

Economic evaluation of an integrated process for lactic acid production from ultrafiltered whey

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Abstract

Lactic acid can be manufactured either by chemical synthesis or by fermentative processes. In recent years, the amount of lactic acid obtained by biotechnological methods has increased. The highest cost in the traditional process of lactic acid production by carbohydrate fermentation lies in the separation steps that are needed to recover and purify the product from the fermentation broth. An integrated process for food grade lactic acid production from whey ultrafiltrate is evaluated in this work. This process consists in the following steps: fermentation, ultrafiltration, ion exchange, reverse osmosis and final concentration by vacuum evaporation. The proposed process was demonstrated to be economically viable. The annual cost resulted to be 1.25 US\$/kg for 50% (w/w) lactic acid. The highest contribution to the total investment cost corresponds to the concentration step, representing 40% of the total cost, whereas the fermentation step requires the highest operating cost (47% of the total operating cost).

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1. Introduction

Whey is a wastewater obtained in the industrial production of cheese. It contains proteins (8.4 g/L), lactose (65 g/L), fat (<2.5 g/L) and mineral salts (5.6–8.4 g/L). It shows a very high chemical oxygen demand (COD) value (between 40 000 and 60 000 mg O₂/L) and therefore it cannot be drained without a treatment. Nowadays, most of the whey is processed by ultrafiltration (UF) to obtain a whey protein concentrate (WPC). The permeate stream does not have proteins, but it contains a great amount of lactose and mineral salts. Therefore the COD remains practically the same and the environmental problems related to whey are not solved. Whey UF permeate can be used as fertiliser, to feed animals or dried to be added to food products.

However, due to the high content and purity of lactose, it could be further processed to obtain lactose or compounds with high added value produced from lactose, such as lactic acid (Zadow, 1992).

Lactic acid is a versatile chemical used in food and chemical industries. Commercial lactic acid can be classified in four groups (National Research Council, 2003; United States Pharmacopeial, 2003) according to their composition and purity: synthetic, fermentative, thermally stable and technical grade. Table 1 shows the specifications that different types of commercial lactic acid must fulfil.

The conventional process for fermentative production of lactic acid is a discontinuous process with low productivity and high capital and operating costs. The highest cost in the traditional process of lactic acid production by fermentation corresponds to the separation processes that are needed to recover and afterwards to purify the lactic acid from fermentation broths. Therefore, alternatives to this

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Table 1
Specifications for different types of commercial lactic acid

Parameter	Lactic acid			
	^a FCC 88	FCC 80	FCC 50	88% ^b USP/FCC, thermally stable
Process	Fermentative	Fermentative	Fermentative	Synthetic
Lactic acid content (%)	87.5–88.5	79.5–80.5	49.5–50.5	88–90
Density at 20 °C (g/mL)	1.20–1.22	1.18–1.20	1.12–1.14	1.2–1.22
Sulphated ashes (%)	max. 0.1	max. 0.1	max. 0.06	max. 0.05
Heavy metals (ppm)	max. 10	max. 10	max. 6	max. 0.001
Iron (ppm)	max. 10	max. 10	max. 6	max. 0.001
Arsenic (ppm)	max. 1	max. 1	max. 1	max. 0.003
Calcium (ppm)	max. 20	max. 20	max. 20	
Chloride (ppm)	max. 10	max. 10	max. 10	Test USP
Sulphate (ppm)	max. 20	max. 20	max. 20	Test USP

^a FCC: food grade lactic acid according to the Food Chemicals Codex (National Research Council, 2003).

^b USP/FCC: lactic acid that accomplishes the quality rules established by the United States Pharmacopeial (2003) and the food regulations indicated in the Food Chemicals Codex (National Research Council, 2003).

manufacturing process are being investigated (Saha & Woodward, 1997). In order to reduce costs, many studies on lactic acid separation have been conducted using different separation techniques such as reactive extraction, membrane technology, ion exchange, electrodialysis and distillation (Baniel, Eyal, Mizarahi, Hazan, & Fisher, 2001; Datta, 1989; Eyal et al., 2001; Kulprathipanja, 1991; Van Nispen & Jonker, 1991; Russo & Kim, 1996). Some researchers have combined the fermentation operation with a separation step to simultaneously purify the lactic acid obtained. Ye, Jin, and Shimizu (1996) used multistage fermentation; Davidson and Scott (1992) combined fluidized bed fermentation with adsorption; Hane et al. (1993) used solvent extraction for purification of the fermentation broths. Each of these research works have only studied single parts of the global process to obtain purified commercial lactic acid. Some reviews about the different technologies that can be used to purify lactic acid from fermentation broths have also been published (Eyal et al., 2001).

