Lactic Acid Production to Purification: A Review

Andrea Komesu,[a,*] Johnatt Allan Rocha de Oliveira,[b] Luiza Helena da Silva Martins,[a] Maria Regina Wolf Maciel,[a] and Rubens Maciel Filho [a]

Lactic acid is a naturally occurring organic acid that can be used in a wide variety of industries, such as the cosmetic, pharmaceutical, chemical, food, and, most recently, the medical industries. It can be made by the fermentation of sugars obtained from renewable resources, which means that it is an eco-friendly product that has attracted a lot of attention in recent years. In 2010, the U.S. Department of Energy issued a report that listed lactic acid as a potential building block for the future. Bearing the importance of lactic acid in mind, this review summarizes information about lactic acid properties and applications, as well as its production and purification processes.

Keywords: Lactic acid; Fermentation; Renewable resources; Separation processes

*Contact information: a: School of Chemical Engineering, University of Campinas, Box 6066, 13083-970, Campinas-SP, Brazil; b: Nutrition College, Federal University of Pará (UFPA), 66075-110, Belém-PA, Brazil; *Corresponding author: andrea_komesu@hotmail.com*

INTRODUCTION

Lactic acid, or 2-hydroxypropionic acid (CAS 50-21-5), is the most widely occurring hydroxycarboxylic acid (Datta and Henry 2006). It is a natural organic acid with a long history of applications in the food, pharmaceutical, textile, and chemical industries (Ouyang *et al.* 2013). In recent years, the demand for lactic acid has increased considerably because of its use as a monomer in the preparation of polylactic acid (PLA) (Abdel-Rahman *et al.* 2013; Ouyang *et al.* 2013; Shi *et al.* 2015), which is a biodegradable and biocompatible polymer that is used in a wide variety of applications. Its uses range from packaging and fibers to foams (Abdel-Rahman *et al.* 2013) and applications in biomedical devices (Lasprilla *et al.* 2012). Lactic acid can be produced by fermentation or chemical synthesis. Production by the fermentation process has attracted interest because of its advantages, which are the production of pure isomers (L(+)- or D(-)-lactic acid), use of renewable and low cost raw materials, low energy consumption, and mild conditions required for operation.

Lactic acid was first discovered in sour milk in 1780 by the Swedish chemist Scheele (Lima *et al.* 2001). In 1839, Fremy carried out lactic acid fermentation with various carbohydrates, such as sugar, milk, starch, and dextrin (Holten *et al.* 1971). In 1857, Pasteur discovered that lactic acid was not a component of milk, but a metabolite that certain microorganisms produced by fermentation (Benninga 1990).

In the last few decades, the production of lactic acid has substantially increased primarily because of the development of new uses and products. Global lactic acid demand was estimated to be 714.2 kilo tons in 2013, and it is expected to grow annually by 15.5% to reach 1,960.1 kilo tons by 2020 (Abdel-Rahman and Sonomoto 2016). The three largest consumer markets in the world are the United States (31% of total lactic acid consumption in 2013), followed by China and Western Europe. China surpassed Western Europe due to

export demand, as well as consumption in the food and beverage industry. The world's top three lactic acid manufacturers, which are Purac, Cargill and Henan Jindan Lactic Acid Technology Co., Ltd., boasted a combined capacity of 505,000 tons in 2013. Cargill mainly supplies lactic acid products to its subsidiary - NatureWorks for production of polylactic acid (PR Newswire 2016)

In 2010, the U.S. Department of Energy issued a report on the chemicals that are considered potential building blocks for the future (Jong *et al.* 2012), and lactic acid was included.

Bearing the importance of lactic acid in mind, this review summarizes information about lactic acid properties and its applications. Production and purification processes are also discussed.

LACTIC ACID PROPERTIES

Lactic acid is a yellow to colorless liquid (at 15 °C and 1 atm), and is odorless. It is the simplest hydroxycarboxylic acid. Thermodynamic properties are shown in detail in Table 1.

Table 1. Thermodynamic Properties of Lactic Acid (Holten *et al*. 1971; Perry and Chilton 1999)

Properties	Values
Density at 20 °C (g/L)	1.249
Melting point (°C)	52.8 (D); 53.0 (L); 16.8 (DL)
Boiling point (°C)	82.0 (DL) a 0.5 mmHg; 122.0 (DL) at 15 mmHg; 103 (D) at 15 mmHg
Dissociation constant (pKa) at 25 °C	3.83 (D); 3.79 (L)
Heat capacity (J/mol·°C) at 20 °C	190 (DL)
Heat of solution (kJ/mol) at 25 °C	7.79 (L)
Heat of fusion (kJ/mol)	16.86 (L); 11.33 (DL)

Lactic acid is both an alcohol and acid, and it has an asymmetric carbon that confers optical activity. It can be found in two optically active forms, L(+)-lactic acid and D(-)-lactic acid, or in racemic form, which is a mixture of L(+)-lactic acid and D(-)-lactic acid. The two isomers have the same physical properties (melting point, solubility, dissociation constant, density, *etc.*) and the same chemical properties, except when in reactions where other compounds with optical activity are present. One consequence of those reactions is the difficulty in separating the compounds through traditional techniques (chromatography, distillation, and fractional crystallization). Thus, it is necessary to select appropriate separation techniques when using substances with optical activity. The pure isomers have greater value than the racemic mixture because they are used for specific industrial applications, *e.g.*, L(+)-lactic acid is used in the synthesis of L(+)-polylactic acid, a biodegradable semi-crystalline and thermosetting polymer. Another application is D(-)-polylactic acid production, where the D(-)-isomer of lactic acid is used.

Additionally, isomers behave differently in living tissues. L(+)-Lactic acid is found in living organisms more often than D(-)-lactic acid. In the human body, only L(+)-lactic acid is produced during muscle contraction (Trindade 2002). For applications in food and in medicine, L(+)-lactic acid is preferred because the metabolic conversion of L(+)-lactic

acid in the body is faster than for D(-)-lactic acid. Different methods of production result in different amounts of isomers. In lactic acid production by chemical synthesis, only a racemic mixture is obtained, where the concentrations of the isomers are equal, whereas fermentation allows for producing one isomer in a greater amount.

APPLICATIONS

Lactic acid has a wide range of applications in chemicals, pharmaceuticals, and food, and it is a precursor to several products. The uses and demand of lactic acid are shown in Fig. 1. Although commercially available long ago, it is only in recent decades that new uses have resulted in a great increase in the demand.

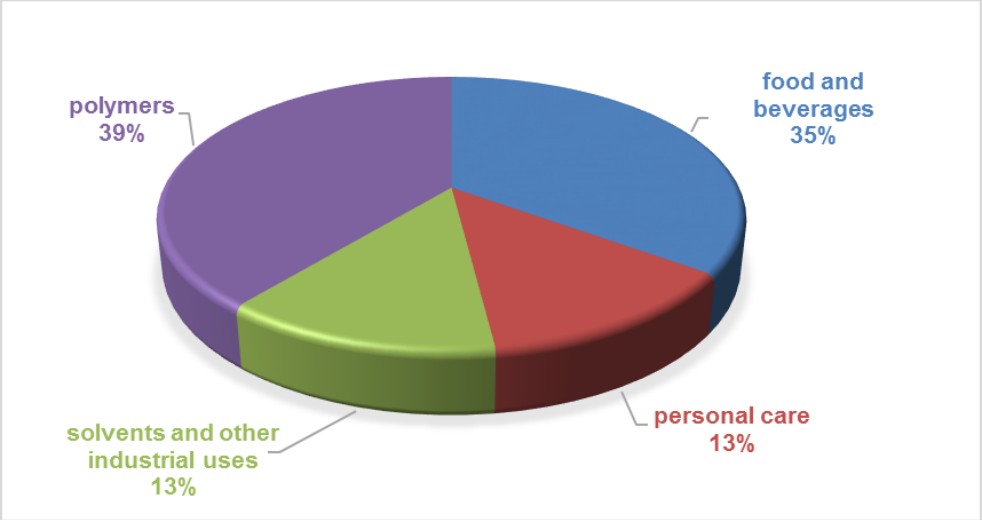

Fig. 1. Uses and demand of lactic acid (The Essential Chemical Industry Online 2013)

In the food industry, which accounts for a large portion of the demand (35%), lactic acid has a number of uses. It is used as an acidulant because of its mild acidic taste when compared with other acids used in food, and as a preservative in olives and pickled vegetables. It is also used as a flavoring agent, pH regulator, and inhibitor of residual bacteria in food processing, such as for sweets, breads, soft drinks, beer, and other products. It is an essential ingredient in fermented foods as well, like yogurt, butter, and canned vegetables.

Lactic acid has applications in the leather tanning industry, in descaling processes, in the textile industry as a mordant (fixative) for dyeing, and can replace ethylene glycol in antifreeze, which results in a higher efficiency and lower cost. In the chemical industry, lactic acid can be converted to ethanol, propylene glycol, and acrylic polymers. Lactic acid derivatives, salts, and esters are used as solvents, emulsifiers, and plasticizers (Trindade 2002). Lactic acid is also used in the production of propylene oxide, acetaldehyde, acrylic acid, propanoic acid, 2,3-pentanedione, ethyl lactate, lactide, and polylactic acid.

