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of the past?
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alternative: the unbalanced turn of deep eutectic solvents**

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History repeats itself again: Will DESs repeat ILs mistakes of the past?

From being considered ionic liquids to become their alternative: the unbalanced turn of deep eutectic solvents

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Abstract

The establishment of the place of Deep Eutectic Solvents (DESs) as a new class of green solvents was essentially grounded on naïve comparisons with Ionic Liquids (ILs), since both are composed of charged compounds. The easiness of DESs preparation afforded the quick preparation and utilization of a massive number of solvents and their use in wide variety of applications with a minimal fundamental knowledge of their thermophysical properties and phase equilibria studies. As time went, the need to define DESs from the thermodynamic point of view and to differentiate them from other classes of solvents was imperative.

This perspective review aims at dispelling some myths about DESs through the use of experimental data and computational chemical calculations and establishing fair comparisons with other classes of solvents, ILs, eutectic solvents (ESs) and volatile organic compounds (VOCs), so that clear and sound conclusions can be drawn. Several important parameters typically used to characterize solvents and that have been much used to justify DESs wide range of applications, such as vapor pressure, thermal stability, polarity, toxicity and water miscibility, were accessed for these different solvents and comparisons were established. Moreover, a comparative analysis in a selected research area, biopolymer dissolution and treatment, was chosen to illustrate the unique potential of ILs and DESs and the challenges that still need to be addressed. Literature available for the diverse polysaccharides selected (cellulose, hemicellulose and chitin) and lignin highlighted pros and cons and the different level of knowledge gained to date for both ILs and DESs. This part is complemented with recycling and techno-economic considerations for the two classes of solvents which are additional key aspects to consider for the development of an effective integrated biorefinery process.

The conclusion is obvious: DESs are a new class of solvents, with distinct properties from other classes of solvents which are essentially dependent on the properties of their constituent compounds. Therefore, when starting compounds are wisely selected, DESs become an additional and promising pathway in the pursuit of environmentally friendly solvents to replace traditional VOCs for a given application. However, some fundamental studies are still needed to fully understand these systems and define their most effective areas of application.

Key words: Deep Eutectic Solvents, Ionic Liquids, Alternative Solvents, Properties, Biomass

1. DESs definition over time

Eutectic mixtures date back to 1884, when Guthrie defined them as mixtures on such proportion that a minimum temperature of liquefaction could be obtained.¹ Nowadays, eutectics solvents (ESs) are a well-known class of multicomponent systems, presenting more or less pronounced melting point temperature depressions relative to the starting compounds. Many examples, in pharmaceutical field to solubilize or liquefy specific compounds,²⁻⁴ as phase change materials⁵⁻⁷, as liquid crystals⁸⁻¹⁰ etc., can be found in the open literature. In 2003, Abbott et al.¹¹ showed that it is possible to obtain remarkably large melting point depressions, using one salt, that acts as hydrogen bond donor (HBD), and one hydrogen bond acceptor (HBA) to obtain liquid mixtures at room temperature, presenting for the first time the so-called deep eutectic solvents (DESs). DESs were then defined as supramolecular complexes formed between one hydrogen bond donor (HBD) and one hydrogen bond acceptor (HBA) and the large decrease in the mixture melting point was attributed to charge delocalization and the extensive hydrogen bond network that occurs between the HBD and the HBA. The first reported DESs was a mixture of ChCl and U, with a melting temperature of 12 °C, much lower than those of the starting materials, 302 °C and 133 °C, respectively, and thus the designation of deep. Since then, a large amount of work has been carried out under the DESs flagship, most of it regarding applications of DESs as tunable solvents, and only a handful addressing the fundamentals of these mixtures. The knowledge of the solid-liquid phase diagram, defining the phase behavior at a given temperature and composition and thus the understanding of the phase coexistence, the depression of the melting point through the intersection of the solubility lines and the liquid window available at a specific temperature, are vital to the design of chemical processes and products using DESs.

Since the dawn of DESs, many authors refer to them as ionic liquids (ILs) analogues.¹²⁻¹⁴ This was mainly due to the presence of salts or solid at room temperature ILs, especially those based on cholinium cation. Contrary to what happened in ILs research, which were very well studied and characterized from the fundamental point of view prior to their use, DESs started to be used in applications, with little fundamental knowledge and molecular understanding. This is probably a consequence of their easy preparation, most often just by mixing and heating the pure components. However, some authors pointed out the unsuitability of this preparation method,^{15,16} especially for DESs composed of carboxylic acids, since their lack of thermal stability might lead to unwanted reactions and thus impurities. Consequently, despite the simple and easy preparation method, the chemical structure of the final DESs should always be verified.

In 2011, Choi and co-workers^{17,18} reported many natural deep eutectic solvents (NADESs) based on natural compounds only, particularly primary metabolites, such as organic acids, amino acids, sugars etc. Soon, the attractive features of NADESs were widely extrapolated to the whole DESs family, which became widely known as easy-to-prepare, inexpensive, environmentally benign, green, sustainable etc. In 2019, Coutinho and co-workers¹⁹ brought some order into the field by defining DESs as a mixture of pure compounds for which the eutectic point temperature is considerably below that of the ideal mixture description, thus presenting significant negative deviations from ideality. This not only clearly sets DESs apart from ESs or eutectic mixtures, but also emphasizes the importance of the knowledge of solid-liquid phase equilibria diagrams, which sometimes are not easy to measure and most of the times are not available. Although most DESs that fall under this definition are ionic, meaning they have salts in their constitution, non-ideal mixtures of fully neutral compounds, such as D,L-menthol:thymol,^{20,21} can also exhibit non-ideal behavior and thus also need

to be considered as DESs. Conversely, not all ESs containing salts present large deviations from the ideal behavior.^{19,22} This distinction between DESs and ESs implies the recognition of the last one as another platform for solvent's development. If both DESs and ESs are to be used as solvents, the temperature depression should be such that a liquid mixture needs to be attained at the operating temperature for a certain composition range. The acknowledgement that DESs composition does not have to be fixed at the eutectic point but can be another variable in the preparation of DESs and ESs, just like in any other mixtures, adds further flexibility to these platforms of designer solvents.

2. ILs and DESs – properties and myths

The boom of designer solvents occurred with the discovery of stable molten salts that are liquid at room temperature or temperatures below room temperature – ILs.²³ Besides the commonly accepted definition for an IL, a salt with a melting temperature below the boiling point of water, this new class of solvents, composed solely by cations and anions, soon attracted the attention of the scientific community. ILs usually consist of a large, asymmetric organic cation coupled with a generally smaller, weakly coordinating anion. Due to the large number of possible cations and anions combinations, that could reach 10^6 according to some authors,²⁴ their physicochemical properties can be easily tuned, making justice to the designation of designer solvents. However, the complex synthetic and purification steps that are often needed to prepare an IL with a purity equivalent to commercial organic solvents was rarely mentioned.

Another important property of (aprotic) ILs is their negligible vapor pressure,^{25,26} typically in the order of units of Pa,²⁷ which eliminated the major problems associated to volatile organic solvents, the damage of the ozone layer, human health hazards and the loss of solvent throughout a process due to its high volatility. This property alone allegedly granted ILs the green solvent label, without considering the different aspects through which ILs might enter the terrestrial ecosystem. The very rich and complex interactions present in ILs and through which they solvate solutes, either gases, liquids, or solids, has also been seen by most authors as a true advantage over other solvents. Nevertheless, there are many examples in the literature where ILs act as sponges, dissolving very high amounts of solutes, which can hardly ever be recovered, thus bringing additional challenges from the sustainability and circular economy point of view.

One of the greatest challenges in the design of ILs was, and still is, the preparation of liquid at room temperature ILs. Despite the ubiquitous place that imidazolium cation has in the IL's portfolio, the introduction of the cholinium cation, and in particular, the ChCl salt was a game changer since it provided a framework to design more benign ILs. However, the fact that the ChCl is a solid at room temperature hindered its application as solvent, until it was used in the preparation of DESs. Thus, the "birth" of DESs from solid ILs prompted many erroneous generalizations. To promote the "beneficial" properties of ILs and DESs, the scientific community made wide generalizations of their properties, instead of recognizing that both these classes of solvents have their independent classes of solvents, with different properties. Even common volatile organic compounds (VOCs) have very different chemical and biological properties among themselves. However, some VOCs can have similar properties to each other, as recognized by the pharmaceutical industry where scales have been created, to replace some solvents by others with similar chemical properties but different toxicity.

The most frequent generalizations are on DESs toxicity and volatility, without paying attention to DESs constituents. Just like the properties of ILs are intimately connected to the properties of their

ions, those of DESs are also dependent on their constituents. Another important point is that unlike ILs, DESs are not pure fluids. Consequently, the properties of DESs depend also on the composition (HBA/HBD molar ratio) and thus the DESs constituents can have a different impact on each property. On the other hand, as non-ideal mixture, DESs might have properties that are not in between those of their parent compounds, depending on the interactions playing a dominant role in their bulk or at the surface, according to the property under consideration.

Table 1 depicts the evolution of the scientific community perception of the ILs properties in early 2000 and today, along with the current perception of DESs. Will DESs repeat ILs mistakes of the past? By critically analyzing the single entries, it can be easily stated that both perceptions of ILs and DESs are not correct. As soon as ionic and non-ionic DESs found their own space outside the ILs family, a race of praising their properties against those of ILs started, instead of recognizing them as another interesting class of media alternative to VOCs. It is evident that errors of the past, experienced before in the ILs research area are repeated nowadays in the DESs research area (overestimating the properties of DESs, often to the detriment of ILs). In conclusion, DESs are not IL's analogues or complexes at a fixed stoichiometric ratio of components, but non ideal mixtures of two or more compounds. DESs are not always green, not always cheap, not always nontoxic: their properties depend on their components and their interactions within the DESs mixture.

Table 1 Evolution of ILs and DESs properties perception.

Property	ILs Early 2000	ILs TODAY	DESs TODAY
Tunability	✓	✓	✓
Thermal stability	✓	✓	✓
Low cost	✓	X	✓
Safety (toxicity/biodegradability)	✓	X	✓
Green character	✓	X	✓
Ease of preparation	✓	X	✓

3. Is there any relationship between ILs and DESs?

The seminal work of Abbott in 2003¹¹ opened the door to the preparation of DESs using ILs. In fact, a large amount of DESs are based on ammonium salts, specially ChCl, as HBA and a wide variety of HBD such as acids, aminoacids, alcohols, glycols etc.^{28,29} More recently, water has also been proposed as HBD and thus mixtures of DESs and water have been investigated to understand up to which composition the DESs structure is maintained.³⁰⁻³⁴ On the other hand, mixtures of imidazole-based ILs, [C₂C₁im]Cl, [C₄C₁im]Cl, [C₆C₁im]Cl, with a large variety of HBD have been widely prepared and

used in several applications.^{35–41} The relevant role of chloride anion, present in the IL, in the establishment of hydrogen bond donors in DESs has also been addressed.^{42–50} Even more, mixtures of ILs could give rise to new DESs. Nevertheless, only for few systems solid-liquid phase diagrams are reported. As shown in Figure 1, although it is possible to convert ILs in DESs, the reverse cannot be attained.

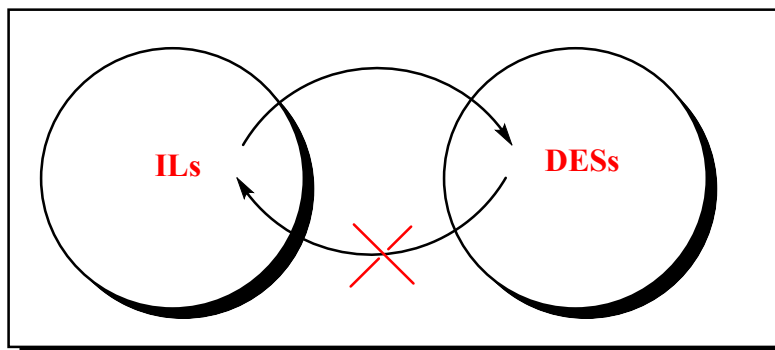


Fig. 1 ILs and DESs relationship (ring dimensions are arbitrary).

Recently this type of transition was already made by adding carboxylic acids, namely acetic acid, to $[\text{C}_2\text{C}_1\text{im}]\text{Cl}$, in various molar ratios led to the formation of DESs with a melting point below $-78\text{ }^\circ\text{C}$. Additionally, NMR and solvatochromic parameters were used to prove that the acid does not ionize and led to the formation of $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$ as it might be expected.⁵¹

4. On DESs, ESs, ILs and VOCs properties

In the following sections some of the most important properties of DESs often freely extrapolated from those of ILs will be discussed and illustrated. Vapor pressure, thermal stability, polarity and toxicity are the properties that were selected to illustrate and discuss the difference between ILs and DESs, also introducing ESs and VOCs properties and how their properties compare with the former classes of solvents.

4.1. Do DESs and ESs have negligible vapor pressure?

With the objective of rebutting the common claim that DESs and ESs have negligible vapor pressure, this section presents a comparison between DESs, ESs, ILs and VOCs. To be noted that as DESs and ESs are mixtures of compounds and thus the difference in volatility of each one of the constituent compounds as well as the nature of their interactions may lead to the preferential evaporation of one of the compounds in detriment of the other. This implies that the composition of the DESs in the vapor phase can thus be quite different from that of the liquid phase, especially for DESs and ESs composed of salts or ILs and other neutral compounds. The isoteniscope is the most used method to measure vapor pressure.⁵² Despite of the recent redesigns of the apparatus,⁵³ this procedure is very demanding on the manipulation of the apparatus and requires large volumes of the sample under study. Thus, recently, this method has been replaced by head-space gas chromatography mass spectrometry (HS-GC-MS), for DESs and ESs, and thermogravimetric analysis (TGA) mainly for ILs. HS-GC-MS has the advantage of clearly identifying DESs and ESs vapor phase composition. Despite the scarcity of data in what concerns DESs and ESs, some conclusions can be already drawn.

