Green Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

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Enhanced tunability afforded by aqueous biphasic systems formed by fluorinated ionic liquids and carbohydrates

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This work unveils the formation of novel aqueous biphasic systems (ABS) formed by perfluoroalkylsulfonate-based ionic liquids (ILs) and a large number of carbohydrates (monosaccharides, disaccharides and polyols) aiming at establishing more benign alternatives to the salts commonly used. The respective ternary phase diagrams were determined at 298 K. The aptitude of the carbohydrates to induce phase separation closely follows their hydration capability, while the length of the IL cation/anion fluorinated chain also plays a crucial role. Finally, these systems were investigated as liquid-liquid extraction strategies for four food dyes. Single-step extraction efficiencies for the carbohydrate-rich phase up to 94% were obtained. Remarkably and contrarily to the most investigated IL-salt ABS, most dyes preferentially migrate for the most hydrophilic and biocompatible carbohydrate-rich phase – an outstanding advantage when envisaging the products recovery and further use. On the other hand, more hydrophobic dyes preferentially partition to the IL-rich phase, disclosing therefore these novel systems as highly amenable to be tuned by the proper choice of the phase-forming components.

Introduction

Aqueous biphasic systems (ABS), originally proposed by Albertsson[1], are formed when two distinct substances, both miscible with water and at least up to a large extent, *e.g.* polymer/polymer, polymer/salt or salt/salt combinations, are dissolved in aqueous media, and for which above given concentrations a spontaneous phase separation takes place – resulting thus in the formation of a liquid-liquid system where both phases are aqueous-rich[2]. As both phases are majorly composed of water, these systems are able to preserve the native conformation and the biological activity of a large number of biomolecules.[1, 2] Due to these features, ABS have been widely used in the separation of cells, membranes, viruses, proteins, nucleic acids, enzymes and other added-value biomolecules in the last decades.[3] These typical polymer-based ABS have been largely explored since the 50's; yet, in the last decade, novel systems employing ionic liquids (ILs)[4] have emerged as a valuable option over polymers since their coexisting phases are of a lower viscosity and provide a faster two-phases separation[5]. Therefore, IL-based ABS also allow to obtain better efficient mixing under gentle stirring and a more rapid partitioning of the target molecules or products being separated. However, the most important feature afforded by IL-based ABS is certainly their outstanding performance in extractions and selectivity for a wide variety of biomolecules, simply achieved by wise selection of the phase-forming components and their compositions.[5]

ILs are salts with low melting temperatures as a result of the delocalized electrical charge distribution and frequent asymmetry of their ions which prevent crystallization. Due to their ionic nature, most ILs are also characterized by a negligible volatility at ambient conditions[6], high thermal and chemical stabilities, and large dissolving capabilities for a wide variety of compounds.[2, 3, 5] Furthermore, ILs are known as designer solvents since their physical and chemical properties can be properly manipulated for a given application by using different ions arrangements. This characteristic is transferrable to aqueous solutions of ILs, where ABS composed of ILs have shown a vast applicability by an adequate control of their phases' polarities.[2] This feature bestows IL-based ABS with an outstanding tailoring ability for extraction and purification routes carried out by liquid-liquid separation processes.[2] IL-based ABS have been successfully used in the extraction, concentration, and purification of the most diverse biomolecules, including proteins, enzymes, antioxidants, synthetic and fermentative produced drugs, biopharmaceuticals, among others.[2, 3]

The chemical properties of ILs are greatly influenced by their constituent ions, and a vast number of combinations may be found in the literature referring to IL-based ABS.[2] The most widely studied are the imidazolium-based salts, combined with simple anions, such as chloride or bromide, or more complex species, such as tetrafluoroborate, acetate, dicyanimide and alkylsulphates. Aprotic ILs are non-volatile at atmospheric conditions, and hence are a better choice than the typical VOCs used in extraction and separation procedures[7]; yet, they may not be considered entirely safe since ILs used in ABS formulations are completely miscible with water (in the whole composition range) and, if accidently discharges occur, they may contaminate the aquatic media and pose threats to the environment and/or biota.[8] Although few successful attempts have been made in the recovery of ILs either using ABS[9] or membranes[10] these procedures are not yet an established routine, and the search for efficient though benign ILs[11] for forming ABS still needs to be addressed. When downstream processes are considered, the toxicity of the substances involved must be pondered alongside other important issues, such as their cost and efficiency. The toxicity and biodegradability of ILs depend on the length of the alkyl chains at the cation or anion, on the degree of functionalization in the side chains, on the cation and anion nature, as well as on synergetic cation-anion effects.[12, 13] So, intensive work must be pursued to provide ampler and more diverse combinations of constituents to broaden and ameliorate the choice of ILs according to a desired purpose, while avoiding detrimental effects.

Aiming at widen up the properties and applications of ILs, fluorinated-based ILs (FILs) have emerged recently due to their remarkable performances, namely in the recovery of contaminants either in gaseous mixtures or in liquid effluents.[14, 15] Anions such as bis(trifluoromethylsulfonyl)imide, hexafluorophosphate, tetrafluoroborate, trifluoromethanesulfonate and trifluoroacetate have been largely characterized and denoted as conventional FILs. Nevertheless, since the formation of two aqueous-rich phases in ABS requires the use of water-miscible ILs, only tetrafluoroborate-, trifluoromethanesulfonate- and trifluoroacetate-based ILs (and with cations with small alkyl side chains) have been used for such a purpose.[2] Novel perfluoroalkylsulfonate-based ILs were recently proposed aiming at developing environmentally benign and selective fluorinated systems[16] with their properties thoroughly studied and compared with other FILs available in the literature.[14] A most important feature of this new class of FILs relays on their low toxicity – a major result of the alkylsulfonate-type anions.[14] When considering transport properties, ethylmethylpyridinium perfluorobutanesulfonate, $[C_2C_1py][C_4F_9SO_3]$, comes up among FILs since it has the lowest viscosity and a behaviour that is very close to that of a strong electrolyte.[17, 18] The presence of long fluorinated alkyl chains at the anion in this class of FILs leads also to a structured liquid phase with three nanodomains - polar, nonpolar and fluorous.[14] On the other hand, fluorocarbon compounds present a handicap because their water solubility is in most cases too low. However, these novel FILs show total miscibility in water and could be used in biological applications.[19]

Although the research on IL-based ABS has been directed to more environmentally benign salting-out species, the use of carbohydrates is still scarce since, up to date, only two ILs were reported to be able to form ABS when combined with carbohydrates, namely 1-butyl-3-methylimidazolium tetrafluoroborate[20, 21], and 1-butyl-3-methylimidazolium trifluoromethanesulfonate[22]. Mono and disaccharides, as well as polyols, have high affinity towards water and were proven capable of "salting-out/sugaring-out" hydrophilic ILs from aqueous media giving rise to ABS.[22] Carbohydrates are weaker salting-out species than high-charge density salts, and thus, only ILs with a lower ability to hydrogen-bond with water (defined by their ability to accept protons) are capable of undergoing liquid-liquid demixing and to create ABS. Even so, the use of tetrafluoroborate-based ILs should be avoided since this anion is not-water stable even at moderate conditions.[23]

In this work, it is demonstrated that a novel class of FILs, based on perfluoroalkylsulfonate anions, is able to form ABS with a large plethora of carbohydrates (including monosaccharides, disaccharides and polyols). In this line, novel ternary phase diagrams, tie-lines and tie-line lengths were determined at 298 K and atmospheric pressure. To evaluate the potential of these new systems as extractive platforms, they were also tested in the extraction of four food dyes – used here as a proof of concept.

