Appl Microbiol Biotechnol (2007) 74:524–534
DOI 10.1007/s00253-006-0779-6

MINI-REVIEW

Fermentative production of lactic acid from biomass: an overview on process developments and future perspectives

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Received: 22 September 2006 / Revised: 21 November 2006 / Accepted: 22 November 2006 / Published online: 16 January 2007

Abstract The concept of utilizing excess biomass or wastes from agricultural and agro-industrial residues to produce energy, feeds or foods, and other useful products is not necessarily new. Recently, fermentation of biomass has gained considerable attention due to the forthcoming scarcity of fossil fuels and also due to the necessity of increasing world food and feed supplies. A cost-effective viable process for lactic acid production has to be developed for which several attempts have been initiated. Fermentation techniques result in the production of either D (−) or L (+) lactic acid, or a racemic mixture of both, depending on the type of organism used. The interest in the fermentative production of lactic acid has increased due to the prospects of environmental friendliness and of using renewable resources instead of petrochemicals. Amylolytic bacteria *Lactobacillus amylovorus* ATCC 33622 is reported to have the efficiency of full conversion of liquefied cornstarch to lactic acid with a productivity of 20 g l^{-1} h^{-1}. A maximum of 35 g l^{-1} h^{-1} was reported using a high cell density of *L. helveticus* (27 g l^{-1}) with a complete conversion of 55- to 60-g l^{-1} lactose present in whey. Simultaneous saccharification and fermentation is proved to be best in the sense of high substrate concentration in lower reactor volume and low fermentation cost. In this review, a survey has been made to see how effectively the fermentation technology explored and exploited the cheaply available source materials for value addition with special emphasis on lactic acid production.

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Keywords Lactic acid · Renewable resource · Agro-industrial residue · Solid-state fermentation

Introduction

The trend towards environmental sustainability and development of renewable resources has significantly increased interest in the recovery of fermentation products, such as organic acids, feed or food additives, and industrial chemicals. Consequently, the range of products produced by fermentation is expanding beyond the traditional high-value low-volume compounds, such as pharmaceuticals, and is beginning to compete with traditional synthetic production of commodity chemicals. As fermentation moves into lower-value higher-volume chemicals, it becomes necessary to maximize efficiency and minimize costs and waste by-products to compete effectively against traditional options. Currently, a great deal of attention is being paid on the biotechnological potential of agro-industrial residues such as cassava bagasse, sugarcane bagasse, sugar beet pulp, coffee husk and pulp, apple pomace, oilcakes, wheat/rice bran etc. for their use as raw materials in the production of value-added products such as enzymes, organic acids, ethanol, amino acids, aroma, single cell protein etc. (Wang 1998; Barbosa et al. 1995; Bramorski et al. 1998; Nampoothiri and Pandey 1996; Shankaranad and Lonsane 1994; Vanwalsum et al. 1996; Zayed and Mostafa 1992; Nampoothiri et al. 2004; Ramachandran et al. 2004; Pandey et al. 2000).

Lactic acid (2-hydroxypropionic acid), CH_3-CHOH COOH, is the most widely occurring hydroxycarboxylic acid, having a prime position due to its versatile applications in food, pharmaceutical, textile, leather, and chemical industries (Vickroy 1985). It was first isolated from sour

milk by CW Scheele in 1780 and was first commercially produced in 1881 by CE Avery in Littleton, MA, USA (Vickroy 1985). Pasteur, Lister, and Delbrueck identified lactic acid as a microbial metabolite (Gregor 1999). Lactic acid is a naturally occurring organic acid that can be produced by chemical synthesis or fermentation. Chemical synthesis of lactic acid is mainly based on the hydrolysis of lactonitrile by strong acids, which provide only the racemic mixture of D- and L-lactic acid. Other possible chemical synthesis routes for lactic acid include base-catalyzed degradation of sugars, oxidation of propylene glycol, reaction of acetaldehyde, carbon monoxide, and water at elevated temperatures and pressures, hydrolysis of chloropropionic acid, and nitric acid oxidation of propylene, among others. None of these routes have led to technically and economically viable processes (Datta et al. 1995).

There have been numerous investigations on the development of biotechnological processes for lactic acid production, with the ultimate objective to enable the process to be more effective and economical. Biological conversion has an important role in waste utilization, and it is likely that various food-processing wastes may contain useful substrates, which can be used for lactic acid production. The biotechnological production of lactic acid offers several advantages compared to chemical synthesis like low cost of substrates, low production temperature, and low energy consumption. High product specificity is yet another advantage of lactic acid fermentation, as it produces a desired stereoisomer, optically pure L-(+)- or D-(−)-lactic acid (Pandey et al. 2001). The potential of microorganisms to synthesize enzymes necessary for the breakdown of complex organic substrates can be exploited for the cost-effective production of lactic acid, as high-cost demanding processes like addition of sugars as carbon source can be avoided.