The truth is that DESs and ESs present a much lower vapor pressure than common solvents. For example, comparing the vapor pressure of VOCs such as dichloromethane and diethyl ether, which exhibit values of 102 kPa and 123 kPa at 40 °C,⁵⁴ respectively, the highest vapor pressure found in literature for ESs is that of 1-tetradecanol:D,L-menthol (1:2), which does not surpass 16 Pa at the same temperature. This difference is even higher when comparing VOCs with ionic DESs/ESs that have a salt as one of the components, being 4 Pa, the highest value of vapor pressure observed for [P₄₄₄₄]Br:sulfolane (1:4), at the same temperature. This difference in vapor pressure is still several orders of magnitude different compared to less volatile VOCs, like ethyl acetate or toluene, which exhibit a vapor pressure of 25 kPa and 8 kPa, at 40 °C,⁵⁴ respectively. Moreover, other common environmentally friendlier solvents, such as ethanol or even water, still have a much higher vapor pressure, 19 kPa and 7 kPa respectively, at the same temperature.⁵⁴

In fact, usually eutectic mixtures have a lower vapor pressure than their pure components as result of the favorable interactions, mostly hydrogen bonds, established between the two compounds. This is true for both ionic and neutral DESs and ESs, even when their components have a very low vapor pressure. For example, considering U-based eutectics, the vapor pressure of ChCl:U (1:2),⁵⁵ is 1.33 Pa at 100 °C, contrasting with 1.97 Pa for pure U at the same temperature.⁵⁶ Additionally, the proportion of each compound in the eutectic mixture plays a decisive role on the difference between the vapor pressure values for the pure components and the DESs or ESs. This can be easily understood considering, for example, the eutectic mixtures of thymol:D,L-menthol at 100 °C, for which the vapor pressure is 975 Pa at the molar ratio (1:2), while at a molar ratio of (1:1) it decreases to 680 Pa.⁵⁵ In this case, the lowest vapor pressure corresponds to the eutectic point (1:1) of the eutectic mixture, which can be interpreted as, at this molar ratio, the two compounds have more favorable interactions, and therefore, are less volatile. On the other hand, mixtures of decanoic acid:D,L-menthol have, at 100 °C, a vapor pressure of 540.9 Pa at (1:1) molar ratio⁵⁷ and 895.8 Pa at a (1:2) molar ratio.⁵⁸ Since (1:2) is closer to the eutectic point (2:3) and it presents a higher vapor pressure, it can be concluded that the vapor pressure of each neat component impacts the tunability of the vapor pressure of the mixture. Another point to consider is how deep is the melting temperature depression of the DESs/ESs is, that is, how much the system deviates from ideality. Similarly, mixtures of thymol:lidocaine, at 100 °C, at a molar ratio of (1:1) has a vapor pressure of 53.9 Pa⁵⁸, while the (1:2) ratio has a vapor pressure of 329.4 Pa⁵⁷ (Figure 2).

Aprotic ILs (AILs) present a much lower vapor pressure than all the above-mentioned DESs/ESs. The fact that ionic DESs/ESs contain a salt or an ionic liquid in their constitution, led to incorrect generalizations about their properties. When compared with ionic DESs/ESs, ILs have a much lower vapor pressure, below 1 Pa at 200 °C, in most cases.⁵⁹ Also, to be mentioned that ionic DESs/ESs usually have lower vapor pressure than neutral DESs/ESs. For example, thymol:lidocaine (1:1) has a vapor pressure of 7.28 Pa at 70 °C, while ChCl:Gly (1:2) presents a vapor pressure of 2.14 Pa at the same temperature.^{57,58} Still both these vapor pressure values are much higher than those of ILs.

In the case of protic ILs (PILs), as they are a mixture of the neat constituents and their respective ionic species, the vaporization phenomenon can be understood through the concept of reactive azeotrope.⁶⁰ In this scenario, it is possible to define an equilibrium between 3 species, namely the two neutral species (Brønsted acid and base) and the formed PIL. The vapor pressure is led by the volatility of the molecular compounds as their respective ionic forms have negligible vapor pressure. This implies that PILs have higher vapor pressure than aprotic ones. Indeed, this vapor pressure can

be calculated for various molar ratios of the two components considering vapor-liquid equilibrium conditions and a reaction constant K for the previously stated equilibrium. In this regard, the pK_a and pK_b of the acid and base are a measurement of the proton exchange process efficiency,^{60,61} and therefore influence the stoichiometry of the azeotropic point. Nevertheless, volatility of the molecular components also plays an essential role on the vapor pressure shown by PILs.⁶⁰ Furthermore, evidence suggest that PILs also displays an equilibrium between ionic and neutral species in the gas phase.⁶¹

In conclusion, the negligible vapor pressure of ILs, even at high temperatures, is an achievement that DESs/ESs cannot match, despite their relatively low vapor pressure when compared to commonly used organic solvents. Of course, that DESs prepared by mixing two ILs will have vapor pressure as low as ILs.

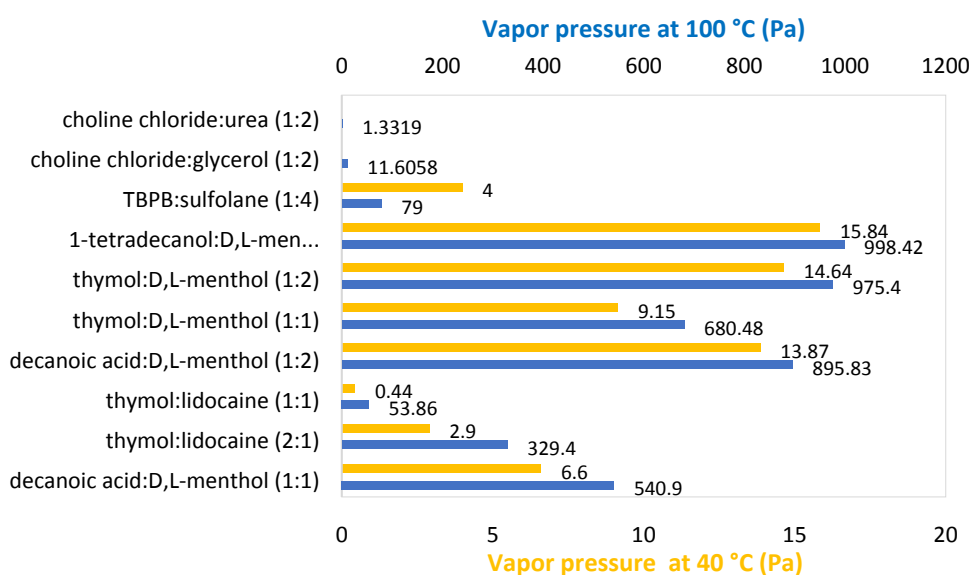


Fig. 2 Vapor pressure of various eutectic solvents at 40 °C (yellow) and 100 °C (blue).^{55,57,58,62}

4.2. Is the thermal stability of DESs, ESs and ILs on the same level?

DESs/ESs are usually wrongly labeled as thermostable as ILs. It is important to highlight the subjectiveness of what can be labeled as thermostable, as it is based not only on the capacity of other similar compounds to remain active, without decomposition or deactivation, but is also connected to its function and often linked to a specific application. Although usually both DESs/ESs and ILs are more thermostable than VOCs, this does not mean that they are on same pace with each other.

The thermostability of solvents is typically evaluated by TGA, in which the sample is gradually heated, and the weight monitored, and the onset temperature (T_{onset}) determined. Although onset temperature is usually used as measure of the thermal stability of compounds, it is usually obtained over short periods of time what leads to divergence between onset temperature and the real degradation temperature when the compound is exposed to temperature for long periods. Furthermore, reported values of T_{onset} have many fluctuations, as measurement conditions such as

sample mass, inert gas flow and heating rate significantly influence the results. For this reason, $T_{z/y}$ is usually calculated where z and y correspond to the degree of decomposition and time of utilization, respectively.⁶³

A plot of the distribution of T_{onset} of 51 DESs/ESs and 165 ILs is shown in Figure 3. It is easy to see that most DESs/ESs have clearly a lower thermal stability than ILs. In fact, almost all DESs/ESs have a T_{onset} between 30 °C and 250 °C,^{64–67} while only about one quarter of the considered ILs have a T_{onset} in this range⁶³. In fact, eutectic mixtures display T_{onset} as low as 34.3 °C for ChCl:acetic acid (1:2),⁶⁴ up to 265.1 °C for ChCl:pentaerythritol (2:1).⁶⁴ For eutectic mixtures composed of ChCl and organic diacids at (1:1) molar ratio, the T_{onset} increases with chain length of the organic acid, from 128.3 °C for malonic acid, 229.1 °C for succinic acid up to 232.3 °C for adipic acid.⁶⁴ Additionally, different counter ions of cholinium salt also have impact on thermal stability of the corresponding eutectic mixtures since larger ions lead to lower T_{onset} . For example, T_{onset} of 128.3 °C for ChCl:malonic acid (1:1), 126.2 °C for ChBr:malonic acid (1:1) and 125.2 °C for ChI:malonic acid (1:1).⁶⁴ Moreover, worthwhile mentioning is also the capacity of easy tuning of thermal stability of these solvents. For example, ChCl:D-fructose (2:1) has a T_{onset} of 161.5 °C, while ChCl:xylitol (2:1) has T_{onset} of 261.1 °C,⁶⁴ despite the fact that both HDBs are sugars that only differ on the oxidation state of one functional group. The scarcity of data on this subject does not allow to take further conclusions and thus it is very important to measure onset temperature for DESs and ESs, as well as decomposition temperatures for long exposure periods, for instance $T_{0.01/10\text{hr}}$, conditions which are commonly used for ILs.⁶³

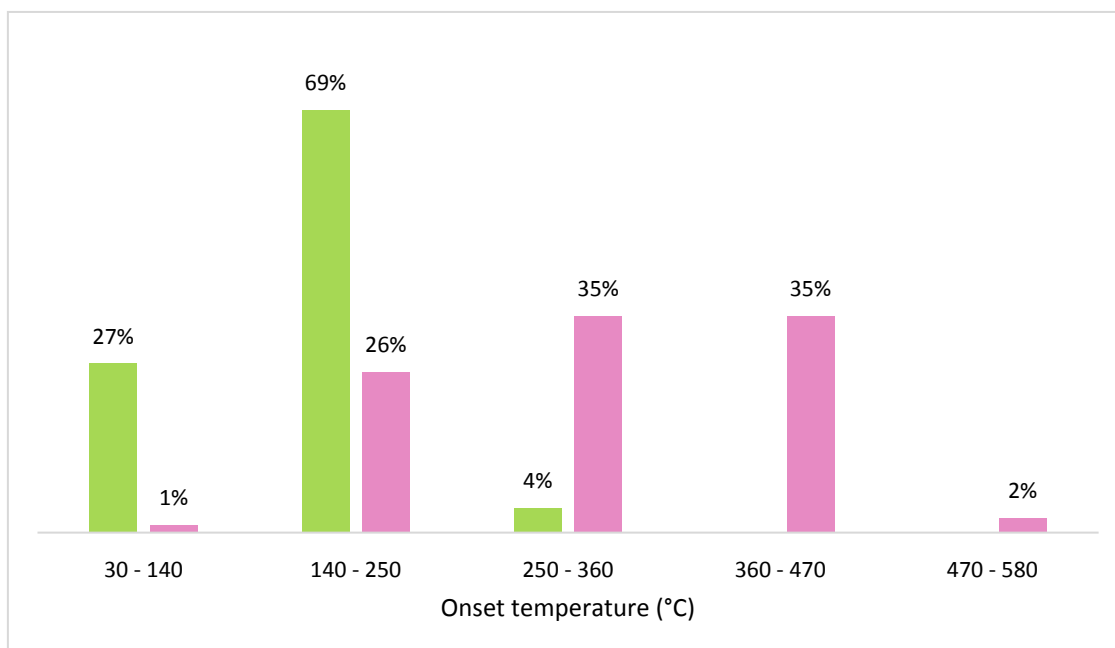


Fig. 3 Distribution of ESs (green) and ILs (pink) based on their T_{onset} (°C), considering intervals of 110 °C.^{63–67}

Another worth mentioning aspect of the TGA methodology is the lack of knowledge about transformations that may occur on the sample that do not result in mass loss. For example, although ChCl:oxalic acid (1:1) have a reported T_{onset} of 162.1 °C,⁶⁴ this same eutectic solvent undergoes esterification with a 34% yield at a temperature of 100 °C after 2 hours¹⁶. Actually, this eutectic solvent shows considerable esterification (10%) after 2 hours at 60 °C,¹⁶ this esterification reactions were also reported in this range of temperatures for other mixtures of ChCl and diacids at diverse

molar ratios.¹⁶ Within this line of thought, techniques like NMR, FTIR and MS that are already used to understand the mechanisms of degradation are also recommended in order to verify the integrity of the sample. In another vein, in some cases TGA methodology might underestimate DESs/ESs thermal stability. Indeed, as eutectic mixtures do present vapor pressure, evaporation of the neutral species under gas flow has been observed. This means that DESs/ESs is more thermally stable than determined by TGA, since the observed mass loss might be due to evaporation and not degradation, as the gas flow in TGA helps the evaporation process.

Focusing on ILs, their T_{onset} range from 100 °C ($[\text{P}_{4440}]\text{NO}_3$) up to 575.2 °C for $[(\text{C}_9(\text{C}_1\text{im})_2)[\text{NTf}_2]_2]$,⁶³ although near 97% of them present a T_{onset} on the range of 140 °C to 470 °C. Nevertheless, they can reach much higher temperatures than most DESs/ESs without degradation. The degradation mechanism and the effect of different anions and cations were already heavily discussed with the order of stability reported over various series of anions for a given cation as well as the other way around.⁶³ Regardless of this, some effects are too complex to be reported over a series of ions, as happens in the case of chain length effect. For instance, T_{onset} of $[\text{C}_2\text{C}_1\text{im}]\text{Phe}$ is 156 °C, $[\text{C}_4\text{C}_1\text{im}]\text{Phe}$ is 158 °C, $[\text{C}_6\text{C}_1\text{im}]\text{Phe}$ is 162 °C, $[\text{C}_8\text{C}_1\text{im}]\text{Phe}$ is 168 °C and $[\text{C}_{10}\text{C}_1\text{im}]\text{Phe}$ is 180 °C, one could conclude that T_{onset} increases as chain length grows,⁶³ contradictorily $[\text{C}_4\text{C}_1\text{im}]\text{OAc}$ and $[\text{C}_8\text{C}_1\text{im}]\text{OAc}$ has a T_{onset} of 216 °C and $[\text{C}_6\text{C}_1\text{im}]\text{OAc}$ of 220 °C, pointing that chain length has no effect over thermal stability of this ILs.⁶³ Finally, predictions of these temperatures and mechanisms of degradation can be made by various models such as quantitative structure-property relationship (QSPR), ab initio quantum chemical calculation, COSMO-RS as well as correlations with physical properties or spectroscopic parameters, for example peak position on the IR spectra.⁶⁸

In the case of PILs, the principal decomposition mechanism is the reverse proton transfer, reason why in this type of ILs the difference between the value of pK_a of both, the acid and the base represent a major factor in thermal stability.⁶³ For instance, taking in account the ILs $[\text{P}_{4440}]\text{NO}_3$, $[\text{P}_{4440}]\text{MsO}$, $[\text{P}_{4440}]\text{TfO}$ and $[\text{P}_{4440}]\text{NTf}_2$, the T_{onset} displayed is, respectively, 100, 210, 220 and 240 °C.⁶³ This is also in accordance with the superior thermal stability of superbases-derived PILs, between 300 ($[\text{BEMPH}]\text{NTf}_2$) and 380 °C ($[\text{mTBDH}]\text{NTf}_2$) as the ΔpK_a is higher than for other PILs. Furthermore, considering phosphonium and ammonium-based PILs the thermal stability increases as the alkyl chain grows, for instance the T_{onset} for $[\text{P}_{4440}]\text{TfO}$ is 220 °C, while for $[\text{P}_{8880}]\text{TfO}$ is 371 °C, the presence of electron-withdrawing groups have the opposite effect, for instance taking in account $[\text{N}_{8880}]\text{TfO}$ and $[\text{Ph}_3\text{NH}]\text{TfO}$ the respective T_{onset} are 362 and 208 °C.⁶³

4.3. Are DESs and ESs less polar than ILs? What about common solvents?

As a complex parameter to evaluate in a one-dimensional scale, polarity is often evaluated using empirical polarity scales. The most widely used method to describe multiple polarity properties of a solvent is the Kamlet–Taft polarity scale. In this scale, polarity is unfolded over 3 factors, α , which accounts for hydrogen bond donor capability, β , which accounts for hydrogen bond acceptor capability and π^* , which accounts for polarizability / dipolarity.

