Ionic Liquid Recovery Alternatives in Ionic Liquid-Based Three-Phase Partitioning (ILTPP)

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Ionic liquid-based three-phase partitioning (ILTPP) is a promising technique to recover high-added value proteins at the liquid–liquid interface. Its economic and environmental performance highly depends on the net ionic liquid consumption. Alternatives to maximize the fraction of ionic liquid that can be recycled are studied. It is demonstrated that the addition of extra salt, previously proposed in literature, has a very limited effect on ionic liquid recovery for relatively high protein concentrations in the feed stream, and that it may even lead to an increase of the ionic liquid losses under certain conditions. However, small additions of salt are shown to be effective and profitable from an economic point of view. Vacuum evaporation is shown to allow for the complete ionic liquid and salt recovery, reinforcing the sustainability and viability of ILTPP processes. © 2014 American Institute of Chemical Engineers *AIChE J*, 60: 3577–3586, 2014
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Introduction

In the last few years, ionic liquids have been used as extraction solvents in a wide variety of separation processes because they have been considered as environmentally friendly solvents that could be applied in green technologies.[1,2] This increasing attention is related to their unique properties, such as negligible vapor pressure, high thermal and chemical stabilities, non-flammability, high-ionic conductivity or wide electrochemical potential window,[3,4] and tunable nature as designer solvents.[5–7] In this way, one of the separation processes based on ionic liquids that have been recently developed is ionic liquid-based three-phase partitioning (ILTPP).

ILTPP is a promising technique to recover proteins by means of their accumulation at the liquid–liquid interface between the aqueous ionic liquid-rich phase and the aqueous salt-rich phase.[8] This technique combines the advantages of ionic liquid-based aqueous two-phase systems (ILATPS) and three-phase partitioning (TPP), because it obtains the interfacial partitioning of the target compound, which is characteristic of TPP,[9–12] with the same ionic liquid/salt systems of ILATPS.[6,13–16] ILTPP has been successfully applied to recover bovine whey proteins such as lactoferrin (LF), which stands out because of its important nutraceutical properties.[17,18] For this purpose, ionic liquid/salt systems that consist of 1-butyl-3-methylimidazolium trifluoromethanesulfonate (BmimTfO) and phosphate salts have been identified as the most suitable for the process.[19]

The economic and environmental profile of ILTPP is highly dependent on the consumption of the reagents involved, and especially of ionic liquid, due to its relatively high price and environmental impact, which may be even higher than some volatile organic solvents.[20] A previous work concluded that between 0.8 and 5% of the ionic liquid used in the ILTPP process could not be reused, depending on the experimental conditions.[21] Despite the apparently low value of these ionic liquid losses, they may lead to both significant economic and environmental impacts, because the ionic liquid constitutes more than the 20% of the ILTPP systems (it is one of the major components). As a result, additional recovery steps should be included in the process to enhance the recovery of the ionic liquid.

The aim of this work is the analysis and modeling of additional ionic liquid recovery steps in the ILTPP process so that the fraction of ionic liquid that cannot be recycled decreases as much as possible. Some previous works based on ILATPS proposed the integration of processes where the solute can be recovered and the ionic liquid recycled, but most of them are developed for tetrafluoroborate-based ionic liquids, which may suffer from hydrolysis when they are in contact with water.[22–28] Furthermore, some of these alternatives require an additional hydrophobic ionic liquid[22,23] or even, volatile organic solvents like dichloromethane[24] or ethyl acetate.[26] Other studies are related to the recovery of ionic liquids from aqueous streams by means of the use of ILATPS,[29,30] but they do not consider the recyclability of the ionic liquid that already constitutes ILATPS. In this sense, Neves et al.[30] proposed a

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recovery of the ionic liquid used in the process based on the evaporation of part of the salt-rich phase. Other works propose an increase in the salt concentration of the system to reduce the fraction of ionic liquid present in the salt-rich phase.[31,32]

The present work investigates the reduction of the ionic liquid losses in ILTPP by means of two different alternatives for its recovery, increase of salt content and evaporation, so that they can be compared in terms of the amount of ionic liquid recycled. The ILTPP systems considered in the present work are based on BmimTfO and phosphate salts as these have been identified as the most suitable to carry out this process.[19] These systems combine very promising results in terms of LF recovery and chemical stability.

Material and Methods

Material

The ionic liquid 1-butyl-3-methylimidazolium trifluoromethanesulfonate, (BmimTfO; 99%), was supplied by IoLiTec (Ionic Liquid Technologies, Germany). Sodium dihydrogenophosphate, NaH_2PO_4 (122018), and sodium hydroxide, NaOH (131687), are the compounds used in the salt fraction of the systems and they were purchased from Panreac Química (Spain). With respect to water, it was obtained by means of double distillation, reverse osmosis and, finally, treated with a Milli-Q plus 185 water purification equipment.

Methods

In the ionic liquid recyclability tests, the ILTPP systems were reused during six cycles. In each cycle, the compositions of the overall system and the two liquid phases were determined by means of the gravimetric method which has been extensively described in literature.[30,33] The ionic liquid of the ILTPP system was recirculated according to the alternatives developed for this purpose. In these tests, protein feed stream was replaced by water because the ionic liquid recovery takes place once most of the protein content, which is accumulated at the liquid–liquid interface, has been removed from the system. Furthermore, the protein mass fraction of the overall system is very low (1.6×10^{-4}), so the overall system composition can be described by means of the three major components: water, ionic liquid, and salt.

In the experiments in which the salt concentration was increased to enhance the ionic liquid reuse, each cycle had two sequential steps. First, a prefixed amount of extra salt was added to the ILTPP system, whose composition had been previously determined. Once the new mixture point was equilibrated and its composition was known, the ionic liquid-rich phase, the fraction of the salt-rich phase that is recycled (established according to the model reported in Section "Addition of extra salt") and the fresh water that simulates the protein feed stream were mixed and a new cycle of the process began.

The alternative based on vacuum evaporation removed the amount of water from the salt-rich phase that is calculated according to the model reported in Section "Concentration of the salt-rich phase by means of evaporation." Then, the amount of water that simulates the feed stream was added to the system to replace the fraction of the salt-rich phase that had been removed, starting a new ILTPP cycle.

All the experiments were replicated, so the results provided are the mean values among them. Very similar results were obtained in all the cases, as the low mean relative experimental deviation (0.5%) for the ionic liquid content in the overall system, which is the key variable in the assessment of the ionic liquid recyclability, demonstrates.

