Influence of Residual Sugars on the Purification of Lactic Acid Using Short Path Evaporation

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Short path evaporation (SPE) is a promising separation technique for the purification of lactic acid from fermentation broth. This study investigated the influence of residual sugars, such as glucose, xylose, and sucrose, on the purification of lactic acid using SPE. A 2^3 factorial experimental design was performed in the experimental range from 5 $g \cdot L^{-1}$ to 15 $g \cdot L^{-1}$ for glucose, xylose, and sucrose concentrations. Glucose and sucrose concentrations did not have significant effects on the process of lactic acid concentration in the range used for this study. Xylose in high concentration was found to reduce the lactic acid concentration process performance. An increase in the boiling temperature of the mixture by the ebullioscopy effect possibly hindered the evaporation of the mixture.

Keywords: Lactic acid; Short path evaporation; Glucose; Xylose; Sucrose

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INTRODUCTION

Lactic acid is a natural organic acid with a long history of applications in food, pharmaceutical products, textiles, cosmetics, and other chemical industries (Ouyang *et al*. 2013; Wang *et al.* 2016). In recent years, the demand for lactic acid has been increasing considerably due to its use as a building block for the production of polylactic acid (PLA) materials (Abdel-Rahman *et al*. 2013; Ouyang *et al.* 2013), which are environmentally friendly, biodegradable, and agro-based alternatives to petroleum-based plastics (Abdel-Rahman *et al.* 2013; Abdel-Rahman and Sonomoto 2016).

Production of lactic acid can be conducted by chemical synthesis or by fermentation. The chemical synthesis method is mainly based on the hydrolysis of lactonitrile by a strong acid, where a racemic mixture of the two forms of (D(-) and L(+)) lactic acid are produced (Lasprilla *et al.* 2012). In contrast, the method of biological fermentation can yield a particular form of lactic acid (L- or D- lactic acid) by selecting specific microorganisms, substrates, and conditions (Wang *et al.* 2015). Biological production of lactic acid has received substantial interest because it is an attractive process in terms of its environmental impact (Lasprilla *et al.* 2012), high product specificity, (Lunelli *et al*. 2010) and, additionally, the production of optically pure L- or D- lactic acid, which have been shown to affect the physical and mechanical properties of PLA (Wee *et al*. 2006). Renewable sources and some industrial wastes, such as sugarcane molasses, kitchen waste, paper sludge, agriculture wastes, and others, can be used as substrates for lactic acid production, because these renewable materials are cheap and abundant.

The main problem in the production of lactic acid by fermentation is its downstream processing. Therefore, development of an efficient and low-cost separation

process is very important, as this can reach up to 50% of the total cost (Wasewar *et al.* 2002; Datta and Henry 2006; Chanukya *et al.* 2013).

Several studies have been conducted on finding attractive separation techniques for the recovery of lactic acid from fermentation broth, such as solvent extraction (Yankov *et al.* 2004; Alkaya *et al*. 2009; Krzyzaniak *et al.* 2013), membrane separation processes, such as reverse osmosis, electrodialysis, and ultrafiltration (Ramchandran *et al.* 2012; Dey and Pal 2013; Pal and Dey 2013), reactive distillation (Asthana *et al*. 2005; Kumar *et al*. 2006; Komesu *et al*. 2015), molecular distillation or short path distillation (Xu *et al*. 2004; Chen *et al*. 2012; Komesu *et al*. 2014), and others. Among the proposed technologies, the molecular distillation may have advantages: short residence time in the zone of the molecular evaporator exposed to heat, and low operating temperature due to vacuum in the space of distillation (Lutisan and Cvengros 1995), which minimizes problems with thermal decomposition. Besides that, as the process does not involve the use of a solvent as in extractive distillation, the product material is not polluted, and no further purification is needed (Gorak and Schoenmakers 2014).

In addition to lactic acid and water, fermentation broth also contains a variety of by-products (Komesu *et al.* 2016), which could hinder the purification. When fermentation-derived lactic acid without prior purification is used in a short path distillation, residual sugars, such as glucose, xylose, sucrose, and others can be present in the fermentation mixture. Thus, the residual sugars in various concentrations can influence the performance of the separation process because of the complexity of having a multicomponent mixture feed. Despite this, the influence of fermentation by-products on short path distillation has not been investigated.

Bearing all this in mind, the objective of this study was to elucidate the effects of fermentation by-products on the separation of lactic acid from fermentation broth using short path distillation. This will enable scientists to optimize fermentation broths to improve the performance of the separation process.