History of lactic acid production

Lactic acid production was around 5,000 kg per year (Inskeep et al. 1952), and in 1982, it was approximately 24,000–28,000 metric tonnes per year (Naveena 2004). By 1990, the worldwide production volume of lactic acid had grown to approximately 40,000 metric tonnes per year with two significant producers, CCA Biochem in The Netherlands, with subsidiaries in Brazil and Spain, and Sterling Chemicals in Texas City, TX, USA, as the primary manufacturers. Musashino in Japan has been a smaller manufacturer. CCA uses carbohydrate feedstocks and fermentation technology, whereas Sterling and Musashino use a chemical technology. Sterling Chemicals manufactured lactic acid synthetically using the lactonitrile route, which was a by-product of acrylonitrile technology. Sterling exited the business in early 1990s. In the Far East, Musashino Chemical used the chemical technology but recently converted to carbohydrate fermentation technology with Chinese partners. In early 1990s, a new manufacturer, Archer Daniels Midland (ADM), entered the business using carbohydrate fermentation technology. ADM's focus has been on lactic acid and its derivatives for conventional and other uses. In late 1997, Cargill joined forces with Dow Chemical and established a Cargill–Dow polylactic acid (PLA) polymer venture based on carbohydrate fermentation technology. In early 2005, Cargill brought out Dow from this joint venture and established NatureWorks LLC as a wholly owned subsidiary. The major manufacturers of fermentative lactic acid include NatureWorks LLC, Purac (The Netherlands), Galactic (Belgium), Cargill (USA), and several Chinese companies (Wee et al. 2006). Currently, NatureWorks LLC (http://www.natureworksllc.com) is the leader in lactic polymer technology and markets, and the development and implementation of their dilactide technology has contributed to their success. More than 100 US patents in this area were assigned to this company. Over the past 10 years, this company has done extensive work on the development of lactic acid-based products, which are of two types—the polydilactide-based resins (NatureWorks PLA®), used for plastics or packaging applications, and the Ingeo™ polydilactide-based fibers that are used in specialty textiles and fiber applications. The US Food and Drug Administration (FDA) and European regulatory authorities have approved the PLA resins for all food-type applications. NatureWorks LLC has recently constructed a major lactic acid plant in Blair, NE, USA, with a nameplate capacity of 300 million pounds per year for the production of lactic acid and PLA, and it began operating in late 2002 (Wee et al. 2006; Datta and Henry 2006). For product commercialization, they have partnered with many potential end-users and polymer processing equipment manufacturers.

Microbial sources for lactic acid

Lactic acid bacteria (LAB) and some filamentous fungi are the chief microbial sources of lactic acid (Litchfield 1996). On the basis of the nature of fermentation, LAB are classified into (1) homofermentative and (2) heterofermentative. Homofermentative LAB produce virtually a single product, i.e., lactic acid, whereas the heterofermentative LAB produce other products such as ethanol, diacetyl, formate, acetoin or acetic acid, and carbon dioxide along with lactic acid. Lactic acid-producing organisms, most of which are anaerobic, utilize pyruvic acid, which is the end-product of Embden–Meyerhof pathway. The conversion of pyruvic acid to lactate can be effected by either of the two enzymes, L-lactate dehydrogenase or D-lactate dehydroge-

nase. The stereospecificity of the lactic acid depends on the type of organism, whose enzyme is involved in the process of lactic acid production. The major homofermentative LAB used in the lactic acid production from different carbon sources are *Lactococcus lactis* (Nolasco-Hipolito et al. 2002), *Lactobacillus delbrueckii* (John et al. 2006a; Kadam et al. 2006), *L. helveticus* (Tango and Ghaly 2002), *L. casei* (Hujanen et al. 2001; Rojan et al. 2005). Some of the homofermentative bacteria like *L. amylophilus*, *L. manihotivorans* etc. can directly consume complex carbohydrates like starch (Naveena et al. 2005; Ohkouchi and Inoue 2006). Amylolytic bacteria *Lactobacillus amylovorus* ATCC 33622 had the efficiency of full conversion of liquefied cornstarch to lactic acid with a productivity of 20 g l^{-1} h^{-1} (Zhang and Cheryan 1991).