In the pharmaceutical industry, lactic acid is used in implants, pills, dialysis, surgical sutures, and controlled drug release systems. In the cosmetic industry, lactic acid is used in the manufacture of hygiene and aesthetic products because of its moisturizing,

antimicrobial, and rejuvenating effects on the skin. It is also used in oral hygiene products (Castillo Martinez *et al.* 2013).

New applications for lactic acid have been developed, such as the production of biodegradable and biocompatible PLA polymers (Abdel-Rahman *et al.* 2013), solvents, and oxygenated chemicals. Polymer production accounts for the largest portion of lactic acid demand (39%). In polymer applications, water is removed from lactic acid ($CH_3CHOHCOOH$) in the presence of acid catalysts to form lactides ($C_6H_8O_4$), as shown in Eq. 1:

$$2CH_3CHOHCOOH \rightarrow C_6H_8O_4 + 2H_2O \quad (1)$$

Lactides are polymerized to obtain the biodegradable thermoplastic polymer, PLA. There is a growing demand for PLA derivatives to substitute conventional plastic materials, as well as for use in materials for medical devices (Gao *et al.* 2011). L(+)-Lactic acid provides a high yield of lactide, which in turn yields polymers with a high molecular weight, high degree of crystallinity, and high tensile strength. These polymers are transparent, which is important for packaging applications; have long shelf lives because they slowly degrade by hydrolysis (which can be controlled by composition and molecular weight adjustment); and their characteristics are similar to polymers generated from fossil fuels. Lactic acid polymers have the advantage of being produced by renewable carbohydrates. Other desired properties can be obtained by copolymerization with other oxygen monomers.

A large number of patents and articles about lactic acid polymers have been published in recent years (Jompang *et al.* 2013; Padee *et al.* 2013; Pivsa-Art *et al.* 2013; Li *et al.* 2014; Shi *et al.* 2015). Although demand for PLA has expanded, its current production capacity of 450 million kg per year is dwarfed by the 200 billion kg of total plastics produced per year. This low production volume is, for the most part, due to the high manufacturing costs. On an industrial scale, the targeted manufacturing cost of the lactic acid monomer is less than 0.8 US$/kg because the selling price of PLA must decrease by roughly half of its present price of 2.2 US$/kg to be able to compete with fossil fuel-based plastics (Wee *et al.* 2006; Okano *et al.* 2010). The majority of the cost of manufacturing PLA is associated with lactic acid monomer production costs (Okano *et al.* 2010).

The use of lactic acid in the manufacture of green solvents, which are environmentally friendly solvents, is another area for potential growth. In particular, using lactate esters from alcohols with low molecular weights in the formulation of pesticides (Sasson *et al.* 2005; Baur *et al.* 2008) and other bioactive components because of its low toxicity has a high potential for growth.

Oxygen chemical derivatives from lactic acid are widely produced, and include propylene glycol, propylene oxide, acrylic acid, and acrylate esters (Datta and Henry 2006).

Although there is a wide range of applications, the use of lactic acid is still limited by the final production costs associated with the downstream processes, which are responsible for 30% to 40% of total production costs of lactic acid (López-Garzón and Straathof 2014).

MANUFACTURING TECHNOLOGIES

The lactic acid molecule is found naturally in plants, microorganisms, and animals, and may also be produced by the fermentation of carbohydrates or by chemical synthesis from coal, petroleum products, and natural gas. Industrially, lactic acid can be produced by chemical synthesis or by fermentation. Figure 2 shows the two main processes of lactic acid production.

Although racemic lactic acid is always produced by chemical synthesis from petrochemical resources, an optically pure L(+)- or D(-)-lactic acid can be obtained by microbial fermentation of renewable resources when the appropriate microorganism is selected (Wee *et al.* 2006). Depending on the application, one form of the optically pure lactic acid is preferable over the other. Additionally, microbial fermentation offers advantages, including cheap renewable substrates, low production temperatures, and low energy consumption (Abdel-Rahman *et al.* 2011). Because of these advantages, it is the production process that is used most often.

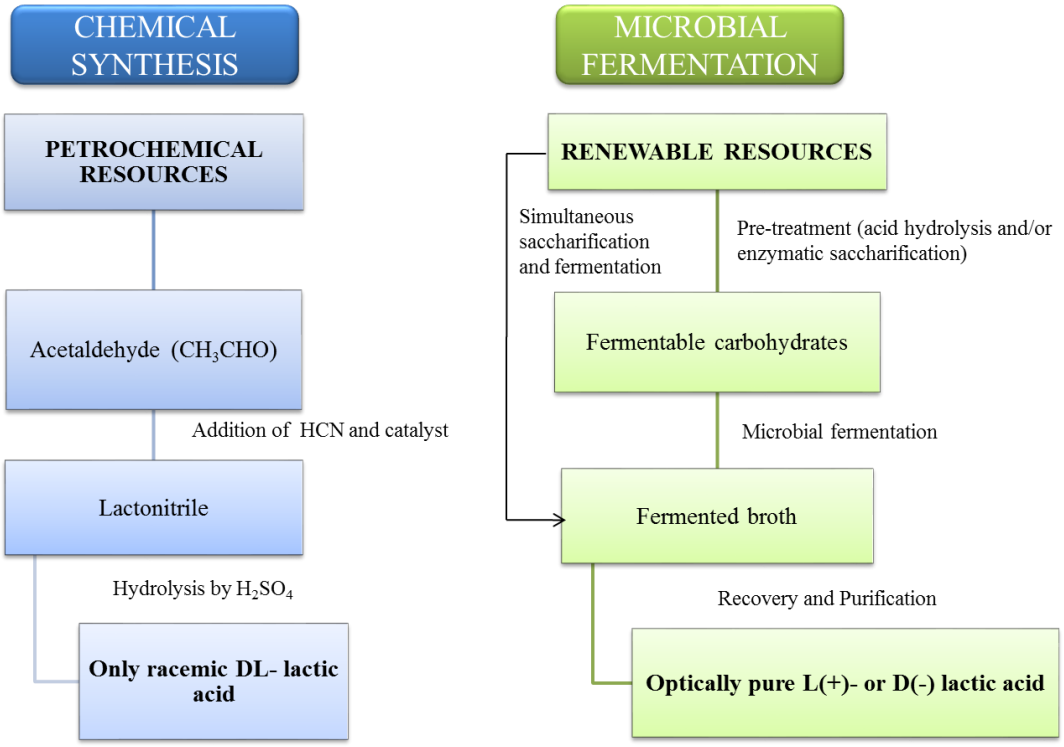

Fig. 2. Overview of the two manufacturing methods of lactic acid, chemical synthesis and microbial fermentation (Wee *et al.* 2006)

Chemical Synthesis

Lactic acid production by chemical synthesis using the lactonitrile route, which was a by-product of acrylonitrile technology, was discovered in 1863 by Wislicenus (Benninga 1990). The reactions involved are described in Eqs. 2 to 5,

$$CH_3CHO + HCN \rightarrow CH_3CHOHCN \quad (2)$$

$$CH_3CHOHCN + 2H_2O + \frac{1}{2}H_2SO_4 \rightarrow CH_3CHOHCOOH + \frac{1}{2}(NH_4)_2SO_4 \quad (3)$$

$$CH_3CHOHCOOH + CH_3OH \leftrightarrow CH_3CHOHCOOCH_3 + H_2O \quad (4)$$

$$CH_3CHOHCOOCH_3 + H_2O \leftrightarrow CH_3CHOHCOOH + CH_3OH \quad (5)$$

In Eq. 2, hydrogen cyanide (HCN) is added to liquid acetaldehyde (CH_3CHO) in the presence of a base catalyst under high pressure when lactonitrile is produced (Pal *et al.* 2009). Then in Eq. 3, lactonitrile is recovered, purified by distillation, and hydrolyzed using sulfuric acid (H_2SO_4) to obtain lactic acid ($CH_3CHOHCOOH$) and ammonium salt ($(NH_4)_2SO_4$). In Eq. 4, lactic acid is esterified with methanol (CH_3OH), and the methyl lactate ($CH_3CHOHCOOCH_3$) formed is recovered, purified by distillation, and hydrolyzed with acidified water to produce lactic acid and methanol. Methanol is separated by distillation and recycled in Eq. 5.

The first company to produce lactic acid by chemical synthesis in significant amounts was Monsanto (Texas, USA) in 1963. They produced 40% (4,500 tons) of the lactic acid consumed in the USA (Trindade 2002). Industrial production by chemical synthesis was also used by Sterling Chemicals, which ended production in early 1990. In the east, Musashino Chemical also used this technology, but recently they changed their production process to fermentation (John *et al.* 2009).