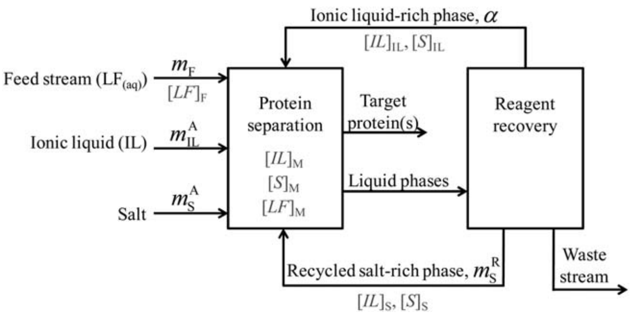

Figure 1. Block diagram of the ILTPP process in which an additional recovery step to reduce the fraction of ionic liquid that is lost in the process is carried out.

Notation: variables in black denote streams whereas variables in gray denote concentrations.

Results and Discussion

Analysis of the ILTPP process for ionic liquid recovery

Previous studies about ILTPP showed that between 0.8 and 5% of the ionic liquid cannot be reused in the process.[21] Figure 1 shows the block diagram of the ILTPP process in which an additional recovery step to reduce the fraction of ionic liquid that is lost in the process is carried out. Also, the notation used to describe the streams is included in Figure 1, where each variable represents a concentration or the mass fraction of the associated stream referred to the total input streams in the first separation tank.

As can be seen, both ionic liquid-rich phase (α) and salt-rich phase are recycled, even though only the former is completely reused. In this way, as the ionic liquid concentration is considerably high in the ionic liquid-rich phase, the complete recirculation of this phase leads to high ionic liquid recoveries even when no additional steps are used, as previously stated.[21] Therefore, only a fraction of the salt-rich phase can be recycled (m_S^R), so that the mass of the overall system is kept constant. The mass introduced with the protein feed stream and the salt and ionic liquid added to the system, so that the concentrations of these components remain constant, constitute the fraction of this salt-rich phase that cannot be reused and, consequently, the waste stream of the process. As a result, in addition to the two previous streams that are recycled, the separation tank has three other feed streams: the protein feed stream (m_F) and the salt (m_S^A) and ionic liquid (m_{IL}^A) that have to be added to keep their concentration constant.

The goal of the additional ionic liquid recovery is to maximize the fraction of ionic liquid that can be recycled in the ILTPP process, R. For this purpose, the general model that is developed in the present work has the following general structure

$$R=f\left([\mathrm{IL}]_{\mathrm{IL}},\ [\mathrm{IL}]_{\mathrm{S}},\ \alpha,\ m_{\mathrm{S}}^{\mathrm{R}}\right) \tag{1}$$

where

$$[\mathrm{IL}]_{\mathrm{IL}},\ [\mathrm{IL}]_{\mathrm{S}},\ [\mathrm{S}]_{\mathrm{IL}},\ [\mathrm{S}]_{\mathrm{S}}=f\left([\mathrm{IL}]_{\mathrm{M}},\ [\mathrm{S}]_{\mathrm{M}}\right) \tag{2}$$

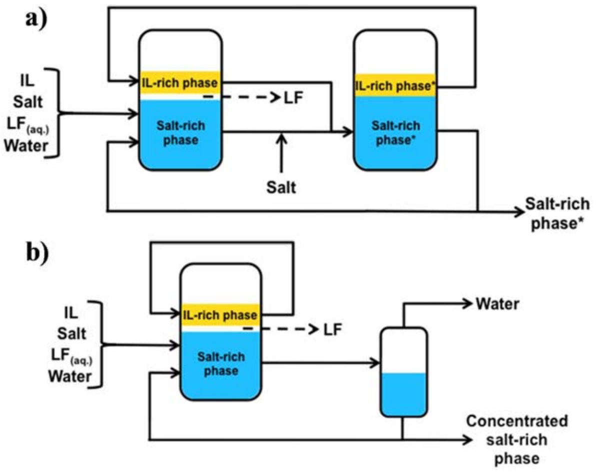

Figure 2. Schematic diagrams of the ILTPP process when: (a) extra salt is added to the system to enhance the ionic liquid recovery; (b) evaporation is used to enhance the ionic liquid recovery.

The asterisk (*) denotes different compositions due to the addition of the extra salt. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

$$\alpha=f\left([\mathrm{S}]_{\mathrm{IL}},\ [\mathrm{S}]_{\mathrm{S}},\ [\mathrm{S}]_{\mathrm{M}}\right) \tag{3}$$

$$m_{\mathrm{F}}=\frac{[\mathrm{LF}]_{\mathrm{M}}}{[\mathrm{LF}]_{\mathrm{F}}} \tag{4}$$

$$m_{\mathrm{S}}^{\mathrm{A}}=f\left([\mathrm{S}]_{\mathrm{M}},\ [\mathrm{S}]_{\mathrm{S}},\ [\mathrm{S}]_{\mathrm{IL}},\ \alpha,\ m_{\mathrm{F}},\ \mathrm{RA}\right) \tag{5}$$

$$m_{\mathrm{S}}^{\mathrm{R}}=f\left(\alpha,\ m_{\mathrm{F}},\ m_{\mathrm{S}}^{\mathrm{A}},\ \mathrm{RA}\right) \tag{6}$$

$$\alpha+m_{\mathrm{F}}+m_{\mathrm{S}}^{\mathrm{A}} \leq 1 \tag{7}$$

where α is the ionic liquid-rich phase mass fraction; $[X]_i$ represents the mass fraction (expressed as percentage) of X (where X can be IL for the ionic liquid and S for the salt) in the phase i (where i can be M for the mixture point in the protein separation tank, IL for the ionic liquid-rich phase and S for the salt-rich phase); $m_{\mathrm{S}}^{\mathrm{R}}$, m_{F}, and $m_{\mathrm{S}}^{\mathrm{A}}$ are the mass fractions of the salt-rich phase that is recycled, the feed stream and the salt that has to be added to the system to remain the salt mass fraction constant, respectively, with respect to the total input streams in the protein separation tank; $[\mathrm{LF}]_{\mathrm{M}}$ is the mass fraction of LF in the mixture point at which the ILTPP is carried out (i.e., in the protein separation tank); $[\mathrm{LF}]_{\mathrm{F}}$ is the mass fraction of LF in the feed stream; and RA is the specific variable(s) of the recovery alternative used to enhance the ionic liquid recyclability. In the model of the ionic liquid recovery in the ILTPP process, the following assumptions are made:

– The amount of ionic liquid that has to be added to the system ($m_{\mathrm{IL}}^{\mathrm{A}}$) can be considered negligible, as the complete recirculation of the ionic liquid-rich phase assures that most of this component can be reused.[21]

– ILTPP leads to the complete recovery of LF at the liquid–liquid interface ($\mathrm{LF_I} = 100\%$) because, on the one hand, values of the fraction of LF recovered at the liquid–liquid interface, $\mathrm{LF_I}$, which are reported in previous works are near 100%,[19] and on the other hand, $\mathrm{LF_I}$ has not a strong effect on 100-R (%) in the range of values analyzed.[21]