EXPERIMENTAL

Materials

The feed solution used in this work was prepared with commercial lactic acid (85%) supplied by Ecibra (São Paulo, Brazil), xylose (99%) supplied by Dinâmica (São Paulo, Brazil), glucose (99.5%), and sucrose (99.5%) supplied by Sigma-Aldrich (São Paulo, Brazil), that was diluted in distilled water. Solution with 50 $g \cdot L^{-1}$ of lactic acid was prepared and glucose, xylose, and sucrose solutions were prepared in various concentrations (5 $g \cdot L^{-1}$, 10 $g \cdot L^{-1}$, and 15 $g \cdot L^{-1}$) according to Table 1. Lactic acid concentration was chosen based on previous studies (Lunelli 2010; Komesu *et al.* 2014) as well as residual sugar concentrations (Evangelista 1994; Oliveira *et al.* 2016).

Short path evaporation

In this study an evaporation system composed of a molecular distiller, Model Pope 2 Wiped Film Still, manufactured by Pope Scientific Inc. (Saukville, WI, USA), was used to study the lactic acid purification. A schematic diagram of the apparatus is shown in Fig. 1. The equipment consists of a cylindrical wiped film evaporator with two condensers, one located internally and the other externally to the evaporator. The surface

area of the evaporator was 0.033 m^2. Details of the equipment can be seen in Komesu *et al*. (2014). In addition, the theoretical aspects can be found in Komesu *et al.* (2016).

Operating conditions

During the experiments, the evaporator temperature was fixed at 100 °C. The internal condenser was positioned inside the body, at a short distance away from the evaporation surface, and was kept constant at 22 °C. To an external condenser, which was fixed at -5 °C, a trap was coupled, and it was continuously fed with liquid nitrogen (-196 °C). Liquid nitrogen was used to freeze and avoid the volatiles from migrating into the pump. The transfer of feed solution (approximately 50 g at room temperature) to the equipment was conducted by using a peristaltic metering pump (Cole Palmer Masterflex model 77200-60, Illinois, USA) with the flow rate of 14 mL/min. Operating pressure was fixed at 1 kPa by a mechanical pump. A rotor containing diagonally slotted wiper blades, for wiping the incoming liquid circumferentially as well as downward at 750 rpm. In this system, it was possible to collect three streams: light (external condenser distillate), residue, and distillate. These streams were collected in glass flasks and were analyzed by liquid chromatography to determine the concentrations of lactic acid and residual sugars.

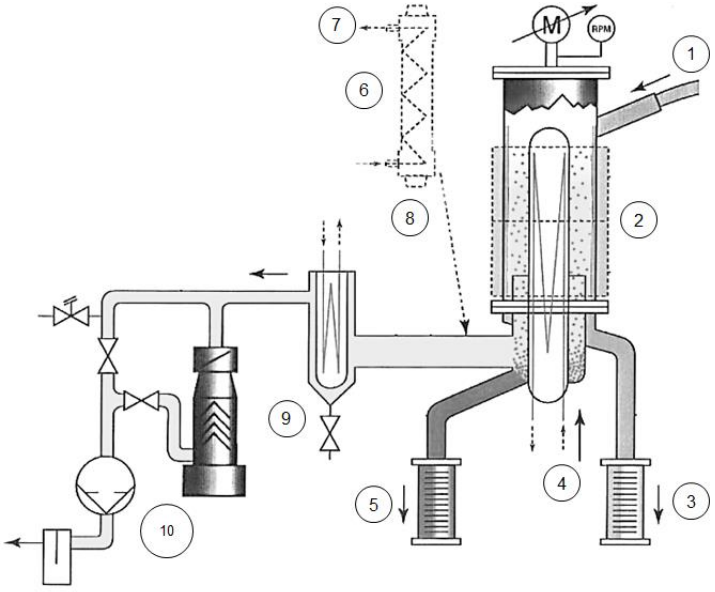

Fig. 1. Schematic diagram of evaporator; (1) Feed; (2) Electric jacket; (3) Residue; (4) Coolant; (5) Internal condenser distillate; (6) External condenser; (7) Coolant; (8) External condenser distillate (light); (9) Cold trap; and (10) Vacuum pump; By permission from Pope Scientific, Inc., Saukville, WI, USA (adapted)

Experimental design

A 2^3 experimental design with 3 factors and 3 replicates at central point, resulting in 11 experiments, was used to investigate the impact of feed solution concentration on the short path evaporation (SPE) process performance. Experiments were performed varying the concentrations of glucose (C_{glu}), xylose (C_{xyl}), and sucrose (C_{suc}) in the feed solution, which were represented by dimensionless coded variables X_1, X_2, and X_3, respectively. The response variables were: residue percentage (R%), light percentage (L%), lactic acid concentration at residue (LA_R), and lactic acid concentration at light

stream (LA_L). The matrix of experiments, and correlation of coded and real values are shown in Table 1.