Experimental Section

Materials

The ABS studied in this work were established using different aqueous solutions of carbohydrates (mono- and disaccharides, and polyols) and aqueous solutions of different ILs. The monosaccharides investigated were: D-(+)-glucose from Scharlau (99.5 wt% pure, 180 $g \cdot mol^{-1}$), D-(+)-galactose from GPR Recaptur (98.0 wt% pure, 180 $g \cdot mol^{-1}$), D-(+)-fructose from Panreac (≥ 98 wt% pure, 180 $g \cdot mol^{-1}$), D-(+)-mannose from Sigma-Aldrich (≥ 99 wt% pure, 180 $g \cdot mol^{-1}$), D-(–)-arabinose from RPE (≥ 99 wt% pure, 150 $g \cdot mol^{-1}$), L-(+)-arabinose from BHD Biochemicals (≥ 99.0 wt% pure, 150 $g \cdot mol^{-1}$) and D-(+)-xylose from Carlo Erba (≥ 99.0 wt% pure, 150 $g \cdot mol^{-1}$). The studied disaccharides were sucrose from Himedia (99.5 wt% pure, 342 $g \cdot mol^{-1}$) and D-(+)-maltose from Sigma-Aldrich (≥ 98 wt% pure, 342 $g \cdot mol^{-1}$). The polyols investigated comprise D-sorbitol from Fluka (≥ 99 wt% pure, 182 $g \cdot mol^{-1}$), maltitol from ACROS Organics (≥ 95 wt% pure, 344 $g \cdot mol^{-1}$) and xylitol from Sigma-Aldrich (≥ 99 wt% pure, 152 $g \cdot mol^{-1}$). The chemical structures of the investigated carbohydrates are depicted in Fig. 1.

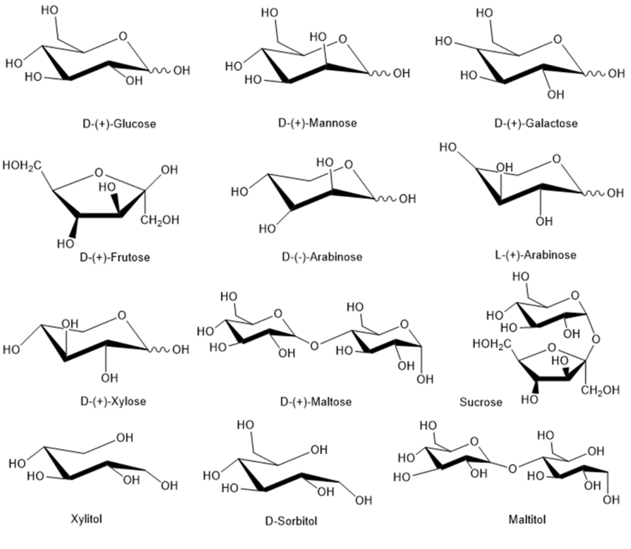

Figure 1. Chemical structure of the studied carbohydrates: monosaccharides, disaccharides and polyols.

1-Ethyl-3-methylpyridinium perfluorobutanesulfonate ($[C_2C_1py][C_4F_9SO_3]$, >99% mass fraction purity, halides (IC) < 100 ppm, cation (IC) > 99.9%, anion (IC) > 99.9%, 421 $g \cdot mol^{-1}$), 1-ethyl-3-methylimidazolium perfluorobutanesulfonate ($[C_2C_1im][C_4F_9SO_3]$, > 98% mass fraction purity, halides (IC) < 1%, cation (IC) > 99.8%, anion (IC) > 99.9%, 410 $g \cdot mol^{-1}$) (2-hydroxyethyl)trimethylammonium (cholinium) perfluorobutanesulfonate ($[N_{1112OH}][C_4F_9SO_3]$, >97% mass fraction purity, halides (IC) < 1%, cation (IC) > 97%, anion

(IC) > 97%, 684 g·mol^{-1}), 1-ethyl-3-methylimidazolium triflate ([C_2C_1im][CF_3SO_3], >99% mass fraction purity, halides (IC) < 1%, cation (IC) > 99%, anion (IC) > 99%, 260 g·mol^{-1}), and 1-ethyl-1-methylpyrrolidinium triflate ([C_2C_1pyr][CF_3SO_3], >99% mass fraction purity, halides (IC) < 1%, cation (IC) > 99%, anion (IC) > 99%, 263 g·mol^{-1}) were purchased from IoLiTec GmbH. Before use, all ILs were dried for a minimum of 24 h at constant agitation, moderate temperature (≈ 353 K) and under vacuum to reduce their volatile impurities to negligible values. After this step, the purity of each IL was confirmed by ^{1}H, ^{13}C and ^{19}F NMR spectra. The chemical structures of the investigated ILs are presented in Fig. 2.

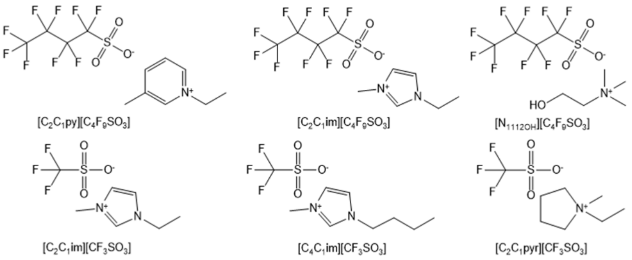

Figure 2. Chemical structures of the studied ILs.

The water used was ultra-pure water, double distilled, passed by a reverse osmosis system and additionally treated with a Milli-Q plus 185 water purification equipment.

The food colouring dyes used were tartrazine (E102), Ponceau 4R (E124), Brilliant Blue FCF (E133) and Green S (E142), commercially available from the food brand Globo (E142 and E124) and Vahiné (E133 and E102). Their structures are depicted in Fig. 3.