Chemical process routes include base-catalyzed degradation of sugars, oxidation of propylene glycol, hydrolysis of chloropropionic acid, nitric acid oxidation of propylene, and the reaction of acetaldehyde, carbon monoxide, and water at high temperatures and pressures (Gao *et al.* 2011). Although there are many possible routes for the production of lactic acid by chemical synthesis, none of these routes are technically and economically feasible (Datta *et al.* 1995; Gao *et al.* 2011), except for the routes that use lactonitrile as the raw material.

Lactic acid production by a chemical route is expensive and dependent on by-products from other industries, which are derived from fossil fuels (Datta and Henry 2006). Furthermore, chemical synthesis produces a racemic mixture of lactic acid (Abdel-Rahman *et al.* 2011; Pal *et al.* 2009) and for many specific applications, only one of the lactic acid isomers is desired. The problems of expensive raw materials, impurity of the product, and dependence on other industries for raw materials can be bypassed by using biotechnological processes based on fermentation (Pal *et al.* 2009).

Carbohydrate Fermentation

Worldwide lactic acid production from microbial fermentation accounts for around 90% of the total lactic acid production (Hofvendahl and Hahn-Hägerdal 2000) and has attracted interest because of its numerous advantages compared with chemical synthesis, such as production of pure isomers and the use of renewable resources as fermentation substrates.

The fermentation process is characterized by the biological degradation of the substrate (glucose) by a population of microorganisms (biomass) into metabolites, such as ethanol, citric acid, and lactic acid (Silveira 2009). Several microorganisms and raw materials can be used in the production of lactic acid (Table 2). A fermentation product with high purity is obtained when a pure substrate is used, such as sucrose from sugarcane and sugar beet, which results in a reduction in the cost of purification.

Table 2. Lactic Acid Production using Different Substrates and Microorganism

Substrate	Microorganism	Fermentation process	Lactic acid			References
			Concentration (g/L)	Yield (g/g)	Productivity (g/L/h)	
Alfalfa fibers	*Lb. plantarum*	Batch	46.4	0.46	0.64	Sreenath *et al.* 2001
Apple pomace	*Lb. rhamnosus* ATCC 9595 (CECT288)	Batch	32.5	0.88	5.41	Gullón *et al.* 2008
Cassava bagasse	*Lb. delbrueckii* NCIM 2025	Batch	81.9	0.94	1.36	John *et al.* 2009
Cellobiose	*E. mundtii* QU 25	Batch	119	0.83	1.12	Abdel-Rahman *et al.* 2011
Cellobiose	*Lb. delbrueckii* mutant Uc-3	Batch	90	0.90	2.25	Adsul *et al.* 2007
Cellulose	*B. coagulans* 36D1	Fed batch	80.0	0.80	0.30	Ou *et al.* 2011
Cheese whey	*Lb. casei* NRRL B-441	Batch	96	0.93	2.2	Büyükkileci and Harsa 2004
Corn stover	*B. coagulans* LA204	Fed batch	97.59	0.68	1.63	Hu *et al.* 2015
Corncob molasses	*Bacillus* sp. strain	Fed batch	74.7	0.50	0.38	Wang *et al.* 2010
Glucose	*Lb. lactis* BME5-18M	Fed batch	210	0.97	2.2	Bai *et al.* 2003
Glycerol	*E. coli* AC-521	Batch	56.8	0.88	0.94	Hong *et al.* 2009
Lignocellulosic hydrolyzates	*Bacillus* sp. NL01	Fed batch	75.0	0.75	1.04	Ouyang *et al.* 2013
Paper sludge	*L. rhamnosus* ATCC 7469	Batch	73.0	0.97	2.90	Marques *et al.* 2008
Sugar cane bagasse	*Lc. lactis* IO-1	Batch	10.9	0.36	0.17	Laopaiboon *et al.* 2010
White rice bran hydrolysate	*Lb. Rhamnosus* LA-04-1	Batch	82.0	0.81	3.73	Li *et al.* 2012
Wood hydrolysate	*E. faecalis* RKY1	Batch	93	0.93	1.7	Wee *et al.* 2004

Unfortunately, the high cost of sugar makes it unfeasible for use. However, waste products from food industries, agricultural industries, sugarcane mills, and biomasses can be used, which is advantageous from an environmental and economic standpoint.

Raw material cost is one of the major factors in the economic production of lactic acid. Since substrate cost cannot be reduced by process scale-up, extensive studies currently are underway to search for novel substrates for lactic acid production (Abdel-Rahman *et al.* 2013).

Starchy materials, such as wheat, corn, maize, cassava, potato, rice, rye, barley (Wang *et al*. 2010; Nakano *et al.* 2012; Li *et al.* 2012; Prückler *et al*. 2015) are potential raw material for lactic acid production. The advantages is that starchy materials can avoid glucose repression, which occurs when high concentration of glucose in the medium would inhibit growth of lactic acid bacteria (Nakano *et al.* 2012). Approximately 90% of the commercially available lactic acid is produced by submerged fermentation of corn (Wang *et al*. 2016).

Lignocellulose biomass is also a promising source for lactic acid production because its represents the most abundant global source of biomass (Hama *et al.* 2015; Hu *et al*. 2015; Eom *et al*. 2015). It can be used to obtain sugar solutions that may be usefully exploited for the production of lactic acid through the following steps: (a) pretreatment to break down the lignocellulosic structure, (b) enzymatic hydrolysis to depolymerize lignocellulose to fermentative sugars, and (c) sugar fermentation to lactic acid (Idler *et al*., 2015). Although the cost of lignocellulose is low, the pretreatment step makes the whole process cost-inefficient. This occurs because of the following reasons: (a) additional cost of enzymes and chemicals, (b) inhibitory compounds generated during chemical hydrolysis (*e.g.* furfural, 5-hydroxymethylfurfural, and some organic acids) that are inhibitory to the microorganisms used in fermentation, (c) production of mixed sugars such as pentoses, which cannot be fermented by the majority of producer strains. To overcome these challenges, direct conversion of polymeric sugars is of great interest (Abdel-Rahman and Sonomoto 2016). In addition, hydrothermal pretreatment is one of the simplest and most promising methods. In this process, only hot water is used as the reaction medium (Eom *et al*. 2015), reducing operating and maintenance costs (Eom *et al*. 2015).

Recently, the manufacturing of cheese has been reported to produce large volumes of whey as a byproduct (Li *et al*. 2006). Several studies have recently reported lactic acid production using whey (Tejayadi *et al*. 1995, Kim *et al.* 2006; Li *et al*. 2006). Whey is a potent and suitable raw material for lactic acid production because it consists of lactose, protein, fats, water-soluble vitamins, mineral salts, and other essential nutrients for microbial growth (Panesar *et al.* 2007).

Food waste is other potential raw material for lactic acid production because it is usually rich in carbohydrates. In addition, it is advantageous as an effective method of environmental waste management (Tashiro *et al*. 2013; Abdel-Rahman and Sonomoto 2016; Tang *et al*. 2016).

Another approach for production of lactic acid is from glycerol, which is a by-product of biodiesel production. The conversion of glycerol to lactic acid can be categorized into hydrothermal (Kishida *et al*. 2005; Yin *et al.* 2016) and heterogeneous catalysis methods (Auneau *et al.* 2012).

Microalgae are another potential raw material for lactic acid fermentation. Microalgae do not contain lignin, which simplifies conversion into fermentation substrate. In addition, microalgae grow almost anywhere, have an extremely short harvesting cycle

of approximately 1 to 10 days (Nguyen *et al*. 2012), and have high fermentable sugar contents.

Several reviews have been published about novel substrates and developments of biotechnology processes for lactic acid production by fermentation (Vaidya *et al*. 2005; Datta and Henry 2006; Abdel-Rahman *et al.* 2011; Abdel-Rahman *et al.* 2013).

Microorganisms used in fermentation can be divided into two groups: bacteria and fungi (Wee *et al.* 2006). The choice of which type of microorganism to use depends primarily on the carbohydrate that is to be fermented, as a microorganism's metabolism differs with different sources of carbon (Lunelli 2010).

Most lactic acid bacteria (LAB) are cocci, with the exception of *Lactobacilli* and *Carnobacterium*, which are rods. LAB are unable to synthesize ATP by respiration, and their major end product from the energy-conserving fermentation of sugars is lactic acid. Most LAB are facultative anaerobic, catalase negative, nonmotile, and non-spore forming. They normally have a high acid tolerance and can survive at pH 5 and lower. Their high acid tolerance gives them a competitive advantage over other bacteria. The optimal temperature for growth varies between the genera from 20 to 45 °C (Hofvendahl and Hahn-Hägerdal 2000). LAB can be classified into two groups according to fermentation end-product, homofermentative and heterofermentative. There are two kinds of heterofermentative LAB, obligatory and facultative. Figure 3 shows the catabolic pathways for LAB.

Homofermentative LAB convert glucose almost exclusively to lactic acid, while heterofermentative LAB catabolize glucose into ethanol, CO_2, and lactic acid. Homofermentative LAB normally metabolizes glucose by the Embden-Meyerhof-Parnas pathway (glycolysis). Glycolysis only results in lactic acid as the end product of glucose metabolism. Two molecules of lactic acid are produced per glucose molecule, which results in a yield of more than 0.90 g/g. *Lactobacillus acidophilus*, *Lactobacillus amylophilus*, *L. bulgaricus*, *Lactobacillus helveticus*, and *L. salivarius* are all homofermentative LAB (Castillo Martinez *et al.* 2013).