As stated before, the polarity measurement is too complex for a one-dimensional scale as this property is result of different intermolecular interactions between the solvent and the solute, namely hydrogen bonding, van der Waals interactions and π -interactions, the complexity of this property is even bigger when the solvent is composed of a mixture of substances, like in eutectic mixtures, as each component has its own capacity to establish interactions with the probes.⁶⁹ Typically, polarity

is measured through the analysis of UV-vis spectra of a set of solvatochromic probes in the desired solvent. Hence, the interaction of the solvent with solvatochromic probes is evaluated through the changes in probes absorption spectrum.⁷⁰ The most used set of solvatochromic probes are those that allow the determination of the so-called Kamlet-Taft parameters, using 4-nitroaniline, *N,N*-diethyl-4-nitroaniline and Reichardt's dye 30 as probes. Usually, the solvatochromic shift of the absorption bands of these probes is measured as positive, bathochromic shift (shift to the red), or negative hypsochromic shift (shift to the blue), and then related with the Kamlet-Taft parameters.⁷¹ It is also important to mention that Reichardt's dye ground state is more stabilized by solvents with a high hydrogen bonding capability than the excited state, reason why in case of these solvents alternative probes are used, namely, Reichardt's betaine dye 33 commonly used for eutectic solvents⁶⁹ or Nile red for ILs.⁷² Although this approach enables a better understanding of the polarity of a solvent, especially DESs, ESs and ILs, these classes of solvents have an added difficulty in the determination of the α parameter, due to their hygroscopic nature, as the water concentration affects the measurement.⁷³ To overcome this problem, ¹³C NMR measurements of this parameter were developed and reported, based on the carbon's chemical shifts of the pyridine-N-oxide probe.⁷⁴ As a matter of fact, some of the α values used in this critical review for comparisons were measured using this method, such as for example those for eutectic solvents comprised of tetraalkylammonium salts,⁷⁵ as each one of Kamlet-Taft parameters are weighted by coefficients (a, b and s) for a given probe, these values of α can be directly compared to the ones obtained by other methodologies as they represent the same scale.⁷⁶

It is important to emphasize that these parameter's values may change if a different probe is used, making it hard to fairly compare different sets of data. Additionally, this method represents an economically and time demanding step, making room for *in silico* prediction of these parameters, a much cheaper and quicker method. COSMO-RS (conductor like screening model for real solvents) is a quantum chemical-based model that calculates thermodynamic properties of molecules.⁷³ This model was already applied to predict Kamlet-Taft parameters based on the equilibrium constant of the tautomerism between a β -keto ester and a β -diketone with their respective enolic forms in various molecular solvents.⁷⁷ A different method was proposed for hydrophilic and hydrophobic eutectic mixtures, by establishing a linear correlation between three calculated energies, namely, hydrogen bonding, van der Waals, and misfit energy and the α and β parameters. These two correlations were then used to predict the values of α and β for other eutectic solvents.⁷³

In order to compare and distinguish each one of these parameters for DESs, ESs, ILs, and VOCs each of these parameters will be analyzed separately. It is important to note that this type of comparison between these classes of solvents is scarce, and usually reported taking in account only a small amount of data.^{69,72}

4.3.1. α - Hydrogen bond donor capability

Eutectic mixtures are mixtures of HBA and HBD and are based on the establishment of hydrogen bonds to form a mixture in liquid state.⁷⁸ Thus, it is obvious that this class of solvents presents the highest values of α when compared to ILs and VOCs. These solvents present values for α ranging from 0.49 (ChCl:glycolic acid (1:1)) up to 1.79 (menthol:dodecanoic acid (2:1)).⁶⁹ This parameter is very sensitive to each one of the DESs/ESs components. For example, menthol:octanoic acid (1:1) has α a value of 1.77⁶⁹, while [N₄₄₄₄]Br:octanoic acid (1:2) has α a value of 0.98. In fact, just changing the counter ion of the tetraalkylammonium salts also has a large impact, as it can be concluded from

the α value (0.84) of $[\text{N}_{4444}]\text{Cl}:\text{octanoic acid (1:2)}$. The length of the alkyl chains of the tetraalkylammonium salts also shows significant influence in the α value. For example, $[\text{N}_{2222}]\text{Cl}:\text{octanoic acid (1:2)}$ and $[\text{N}_{3333}]\text{Cl}:\text{octanoic acid (1:2)}$ have α value of 0.96 and 0.90, respectively, allowing the conclusion that this parameter decreases with the increase in length of the alkyl chain of the ammonium salt.⁷⁵ This is probably due to the fact that smaller alkyl chains have a lower electronic contribution to the nitrogen atom, thus increasing its capability to be hydrogen bonding acceptors and therefore increasing the HBD capacity (α) of the other component. This influence of the alkyl chains can be appreciated comparing the α values of eutectic mixtures with ChCl , where a decrease of the value of α as the alkyl chain length of the carboxylic acid increases is also noticeable for different tetraalkylammonium salts.⁷⁵ Changing the proportion of the components also has impact on the value of α . For instance, $[\text{N}_{4444}]\text{Cl}:\text{decanoic acid (1:2)}$ has a α value of 0.85, while for the molar ratio of (1:1) a value of 0.91 was reported.⁷⁵

Similarly, ILs show also a wide range of α values, between 0.38 for $[\text{C}_4\text{C}_1\text{im}]\text{NTf}_2$ and 1.55 for $[\text{Ch}]\text{Mal}$. Nevertheless, the majority of ILs (typically based on imidazolium and pyridinium cations) present an average value around 0.63, usually, while ILs containing $[\text{HOC}_2\text{C}_1\text{im}]$ or cholinium cations present higher values of α . This is probably due to the presence of the OH group, corroborating the importance of hydrogen bond interactions within ILs.⁷⁹ The influence of the IL's anion in the α value can be appreciated considering the ILs $[\text{HOC}_2\text{C}_1\text{im}]\text{Cl}$, $[\text{HOC}_2\text{C}_1\text{im}]\text{NO}_3$, $[\text{HOC}_2\text{C}_1\text{im}]\text{DCA}$, $[\text{HOC}_2\text{C}_1\text{im}]\text{ClO}_4$, $[\text{HOC}_2\text{C}_1\text{im}]\text{PF}_6$ and $[\text{HOC}_2\text{C}_1\text{im}]\text{NTf}_2$ which display α values of 0.73, 0.77, 0.80, 1.06, 1.17 and 1.17, respectively.⁷² It is also interesting to refer that, similarly to what happens with eutectic mixtures composed of carboxylic acids, comparing ILs composed of cholinium and two distinct acids, the value of α decreases with the increase of the alkyl chain length of the acids. For example, $[\text{Ch}]\text{Mal}$ has a α value of 1.55, while $[\text{Ch}]\text{Lev}$ has a α value of 1.07.⁶⁹ Another interesting fact is that the α values obtained for ILs are usually higher than those obtained for eutectic mixtures composed of the same compounds, such as for example, $[\text{Ch}]\text{Gl}$ has α value of 1.29, while $\text{ChCl}:\text{glycolic acid (1:1)}$ shows a value of 0.49.⁶⁹ Nevertheless, in general, the eutectic mixtures have higher values of α than ILs, which can be explained by the different type of compounds present in each one of these classes of solvents. For example, eutectic mixtures containing carboxylic acids present a much higher acidity than the most common IL's cations, imidazolium, pyridinium and pyrrolidinium, combined with the corresponding carboxylic basis.

Protic ILs display α values between -0.06 for $[\text{HC}_1\text{im}]\text{OEt}$ and 1.415 for $[\text{HC}_4\text{im}]\text{HSO}_4$. Just like AILs, for protic ILs this parameter is also mainly controlled by the anion. For example, considering PILs based on the nitrate anion, the α values are 1.09 for ethylammonium nitrate, 1.1 for ethanolammonium nitrate, 1.09 for propylammonium nitrate and 1.08 for butylammonium nitrate.⁸⁰ Changing the anion has a much more pronounced effect on the α value, which increases with the strength of the conjugated acid of the anion, such as for example $[\text{HC}_1\text{im}]\text{HSO}_4$ has an α value of 1.225, while $[\text{HC}_1\text{im}]\text{OF}$ 0.812 and $[\text{HC}_1\text{im}]\text{OPr}$ 0.506.⁸¹ In comparison to AILs, PILs have usually a higher α as expected since they are based on a proton transfer mechanism.

On the other hand, VOCs have usually an α value very close or equal to zero, apart from alcohols that usually display an α between 0.76, for isopropanol, and 0.93 for methanol, given their known capability of acting as HBD as well as HBA, to some extent. VOCs that have a labile hydrogen atom also have a high value of α , like chloroform (0.44) and dichloromethane (0.30), as α is a measure of acidity of hydrogen-bond.^{82,83}

4.3.2. β Hydrogen bond acceptor capability

Regarding DESs, ESs and ILs, the distribution of each solvent over the β parameter axis is similar to the distribution over the α axis, with eutectics mixtures presenting higher values than ILs. As stated before, this is probably due to the different constituent components of these classes of solvents.

However, there is a wider distribution of the β parameter values compared to the α parameter, even reaching values near zero. Overall, it can be observed that eutectic mixtures and ILs both present similar values of α and β . Nonetheless, tetraalkylammonium salts eutectic mixtures show higher values of β than ILs and other DESs and ESs, showing increasingly high values of β with the increase of the alkyl chains length of the tetraalkylammonium salts. For instance, (2:1) eutectic mixtures of octanoic acid with $[N_{2222}]Cl$, $[N_{3333}]Cl$ and $[N_{4444}]Cl$ have β values of 0.87, 0.96 and 1.19,⁷⁵ respectively. Other eutectic mixtures (based on D,L-menthol or ChCl) have similar β values, around 0.53, while ILs exhibit a wider variety of values.

It is also important to compare the β parameter of eutectic mixtures and ILs composed of the same compounds. It has been showed that eutectic mixtures of ChCl with levulinic, malonic or glycolic acid present a lower β value than their respective ILs. For example, ChCl:glycolic acid (1:1) shows a β value of 0.50, while [Ch]GI has a β value of 0.79, thus supporting the conclusion that the formation of eutectic mixtures by the establishment of hydrogen bonds decreases their capacity to form additional hydrogen bonds.⁶⁹

Concerning PILs, they also present a wide range of β values which are slightly above the average of ALLs. Again this parameter is mainly controlled by the anion, as it can be seen from the β values of $[N_{2200}]OF$, $[N_{4000}]OF$ and $[N_{5000}]OF$, which are 0.91, 0.93 and 0.93, respectively.⁸⁰ In contrast to what happens with the α parameter, the β parameter values increases with the decrease in acidity, such as for example for $[HC_1im]HSO_4$, $[HC_1im]OF$, $[HC_1im]OAc$ the β value respectively displayed is 0.61, 0.81 and 0.85.⁸¹

Concerning VOCs, the alcohols present values of β values between 0.62, for methanol, and 0.95, for isopropanol. The remaining VOCs present a different distribution over the β axis, as amides, ethers, esters, and ketones have distinct β values from the more apolar solvents like alkanes, presenting β values between 0.37 for 1,4-dioxane and 0.69 for dimethylformamide.^{82,83}

4.3.3. π^* polarizability / dipolarity

The distribution over the π^* parameter axis is much different from the previous ones, as ILs present an average value of 1.05, for $[C_4C_1im]BF_4$,⁷² while for lower π^* average values are found for eutectic mixtures, such as 0.85 obtained for $[N_{2222}]Cl$:hexanoic acid (1:2).⁷⁵ This fact was expected since ILs are composed of ions, whose charges confer a strong dipole moment and thus a larger polarizability. On the other hand, π^* value of neutral eutectic mixtures is usually lower than those of ionic eutectic mixtures, as there is no charged species on the former. For example, the highest π^* value (0.66) for neutral eutectic solvents was obtained for D,L-menthol:levulinic acid (1:1), while the lowest π^* value (0.69) for ionic eutectic mixtures was observed for $[N_{4444}]Cl$:decanoic acid (1:2)^{69,75}. In fact, these mixtures have a π^* values comparable to those of VOCs such as ethers, esters, ketones, and alcohols, as the presence of heteroatoms forms a dipole on these molecules, thus showing higher π^* when

compared with other organic apolar solvents, like alkanes. VOCs also exhibit a larger π^* parameter values distribution, when compared to the other classes of solvents, between 0.18 exhibited by butyl ether and 1.00 by dimethyl sulfoxide.^{82,83}

Focusing on PILs, the values of π^* are similar to those displayed by AILs. In contrast with the other parameters, the π^* parameter values vary when the cation of the PIL is changed. For instance, [N₅₀₀₀]OF has a π^* value of 0.66, [N₄₀₀₀]OF 0.7 and [N₂₂₀₀]OF 1.06,⁸⁰ indicating that for PILs as the alkyl chain length of the amine increases, the value of π^* decreases. The anion has also an important effect over the π^* parameter, as stronger acids lead to the formation of PILs with higher π^* values. For instance, [HC_{1im}]OAc, [HC_{1im}]OF and [HC_{1im}]HSO₄ have π^* values of 1.03, 1.10 and 1.17, respectively.⁸¹

An overall analysis of the 3 solvation parameters is now due. Exchanging one of the components from a salt and an organic compound has a huge influence over α and β . For instance, eutectic mixtures of D,L-menthol and carboxylic acids have a higher α value and lower β value than eutectic mixtures of the same acids with tetra alkyl ammonium salts, as they are better hydrogen bond acceptors but worst donors compared to D,L-menthol. For example, the α and β values of D,L-menthol:dodecanoic acid (2:1) and [N₄₄₄₄]Br:dodecanoic acid (1:2) are respectively, 1.79, 0.57 and 1.45, 1.04.⁶⁹ Even the presence of a different counterion has influence on these parameters, as eutectic mixtures with ammonium chloride salts have lower values of α and higher values for β than those with bromide ammonium salts. For example, the α and β values for eutectic mixture (2:1) of decanoic acid and [N₄₄₄₄]Br and [N₄₄₄₄]Cl are, respectively, 0.95, 1.05 and 0.85, 1.28.⁷⁵ Furthermore, changes on the HBD also have a great impact on these parameters. For example, ChCl eutectic mixtures with levulinic acid have less than half the value of α parameter (0.51) than mixtures of ChCl with better hydrogen bond donors like malonic acid (1.39) or EG (1.47).⁶⁹

In Figure 4, a 3-dimensional representation of the Kamlet-Taft parameters for the classes of solvents, described above, VOCs, ILs, eutectic mixtures, is shown. A quick glance shows that there are no overlapped points, meaning that no IL or DESs/ESs, from those here considered, could fully replace a VOC.

As mentioned before, the difference in the values of α parameters for these classes of solvents can clearly be appreciated, with VOCs displaying very low α , apart from acetonitrile and alcohols, followed by ILs and eutectic mixtures, which show the highest values for this parameter. Nevertheless, these families of solvents have members with intermediate values of α (around the unity), meaning that it is possible to replace VOCs for ILs and eutectic mixtures in what concerns the α values.