About 90% of the literature on lactic acid production is focused on bacterial fermentation. Bacterial species belonging to *Lactobacillus*, *Streptococcus*, *Leuconostoc*, and *Enterococcus* (Naveena 2004) are most common producers, although fungal strains such as *Mucor*, *Monilia*, and *Rhizopus* (Prescott and Dunn 1959) also produce lactic acid. The best-known fungal source of lactic acid is *Rhizopus oryzae* (Yu and Hang 1989). The first report of an efficient submerged fermentation for the fungal production of L-lactic acid was in 1936 (Lockwood et al. 1936). This was the era in which the efficiencies of submerged fungal fermentations first became widely recognized. Ward et al. (1938) described a fermentation process utilizing *Rhizopus* and *Actinomucor* in general and *R. oryzae* specifically, which resulted in 63–69% yields of L-lactic acid from chemically defined media containing 15% glucose. They also delineated the advantages of the fungal process over the bacterial process that remain true today such as the use of a chemically defined medium (including inorganic nitrogen sources), which simplifies product purification, and the ability to metabolize high concentrations of glucose resulting in high product concentrations and also produce enantiomerically pure L-lactic acid, which is necessary for food applications and preferred for polylactide manufacture. The principal disadvantage of the *R. oryzae*-based process is the diversion of carbon away from the desired product into the by-products ethanol and fumaric acid. Improvement in the L-lactic acid yield (up to 72–79%) of the *R. oryzae* fermentation as described by Snell and Lowery (1964) consisted primarily of introducing calcium carbonate and increasing the temperature in the late production phase. These studies have taken two basic approaches, immobilization of cells (Hamamci and Ryu 1994; Dong et al. 1996) and promotion of mycelial pellet (Yin et al. 1998; Zhou et al. 2000). The pellets of less than about 1 mm are associated with high production rates and yields, whereas larger pellets are not. This is due to mass transfer limitations with regard to oxygen, substrates, and products. A number of studies have reported improved yields of 85 to 88% (Yin et al. 1997; Du et al. 1998; Zhou et al. 1999). These yields are comparable to the yields routinely obtained with the bacterial process, and if consistently obtained, would contribute greatly to the economic competitiveness of the fungal process.

Lactic acid production from renewable resources

Crop residues are annually renewable sources of energy. Approximately 3.5 billion tons of agricultural residues are produced per annum in the world. The use of a specific carbohydrate feedstock depends on its price, availability, and purity. Although agro-industrial residues are rich in carbohydrates, their utilization is limited due to low protein content and poor digestibility (Pandey et al. 2001).

The carbon source for microbial production of lactic acid can be either sugar in pure form such as glucose, sucrose, lactose etc. or sugar-containing materials such as molasses, whey, sugarcane bagasse, cassava bagasse, and starchy materials from potato, tapioca, wheat, barley, and carrot (Pandey et al. 2001; Anuradha et al. 1999). The economics of production of lactic acid and its derivatives is dependent on many factors of which the cost of raw material is very significant (Nolasco-Hipolito et al. 2002). It is very expensive when purified sugars like glucose, sucrose etc. are given as the feedstock for lactic acid production. Different food/agro-industrial products or residues form the cheaper alternatives to refined sugars for lactic acid production. Sucrose-containing materials such as molasses are commonly exploited raw materials for lactic acid production. The utilization of starchy materials in the place of expensive refined sugars is most economical (Yumoto and Ikeda 1995). Sugarcane bagasse is reported to be used as support for lactic acid production by *R. oryzae* and *Lactobacillus* in solid-state fermentation (SSF) by supplementing sugars or starch hydrolyzate as carbon source (Soccol et al. 1994; Rojan et al. 2005). Some agricultural by-products that are potential substrates for lactic acid production are cornstarch (Cheng et al. 1991; Hang 1990), cassava starch (Yumoto and Ikeda 1995), lignocellulose/hemicellulose hydrolyzates (Karel et al. 1997), cottonseed hulls, Jerusalem artichokes, corn cob, corn stalks (Vickroy 1985), beet molasses (Goksungur and Guvenc 1999; Kotzamanidis et al. 2002), wheat bran (Naveena et al. 2005), rye flour (Raccach and Mamiro 1997), sweet sorghum (Richter and Trager 1994), sugarcane press mud (Xavier and Lonsane 1994), cassava (Xiaodong et al. 1997; Rojan et al. 2005; John et al. 2006a,b), barley starch (Linko and Javaneinen 1996), cellulose (Venkatesh 1997), carrot processing waste (Pandey et al. 2001), molasses spent wash (Sharma et al. 2003), corn fiber hydrolyzates (Saha and

Nakamura 2003), and potato starch (Yumoto and Ikeda 1995; Anuradha et al. 1999).

Generally, LAB is deficient in cellulolytic and amylolytic characters necessitating the prior hydrolysis of cellulosic and starchy wastes for their better utilization. Acid or enzymatic hydrolysis is preferred for this purpose. Hydrolysis of coffee husk was studied by using dilute acid or steam treatment (Pandey and Soccol 2000) or by lignocellulolytic enzymes (Pandey 1991; Pandey et al. 2000). The woody material can be mashed to a cellulose pulp with calcium bisulfate to release the hexoses and pentoses. This sulfite waste liquor can be utilized for lactic acid fermentation by microorganisms like *L. pentosus* (Sethi and Maini 1999). The utilization of acid- or enzyme-hydrolyzed starchy wastes like cassava bagasse for value addition is well documented (Woiciechowski et al. 2002). Gelatinization of starchy wastes enables easy action of the hydrolyzing enzyme. The gelatinized bagasse can be treated with alpha amylase (liquefaction) and glucoamylase (saccharification). Woiciechowski et al. (2002) studied the economic aspects of the recovery of reducing sugars by acid and enzymatic hydrolysis of cassava bagasse. Although both the acid and the enzyme hydrolysis are almost equally efficient based on the yield of reducing sugars (94.5% from acid hydrolysis and 97.3% from enzyme hydrolysis), acid hydrolysis is economically more advantageous, as the energy consumption cost for enzyme hydrolysis is 24.92% more than that of acid hydrolysis (Woiciechowski et al. 2002). Cellulosic and hemicellulosic fractions can be gelatinized with 72% sulfuric acid and then diluted to get the sugars (Pandey and Soccol 2000). Simultaneous saccharification and lactic acid production is done with the addition of amylolytic enzymes and inoculated with *L. delbrueckii* (Anuradha et al. 1999). Co-immobilization of starch-degrading organisms like *Aspergillus awamori* and lactic acid-producing bacteria *Streptococcus lactis* is also done for the simultaneous saccharification and lactic acid production (Kurusava et al. 1988).