Obligatory heterofermentative LAB ferment sugar by the 6-phosphogluconate/ phosphoketolase pathway, while facultative heterofermentative LAB use both pathways for fermentation. *Lactobacillus brevis*, *L. fermentum*, *L. parabuchneri*, and *L. reuteri* are obligatory heterofermentative LAB. Facultative heterofermentative LAB are *L. alimentarius*, *Lactobacillus plantarum*, *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactococcus lactis*, *Lactobacillus pentosus*, and *Lactobacillus xylosus* (Castillo Martinez *et al.* 2013).

LAB have complex nutrient requirements because of their limited ability to synthesize B vitamins and amino acids (Hofvendahl and Hahn-Hägerdal 2000) and so require a nutritionally rich medium for growth.

Many LAB produce only one isomer of lactic acid, but sometimes, depending on operating conditions, small amounts of both isomers can be produced. Organisms that produce the D(-)- or L(+)-isomer have two lactate dehydrogenase enzymes (LDH), which differ in their stereospecificity. Some *Lactobacillus* species produce the L(+)-isomer, and when those isomers accumulate, lactic acid is converted into the D(-)-isomer until equilibrium is reached and a racemic mixture is formed (Narayanan *et al.* 2004). *Lactobacillus helveticus* and *Lactobacillus plantarum* produce a racemic mixture (Hofvendahl and Hahn-Hägerdal 2000).

Although the majority of lactic acid processes are carried out with LAB, there are filamentous fungi, such as *Rhizopus*, that can utilize glucose aerobically to produce lactic

acid. *Rhizopus* species, such as *R. oryzae* and *R. arrhizus*, have amylolytic enzymatic activity, which enables them to convert starch directly to L(+)-lactic acid. Several studies have reported on the use of *Rhizopus* for lactic acid production (Yin *et al.* 1998; Liu *et al.* 2006; Yu *et al.* 2007; Guo *et al.* 2010; Wu *et al.* 2011; Saito *et al.* 2012).

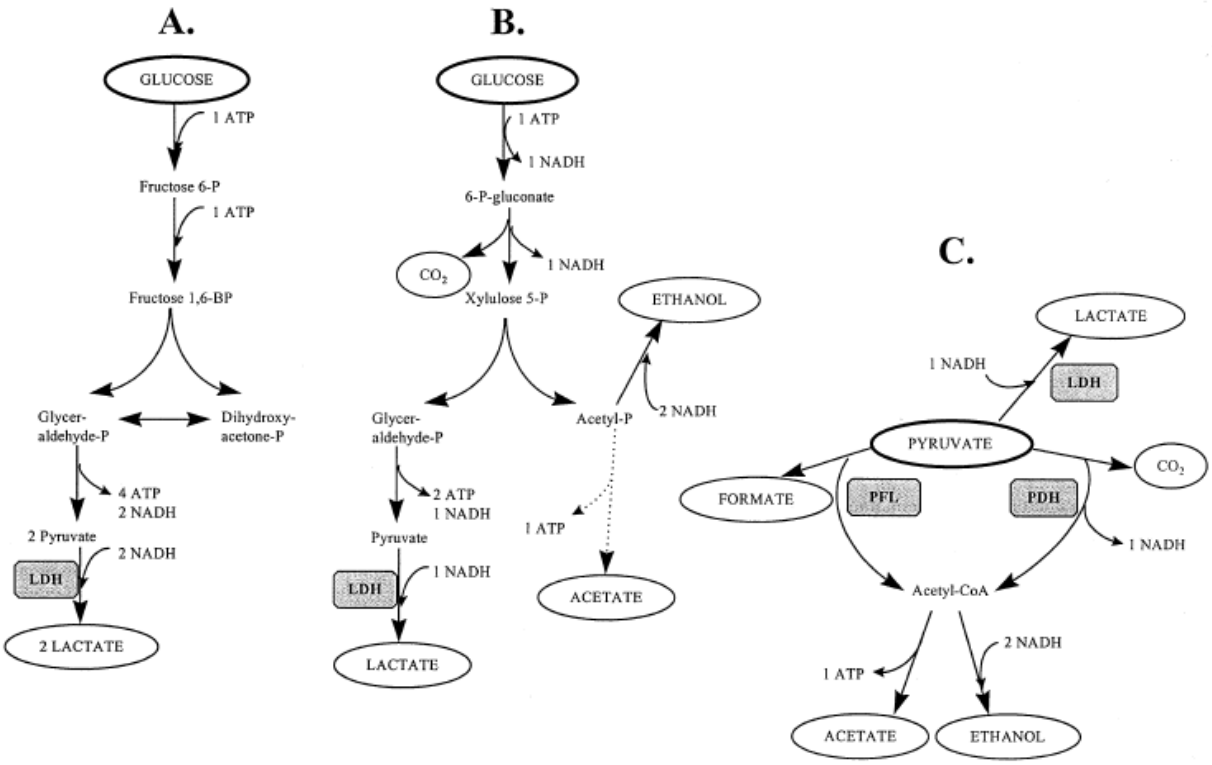

Fig. 3. The catabolic pathways for lactic acid bacteria are (A) homofermentation, (B) heterofermentation, and (C) mixed acid fermentation. P= phosphate, BP= biphosphate, LDH= lactate dehydrogenase, PFL= pyruvate formate lynase, and PHD= pyruvate dehydrogenase (Hofvendahl and Hahn-Hägerdal 2000)

Fungal fermentation has some advantages. For example, *R. oryzae* requires only a simple medium and produces L(+)-lactic acid, but it also requires vigorous aeration because *R. oryzae* is an obligate aerobe. The low production rate in fungal fermentation, below 3 g/L/h, is most likely due to the low reaction rate caused by mass transfer limitations. Lower product yields in fungal fermentation are also partially attributed to the formation of by-products, such as fumaric acid and ethanol (Wee *et al.* 2006).

Other than the substrate source and microorganism, some parameters that may affect the fermentation efficiency are the pH and temperature of the medium, nitrogen and vitamins sources, fermentation operation, and by-products formation.

The pH of the fermentation decreases according to the amount of lactic acid that is produced. To control the pH, a base is added to the medium, such as calcium carbonate, calcium hydroxide, or sodium hydroxide, because in an acidic medium, lactic acid production is either zero or minimal. The pH control can also be done by extraction, adsorption, or electrodialysis of lactic acid (Hofvendahl and Hahn-Hägerdal 2000). Several studies show that a pH value of approximately 6.5 is the optimal pH for growth and lactic acid production (Silveira 2009). A pH below 5.7 is only optimal for *Lactobacillus* strains,

which are known to tolerate lower pHs than *Lactococci* (Hofvendahl and Hahn-Hägerdal 2000). The batch fermentation process at a controlled pH significantly improves lactic acid production, yield, and productivity by different LAB strains, *e.g.*, *Lb. Delbrueckii*, *E. mundtii* QU 25 and *E. faecium* (Abdel-Rahman *et al.* 2011).

Temperature is an important parameter for bacteria growth (Silveira 2009) and relates to the growth kinetics parameters of LAB, lactic acid production, and substrate consumption. Among LAB, most lactic acid productivity studies have been conducted at temperatures ranging from 30 to 43 °C (Abdel-Rahman *et al.* 2011).

Nitrogen sources and vitamins are important primarily because of the limited ability of bacteria to synthesize B vitamins. The main sources of nitrogen are yeast extract and ammonium sulfate (Yin *et al.* 1997; Zhou *et al.* 1999; Jin *et al.* 2003). In terms of industrial processes, the use of yeast extract has a high cost, although it is best for the cultivation of lactic acid bacteria. Ammonium sulfate is a practical alternative, mostly because of its lower cost. Inexpensive nitrogen sources supplements (*e.g.* flour of pigeon pea, red lentil gram, black gram, bengal gram, green gram, soya bean, baker's yeast) have been studied to replace commercial peptone and yeast extract (Altaf *et al*. 2005, 2007). The addition of other nutrients into the medium generally has a positive effect on the lactic acid production; sources include peptone and meat extract (Hofvendahl and Hahn-Hägerdal 2000).

Lactic acid is usually produced in batch mode, but continuous and fed-batch modes can also be used. Fermentation in batch mode has superior conversion and yield compared to continuous fermentation, but the volumetric productivity is lower. In a batch process, all of the substrate gets used, whereas in a continuous process, there is a residual substrate concentration that is always present. The highest productivity possible for continuous fermentation is due to the high dilution ratio and the possibility of maintaining the process for a long period of time. The choice of operation mode depends on the costs of the substrate and the capital investment. If the substrate is expensive, the yield is maximized, by either batch or semicontinuous operation. If investment costs are high, the volumetric productivity is maximized by continuous operation (John *et al.* 2007). A high volumetric productivity is achieved by a cell recycle system, which results in a high cell density with complete glucose conversion (Ohleyer *et al.* 1985).