The difference between β values for the 3 classes of solvents is more subtle than for the α values, as there are members of the 3 classes that can have similar values of this parameter. Nevertheless, eutectic solvents reach higher β values than the other two classes of solvents, meaning that in what concerns this parameter is easier to design an IL to replace a VOC than DES/ES. Nevertheless, and just like for the α values, it is possible to find members of the 3 classes of solvents with intermediate β values.

In what concerns the π^* values, it can be observed that ILs present the highest π^* values amongst the 3 studied families, while VOCs and eutectic solvents share similar π^* values. In this case, it would

be difficult to replace a common solvent for an IL, but it would be possible to find a eutectic mixture as a replacement of a VOC, since they share the same π^* values. Nevertheless, only VOCs (hexane, cyclohexane, butyl ether, isopropyl ether, carbon tetrachloride, ethyl ether and tetrachloroethylene) display very low π^* values.^{82,83}

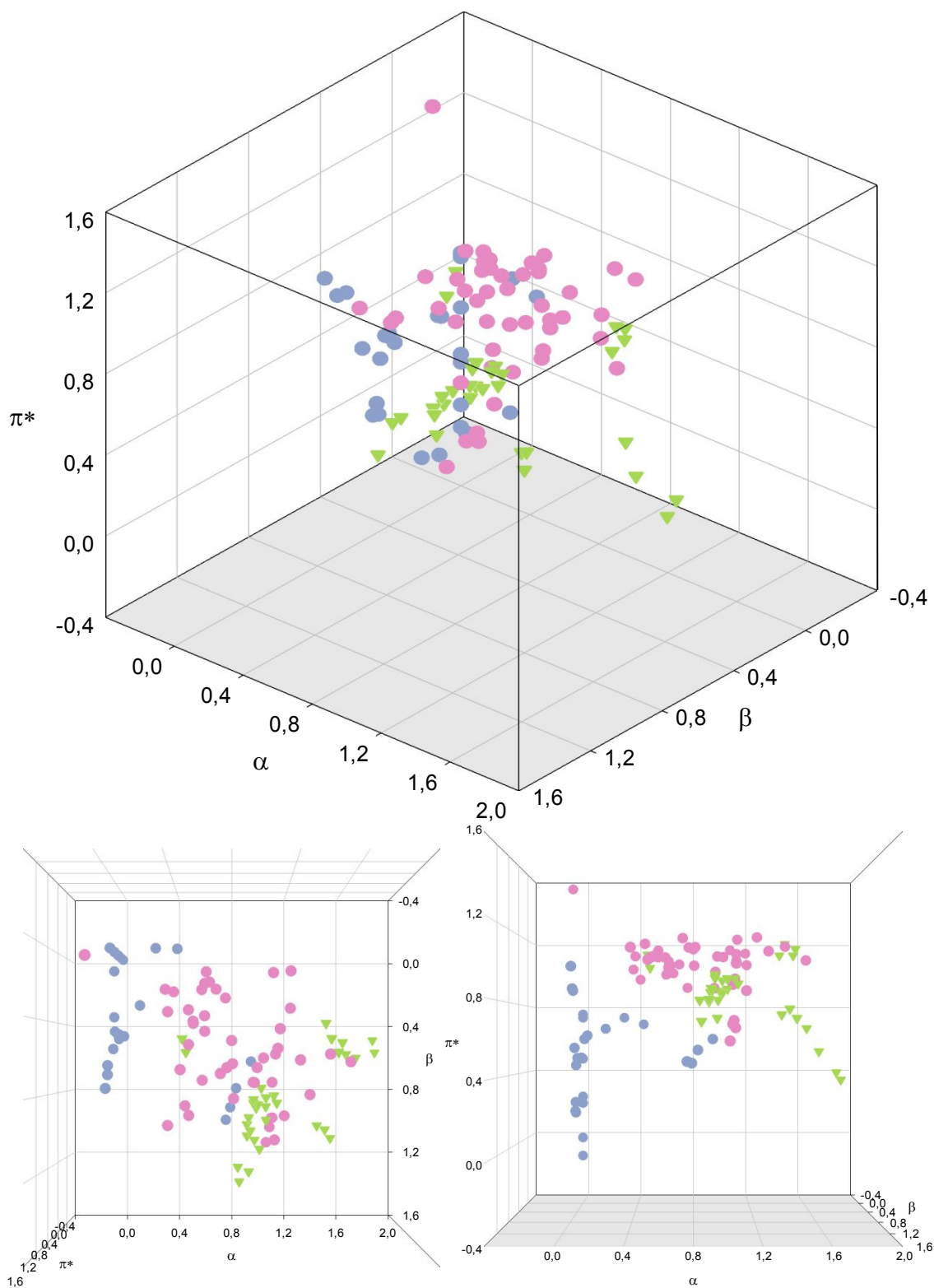


Fig. 4. Kamlet-Taft parameters for VOCs (blue), ILs (pink) and DESs and ESs (green).^{69,72,75,84}

Also, aqueous solutions of eutectic mixtures have distinct Kamlet-Taft parameters than their respective neat solvents, since water molecules interfere in hydrogen bonding network between constituents of eutectic mixture, establishing stronger interactions with them and leading to decrease on the capability of the solvent to establish new hydrogen bonds, which translates in lower values of α and β as the water content increases. Consequently, these hydrogen bond interactions with water molecules reduce ionic and dipole interactions within eutectic mixtures leading to an increase of π^* value with the water content in the mixture. It is important to refer that although the β value of pure water is the limit value for these diluted solutions, the other two parameters do not follow this tendency. This provides new insights on the interaction between water and these solvents as they do not act as simple aqueous solutions of the eutectic mixture constituents, but have a more complex mechanism of interaction, at least up to a water content of 50%.^{85,86} To illustrate this, Table 2 compiles the Kamlet-Taft parameters of two eutectic mixtures of ChCl: U and ChCl:EG, both at (2:1) molar ratio, with different content of water as well as pure water.

Table 2 Kamlet-Taft parameters ChCl:U (2:1) and ChCl:EG (2:1) as function of water content.^{85,86}

Water content % (w/w)	ChCl:U (2:1)				ChCl:EG (2:1)				water
	0	10	30	50	0	10	30	50	
A	0.79	0.69	0.62	0.60	0.67	0.63	0.45	0.40	1.17
B	0.84	0.79	0.71	0.66	0.69	0.67	0.53	0.47	0.47
π^*	1.14	1.18	1.25	1.27	1.08	1.10	1.39	1.55	1.09

It can be observed that the Kamlet-Taft parameters for water are not the lower/upper limiting values of these eutectic mixtures, thus indicating that the evolution of complex solvation phenomena as the water content changes.

To be highlighted that although ILs and eutectic mixtures can both have their polarity tuned, it is possible for latter to do slight variations of α , β and π^* with simple changes on the proportion of the constituents.

4.4. Are DESs and ESs nontoxic?

The ecotoxicological profile of a solvent is of extreme importance as it can be a restriction on its applicability. The toxicity of a given solvent can be measured over different scales, such as for example, minimum inhibitory concentration (MIC), half maximal inhibitory concentration (IC_{50}), half maximal effective concentration (EC_{50}), median lethal dose (LD_{50}) and many others that can be more or less specific to a group of model living beings. In fact, ecotoxicity evaluation of solvents is rarely reported against more than one model organisms, namely, zebrafish, *Vibrio fischeri*, *Escherichia coli*, *Daphnia magna*, *Lemna minor* and even human cellular lines. This diversity of models to evaluate the ecotoxicity rises unfair and unprecise comparisons between different datasets, which can lead to erroneous conclusions. Some correlations for given scales between different organisms have been developed, although they are only accurate for highly similar species.⁸⁷ This unevenness of the reported ecotoxicological data led to attempts to uniformize different values on a single scale to enable predictions on the toxicity of a given solvent not yet studied.⁸⁸

Toxicity studies on the gram-negative bacteria *Vibrio fischeri* are rather common, as these bioluminescent bacteria are trademarked as a toxicological test over the name of Microtox[®], the effects of compounds can be visualized on the decrease of the luminescence produced by the bacteria cellular respiration.⁸⁹ In this scenario, it is usual to report the toxicity as EC₅₀, the half maximal effective concentration, which is the concentration at which the toxicant induces a response of 50% of the effect, in this case the reduction of bioluminescence. For this test, the bacteria are exposed to a known concentration of each pollutant and after an incubation time (usually 5, 15 and 30 minutes) the luminescence produced is measured and compared to the control. This procedure is repeated to different concentrations of the pollutant under study and the concentration of 50% inhibition is calculated.⁹⁰ As there are reports over the ecotoxic effects of eutectic mixtures,^{90–93} ILs,⁹⁴ and VOCs⁹⁵ for this system, it was here chosen for comparison. Figure 5 shows the EC₅₀ (mM) value for several solvents belonging to the 3 different classes of solvents under study.

In general, ILs seem to have lower values of EC₅₀, than VOCs and DESs/ESs. In fact, 56% of the ILs considered have EC₅₀ < 1 mM (Figure 6), which means that lower concentrations are required to attain 50% of inhibition of the bioluminescence and, therefore, they are the most ecotoxic of these 3 classes of solvents. However, ILs also display the wider range of EC₅₀ values, from 0.4 μM ([C₁₀C₁IM]FeCl₄) to 398.11 mM ([C₂DABCO]Br),⁹⁴ the last one having a value of EC₅₀ similar to the majority of eutectic mixtures and VOCs. This huge variety of ecotoxicity values is also present in ILs of the same family. For instance, [C₂DABCO]Br, [C₄DABCO]Br, [C₆DABCO]Br, [C₈DABCO]Br, [C₁₀DABCO]Br have EC₅₀ values of 398.11 mM, 70.79 mM, 5.01 mM, 0.19 mM and 0.02 mM, respectively. The anion also has high impact in IL ecotoxicity. For example, the ILs [C₁C₄mor]NTf₂, [C₁C₄mor]CF₃SO₃, [C₁C₄mor]N(CN)₂ and [C₁C₄mor]Br exhibit EC₅₀ of 0.31 mM, 25.12 mM, 77.62 mM and 281.84 mM, respectively.⁹⁴ As both cation and anion are very impactful on the toxicity of the final IL, it is not possible to assign a given family of ILs as more or less ecotoxic than the majority.

Considering PILs, they present a narrower range of EC₅₀ values, between 1.69 mM for [H₂N(CH₂CH₂OH)₂]OEt and 15.13 mM for [H₃N(CH₂CH₂OH)]OPr.⁹⁴ In similarity to what happens for ALLs, the ecotoxicity of PILs also varies based on changes in both ions, for instance considering the PILs [HN(CH₂CH₂OH)₃]OBut, [H₂N(CH₂CH₂OH)₂]OBut and [H₃N(CH₂CH₂OH)]OBut the values of EC₅₀ are, respectively, 2.11, 4.15 and 15.13 mM. This also can lead us to the conclusion that ethanolamine based PILs are less ecotoxic than di and triethanolamine based ones considering the same anion, and therefore, the ecotoxicity of these PILs increases with the number of hydroxy-ethyl chains. The anion also plays an important role in the ecotoxicity, and for the same cation the ecotoxicity of PILs increases as the carboxylic aliphatic chain length increases. For instance, considering the PILs [H₂N(CH₂CH₂OH)₂]OAc, [H₂N(CH₂CH₂OH)₂]OBut and [H₂N(CH₂CH₂OH)₂]OPent the EC₅₀ are respectively 10.61 mM, 4.15 mM and 1.69 mM. Ramifications on the side chain of the acids seem to slightly decrease the ecotoxicity of these PILs, as [H₂N(CH₂CH₂OH)₂]OiBut has an EC₅₀ of 4.40 mM.⁹⁴

Similarly, for VOCs, the range of values for EC₅₀ is very wide, from 0.04 mM for carbon tetrachloride to 10 M for methanol. Nevertheless, this value for methanol is almost ten times the EC₅₀ of the second less ecotoxic VOC, dimethyl sulfoxide which has a EC₅₀ value of 1.259 M. In general, alcohols until three carbons, acetone, acetonitrile, dimethyl sulfoxide, dimethylformamide have EC₅₀ values above 150 mM, while chlorinated solvents, ethers aromatic compounds, other alcohols and ketones have much lower values, below 75.86 mM for ether.⁹⁵ Considering linear alcohols, the ecotoxicity seems to increase with the length of the chain, as methanol has a EC₅₀ of 10 M, while the value of

this parameter for ethanol is 758.58 mM, for propanol 154.88 mM and for butanol 50.12 mM. This increase of ecotoxicity with longer alkyl chains also occurs on ethers, as, for instance, ethyl ether has an EC₅₀ of 75.86 mM, while butyl ether 0.48 mM. Also, for chlorinated compounds the ecotoxicity increase as more atoms of chlorine are present. For example, considering dichloromethane, chloroform, and carbon tetrachloride, the EC₅₀ values are 33.88 mM, 5.62 mM and 0.04 mM, respectively.⁹⁵

Eutectic mixtures have a narrower range of values for EC₅₀, ranging from 0.07 mM for ChCl:propionic acid (1:4)⁹³ up to 1681.41 mM for ChCl:Gly:water (1:2:1)⁹¹. However, and despite the wide range of EC₅₀ values, with several orders of magnitude, more than 60% of these values are above 0.1 M, while for VOCs less 30% have EC₅₀ above this value.