Some economic studies of the fermentative production of lactic acid have been reported (Akerberg & Zacchi, 2000; Tejayadi & Cheryan, 1995). Most of these studies have only considered parts of the overall process, and in some investigations, the final product consisted mainly of lactate rather than lactic acid. Akerberg and Zacchi (2000) conducted an economic evaluation of the fermentative production of lactic acid from wheat flour, obtaining results ranging between 1.10 US\$/kg and 1.15 US\$/kg.

In the present study, the production cost of 50% lactic acid from whey permeate was estimated. The proposed process is described in Fig. 1 where the operating conditions selected have been included. Most of the steps considered (fermentation, ultrafiltration, ion exchange and reverse osmosis) were performed at laboratory scale using real whey permeate from a dairy company as feed stream. The main results obtained were compared with those reported by other authors in order to perform a reliable economic evaluation. The evaporation step was not studied at laboratory scale in this work; therefore the necessary

information was taken from the literature and from lactic acid manufacturing companies.

The fermentation step was performed at constant pH (pH 5.6). The product obtained was mainly lactate. The fermentation broth was then clarified by ultrafiltration and afterwards lactate was converted to lactic acid and purified by ion exchange in two steps (González, Álvarez, Riera, & Álvarez, 2006). In the first step, the clarified fermentation broth was passed through a cation-exchange resin, which retains the cations present in the broth and at the same time, the stream is acidified, thus converting lactate into lactic acid. Afterwards an anion exchanger was used to remove the other anions present in the broth (mainly chloride and phosphate) obtaining a highly purified (>99%) and diluted lactic acid solution (32.7 g/L). Finally, the lactic acid solution was concentrated by reverse osmosis and evaporation to 50% (w/w). The plant was designed to treat 100 m³/day of whey permeate.

2. Methods

2.1. Raw material

The raw material used is sweet cheese whey ultrafiltration permeate supplied by ILAS, S.A. (Navia, Spain). This company processes around 1 million L/day of whey that comes from many different cheese companies in the area, which produce different types of cheese. The ultrafiltration permeate is supplemented with 2.5 g/L yeast extract. Cheese whey is used for the inoculum preparation. The composition of the whey permeate used as raw material is summarised in Table 2.

3. Experimental

In this section the main experimental results obtained in each step are detailed. In Table 3, a summary of the operating conditions selected to perform the experiments is shown as well as the experimental results obtained. Table

