



Thermodynamic study of ATPS involving ethyl lactate and different inorganic salts

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ABSTRACT

In this work, three Aqueous Two-Phase Systems (ATPS) involving ethyl lactate and the inorganic salts $(\text{NH}_4)_2\text{SO}_4$, K_2HPO_4 and NaH_2PO_4 have been studied. To analyse the separation process, binodal curves and tie lines were experimentally determined at $T = 298.15$ K and atmospheric pressure. The experimental binodal data were successfully fitted using several empirical equations: Merchuk *et al.*, Hu *et al.*, Han *et al.* and Jayapal *et al.*, and the degree of consistency of the tie line compositions was evaluated using Othmer-Tobias and Brancoft equations. The liquid–liquid equilibria were fitted using the Pitzer-Debye-Hückel + UNIQUAC and the UNIQUAC thermodynamic models. For all systems, the modelled tie lines were very similar to the experimental ones, but the first model presented somewhat smaller deviations, which allows to conclude that long-range forces present in these systems with strong salts should be considered.

1. Introduction

Aqueous Two-Phase Systems (ATPS) is a separation technique based on the formation of two immiscible phases by mixing different water-soluble compounds [1]. Due to the high water-content in both immiscible phases and to the use of non-toxic chemical compounds, this technique provides a suitable environment to separate different biomolecules without modifying their chemical structure and, at the same time, preventing their denaturation. This fact is a crucial advantage of the ATPS, since the conventional liquid-liquid extraction presents serious drawbacks such as long residence times, high temperatures and pressures, as well as the presence of toxic organic solvents, which could irreversibly damage the bio-compounds [1–3].

The most common ATPS are based on two polymers, on a polymer and a salt or on an ionic liquid and a salt [1,2,4,5]. With the need to find new green chemical compounds capable of forming biphasic aqueous systems, in this work, ethyl lactate (EL) has been chosen as component for the formation of ATPS, since it is a biodegradable solvent which can be produced from bio-renewable sources as corn fermentation [7]. Therefore, it is a promising solvent due to its attractive chemical and physical properties, such as low toxicity [6], low corrosivity, high biodegradability and good solvent power [8].

Besides, several reported studies show promising results in the application of ethyl lactate as extraction agent for different biomolecules [9–13]. In a previous work [14], the separation of flavonoids with ATPS formed by ethyl lactate and organic salts was studied, and good partitioning results were obtained. Hence, in this work, new ATPS formed with ethyl lactate and inorganic salts are studied with the aim of analysing their behaviour and suitability to future applications in the extraction of biomolecules.

The knowledge on how biomolecules are distributed in the two phases of the ATPS is still scarce, so the study of the LLE is essential, and it usually relies on understanding the influence of the hydrophobicity of the ATPS-forming compounds and the influence of temperature [2,1,15–17]. Hydrophobicity is an especially important factor in the partitioning of biomolecules such as proteins and the salting-out effect is believed to heavily influence the hydrophobic interactions [5]. The addition of a salt composed by ions of different hydrophobicity to a system leads to a preferential distribution of the biomolecules from the salt-rich phase to the solvent-rich phase (partitioning) [5,15].

Therefore, the experimental determination of ATPS is necessary to better understand the extraction process, to develop predictive models for the mechanisms involved in the partitioning of biomolecules and

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thus to be able to select the most suitable ATPS based on the physico-chemical properties of a specific biomolecule.

In this way, binodal curves and tie lines for three ATPS containing ethyl lactate and one inorganic salt (ammonium sulphate, $(\text{NH}_4)_2\text{SO}_4$, or di-potassium hydrogen phosphate, K_2HPO_4 , or sodium dihydrogen phosphate, NaH_2PO_4) have been measured at $T = 298.15$ K and atmospheric pressure. The binodal curves were fitted using several equations widely used in this kind of systems [19–22] and the degree of consistency of the tie line compositions was evaluated using Othmer-Tobias [23] and Bancroft [24] equations.

Furthermore, the thermodynamic modelling of the studied ATPS was performed using two different approaches: the Pitzer-Debye-Hückel + UNIQUAC (PDH + UNIQUAC) and the UNIQUAC models. As UNIQUAC was not originally developed for electrolytes, the salts were considered as if they were in their molecular and neutral form and only short-range interaction forces were accounted for (three different chemical compounds in the system). However, it is known that strong salts dissociate when mixed with some solvents, namely water. Therefore, the PDH + UNIQUAC model was adopted in this study to describe long-range interactions. In this model, salts are considered as fully dissociated (four different chemical species in the system). Although very good results were obtained for both models, it is worth mentioning that PDH + UNIQUAC provides calculated tie lines that are in slightly better agreement with the experimental ones. This means that the assumption that the salt is dissociated is more realistic.

2. Experimental section

2.1. Chemicals

Ethyl lactate with purity higher than 0.99 in mass fraction was purchased from Sigma-Aldrich and it was used without any further purification. Inorganic salts: ammonium sulphate, $(\text{NH}_4)_2\text{SO}_4$, di-potassium hydrogen phosphate, K_2HPO_4 , and sodium dihydrogen phosphate, NaH_2PO_4 , were procured from commercial suppliers with purities greater than 0.98 in mass fraction in all cases. All salts are anhydrous species and they were used after drying with heating in order to prevent water adsorption. A summary of purities and suppliers of all chemicals employed are listed in Table 1.