Production of other organic acids during lactic acid fermentation depends on the purity and quality of the inoculum, metabolic route used, and process conditions, which should prevent external contamination. By-products, such as acetic acid, formic acid, carbon dioxide, and ethanol, can be produced, but for efficient lactic acid production, formation of by-products should be avoided or kept to a minimum (Hofvendahl and Hahn-Hägerdal 2000).

The manufacturer Archer Daniels Midland began using the fermentation process for lactic acid production in the early 1990s. At the end of 1997, Cargill joined Dow Chemical, creating Cargill-Dow, and started producing a polymer by PLA-based fermentation technology. In early 2005, Cargill broke away from Dow and established NatureWorks LLC. The biggest producers of lactic acid by fermentation now include NatureWorks LLC, Purac (Netherlands), Galactic (Belgium), Cargill (USA), and several Chinese companies, such as CCA (Changzhou) Biochemical Co. Ltd., Henan Jindan Lactic Acid Co. Ltd., and Mushashino Chemical Co. Ltd. Currently, NatureWorks LLC is leading the lactic acid polymers market in terms of production and technology (John *et al.* 2009; Abdel-Rahman *et al.* 2013). NatureWorks LLC built a lactic acid plant in Blair, USA, with a production capacity of 180,000 tons per year, which started operation in 2002 (Wee *et al.* 2006; John *et al.* 2009).

SEPARATION AND PURIFICATION PROCESSES

Separation processes are essential to the chemical industry and other related industries. Approximately 40% to 70% of operating and capital costs are associated with the separations steps (Wankat 2007). In lactic acid production processes, development of an effective method of lactic acid separation and purification from fermentation broth is extremely important for economic viability. Although the difference between the boiling point of lactic acid and water is relatively large, it is almost impossible to obtain pure crystalline lactic acid. This is because lactic acid has a high affinity for water and a dimer of lactate is formed when lactic acid concentrations are sufficiently high (Lunelli 2010).

Lactic acid process in a classical way involves a series of downstream treatments such as precipitation, conventional filtration, acidification, carbon adsorption, evaporation, crystallization, and others (Pal *et al.* 2009). The number of downstream processing steps strongly influences the quality and the price of the product (Idler *et al*. 2015).

Open sources provide only limited data about industrial product recovery processes (Idler *et al*. 2015). Otherwise, the separation steps are widely discussed in literature, such as precipitation (Rauch *et al.* 1960; Min *et al.* 2011; Kwak *et al.* 2012; Nakano *et al.* 2012), solvent extraction (Malmary *et al.* 2000; Wasewar *et al.* 2002; Matsumoto *et al.* 2003; Yankov *et al.* 2004; Alkaya *et al.* 2009; Krzyzaniak *et al.* 2013), membrane separation processes, and others. Membrane separation processes that have been studied include reverse osmosis, electrodialysis, and ultrafiltration (Kim and Moon 2001; Choi *et al.* 2002; Madzingaidzo *et al.* 2002; Li and Shahbazi 2006; González *et al.* 2008; Ecker *et al.* 2012; Lu *et al.* 2012; Ramchandran *et al.* 2012; Sikder *et al.* 2012; Dey and Pal 2013; Pal and Dey 2013; Wang *et al.* 2014).

Efficient lactic acid yields and purities can be obtained from these purification technologies, and several advances have been developed, but many drawbacks are still reported. In the precipitation process, the drawbacks include high cost of reagents and the necessity of filtration and other separation processes, especially when a product of higher purity is required. From an environmental standpoint, the generation of large amounts of wastewater is a major drawback. Furthermore, to produce one ton of lactic acid, approximately one ton of low-cost calcium sulfate is needed (Pal *et al.* 2009), which poses serious problems in terms of waste treatment. In solvent extraction, a high exchange area for efficient separation is necessary, which requires expensive equipment. Its application in *in situ* extractive fermentation is limited by solvent recovery done in stripping steps and the high toxicity of the extractant to the microorganisms (Gao *et al.* 2009). Membrane separation processes are promising technologies, but the high cost of membranes and the polarization and fouling problems limit the use of electrodialysis processes on a large scale.

In recent years, many studies have been completed that attempt to solve the problems of traditional separation process by instead using non-traditional distillation separations (Komesu *at al*. 2016), such as reactive distillation (Asthana *et al.* 2005; Kumar *et al.* 2006; Lunelli *et al.* 2010) and molecular distillation (Wei *et al.* 2004; Xu *et al.* 2004; Chen *et al.* 2012; Komesu *et al.* 2014). Another worthwhile approach is the direct fermentation of organic lactates, such as aminium lactates (piperazinium dilactate, imidazole lactate and hexamethylenediamine dilactate), for the manufacture of high purity lactic acid (Idler *et al.* 2015).

Furthermore, new studies on lactic acid recovery processes are required to develop a more efficient and economically attractive process for industrial applications.

CONCLUSIONS

According to this review, it is possible to observe the importance of lactic acid because of its widespread use and applications. The literature reports many lactic acid applications, such as cosmetics, pharmaceutical products, chemistry, food, and more recently in the medical area. The largest demand is in food and polymers application. Lactic acid produced by fermentation offers several advantages: low substrate costs, production temperature and energy consumption. However, lactic acid production is still limited by the final production cost, which is associated with the downstream process that requires many steps and makes the process expensive. Therefore, it is necessary to develop more efficient and viable technologies.

ACKNOWLEDGEMENTS

The authors are grateful for the financial support from the São Paulo Research Foundation (FAPESP), Project 2015/12783-5.

REFERENCES CITED

Abdel-Rahman, M. A., and Sonomoto, K. (2016). "Opportunities to overcome the current limitations and challenges for efficient microbial production of optically pure lactic acid," *J. Biotechnol.* 236, 176-192. DOI: 10.1016/j.jbiotec.2016.08.008

Abdel-Rahman, M. A., Tashiro, Y., and Sonomoto, K. (2011). "Lactic acid production from lignocellulose-derived sugars using lactic acid bacteria: Overview and limits," *J. Biotechnol.* 156(4), 286-301. DOI: 10.1016/j.jbiotech.2011.06.017

Abdel-Rahman, M. A., Tashiro, Y., and Sonomoto, K. (2013). "Recent advances in lactic acid production by microbial fermentation processes," *Biotechnol. Adv.* 31(61), 877-902. DOI: 10.1016/j.biotechadv.2013.04.002

Adsul, M. G., Khire J. M., Bastawade, K. B., and Gokhale, D. V. (2007). "Lactic acid production from cellobiose and cellotriose by *Lactobacillus delbrueckii* mutant Uc-3," *Appl. Environ. Microb.* 73(15), 5055-5057. DOI: 10.1128/AEM.00774-07

Alkaya, E., Kaptan, S., Ozkan, L., Uludag-Demirer, S., and Demirer, G. N. (2009). "Recovery of acids from anaerobic acidification broth by liquid–liquid extraction," *Chemosphere* 77(8), 1137-1142. DOI: 10.1016/j.chemosphere.2009.08.027

Altaf, M., Naveena, B. J., and Reddy, G. (2005). "Screening of inexpensive nitrogen sources for production of L(+) lactic acid from starch by amylolytic *Lactobacillus amylophilus* GV6 in single step fermentation," *Food Technol. Biotechnol*. 43, 235-239.

Altaf, M., Naveena, B.J., and Reddy, G. (2007). "Use of inexpensive nitrogen sources and starch for L(+) lactic acid production in anaerobic submerged fermentation," *Bioresource Technology*. 98, 498-503. DOI: 10.1016/j.biortech.2006.02.013

Asthana, N., Kolah, A., Vu, D. T., Lira, C. T., and Miller, D. (2005). "A continuous reactive separation process for ethyl lactate formation," *Org. Process Res. Dev.* 9(5), 599-607. DOI: 10.1021/op0500640

Auneau, F., Arani, L.S., Besson, M., Djakovitch, L., Michel, C., Delbecq, F., Sautet, P., and Pinel, C. (2012). "Heterogeneous transformation of glycerol to lactic acid," *Top. Catal*. 55, 474-479.

Bai, D., Wei, Q., Yan, Z., Zhao, X., Li, X., and Xu, S. (2003). "Fed-batch fermentation of *Lactobacillus lactis* for hyper-production of l-lactic acid," *Biotechnol. Lett.* 25(21), 1833–1835. DOI: 10.1023/A:1026276925649

Baur, P., Davies, L. E., Pontzen, R., and Rochling, A. (2008). "Use of lactate esters for improving the action of agricultural pesticides," U. S. Patent No. 20080318791 A1.

Benninga, H. A. (1990). *A History of Lactic Acid Making*, Kluwer Academic Publishers, Dordrecht, Netherlands.