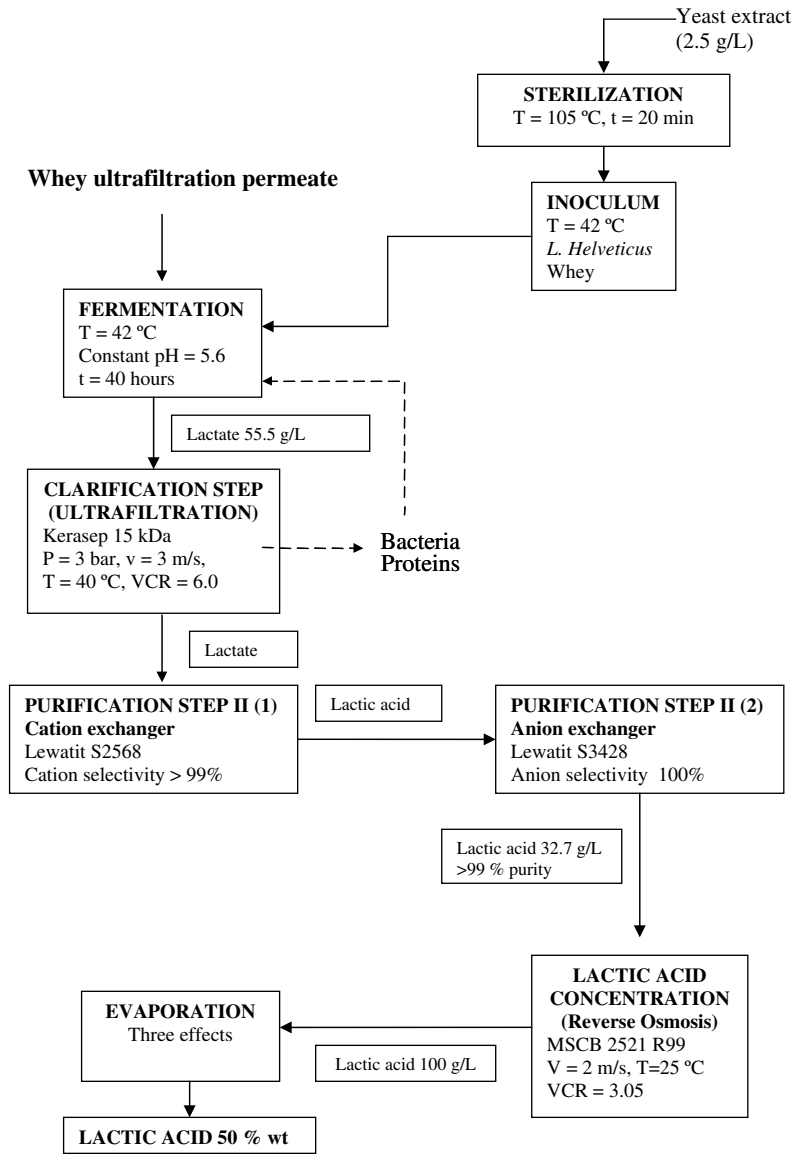


Fig. 1. Proposed process for 50% food grade lactic acid production.

4 summarises the mass balance for each step of the overall process and Table 5 contains the basis used to perform the cost estimations.

Table 2
Composition of whey ultrafiltration permeate used as feed

Parameter	Composition
pH	5.7–6.0
Density (g/L)	1023
Lactose (%) ^a	84.0
Ash (%) ^a	9.42
TKN ^b (%) ^a	4.78
Phosphorous (%) ^a	0.683
Lactic acid (%) ^a	3.3
Fat (%) ^a	0

^a Composition on dry weight basis.

^b Total Kjeldahl nitrogen.

3.1. Fermentation step

Batchwise fermentation is considered. The fermentors are designed to have a capacity of 100 m³. Two fermentors are needed to treat 100 m³ of whey permeate per day. The fermentors require stirring and temperature and pH control. The fermentation is performed at constant pH. The optimum pH value for this step was 5.6, according to the tests carried out at laboratory scale. Sodium hydroxide was added to adjust the pH. The inoculum is prepared in a 10 m³ culture tank. The microorganism used is *Lactobacillus helveticus* (LH100, Rhodia, France). Whey permeate is supplemented with 2.5 g/L yeast extract (DSM Food Specialties, The Netherlands). The operating conditions have been selected from the results obtained in the laboratory experiments. An example of the evolution of the fermentation step is shown in Fig. 2.

Table 3
Summary of the operating conditions selected and the experimental results obtained in each step

<i>Fermentation</i>	
Feed:	ultrafiltered whey
Supplement:	2.5 g/L yeast extract
Constant pH:	5.6
Microorganism:	<i>Lactobacillus helveticus</i> (LH100, Rhodia, France)
Initial Lactose concentration:	55 g/L
Final Lactose concentration:	0.605 g/L
Lactose conversion:	99%
Final lactate concentration:	55 g/L
<i>Clarification by ultrafiltration</i>	
Membrane:	KERASEP 482/1T Tubular ceramic membrane (Rhodia, France)
Membrane area:	0.254 m ²
Membrane molecular weight cut-off (MWCO):	15 kDa
Operating temperature:	40 °C; Operating pressure: 3 bar
Cross flow velocity:	3 m/s; pH = 5.6
Volume concentration ratio (VCR) =	6
Permeate flux (average):	18 L/h m ²
<i>Rejection</i>	
Microorganisms:	100%
Proteins:	100%
Ashes:	3.3%
NPN:	42.4%
Lactate:	1.4%
<i>Purification by ion exchange</i>	
Cation exchanger	
Resin:	Lewatit S2568 (total capacity > 1.6 eq./L, Bayer, Germany)
Selectivity for cations:	>99% (4 BV of treated fermentation broth)
Anion exchanger	
Resin:	Lewatit S3428 (Bayer, Germany)
Selectivity for anions:	100% (25 BV of purified lactic acid)
Final purity of lactic acid after the ion exchange step	> 99%
<i>Preconcentration by reverse osmosis</i>	
Membrane:	MSCB 2521 R99 spiral wound membrane (Separeem Spa., Italy)
Membrane area:	0.8 m ²
Membrane MWCO:	99% NaCl rejection
Operating temperature:	25 °C; Operating pressure: 30 bar
Cross flow velocity:	2 m/s
VCR:	3
Permeate flux (average):	12 L/h m ²
Initial lactic acid concentration:	32.7 g/L
Final lactic acid concentration:	100 g/L