Like different agriculture resources, some waste materials of animal origin are also used as the carbon sources for the lactic acid fermentation. Whey is a by-product from cheese industry that contains lactose as carbon source, and it contains proteins, vitamins, and minerals. Podlech et al. 1990, Roukas and Kotzekidou 1998 etc. studied lactic acid fermentation using different types of LAB under free cell or immobilized condition. Mussel processing wastes are an underexploited liquid by-product generated in large volume in the industrial steam treatment of mussels that contain glycogen as main component. Pintado et al. 1999 used amylolytic strains of LAB to direct utilization of this waste material.

Processes in lactic acid fermentation

Lactic acid can be produced from the sugars or sugar-containing hydrolyzates or the single-step conversion of starchy or cellulosic wastes by direct conversion by amylolytic lactic acid-producing microorganisms or by the simultaneous hydrolysis and fermentation by adding enzymes and inoculum together. Different lactic acid fermentation processes adopted by the researchers are shown in Fig. 1. Generally, hydrolyzate is used for replacing refined sugar and can be utilized for the submerged fermentation or solid-state fermentation (Tiwari et al. 1979; Rojan et al. 2005; John et al. 2006a). The reducing sugar concentration in the hydrolyzate affects fermentation, as bacterial cells reduce lactic acid production in higher sugar concentration. The conversion of starch or cellulose to sugar consumes energy during liquefaction or

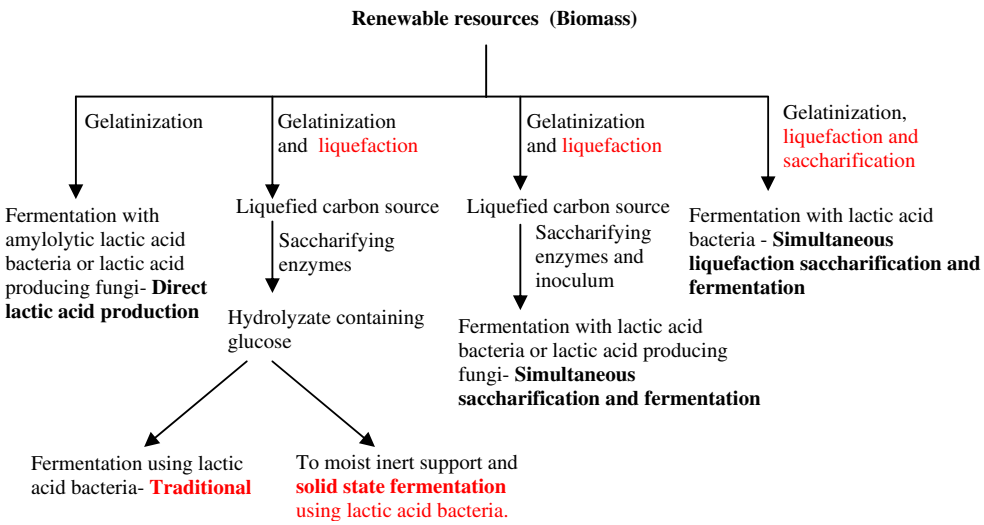

Fig. 1 Different processes for lactic acid fermentation using renewable resources

saccharification and increases the cost of production. The lactic acid-producing fungi can directly convert starch to lactic acid by producing enzymes. There are many reports of amylolytic lactobacilli like *L. manihotivorans*, *L. amylovorous*, *L. amylophilus* etc. Yumoto and Ikeda (1995) reported that *L. amylophilus* JCM 1125 produced 53.4 g l^{-1} of lactic acid from 100-g l^{-1} liquefied starch. *Lactobacillus plantarum* NCIM 2084 produced 72.9 g l^{-1} of lactic acid when provided with 100 g l^{-1} of liquefied starch (Krishnan et al. 1998). *Lactobacillus amylophilus* (NRRL B 4437) produced 29-g l^{-1} lactic acid from 45 g l^{-1} of cornstarch, and *L. amylovorous* was used in conversion of 120-g l^{-1} liquefied starches to 92.5-g l^{-1} lactic acid in submerged fermentation (Zhang and Cheryan 1991). But these processes all need the hydrolysis of starch. Direct conversion of starchy substrate to lactic acid can be done using these amylolytic organisms (Ohkouchi and Inoue 2006; Altaf et al. 2006). Simultaneous saccharification and fermentation can solve inhibition of high sugar concentration in the medium. In this mode of fermentation, the hydrolyzing enzymes are added along with the inoculum. Enzymes release sugars from the substrate, and the organism simultaneously uses it and no inhibition of substrate in case. Many researchers have carried out simultaneous saccharification and fermentation of starchy wastes using amylase and cellulosic wastes using cellulase. This approach can reduce the cost on energy consumption, and it will reduce the negative influence of higher glucose concentration in the media where the refined sugar and hydrolyzate are used. In some instances, proteases are employed to degrade the protein part of residues to reduce the supplementation of extra nutrients (Hofvendahl et al. 1999; John et al. 2006b).