As a result, the variable R can be used to measure the effectiveness of the alternatives to reduce the ionic liquid losses in the ILTPP process and it should be maximized. For its calculation, data obtained from the thermodynamic equilibrium and mass balances are required. In this regard, the thermodynamic equilibrium of the ILTPP systems, which is summarized by Eqs. 2 and 3, has been previously described by Alvarez-Guerra et al.[21] In this work, the values of the parameters involved in the equilibrium description are reported: A, B, C, k_1, k_2, m_1, and n_1. It should be noted that there is no other parameters in the model. The thermodynamic equilibrium provides the composition of the two liquid phases as well as the relative mass fraction of each phase, so α can be known from thermodynamics relations. Equations 4–6 are derived from the mass balances of the process and they determine the mass flow of the input streams, with the exception of α that has already been calculated and $m_{\mathrm{IL}}^{\mathrm{A}}$, which is considered negligible. The expression to calculate m_{F} is so simple because of the second assumption that was previously stated. Eventually, the constraint imposed by Eq. 7 introduces the idea that the total mass in the system should be kept constant, so that the sum of the mass fractions of the ionic liquid-rich phase (which is completely recycled), the feed stream, and the salt added to remain its mass fraction constant, cannot be greater than 1. If this sum was equal to 1, any fraction of the salt-rich phase would not be recirculated.

Modeling of the alternatives to enhance the ionic liquid recyclability

Two different alternatives are considered to reduce the amount of ionic liquid lost in the ILTPP process:

– Once the protein accumulated at the liquid–liquid interface is recovered, the addition of an extra amount of salt (Figure 2a) to reduce the concentration of the ionic liquid in the salt-rich phase increasing it in the ionic liquid-rich phase.[31,32]

– Removal of water from the salt-rich phase by means of evaporation (Figure 2b) so that a higher fraction of the ionic liquid and salt contained in this phase is recycled.[30,34]

The model reported in the previous section is specifically developed to describe the net consumption of ionic liquid obtained with these two alternatives when the ILTPP process is performed in continuous. The study is focused on the two systems that showed promising results for the LF recovery: BmimTfO (23.3 wt %)/$\mathrm{NaH_2PO_4}$ (26.3 wt %) and BmimTfO (24.6 wt %)/($\mathrm{NaH_2PO_4}$/$\mathrm{Na_2HPO_4}$) (22.0 wt %).[19,21] In this last system, BmimTfO/($\mathrm{NaH_2PO_4}$/$\mathrm{Na_2HPO_4}$), the salt fraction is also considered as a single component because the $\mathrm{NaH_2PO_4}$:NaOH mass ratio used to prepare it was kept constant at a value of 18.

Addition of Extra Salt. The schematic diagram of this alternative is represented in Figure 2a. The ILTPP is developed in two sequential separation tanks: in the first tank, the protein separation takes place; whereas the ionic liquid recovery occurs in the second tank. Between the two tanks, a stream of salt is added to the system to enhance the ionic liquid recovery in the second tank. The new salt mass fraction of the mixture point in this second tank, $[\mathrm{S}]_{\mathrm{M}}$, is calculated as follows

$$[\mathrm{S}]_{\mathrm{M}}=\frac{[\mathrm{S}]_{\mathrm{M},0}+100m_{\mathrm{S}}^{\mathrm{extra}}}{\left(1+m_{\mathrm{S}}^{\mathrm{extra}}\right)} \tag{8}$$

where $[\mathrm{S}]_{\mathrm{M},0}$ is the salt mass fraction in the mixture point (expressed as wt %) at which the protein recovery is performed, that is, before the addition of salt. As can be appreciated in this alternative, the general variable RA is described by m_S^{extra}, which denotes the mass fraction of extra salt added to the system referred to the total input streams in the first separation tank

$$m_S^{\mathrm{extra}}=\frac{M_M}{M_{M,0}}-1 \tag{9}$$

where $M_{M,0}$ is the total mass flow of the input streams to the first separation tank (before the addition of the extra salt) and M_M is equal to the sum of $M_{M,0}$ and the extra salt added to the system.

The fraction of the ionic liquid that can be reused, R, is specifically assessed in this case according to Eq. 10

$$R=\frac{\alpha[\mathrm{IL}]_{\mathrm{IL}}+m_S^R[\mathrm{IL}]_S}{\alpha[\mathrm{IL}]_{\mathrm{IL}}+(1-\alpha)[\mathrm{IL}]_S} \tag{10}$$

With respect to the fraction of the salt-rich phase that can be recirculated, m_S^R, it can be limited by two different constraints depending on the operating conditions. At relatively low amounts of extra salt added and low protein concentrations in the feed stream, m_S^R is limited by the protein feed stream and the salt that has to be added to the system, so that the concentrations of both LF and salt remain constant without increasing the overall mass of the system. However, for relatively high amounts of both m_S^{extra} and $[\mathrm{LF}]_F$, m_S^R can be limited by the mass of salt that is recirculated with the salt-rich phase so that the mass fraction of the mixture point in the first separation tank does not vary with the performance of ILTPP.

The partial mass balance to the salt is represented by Eq. 11

$$[\mathrm{S}]_{M,0}=100m_S^A+\alpha(1+m_S^{\mathrm{extra}})[\mathrm{S}]_{\mathrm{IL}}+m_S^R[\mathrm{S}]_S \tag{11}$$

where all the concentrations are referred to the mixture point after the addition of the extra salt content (with the exception of $[\mathrm{S}]_{M,0}$) and m_S^A is the mass fraction of the salt added to the first separation tank (maintaining the salt mass fraction constant) with respect to the total input streams in the first tank. An auxiliary variable, denoted by Q_1, is defined to determine which is the constraint that is limiting m_S^R under certain operating conditions

$$Q_1=\frac{[\mathrm{S}]_{M,0}-\alpha(1+m_S^{\mathrm{extra}})[\mathrm{S}]_{\mathrm{IL}}-\left[1-\alpha(1+m_S^{\mathrm{extra}})-m_F\right][\mathrm{S}]_S}{100-[\mathrm{S}]_S} \tag{12}$$

Q_1 represents the mass fraction of salt that has to be added to the system to remain the salt mass fraction constant, m_S^A, when m_S^R is limited by m_F and m_S^A, which also implies that $Q_1 \geq 0$. Otherwise, the addition of salt to remain its mass fraction constant is not required, $m_S^A=0$, and m_S^R can be directly calculated from Eq. 11. Mathematically, these two scenarios are modeled by means of two binary variables, Y_1 and Y_2

$$m_S^A=Y_1\cdot Q_1 \tag{13}$$

$$m_S^R=Y_1\cdot\left[1-\alpha(1+m_S^{\mathrm{extra}})-m_F-m_S^A\right]+Y_2\cdot\frac{[\mathrm{S}]_{M,0}-\alpha(1+m_S^{\mathrm{extra}})[\mathrm{S}]_{\mathrm{IL}}}{[\mathrm{S}]_S} \tag{14}$$

where:

– If $Q_1 \geq 0$: $Y_1=1$, $Y_2=0$
– If $Q_1 < 0$: $Y_1=0$, $Y_2=1$

In this approach, the constraint of Eq. 7 is slightly modified because the ionic liquid-rich phase mass fraction that is recirculated is referred to a system that contains higher mass than the input streams of the first separation tank due to the addition of the extra salt

$$\alpha(1+m_S^{\mathrm{extra}})+m_F+m_S^A \leq 1 \tag{15}$$

The fraction of the ionic liquid that cannot be reused in the ILTPP process is assessed for different amounts of extra salt added (i.e., for different mixture compositions in the second separation tank) and for both systems of interest (Figure 3). In this figure, the curve that corresponds to the lowest value of $[\mathrm{S}]_M$ represents the scenario when additional salt is not added to the system. As can be seen, this approach makes it possible to reduce the losses of ionic liquid to 0.5% in the best scenarios. In both systems, the same trend is observed: for a given amount of extra salt added, 100-R (%) decreases with the protein concentration in the feed stream. However, there is a value of $[\mathrm{LF}]_F$ for which higher protein concentrations cannot achieve any further decrease in 100-R (%). Even though, in the region where 100-R (%) remains constant, a higher amount of the salt-rich phase can be recycled without increasing the total mass of the system, the bottom phase is not recirculated in a greater fraction because in this case, the overall salt mass fraction in the first separation tank will increase, due to the very high content in salt of this bottom phase. This protein concentration that limits the region in which 100-R (%) is constant, decreases with the amount of extra salt added, as the higher the m_S^{extra}, the

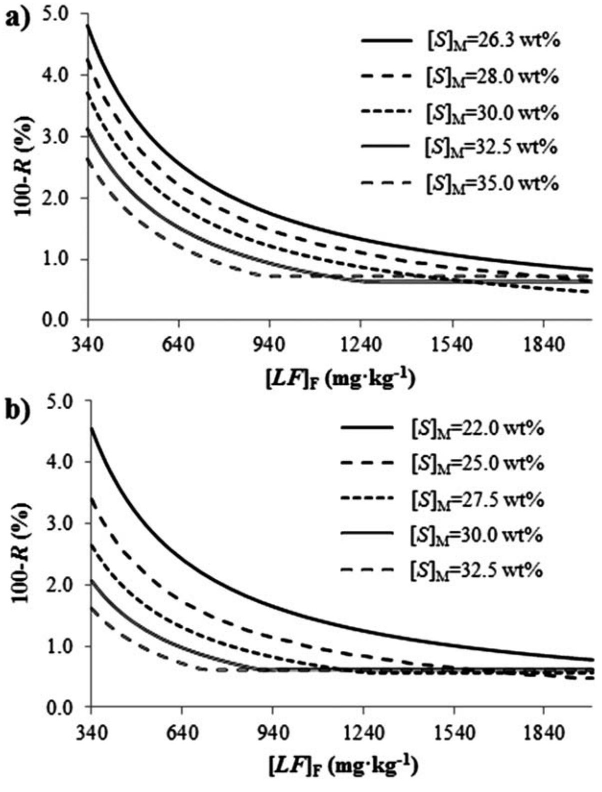

Figure 3. Percentage of ionic liquid lost in each cycle, 100-*R* (%), when the process is developed at different salt mass fractions in the second separation tank with: (a) BmimTfO/NaH_2PO_4 system; (b) BmimTfO/(NaH_2PO_4/Na_2HPO_4) system.

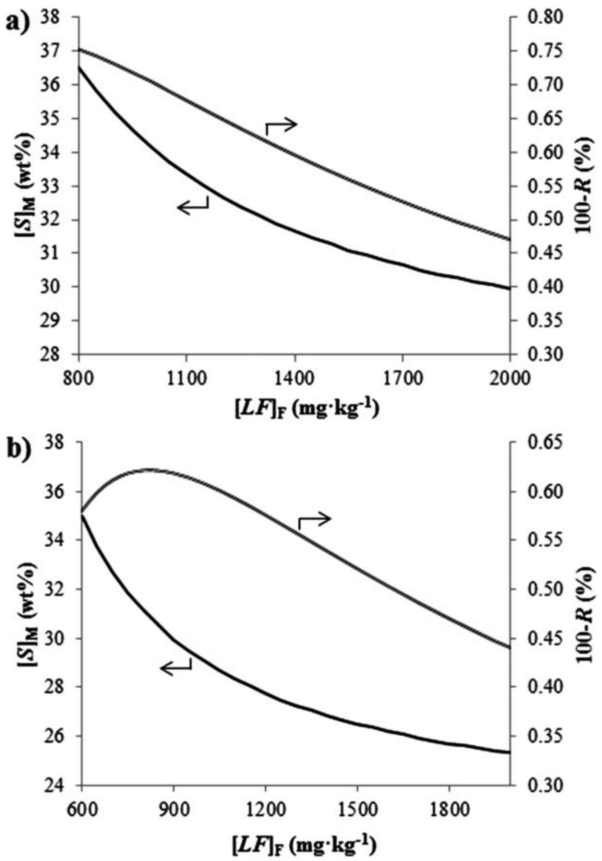

Figure 4. Value of the overall salt mass fraction in the second separation tank that makes $Q_1 = 0$ and the corresponding value of 100-*R* (%) which are obtained for each protein concentration, $[LF]_F$, with: (a) BmimTfO/NaH_2PO_4 system; (b) BmimTfO/(NaH_2PO_4/Na_2HPO_4) system.

lower the fraction of the salt-rich phase that is needed to reach the desired mass fraction in the mixture point used to perform the protein recovery.

This behavior explains why the addition of salt is much more effective in terms of ionic liquid recovery for low values of $[LF]_F$. In this way, whereas the addition of extra salt can lead to a reduction in the ionic liquid losses higher than 60% at low protein concentrations in scenarios with the highest extra salt additions, the enhancement in the ionic liquid recovery decreases to values lower than 20% at high $[LF]_F$. This implies that the addition of extra salt does not introduce notable reductions in the losses of ionic liquid with respect to the case in which no additional recovery steps are introduced at high protein concentrations of the feed stream. Moreover, for high values of $[LF]_F$, the addition of higher amounts of extra salt may increase 100-*R* (%), as can be observed in Figure 3. On the one hand, the fraction of ionic liquid that cannot be reused is very low at high protein concentrations even when no additional steps are used, on the other hand, the constraint for which the overall mass salt fraction must be kept constant is more restrictive when high amounts of extra salt are added. For instance, the curves that correspond to the highest values of $[S]_M$ in both systems show higher ionic liquid losses (100-*R*) than the curves of slightly lower content of salt at high protein concentrations in the feed stream. Under these experimental conditions, as the protein is concentrated in the feed stream, a reduced amount of water is introduced with the feed stream so a high fraction of the salt-rich phase could be recycled without increasing the overall mass of the system. However, due to the extra salt added, if these high fractions of the salt-rich phase were recirculated, the salt mass fraction at which the protein recovery takes place would increase. For this reason, only a lower fraction of the salt-rich phase can be recycled to avoid this increase in the salt content, so slightly lower additions of extra salt would allow a higher recycling of the salt-rich phase and, consequently, a reduction in the ionic liquid losses. Therefore, these ideas explain why, for $[LF]_F > 1500$ mg kg^{-1}, the ionic liquids losses follow the following trends for the BmimTfO/NaH_2PO_4 and BmimTfO/(NaH_2PO_4/Na_2HPO_4) systems, respectively:

$$100-R|_{[S]_M=35.0\%} > 100-R|_{[S]_M=32.5\%} > 100-R|_{[S]_M=30.0\%} \text{ and}$$

$$100-R|_{[S]_M=32.5\%} > 100-R|_{[S]_M=30.0\%} > 100-R|_{[S]_M=27.5\%}$$

Figure 4 shows, for each protein concentration in each system studied, the value of the overall salt mass fraction in the second separation tank that makes that $Q_1 = 0$ and the value of 100-*R* (%) obtained under these conditions. This value of 100-*R* (%) is the minimum ionic liquid loss that can be achieved at the corresponding $[LF]_F$ and, for the same value of $[S]_M$, the value of 100-*R* (%) is constant for higher protein concentrations, as previously explained. For instance, in the BmimTfO/NaH_2PO_4 system, the value of $[S]_M$ that minimizes the losses of ionic liquid at 1000 mg LF kg^{-1} is 34.2 wt %, so for protein concentrations greater than 1000 mg LF kg^{-1}, the fraction of the ionic liquid that cannot be recycled is 0.705% when $[S]_M$ is fixed at 34.2 wt %. The range of values of protein concentrations plotted in Figure 4 leads to component concentrations of the overall system and the individual phases which are feasible, because the values of $[S]_M$ for which $Q_1 = 0$ at lower values of $[LF]_F$ are too high and unfeasible phase compositions are obtained. Figure 4 reinforces the idea that, when $[LF]_F \geq 800$ mg kg^{-1}, the higher the mass protein concentration, the lower the value of 100-*R* (%) and the lower the salt mass fraction that leads to this minimum ionic liquid losses, because the slopes of both $[S]_M$-$[LF]_F$ and (100-*R* (%))-$[LF]_F$ relationships are negative. As a result, for a certain value of $[LF]_F$, it is useless the addition of amounts of extra salt higher than the amount required to obtain the value of $[S]_M$ reported in Figure 4, because greater values of $[S]_M$ will increase the fraction of the ionic liquid that cannot be recovered.

The values of $[S]_M$ shown in Figure 4 should be considered as the upper bound of the addition of extra salt because they minimize the losses of ionic liquid for each protein concentration. However, it should not be interpreted as the optimum value for $[S]_M$, as even though a minimum loss of ionic liquid can provide several advantages from an environmental point of view, this high addition of extra salt to enhance the ionic liquid recovery in a small fraction may not be profitable from an economic point of view. The following economic criterion for the addition of extra salt is proposed, which can be seen as an additional constraint for the general model reported by Eqs. 1–7

$$\frac{dM_S^{IL}}{dM_M^S} \geq \frac{\text{Price of S}}{\text{Price of IL}} \tag{16}$$

where M_S^{IL} is the mass of ionic liquid present in the salt-rich phase and M_M^S is the mass of salt present in the overall

Table 1. Values of the Adjusted Parameters when the Mass Fractions are Expressed as Percentage and R^2 of Eqs. 19 and 20 for Both BmimTfO/NaH$_2$PO$_4$ and BmimTfO/(NaH$_2$PO$_4$/Na$_2$HPO$_4$) Systems

Parameter/ Coefficient	BmimTfO/ NaH$_2$PO$_4$	BmimTfO/(NaH$_2$PO$_4$/ Na$_2$HPO$_4$)
Equation 19: $\alpha = m_2[\mathrm{S}]_\mathrm{M} + n_2$		
m_2	$(-5.937 \pm 0.364) \times 10^{-3}$	$(-7.393 \pm 1.045) \times 10^{-3}$
n_2	0.4157 ± 0.0106	0.4570 ± 0.0277
R^2	0.9981	0.9897
Equation 20: $[\mathrm{S}]_\mathrm{M} = m_3[\mathrm{S}]_\mathrm{S} + n_3$		
m_3	0.9477 ± 0.0469	0.9678 ± 0.0492
n_3	-7.034 ± 1.784	-7.824 ± 1.739
R^2	0.9987	0.9987

system. The idea that supports Eq. 16 is that the value of the ionic liquid recovered from the salt-rich phase because of the addition of salt must not be lower than the value of the extra salt added. If Eq. 16 is developed, the following expression is obtained

$$\frac{\mathrm{d}M_\mathrm{S}^\mathrm{IL}}{\mathrm{d}M_\mathrm{M}^\mathrm{S}} = \frac{(1-\alpha)[\mathrm{IL}]_\mathrm{S}\mathrm{d}M_\mathrm{M} + [\mathrm{IL}]_\mathrm{S}M_\mathrm{M}\mathrm{d}(1-\alpha) + M_\mathrm{M}(1-\alpha)\mathrm{d}[\mathrm{IL}]_\mathrm{S}}{[\mathrm{S}]_\mathrm{M}\mathrm{d}M_\mathrm{M} + M_\mathrm{M}\mathrm{d}[\mathrm{S}]_\mathrm{M}} \tag{17}$$

where

$$[\mathrm{IL}]_\mathrm{S} = k_1 \cdot \exp\left(k_2[\mathrm{S}]_\mathrm{S}\right) \tag{18}$$

$$\alpha = m_2[\mathrm{S}]_\mathrm{M} + n_2 = m_2 m_3[\mathrm{S}]_\mathrm{S} + m_2 n_3 + n_2 \tag{19}$$

$$[\mathrm{S}]_\mathrm{M} = m_3[\mathrm{S}]_\mathrm{S} + n_3 \tag{20}$$

$$M_\mathrm{M} = M_{\mathrm{M},0}\left[\frac{100-[\mathrm{S}]_{\mathrm{M},0}}{100-(m_3[\mathrm{S}]_\mathrm{S}+n_3)}\right] \tag{21}$$

$$\mathrm{d}[\mathrm{IL}]_\mathrm{S} = k_1 k_2 \cdot \exp\left(k_2[\mathrm{S}]_\mathrm{S}\right) \cdot \mathrm{d}\,[\mathrm{S}]_\mathrm{S} \tag{22}$$

$$\mathrm{d}[\mathrm{S}]_\mathrm{M} = m_3 \cdot \mathrm{d}\,[\mathrm{S}]_\mathrm{S} \tag{23}$$

$$\mathrm{d}(1-\alpha) = -m_2 m_3 \cdot \mathrm{d}\,[\mathrm{S}]_\mathrm{S} \tag{24}$$

$$\mathrm{d}M_\mathrm{M} = M_{\mathrm{M},0}\left[\frac{m_3\left(100-[\mathrm{S}]_{\mathrm{M},0}\right)}{\left[100-(m_3[\mathrm{S}]_\mathrm{S}+n_3)\right]^2}\right] \cdot \mathrm{d}\,[\mathrm{S}]_\mathrm{S} \tag{25}$$