It is worth underlining the importance of reporting the water content of eutectic mixtures in this type of measurements, as 2 of the datasets here considered report different values of EC₅₀ for ChCl:U (1:2) and ChCl:Gly (1:2), as eutectics with a high-water content present low ecotoxicity. For instance, ChCl:Gly (1:2) presents EC₅₀ values of 803.50 mM⁹¹ and 969.20 mM⁹³ for 0.0275 % and 0.9% (w/w) of water. In fact, the effect of the presence of water on the ecotoxicity of these eutectic mixtures was already reported⁹¹ and corroborated this ecotoxicity trend. For example, EC₅₀ values of 304.30 mM and 1592.89 mM were obtained for ChCl:U (1:2) and ChCl:U:water (1:2:1.7),⁹¹ respectively. Similarly, the EC₅₀ values for ChCl:Gly (1:2) and ChCl:Gly:water (1:2:1) are, respectively, 803.50 mM and 1681.41 mM, and for ChCl:EG (1:2) and ChCl:EG:water (1:2:1) the EC₅₀ values are 1234.37 mM and 1638.89 mM, respectively.⁹¹

In general, it can be concluded that eutectic mixtures have higher EC₅₀ values than that of their most ecotoxic components, which allows the comparison of eutectics mixtures that have one component in common. For instance, eutectic mixtures of ChCl:propanol, that have EC₅₀ values between 228.33 mM for the molar ratio of (1:4) and 393.31 mM for (2:1) 30, are less ecotoxic than eutectic mixtures of this alcohol with tetraalkylammonium chloride salts, that show values ranging from 9.26 mM ([N₃₃₃₃]Cl:propanol (2:1)) to 245.98 mM ([N₁₁₁₁]Cl:propanol (1:1)).⁹² However, ChCl has a lower value of EC₅₀ value (2.89 mM)⁹³ than [N₁₁₁₁]Cl (207.03 mM) and [N₂₂₂₂]Cl (116.11 mM).⁹² Thus, the ecotoxicity of a eutectic solvent is different from the ecotoxicity of each one of its neat components and a more complex mechanism needs to be considered. To rationalize these results, the mixture toxicity theory was proposed. This is based on two different toxicity action models working simultaneously, namely the Concentration Addition (CA), where the mixture of toxicants aims the exact same site of action, and the Independent Action (IA), where instead different sites of action are targeted.⁹² This approach is also supported by the evidence of the dissociation of the components of a eutectic mixture above a specific concentration of water, that is easily surpassed in this type of assay.^{92,93} Consequently, the ecotoxicity of a given eutectic mixture is studied as a mixture of compounds and enabling the application of these models. In the case of *Vibrio fischeri*, it is suggested that these individual compounds act as membrane disruptors in these organisms,⁹³ which is in agreement with the superior data description of the CA model, in which each component of the eutectic mixture acts as diluter of the other, reason why it is unusual to have a trend of values linear with the molar fraction of one of the components. For instance, mixtures of [N₃₃₃₃]Cl with EG have EC₅₀ values of 5.76 mM, 25.82 mM, 8.20 mM and 13.67 mM for molar ratios of 1:2, 1:1, 2:1 and 4:1, respectively.⁹²

When the components of the eutectic mixture have identical targets, they can act as synergists or antagonist of each other, this means that each of them can boost or attenuate the ecotoxicity of the other. Eutectic mixtures based on ChCl, with different HBD (EG, U, Gly, 1,2-propanediol, propanol) all presented an antagonistic character,⁹³ meaning that these DESs/ESs display lower ecotoxicity than their neat compounds. ChCl:propionic acid was the exception, displaying synergistic character for some molar ratios, in agreement with the theory that the HBD commands the ecotoxicity of eutectic mixtures.⁹³ For these eutectic mixtures based on ChCl, a ecotoxicity sequence can be proposed, from less to more ecotoxic, Gly < 1,2-propanediol and EG < U < propanol < propionic acid < acetic acid < lactic acid < glycolic acid < citric acid.⁹³ In fact, with the exception of EG, this series is identical to that of neat compounds. Tetraalkylammonium chloride based eutectic mixtures composed of EG presented lower ecotoxicity than propanol containing ones, for example [N₁₁₁₁]Cl:EG (1:4) exhibits an EC₅₀ of 916.79 mM, while [N₁₁₁₁]Cl: propanol (1:4) displays a EC₅₀ of 219.45 mM.⁹³

On a final note, it is important to keep in mind that even though eutectic mixtures presented the lowest ecotoxicity among the 3 families of solvents here considered, *Vibrio fischeri*, represents only a small fraction of the biodiversity present on the Earth's environment, demanding for deeper knowledge on the mode of action and potency of alternative solvents like ILs and eutectic mixtures as pollutants to ensure their "greenness". On the other hand, it should be kept in mind that eutectic mixtures can be quite ecotoxic, depending on their constituents.

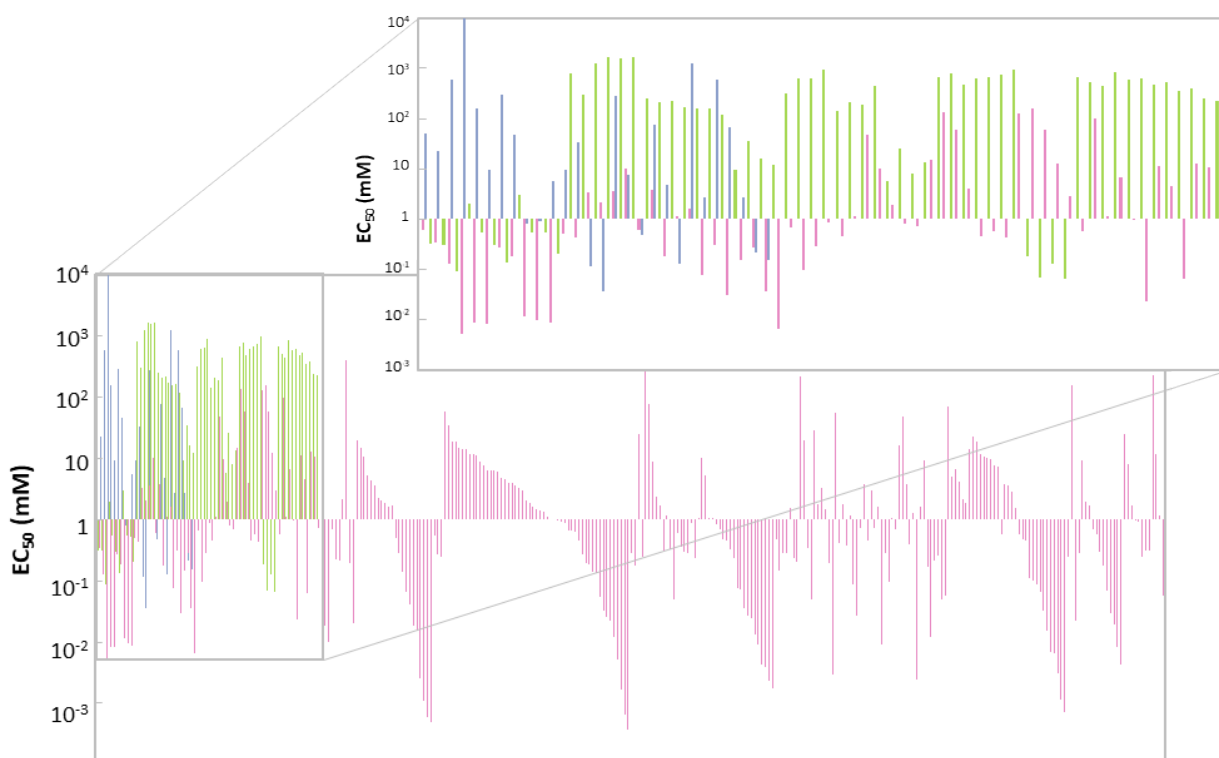


Fig. 5 Ecotoxicity in EC₅₀ (mM), against *Vibrio fischeri*, of each one of the considered solvents.^{90–95} VOCs (blue), ILs (pink) and DESs and ESs (green).

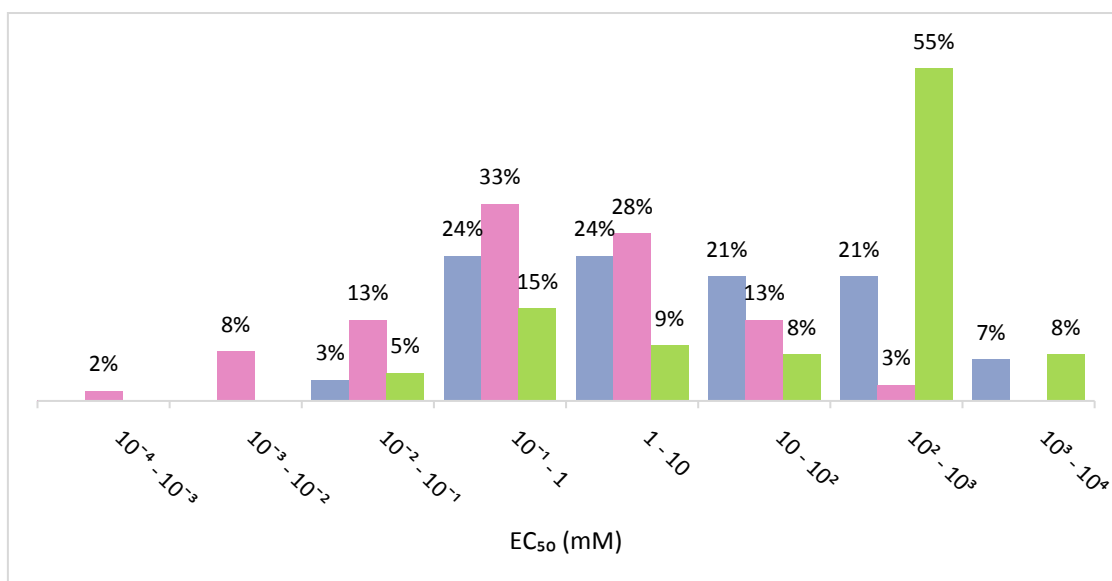


Fig. 6 Distribution of EC₅₀ (mM) against *Vibrio fischeri* considering intervals of 1 order of magnitude.⁹⁰⁻⁹⁵ Organic solvents (blue), ILs (pink) and eutectic solvents (green).

Switching to a human focused perspective, information on cytotoxicity of alternative solvents is very scarce and mostly, only available against a specific skin cell line (HaCaT). As these solvents are a “greener” option to VOCs, it is important to address this lack of knowledge. Despite the diversity of the data found in literature, this work presents a comparison between the reported values of IC₅₀ against HaCaT cells displayed by VOCs⁹⁶ and eutectic mixtures,⁹⁷ with an exposure time of 72 hours, as well as PILs⁹⁸ and AILs⁹⁹, with an exposure time of 24 hours.

According to Figure 7, eutectic mixtures are clearly less cytotoxic than VOCs and ILs, and the difference between the reported values of IC₅₀ may be even larger considering the lower period of exposure of ILs relatively to DESs and ESs. In fact, these are the only class of solvents with values of IC₅₀ in the two upper categories (10 to 1000 mM). PILs and VOCs share the middle categories (0.1 to 10 mM) although, as stated before this is not a fair comparison due to the different time of exposure. Finally, AILs are the only representative of the two lowest categories (0.001 to 0.1 mM) and therefore are the most cytotoxic to HaCaT cell line from the solvents considered.

Focusing on eutectic mixtures, the cytotoxicity of [N₄₄₄₄]Cl based eutectic seems higher than that of ChCl or [N₁₁₁₁]Cl based ones, as all eutectic mixtures based on these latter HBAs increased cell viability, even at the highest concentrations tested for most cases.⁹⁷ Thus, it is impossible to calculate a reasonable IC₅₀ value for these eutectic mixtures, while meaningful information can be obtained from the [N₄₄₄₄]Cl based eutectics. For instance, the cytotoxicity of mixtures of this tetraalkylammonium salt and carboxylic acids seems to decrease as the length of the alkyl chain of the acid increases. For example [N₄₄₄₄]Cl:butanoic acid (1:1) and [N₄₄₄₄]Cl:hexanoic acid (1:1) have a IC₅₀ of 108.7 and 112 mM, respectively. These two eutectic mixtures are also the less toxic to the HaCaT cell line displaying the highest values of IC₅₀, in contrast to [N₄₄₄₄]Cl:EG (1:1), which showed the lowest IC₅₀ of 34.1 mM.⁹⁷ Moving on to VOCs, the reported values of IC₅₀ are between 0.14 mM

for dimethylformamide and 2.27 mM for 2-methoxyethanol.⁹⁶ However, due to the reduced number of VOCs tested and the heterogeneity in IC_{50} values, it is impossible to take conclusions from this set of data. Additionally, the scarcity of information over the cytotoxicity of VOCs is frightening as they are widely and intensively used all over the world.

Focusing on ILs, as mentioned before PILs showed higher values of IC_{50} than AILs. AILs have IC_{50} ranging from as low as 0.001 mM, for $[C_{14}Qn]Br$, up to 0.035 mM, for $[C_8C_1im]Cl$. Both the cation and anion seem to have influence on the cytotoxicity of aprotic ILs against HaCaT cell line. For instance, imidazolium based ILs showed a lower IC_{50} for long alkyl side chains, namely $[C_8C_1im]Cl$, $[C_{14}C_1im]Cl$ and $[C_{16}C_1im]Cl$ which have a IC_{50} of 0.035, 0.005 and 0.004 mM, respectively. The effect of the anion is evident when the IC_{50} of $[C_{16}C_1im]Cl$ (0.004 mM) is compared with that of $[C_{16}C_1im]NTf_2$ (0.017 mM).⁹⁹ PILs have IC_{50} ranging from around 0.4 mM for $[H_3N(CH_2CH_2OH)]OF$ and 2.5 mM for $[H_3N(CH_2CH_2OH)]OF$ and similarly to AILs, their cytotoxicity is influenced by both ions. For example, both $[N_{2000}]OF$ and $[N_{2000}]NO_3$ display a IC_{50} below 0.4 mM, while $[N_{2000}]GI$ has a value of 1.3 mM and $[N_{2000}]OAc$ shows the highest value of 2.4 mM. The cation role can also be illustrated by considering the case of $[H_3N(CH_2CH_2OH)]OAc$ with a IC_{50} of 2.5 mM, $[H_2N(CH_2CH_2OH)_2]OAc$ with a IC_{50} of 0.9 mM and $[HN(CH_2CH_2OH)_3]OAc$ with a IC_{50} of 1.6 mM.⁹⁸

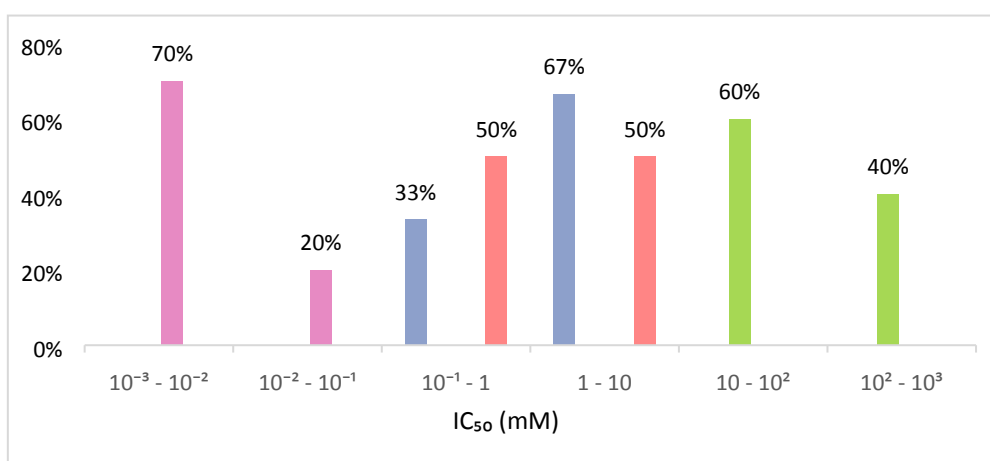


Fig. 7 Distribution of IC_{50} (mM) against HaCaT cell line considering intervals of 1 order of magnitude.^{96–99} VOCs (blue), AILs (pink), PILs (red) and DESs and ESs (green).