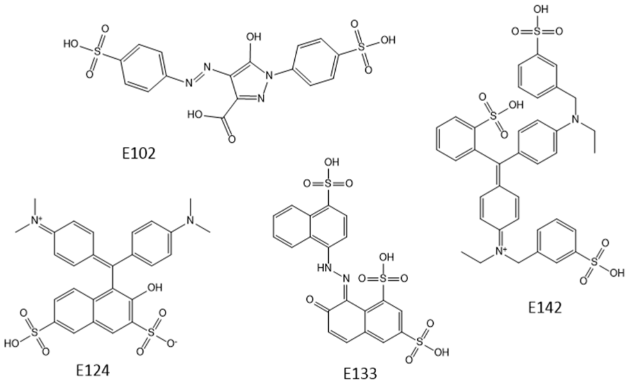

Figure 3. Chemical structures of the studied dyes.

The colorants are provided as 1g·mL^{-1} aqueous solutions acidified with acetic acid and were used as received.

Phase diagrams (solubility curves and tie-lines)

For the phase diagrams determination, aqueous solutions of the diverse carbohydrates at different concentrations were initially prepared; those values varied from 23 wt% for D-(+)-xylose to 67 wt% for D-(+)-fructose, and were established by their saturation solubility values in water at 298 K. On the other hand, aqueous solutions containing 95 wt % of each IL were used.

The binodal curves were determined at room temperature (298 ± 1) K and at atmospheric pressure by the cloud point titration method.[24] The method consists on the drop-wise addition of each carbohydrate aqueous solution to the IL aqueous solution, or *vice-versa*, under constant stirring, until the cloud point is reached, that is, the solution becomes cloudy - which means that the biphasic region was formed. Then, drop-wise addition of water is carried out until a clear and limpid solution is obtained, evidencing that the monophasic region was attained. This procedure was carried out consecutively until no more turbidity was detected upon carbohydrate or IL addition. The compositions were determined by weight within ±10^{-4} g at each point of turbidity and clear solution, using a Mettler Toledo Excellence XS205 Dual Range balance.

The determination of the tie-lines (TLs) was based on the gravimetric method originally proposed and described by Merchuk et al.[25]. Ternary weight fraction compositions, chosen from the biphasic region, were prepared in small glass vials (with *circa* 2 g of total mixture) by weighing the necessary amounts of IL, carbohydrate and water with an uncertainty of 10^{-4} g. The mixtures were homogenized using a mechanical vortex stirrer, from VWR^{TM} International, VV3, and then centrifuged at 3500 rpm to favor phase separation. After 12 h at (298 ± 1) K to reach equilibrium, both top and bottom phases were carefully separated, making use of a syringe, and weighted. Each individual TL was determined by application of the lever rule to the relationship between the top phase and the overall system composition [25].

The following system of four equations (Equations 1 to 4) was used to determine the coordinates of the top and bottom phases as proposed originally by Merchuk et al[25]:

$$[\mathrm{IL}]_{\mathrm{IL}} = \mathrm{A}\ exp[(\mathrm{B}[\mathrm{CH}]_{\mathrm{IL}}^{0.5}) - (\mathrm{C}[\mathrm{CH}]_{\mathrm{IL}}^{3})] \quad (1)$$

$$[\mathrm{IL}]_{\mathrm{CH}} = \mathrm{A}\ exp[(\mathrm{B}[\mathrm{CH}]_{\mathrm{CH}}^{0.5}) - (\mathrm{C}[\mathrm{CH}]_{\mathrm{CH}}^{3})] \quad (2)$$

$$[\mathrm{IL}]_{\mathrm{IL}} = \frac{[\mathrm{IL}]_{\mathrm{M}}}{\alpha} - \left(\frac{1-\alpha}{\alpha}\right)[\mathrm{IL}]_{\mathrm{CH}} \quad (3)$$

$$[\mathrm{CH}]_{\mathrm{IL}} = \frac{[\mathrm{CH}]_{\mathrm{M}}}{\alpha} - \left(\frac{1-\alpha}{\alpha}\right)[\mathrm{CH}]_{\mathrm{CH}} \quad (4)$$

where CH, IL and M designate the carbohydrate-rich phase (top phase), the IL-rich phase (bottom phase) and the mixture composition, respectively. [IL] and [CH] are the IL and carbohydrate weight fractions, respectively; coefficients *A*, *B* and *C* are parameters obtained by the regression of the experimental data; and α is the ratio between the weight of the IL-rich phase and the total weight of both phases.

The tie-line length (TLL) was calculated using Equation 5:

$$\mathrm{TLL} = \sqrt{([\mathrm{CH}]_{\mathrm{IL}} - [\mathrm{CH}]_{\mathrm{CH}})^2 + ([\mathrm{IL}]_{\mathrm{IL}} - [\mathrm{IL}]_{\mathrm{CH}})^2} \quad (5)$$

Dyes extraction

To evaluate the extracting potential of the investigated IL-based ABS, they were employed in single-step extractions of 4 food dyes. In the extraction procedures, a fixed IL and common mixture composition were used to directly compare the behaviour in partitioning of the different dyes

(ABS mixture composition: 40 wt% of $[C_2C_1py][C_4F_9SO_3]$ + 18 wt% of D-(+)-maltose + 42 wt% of water). For each system, a small amount (≈ 0.30 mg) of the commercial dye solution was added to 3 g of the overall ABS mixture in a glass tube. Then, it was vigorously stirred, centrifuged at 3500 rpm for 30 min, and left to equilibrate for more 10 min, at (298 ± 1) K, to ensure the complete separation of both phases. After a careful separation of both phases, the quantification of the dyes in each phase was carried out by UV-Vis spectroscopy, using a Shimadzu UV-1700, Pharma-Spec Spectrometer, at a wavelength of 520 nm for Ponceau 4R (E124), 414 nm for Green S (E142), 430 nm for tartrazine (E102) and 630 nm for Brilliant Blue FCF (E133). These wavelengths correspond to the respective maximum absorbance peaks in the visible region. At least three individual experiments were performed in order to determine the average in the extraction efficiency, as well as the respective standard deviations. The interference of the carbohydrates and IL in the quantification method was also taken into account and blank control samples were always employed.

The extraction efficiency (EE_{Dye}%) is then defined as the percentage ratio between the weight of each dye that is present in the carbohydrate-rich phase and the total amount of dye (sum of the two phases). The partition coefficient of the studied dyes (K_{Dye}) is defined as the ratio of the concentration of each dye in the carbohydrate- to that in the IL-rich aqueous phases.

The pH values of each phase were measured with an uncertainty of ± 0.02 pH units using a Mettler Toledo S47 SevenMulti^{TM} pH meter. The calibration of the pH meter was carried out with two buffers that bracketed the measured values (pH values of 4.00 and 7.00).