It can be observed that after 40 h of fermentation lactose is completely fermented and lactate concentration in the broth is around 5.5% on a weight basis. The microorganism selected in this work produces a racemic lactate mixture. The experimental results obtained agree with the results published by other authors (Aeschlimann & Von Stockar, 1989; Amrane & Prigent, 1998; Kulozik & Wilde, 1999; Tango & Ghaly, 1999). Table 6 shows the composition of the clarified fermented broth.

For the scale-up of this step the following equation was used:

$$C_1 = C_0(Cap_1/Cap_0)^n$$

where C represents the cost of the equipment, Cap is the plant capacity, n is the scale-up factor and the subscripts 0 and 1 represent the reference unit and unit under study, respectively. For fermentors and mixing tanks, n is assumed to be 0.65 (Akerberg & Zacchi, 2000; Peters, Timmerhaus, & West, 2003).

Costs have been updated to October 2003 using the Chemical Engineering Cost Index (www.che.com/pindex). A pay-off period of 15 years and an interest rate of 5% have been assumed.

3.2. Clarification step

Proteins and biomass are removed by ultrafiltration. Tubular multichannel ceramic membranes with a molecular weight cut-off (MWCO) of 15 kDa are used (KERASEP 482/1T model, Rhodia, France) in this step. Ceramic membranes are chosen because of their higher chemical and temperature resistance that makes possible their sterilisation. The plant is designed to operate in feed and bleed mode as it is the most common in industrial processes. The plant is designed for a permeate flow rate of 9 m³/h. The data used for this step were obtained from the experiments performed at laboratory scale. Fig. 3 shows an example of the evolution of the membrane permeability with the volume concentration ratio (VCR). Proteins and bacteria are totally removed from the broth by means of this membrane, obtaining a permeate basically

Table 4
Mass balance of the global process (basis for the calculation: Annual production of 1800 Tm/year; 320 days/year)

	Fresh whey	UF permeate	Clarified fermentation broth	Purified lactic acid solution	RO concentrations	Final product lactic acid (50 wt%)
Production (L/day)	500 000	100 000	83 300 ^a	83 300	28 000 ^e	5000
Lactose concentration (g/L)	56	55	–	–	–	–
Lactose purity (%) ^d	65	84	–	–	–	–
Lactose (kg/day)	28 000	5500	–	–	–	–
Lactic acid/lactate concentration (g/L)	–	0.2	55.5 ^b	32.7 ^c	100 ^c	–
Purity (% lactic acid) ^d	–	3.3	73.3	>99	>99	>99
Lactic acid production (kg/day)	–	20	4600	2800	2800	2800

^a VCR = 6.

^b Lactate.

^c Lactic acid.

^d wt% on a dry basis.

^e VCR = 3.

Table 5
Basis for costs estimations for each step of the process

	Fermentation	Ultrafiltration	Ion exchange	Reverse osmosis pre-concentration	Evaporation
Reference	Akerberg and Zacchi (2000), Peters et al. (2003)	Wiesner et al. (1994), Cheryan (1998), Sethi and Wiesner (1995)	González et al. (2006), Peters et al. (2003)	Wiesner et al. (1994), Cheryan (1998)	Peters et al. (2003), Akerberg and Zacchi (2000), Anaya (1996)
Energy consumption (kW h/year)	5400000	558000	8778	83472	21300
Other parameters	NaOH (50 wt%) consumption: 924 Tm/year	Cleaning agents (kg/year): DIVOS, LS ¹ = 600 HNO ₃ = 800	NaOH for regeneration: 161 Tm/year HCl for regeneration: 1500 Tm/year	Cleaning agents (kg/year): DIVOS110 ² = 6000, DIVOS2 ² = 3000	
Equipment	2 fermentors 100 m ³ each	Membrane area: 500 m ²	8 m ³ cation exchanger; 1.1 m ³ anion exchanger	Membrane area: 525 m ²	82.5 m ² exchange area, 3 effects Vapour consumption: 2445642 kg/year

Pay-off period: 15 years.