Many starch-degrading LAB, *Lactobacillus* spp., can be also used for the one-step lactic acid production. The starch-degrading *Lactobacillus* spp. are *L. amylophilus* (Yumoto and Ikeda 1995; Vishnu et al. 2000), *L. amylovorus* (Cheng et al. 1991), amylolytic strains of *L. plantarum* (Saha and Nakamura 2003), and *L. amylolyticus* (Bohak et al. 1998). Semi-solid-state fermentation is adopted in the case of certain amylolytic bacteria because they prefer to grow at higher moisture level (Naveena 2004).

The filamentous fungus *R. oryzae* is very much utilized in the solid-state fermentation for the production of L-lactic acid (Yu and Hang 1989). *Rhizopus oryzae*, *R. arrhizus* etc. can aerobically convert starch to lactic acid (Hang 1989, 1990; Hang et al. 1989; Kristoficova et al. 1991). Fungal species of *R. arrhizus* 36017 and *R. oryzae* 2062 produced lactic acid in a single-stage simultaneous saccharification and fermentation process using potato, corn, and wheat and pineapple waste streams as production media. *Rhizopus arrhizus* gave a high lactic acid yield up to 0.94–0.97 g g^{-1} of starch or sugars, whereas a lactic acid yield of 0.65–0.76 g g^{-1} was produced by the *R. oryzae* in 36- to 48-h fermentation. Supplementation of 2 g l^{-1} of ammonium sulfate, yeast extract, and peptone stimulated an increase in 8–15% lactic acid yield (Jin et al. 2005). Research on lactic acid production by *Rhizopus* spp. has continued basically because of the ease of product separation and purification and the ability of the fungus to utilize both complex carbohydrates and pentose sugars (Jin et al. 2005).

The selection of mode of fermentation may vary with respect to different processes. Batch fermentation was superior to continuous fermentation in all respects but the volumetric productivity. Repeated or semicontinuous batch modes increase the yield further. If the substrate is expensive, the yield should be maximized, as in batch or semicontinuous operation, whereas the volumetric productivity is maximized by continuous operation if investment costs are high. A high productivity is achieved by recycling the cells, resulting in a high cell mass without reducing the yield. Immobilization of cells helps to increase the cell density for getting the better productivity and yield, but many of the works have not been very successful in terms of increasing the yield and productivity. In about half of the studies, better results were obtained using free cells (Hofvendahl and Hahn-Hägerdal 2000). Report showed that high cell density *L. helveticus* (27 g l^{-1}) increased the productivity of lactic acid up to 35 g l^{-1} h^{-1} with a complete conversion of 55- to 60-g l^{-1} lactose (Kulozik and Wilde 1999). The production of lactic acid by mixed cultures of free and coimmobilized *L. casei* and *L. lactis* cells in batch and fedbatch culture was investigated by Roukas and Kotzekidou (1998). Fedbatch culture proved to be a better fermentation system for the production of lactic acid than batch culture. The maximum lactic acid concentration (46 g l^{-1}) in fedbatch culture was obtained with both free cell mixture and coimmobilized cells at a substrate concentration of 100 g l^{-1} and a feeding rate of 250 ml h^{-1}. In repeated fedbatch culture, coimmobilized cells gave a higher overall lactic acid concentration compared with the free cell mixture. The coimmobilized cells in Ca-alginate beads retained their ability to produce lactic acid for 20 days. From whey, there was a productivity of 29 g l^{-1} h^{-1} lactic acid in a continuous mode of operation using immobilized *L. helveticus*.

On the other hand, recirculation of cells gave higher lactic acid concentrations and higher or equal yields. Continuous removal of the acid with extraction or electrodialysis results in even higher lactic acid concentrations and yields. The extracting material must be biocompatible so as not to harm the organism, and one way of achieving this is aqueous two-phase systems, which provide good separation of lactic acid and cells when combined with a tertiary amine (Hofvendahl and Hahn-Hägerdal 2000).