Results and Discussion

Phase diagrams (solubility curves)

In this work, novel systems combining perfluoromethanesulfonate- and perfluorobutanesulfonate-based ILs and low molecular weight carbohydrates were investigated concerning their ability to form aqueous two-phase systems. Since different FILs and carbohydrates were used, the influence of the structures of both components in the solubility curves could be evaluated. To this aim, the binodal curves and respective tie-lines were determined for each system, at 298 K and atmospheric pressure. In the studied systems the bottom phase is majorly composed of IL, while the upper phase is enriched in carbohydrates. The results obtained will be discussed by different effects regarding their impact on the ternary phase diagrams.

Each of the following small molecular weight carbohydrates, namely maltitol, D-sorbitol, xylitol, D-(+)-maltose, sucrose, D-(+)-glucose, D-(+)-mannose, D-(+)-galactose, D-(+)-fructose, D-(-)-arabinose, L-(+)-arabinose and D-(+)-xylose, was combined with $[C_2C_1py][C_4F_9SO_3]$ to form a ternary system with water and to create ABS. All the studied carbohydrates, with the exception of L-(+)-arabinose and D-(+)-xylose, were able to form ABS at 298 K. To ascertain on the effect of the IL cation, two other ILs containing the same anion, namely $[C_2C_1im][C_4F_9SO_3]$ and $[N_{1112OH}][C_4F_9SO_3]$, were also combined with the carbohydrate that behaved as the strongest two-phase promoter, maltose; though, only $[C_2C_1im][C_4F_9SO_3]$ formed ABS. The influence of the anion, in particular the size of the fluorinated alkyl chain length, was further assessed by studying an IL comprising the same cation, $[C_2C_1im]^+$, with the shorter fluoroalkyl chained anion $[CF_3SO_3]^-$. However, $[C_2C_1im][CF_3SO_3]$ was not able to undergo liquid-liquid demixing with maltose at 298 K, indicating that the size of the fluoroalkyl chain of the anion has a relevant role in the formation of two-phase systems with carbohydrates. Also a similar IL ($[C_2C_1pyr][CF_3SO_3]$ - that bears the same perfluoromethanesulfonate anion combined with $[C_2C_1pyr]^+$) was tested, but was also unable to produce a two-phase splitting when mixed with maltose.

Effect of the carbohydrate nature. Mono- and disaccharides are polyhydroxy aldehydes or ketones, whereas the hydrogenated forms of such aldoses or ketoses are known as polyols. All the structures have diverse –OH groups with dual donor–acceptor character, and can establish hydrogen bonds with water and act as salting-out/sugaring-out species. In general, the FIL $[C_2C_1py][C_4F_9SO_3]$ was able to form ABS with all the carbohydrates investigated, except with D-(+)-xylose and L-(+)-arabinose. Two-phase systems were obtained for the monosaccharides: D-(+)-glucose, D-(+)-galactose, D-(+)-fructose, D-(+)-mannose, D-(-)-arabinose; the disaccharides: D-(+)-maltose and sucrose; and the polyols: maltitol, D-sorbitol and xylitol. The corresponding phase diagrams are depicted in Fig. 4 (monosaccharides), Fig. 5 (disaccharides) and Fig. 6 (polyols).

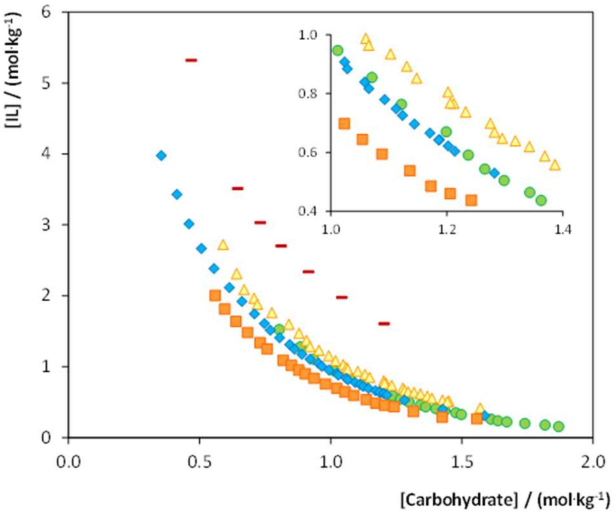

Figure 4. Ternary phase diagrams for ABS composed of $[C_2C_1py][C_4F_9SO_3]$ + monosaccharide + water, at 298 K and atmospheric pressure: (■) D-(+)-galactose; (◆) D-(+)-glucose; (●) D-(+)-mannose; (▲) D-(+)-fructose; (—) D-(–)-arabinose.

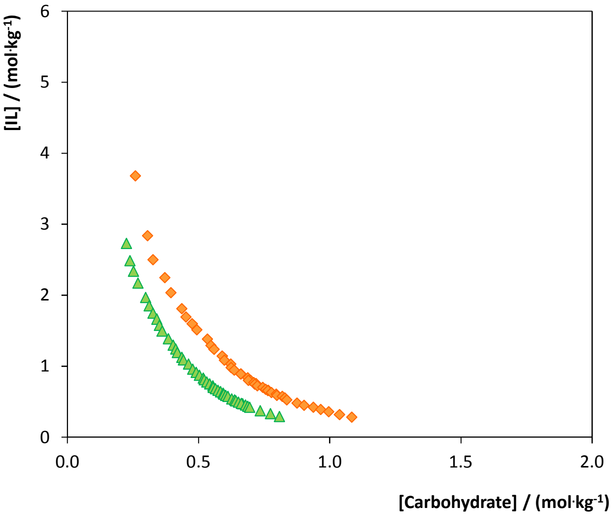

Figure 5. Ternary phase diagrams for ABS composed of $[C_2C_1py][C_4F_9SO_3]$ + disaccharide + water, at 298 K and atmospheric pressure: (▲) D-(+)-maltose; (♦) sucrose.

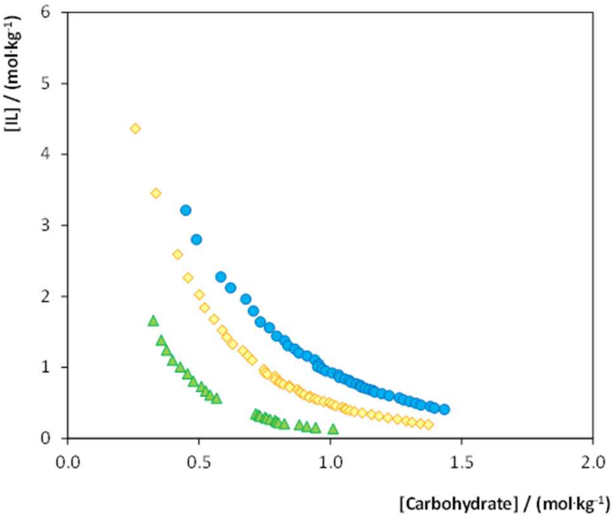

Figure 6. Ternary phase diagrams for ABS composed of $[C_2C_1py][C_4F_9SO_3]$ + polyol + water, at 298 K and atmospheric pressure: (▲) maltitol; (♦) D-sorbitol; (●) xylitol.