Costs updated: October 2003.

¹ Alkaline reagent recommended by ultrafiltration membrane supplier.

² Cleaning agents recommended by RO membrane supplier.

composed of mineral salts and lactate (pH = 5.6). The selected operating conditions are 3 m/s, 40 °C and 3 bar. Permeate flux was observed to be steady at 18 L/hm² (Fig. 3). This value can be improved by increasing the cross flow velocity, but the results obtained agree quite well with those obtained by other authors for the clarification of different types of fermentation broths (Aeschlimann & Von Stockar, 1991; Milcent & Carrère, 2001; Tejayadi & Cheryan, 1988; Xavier, Gonçalves, Moreira, & Carrondo, 1995). Using this value as reference, the total membrane area required resulted to be 500 m².

The cost of the plant was calculated from the equation proposed by Wiesner, Sethi, Hackney, Jacangelo, and Lainé (1994). The energy required for pumping and the overall energy costs were estimated as proposed by Cheryan (Cheryan, 1998). The price of the membranes and housings was given by the supplier (Profilta, Spain).

Operating costs include energy consumption, membrane replacement, water and chemicals needed to clean the membranes. The life of the membranes was assumed to

be 10 years, according to the manufacturer, with a plant pay-off period of 15 years.

3.3. Ion exchange step

The clarified fermentation broth (pH = 5.6) is mainly composed of lactate and inorganic salts. The cations are basically sodium, magnesium, calcium and potassium, while the anions present in the broth, apart from lactate, are phosphate and chloride. Most of these ionic impurities must be removed to obtain food grade lactic acid. The composition of the ultrafiltered fermentation broth is shown in Table 3.

Different technologies were investigated in this work to purify the lactic acid fermentation broth. Nanofiltration (NF) was the first technology considered, as it is contemplated as a “clean technique”. However, lactic acid purification by NF was not successful due to the similar size and charge of the species to be separated (González, Álvarez, Riera, & Álvarez, submitted for publication). Similar conclusions were obtained by other authors (Gyo, Kang, & Chang, 1999; Schlicher & Cheryan, 1990; Timmer, van der Horst, & Robbertsen, 1993). There are not available in the market selective enough membranes to separate these compounds.

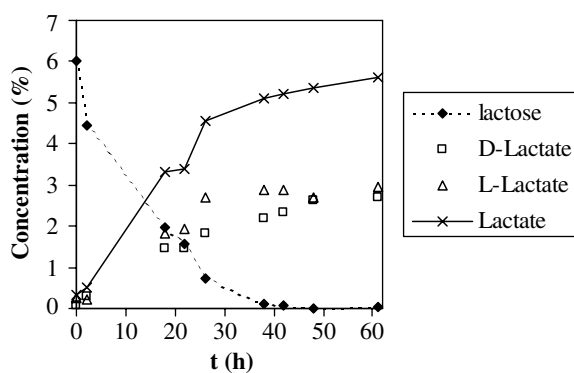


Fig. 2. Lactic acid production by fermentation of whey ultrafiltrate supplemented with 2.5 g/L yeast extract at pH 5.6.

Table 6
Ionic composition of the clarified fermentation broth

Component	Concentration, g/L
Sodium	12.07
Potassium	2.22
Magnesium	0.17
Calcium	0.49
Lactate	55.55
Chloride	2.90
Phosphate	1.78

Ion exchange was the other alternative considered in this work. It was finally selected to perform the purification of the fermentation broth because of the good results obtained at laboratory scale (González et al., 2006). Ion exchange allows both lactate conversion into undissociated lactic acid and salt removal. A novel process for lactic acid purification based on ion exchange is selected. The ion exchange process consists of two steps. In the first one, a cation exchanger (Lewatit[®] S2568) is used to remove the main cations in the broth (sodium, potassium, calcium, magnesium) and to acidify the broth converting lactate into undissociated lactic acid as well as creating the adequate operating conditions (a pH below lactic acid pK_a) for the second purification step. The cation exchanger retains the cations present in the broth with an apparent capacity of 1.7 eq/L and is able to reduce the broth pH below 3.86 (lactic acid pK_a). In the second step, an anion exchanger (Lewatit[®] S3428) is used to remove the non-desired anions present in the broth (chloride, phosphate), thus obtaining a very pure (>99%) aqueous solution of lactic acid. Fig. 4 shows an example of the behaviour of the anionic resin. Lactate is hardly retained by the anion exchanger while phosphate and chloride are selectively retained. It is possible to obtain 25 bed volumes (BV) of purified lactic acid with a good selectivity (greater than 99.9%). The final purity of lactic acid is higher than 99%. The amount of ion exchange resin necessary is much lower than those previously reported (Evangelista & Nikolov, 1996). Moreover no inorganic or organic solvent is added, obtaining a dilute lactic acid solution with high purity that can be easily concentrated to obtain food grade lactic acid.