Nutrient supplementation for lactic acid fermentation

As the LAB require high level of nutrient supplementation like amino acids, vitamins etc., yeast extract was supplemented as best nutrient sources (Stanier et al. 1986; Naveena 2004; Rojan et al. 2005; John et al. 2006a). The addition of malt-combing nuts, waste from the industry of barley malting, were employed to reduce the high cost of such supplements (Pauli and Fitzpatrick 2002). Whey protein hydrolyzate was supplemented for lactic acid production from whey (Fitzpatrick and Keeffe 2001). According to Goksungur and Guvenc (1999), malt sprout was the second best nitrogen source. Soybean meal and cottonseed were used as the inexpensive nitrogen source (Sethi and Maini 1999; Zhou et al. 1995). Addition of mustard powder in pickle brine increases the rate of acid production (Sethi and Maini 1999). Those nutrients could substitute partially for yeast extract. However, large amount of their supplementation contributed to an increase in the concentration of impurities, corresponding to the increase in separation cost and the decrease in lactic acid recovery. Wheat bran hydrolyzate or wheat bran extract was also used as the nitrogen source (Krishnan et al. 1998; Kotzamanidis et al. 2002). Nutrient supplementation raises the cost of production, as unutilized nutrients will raise the purification cost. Yun et al. (2004) used the amylase-treated rice bran and wheat bran for the DL lactic acid production by *Lactobacillus* sp., as they contain several nutritional factors besides carbohydrate. Nancib et al. (2005) tried the different nitrogen sources, both organic and inorganic nutrients, for the lactic acid using date juice. Their study revealed that yeast extract gave the highest yield, but it can replace with ammonium sulfate when supplemented with vitamins. Hofvendahl et al. (1999) studied the lactic acid production with wheat starch. The addition of protease in the medium enhances the lactic acid production; the productivity increased up to 1.5 g l^{-1} h^{-1} from 0.23 g l^{-1} h^{-1}. When the protease, along with wheat starch, was supplemented with peptide, vitamins, and amino acids, the yield raised to 2.2, 2.4, and 2.8 g l^{-1} h^{-1}, respectively. Interesting to note that John et al. (2006b) reported that using protease-treated wheat bran, around tenfold decrease in supplementation of the costly medium component, like yeast extract, was achieved together with a considerable increase in the lactic acid production level. Maximum lactate yield after various process optimizations was 123 g l^{-1} with a productivity of 2.3 g l^{-1} h^{-1} corresponding to a conversion of 0.95-g lactic acid per gram starch after 54 h at 37°C.

Timbuntam et al. (2006) tried various nitrogen sources like silkworm larvae, yeast autolyzate, dry yeast, and shrimp waste as a replacement of yeast extract in cane juice medium (Table 1). At the same concentration of nitrogen sources (1% w/v), addition of silkworm larvae, yeast autolyzate, and shrimp waste all led to increases in lactic acid production more than that attained with yeast extract. But colony forming unit and cell dry weight were highest with yeast extract.

Gao et al. (2006a,b) used low-cost nutrients by the acid hydrolyzate of fish waste or spent cells as fully or partial substitute for high-cost nutrients like yeast extract with less impurities in fermented medium.

Novel applications

Food and food-related applications account for approximately 85% of the demand for lactic acid, whereas the non-food industrial applications account for only 15% of the demand. Lactic acid has been used as a preservative and acidulant in food and beverage sector for several decades. Calcium lactate is a good dough conditioner, whereas sodium lactate acts both as conditioner and as emulsifier. Lactic acid is considered as generally recognized as safe (GRAS) for use as food additive by the regulatory agencies like FDA in USA. It is used as acidulant/flavoring/pH-buffering agent or inhibitor of bacterial spoilage in a wide variety of processed foods, such as candy, breads and bakery products, soft drinks, soups, sherbets, dairy products, beer, jams and jellies, mayonnaise, and processed eggs, often in conjunction with other acidulants (Datta et al. 1995). Lactic acid or its salts are now used in the disinfection and packaging of carcasses, particularly those of poultry and fish, where the addition of their aqueous solutions during processing increased shelf life and reduced microbial spoilage by *Clostridium botulinum* (Datta et al. 1995). The esters of calcium and sodium salts of lactate with longer chain fatty acids have been used as very good dough conditioners and emulsifiers in bakery products.

The water-retaining capacity of lactic acid makes it suitable for use as moisturizer in cosmetic formulations. The ability of lactic acid to suppress the formation of tyrosinase is responsible for its effects like skin lightening and rejuvenation. As humectants, the lactates are often superior to natural products and more effective then polyols (Datta et al. 1995). Ethyl lactate is the active ingredient in many anti-acne preparations. The natural occurrence of lactic acid in human body makes it very useful as an active ingredient in cosmetics (Wee et al. 2006). Lactic acid has long been used in pharmaceutical formulations, mainly in topical ointments, lotions, and parenteral solutions. It also finds applications in the preparation of biodegradable polymers for medical uses such as surgical sutures, prostheses, and controlled drug delivery systems (Wee et al. 2006). The presence of two reactive functional groups makes lactic acid the most potential feedstock monomer for chemical conversions to potentially useful chemicals such