The experiments were performed in a randomized order and three replicates at the central point of the design were performed to allow the estimation of the pure error (runs 9, 10, and 11). The effect of each process variable and their interactions in the response variables were calculated using the software Statistica 7.0 from Statsoft Inc., Oklahoma, USA (2004). The relationship between factors and each response variable was modeled by fitting the polynomial equation given by Eq. 1. The quality of the fitted models was validated by analysis of variance (ANOVA).

$$Y = \alpha_0 + \alpha_1 X_1 + \alpha_2 X_2 + \alpha_3 X_3 + \alpha_{12} X_1 X_2 + \alpha_{13} X_1 X_3 + \alpha_{23} X_2 X_3 \quad (1)$$

where X_1, X_2, and X_3 denotes the independent coded variables in dimensionless form, α_0, α_1, α_2, α_3, α_{12}, α_{13}, and α_{23} represent the regression coefficients, and Y is the response function.

Table 1. Design Matrix of Experiments

	Coded Variables			Real Variables		
Runs	X_1	X_2	X_3	C_{glu} ($g \cdot L^{-1}$)	C_{xyl} ($g \cdot L^{-1}$)	C_{suc} ($g \cdot L^{-1}$)
1	-1	-1	-1	5	5	5
2	1	-1	-1	15	5	5
3	-1	1	-1	5	15	5
4	1	1	-1	15	15	5
5	-1	-1	1	5	5	15
6	1	-1	1	15	5	15
7	-1	1	1	5	15	15
8	1	1	1	15	15	15
9 (C)	0	0	0	10	10	10
10 (C)	0	0	0	10	10	10
11 (C)	0	0	0	10	10	10

C_{glu}: Glucose concentration; C_{xyl}: Xylose concentration, and C_{suc}: Sucrose concentration

Methods

Lactic acid and residual sugars (glucose, xylose, and sucrose) were determined by high performance liquid chromatography (HPLC) (Agilent Technologies, California, USA). For lactic acid, the column used was Bio-Rad Aminex, model HPX-87H (Bio-Rad, California, USA) (300 mm x 7.8 mm). Sulfuric acid solution (5 mM) was used as mobile phase at a flow rate of 0.6 mL/min. The column temperature was kept constant at 35 °C. For lactic acid detection and quantification, the wavelength of 215 nm was used in the UV detection system. For residual sugars, the column used was Bio-Rad Aminex, model HPX-87P (Bio-Rad, California, USA) (300 mm x 7.8 mm). Milli-Q water was used as the mobile phase at a flow rate of 0.5 mL/min. The column temperature was kept constant at 55 °C.

RESULTS AND DISCUSSION

Separation Process Evaluation

Experimental results for the residue (R%) and light (L%) mass percentages, lactic acid concentrations (LA_R and LA_L), and glucose (C_{glu}), xylose (C_{xyl}), sucrose (C_{suc}), and fructose (C_{frut}) concentrations at residue and light streams are shown in Table 2. The mass percentages of residue or light stream were defined according to Eq. 2,

$$Percentage\ (\%) = \frac{m_{\text{residue or light}}}{m_{\text{total}}} \quad (2)$$

where $m_{\text{residue or light}}$ denotes the mass of the residue or light (g) and m_{total} is the sum of the masses of residue and light after evaporation (g).

