWLEDGEMENTS

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