Table 1 Nutrient supplements used in the lactic acid production

Organism	Carbon source	Nitrogen source	Yield (g g^{-1}) or g l^{-1})/ productivity (g l^{-1} h^{-1})	Reference
L. delbrueckii subsp. *bulgaricus*	WFH	–	0.11 g g^{-1}	Hofvendahl and Hahn-Hägerdal 1997
		YE	0.18 g g^{-1}	
L. delbrueckii subsp. *delbrueckii*	WFH	–	0.82 g g^{-1}	Hofvendahl and Hahn-Hägerdal 1997
		YE	0.91 g g^{-1}	
L. delbrueckii subsp. *lactis*	Potato waste hydrolysate	–	1.0 g g^{-1}	Tsai and Millard 1994
		CSL	0.78 g g^{-1}	
L. paracasei	Sweet sorghum	–	0.79 g g^{-1}	Richter and Trager 1994
		YE + peptone	0.91 g g^{-1}	
L. delbrueckii NRRL B-445	Molasses	–	0.81 g g^{-1}	Aksu and Kutsal 1986
		YE + peptone	0.70 g g^{-1}	
L. salivarious NRRL B-1950	Soy molasses	–	0.76 g g^{-1}	Montelongo et al. 1993
		YE	0.85 g g^{-1}	
L. lactis sub sp. *lactis* AS211	WFH	–	0.77 g g^{-1}	Hofvendahl and Hahn-Hagerdal 1997
		YE	0.91 g g^{-1}	
L. lactis subsp. *lactis* ATCC 19435	WFH	–	0.76 g g^{-1}	Hofvendahl and Hahn-Hagerdal 1997
		YE	0.88 g g^{-1}	
L. lactis subsp. *lactis* ATCC 19435	WFH + protease	–	1.5 g l^{-1} h^{-1}	Hofvendahl et al. 1999
	WFH + protease	Vitamins	2.4 g l^{-1} h^{-1}	
	WFH + protease	Amino acids	2.8 g l^{-1} h^{-1}	
	WFH + protease	Peptides	2.2 g l^{-1} h^{-1}	
	WFH	–	0.23 g l^{-1} h^{-1}	
L. casei ATCC 10863	Glucose	RHH (1%)	0.08 g g^{-1}	Kurbanoglu and Kurbanoglu 2003
	Glucose	RHH (6%)	0.44 g g^{-1}	
	Glucose	RHH (7%)	0.28 g g^{-1}	
Lactobacillus sp.	Cane juice	–	8.1 g l^{-1}	Timbuntam et al. 2006
		1% YE	10.8 g l^{-1}	
		1% SWL	13.5 g l^{-1}	
		1% YA	15.3 g l^{-1}	
		1% SW	12.6 g l^{-1}	
L. delbrueckii	Alfalfa extract	–	0.55 g g^{-1}	Sreenath et al. 2001
		YE + PP	0.58 g g^{-1}	
L. plantarum	Alfalfa extract	–	0.58 g g^{-1}	Sreenath et al. 2001
		YE + PP	0.62 g g^{-1}	
L. amylovorus	Cassava starch	–	4.8 g l^{-1}	Xiaodong et al. 1997
		peptone	7.7 g l^{-1}	

WFH wheat flour hydrolyzate, *MS* malt sprout, *YE* yeast extract, *CSL* corn steep liquor, *RHH* ram horn hydrolyzate, *SWL* silk worm larvae, *YA* yeast autolyzate, *SW* shrimp waste, *PP* polypeptone

as propionic acid, acetic acid, acrylic acid etc. (Dimerci et al. 1993).

Technical-grade lactic acid is extensively used in leather-tanning industries as an acidulant for deliming hides and in vegetable tanning. Lactic acid is used as descaling agent, solvent, cleaning agent, slow acid-releasing agent, and humectants in a variety of technical processes.

The demand for lactic acid has been increasing considerably, owing to the promising applications of its polymer, the polylactic acid (PLA), as an environment-friendly alternative to plastics derived from petrochemicals. PLA has received considerable attention as the precursor for the synthesis of biodegradable plastic (Senthuran et al. 1997). The lactic acid polymers, with tremendous advantages like biodegradability, thermo plasticity, high strength etc., have potentially large markets in the packaging of goods, fabrication of prosthetic devices, and controlled delivery of drugs in humans. The substitution of existing synthetic polymers by biodegradable ones would also significantly alleviate waste disposal problems. As the physical properties of PLA depend on the isomeric composition of lactic acid, the production of optically pure lactic acid is essential for polymerization. L-Polylactide is a semi-crystalline polymer exhibiting high tensile strength and low elongation with high modulus suitable for medical products in orthopedic fixation (pins, rods, ligaments etc.), cardio-vascular applications (stents, grafts etc.), dental applications, intestinal applications, and sutures. L-Polylactic acid has a melting point of 175–178°C and slow degradation time.