2.2. Apparatus

Aqueous solutions used in the experimental procedure were prepared by weighing using a Mettler AX-205 Delta Range scaler with a measurement uncertainty of $\pm 3 \cdot 10^{-4}$ g. The physical properties, density (ρ) and refractive index (n_D) of the binary and ternary mixtures were measured using an Anton Paar DSA-5000 M digital vibrating tube densimeter with a measurement uncertainty of $\pm 3 \cdot 10^{-5}$ g·cm $^{-3}$ and an automatic refractometer Abbemat-HP Dr. Kernchen with an uncertainty in the measurement of $\pm 4 \cdot 10^{-5}$, respectively. The equilibrium temperature was maintained at $T = 298.15$ K using a PoliScience thermostat bath digital temperature controller. The temperature was controlled with a digital thermometer ASL model F200 with an uncertainty of ± 0.01 K. The pH measurements of both phases in equilibrium were measured at $T = 298.15$ K and atmospheric pressure using a pHmeter Crison Basic 20 with a measurement uncertainty of pH and

Table 1
Purity and suppliers of pure compounds used in this work.

Compound	Supplier	Purity ^a
(-) Ethyl L-lactate	Sigma-Aldrich	≥ 99%
Ammonium sulphate	Sigma-Aldrich	≥ 99%
di-Potassium hydrogen phosphate	Scharlau	≥ 98%
Sodium di-hydrogen phosphate	Panreac	≥ 99%

^a purity given by the suppliers.

temperature of ± 0.01 and ± 0.1 K, respectively. pH standard solutions (pH = 4.01, 7.00 and 9.21) were used for pHmeter calibration prior to measurements.

2.3. Binodal curves

Binodal curves of the ternary systems {ethyl lactate (1) + inorganic salt (2) + water (3)}, being the inorganic salts: $(\text{NH}_4)_2\text{SO}_4$, K_2HPO_4 , and NaH_2PO_4 , were experimentally determined at $T = 298.15$ K and atmospheric pressure using the cloud point method [18]. This technique has been extensively used for the measurement of ATPS, namely those containing ethyl lactate and different organic salts, and has already been thoroughly described [14]. So, to build binodal curves, drops of pure ethyl lactate were added to a known amount of the corresponding aqueous salt solution until a turbid mixture was reached. Composition of cloudy mixtures was reached by weighing. Afterwards, drops of water were added until one homogeneous mixture was observed. This procedure was repeated until enough data was obtained. In a similar way, to cover the whole range of compositions of the solubility curve, a known amount of ethyl lactate was titrated with the corresponding aqueous salt solution, following the abovementioned procedure.

Pure ethyl lactate and aqueous salt solutions of $(\text{NH}_4)_2\text{SO}_4$ (40.88 wt%), K_2HPO_4 (50.00 wt%) and NaH_2PO_4 (44.44 wt%) were used in the preparation of ATPS. These compositions correspond to the maximum solubility of the corresponding salt in water at room temperature (stock solutions).

2.4. Tie lines

The experimental determination of tie lines of the three aqueous two-phase systems {ethyl lactate (1) + $(\text{NH}_4)_2\text{SO}_4/\text{K}_2\text{HPO}_4/\text{NaH}_2\text{PO}_4$ (2) + water (3)} was undertaken at $T = 298.15$ K and atmospheric pressure. Ternary mixtures of the studied components within the immiscible region were prepared by weighing and were placed into glass cells sealed with rubber covers to avoid moisture absorption. Then, they were vigorously stirred for 6 h to achieve a good contact among the two phases and they were allowed to settle overnight to ensure a complete phase separation. Both stirring and settling were carried out in a thermostatic bath with temperature control. After equilibrium was reached, samples from both phases were withdrawn to measure their concentrations.

The composition of the tie lines was calculated through a method based on the measurement of two physical properties: density (ρ) and refractive index (n_D) at $T = 298.15$ K and atmospheric pressure. First, binary and ternary mixtures with known composition were gravimetrically prepared. Second, mixture compositions were carefully chosen within the miscible region of the corresponding phase diagram to homogeneously cover it. Then, density and refractive index were measured for each mixture at $T = 298.15$ K and atmospheric pressure. Experimental data of both physical properties were fitted to a polynomial expression that relates the corresponding physical property to mixture composition, as follows:

$$Q = \sum_{i=1}^n \sum_{j=1}^m A_{ij} w_i^m \quad (1)$$

where Q is the physical property (ρ or n_D), n is the number of components of the ternary mixtures, m is the degree of polynomial expression, w_i is the mass fraction of component i and A_{ij} are the fitting parameters.

Following a very common approach [14], the compositions of the tie lines were calculated by combining the two polynomial expressions (eq. (1)) with the experimental data of density and refractive index measured for the corresponding phases of each tie line.

To assess the behaviour of the tie lines, the tie line length (TLL) and the tie line slope (STL) were calculated using the following expressions:

$$\text{TLL} = \sqrt{(w_{\text{EL}}^{\text{top}} - w_{\text{EL}}^{\text{bot}})^2 + (w_{\text{salt}}^{\text{top}} - w_{\text{salt}}^{\text{bot}})^2} \quad (2)$$

$$\text{STL} = (w_{\text{EL}}^{\text{top}} - w_{\text{EL}}^{\text{bot}}) / (w_{\text{salt}}^{\text{top}} - w_{\text{salt}}^{\text{bot}}) \quad (3)$$

where the subscripts EL and salt denote ethyl lactate and salt compositions in mass fraction and the superscripts top and bot refer to the top and bottom phases, respectively.

The degree of consistency of the composition of the phases in equilibrium was ascertained through the equations proposed by Othmer-Tobias (Eq. (4)) and Bancroft (Eq. (5)) [23,24]:

$$\log \left[\frac{1 - w_{\text{EL}}^{\text{top}}}{w_{\text{EL}}^{\text{top}}} \right] = K_1 + n \cdot \log \left[\frac{1 - w_{\text{salt}}^{\text{bot}}}{w_{\text{salt}}^{\text{bot}}} \right] \quad (4)$$

$$\log \left[\frac{1 - w_{\text{water}}^{\text{bot}}}{w_{\text{salt}}^{\text{bot}}} \right] = K_2 + r \cdot \log \left[\frac{1 - w_{\text{EL}}^{\text{top}}}{w_{\text{EL}}^{\text{top}}} \right] \quad (5)$$

where $w_{\text{water}}^{\text{top}}$ and $w_{\text{water}}^{\text{bot}}$ are the mass fractions of water in the top and bottom phases in equilibrium, respectively, and where $w_{\text{EL}}^{\text{top}}$ and $w_{\text{salt}}^{\text{bot}}$ are the compositions, in mass fraction, of ethyl lactate in the top phase and salt in the bottom phase, respectively.