Table 2. Experimental Results for the Factorial Design

Residue Stream						
Runs	R (%)	LA_R ($g \cdot L^{-1}$)	C_{glu} ($g \cdot L^{-1}$)	C_{xyl} ($g \cdot L^{-1}$)	C_{suc} ($g \cdot L^{-1}$)	C_{frut} ($g \cdot L^{-1}$)
1	34.38	125.63	22.58	16.84	6.61	16.43
2	35.25	130.83	42.00	14.82	6.14	15.36
3	40.79	110.87	17.89	30.64	4.55	10.64
4	38.78	120.10	38.49	37.81	4.87	11.74
5	38.21	121.36	26.80	16.96	14.14	28.86
6	39.02	118.78	46.86	13.06	14.74	30.48
7	39.49	106.58	24.81	30.14	13.95	29.05
8	47.47	104.66	38.36	30.29	11.85	25.43
9 (C)	37.38	138.42	39.96	29.47	12.62	25.00
10 (C)	34.04	126.93	32.88	25.79	11.17	21.17
11 (C)	29.21	133.47	40.11	29.76	12.89	26.66
Light Stream						
Runs	L (%)	LA_L ($g \cdot L^{-1}$)	C_{glu} ($g \cdot L^{-1}$)	C_{xyl} ($g \cdot L^{-1}$)	C_{suc} ($g \cdot L^{-1}$)	C_{frut} ($g \cdot L^{-1}$)
1	65.09	4.78	0.85	0.45	0.26	0.32
2	64.32	5.42	0.86	0.47	0.26	0.36
3	59.21	5.97	0.96	0.54	0.26	0.75
4	59.34	5.55	0.87	0.46	0.25	0.60
5	60.81	5.07	0.81	0.43	0.24	0.55
6	59.78	5.04	0.56	0.29	0.17	0.36
7	60.51	5.74	0.33	0.18	0.10	0.22
8	52.11	6.09	0.22	0.20	0.00	0.14
9 (C)	75.05	6.39	0.00	0.11	0.00	0.00
10 (C)	65.96	7.57	1.15	0.60	0.32	0.82
11 (C)	70.79	7.25	1.03	0.57	0.30	0.93

R%: Mass percentage of residue; LA_R: Lactic acid concentration at residue; C_{glu}: Glucose concentration; C_{xyl}: Xylose concentration; C_{suc}: Sucrose concentration, C_{frut}: Fructose concentration; L%: Mass percentage of light; and LA_L: Lactic acid concentration at light

The runs identified by 9, 10, and 11 corresponded to the central points, which were used to determine experimental error. The residue mass percentage (33.54% ± 4.11%) and light mass percentage (70.60% ± 4.55%) indicated low standard deviations.

Experimental data of distillate stream were not reported here. The amount of distillate collected for analysis was too small. Considering the sum of residue and light streams, the amount of distillate produced can be calculated as 100 – *R*% – *L*%. The highest mass percentage of distillate produced was 1.88%, which was about 1 g of material. This amount of material was not sufficient to flow inside the evaporator.

Table 2 shows the presence of fructose at residue and light streams. Although fructose was not present in the feed solution, it was produced by the hydrolysis of sucrose to fructose and glucose. The hydrolysis was catalyzed by acidic medium and high temperatures on SPE. The fructose concentrations varied from 10.64 $g \cdot L^{-1}$ to 30.48 $g \cdot L^{-1}$ at residue stream and from 0.00 $g \cdot L^{-1}$ to 0.93 $g \cdot L^{-1}$ at light stream.

In terms of lactic acid and residual sugars concentrations, the richer fractions were obtained at the residue stream. This was expected because water has higher vapor pressure than lactic acid, which can be expected to volatilize preferentially. So, substances of higher vapor pressure were collected predominantly in the light stream, while substances with lower vapor pressure were predominantly in the residue.

Depending on the lactic acid application, the presence of residual sugars were undesirable and should be minimized in the fermentation process. Another option was separating sugars using crystallization or liquid chromatographic methods.

Mass Percentages Evaluation

Table 3 presents the variable effects on the residue and light streams percentages. Considering a confidence level of 90%, it can be realized that the concentrations of glucose, xylose, and sucrose were not significant to the mass percentages at residue and light streams ($p < 0.1$). It was possible that the range of sugar concentrations (from 5 $g \cdot L^{-1}$ to 15 $g \cdot L^{-1}$) were not enough to promote the effect in residue and light streams.

Observing Table 2, the mass percentage range varied from 29.21% to 47.47% at residue stream and from 52.11% to 75.05% at light stream. This meant that more material tended to migrate to the light stream at the evaporator temperature of 100 °C.

Table 3. Factor Effects on Mass Percentages (Confidence Level of 90%)

Residue Percentage				
Factor	Effect	Error	t(2)	p
Mean	**37.63818**	**1.238483**	**30.39056**	**0.001081**
(1) C_{glu}	1.91250	2.904499	0,65846	0.577907
(2) C_{xyl}	4.91750	2.904499	1.69306	0.232521
(3) C_{suc}	3.74750	2.904499	1.29024	0.326015
(1)*(2)	1.07250	2.904499	0.36925	0.747367
(1)*(3)	2.48250	2.904499	0.85471	0.482757
(2)*(3)	-0.05250	2.904499	-0.01808	0.987220

Table 3. Factor Effects on Mass Percentages (Confidence Level of 90%) (Cont.)