Mixtures with compositions above the binodal curve undergo liquid-liquid demixing (biphasic region), while those below fall into the homogeneous and monophasic region. The closer the binodal curve to the axis origin (larger biphasic region) the higher is the system's ability to undergo two-phase separation. Since these systems share the same IL, the closer the curve to the origin, the higher the carbohydrate ability to promote phase separation. As Fig. 4 depicts, and with the exception of D-(-)-arabinose, there are slight differences among the solubility curves of the studied monosaccharides although a trend for their ABS promoting ability may be devised: D-(+)-galactose ≥ D-(+)-glucose ≥ D-(+)-mannose ≥ D-(+)-fructose > D-(-)-arabinose (with the latter as the weakest ABS promoter). A closer look to the solubility curves unveils differences among the ones corresponding to galactose, mannose and fructose, in spite of all being carbohydrates with a total of 5 –OH groups.

The ability of a solute to promote phase separation in aqueous media is related to its characteristics and particularly to its hydration extension. Both the IL and carbohydrate entities are solvated by water molecules; when the carbohydrate aqueous solution is added to the aqueous solution of the IL, the two solutes compete for the solvent molecules. The competition is likely to be won by the sugar molecules, since they have *a priori* a higher affinity for water molecules than the FIL and hence are able to establish stronger interactions with the solvent, as expected. In fact, significantly higher water content is present at the carbohydrate-rich phase and as will be shown below when discussing the tie-lines data. In general, there is a "migration" of solvent molecules away from the ions of the IL towards the carbohydrate, which decreases the hydration and therefore the solubility of the ionic solute in water. The competition for water molecules is thus a process that leads to the dehydration of IL ions and promotes phase separation, with the carbohydrates acting usually as salting-out agents.[22, 26] As a consequence, a phase rich in IL separates from the rest of the solution and an ABS is formed. On the other hand, the ability of each carbohydrate to interact with water depends mainly on its ability to hydrogen bond, which is further dependent on the number of its hydroxyl groups.[27] In this line, arabinose, bearing 4 hydroxyl groups is expected to be a weaker two-phase promoter than all the other monosaccharides investigated with 5 hydroxyl groups. An appreciation of the solubility curves experimentally obtained (Fig. 4) confirms this expectation, since for the same amount of carbohydrate, arabinose requires the largest amount of IL to cause phase splitting.

The gathered phase diagrams for the disaccharides investigated are depicted in Fig. 5. In general, and as observed before with a different IL[28], maltose is more able to induce the separation of an IL-rich phase when compared to sucrose. Although both dissacharides present the same number of –OH groups, six-membered pyranose rings in maltose interact more favorably with water than the five-membered furanose ring in sucrose and hence display a higher ability to salt-out the IL.

The studied polyols (Fig. 6) also lead to noticeably different curves following the order: maltitol > D-sorbitol > xylitol. As the molecular structures reveal (Fig. 1), maltitol is the largest polyol with more –OH groups, followed by D-sorbitol that has one more –OH group than xylitol. Indeed, this latter alcohol reveals a two-phase promoting ability very similar to the isomers D-(+)-galactose, D-(+)-glucose and D-(+)-mannose (with the same number of hydroxyl groups).

The relation between -OH content and ABS forming ability was observed before[22] for carbohydrates combined with a different IL, $[C_4C_1im][CF_3SO_3]$. A similar and overall rank on the carbohydrates potential to form ABS was observed in this work. The order observed in the two-phase forming capability of these carbohydrates persists even when they are involved in the formation of ABS with molecular solvents, *e.g.*, acetonitrile.[29] These trends clearly emphasize the importance of the number of hydroxyl groups in saccharides and further solvation ability.

Overall, the following rank on the carbohydrates potential to form ABS was observed: maltitol ≈ D-(+)-maltose > sucrose > D-sorbitol > D-(+)-galactose > D-(+)-glucose ≈ xylitol ≈ D-(+)-mannose > D-(+)-fructose > D-(–)-arabinose. The overall representation of all phase diagrams is depicted in the ESI†, Fig. S1. The representation of the phase diagrams in weight fraction percentage is also depicted in the ESI†, Fig. S2. The isomer D-(+)-glucose is an aldose with a 6-sided ring while D-(+)-fructose is a ketose with a 5-sided ring, which suggests that ketoses are less effective in inducing the phase separation. The same trend was noticed when comparing sucrose and maltose. The fact that sugar molecules bearing the same number of hydroxyl groups do not present exactly the same two-phase separation ability, evidences that their hydration extension is not strictly ruled by the number of hydroxyl groups. In fact, the interaction of carbohydrates with water has been the subject of several studies.[27, 30] It was concluded that the compatibility of a carbohydrate with the three dimensional hydrogen-bonded network of water is governed by the carbohydrate stereochemistry, with the hydration of carbohydrates depending not only on the number of hydroxyl groups, but also on their position in the pyranose ring. Overall, the results show that the curve corresponding to D-(+)-maltose (Fig. 5) is visibly closer to the axes than the one of sucrose, meaning thus a higher two phase separation ability of the former. Furthermore, in spite of having the same number of total hydroxyl groups, D-(+)-maltose has more –OH groups in the equatorial position. Similarly, D-(+)-galactose is a stronger ABS producer than D-(+)-mannose, while L-(+)-arabinose and D-(+)-xylose were not even able to produce a two phase system with [C_2C_1py][$C_4F_9SO_3$].

As mentioned before, the influence of saccharides in the formation of ABS has been the focus of several research works[20, 22, 28, 31], where it was also found that the required amount of saccharide to achieve ABS formation generally decreases with the increase on the number of equatorial –OH groups. However, these numbers (total and equatorial) are not the sole influence in the phase diagrams behavior of carbohydrates and ILs, as the difference in the curves obtained for D-(+)-galactose and D-(+)-mannose depict (Fig. 4). The orientation of the hydroxyl group at carbon 4 is not the same for D-(+)-galactose and D-(+)-mannose, and bestows the former a stronger hydration and enhanced ability to induce ABS formation.