3. Results and discussion

3.1. Phase diagrams: Binodal curves and tie lines

3.1.1. Tests of ATPS formation

Prior to the experimental determination of the presented phase diagrams, a preliminary study of the formation of ATPS containing ethyl lactate and different inorganic salts (KH_2PO_4 , Na_3PO_4 , Na_2HPO_4 , KHCO_3 , Na_2CO_3 , NaHCO_3 , NH_4Cl , K_2SO_4 and Ca_2SO_4) at $T = 298.15$ K and atmospheric pressure was performed. Table 2 displays a summary of the obtained results. These tests showed that ethyl lactate can form ATPS with the following salts: K_3PO_4 , K_2HPO_4 , NaH_2PO_4 , and $(\text{NH}_4)_2\text{SO}_4$. Ethyl lactate also forms two immiscible phases with Na_3PO_4 , however, due to the very low salt solubility in water (10.5 wt%), the phase diagram is very reduced.

Conversely, ethyl lactate is not able to generate ATPS with the inorganic salts: KHPO_4 , Na_2HPO_4 , KHCO_3 , Na_2CO_3 and NaHCO_3 , due to the salt precipitation in the whole range of compositions. With the salts: K_2SO_4 , Ca_2SO_4 and NH_4Cl , the phase splitting is not produced throughout the range of compositions.

These results agree with previous works related to ATPS formation with PEG and ionic liquids with different salts [1,25–27]. Moreover, the contribution of the salt anion is more important than that of the cation in the phase splitting. Besides, trivalent anions (trivalent) are more effective in inducing phase separation than divalent ones, and these are stronger than monovalent anions. These assessments are in accordance with the widely known Hoffmeister series, which is a classification of ions based on the salting-out capability [28].

Table 2

Study of the ATPS formation in the ternary systems {ethyl lactate (1) + inorganic salt (2) + water (3)} at $T = 298.15$ K and $p = 0.1$ MPa^a.

Salt	ATPS	Salt	ATPS	salt	ATPS
K_3PO_4	√ ^c	KH_2PO_4	Precipitation	Na_2HPO_4	Precipitation
K_2HPO_4	√ ^{b,c}	Na_3PO_4	√	NaH_2PO_4	√ ^b
Na_2CO_3	Precipitation	$(\text{NH}_4)_2\text{SO}_4$	√ ^b	NH_4Cl	×
KHCO_3	×	NaHCO_3	Precipitation	K_2SO_4	×
Ca_2SO_4	×				

√ denotes ATPS can be formed by EL and salt.

× denotes ATPS cannot be formed by EL and salt.

Precipitation denotes EL and salt generates precipitation.

^a Standard uncertainties u are $u(T) = 0.01$ K and $u(p) = 1$ kPa.

^b denotes ATPS experimental data reported [13].

^c denotes ATPS experimental data presented in this work.

3.1.2. Phase diagrams: Binodal curves and tie lines

The phase diagram is very specific to a system under detailed conditions and shows the potential working area of the ATPS. The analysis of the binodal curves and tie lines provides important information about the concentration of components for two phase formation and the composition of the top and bottom phases [1,5].

In this work, the binodal curves for the ATPS containing ethyl lactate and the salts: $(\text{NH}_4)_2\text{SO}_4$, K_2HPO_4 and NaH_2PO_4 were experimentally determined at $T = 298.15$ K and atmospheric pressure. Experimental binodal curve data are drawn in Fig. 1. Besides, the reported data for the ternary system {ethyl lactate (1) + K_2HPO_4 (2) + water (3)} by Kamilanathan et al. [13] are also plotted in Fig. 1. As it can be observed, the experimental data from this essay for the ATPS involving K_2HPO_4 agree with the values reported in the literature, within the errors associated with the cloud point method.

As shown in Fig. 1, the binodal curves of the systems exhibit a very similar behaviour, indicating that these three salts have a similar phase-forming ability. This trend is in accordance with the well-known Hofmeister series [28] and the results reported by other authors for IL-based ATPS [29–39].

Experimental binodal data of {ethyl lactate (1) + $(\text{NH}_4)_2\text{SO}_4$ / K_2HPO_4 / NaH_2PO_4 (2) + water (3)} were fitted using the following equations proposed by Merchuk et al. [19] (Eq. (6)), Hu et al. [20] (Eq. (7)), Han et al. [21] (Eq. (8)) and Jayapal et al. [22] (Eq. (9)), respectively:

$$[\text{EL}] = A \cdot \exp(B[\text{salt}]^{0.5} - C[\text{salt}]^3) \quad (6)$$