Büyükkileci, A. O., and Harsa, S. (2004). "Batch production of L(+) lactic acid from whey by *Lactobacillus casei* (NRRL B-441)," *J. Chem. Technol. Biot.* 79(9), 1036-1040. DOI: 10.1002/jctb.1094

Castillo Martinez, F. A., Balciunas, E. M., Salgado, J. M., González, J. M. D., Converti A., and Oliveira, R. P. S. (2013). "Lactic acid properties, applications and production: A review," *Trends Food Sci. Tech.* 30(1), 70-83. DOI: 10.1016/j.tifs.2012.11.007

Chen, L., Zeng, A., Dong, H., Li, Q., and Niu, C. (2012). "A novel process for recovery and refining of L-lactic acid from fermentation broth," *Bioresour. Technol.* 112, 280-284. DOI: 10.1016/j.biortech.2012.02.100

Choi, J., Kim, S., and Moon, S. (2002). "Recovery of lactic acid from sodium lactate by ion substitution using ion-exchange membrane," *Separ. Purif. Technol.* 28(1), 69-79. DOI: 10.1016/S1383-5866(02)00014-X

Datta, R., and Henry, M. (2006). "Lactic acid: Recent advances in products, processes and technologies – A review," *J. Chem. Technol. Biot.* 81(7), 1119-1129. DOI: 10.1002/jctb.1486

Datta, R., Tsai, S., Bonsignore, P., Moon, S., and Frank, J. R. (1995). "Technological and economic potential of poly (lactic acid) and lactic acid derivatives," *FEMS Microbiol. Rev.* 16(2-3), 221-231. DOI: 10.1016/0168-6445(94)00055-4

Dey, P., and Pal, P. (2013). "Modelling and simulation of continuous L (+) lactic acid production from sugarcane juice in membrane integrated hybrid-reactor system," *Biochem. Eng. J.* 79, 15-24. DOI: 10.1016/j.bej.2013.06.014

Ecker, J., Raab, T., and Harasek, M. (2012). "Nanofiltration as key technology for the separation of LA and AA," *J. Membrane Sci.* 389, 389-398. DOI: 10.1016/j.memsci.2011.11.004

Eom, I.-Y., Oh, Y.-H., Park, S. J., Lee, S.-H., and Yu, J.-H. (2015). "Fermentative L-lactic acid production from pretreated whole slurry of oil palm trunk treated by hydrothermolysis and subsequent enzymatic hydrolysis," *Bioresource Technol*.185, 143-149.

Gao, C., Ma, C., and Xu, P. (2011). "Biotechnological routes based on lactic acid production from biomass," *Biotechnol. Adv.* 29(6), 930-939. DOI: 10.1016/j.biotechadv.2011.07.022

Gao, M., Shimamura, T., Ishida, N., Nagamori, E., Takahashi, H., Uemoto, S., Omasa, T., and Ohtake, H. (2009). "Extractive lactic acid fermentation with tri-n-decylamine as the extractant," *Enzyme Microb. Tech.* 44(5), 350-354. DOI: 10.1016/j.enzmictec.2008.12.001

González, M. I., Alvarez, S., Riera, F. A., and Álvarez, R. (2008). "Lactic acid recovery from whey ultrafiltrate fermentation broths and artificial solutions by nanofiltration," *Desalination* 228(1-3), 84-96. DOI: 10.1016/j.desal.2007.08.009

Gullón, B., Yáñez, R., Alonso, J. L., and Parajó, J. C. (2008). "L-lactic acid production from apple pomace by sequential hydrolysis and fermentation," *Bioresour. Technol*. 99(2), 308-319. DOI: 10.1016/j.biortech.2006.12.018

Guo, Y., Yan, Q., Jiang, Z., Teng, C., and Wang, X. (2010). "Efficient production of lactic acid from sucrose and corncob hydrolysate by a newly isolated *Rhizopus oryzae* GY18," *J. Ind. Microbiol. Biot.* 37(11), 1137-1143. DOI: 10.1007/s10295-010-0761-2

Hama, S., Mizuno, S., Kihara, M., Tanaka, T., Ogino, C., Noda, H., and Kondo, A. "Production of D-lactic acid from hardwood pulp by mechanical milling followed by simultaneous saccharification and fermentation using metabolically engineered Lactobacillus plantarum," *Bioresource Technology*. 187, 167-172. DOI: http://dxdoiorg/101016/jbiortech201503106 2015

Hofvendahl, K., and Hahn-Hägerdal, B. (2000). "Factors affecting the fermentative lactic acid production from renewable resources," *Enzyme Microb. Tech.* 26(2-4), 87-107. DOI: 10.1016/S0141-0229(99)00155-6

Holten, C. H., Müller, A., Rehbinder, D., and Ilra, S. (1971). *Lactic Acid: Properties and Chemistry of Lactic Acid and Derivatives*, Chemie, Weinheim, Germany.

Hong, A. C., Tanino, K., Peng, F., Zhou, S., Sun, Y., Liu, C., and Liu, D. H. (2009). "Strain isolation and optimization of process parameters for bioconversion of glycerol to lactic acid," *J. Chem. Technol. Biot.* 84(10), 1576-1581. DOI: 10.1002/jctb.2209

Hu, J., Zhang, Z., Lin, Y., Zhao, S., Mei, Y., Liang, Y., and Peng, N. (2015). "High-titer lactic acid production from NaOH-pretreated corn stover by *Bacillus coagulans* LA204 using fed-batch simultaneous saccharification and fermentation under non-sterile condition," *Bioresour. Technol.* 182, 251-257. DOI: 10.1016/j.biortech.2015.02.008

Idler, C., Venus, J., and Kamm, B. (2015). "Microorganisms for the production of lactic acid and organic lactates," *Microbiology Monographs* 26. DOI 10.1007/978-3-662-45209-7_9

Jin, B., Huang, L. P., and Lant, P. (2003). "*Rhizopus arrhizus* – A producer for simultaneous saccharification and fermentation of starch waste materials to L(+)-lactic acid," *Biotech. Lett.* 25(23), 1983-1987. DOI: 10.1023/B:BILE.0000004389.53388.d0

John, R. P., Anisha, G. S., Nampoothiri, K. M., and Pandey, A. (2009). "Direct lactic acid fermentation: Focus on simultaneous saccharification and lactic acid production," *Biotechnol. Adv.* 27(2), 145-152. DOI: 10.1016/j.biotechadv.2008.10.004

John, R. P., Nampoothiri, M., and Pandey, A. (2007). "Fermentative production of lactic acid from biomass: An overview on process developments and future perspectives," *Appl. Microbiol. Biot.* 74(3), 524-534. DOI: 10.1007/s00253-063-0779-6

Jompang, L., Thumsorn, S., On, J. W., Surin, P., Apawet, C., Chaichalermwong, T., Kaabbuathong, N., O-Charoen, N., and Srisawat, N. (2013). "Poly(lactic acid) and poly(butylene succinate) blend fibers prepared by melt spinning technique," *Energy Procedia* 34, 493-499. DOI: 10.1016/j.egypro.2013.06.777

Jong, E., Higson, A., Walsh, P., and Wellisch, M. (2012). *Bio-based Chemicals Value Added Products from Biorefineries*, IEA Bioenergy Task 42 Biorefinery, Amsterdam, Netherlands.

Kim, Y. H., and Moon, S. (2001). "Lactic acid recovery from fermentation broth using one-stage electrodialysis," *J. Chem. Technol. Biot.* 76(2), 169-178. DOI: 10.1002/jctb.368

Kim, H.O., Wee, Y.J., Kim, J.N., Yun, J.S., and Ryu, H.W. (2006). "Production of lactic acid from cheese whey by batch and repeated batch cultures of *Lactobacillus* sp. RKY2," *Appl. Biochem. Biotechnol*. 131, 694-704.

Kishida, H., Jin, F., Zhou, Z., Moriya, T., and Enomoto, H. (2005) "Conversion of glycerin into lactic acid by alkaline hydrothermal reaction," *Chem. Lett.* 34, 1560-1561.