When globally considering the solubility curves herein obtained, a close relation is observed between the carbohydrates hydration potential and ABS forming ability. From this analysis, it can be concluded that the IL is salted-out by the saccharides. Although ILs are charged molecules and this behavior could not be the expected one, it should be highlighted that only more hydrophobic ILs, within the set of water-soluble ILs, are able to form ABS with carbohydrates.[21, 22, 31, 32] These ILs seem thus to display a much lower affinity for water than the sugar molecules. These FILs are almost in the limit of hydrogen-bond basicity, where lower values correspond to ILs that immediately form two phases with water without the need of a third species.[33] Furthermore, when the size of hydrogenated alkyl chain increases in the imidazolium cation for the same perfluorobutanesulfonate-based ILs (from [C_2C_1im][$C_4F_9SO_3$] to [C_6C_1im][$C_4F_9SO_3$], [C_8C_1im][$C_4F_9SO_3$] and [$C_{12}C_1$im][$C_4F_9SO_3$]), FILs show partial solubility with water.[34]

Effect of the ionic liquid chemical structure. In order to gain a better insight into ABS formation involving ILs and carbohydrates, different ILs were combined with maltose, since this showed to be one of the two strongest phase promoters among the carbohydrates investigated. Amongst the studied ILs, [N_{1112OH}][$C_4F_9SO_3$], [C_2C_1im][CF_3SO_3] and [C_2C_1pyr][CF_3SO_3] were not able to produce ABS irrespectively of the proportions of IL and carbohydrate used.

From the solubility curves obtained with [C_2C_1py][$C_4F_9SO_3$] and [C_2C_1im][$C_4F_9SO_3$], that are shown in Fig. 7, and based on the chemical structures of the ILs that were not able to create ABS, some major insights can be derived. Since [C_2C_1im][$C_4F_9SO_3$] and [C_2C_1py][$C_4F_9SO_3$] are able to form ABS in contrast to [C_2C_1im][CF_3SO_3] or [C_2C_1pyr][CF_3SO_3], this means that the anion [$C_4F_9SO_3$]$^-$ has a higher ability to promote the phase splitting than [CF_3SO_3]$^-$. The longer fluorinated alkyl chain of the anion renders it more hydrophobic, and diminishes its affinity towards water, thus enhancing the two-phase separation. Although the fluorine containing anions are not the same, it was also shown[35] that the increment of fluorinated alkyl chain length of the anion [$P(C_2F_5)_3F_3$]$^-$ rendered [C_2C_1im][$P(C_2F_5)_3F_3$] much less soluble in water than [C_2C_1im][PF_6]. ILs interact with water molecules essentially *via* hydrogen-bonds with their anions, which are stronger for anions with higher basicity values.[36]

The disruption in the water hydrogen-bonding network results from a combined effect of the ability of the IL anion to hydrogen bond with water and the molar volume of the ions.[37] The binding strength of the anions with the cations as well as the hydrophobicity and steric hindrance of the cations are further elements suggested to play important roles in water/IL interactions.[38] The influence of the cation core in the process of phase splitting was also evaluated, with the phase diagrams of the only two ILs able to form ABS with maltose shown in Fig. 7. In spite of the wide range of compositions tested, no two-phase formation was achieved with the IL containing the cholinium cation. The higher hydrophilicity of cholinium-based ILs has been previously reported[11], being thus not amenable to undergo through phase separation in presence of a carbohydrate aqueous solution. Indeed, cholinium-based ILs only form ABS with strong salting-out salts, such as K_3PO_4 [11], or with polymers where the effect seems to be the reverse with the IL acting as the salting-out agent[39] or where more complex molecular phenomena seem to takes place[40]. From the inspection of Fig. 7, the ability to form two phase systems is higher for [C_2C_1py]$^+$ than for [C_2C_1im]$^+$; the former cation has a 6-carbon ring, and the imidazolium only a 5-carbon one. This agrees with previous studies where it was shown that ILs having cations containing 6-carbon rings (pyridinium and piperidinium) formed ABS more easily than those with cations containing 5-carbon rings (imidazolium and pyrrolidinium). According to this study[24], aromaticity is not expected to play a significant role in ABS capability, that emerges to be strongly correlated with the cation size. Our data further corroborates this evidence: $[C_2C_1im][CF_3SO_3]$ was not able to produce two-phase splitting when combined with maltose, neither did $[C_2C_1pyr][CF_3SO_3]$, a similar IL also composed of a 5-membered core cation bearing similar chains but no double bonds.

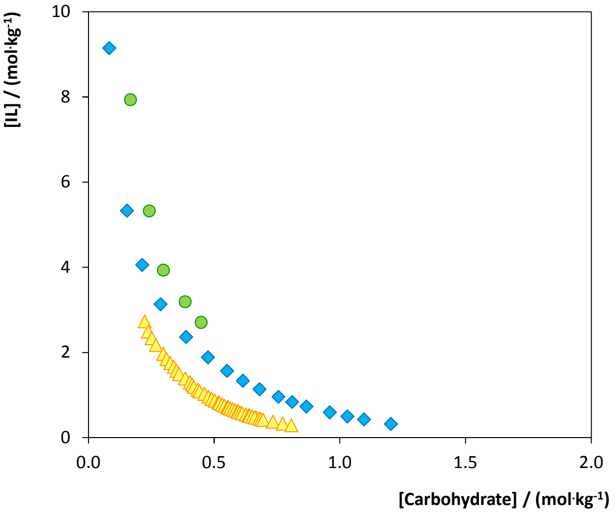

Figure 7. Ternary phase diagrams for ABS composed of IL + maltose + water, at 298 K and atmospheric pressure: (▲) $[C_2C_1py][C_4F_9SO_3]$, (◆) $[C_2C_1im][C_4F_9SO_3]$ and (●) $[C_4C_1im][CF_3SO_3]$[22].

In summary, and while overviewing a general salting-out phenomenon governing the formation of ABS composed of ILs and carbohydrates, the hydrophilic cholinium cation is not as prone to be salted-out by the sugar molecule as $[C_2C_1py]^+$ or $[C_2C_1im]^+$ are. Moreover, the competition between the IL ions and the carbohydrate for water molecules is more balanced when the IL contains cholinium than when it has pyridinium or imidazolium cations. It must be highlighted also that not only the size of the cation core but also the size of the side alkyl chains of the cation have great influence in ABS formation; the ability of the cation to produce two phases increases with the length of its side chain; when combined with maltose, $[C_2C_1im][CF_3SO_3]$ and $[C_2C_1pyr][CF_3SO_3]$, were unable to produce ABS, but $[C_4C_1im][CF_3SO_3]$ was, as results from a previous work[22] and depicted in Fig. 7. Moreover, and as highlighted before, the aromaticity of the core cation does not appear to play a significant role in the two-phase splitting.