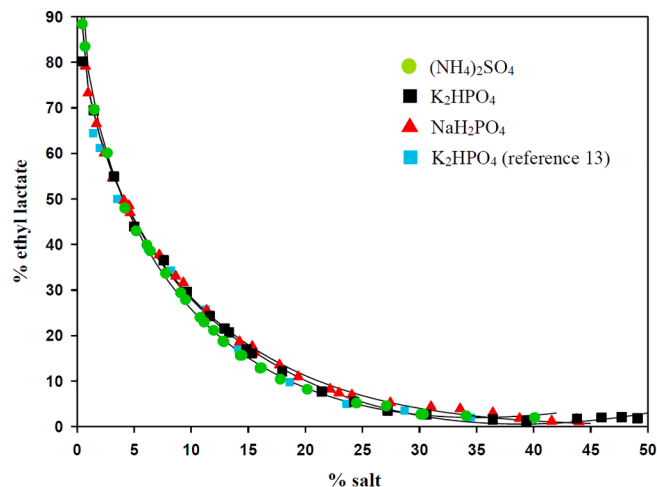


Fig. 1. Binodal curve of the studied ternary systems {ethyl lactate (1) + salt (2) + water (3)} determined at $T = 298.15$ K and atmospheric pressure. The symbols represent the experimental data and the line corresponds to the best fit obtained for each system. Salts: (●) $(\text{NH}_4)_2\text{SO}_4$, (■) K_2HPO_4 and (▲) NaH_2PO_4 (data presented in this work) and (■) K_2HPO_4 (reference [13]).

$$[\text{EL}] = A + B[\text{salt}]^3 + C[\text{salt}] + D[\text{salt}]^2 \quad (7)$$

$$[\text{EL}] = \exp(A + B[\text{salt}]^3 + C[\text{salt}] + D[\text{salt}]^2) \quad (8)$$

$$[\text{EL}] = A + B[\text{salt}]^{0.5} + C[\text{salt}] \quad (9)$$

where [EL] and [salt] are the compositions of ethyl lactate and salt in weight percentages, respectively, and A, B, C, and D are the adjustable parameters. Although the most common equation for the fitting of the binodal curves is equation (6), other equations have also been applied for fitting of binodal data of aqueous two-phase systems involving polymers, ionic liquids and salts [40–44]. Being so, the fitted parameters obtained for each ternary system with the corresponding standard deviations (σ) of Eqs. (1), (2), (3) and (4) are given in Table 3 and the best fit for each ternary system is presented in Fig. 1, with the objective of comparing their performance in the description of the experimental data. Based on the values of σ , it can be concluded that Eq. (7) shows a better fit for the systems involving the inorganic salts: $(\text{NH}_4)_2\text{SO}_4$ and K_2HPO_4 whereas for the ATPS containing NaH_2PO_4 the best result is obtained with Eq. (8). As can be seen in Table 3, Merchuk's equation does not convey the smallest deviations for any of the studied systems.

Experimental feed and tie lines' compositions, as well as their corresponding length (TLL) and slopes (STL), are shown in Table 4. The tie lines' compositions were calculated using the method based on the measurement of the physical properties density and refractive index previously described. The adjustable parameters of the polynomial expressions (Eq. (1)) for each physical property are presented in Table 4.

The tie line length (TLL) is a widely used parameter to study aqueous two-phase systems since it gives relevant information on the broadness of the two-phase region in the phase diagram [45]. As it can be inferred from Table 5, an increase of ethyl lactate composition in the feed leads to an increase in the concentration of EL and salt in the top and bottom phases, respectively, and higher TLL values. Hence, the top phase is the EL-rich phase whereas the bottom phase is the salt-rich phase. The TLL

Table 3

Fitting parameters obtained with eqs. (6), (7), (8) and (9) and standard deviation for the experimental binodal curves data^a.

System	A	B	C	D	σ^a
Merchuk <i>et al.</i> equation (6)					
EL + $(\text{NH}_4)_2\text{SO}_4$ + water	122.383	-0.457	$8.79 \cdot 10^{-5}$	—	1.203
EL + K_2HPO_4 + water	108.762	-0.393	$8.76 \cdot 10^{-5}$	—	1.317
EL + NaH_2PO_4 + water	112.874	-0.412	$5.83 \cdot 10^{-5}$	—	1.279
Hu <i>et al.</i> equation (7)					
EL + $(\text{NH}_4)_2\text{SO}_4$ + water	112.077	-37.344	3.181	$-4.16 \cdot 10^{-4}$	0.603
EL + K_2HPO_4 + water	100.945	-29.030	1.820	$6.52 \cdot 10^{-3}$	0.719
EL + NaH_2PO_4 + water	102.263	-30.314	2.177	$2.42 \cdot 10^{-3}$	0.780
Jayapal <i>et al.</i> equation (8)					
EL + $(\text{NH}_4)_2\text{SO}_4$ + water	111.970	-37.218	3.149	—	0.603
EL + K_2HPO_4 + water	103.829	-32.053	2.499	—	0.901
EL + NaH_2PO_4 + water	103.287	-31.350	2.412	—	0.795
Han <i>et al.</i> equation (9)					
EL + $(\text{NH}_4)_2\text{SO}_4$ + water	4.725	-0.342	-0.027	$-1.26 \cdot 10^{-3}$	0.666
EL + K_2HPO_4 + water	4.586	-0.252	-0.033	$-1.23 \cdot 10^{-6}$	0.998
EL + NaH_2PO_4 + water	4.614	-0.280	-0.029	$-9.07 \cdot 10^{-4}$	0.773

^a Standard deviation; $\sigma = \left\{ \sum_i^{n_{\text{dat}}} ((z - z_{\text{cal}}))^2 / n_{\text{dat}} \right\}^{1/2}$ (z and z_{cal} are the values of the experimental and calculated property and n_{dat} is the number of experimental data points)

Table 4

Polynomial expressions for density and refractive index as function of the composition for the studied ternary systems.