Light Percentage				
Factor	Effect	Error	t(2)	p
Mean	**62.99727**	**1.371267**	**45.94093**	**0.000473**
(1) C_{glu}	-2.51750	3.215906	-0.78283	0.515703
(2) C_{xyl}	-4.70750	3.215906	-1.46382	0.280813
(3) C_{suc}	-3.68750	3.215906	-14.664	0.370203
(1)*(2)	-1.61750	3.215906	-0.50297	0.664909
(1)*(3)	-2.19750	3.215906	-0.68332	0.564942
(2)*(3)	0.72250	3.215906	0.22466	0.843106

Lactic Acid Concentration Evaluation

The main motivation for the lactic acid separation process is to obtain richer lactic acid fractions. Because, in the present work, a fermentation broth was a mixture of residual sugars, organic acid, and others, the separation process of a multicomponent feed is more complex compared to binary mixtures. Thus, the experimental design was performed to verify the influence of these sugars in the separation process.

Table 4 shows the effects of various sugar concentrations on lactic acid process concentration at residue and light streams.

Table 4. Factor Effects on Lactic Acid Concentration (Confidence Level of 90%)

Residue Stream				
Factor	Effect	Error	t(2)	p
Mean	**121.6026**	**1.737944**	**69.96923**	**0.000204**
(1) C_{glu}	2.4813	4.075840	0.60878	0.604605
(2) C_{xyl}	**-13.5971**	**4.075840**	**-3.33601**	**0.079313**
(3) C_{suc}	-9.0137	4.075840	-2.21151	0.157530
(1)*(2)	1.1733	4.075840	0.28786	0.800543
(1)*(3)	-4.7316	4.075840	-1.16090	0.365515
(2)*(3)	-0.8565	4.075840	-0.21014	0.853019
Light Stream				
Factor	Effect	Error	t(2)	p
Mean	**5.897273**	**0.183996**	**32.05108**	**0.000972**
(1) C_{glu}	0.135000	0.431509	0.31286	0.784000
(2) C_{xyl}	0.760000	0.431509	1.76126	0.220256
(3) C_{suc}	0.055000	0.431509	0.12746	0.910236
(1)*(2)	-0.170000	0.431509	-0.39397	0.731642
(1)*(3)	0.025000	0.431509	0.05794	0.959067
(2)*(3)	0.100000	0.431509	0.23174	0.838288

Considering a 90% confidence level at residue stream, the xylose concentration was significant in the lactic acid concentration process in the range under study ($p < 0.1$). Considering a confidence level of 90% at light stream, the effects of glucose, the xylose and sucrose concentrations were not statistically significant as well as their interactions.

Sucrose, glucose, and xylose are carbohydrate molecules with the molar mass of 342.30 $g \cdot mol^{-1}$, 180.16 $g \cdot mol^{-1}$, and 150.13 $g \cdot mol^{-1}$, respectively. For the small carbohydrate molecules, the solubilities are higher in water. Therefore, xylose is more soluble in water than glucose and sucrose, as reported by Cardoso *et al*. (2012). Consequently, when xylose was used in high concentrations (15 $g \cdot L^{-1}$, in runs 3, 4, 7, and 8), a considerable amount of non-volatile solute was present in the solution of lactic acid and water. Based on the ebullioscopy effect, the added xylose increased the boiling temperature of the mixture (vapor pressure was reduced), which made it difficult to volatilize. As a result, less amount of water volatilized and lactic acid with lower concentrations were obtained in runs 3, 4, 7, and 8, which were 110.87 $g \cdot L^{-1}$, 120.10 $g \cdot L^{-1}$, 106.58 $g \cdot L^{-1}$, and 104.66 $g \cdot L^{-1}$, respectively. This fact justified the significant effect of xylose concentrations in the process of lactic acid separation.

Experimental data of lactic acid concentration obtained by SPE in residue stream (LA_R) were modeled by a polynomial equation (Eq. 3) considering only the statistically significant factors. Factor X_2 represents the coded value of xylose concentration.

$$LA_R = 121.6026 - 6.7985 \times X_2 \quad (3)$$

To evaluate the model, the F-test was applied. Table 5 shows the ANOVA for lactic acid concentration at residue stream. For Eq. 3, the $F_{1,9}$ calculated (4.05) was higher than $F_{1,9}$ tabulated (3.36), and $F_{7,2}$ calculated (3.25) was lower than $F_{7,2}$ tabulated (9.35), in the F-tests. Thus, this model depicted by Eq. 3 is well adjusted to the experimental data.