It should be noted that $M_{\mathrm{M},0}$ is not required to be known because it is mutually canceled in Eq. 17 and all the variables are expressed as a function of $[\mathrm{S}]_\mathrm{S}$ to cancel differential terms. For this last purpose, the α-$[\mathrm{S}]_\mathrm{M}$ and $[\mathrm{S}]_\mathrm{M}$-$[\mathrm{S}]_\mathrm{S}$ relationships are developed by means of Eqs. 19 and 20, where m_2, m_3, n_2, and n_3 are adjusted parameters whose values are stated in Table 1. These correlations are obtained from data reported by Alvarez-Guerra et al.[21] in a previous work and they are perfectly described by Eqs. 19 and 20, as the high values of R^2 reflects.

Considering the prices obtained from commercial suppliers (Panreac Química for the salt, NaH$_2$PO$_4$, and IoLiTec for the ionic liquid, BmimTfO) for the same quantity of product (1 kg), the ratio of prices reported in Eq. 16 is equal to 0.0508. The application of this economic criterion to the systems of interest for the LF recovery reveals that the maximum overall salt mass fractions that should be reached so that the addition of extra salt is profitable are 27.5% for the BmimTfO/NaH$_2$PO$_4$ system and 26.5% for the BmimTfO/(NaH$_2$PO$_4$/Na$_2$HPO$_4$) system. As a result, these salt concentrations are considerably lower than those reported in Figure 4, so the reuse of the maximum amount of ionic liquid when extra salt is used is not the most advantageous option from the economic point of view.

Therefore, despite the fact that previous works report that the higher the salt mass fraction, the higher the ionic liquid recovery,[31,32] the study of the present section demonstrates that this trend is not true under some conditions due to operational constraints. Furthermore, even though the fraction of ionic liquid reused with this approach can reach 99.5%, the effect of the addition of extra salt on the reduction of losses of ionic liquid is not very high when concentrated protein feed solutions are used. The higher salt consumption that may be required due to the extra addition of this component should also be considered and the additions of extra salt that are profitable from an economic point of view are considerably lower than those required to maximize the ionic liquid recovered. As a consequence, the increase of the salt mass fraction of the system may be useful for limited salt additions and, especially, for low protein concentrations, but this approach presents several constraints that should be taken into account.

Concentration of the Salt-Rich Phase by Means of Evaporation. The addition of the LF to the system implies the introduction of a significant amount of water to the system, which prevents the complete salt-rich phase recirculation. However, if the same amount of water added with the protein feed stream is previously removed from the salt-rich phase, all the ionic liquid and salt contained in the bottom phase can be recycled, without increasing the mass of the overall system. It should be considered that the ionic liquid losses are due to the amount of this component which is contained in the salt-rich phase and cannot be recycled. Due to the negligible vapor pressure of both the ionic liquid and salt, water can be easily separated from these components by means of evaporation.[30,34] Vacuum evaporation at room temperature is used to prevent the degradation with higher temperatures of either ionic liquid or protein that might remain in the salt-rich phase. The schematic diagram of this approach is shown in Figure 2b.

The fraction of the salt-rich phase that is evaporated should be equal to the amount of protein feed stream and salt that has to be added to the system so that their concentrations are constant. However, at relatively low protein concentrations, the fraction of the salt-rich phase that should be evaporated may be greater than its water content, so in these cases, a complete removal of water from the bottom phase takes place, and the maximum fraction of salt-rich phase that can be evaporated is equal to its water mass fraction. An auxiliary variable denoted by Q_2 is defined to identify the case that corresponds to a certain operating condition

$$Q_2 = \frac{m_\mathrm{F} + m_\mathrm{S}^\mathrm{A}}{1-\alpha} \tag{26}$$

Q_2 represents the salt-rich phase fraction that is evaporated when its value is lower than the water mass fraction in this bottom phase. For its calculation, m_F is obtained from Eq. 4, whereas m_S^A and m_S^R are determined as follows

$$m_\mathrm{S}^\mathrm{A} = \frac{\left([\mathrm{S}]_\mathrm{M} - \alpha[\mathrm{S}]_\mathrm{IL}\right)\left(1-m_\mathrm{S}^\mathrm{E}\right) - (1-\alpha-m_\mathrm{F})[\mathrm{S}]_\mathrm{S}}{100-[\mathrm{S}]_\mathrm{S}-100m_\mathrm{S}^\mathrm{E}} \tag{27}$$

$$m_\mathrm{S}^\mathrm{R} = 1-\alpha-m_\mathrm{F}-m_\mathrm{S}^\mathrm{A} \tag{28}$$

where m_S^E is the mass fraction of the salt-rich phase that is evaporated, which is the variable that corresponds to RA in

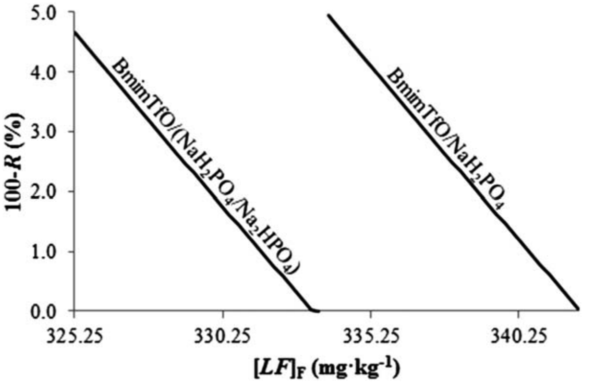

Figure 5. Percentage of ionic liquid lost in each cycle, 100-*R* (%), when evaporation is used to enhance the ionic liquid recovery.

the general model that corresponds to Eqs. 1–7. Considering that Q_2 can be equivalent to m_S^E and combining Eqs. 26 and 27, it is obtained

$$Q_2=\frac{-b-\sqrt{b^2-4ac}}{2a} \tag{29}$$

where

$$a=1-\alpha \tag{30}$$

$$b=-\left[(1-\alpha)(1-0.01[\mathrm{S}]_\mathrm{S})+m_\mathrm{F}+0.01[\mathrm{S}]_\mathrm{M}-0.01\alpha[\mathrm{S}]_\mathrm{IL}\right] \tag{31}$$

$$c=(1-0.01[\mathrm{S}]_\mathrm{S})m_\mathrm{F}+0.01[\mathrm{S}]_\mathrm{M}-0.01\alpha[\mathrm{S}]_\mathrm{IL}-0.01(1-\alpha-m_\mathrm{F})[\mathrm{S}]_\mathrm{S} \tag{32}$$