Future perspectives of lactic acid production

Lactic acid can be used for products that potentially have very large-volume uses in industrial applications and consumer products. The primary classes of such products are polymers for plastics and fibers, solvents for formulations and cleaning and oxygenated industrial chemicals. NatureWorks LLC, the current leader of lactic acid-based polymers and products, has stated publicly its belief that the PLA market will reach 500,000 (metric) tonnes per year worldwide by 2010, and the construction of two additional PLA plants are being considered presently (http://www.natureworksllc.com; Wee et al. 2006).

Environmentally friendly, 'green' solvents are another potential area for lactic acid derivatives, particularly lactate esters of low-molecular-weight alcohols such as ethyl, propyl, and butyl lactate. Several specialized applications of lactate esters in electronics and precision cleaning were developed and commercialized by Purac. Blends of these esters with other biologically active solvents with a wide range of solvating and cleaning properties have been developed and commercialized very recently by Vertec Biosolvents (http://www.vertecbiosolvents.com). The US Environmental Protection Agency (EPA) has approved the lactate ester solvents as inert ingredients with negligible toxicity and an excellent environmental profile. This has opened up a chance for the development and commercialization of a good range of specialty applications with these non-toxic, environmentally friendly lactate ester solvents with other biologically derived solvents (Datta and Henry 2006).

Lactic acid could be potentially used for the manufacturing of large-volume oxygenated chemicals, such as propylene glycol, propylene oxide, acrylic acid, and acrylate esters, and other chemical intermediates such as lactate ester plasticizers. The advances made in hydrogenolysis technology can be further developed and integrated to make propylene glycol from lactic acid in the future (Datta and Henry 2006).

In various textile finishing operations and acid dying of wool, technical-grade lactic acid was used extensively. Cheaper inorganic acids are now more commonly used in these applications. The future availability of lower cost lactic acid and the increasing environmental restrictions on waste salt disposal may reopen these markets for lactic acid. The use of chirality of lactic acid for the synthesis of drugs and agrichemicals is an opportunity for new applications for optically active lactic acid or its esters. Another use as an optically active liquid crystal whereby lactic acid is used as a chiral synthon has been recently described (Datta et al. 1995). These advances could open new small-volume specialty chemical opportunities for optically active lactic acid and its derivatives.

The current worldwide demand of lactic acid is estimated to be 130,000–150,000 (metric) tonnes per year, and the commercial prices of food-grade lactic acid range between 1.38 US$/kg (for 50% purity) and 1.54 US$/kg (for 88% purity). Technical-grade lactic acid with 88% purity has been priced as much as 1.59 US$/kg (Wee et al. 2006). Lactic acid consumption in chemical applications, which include PLA polymer and new green solvents, such as ethyl lactate, is expected to expand 19% per year (Wee et al. 2006).

On an industrial scale, the manufacturing cost of lactic acid monomer will be targeted to less than 0.8 US$/kg because the selling price of PLA should decrease roughly by half from its present price of 2.2 US$/kg. According to the cost analysis by Datta et al. (1995), the base manufacturing cost of lactic acid was estimated to be 0.55 US$/kg. There are several issues that need to be addressed for the biotechnological production of lactic acid, such as the development of high-performance lactic acid-producing microorganisms and the lowering of the costs of raw materials and fermentation processes. The biotechnological processes for the production of lactic acid from cheap raw materials should be improved further to make them competitive with the chemically derived one.

With increasing demand for lactic acid and increasing concern over environmental impact of gypsum accumulation as a by-product of traditional fermentative production of lactic acid, enhanced efforts for development of alternative technologies are being made. The genetic-engineering approaches have been exploited in a big way for improvement of LAB, and the different metabolic engineering approaches for lactic acid production have been recently reviewed extensively by Singh et al. (2006). Owing to the intrinsic problems of growth under anaerobic conditions and inability of LAB to produce lactic acid under low pH conditions, concerted efforts are required to develop LAB with tolerance to low pH/product inhibition and identification of suitable target sites to develop lactic acid-hyperproducing strains at low pH, making recovery of lactate easier and resulting in less accumulation of gypsum. Development of tolerant LAB systems seems to be more economic in terms of production and overall yields.

Conclusion

Lactic acid is one of the primary platform chemicals that can be derived from renewable carbohydrates and used to make a wide variety of useful products. In the last decade, lactic acid production has grown considerably, mainly owing to the development of new uses, and the production technology is now primarily based on carbohydrate fermentation. Lactic acid fermentation has received a

significant amount of interest in recent times because it offers an alternative to environmental pollution caused by the petrochemical industry and also solves the problems of limited supply of petrochemical resources. Although considerable pioneering effort has been invested by a few companies in the development and commercialization of lactic acid-based products, lactic acid production technologies need to be further advanced and implemented to become technically and economically feasible and environmentally sound. The use of nutrient-rich renewable resources such as various agro-wastes opens an avenue in a dual working manner for value addition through an ecofriendly green technology.

Acknowledgment The authors would like to thank Council of Scientific and Industrial Research (CSIR) Task force (CMM 0006) program for providing the financial support. One of the authors (RPJ) is deeply indebted to CSIR for the award of Senior Research Fellowship.

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