Switching to a more realistic model to analyze the toxicity of DESs, a mixture of Bet and Gly at a molar ratio of 1:2 and with 10% (v/v) water was used to extract antioxidant phenolic compounds from green coffee beans, this extract besides being composed of only natural occurring compounds proved to be lethal to rats. Even though Bet and the extracted phenolic compounds having very positive effects in rats, namely antioxidative, Gly is known to be harmful to these mammals leading to renal failure and therefore the prepared DES had a similar effect. This is also in accordance with the dissociation of the DES at high percentage of water, possibly at the stomach.¹⁰⁰

4.5. Water in DESs and DESs in water

Trace amounts of water is often unavoidable as impurity in ILs and DESs/ESs, as these solvents have proven to be very hygroscopic. Nonetheless, the addition of specific amounts of water has been a strategy followed by many researchers to overcome two major drawbacks of both these classes of fluids: their high viscosity and high price.¹⁰¹ Consequently, understanding the effects of different amounts of water on the liquid structure of ILs and DESs/ESs at the molecular level is highly important, since it allows to control their macroscopic properties. Although the effect of water in ILs structure is well understood and a substantial amount of work has been published,¹⁰² the same cannot be said for DESs/ESs. Chunyan published a comprehensive review¹⁰³ of similarities and differences of water in ILs/ionic DESs and ILs/ionic DESs in water. The mechanisms of solubilization of both these classes of solvents in water as well as inorganic salts are summarized in Figure 8.

A given IL exposed to a small quantity of water can embed water molecules without breaking the liquid structure of the pure IL. As the addition of water increases, the cluster starts to dissociate, and the anions begin to strongly hydrate and finally the addition of more water molecules completely dissociates the IL ions and fully hydrate them. Even though this is true for many ILs, some larger anions, like BF_4^- , do not get fully hydrated and hydrophobic anions, such as NTf_2^- , do not even get hydrated. This feature is another proof of IL's tunability, as switching from smaller and hydrophilic ions to larger and more hydrophobic anions the resulting IL will be less capable of insert water molecules in its structure but also more stable in highly diluted solutions.¹⁰³ For example, MD simulations show that $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ when mixed with water, ion pairs can be found even at IL molar fraction of 0.001. Even though these simulation studies lack experimental validation, it is helpful to understand the difference between the effect of water in ILs and in salts.¹⁰⁴ As for this last case, a solution of a given salt at its saturation point will result in the complete dissociation of the ions that compose the salt and finally the addition of more water will carry the full hydration of these ions.¹⁰³

It is also important to point out that the stability of a given IL cluster depends on both the structure of the cation and the anion, meaning that it is not possible to make a general rule as 2 distinct ILs may have different concentrations of water that results in dissociation and hydration and as exposed above this can even not happen to some ILs.¹⁰³ In fact, MD simulations of aqueous solutions of ILs based on $[\text{C}_{10}\text{C}_1\text{IM}]$ and different anions, all in the concentration of 1 M, show very distinct arrangements. For instance, $[\text{C}_{10}\text{C}_1\text{IM}]\text{NTf}_2$ at this concentration still remains as a cluster with few water molecules embedded in it, while $[\text{C}_{10}\text{C}_1\text{IM}]\text{PF}_6$ at the same concentration, is already dissociating and hydrating.¹⁰⁵

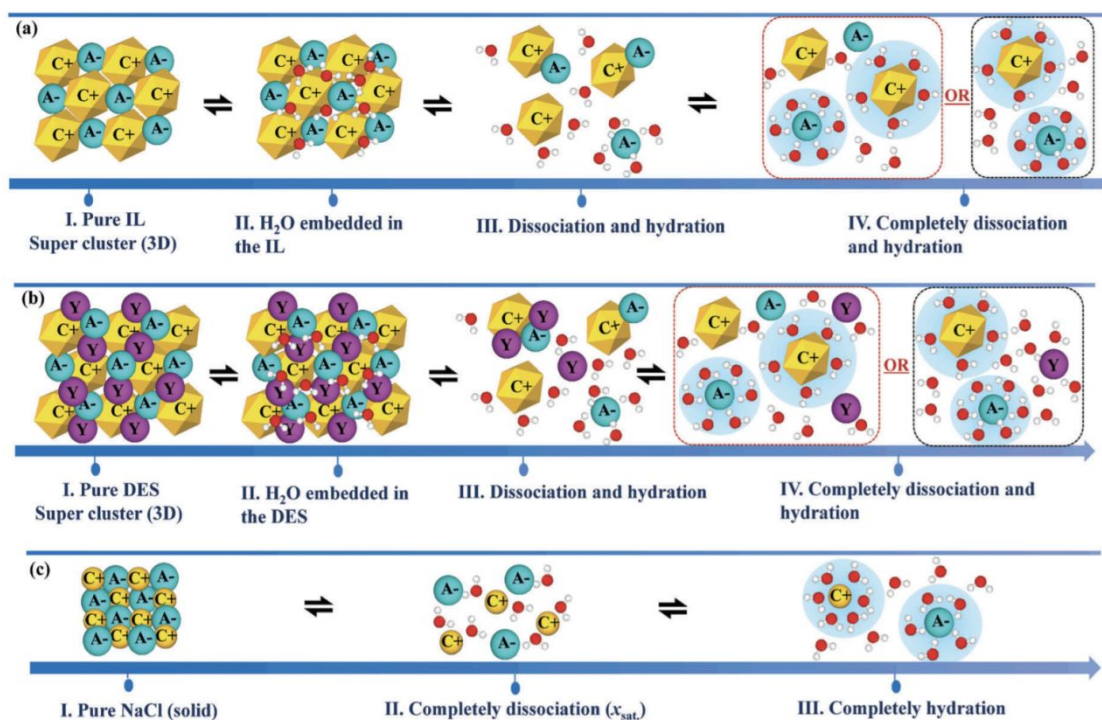


Fig. 8 Structural effects of the addition of water to ILs (a), DESs (b) and NaCl (c).¹⁰³

The structural modifications on pure DESs clusters due to the addition of water are similar to those of ILs, starting with the embedding of water molecules in the cluster, going through dissociation and hydration as more water is added, until the full dissociation and hydration is achieved. Also once again, it is not possible to make a general rule as different combinations of HBA and HBD can result in DESs with different affinity for water and, therefore, more or less stable clusters at high water content.¹⁰³ Either way, the concepts of water in DES and DES in water are already established, as water in DES refers to the embedding of water molecules into the DES structure while DES in water corresponds to the dissociation of the cluster.

Solubility of DESs in water is complex because DESs are mixtures and thus the DESs components are going to solubilize in water according to their individual solubility in water. Considering a binary DES, if it is composed of two hydrophilic compounds, one phase solution is obtained, but if one of the components is hydrophobic a two-phase equilibrium will be obtained, with one aqueous phase and one hydrophobic phase. Note that in this last case, both the hydrophilic and the hydrophobic components will solubilize in the water phase according to their solubility.¹⁰⁶ Thus, the hydrophobic phase will be mainly composed of the hydrophobic component since the hydrophilic components will leach to the water phase. In fact, this was proved by contacting eutectic solvents with water and analyzing both phases through ¹H-NMR, as for DESs composed of [N₄₄₄₄]Cl and various carboxylic acids, the ammonium salt was always present in water and the carboxylic acids with short alkyl chain, for example, acetic acid also did leach to the aqueous phase, to some extent. Switching from the ammonium salt to neutral compounds, such as D,L-Menthol, only the DESs composed of short carboxylic acids showed the presence of these acids in the water phase, while for acids with long alkyl chains like octanoic, decanoic and dodecanoic acids, none of the components were identified in the water phase. Of course, this does not mean that these DESs are not soluble in water, but that their concentration in aqueous phase is below the limit of detection of the ¹H-NMR technique.¹⁰⁷

Even for a hydrophobic DES composed of two hydrophobic compounds, the final DES composition will always slightly change, since the two compounds will not have the same solubility in water. This does not hinder the use of hydrophobic DESs as extractants of compounds from aqueous phases as the quantity of leached compounds will be, most of the times, negligible when compared to the extracted compounds. For example, taking in account two DESs composed of decanoic acid and either D,L-menthol or $[N_{4444}]Cl$ in the proportion 2:1, for the latter one the water solubility into DES is 6.9 wt % at 298 K and the solubility of the ammonium salt in water is 13.5 wt % at 298 K, while for the former DES the solubility of water in DES is 2.1 wt % at 295 K and the total solubility of both compounds in water is 0.04 wt % at 295 K.¹⁰⁸ Consequently, it is possible to conclude that even hydrophobic DESs have some solubility in water that should not be ignored. Moreover, various authors present the solubility of a DES in water as if it is an individual compound or only measure the water solubility for one of the compounds (typically the hydrophilic or charged compound), instead of presenting the water solubility of all the individual compounds of the eutectic mixture. It is also important to point out that changing one of the constituents of the DES can lead to significant changes in the solubility of water in DES and vice versa. Finally, it is worth noticing that when in contact with water the remaining DES phase will have a different molar ratio compared to the initial one as each compound solubilizes to a different extent from the other.¹⁰⁶

5. Comparative analysis in a selected research area: is there a clear winner and a clear loser between ILs and DESs?

When reading the general statements found in the introduction of the vast majority of papers, one has the impression that DESs are by nature greener and better performing systems than ILs, not to mention other solvents.

As mentioned in the previous sections, DESs and ILs share several common features which make them suited for sustainable development. For instance, they can be made up of natural molecules that originate from renewable feedstock such as sugars and sugar-based compounds,^{109–112} amino acids,^{113–115} fatty acids^{116–119} and lignin monomers.^{120,121} This peculiarity, presents for the first time the option of using largely available, non petroleum-derived materials for the preparation of a wide range of liquid media. In an attempt to answer the heading question of this article, we focused the present analysis on the research area which, in our opinion, will likely play the lion's share in sustainable chemistry, namely the exploitation of lignocellulose materials. From this point onwards, this comparative analysis is directed towards selected examples concerning the dissolution and treatment of the most available biopolymers: cellulose, hemicellulose, lignin and chitin. In this chosen area of research, new media are always sought given the limited applicability of most of the traditional organic solvents.

Before starting this analysis, a word of caution is needed when considering the results reported by different authors, even considering the same kind of biopolymers. Indeed, different publications are based on polymers with different degrees of polymerization, crystallinity, composition (for hemicellulose) and polymorphism as well as various degrees of acetylation (for chitin). Also, it is not always trivial to organize this information, which hinders the correct comparison and evaluation of the proposed systems' performances. Moreover, when considering complex biomasses, factors like the natural heterogeneity of lignocellulosic material, the size of the material and possible additional pretreatments all render critical comparisons less reliable.

5.1. Lignocellulosic biomass

Cellulose is the most abundant biopolymer in nature, being present in 30 to 50 wt% of terrestrial biomass and even more prominent in marine biomass. The exploitation of this resource is essential in the current scenario of sustainable development and circular economy, and requires the development of solvents to extract, purify, dissolve and process it effectively.¹²² Although cellulose has been used to make yarns and paper for centuries, most of the protocols used in these processes are not environmentally sustainable.¹²³ For example, the cultivation of cotton produces high purity cellulose but at the same time it is very expensive (2.7 € Kg⁻¹,¹²⁴ price for 1 ton) and above all has a marked environmental impact in terms of water footprint (10000 L of water per 1 Kg of cotton) and massive use of pesticides.¹²⁵ Instead, pulp for paper production is obtained more economically (0.4 € Kg⁻¹,¹²⁴ price for 1 ton) using the Kraft process, which, however, needs harsh conditions (high temperature as well as pressure in addition to the use of reagents harmful to the environment) and employs only cellulose-rich biomass. This latter aspect raises serious concerns as some areas of the planet are being deforested and certain types of trees are preferred to the detriment of biodiversity. In addition, cellulose from the Kraft process typically contains 15-25 wt% of hemicelluloses and 5-10 wt% of lignin and therefore needs to be purified to make it suitable for other applications.^{126,127} These purification processes are called "pulping" and also involve the use of hazardous chemicals and severe conditions.

Nowadays, the Kraft process accounts for about 80% of cellulose pulp production. As mentioned above, this protocol operates under harsh conditions (150-180 °C) and utilises hazardous sodium hydroxide (NaOH) and sodium sulfate (Na₂SO₄) as reagents.¹²⁸ Although the optimised Kraft process has improved energy efficiency, serious issues remain, firstly related to corrosion due to the alkaline environment, but also to the disposal of process water. In addition, the resulting cellulose is intensely coloured due to the degradation products of lignin and hemicellulose, and therefore requires many bleaching treatments. Lastly, the Kraft process breaks down the hemicellulose almost completely and the obtained lignin is of very poor quality due to its strongly degraded and sulfur-rich content.¹²⁹ In view of an integrated biorefinery process, these issues are critical and need to be addressed.

The sulfite pulping process has been developed as an alternative to the Kraft process, its main advantage being the flexibility to treat a wide variety of biomasses. In fact, by varying the dosage and the composition of the chemicals, the entire pH range can be covered.¹²⁹ Sulfite pulping enables the valorisation of the hemicellulose and the lignin fractions through their transformation into chemicals such as liginosulfonates, ethanol, fodder yeast, soda, vanillin, acetic acid and furfural. However, the quality of the cellulose fibres obtained is worse than that obtained in the Kraft process.¹²⁹

Overall, the best industrial process is the Organosolv pulping process, which makes it possible to obtain good quality cellulose fibres while preserving the structure of the other components. For example, the lignin obtained from the Organosolv process is sulfur-free and presents a structure more similar to the native one in comparison with that obtained with the processes described above. This allows for an effective further exploitation and facilitates the valorisation of lignin as high value material. The Organosolv process patented in 1971 used water or water/volatile organic solvent mixtures of different nature in the presence of a catalyst.¹³⁰ The most widely used industrial mixtures are methanol/water 50-100 wt% and ethanol/water 40-60 wt% in the presence of mineral acids or calcium and magnesium salts as catalysts.¹³¹ Although the Organosolv process represents a

significant improvement over the Kraft and sulfite processes, the poor solubility of lignin still gives rise to major issues: the significant quantities of volatile and flammable organic solvents needed, combined with the high energy consumption for their recovery, makes it environmentally but also economically unsustainable.^{129,132} For these reasons, further improvement in the form of new processes that are economically as well as environmentally sustainable, is very much needed.

5.2. Pretreatment of biomass

The main challenge is to develop systems that yield cellulose from all sorts of biomasses in a sustainable way, while simultaneously allowing the valorisation of all biomass components without altering their structure and properties. This advanced biorefinery concept must be implemented in harmony with the principles of green chemistry in order to be fully sustainable. In this context, ILs and DESs can play a key role, separately or even synergistically, as sustainable media capable of selectively solubilising each individual biomass component and thereby resulting in an “integrated biorefinery”.

Over the years, many biomass pretreatment processes aimed at obtaining raw cellulose for use in saccharification processes have been based on the use of ILs and more recently of DESs. These processes, commonly referred to as pretreatment processes, afford cellulose suitable for enzymatic hydrolysis into glucose which is eventually transformed into ethanol using second-generation (2G) protocols.