Komesu, A., Martins, P. F., Lunelli, B. H., Oliveira, J., Maciel Filho, R., and Wolf Maciel, M. R. (2014). "Evaluation of lactic acid purification from fermentation broth by hybrid short path evaporation using factorial experimental design," *Separ. Purif. Technol.* 136, 233-240. DOI: 10.1016/j.seppur.2014.09.010

Komesu, A., Wolf Maciel, M. R., Oliveira, J., Martins, L. H. S., and Maciel Filho, R. (2016). "Purification of lactic acid produced by fermentation: Focus on non-traditional distillation processes," *Separation &Purification Reviews*. DOI: 10.1080/15422119.2016.1260034

Krzyżaniak, A., Leeman, M., Vossebeld, F., Visser, T. J., Schuur, B., and Haan, A. B. (2013). "Novel extractants for the recovery of fermentation derived lactic acid," *Separ. Purif. Technol.* 111, 82-89. DOI: 10.1016/j.seppur.2013.03.031

Kumar, R., Mahajani, S. M., Nanavati, H., and Noronha, S. B. (2006). "Recovery of lactic acid by batch reactive distillation," *J. Chem. Technol. Biot.* 81(7), 1141-1150. DOI: 10.1002/jctb.1444

Kwak, H., Hwang, D. W., Hwang, Y. K., and Chang, J. (2012). "Recovery of alkyl lactate from ammonium lactate by an advanced precipitation process," *Separ. Purif. Technol.* 93, 25-32. DOI: 10.1016/j.seppur.2012.03.025

Laopaiboon, P., Thani, A., Leelavatcharamas, V., and Laopaiboon, L. (2010). "Acid hydrolysis of sugarcane bagasse for lactic acid production," *Bioresour. Technol.* 101(3), 1036-1043. DOI: 10.1016/j.biortech.2009.08.091

Lasprilla, A. J. R., Martinez, G. A. R., Lunelli, B. H., Jardini, A. L., and Maciel Filho, R. (2012). "Poly-lactic acid synthesis for application in biomedical devices – A review," *Biotechnol. Adv.* 30(1), 321-328. DOI: 10.1016/j.biotechadv.2011.06.019

Li, W., Xu, Z., Chen, L., Shan, M., Tian, X., Yang, C., Lv, H., and Qian, X. (2014). "A facile method to produce graphene oxide-*g*-poly(L-lactic acid) as an promising reinforcement for PLLA nanocomposites," *Chem. Eng. J.* 237, 291-299. DOI: 10.1016/j.cej.2013.10.034

Li, Y., and Shahbazi, A. (2006). "Lactic acid recovery from cheese whey fermentation broth using combined ultrafiltration and nanofiltration membranes," *Appl. Biochem. Biotech.* 129-132, 985-996. DOI: 10.1385/ABAB:132:1985

Li, Z., Lu, J., Yang, Z., Han, L., and Tan, T. (2012). "Utilization of white rice bran for production of L-lactic acid," *Biomass Bioenerg.* 39, 53-58. DOI: 10.1016/j.biombioe.2011.12.039

Lima, U. A., Aquarone, E., Borzani, W., and Schmidell, W. (2001). *Biotecnologia Industrial Processos Fermentativos e Enzimáticos*, Blucher, São Paulo, Brazil.

Liu, T., Miura, S., Yaguchi, M., Arimura, T., Park, E. Y., and Okabe, M. (2006). "Scale-up of L-lactic acid production by mutant strain *Rhizopus* sp. Mk-96-1196 from 0.003 m^3 to 5 m^3 in airlift bioreactors," *J. Biosci. Bioeng.* 101(1), 9-12. DOI: 10.1263/jbb.101.9

López-Garzón, C. S., and Straathof, A. J. J. (2014). "Recovery of carboxylic acids produced by fermentation," *Biotechnol. Adv.* 32(5), 873-904. DOI: 10.1016/j.biotechadv.2014.04.002

Lu, Z., Wei, M., and Yu, L. (2012). "Enhancement of pilot scale production of L(+)-lactic acid by fermentation coupled with separation using membrane bioreactor," *Process Biochem.* 47(3), 410-415. DOI: 10.1016/j.procbio.2011.11.022

Lunelli, B. H. (2010). *Produção e Controle da Síntese do Éster de Ácido Acrílico Através da Fermentação do Ácido Láctico*, Ph.D. Dissertation, University of Campinas, Campinas, Brazil.

Lunelli, B. H., Andrade, R. R., Atala, D. I. P., Wolf Maciel, M. R., Maugeri Filho, F., and Maciel Filho, R. (2010). "Production of lactic acid from sucrose: Strain selection, fermentation and kinetic modeling," *Appl. Biochem. Biotech.* 161(1), 227-237. DOI: 10.1007/s12010-009-8828-0

Madzingaidzo, L., Danner, H., and Braun, R. (2002). "Process development and optimisation of lactic acid purification using electrodialysis," *J. Biotechnol.* 96(3), 223-239. DOI: 10.1016/S0168-1656(02)00049-4

Malmary, G., Albet, J., Putranto, A., Hanine, H., and Molinier, J. (2000). "Recovery of aconitic and lactic acids from simulated aqueous effluents of the sugar-cane industry through liquid-liquid extraction," *J. Chem. Technol. Biot.* 75(12), 1169-1173. DOI: 10.1002/1097-4660(200012)75:12<1169::AID-JCTB334>3.0.CO;2-F

Marques, S., Santos, J. A. L., Gírio, F. M., and Roseiro, J. C. (2008). "Lactic acid production from recycled paper sludge by simultaneous saccharification and fermentation," *Biochem. Eng. J.* 41(3), 210-216. DOI: 10.1016/j.bej.2008.04.018

Matsumoto, M., Takahashi, T., and Fukushima, K. (2003). "Synergistic extraction of lactic acid with alkylamine and tri-*n*-butylphosphate: Effects of amines, diluents and temperature," *Separ. Purif. Technol.* 33(1), 89-93. DOI: 10.1016/S1383-5866(03)00002-9

Min, D., Choi, K. H., Chang, Y. K., and Kim, J. (2011). "Effect of operating parameters on precipitation for recovery of lactic acid from calcium lactate fermentation broth," *Korean J. Chem. Eng.* 28(10), 1969-1974. DOI: 10.1007/s11814-011-0082-9

Nakano, S., Ugwu, C. U., and Tokiwa, Y. (2012). "Efficient production od D-(-)-lactic acid from broken rice by *Lactobacillus delbrueckii* using $Ca(OH)_2$ as a neutralizing agent," *Bioresour. Technol.* 104, 791-794. DOI: 10.1016/j.biortech.2011.10.017

Narayanan, N., Roychoudhury, P. K., and Srivastava, A. (2004). "L (+) lactic acid fermentation and its product polymerization," *J. Biotechnol.* 7(2), 167-179. DOI: 10.2225/vol7-issue2-fulltext-7

Nguyen, C.M., Kim, J-S., Hwang, H.J., Park, M.S., Choi, G.J., Choi, Y.H., Jang, K.S., Kim, J-C. (2012). "Production of L-lactic acid from a green microalga, Hydrodictyon reticulum, by *Lactobacillus paracasei* LA 104 isolated from the traditional Korean food, makgeolli. *Bioresource Tehcnology* 110, 552-559.

Ohleyer, E., Blanch, H. W., and Wilke, C. R. (1985). "Continuous production of lactic acid in a cell recycle reactor," *Appl. Biochem. Biotech.* 11(4), 317-332. DOI: 10.1007/BF02798444

Okano, K., Tanaka, T., Ogino, C., Fukuda, H., and Kondo, A. (2010). "Biotechnological production of enantiomeric pure lactic acid from renewable resources: Recent achievements, perspectives, and limits," *Appl. Microbiol. Biot.* 85(3), 413-423. DOI: 10.1007/s00253-009-2280-5

Ou, M. S., Ingram, L. O., and Shanmugam, K. T. (2011). "L(+)-Lactic acid production from non-food carbohydrates by thermotolerant *Bacillus coagulans*," *J. Ind. Microbiol. Biot.* 38(5), 599-605. DOI: 10.1007/s10295-010-0796-4

Ouyang, J., Ma, R., Zheng, Z., Cai, C., Zhang, M., and Jiang, T. (2013). "Open fermentative production of L-lactic acid by *Bacillus* sp. strain NL01 using lignocellulosic hydrolyzates as low-cost raw material," *Bioresour. Technol.* 135, 475-480. DOI: 10.1016/j.biortech.2012.09.096

Padee, S., Thumsorn, S., On, J. W., Surin, P., Apawet, C., Chaichalermwong, T., Kaabbuathong, N., O-Charoen, N., and Srisawat, N. (2013). "Preparation of poly(lactic acid) and poly(trimethylene terephthalate) blend fibers for textile application," *Energy Procedia* 34, 534-541. DOI: 10.1016/j.egypro.2013.06.782

Pal, P., and Dey, P. (2013). "Process intensification in lactic acid production by three stage membrane integrated hybrid reactor system," *Chem. Eng. Process. Intens.* 64, 1-9. DOI: 10.1016/j.cep.2012.12.006

Pal, P., Sikder, J., Roy, S., and Giorno, L. (2009). "Process intensification in lactic acid production: A review of membrane based processes," *Chem. Eng. Process. Intens.* 48(11-12), 1549-1559. DOI: 10.1016/j.cep.2009.09.003

Panesar, P. S., Kennedy, J. F., Gandhi, D. N., and Bunko, K. (2007). "Bioutilisation of whey for lactic acid production," *Food Chemistry* 105, 1-14.

Perry, R. H., and Chilton, C. H. (1999). *Perry's Chemical Engineers' Handbook*, McGraw-Hill, New York, NY.

Pivsa-Art, S., Tong-Ngok, T., Junngam, S., Wongpajan, R., and Pivsa-Art, W. (2013). "Synthesis of poly(D-lactic acid) using a 2-steps direct polycondensation process," *Energy Procedia* 34, 604-609. DOI: 10.1016/j.egypro.2013.06.791

PR Newswire (2016). "Lactic acid market and derivatives 2016 forecasts (global, China) in new research report," (http://www.prnewswire.com/news-releases/lactic-acid-market-and-derivatives-2016-forecasts-global-china-in-new-research-report-279286152.html), accessed 25 February January 2017.