Table 5. ANOVA of Lactic Acid Concentration Model at 90% of Confidence Level

Source of Variation	Sum of Squares	Degrees of Freedom	Mean Square	$F_{calculated}$	$F_{tabulated}$
Regression	369.76	1	369.76	$F_{1,9} = 4.05$	$F_{1,9} = 3.36$
Residues	821.74	9	91.30	$F_{7,2} = 3.25$	$F_{7,2} = 9.35$
Lack of Fit	755.29	7	107.90	-	-
Pure Error	66.45	2	33.22	-	-
Total	1191.50	10	-	-	-

Equation 3 shows that, by increasing the xylose concentration, the lactic acid concentration decreased. This was due to the ebullioscopic effect. Lactic concentration as a function of xylose concentration is shown in Fig. 2.

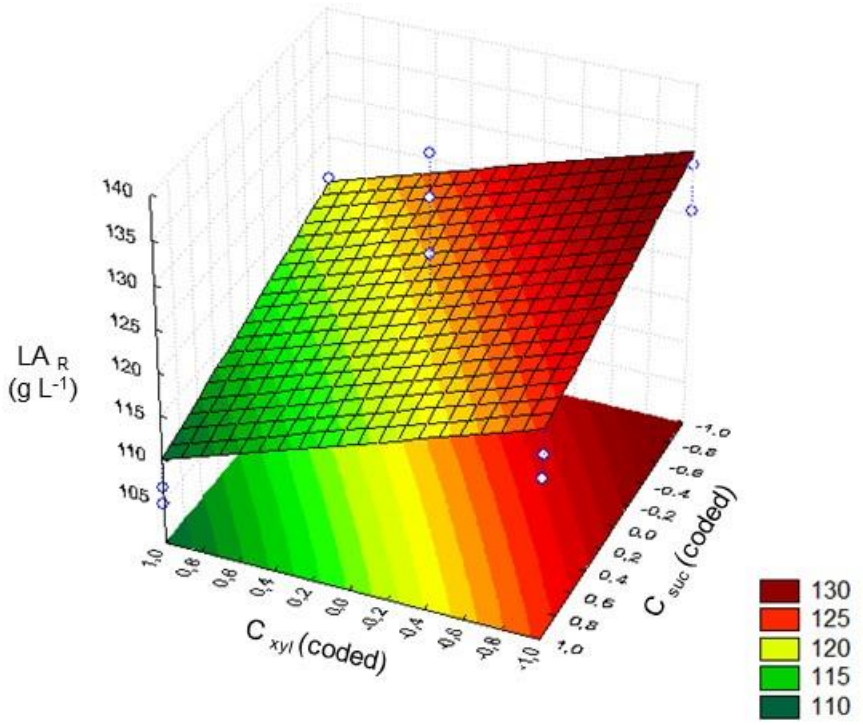

Fig. 2. Response surface diagram of lactic acid concentration at residue stream (LA_R) as a function of xylose (C_{xyl}) and sucrose (C_{suc}) concentrations at a constant concentration of glucose in central point

Considering the interest in maximizing the content of lactic acid in residue stream, it was verified that higher concentrations were obtained in the -1 level. Taking into account the average values obtained at -1 levels, the lactic acid was concentrated in 2.5 times, because the initial concentration of the lactic acid in feed solution was 50 $g \cdot L^{-1}$.

CONCLUSIONS

1. Fermentation systems during lactic acid production generally contained some by-products, such as residual sugars. The effects of the fermentation broth components on the short path evaporation (SPE) performance were analyzed through adding glucose, xylose, and sucrose in various concentrations into the binary lactic acid/water mixtures.

2. The results showed that xylose in high concentrations reduced the lactic acid concentration performance, possibly due to an increase in the boiling temperature of the mixture. Glucose and sucrose had no clear influence on the lactic acid concentration.

3. Further work will be focused on the effect of residual sugars in lactic acid concentration by the SPE from the real fermentation broths.

ACKNOWLEDGEMENTS

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

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Article submitted: February 16, 2017; Peer review completed: April 13, 2017; Revised version accepted: April 27, 2017; Published: May 1, 2017.
DOI: 10.15376/biores.12.2.4352-4363