Given the amount of knowledge in the area, the use of ILs affords a more mature technology compared to DESs based methods. There are two different approaches in the pretreatment of biomass with ILs: the dissolution process and the Ionosolv process.¹³³ In the dissolution process, the entire biomass is completely dissolved and the individual components are obtained by precipitation. This enables a more efficient separation of lignin and cellulose. Furthermore, the recovered cellulose is completely amorphous and thus more readily attacked in hydrolysis processes.¹³³ These processes employ aprotic ionic liquids (AILs) with imidazolium cation, which, besides their high cost (\$50/Kg)¹³⁴ and low water tolerance, have a strong depressing effect on hydrolysis and fermentation processes even if present in traces (as little as 0.25% residual [C₂C₁im]OAc in the fermentation broth will completely inhibit yeast growth and biofuel production)¹³⁵. The limited numbers of papers in the literature that use the dissolution process suggest that it has not yet been fully optimised. Conversely, numerous examples of Ionosolv processes have been reported. The Ionosolv process, whose name is deliberately similar to the Organosolv process, involves the use of ILs in pure form or in a mixture with organic solvents (or water) for the dissolution of lignin and hemicellulose, while cellulose remains undissolved and is not appreciably decrystallised. This way, the raw cellulosic material obtained remains suitable for use in applications where the crystalline cellulose fraction is needed, such as for nano-crystalline cellulose production or as a polymer additive. In addition, ILs can be used in a mixture with water or alcohol. This feature, in spite of a significant reduction of solvent cost, reduces contamination due to entrapment in the cellulose fibres obtained after the re-precipitation step. Thus, the use of ILs has a dual benefit: it allows for a higher percentage of recycled solvents and produces pure cellulose suitable for enzymatic hydrolysis and fermentation processes. The effectiveness of this approach is confirmed by the Ionosolv process marketed by Imperial College London under the name BioFlex process.¹³⁶ This pretreatment process, which uses aqueous solutions of PIL triethylammonium hydrogensulfate ([N₂₂₂₀]HSO₄), demonstrated high feedstock flexibility. Indeed, by modifying the operating conditions, it proved to be efficient with biomasses such as

hardwood,¹³⁷ softwood,¹³⁸ forest residues and switchgrass,¹³⁹ agricultural wastes such as rice straw, rice husk, wheat straw, sugarcane bagasse and coconuts waste.^{140–142} This process has been scaled-up to pilot plants of 200 L capacity and plans for a unit able to produce ca. 200 t/year of pulp have been drafted.¹³⁶ The selection of PILs has been the best in economic terms.¹⁴³ In addition to [N₂₂₂₀]HSO₄, other PILs with hydrogen sulfate as anion such as tetramethylguanidinium, monoethanolammonium, diethanolammonium, triethanolammonium, and diisopropylammonium have also performed excellently.¹⁴⁴ Apart from the type of solvent, the effect of water as well as pretreatment conditions such as biomass loading, acidity, particle size, time, and temperature have been studied extensively.^{145,146} The impact of different kinds of treatment on hemicellulose and lignin will be discussed in sections 5.3 and 5.5. The cellulose obtained is characterised by partial hydrolysis of the amorphous portion and consequent decrease in the molecular weight, as a result of the severe conditions used in these processes. Although this is desirable for some downstream uses such as saccharification and nanocellulose production, it should be avoided for applications such as fibre manufacturing. For this reason, both the type of solvent and the operating conditions must be appropriately selected in order to match with the target use of the cellulosic material.

The hybrid Ionosolv-Organosolv process developed by Chen *et al.* is certainly noteworthy.¹⁴⁷ In this hybrid fractionation process, a mixture of organic solvents (ethanol, butanol or acetone) and [N₂₂₂₀]HSO₄ shows very good fractionation efficiency both on Miscanthus and on recalcinant biomass such as pine wood. Pretreatments using butanol 60 wt% or ethanol 40 wt% with [N₂₂₂₀]HSO₄ show a glucose yield of 85%, which is 10% higher than that obtained with the Ionosolv process. This could be explained by the improved delignification of the biomass during fractionation, confirmed by compositional analysis of the pulps. Moreover, the Ionosolv-Organosolv pretreatment demonstrates the ability to operate at high biomass loading (up to 50 wt%) and to simultaneously generate a highly enzyme-accessible cellulose fraction and high-quality lignin, with excellent potential for high value-added uses.¹⁴⁷ The effect of pretreatments on lignin will be discussed in the dedicated section (section 5.3).

PILs with hydrogen sulphate anion are not the only ones that show great promise. Ferrari *et al.*¹⁴⁸ reported a Ionosolv pretreatment process followed by enzymatic hydrolysis based on a mixture of [H₃N(CH₂CH₂OH)]OAc/ [H₃N(CH₂CH₂OH)]OH₆ PILs in a 1:1 molar ratio. For this process, integrated within a 2G ethanol production process, an in-depth techno-economic analysis was carried out,¹⁴⁹ showing its effectiveness despite the fact that acetate is a proven metabolic inhibitor of most yeast systems.¹³³

In biomass pretreatment processes, DESs are extremely competitive compared to ILs due to their low cost and their low toxicity. The great number of publications in this area is tangible evidence of their effectiveness in this application. Similarly to ILs, the majority of papers focus on the pretreatment of different types of biomasses, from forestry and agricultural sources, and its impact on cellulose saccharification and ethanol production. Various kinds of DESs and NADESs, with HBD and HBA of different nature and molar ratio, have been employed in pretreatment processes. Very often, the pretreatment processes were Ionosolv-like, where cellulose was extracted by reactive and non-reactive solubilisation of lignin and hemicellulose. The solubilisation of hemicellulose and lignin by DESs and NADESs will be discussed in section 5.5. Investigating the contribution of the HBD portion in the pretreatment process reveals that mono- and di-carboxylic acids have superior efficiencies compared to polyols and U.¹⁵⁰ A comparative study was carried out on DESs with the same HBD

moiety (lactic acid, LA) and different HBA parts, which showed that hydrogen bond acidity (α of K-T parameter) had a positive linear relationship with pretreatment efficacy.¹⁵¹ Among the various carboxylic acids used as HBDs, LA is by far the most popular despite its known inhibitory effect on enzymatic hydrolysis processes¹⁵². Finally, the effect of the molar ratio on the pretreatment efficiency was evaluated for the DES ChCl:LA. The best results were obtained with ChCl:LA (1:4) at 130 °C. The cellulosic material obtained had a high degree of crystallinity and a low degree of polymerisation due to the hydrolysis of the amorphous cellulose portion.¹⁵³

Although DESs with carboxylic acids as HBDs are apparently the best performing systems, they present problems during recycling. In fact, it is well known that for cholinium-based DESs, an esterification reaction between the acid and the hydroxyl group of the cholinium occurs. However, it is also true that this phenomenon only affects a DES fraction and remains constant over time. Furthermore, Morais et al.¹⁵⁴ investigated the effect of DES ChCl:LA (1:10) on the polysaccharide portion during the pretreatment process at 130 °C at different time points (0.5-24 h). Surprisingly, the DES had a negative impact already at pretreatment times beyond 4 h, resulting in variety of undesired events such as the esterification of cellulose by LA, the shortening of fiber length and their agglomeration. Moreover, the authors noted side reactions of the hemicelluloses fraction such as furfural and humin formation as well as LA grafting. In addition, this DES also undergoes transformations due to lactide formation and polymerisation. For these reasons, treatments with lactic acid-based DESs are recommended only for a short period of time.¹⁵⁴ Based on this DES, Kumar et al. carried out a technical-economic analysis for a biorefinery process that utilises different types of biomasses for the production of cellulose, lignin, and silicates in a plant- and economically viable way.¹⁵⁵

Although the inhibition effect of the LA component of DES was easily overcome by optimising one-pot saccharification pretreatment processes,¹⁵² the remaining problems were more difficult to solve. Replacing LA with other organic acids only partially solved the difficulties described above. From a circular economy perspective, the use of lignin-derived DESs reported by Kim et al.¹⁵⁶ is of particular interest. These DESs, which are based on ChCl and 4-hydroxybenzyl alcohol, catechol, vanillin, and p-coumaric acid, showed good results and high recyclability as solvents for biomass pretreatment in terms of lignin removal and sugar release after enzymatic saccharification. A viable alternative to acid HBDs is represented by DESs based on Gly, a natural product widely available for large-scale applications and a well-known enzyme-stabilizing agent.¹⁵⁷ The performance of glycerol-based DES, ChCl:Gly (1:1) and Bet:Gly (1:1), was compared with IL [C₂C₁im]OAc.¹⁵⁸ The pretreatment efficiency of the different media was evaluated by comparing the enzymatic digestibility of the cellulose obtained. Pretreatment tests were carried out using 90 wt% DES in water or [C₂C₁im]OAc at 80 °C for 24 h with a 5 wt% loading of different cellulose types. The enzymatic digestibility of the pretreated substrates was evaluated in buffer and in the presence of 30 wt% and 80 wt% of DES or [C₂C₁im]OAc.¹⁵⁸ Although the stability analysis identified glycerol-based DESs as stabilising agents for cellulases, the overall efficiency of the process appeared to be in favour of [C₂C₁im]OAc. This can mainly be attributed to a lower pretreatment efficiency of the DES compared to the IL. Pretreatment efficiency can be, however, improved by coupling DES treatment with ultrasonic irradiation or mechanical manipulation. Sharma et al.¹⁵⁹ reported excellent results in the pretreatment of sugarcane bagasse using ChCl:Gly (1:10) coupled with ultrasonication. Under these conditions, the neutral DES was found to be the best choice even when compared to DESs containing acids as HBDs.¹⁵⁹ Of great interest is the pretreatment procedure devised by Ai et al.¹⁶⁰ that combines

ChCl:Gly (1:2) with a twin-screw extruder. The use of ChCl:Gly-mediated extrusion preserved the basic lignin structural characteristics with no significant differences between extruded biomasses at a solid loading of 30% and 50%.¹⁶⁰ Besides the excellent results obtained, it is important to point out that the use of an acidic DESs in pretreatment would lead to major corrosion concerns.

5.3. ILs and DESs for the 'lignin first' biorefinery process

When it comes to biomass utilisation processes, lignin is regarded as the “ugly duckling” when compared to the various other components.¹⁶¹ The recalcitrant character of biomass materials is in fact mostly due the properties of this very component. The origin of lignin’s bad reputation goes back to well-known problems in both papermaking and ethanol production processes, where the presence of lignin and its derivatives leads to the darkening of the final product and enzyme inhibition, respectively. Lignin derived from traditional pulping and pretreatment processes is quite different from native lignin. In fact, of the various components of lignocellulosic biomass, lignin is the one undergoing the largest structural changes. The resulting material, which is often named after the process employed (e.g. Kraft lignin), only partially retains its pristine structure and loses many of its original properties with a dramatic reduction in applicability. Therefore, it comes to no surprise that only 2% of the extracted lignin is used in industry and agriculture while the rest is discarded as waste.¹⁶²

Lignin cannot yet be isolated in its native unaltered state and for this reason the native structure has not yet been completely elucidated. Despite this, this peculiar chemical species is thought to be a complex amorphous long-chain heterogeneous polymer of phenylpropane linked by ether bonds with a molecular weight in the range of 2,500-10,000 g mol⁻¹.¹⁶³ The polymer is composed of aromatic subunits called monolignols like guaiacyl (G), syringyl (S) and p-hydroxyphenyl (H) subunits derived by sinapyl (3,5-dimethoxy-4-hydroxycinnamyl), coniferyl (3-methoxy-4-hydroxycinnamyl) and p-coumaryl (4-hydroxycinnamyl) alcohols respectively (Figure 9).

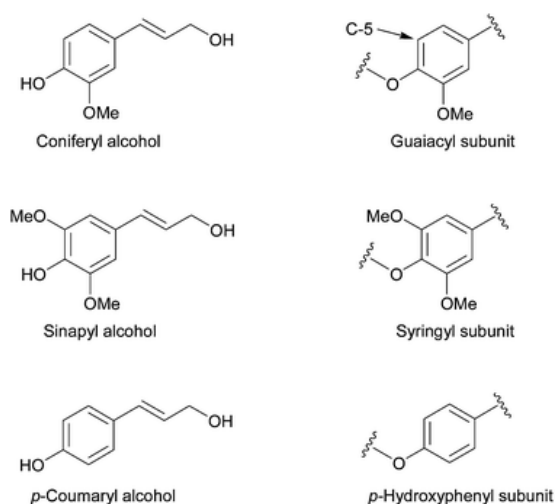


Fig. 9 The three monolignols from which lignin is synthesised and derived aromatic subunit.¹⁶⁴

Non-canonical subunits that have been identified include ferulates (which form linkages between hemicellulose and lignin), coniferaldehyde, sinapaldehyde, 5-hydroxyconiferyl.¹⁶⁵ Lignin monolignols are predominantly linked either through ether or C–C bonds. In native lignin, two-thirds or more of the total linkages are ether bonds, while the other linkages are C–C bonds. The predominant linkages

between the structural units of lignin are β -O-4' (β -arylether), β - β' (resinol), and β -5' (phenylcoumaran) but β -5, β -1, dibenzodioxocin, 5-5', and α -O-4' are also present (Figure 10). Roughly half of the total lignin linking is represented by the β -O-4' ether type. The latter kind are the bonds that allow to elongate the lignin chains through the formation of linear strands from which branches are connected through ether and C-C bonds.¹⁶⁵

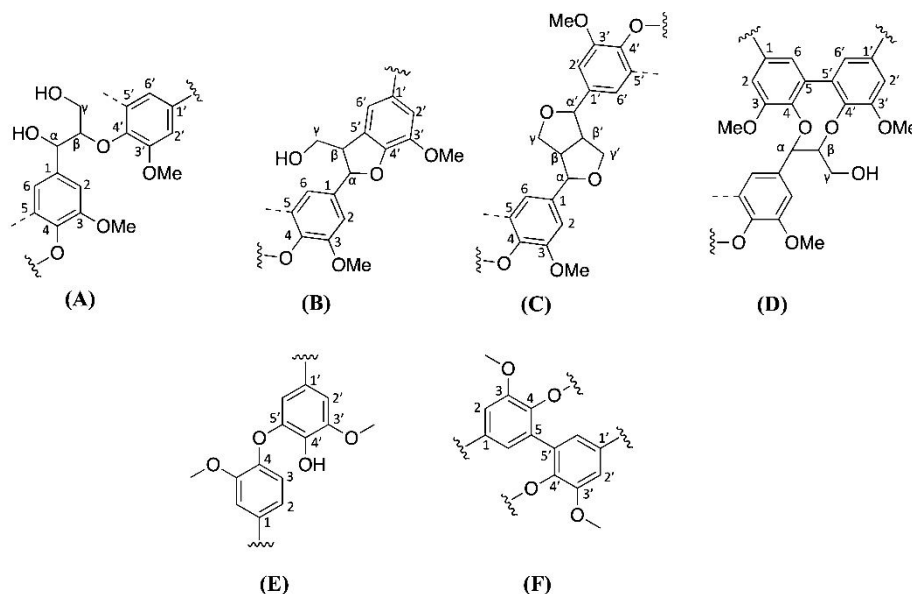


Fig. 10 Common lignin interunit linkages: (A) β -O-4', (B) β -5', (C) β - β' , (D) dibenzodioxocin, (E) 4-O-5', and (F) 5-5' linkage. Adapted with permission from Dutta et al.¹⁶⁵. Copyright 2017 American Chemical Society.