Prückler, M., Lorenz, C., Endo, A., Kraler, M., Dürrschmid, K., Hendriks, K., Da Silva, F.S., Auterith, E., Kneifel, W., and Michlmayr, H. (2015). "Comparison of homo- and heterofermentative lactic acid bacteria for implementation of fermented wheat bran in bread," *Food Microbiology* 49, 211-219.

Ramchandran, L., Sanciolo, P., Vasiljevic, T., Broome, M., Powell, I., and Duke, M. (2012). "Improving cell yield and lactic acid production of *Lactococcus lactis* ssp. *cremoris* by a novel submerged membrane fermentation process," *J. Membrane Sci.* 403-404, 179-187. DOI: 10.1016/j.memsci.2012.02.042

Rauch, M., Gerner, F., and Wecker, A. M. (1960). *Ullmann's Encyklopädie der technischen Chemie [Ullman's Encyclopedia of Industrial Chemistry]*, Verlag Chemie, Weinheim, Germany.

Saito, K., Hasa, Y., and Abe, H. (2012). "Production of lactic acid from xylose and wheat straw by *Rhizopus oryzae*," *J. Biosci. Bioeng.* 114(2), 166-169. DOI: 10.1016/j.jbiosc.2012.03.007

Sasson, Y., Toledano, O., and Levi-Ruso, G. (2005). "Pesticidal composition comprising a lactate ester as crystal growth inhibitor," U.S. Patent 20050169951 A1.

Shi, D., Hua, J., Zhang, L., and Chen, M. (2015). "Synthesis of bio-based poly(lactic acid-*co*-10-hydroxy decanoate) copolymers with high thermal stability and ductility," *Polymers* 7(3), 468-483. DOI: 10.3390/polym7030468

Sikder, J., Roy, M., Dey, P., and Pal, P. (2012). "Techno-economic analysis of a membrane-integrated bioreactor system for production of lactic acid from sugarcane juice," *Biochem. Eng. J.* 63, 81-87. DOI: 10.1016/j.bej.2011.11.004

Silveira, M. S. (2009). *Utilização do Suco de Caju Clarificado para Produção de Ácido Lático pelo Lactobacillus casei B-442*, MSc Thesis, Universidade Federal do Ceará, Ceará, Brazil.

Sreenath, H. K., Moldes, A. B., Koegel, R. G., and Straub, R. J. (2001). "Lactic acid production by simultaneous saccharification and fermentation of alfalfa fiber," *J. Biosci. Bioeng.* 92(6), 518-523. DOI: 10.1007/s11274-006-9150-4

Tang, J., Wang, X., Hu, Y., Zhang, Y., Li, Y. (2016). "Lactic acid fermentation from food waste with indigenous microbiota: Effects of pH, temperature and high OLR," *Waste Management*. 52, 278-285. DOI: 10.1016/j.wasman.2016.03.034

Tashiro, Y., Matsumoto, H., Miyamoto, H., Okugawa, Y., Pramod, P., Miyamoto, H., and Sakai, K. (2013). "A novel production process for optically pure L-lactic acid from kitchen refuse using a bacterial consortium at high temperatures," *Bioresour. Technol.* 146, 672-681.

Tejayadi, S., and Cheryan, M. (1995). "Lactic acid from cheese whey permeate. Productivity and economics of a continuous membrane bioreactor," *Appl. Microbiol. Biotechnol*. 43, 242-248.

The Essential Chemical Industry Online (2013). "Biotechnology in the chemical industry," (http://www.essentialchemicalindustry.org/materials-and-applications/biotechnology-in-the-chemical-industry.html), accessed 25 February 2016.

Trindade, M. C. (2002). *Estudo da Recuperação de Ácido Lático Proveniente Do Soro De Queijo pela Técnica de Membranas Líquidas Surfactantes*, MSc Thesis, Universidade Federal de Minas Gerais, Minas Gerais, Brazil.

Vaidya, A.N., Pandey, R.A., Mudliar, S., Suresh Kumar, M., Chakrabarti, T., and Devotta, S. (2005). "Production and recovery of lactic acid for polylactide—An overview," *Crit. Rev. Env. Sci. Technol*. 35, 429-467. DOI: 10.1080/10643380590966181

Wang, C., Li, Q., Wang, D., and Xing, J. (2014). "Improving the lactic acid production of *Actinobacillus succinogenes* by using a novel fermentation and separation integration system," *Process Biochem.* 49(8), 1245-1250. DOI: 10.1016/j.procbio.2014.04.009

Wang, L., Zhao, B., Liu, B., Yu, B., Ma, C., Su, F., Hua, D., Li, Q., Ma, Y., and Xu, P. (2010). "Efficient production of L-lactic acid from corncob molasses, a waste by-product in xylitol production, by a newly isolated xylose utilizing *Bacillus* sp. strain," *Bioresour. Technol.* 101(20), 7908-7915. DOI: 10.1016/j.biortech.2010.05.031

Wang, Y., Meng, H., Cai, D., Wang, B., Qin, P., Wang, Z., and Tan, T. (2016) "Improvement of L-lactic acid productivity from sweet sorghum juice by repeated batch fermentation coupled with membrane separation," *Bioresour. Technol.* 211, 291-297. DOI: 10.1016/j.biortech.2016.03.095

Wankat P. C. (2007). *Equilibrium Staged Separations*, Prentice Hall, New York, NY.

Wasewar, K. L., Heesink, A. B. M., Versteeg, G. F., and Pangarkar, V. G. (2002). "Reactive extraction of lactic acid using alamine 336 in MIBK: Equilibria and kinetics," *J. Biotechnol.* 97(1), 59-68. DOI: 10.1016/S0168-1656(02)00057-3

Wee, Y., Kim, J., and Ryu, H. (2006). "Biotechnological production of lactic acid and its recent applications," *Food Technol. Biotech.* 44(2), 163-172.

Wee, Y., Yun, J., Park, D., and Ryu, H. (2004). "Biotechnological production of L(+) lactic acid from wood hydrolyzate by batch fermentation of *Enterococcus faecalis*," *Biotechnol. Lett.* 26(1), 71-74. DOI: 10.1023/B:BILE.0000009464.23026.e0

Wei, Q., Han, Z. W., Bai, D. M., Yan, Z. H., and Zhao, X. M. (2004). "Study on recovery and purification of l-lactic acid," in: *4th International Conference on Separation Science and Technology: Frontiers on Separation Science and Technology*, Nanning, Guangxi, China, pp. 717-723.

Wu, X., Jiang, S., Liu, M., Pan, L., Zheng, Z., and Luo, S. (2011). "Production of L-lactic acid by *Rhizopus oryzae* using semicontinuous fermentation in bioreactor," *J. Ind. Microbiol. Biot.* 38(4), 565-571. DOI: 10.1007/s10295-010-0804-8

Xu, S., Zheng, T., and Xu, S. (2004). "The study of refining L-Lactic acid by molecular distillation," *J. Chem. Eng. Chin. Univ.* 18, 246-249.

Yankov, D., Molinier, J., Albet, J., Malmary, G., and Kyuchoukov, G. (2004). "Lactic acid extraction from aqueous solutions with tri-*n*-octylamine dissolved in decanol and dodecanol," *Biochem. Eng. J.* 21, 63-71.

Yin, P., Nishina, N., Kosakai, Y., Yahiro, K., Park, Y., and Okabe, M. (1997). "Enhanced production of L(+)-lactic acid from corn starch in a culture of *Rhizopus oryzae* using an air-lift bioreactor," *J. Ferment. Bioeng.* 84(3), 249-253. DOI: 10.1016/s0922-338x(97)82063-6

Yin, H., Zhang, C., Yin, H., Gao, D., Shen, L., and Wang, A. (2015). "Hydrothermal conversion of glycerol to lactic acid catalyzed by Cu/hydroxyapatite, Cu/MgO, and Cu/ZrO_2 and reaction kinetics," *Chemical Engineering Journal* 288, 332-343.

Yin, P., Yahiro, K., Ishigaki, T., Park, Y., and Okabe, M. (1998). "L(+)-lactic acid production by repeated batch culture of *Rhizopus oryzae* in air-lift bioreactor," *J. Ferment. Bioeng.* 85(1), 96-100. DOI: 10.1016/S0922-338X(97)80361-3

Yu, M., Wang, R., Wang, C., Duan, K., and Sheu, D. (2007). "Enhanced production of L(+)-lactic acid by floc-form culture of *Rhizopus oryzae*," *J. Chin. Inst. Chem. Eng.* 38(3-4), 223-228. DOI: 10.1016/j.jcice.2007.02.005

Zhou, Y., Domínguez, J., Cao, N., Du, J., and Tsao, G. (1999). "Optimization of L-lactic acid production from glucose by *Rhizopus oryzae* ATCC 52311," *Appl. Biochem. Biotech.* 77-79, 401-407. DOI: 10.1385/ABAB:78:1-3:401

Article submitted: August 22, 2016; Peer review completed: December 29, 2016; Revised version received: January 26, 2017; Accepted: January 29, 2017; Published: February 6, 2017.
DOI: 10.15376/biores.12.2.Komesu