The optimum operating conditions were selected from the experiments performed at laboratory scale, which are described in a previous paper by the authors (González et al., 2006), and are the following: a feed flow rate of 5 m/h and a temperature of 40 °C. Taking into account the experimental results and the feed flow rate selected, 8 m³ of cation exchange resin and 1.12 m³ of anion exchange resin are required. Counter-current regeneration is chosen in order to reduce the amount of chemicals needed. Before regeneration, the column is backwashed

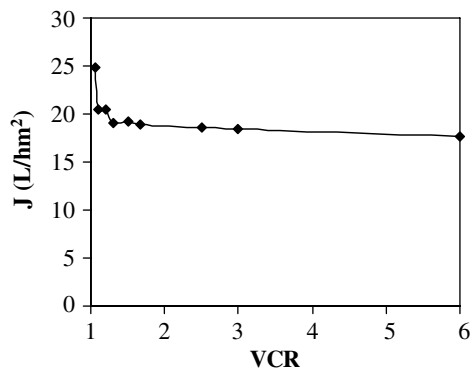


Fig. 3. Permeate flux obtained in the clarification of lactic acid fermentation broths by ultrafiltration with the inorganic membrane KERASEP 482/1T (Rhodia, France) at 3 bar and 40 °C.

with 2 BV of demineralised water. The regeneration of the cation exchanger is carried out with HCl 1 M at 5 m/h and room temperature. The anion exchanger is regenerated with NaOH 0.75 M at the same operating conditions. After regeneration, the column is rinsed with demineralised water at 5 m/h and room temperature.

Investment costs include ion exchangers, columns and auxiliary equipment. Operating costs include the replacement of ion exchangers, water for the washing step and chemicals for column regeneration. The prices of the resins have been obtained from the supplier. The costs of this step have been estimated from our own data.

3.4. Concentration step

Finally, lactic acid concentration is carried out in two steps. Firstly, lactic acid is concentrated by reverse osmosis (RO) to 100 g/L. This is the maximum concentration obtained from the experiments carried out at laboratory scale with a 45 g/L lactic acid solution as feed. In spite of the fact that the lactic acid from the previous step is very pure, the osmotic pressures of the lactic acid concentrated solutions is the limiting factor for this step. The aromatic polyamide MSCB 2521 R99 membrane (Separem Spa., Italy) was selected. The optimum operating conditions were 2 m/s, 25 °C, 30 bar and a volume concentration ratio (VCR) of 3.05. A steady-state permeate flux of 12 L/hm² was assumed. The RO plant was designed to treat 10.5 m³/h. The total membrane area required resulted to be 525 m². The cost of the plant was calculated from the equation proposed by Wiesner et al. (1994). The price of the membranes and housings was given by the supplier. The operating costs include energy consumption, membrane replacement, water and chemicals needed to clean the membranes. Membrane life was assumed to be 2 years with a plant pay-off period of 15 years.

Secondly, the solution containing 100 g/L lactic acid is concentrated by evaporation to 50% (w/w) lactic acid.

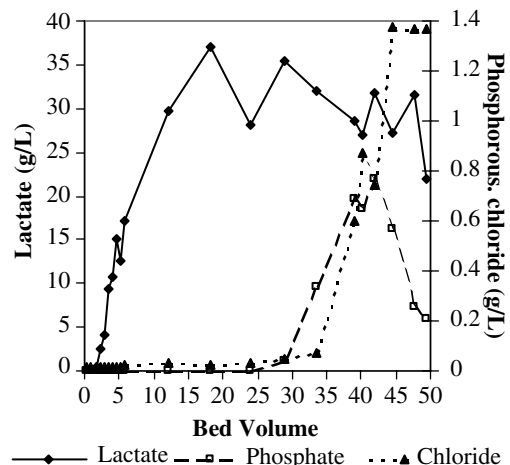


Fig. 4. Effluent profile of Lewatit[®] S3428 column when the demineralised fermentation broth is treated.