As a result, the calculation of m_S^E and the fraction of ionic liquid contained in the salt-rich phase that is recycled, IL_S^R, can be done with Eqs. 33 and 34

$$m_S^E=Y_3\left[1-0.01([\mathrm{S}]_\mathrm{S}+[\mathrm{IL}]_\mathrm{S})\right]+Y_4\cdot\ Q_2 \tag{33}$$

$$\mathrm{IL}_S^R=Y_3\frac{m_S^R}{(1-m_S^E)(1-\alpha)}+Y_4 \tag{34}$$

where:

– If $Q_2 \geq 1-0.01\left([\mathrm{S}]_\mathrm{S}+[\mathrm{IL}]_\mathrm{S}\right)$: $Y_3=1,\ Y_4=0$
– If $Q_2 < 1-0.01\left([\mathrm{S}]_\mathrm{S}+[\mathrm{IL}]_\mathrm{S}\right)$: $Y_3=0,\ Y_4=1$

In the first case ($Y_3=1,\ Y_4=0$), m_S^E is limited by the water concentration in the salt-rich phase, whereas in the second case, the mass of the bottom phase is reduced in the same quantity as the mass that has to be added to the system due to m_F and m_S^A. Therefore, the specific expression to calculate the fraction of the ionic liquid that can be recycled, *R*, is equal to

$$R=\frac{\alpha[\mathrm{IL}]_\mathrm{IL}+\mathrm{IL}_S^R(1-\alpha)[\mathrm{IL}]_\mathrm{S}}{\alpha[\mathrm{IL}]_\mathrm{IL}+(1-\alpha)[\mathrm{IL}]_\mathrm{S}} \tag{35}$$

As can be seen, the variable m_S^R is replaced by IL_S^R, since in this alternative, the waste stream has different composition than the part of the salt-rich phase that is recycled and the fraction of ionic liquid that is recycled is the variable that is actually of importance for *R*. In the previous alternative, both the waste stream and the salt-rich phase that is reused have the same composition, $m_S^R=\mathrm{IL}_S^R(1-\alpha)$.

According to the model that describes the recyclability of ionic liquid by means of vacuum evaporation, a complete recovery of both ionic liquid and salt is achieved for almost all protein feed concentrations, with the exception of a narrow range of $[\mathrm{LF}]_\mathrm{F}$, which is plotted in Figure 5 for both systems. For higher values of $[\mathrm{LF}]_\mathrm{F}$, the fraction of salt-rich phase evaporated is lower than its water mass fraction $[Q_2 < 1-0.01\left([\mathrm{S}]_\mathrm{S}+[\mathrm{IL}]_\mathrm{S}\right)]$, so 100% of the ionic liquid and salt can be reused. For lower values of $[\mathrm{LF}]_\mathrm{F}$ than those shown in Figure 5, the feed stream introduces such a high water content that the desired mixture point for each system cannot be reached. In the range of $[\mathrm{LF}]_\mathrm{F}$ depicted in Figure 5, the fraction of ionic liquid that is lost in each cycle decreases from values higher than 4.5 to 0%. In this case, the amount of water that should be removed is greater than the water content in the salt-rich phase, so only a partial recirculation of the ionic liquid present in this bottom phase can be achieved. Therefore, at the lowest value $[\mathrm{LF}]_\mathrm{F}$ at which 100-*R* (%) = 0, a complete water evaporation from the salt-rich phase takes place, so the stream of bottom phase that is recirculated is only composed of salt (mainly) and ionic liquid. If the concentrated salt-rich phase (after evaporation) was constituted only by salt, it would be equivalent to m_S^A, so all the salt of the system would be reused and $m_S^A=0$. However, the actual salt-rich phase also contains ionic liquid, so only part of this bottom phase can be recycled to avoid an increase of the mass of the system. Consequently, both 100-*R* (%) and m_S^A are greater than 0. As the ionic liquid concentration is very low, this is the reason for which this behavior is exhibited in a very narrow range of $[\mathrm{LF}]_\mathrm{F}$. Comparing both systems, the slopes of each curve are almost identical although they are not exactly the same, due to the strong similarities that the thermodynamic equilibria of these two systems exhibit,[21] as the slopes are functions of the system compositions and the phase ratio.

Eventually, it should be noted that if the complete water removal from the bottom phase is carried out, a phase formed mainly by salt and, in a lower content, of ionic liquid is obtained. Even though it may be more difficult to handle than other streams of the process, it does not lead to any unfeasible system.

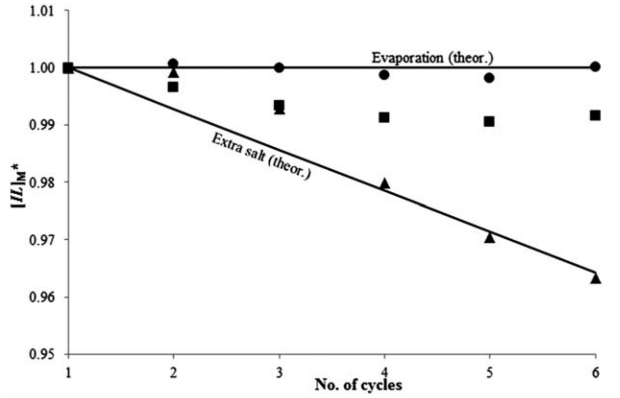

Figure 6. Evolution of both theoretical and experimental dimensionless values of $[\mathrm{IL}]_\mathrm{M}$ for the different recyclability tests.

Notation of experimental points: (■) Evaporation applied to BmimTfO/NaH$_2$PO$_4$ system; (●) Evaporation applied to BmimTfO/(NaH$_2$PO$_4$/Na$_2$HPO$_4$) system; (▲) Addition of extra salt applied to BmimTfO/NaH$_2$PO$_4$ system.

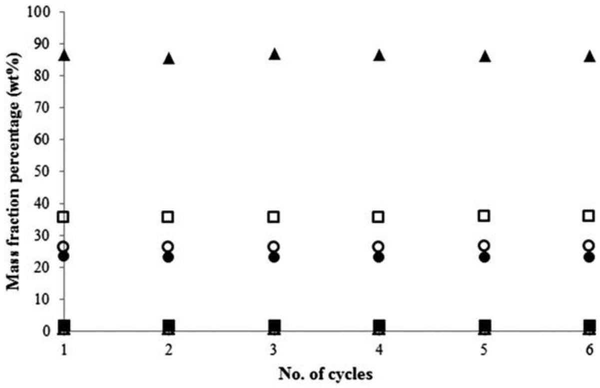

Figure 7. Evolution of the system and phase compositions when the BmimTfO/NaH_2PO_4 system is used and the fraction of ionic liquid recovered is increased by means of evaporation.