The solubility of carbohydrates in ILs should not be discarded and could be also a process that interferes with ABS formation, particularly at low water contents. The solubility of low molecular weight carbohydrates in ILs depends on the nature of the IL[41] and also on the molecular weight of the carbohydrate[42]. The solubility of various mono and disaccharides, such as xylose, fructose, glucose and sucrose in ILs drastically decreased when hexafluorophosphate is replaced by the chloride anion.[42] Furthermore, high solubility values were found for $[C_1C_1im][Me_2PO_4]$ and $[C_2C_1im][N(CN)_2]$ but negligible values were observed in $[C_2C_1im][MeSO_4]$ and $[C_6C_1im]Cl$.[41] It was also demonstrated that glucose, sucrose, lactose and cyclodextrin are only sparingly soluble in weakly coordinating ILs, such as $[C_2C_1im][BF_4]$. In contrast, the solubility values in ILs that contain the dicyanamide anion may reach nearly 200 g·dm^{-3}.[43] These studies demonstrate that the cation, and particularly the length of its alkyl chains negatively affects the solubility of carbohydrates in ILs.[44] Notwithstanding, the anion of the ILs produced also significant differences in the solubility of the carbohydrates: the weak coordinating character of the IL anion contributes to a decreasing on the carbohydrate solubility in ILs. This interaction evidences the decisive role of the anion in the IL/carbohydrate mutual solubility, that is determinant in relevant industrial processes, such as in the dissolution of cellulose.[45] It may be recognized that both constituent ions have a significant influence in the dissolution process of carbohydrates in ILs, as well as in the formation of the respective ABS, a fact that emphasizes the tunable character of ILs by the proper choice of their ions according to a specific application.

Tie-lines

The binodal curves obtained for the studied systems, combining the different carbohydrates with two different FILs, $[C_2C_1py][C_4F_9SO_3]$ and $[C_2C_1im][C_4F_9SO_3]$, were fitted using Eq. (1) and the respective A, B and C parameters were estimated by least-squares regression.[25] Those parameters, as well as the corresponding standard deviations (σ) and regression coefficients (R^2), are reported in Table S6 in the ESI†. As the R^2 values indicate, the good quality of fitness of the results may provide experimentally unavailable data for these systems if needed. The detailed compositions of the coexisting phases are given in the ESI†, Table S7. In general, it can be observed that the IL-rich phase contains much less water than the carbohydrate-rich layer, supporting thus the higher affinity of the carbohydrates for water when compared with the FILs investigated in this work.

Dyes extraction

The extracting capability of the new systems investigated was also evaluated, as a proof of concept, using sulphonated azo dyes. These dyes are most used in the food and textile industries[46] and may be commercialized as pigments or water soluble pigments. The system composed of $[C_2C_1py][C_4F_9SO_3]$ (40 wt %) + D-(+)-maltose (18 wt %) + H_2O (42 wt%) was used to extract four azo dyes, namely Brilliant Blue FCF (E133), Green S (E142), tartrazine (E102) and Ponceau 4R (E124), at 298 K.

In all the investigated ABS, the sugar-rich aqueous phase corresponds to the top phase (as confirmed by us by UV-spectroscopy) while the bottom phase is majorly composed of IL. The results obtained are presented in Table 1 (both in extraction efficiencies and partition coefficients) and depicted in Fig 8. Almost all dyes preferentially migrate to the carbohydrate-rich phase with extraction efficiencies obtained in a single-step ranging between 38 and 94%. However, one of the dyes investigated (Brilliant Blue FCF, E133) preferentially migrates for the IL-rich phase, revealing an extraction efficiency of 38% for the phase enriched in maltose. The extraction efficiencies for the carbohydrate-rich phase increase in the order: Brilliant Blue FCF (E133) < Green S (E142) < tartrazine (E102) < Ponceau 4R (E124).

Table 1. EE_{Dye}% and K_{Dye} for the carbohydrate-rich phase, and respective standard deviation (σ), for Ponceau 4R (E124), tartrazine (E102), green S (E142) and brilliant blue FCF (E133), using the ABS composed of $[C_2C_1py][C_4F_9SO_3]$ (40 wt %) + maltose (18 wt %) + H_2O (42 wt %) at 298 K.

Dye	EE_{Dye} (%)	K_{Dye}
E133	38.08 ± 0.99	0.50 ± 0.02
E142	84.22 ± 1.85	4.42 ± 0.57
E102	93.63 ± 1.25	12.50 ± 2.68
E124	94.35 ± 0.31	13.65 ± 0.74

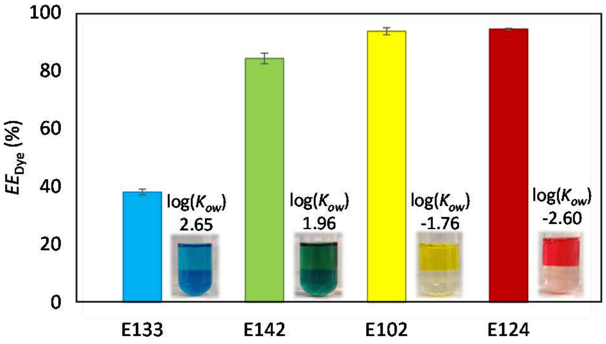

Figure 8. EE_{Dye}% for the carbohydrate-rich phase for Brilliant Blue FCF (E133), Green S (E142), tartrazine (E102) and Ponceau 4R (E124), using the ABS composed of [C2C1py][C4F9SO3] (40 wt %) + D-(+)-maltose (18 wt %) + H2O at 298 K. The log(K_{ow}) values of each dye are also presented.[47]

The pH of the coexisting phases of the studied ABS were also determined and are around 5 – *cf.* the ESI† with detailed data, Table S7. At these pH values, with the exception of Ponceau 4R, all the dyes already exist in a significant amount in a charged state. Even so, and among the charged dyes, E133 preferentially migrates for the IL-rich phase while the reverse was observed with E102 and E124, meaning that electrostatic interactions do not play a major role alongside the dyes partitioning. On the other hand, the K_{ow} values[47] of the four different dyes are a few orders of magnitude apart and seem to support the different partitioning behaviours observed. The values K_{ow} for the studied food dyes are shown in Fig. 8. In general, the higher the K_{ow}, the less the molecule is likely to migrate to the most hydrophilic phase (carbohydrate-rich phase). Further, as Fig. 8 illustrates, the extraction efficiencies for the carbohydrate-rich phase strictly follow the opposite pattern of the K_{ow} values.

Previous works on the extraction of dyes using ABS usually report their preferential migration for the IL-rich phase.[48, 49] Contrarily to the ones demonstrated in this work, these systems are composed of ILs and high-charge density salts - strong salting-out agents favoring thus the migration of dyes for the phase enriched in IL. In this work, carbohydrates with a weak salting-out effect were employed, leading to remarkable opposite behaviors which mainly depend on the hydrophobicity of the dye and polarity of the phase. Therefore, IL-based ABS formed with carbohydrates seem to be more amenable to tailor the extraction efficiencies and, more importantly, to determine the phase for which the target product migrates. This tuning ability if of outstanding importance when dealing with the purification of added-value products from more complexes and real matrices.