Evaporation is performed in a three-effect evaporator below atmospheric pressure in order to avoid lactic acid polymerisation. The evaporator was designed using the method proposed by Anaya (1996). The temperatures for the three steps and the heat transfer coefficients reported by Akerberg and Zacchi (2000) were considered. The operating costs include mainly the cost of steam production, together with the cooling water cost.

The permeate obtained in the reverse osmosis pre-concentration step was used to backwash the ion exchangers before the regeneration step. Thus, the effluent volume as well as the demineralised water consumption were reduced.

4. Results and discussion

The capital and annual costs for the proposed process were calculated taking into account the approaches mentioned in the experimental section. The results are summarised in Table 7. The total cost of the plant resulted to be 2523 125 US\$ and the annual costs 2262 625 US\$/year.

Fig. 5 shows the contribution of each step to the total cost of the process. The concentration step, representing 40% of the investment cost, followed by ultrafiltration (38%) are the main contributors to the capital cost of the plant, while fermentation (50%) followed by ion exchange (28%) are the steps with the highest annual costs.

In Fig. 6, the contributions to the annual costs in each step are shown. It can be observed that the main cost in the concentration step is the depreciation of the equipment; while in the clarification step, the major contributor is the cost of membrane replacement (ceramic membranes are still expensive).

The total annual costs of the fermentation step are high, the major contributor being the cost of the yeast extract used as supplement. Other products could be used to supplement the feed stream, but the experiments carried out at laboratory scale demonstrated that some nutrients present in the yeast extract are very important for the productivity of the fermentation step. Cheaper products, such as whey proteins and mineral salts, were also tested, but lower productivity was obtained and therefore longer fermentation time was required. The cost of the yeast extract accounts for 54% of the annual fermentation costs, followed by

the cost of sodium hydroxide (15%) and steam (10%). The cost of the yeast extract represents about 25% of the total annual costs. The operating costs of the fermentation step could be reduced by operating in continuous mode, recycling the ultrafiltration concentrate (proteins and biomass) to the bioreactor. This way of operation would reduce microorganisms and yeast extract consumption as well as effluent generation and would increase bioreactor productivity (Aeschlimann & Von Stockar, 1991; Bibal, Vayssier, Goma, & Pareilleux, 1991; Jeantet, Maubois, & Boyaval, 1996; Tejayadi & Cheryan, 1995). Regarding the ion exchange step, the chemicals used to regenerate the resins represent 91% of the operating costs and account for 22% of the total operating costs.

The plant was designed for an annual production of 1800 Tm of 50% lactic acid; therefore the final production

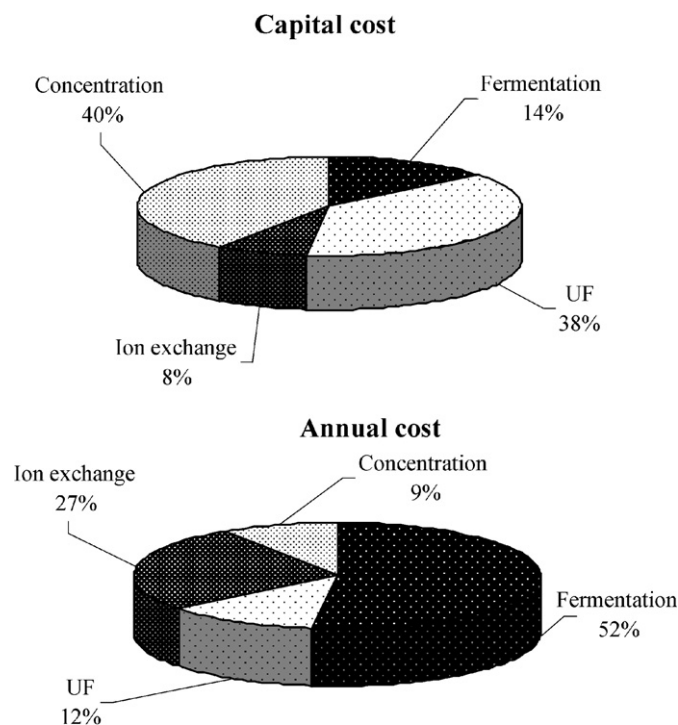


Fig. 5. Economic evaluation of the process designed for lactic acid production from whey ultrafiltrate.