{EL (1) + $(\text{NH}_4)_2\text{SO}_4$ (2) + water (3)}
$\rho = 0.0870 \cdot w_1 + 1.0699 \cdot w_1^2 - 0.1218 \cdot w_1^3 + 0.0704 \cdot w_2 + 1.5542 \cdot w_2^2 - 0.0046 \cdot w_2^3 + 0.2363 \cdot w_3 + 0.9010 \cdot w_3^2 - 0.1412 \cdot w_3^3$
$n_D = -0.0108 \cdot w_1 + 1.4281 \cdot w_1^2 - 0.0050 \cdot w_1^3 + 0.0123 \cdot w_2 + 1.4857 \cdot w_2^2 - 0.0588 \cdot w_2^3 - 0.0051 \cdot w_3 + 1.3371 \cdot w_3^2 + 0.0002 \cdot w_3^3$
{EL (1) + K_2HPO_4 (2) + water (3)}
$\rho = 0.0458 \cdot w_1 + 1.0209 \cdot w_1^2 - 0.0322 \cdot w_1^3 + 0.2598 \cdot w_2 + 1.7563 \cdot w_2^2 + 0.5306 \cdot w_2^3 - 0.0172 \cdot w_3 + 1.0476 \cdot w_3^2 - 0.0340 \cdot w_3^3$
$n_D = 0.0240 \cdot w_1 + 1.4562 \cdot w_1^2 - 0.0668 \cdot w_1^3 + 0.0446 \cdot w_2 + 1.5012 \cdot w_2^2 - 0.0301 \cdot w_2^3 + 0.1635 \cdot w_3 + 1.2407 \cdot w_3^2 - 0.0724 \cdot w_3^3$
{EL (1) + NaH_2PO_4 (2) + water (3)}
$\rho = -0.0125 \cdot w_1 + 1.0734 \cdot w_1^2 - 0.0245 \cdot w_1^3 + 0.3395 \cdot w_2 + 1.7041 \cdot w_2^2 + 0.1201 \cdot w_2^3 + 0.0404 \cdot w_3 + 0.9951 \cdot w_3^2 - 0.0391 \cdot w_3^3$
$n_D = -0.0114 \cdot w_1 + 1.4429 \cdot w_1^2 - 0.0171 \cdot w_1^3 - 0.0423 \cdot w_2 + 1.4786 \cdot w_2^2 + 0.0953 \cdot w_2^3 + 0.0519 \cdot w_3 + 1.3030 \cdot w_3^2 - 0.0234 \cdot w_3^3$

values obtained were similar for the four ternary systems presented in this work. Regarding the tie line slopes (STL), a slight variation is observed between the STL values, which means that the tie lines are almost parallel. The steepest STL values among the studied systems were obtained for the ATPS formed by the salt $(\text{NH}_4)_2\text{SO}_4$.

Finally, the degree of consistency of the tie lines was confirmed using the Othmer-Tobias (Eq. (4)) and Bancroft (Eq. (5)) equations [23,24]. The adjustable parameters and their calculated coefficient of determination (R^2) values are given in Table 6.

Table 5 also shows the pH values of the top and bottom phases. The knowledge of the pH values of phases is very important to choose an adequate ATPS for the partition of a specific biomolecule. Different pH values may alter the charge and surface properties of the solute, which affects the partition of biomolecule [1,2]. The pH values of both phases are very similar for the ATPS based on the salts $(\text{NH}_4)_2\text{SO}_4$, K_2HPO_4 and NaH_2PO_4 , being the mean values around 8, 5 and 4, respectively. Therefore, considering that the behaviour of the phase diagrams of the ternary systems involving the inorganic salts $(\text{NH}_4)_2\text{SO}_4$, K_2HPO_4 and NaH_2PO_4 are similar, the corresponding TLL are comparable for the three ATPS. A first selection of the most suitable ATPS to separate a specific biomolecule between the systems presented in this work would depend on the pH range at which the biomolecule to be separated is chemically stable.

3.2. Thermodynamic modelling

Thermodynamic modelling of phase equilibria is very important since it allows to accurately predict the composition of the different phases and since it can be useful as a support for the design and simulation of unit operations [46]. So far, for ATPS, salts have been modelled in their neutral molecular form and there is a lack of studies considering them as ionised species. Therefore, two different approaches were used to represent the tie lines composition of the studied ATPS: the PDH + UNIQUAC and the UNIQUAC models. In the literature, no previous works were found concerning the application of thermodynamic models in the description of these particular ATPS.

UNIversal QUAsi-Chemical (UNIQUAC) [47] is an excess Gibbs free energy equation widely used in the modelling of non-charged species. Although it was not developed for electrolytes, it has been successfully applied in vapor–liquid equilibria (VLE) and liquid–liquid equilibria (LLE) systems involving organic and inorganic salts [5,48], which are considered in their molecular form, since the model only accounts for short-range interaction forces. UNIQUAC requires two structural parameters for each pure component: the volume, r_i , and the surface area, q_i . These were calculated by summing the structural parameters of the ions that constitute them, which can be observed in Table 7. Following this approach (equations for the UNIQUAC model are not given here, as they are well known),

Table 5

Experimental phase equilibrium compositions (in weight percentages), together with their corresponding tie line lengths (TLL) and tie line slopes (STL) for the systems {EL(1) + inorganic salt (2) + water (3)} as well as pH measurements of each phase at $T = 298.15$ K and $p = 0.1$ MPa^a.