Notation: (●) $[IL]_M$; (○) $[S]_M$; (▲) $[IL]_{IL}$; (△) $[S]_{IL}$; (■) $[IL]_S$; (□) $[S]_S$.

Consequently, in contrast with the alternative based on the addition of extra salt, which shows several constraints and a limited enhancement of the ionic liquid recovery, the concentration of salt-rich phase by means of evaporation makes it possible to reuse 100% of both ionic liquid and salt, under almost all operating conditions. As a result, the ILTPP process with an ionic liquid recovery based on vacuum evaporation does not require a net consumption of reagents.

Experimental tests to recycle the ionic liquid of ILTPP systems

The models developed in previous sections to recover the ionic liquid by means of the addition of extra salt and evaporation are experimentally validated. Although these models have been developed for the ILTPP process operating in continuous, the experimental tests to validate them have been carried out in discontinuous mode because the models can be adapted to a discontinuous ILTPP process by means of the replacement of the concept of stream by the concept of load. These experiments are performed for the case in which $[LF]_F = 1000$ mg kg^{-1}, because it is an intermediate concentration of the range of studied values of $[LF]_F$ and it corresponds to the concentration of the protein solutions used in previous works on ILTPP.[8,19] The reuse of the ionic liquid is assessed during six cycles for both BmimTfO/NaH_2PO_4 and BmimTfO/(NaH_2PO_4/Na_2HPO_4) systems for the approach based on evaporation (22% of the salt-rich phase is evaporated in each cycle), because it is the alternative which offers the highest ionic liquid and salt recirculation. Regarding the use of extra salt, it is also assessed for the BmimTfO/NaH_2PO_4 system using mixture points in which $[S]_M = 35$ wt %, because it assures the highest ionic liquid recovery when $[LF]_F = 1000$ mg kg^{-1}.

In Figure 6, the ionic liquid mass fraction of the mixture point, $[IL]_M$, in the different cycles of the recyclability tests is plotted. As can be seen, $[IL]_M$ remains approximately constant equal to the initial ionic liquid mass fraction when evaporation is used to recover it. It demonstrates that evaporation can recover all the ionic liquid used in the ILTPP process, as the model stated in Section "Concentration of the salt-rich phase by means of evaporation" predicts. The slight decrease of the points of BmimTfO/NaH_2PO_4 can be attributed to experimental error, because, on the one hand, the decrease is very similar to the mean relative experimental deviation between the replicates (0.5%) and, on the other hand, it is not observed for BmimTfO/(NaH_2PO_4/Na_2HPO_4) and the model developed in the previous section is the same for both systems. With respect to the recyclability test in which extra salt is added, the loss of ionic liquid in each cycle corresponds to the value predicted by the model developed in Section "Addition of extra salt" (0.72%). After six cycles, the experimental value of $[IL]_M$ is equal to 96.3%, whereas the model predicts a value of 96.4%.

Figure 7 shows the concentrations of both ionic liquid and salt of the overall BmimTfO/NaH_2PO_4 system and the ionic liquid and salt-rich phases when evaporation is used to enhance the recyclability of the ionic liquid. As can be seen, all the concentrations are constant without any addition neither ionic liquid nor salt, during six cycles. As a result, the feasibility of the complete ionic liquid and salt recyclability when vacuum evaporation is used to recover the reagents involved in the ILTPP process is also experimentally demonstrated. Nevertheless, the process optimization should be carried out as future work and the energy penalty due to evaporation must be considered in this analysis.

Conclusions

ILTPP is a promising technique to recover proteins at the liquid–liquid interface, whose economic and environmental profiles highly depend on the recyclability of the reagents required, and especially, the ionic liquid. Two alternatives are analyzed and modeled in this work to enhance the ionic liquid recyclability: (a) the addition of extra salt to increase the concentration in this component and (b) the concentration of the salt-rich phase by means of vacuum evaporation. Even though the increase of the salt concentration is reported in literature as a very attractive option, it is here demonstrated that its effect is limited at high protein concentrations of the feed stream, and that higher salt content may lead to higher ionic liquid losses under certain operating conditions. Furthermore, it may imply a higher salt consumption that only for small salt additions is profitable from an economic point of view. In contrast, the use of vacuum evaporation makes it possible to reuse all the ionic liquid and the salt required in the ILTPP process. Consequently, ILTPP can be seen as a promising alternative to recover LF from waste streams that does not require net reagent consumption, when water is removed from the salt-rich phase by means of evaporation, which is especially important due to the relatively high cost of ionic liquids.

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Notation

a = auxiliary variable
b = auxiliary variable
c = auxiliary variable
A = adjusted parameter
B = adjusted parameter
C = adjusted parameter
k_1 = adjusted parameter
k_2 = adjusted parameter
IL_S^R = fraction of the ionic liquid contained in the salt-rich phase which is recycled
LF_I = fraction of lactoferrin that can be recovered at the liquid–liquid interface
m_F = mass fraction of the feed stream
m_{IL}^A = mass fraction of the ionic liquid added to the first separation tank (so that the salt mass fraction remains constant) with respect to the total input streams in the first tank
m_S^A = mass fraction of the salt added to the first separation tank (so that the salt mass fraction remains constant) with respect to the total input streams in the first tank
m_S^E = mass fraction of the salt-rich phase which is evaporated
m_S^{extra} = mass fraction of extra salt added to the system referred to the total input streams in the first separation tank
m_S^R = mass fraction of the salt-rich phase which is recycled with respect to the total input streams in the first tank
m_1 = adjusted parameter
m_2 = adjusted parameter
m_3 = adjusted parameter
M_M = sum of $M_{M,0}$ and the extra salt added to the system, g s^{-1}
$M_{M,0}$ = total mass flow of the input streams to the first separation tank (before the addition of the extra salt), g s^{-1}
M_M^S = mass of salt contained in the overall system, g
M_S^{IL} = mass of ionic liquid contained in the salt-rich phase, g
n_1 = adjusted parameter
n_2 = adjusted parameter
n_3 = adjusted parameter
Q_1 = auxiliary variable
Q_2 = auxiliary variable
R = fraction of ionic liquid recycled
RA = specific variable(s) of the recovery alternative used to enhance the ionic liquid recyclability
Y_i (i = 1–4) = binary variables
$[S]_{M,0}$ = salt mass fraction in the overall system before the addition of the salt to increase its concentration (m_S^{extra})
$[X]_i$ = mass fraction, expressed as percentage (wt %), of the component X in the phase/stream i, where X can be: IL, ionic liquid; LF, lactoferrin; S, salt; and i can be: F, feed stream; IL, ionic liquid-rich phase; M, mixture (IL + S); S, salt-rich phase
α = mass fraction of the ionic liquid-rich phase
$1-\alpha$ = mass fraction of the salt-rich phase

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