Table 7

Investment and annual costs for the proposed lactic acid production plant

	Capital costs (US\$)	Reference	Annual costs (US\$/year)	Reference
Fermentation	545000	1, 2	1062500	6, 7
Clarification	873250	3, 4	246375	6, 3
Ion Exchange	174250	5, 1	543500	6, 5
Concentration				
RO	266500	4	68750	6
Evaporation	664125	1	121000	6
Labour			220500	6
	2523125		2262625	

(1) Peters et al. (2003). (2) Akerberg and Zacchi (2000). (3) Proflita (2003). (4) Wiesner et al. (1994). (5) Bayer Chemicals (2003). (6) ILAS SA (2003). (7) DSM Food Specialties Spanien (2003).

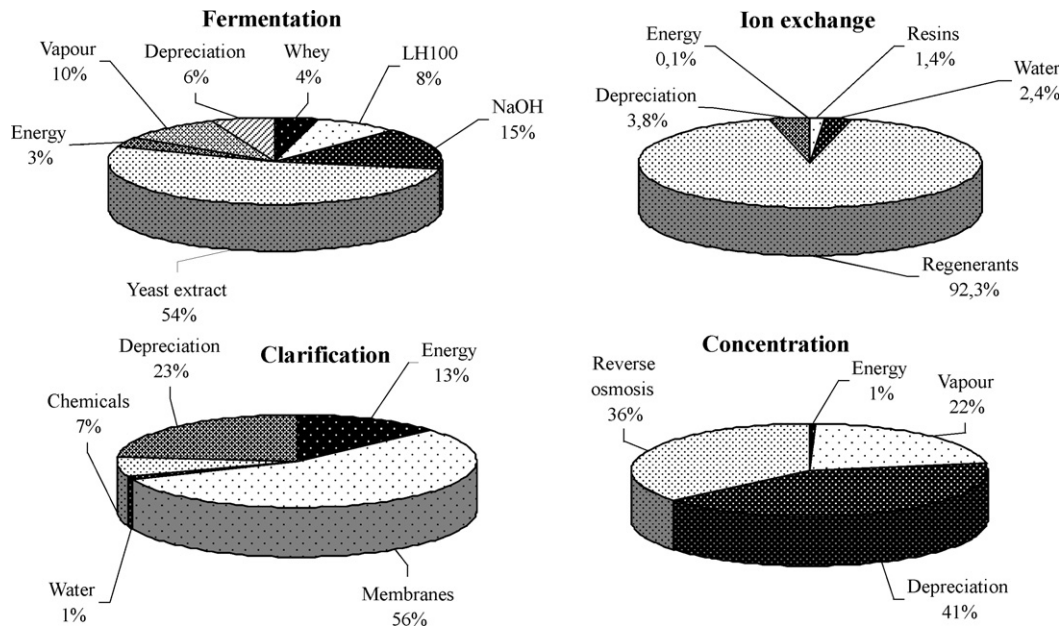


Fig. 6. Contributions to the annual costs of the plant.

cost of 50% lactic acid resulted to be 1.25 US\$/kg. The price of 50% food grade lactic acid, according to the prices published in the Chemical Market Reporter (www.chemicalmarketreporter.com) and to those provided by Purac Bioquímica, SA (Montmeló, Spain), ranges between 1.38 and 1.60 US\$/kg. Thus, the annual profits of the proposed process would range between 217 375 and 554 875 US\$/year.

5. Conclusions

The integrated process proposed for the production of 50% food grade lactic acid was economically evaluated using technical data obtained at laboratory scale. Each step was optimised in previous works by the authors. The process consisted of the following steps: fermentation, ultrafiltration, ion exchange, reverse osmosis and vacuum evaporation.

The production cost of 50% lactic acid was evaluated to be 1.25 US\$/kg. The concentration step, representing 40% of the investment costs, followed by ultrafiltration, are the main contributors to the capital costs of the plant; while fermentation, at 50%, followed by ion exchange, at 28%, require the highest annual costs.

The cost of the yeast extract is the major contributor to the operating costs (25% of total annual costs), although the results obtained at laboratory scale indicated that the fermentation was not possible without a supplement if high yields are desired. Other supplements, such as whey proteins and inorganic salts might be used, but fermentation time would be longer. However, continuous operation in a membrane bioreactor coupling fermentation and ultrafiltration steps would lead to lower raw material consumption.

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