Tie line (TL)	Feed		Top phase			Bottom phase			STL	TLL
	[EL] _{feed}	[salt] _{feed}	[EL] _{top}	[salt] _{top}	pH _{top}	[EL] _{bot}	[salt] _{bot}	pH _{bot}		
{ethyl lactate (1) + (NH ₄) ₂ SO ₄ (2) + water (3)}										
TL1	30.0	12.0	63.6	1.3	4.89	10.5	18.3	4.62	-3.14	55.75
TL2	33.0	12.6	68.9	0.9	4.95	7.2	21.1	4.77	-3.06	64.95
TL3	36.0	13.2	72.4	0.7	4.96	5.9	23.9	4.90	-2.86	70.36
TL4	39.0	13.8	75.6	0.5	5.04	3.9	26.7	4.69	-2.73	76.33
TL5	41.9	14.6	78.3	0.4	5.06	2.6	30.0	4.72	-2.55	81.25
TL6	45.0	15.2	81.3	0.2	4.94	2.3	32.8	4.73	-2.42	85.41
{ethyl lactate (1) + K ₂ HPO ₄ (2) + water (3)}										
TL1	30.0	12.0	50.8	3.0	8.17	12.0	19.0	8.39	-2.44	42.00
TL2	33.0	12.6	59.3	1.9	7.90	7.5	22.8	8.23	-2.48	55.89
TL3	36.0	13.2	64.1	1.4	8.12	4.6	25.8	8.60	-2.43	64.30
TL4	39.0	13.9	69.1	0.9	7.79	3.3	29.0	8.40	-2.35	71.53
TL5	41.9	14.5	73.0	0.7	8.08	2.0	32.0	8.48	-2.27	77.67
TL6	45.0	15.2	76.8	0.6	7.93	0.8	35.2	8.66	-2.20	83.51
{ethyl lactate (1) + NaH ₂ PO ₄ (2) + water (3)}										
TL1	29.95	12.00	55.0	2.9	4.07	13.37	18.19	3.96	-2.72	44.35
TL2	33.02	12.59	61.0	1.9	4.17	10.01	21.59	3.98	-2.60	54.69
TL3	35.99	13.18	65.9	1.4	4.15	7.73	24.80	3.79	-2.48	62.66
TL4	38.94	13.88	70.1	1.0	4.13	4.80	28.15	3.81	-2.40	70.68
TL5	41.95	14.50	73.5	0.7	4.12	3.51	31.41	3.93	-2.28	76.41
TL6	45.01	15.24	76.9	0.5	4.1	2.69	35.11	3.64	-2.14	81.86

^a Standard uncertainties, u , are: $u(T) = 0.2$ K, $u(p) = 10$ kPa, $u(w, \text{weight percentage}) = 10^{-1}$, $u(\text{pH}) = 10^{-2}$.

Table 6

Parameters obtained using Othmer-Tobias Eq. (3) and Bancroft Eq. (4) with the correlation coefficients.

ATPS	Othmer-Tobias			Bancroft		
	n	K_1	R^2	r	K_2	R^2
{ethyl lactate (1) + (NH ₄) ₂ SO ₄ (2) + water (3)}	1.128	-0.984	0.997	0.790	0.805	0.995
{ethyl lactate (1) + K ₂ HPO ₄ (2) + water (3)}	1.371	-0.883	0.999	0.625	0.594	0.998
{ethyl lactate (1) + NaH ₂ PO ₄ (2) + water (3)}	1.124	-0.824	0.999	0.782	0.670	0.998

Table 7

UNIQUAC volume, r_i , and surface area, q_i , structural parameters.

Ion ^b	r	Q	References
K ⁺	0.437	0.578	[54]
Na ⁺	0.176	0.315	[54]
NH ₄ ⁺	0.686	0.471	[55]
HPO ₄ ²⁻	2.270	1.206	[55]
H ₂ PO ₄ ⁻	2.408	1.206	[55]
SO ₄ ²⁻	1.328	1.284	[55]

^b The structural parameters of each molecule were calculated by summing the ones of the ions present.

the six adjustable parameters, a_{ij} , which appear in the τ parameter of the UNIQUAC model, as Eq. (10) shows, and their respective root-mean-square deviation of the molar composition, σ_x , are given in Table 8.

$$\tau_{ij} = \exp\left(-\frac{a_{ij}}{T}\right) \quad (10)$$

The root-mean-square deviations were determined using Eq. (11):

$$\sigma_x = \sqrt{100 \left(\frac{\sum_i^m \sum_j^{n-1} (x_{ij}^{\text{I,exp}} - x_{ij}^{\text{I,cal}})^2 + (x_{ij}^{\text{II,exp}} - x_{ij}^{\text{II,cal}})^2}{2mn} \right)} \quad (11)$$

Table 8

UNIQUAC parameters (a_{ij} and a_{ji}) and deviation obtained from LLE modelling, σ_x .

$i-j$	a_{ij}/K	a_{ji}/K	σ_x^b
{ethyl lactate (1) + (NH ₄) ₂ SO ₄ (2) + water (3)}			
1-2	-154	247	6.9·10 ⁻²
1-3	-169	-696	
2-3	-754	-413	
{ethyl lactate (1) + K ₂ HPO ₄ (2) + water (3)}			
1-2	850	481	5.7·10 ⁻²
1-3	619	549	
2-3	-775	-897	
{ethyl lactate (1) + NaH ₂ PO ₄ (2) + water (3)}			
1-2	619	381	4.1·10 ⁻²
1-3	511	410	
2-3	-1201	-1432	

^b The results were obtained minimising the function described by equation (12).

where m is the total number of tie lines and n is the total number of components in the mixture. The superscripts I and II refer to the top and bottom phase, respectively, and x_i^{exp} and x_i^{cal} are the experimental and calculated compositions in mole fraction of component i , respectively.

The objective function used for both approaches is given by the following equation:

$$\text{O.F.} = \sum_j^m \sum_i^n \left[\ln(x_{ij}^{\text{I,cal}} \gamma_{ij}^{\text{I}}) - \ln(x_{ij}^{\text{II,cal}} \gamma_{ij}^{\text{II}}) \right] \quad (12)$$

where γ stands for the activity coefficients.