Most of the food dyes are enriched in a benign and biocompatible carbohydrate-rich phase instead of the usual IL-rich phase. In the past, we have been dealing with the development of novel strategies for the recovery of the extracted compounds followed by the IL-rich phase recovery and reuse.[9, 49-51] In all of these studies, the target compounds are mainly enriched in the IL-rich phase. Contrarily, in this work, the majority of the target compounds migrate to the carbohydrate-rich phase - an outstanding advantage when envisaging the products recovery and further use since they are in a more biocompatible medium. Moreover, in this situation, the IL-rich phase can be recycled and reused directly unless it is saturated with contaminants.

Based on the overall results, further improvements on the performance of the extraction procedure could be made so as to achieve a better selectivity and afford the separation of Brilliant Blue FCF from Ponceau 4R since they partition for different phases. The studies to be implemented could involve changing the media conditions or using a wider set of carbohydrates or ILs. Notwithstanding, ABS formed with FILs and carbohydrates are remarkable systems to extract either hydrophobic or hydrophilic dyes, taking into consideration that hydrophobic dyes could be recovered at the IL-rich phase whereas more hydrophilic ones could be recovered at the carbohydrate-rich phase.

Conclusions

This work discloses novel ABS composed of FILs and a wide diversity of low molecular weight carbohydrates (monosaccharides, disaccharides and polyols). The ternary phase diagrams, tie-lines and tie-line lengths were determined at 298 K and at atmospheric pressure. The ability of carbohydrates to form ABS decrease in the order (in molality units): maltitol ≈ D-(+)-maltose > sucrose > D-sorbitol > D-(+)-galactose > D-(+)-glucose ≈ xylitol ≈ D-(+)-mannose > D-(+)-fructose > D-(–)-arabinose. This trend reveals that the carbohydrate acts as the major salting-out/sugaring-out species, leading to the formation of a second aqueous phase enriched in FIL, and where the hydration ability of the carbohydrate plays a decisive role. The total number of hydroxyl groups, although important, is not the sole player in the carbohydrate salting-out effect; the size of the pyranose ring and the relative position of the hydroxyl groups also have an impact on the hydration ability of the sugar in respect to the ABS formation ability. Furthermore, the hydration aptitude of each IL ion (cation and anion) also plays a significant role. Only those ILs with larger cations and anions with long fluorinated alkyl chain length are able to form ABS with carbohydrates.

This work contributed to expand the range of ILs available for ABS separation processes and demonstrated that these can be used to extract food dyes - Brilliant Blue FCF (E133), Green S (E142), tartrazine (E102) and Ponceau 4R (E124). Extraction efficiencies up to 94% were attained in a single-step for the carbohydrate-rich phase. Contrarily to ABS formed by ILs and high-charge density salts, where the salting-out effect of the salt seems to favor the extraction of target products to the IL-rich phase, the ABS investigated in this work seem more amenable to be tuned. In fact, both the dye hydrophobicity and the polarity of the phases have a large impact on the dyes partitioning behavior. These novel systems are more versatile and may be further modified to achieve higher selectivity upon a judicious choice of the IL constituent ions and of the carbohydrate. Overall, most of the food dyes can be enriched in a benign and biocompatible carbohydrate-rich phase instead of the usual IL-rich phase.

Acknowledgments

This work was developed in the scope of the project CICECO-Aveiro Institute of Materials (Ref. FCT UID/CTM/50011/2013), financed by national funds through the FCT/MEC and when applicable co-financed by FEDER under the PT2020 Partnership Agreement. A. M. Ferreira acknowledges FCT for the PhD grant SFRH/BD/92200/2013. A. B. Pereiro is gratefully acknowledged FCT/MCTES (Portugal) for the financial support through FCT Investigator 2014 and through projects PTDC/EQU-FTT/118800/2010 and UID/Multi/04551/2013. M. G. Freire acknowledges the European Research Council (ERC) for the Starting Grant ERC-2013-StG-337753.

Notes

†Electronic Supplementary Information (ESI) available: Weight fraction data and respective correlation of the binodal curves, tie-lines and tie-line lengths, weight fraction compositions of the systems used in the extractions, extraction efficiencies and pH of the coexisting phases of the different systems. See DOI: 10.1039/b000000x/.

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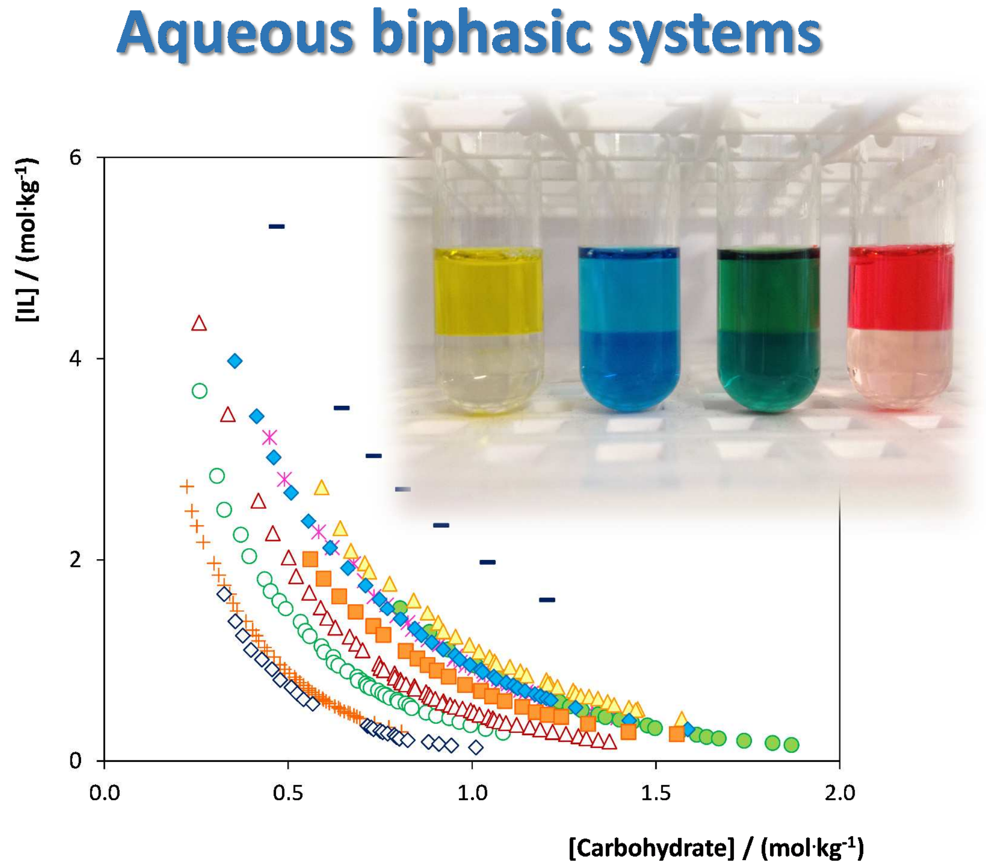

Aqueous biphasic systems formed by fluorinated ionic liquids and carbohydrates are more amenable to be tunned.