On the other hand, to account for salt dissociation and consequent long-range interactions among the chemical compounds, the UNIQUAC model combined with a Pitzer-Debye-Hückel (PDH) [49] term was applied. Hence, four species were considered to be present in the system (EL, cation, anion and water). Based on the assumption that the symmetric molar excess Gibbs free energy for the system (G^E) is given by Eq. (13), the rational symmetric activity coefficient of all the chemical species (solvents or ions) is given by Eq. (14):

$$G^E = G_{\text{UNIQUAC}}^E + G_{\text{PDH}}^E \quad (13)$$

where G_{UNIQUAC}^E is the molar excess Gibbs free energy determined by the UNIQUAC model and G_{PDH}^E is the molar excess Gibbs free energy obtained by the PDH term.

$$\ln(\gamma_i) = \ln(\gamma_i^{\text{UNIQUAC}}) + \ln(\gamma_i^{\text{PDH}}) \quad (14)$$

where γ_i is the activity coefficient of the i species, $\gamma_i^{\text{UNIQUAC}}$ the UNIQUAC contribution for the activity coefficient and γ_i^{PDH} is the PDH term contribution for the activity coefficient.

As mentioned above, the UNIQUAC method [47] is well reported in the literature. To what concerns the PDH contribution of the activity coefficients, it is given for ions, in the symmetric convention, as presented by this group [52]:

$$\ln(\gamma_i^{\text{PDH}}) = -z_i^2 A_{\text{DH},x} \left[\frac{2}{b} \ln \left(\frac{1 + b\sqrt{I_x}}{1 + b\sqrt{I_x^\circ}} \right) + \sqrt{I_x} \frac{1 - I_x/I_x^\circ}{1 + b\sqrt{I_x}} \right] \quad (15)$$

where i is the ion being studied, b is a model parameter related to short-range interactions which is normally fitted, I_x is the ionic strength, I_x° is the ionic strength of the pure salt, and $A_{\text{DH},x}$ is a composition-dependent parameter which is obtained from Eq. (16):

$$A_{\text{DH},x} = \frac{1}{3} \frac{\sqrt{2N_A}}{8\pi} \left(\frac{e^2}{\epsilon_0 k} \right)^{1.5} \frac{\rho_0^{0.5}}{(\epsilon T)^{1.5}} \quad (16)$$

where N_A is the Avogadro's number, e is the electronic charge (C), k is the Boltzmann constant ($\text{J}^{-1} \cdot \text{K}^{-1}$), ϵ_0 is the vacuum permittivity ($\text{C}^2 \cdot \text{J}^{-1} \cdot \text{m}^{-1}$), ϵ is the dielectric constant of the solvent and ρ_0 is the molar density of the solvent (mol/m^3).

The ionic strength, which appears in Eqs. (15) and (16), is determined using Eq. (17).

$$I_x = \frac{1}{2} \sum_{i=1}^{N_{\text{ions}}} z_i^2 x_i \quad (17)$$

where N_{ions} is the total number of ions, z_i is the ionic charge of ion i and x_i is its mole fraction.

However, for solvents, since no charges are accounted, Eq. (15) is reduced to [50]:

$$\ln(\gamma_m^{\text{PDH}}) = A_{\text{DH},x} \frac{2I_x^{1.5}}{1 + b\sqrt{I_x}} \quad (18)$$

where m refers to the solvents under study.

The particular PDH expression used in this work was first written by Achard et al. [51] having in consideration the modified concentrations after salt dissociation. Moreover, the density of the solvent mixture (EL and water) was calculated according to the works by Sander et al. [52] and Macedo et al. [53]. Following this second approach, the twelve a_{ij} parameters needed, as well as the parameter b and the respective root-mean-square deviation of the mole fractions (σx), are given in Table 9. The b parameter was fitted in the theoretical range from 8 to 15, as suggested by Pitzer [49].

Comparing the results for the UNIQUAC equation, displayed in Table 8, with the ones obtained for the PDH + UNIQUAC model, observed in Table 9, it is clear that the deviations are smaller for the latter approach in the three ATPS systems. Hence, the inclusion of a term accounting for long-range interactions (caused by charged components) provided a better fitting of the experimental results. This supports the assumption of the dissociation of the salt.

In Fig. 2, the binodal curves and tie lines for the ternary systems studied can be seen, as well as the predicted tie lines (values converted into mass fraction) for each of the thermodynamics models applied. Once again, the tie lines predicted by PDH + UNIQUAC are the closest to the experimental results, even generally overlapping them.

Table 9

PDH + UNIQUAC parameters (a_{ij} , a_{ji} and b), and deviation obtained from LLE modelling, σx .

$i-j$	a_{ij}/K	a_{ji}/K	b	σx^b
{ethyl lactate (1) + (NH ₄) ₂ SO ₄ (2) + water (3)}				
1-2	-502	-502	12.69	9.2·10 ⁻³
1-3	-264	-496		
1-4	-497	-951		
2-3	-495	-498		
2-4	-1097	-915		
3-4	-514	-490		
{ethyl lactate (1) + K ₂ HPO ₄ (2) + water (3)}				
1-2	667	658	11.70	5.7·10 ⁻³
1-3	427	592		
1-4	577	651		
2-3	588	644		
2-4	474	-1208		
3-4	688	-1353		
{ethyl lactate (1) + NaH ₂ PO ₄ (2) + water (3)}				
1-2	656	616	11.67	1.8·10 ⁻²
1-3	406	619		
1-4	615	645		
2-3	542	644		
2-4	442	-1304		
3-4	692	-1483		

^b The results were obtained minimising the function described by Eq. (12).

4. Conclusions

A successful liquid–liquid–equilibria study was performed in three novel ethyl lactate/inorganic salts-based ATPS for future applications in extractive processes. Binodal curves and tie lines were experimentally determined at $T = 298.15$ K and atmospheric pressure.

The results for one of the ternary systems, {ethyl lactate (1) + K₂HPO₄ (2) + water (3)}, were compared with data from the literature and they were considered very consistent. The capability of phase separation follows the order: (NH₄)₂SO₄ > K₂HPO₄ > NaH₂PO₄. Several equations were applied to fit the experimental binodal curves, and the best results were obtained with the equation proposed by Han et al. for the ATPS containing NaH₂PO₄ and for the other two ATPS the best fit was achieved using the equation proposed by Hu et al. Merchuk's equation did not present the best description of the experimental data for any of the studied systems.

Two different approaches were used to model the tie lines composition of the studied ATPS: the UNIQUAC model, which considers salts as neutral and molecular species, and the PDH + UNIQUAC model, which considers them as fully dissociated (anion and cation). Both models successfully predicted the phase distribution of the components, but the PDH + UNIQUAC model obtained slightly smaller deviations between the experimental results and the calculated molar concentrations in the three studied systems. Being so, the additional term accounting for long-range interactions improved the predictions of the systems compositions. Therefore, the PDH + UNIQUAC model should be preferred in systems in which electrolyte species are present.

CRedit authorship contribution statement

Pedro Velho: Investigation, Formal analysis, Writing - review & editing. **Patricia F. Requejo:** Investigation, Writing - review & editing, Visualization. **Elena Gómez:** Writing - review & editing, Conceptualization, Supervision, Validation. **Eugénia A. Macedo:** Conceptualization, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

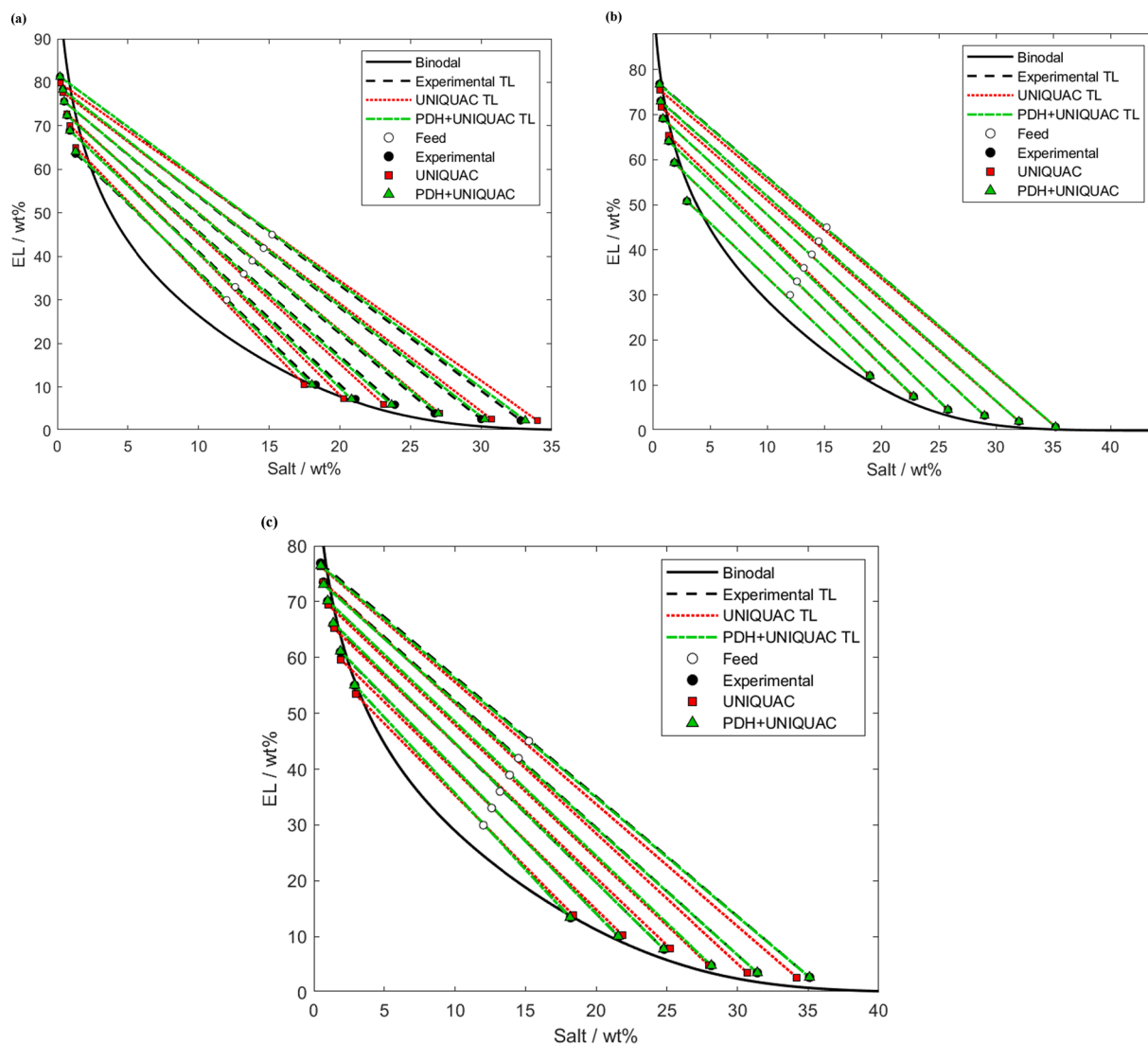


Fig. 2. Binodal curves and tie lines for the ternary systems composed of {ethyl lactate (1) + salt (2) + water (3)} at $T = 298.15$ K and atmospheric pressure. (○) feed compositions, (—) fit of the binodal data, (■) experimental tie line data, (■) calculated tie lines data by the UNIQUAC thermodynamic model and (...) respective tie lines, (▲) calculated tie lines data by the PDH + UNIQUAC thermodynamic model and respective (---) tie lines. (a) {EL + $(\text{NH}_4)_2\text{SO}_4$ + water}, (b) {EL + K_2HPO_4 + water} and (c) {EL + NaH_2PO_4 + water}.

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