The amount, structure and composition of the aromatic subunits are highly dependent on plant taxonomy and whether the source of lignin is softwood (gymnosperm), hardwood (angiosperm) or grasses. Softwoods contain between 27-33 wt% lignin, consisting almost exclusively of G units (90-95%) while hardwoods contain 18-25 wt% of lignin, which is rich in S units (45-75%) with a lower amount of G units (25-50%). Grasses contain a low amount of lignin (17-24 wt%) and a higher amount of H units (5-35%), which is negligible in hardwood and softwood.¹⁶⁶ The composition of lignin has a strong impact on both its potential utilisation and its stability to the biomass deconstruction processes. In fact, during classical delignification processes, lignin is solubilised via the breaking of the β -O-4' bond with concomitant lowering of the molecular weight. However, under the same conditions the guaiacyl groups tend to form stable C-C bonds with other units at the C-5 position that are stable to hydrolysis. This leads to an increase in molecular weight and to the formation of a stable lignin-like solid. This material is often insoluble and can deposit on other lignocellulosic components, lowering their quality.¹⁶⁴ Lignin with a high number of C-C bonds is of poor quality and cannot be used in the production of chemicals given its resistance to degradation. This phenomenon makes the delignification of softwood biomass more difficult than hardwood. This is essentially due to hardwood's lower amount of G groups together with the fact that in S groups the C-5 position is unreactive to crosslinking due to the presence of the methoxyl group.¹⁶⁴

The myth of lignin's recalcitrance is attributable not to pristine lignin, but to the material obtained by classical pretreatment processes. The so-called technical lignin has a low number of ether bonds,

a high sulfur content and a high number of C-C bonds, which makes dissolution and transformations difficult. Figure 11 shows the characteristics of three common types of technical lignin.

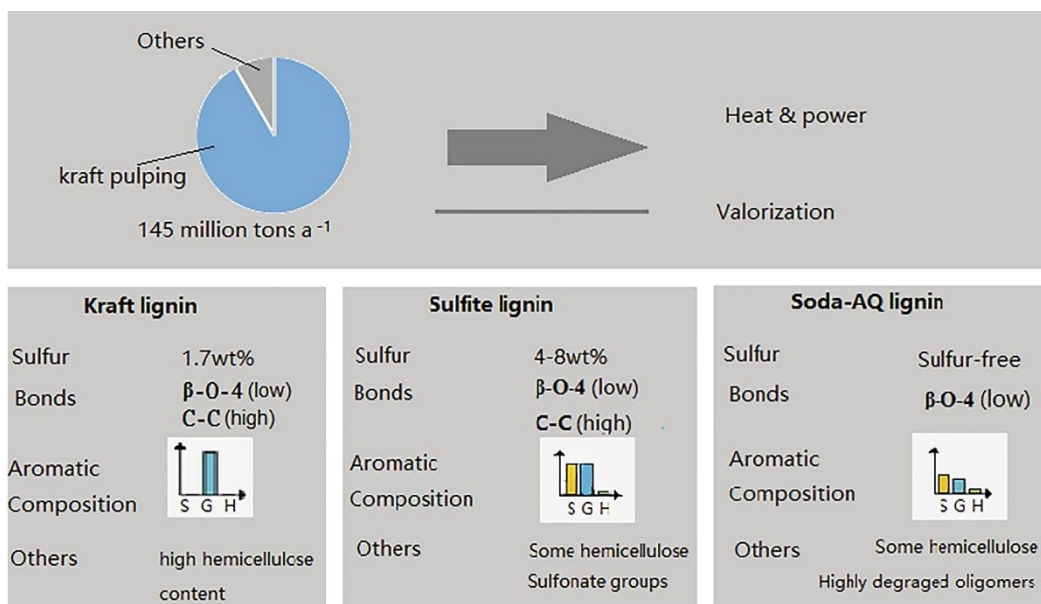


Fig. 11 Structural characteristics of Kraft, Sulfite and Soda-AQ technical lignin.¹⁶²

In order to exploit the full potential of lignin, the spotlight has shifted in recent years to the so-called 'lignin first' biorefinery processes. According to the protocols here used, the removal of lignin takes place through a solubilisation process that limits the modification of the primary structure and thereby restricts recondensation phenomena.¹⁶⁷ The price of lignin can vary between 250 and 750 USD ton⁻¹ for low- and medium-quality lignin, respectively, depending on the degree of purity. This price can rise significantly in the case of low molecular weight native and/or high purity lignin, thus showing the economic relevance of the above described 'lignin first' processes.¹⁶⁸

Of the industrial-scale pretreatment processes, Organosolv processes are the mildest towards the structure of lignin and thus the most suitable for the 'lignin-first' biorefinery.¹⁶⁹ Although the limitations of such processes have previously been pointed out both economically and environmentally, lignin obtained by Organosolv processes is nowadays the reference material in the lignin field.¹⁷⁰ In this context, it can be argued that the use of ILs and DESs in this field has great potential. Numerous papers and reviews on the processing of lignin have been reported in recent years with a focus on the amount of solubilised lignin, the mechanism of solubilisation and structure modification.

The most interesting ILs in lignin removal are AILs with acetate anion and PILs with hydrogen sulfate anion. In addition, cholinium ILs with aminoacidic anion are also a viable alternative to AILs with imidazole cations as they are cheaper, biobased, and biodegradable. Given the high structural variability of lignin and the fact that many solubilisation studies have been carried out with different technical lignins, a comparison of the solubilisation capacity of different ILs is unrealistic and of little interest. Instead, the solubilisation mechanism and the modification of the lignin structure by ILs are certainly topics of interest, especially in view to employing this valuable resource in biorefinery processes.

ALLs were the first ILs to be used for lignin processing, and the material obtained from such processes is often used as a reference. The lignin-removing capabilities of $[C_2C_1im]OAc$ were tested on hardwood (*Eucalyptus globulus*) and switchgrass (*Panicum virgatum*) biomasses under different pretreatment conditions and the effect on the structure of the obtained material was evaluated.¹⁷¹ In particular, it was observed that temperature has the greatest effect on structure with a preferential breakdown of S-lignin at high pretreatment temperature (160 °C) in both hardwood and switchgrass while breakdown of G-lignin for hardwood was observed at 120 °C. In contrast, no preferential breakdown of either S- or G-lignin was observed in switchgrass at low temperature.¹⁷¹

Exploiting this system, Sathitsuksanoh et al.¹⁷² developed a versatile system for the pretreatment and subsequent enzymatic hydrolysis of wheat straw, *Miscanthus*, and *Loblolly* pine. This protocol has been used successfully in the treatment of diverse biomasses so that lignins with different structures can be obtained by varying the reaction conditions. Lignin partitioning into the diverse streams can be controlled by altering the pretreatment parameters. Processing with $[C_2C_1im]OAc$ produces lignins with various molecular masses that can be isolated in the different streams (Figure 12).

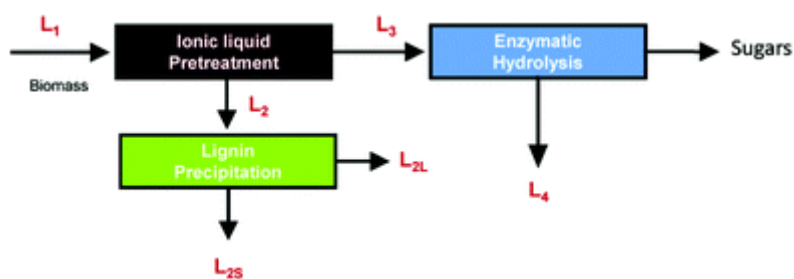


Fig. 12 Diagram of extracted lignin from different streams during IL pretreatment and enzymatic hydrolysis. L_1 : lignin from untreated biomass, L_2 : solubilized lignin in $[C_2C_1im]OAc$, L_{2s} : precipitated solid lignin from L_2 , L_{2L} : remaining lignin in the supernatant after L_{2s} precipitation, L_3 : lignin in pretreated biomass, and L_4 : lignin remaining after enzymatic hydrolysis.¹⁷²

Indeed, at the end of the treatment process, the higher molecular weight lignin is precipitated from IL (L_{2s}) by the addition of 1:1 acetone-water (v/v) while the low molecular weight fraction (L_{2L}) remains in solution. In addition, a high molecular weight and chemically unmodified lignin (L_4) is recovered at the end of the enzymatic hydrolysis reaction. Lignin extraction can be tuned by changes to the pretreatment conditions. With milder conditions the amount of lignin removed is low and the recovered lignin is of high molecular weight and has its structure largely unmodified. In contrast, harsher conditions favour lower molecular mass lignin products formation in the IL. The major benefit of using $[C_2C_1im]OAc$ in these protocols is that the formation of lignin condensation products is not observed even under the most extreme conditions.¹⁷² Although the cost of $[C_2C_1im]OAc$ is rather high, the inherent flexibility of the process is an overwhelming positive feature, especially in view of bulk scale production of high value-added products.

To overcome the issue of $[C_2C_1im]OAc$'s cost drawback, Sun and Xue¹⁷³ studied the effect of water on the dissolution performance of this IL against two different materials: Alcell lignin and *Eucalyptus urophylla* lignin (obtained by an enzymatic process). The study shows that, in addition to lowering the cost of solvent medium, the addition of water also has a beneficial effect on the solvent capacity. The optimal amount of water is dependent on the type of lignin. Furthermore, a different lignin removal mechanism was observed. Indeed, for lignin from enzymatic hydrolysis, an increase in the

syringyl (S) to guaiacyl (G) ratio (S/G) indicated the preferential breakdown of G-unit lignin. In contrast, for Alcell lignin, the S-unit lignin was easily removed from the mixture, indicating a different mechanism of lignin depolymerisation.¹⁷³

ALLs with cholinium cations and amino acid anions [Ch]AA provide a viable alternative to [C₂C₁im]OAc. Since their discovery, there has been much attention paid to their use for the treatment of biomass.¹⁷⁴ The main advantage of these ILs is related to their fully biobased nature and associated biodegradability.¹⁷⁵ The appeal of using biobased solvents for the treatment of biomass immediately fascinated researchers. [Ch]AA ILs have been successfully employed in the treatment of various biomasses such as rice straw, sugarcane bagasse, eucalyptus, and pine. Amongst many, cholinium arginate and cholinium lysinate ([Ch]Arg and [Ch]Lys respectively) were found to be the best performing ILs.¹⁷⁶ [Ch]Lys was also used for the pretreatment of switchgrass, eucalyptus as well as pine and the respective lignins obtained were analysed in depth.¹⁷⁷ Pine delignification was found to be the most difficult process in comparison to eucalyptus and switchgrass, as can be seen from the amount of residual lignin after the hydrolysis process (Figure 13).

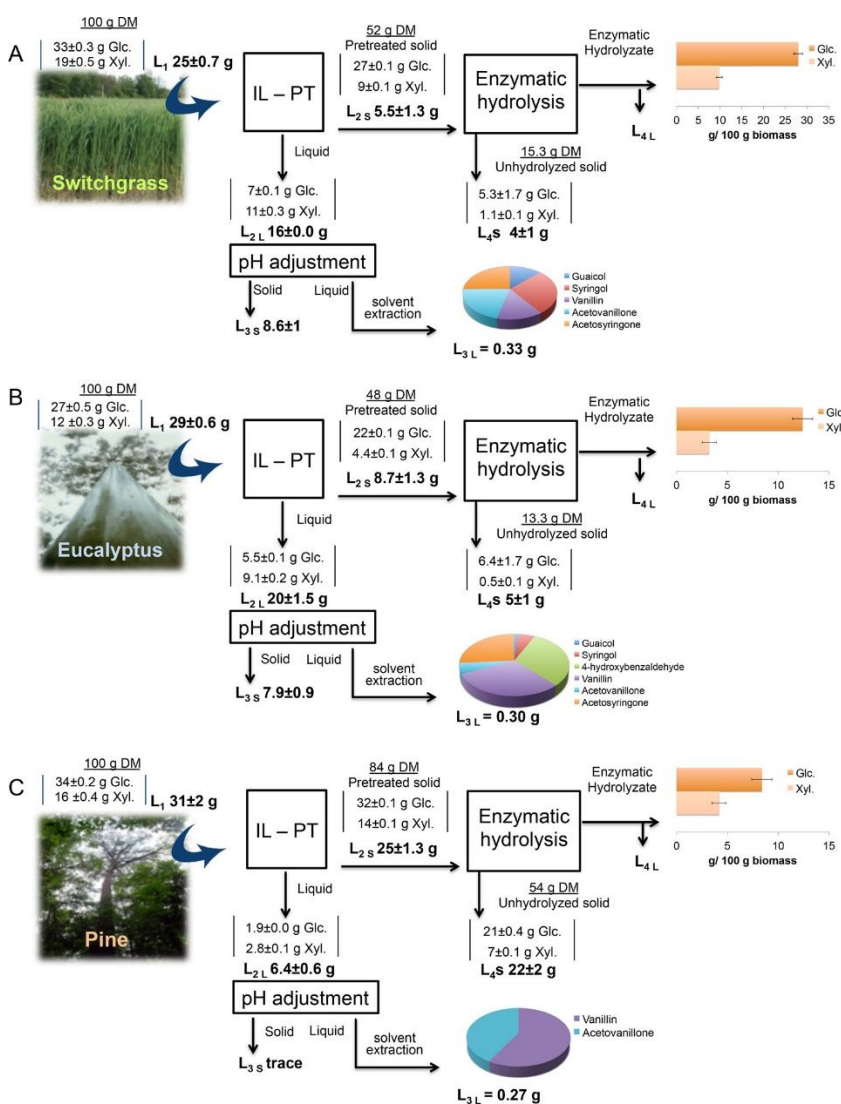


Fig. 13 Schematic representation of the pretreatment of switchgrass, hardwood, and softwood with [Ch]Lys at 140 °C for 1 h. Reprinted with permission from Dutta et al.¹⁷⁷ Copyright 2018 American Chemical Society.

Furthermore, from the analysis of the soluble fraction present in the ILs, the pine treatment shows a limited variety of hydrolysis compounds. Subsequently, in a study conducted on Kraft lignin treated with different [Ch]AA, [Ch]Lys was found to be the gentler option in terms of depolymerisation and of reduction of β -O-4' as well as β - β' bonds.¹⁷⁸

As mentioned in the previous section, the use of PILs in pretreatment processes is currently the most promising in the development of Ionosolv-type industrial processes. For this reason, the study of the effects of this pretreatment on lignin is prominent in the recent literature.

Brandt et al.¹⁷⁹ described the mechanism of lignin solubilisation through the use of 1-butylimidazolium hydrogen sulfate [HC₄im]HSO₄ as solvent in a Ionosolv process. This particular PIL breaks lignin-polysaccharide linkages and depolymerizes the lignin through the cleavage of glycosidic, ester and β -O-4 ether bonds. The partially depolymerized lignin then becomes soluble and is separated from the rest of the biomass. By increasing the pretreatment time, the lignin fragments tend to condense through the formation of C-C bonds. The process is flexible with the possibility of obtaining low molecular weight aromatic molecules or alternatively high molecular weight lignin with a low sulfur content.

The Ionosolv BioFlex process is predominantly based on an aqueous solution of [N₂₂₂₀]HSO₄ at 80 wt%. Weigand et al.¹⁸⁰ analysed the lignin obtained from BioFlex pretreatment of willow hardwood as a function of the severity of the process. In particular, the effect of temperature (120-170 °C), time (0.3-8 h) and acid/base ratio (1.02 and 0.98) was studied. The acid/base ratio of PILs in solution appears to have little impact on the amount of linkages present in the recovered lignin. At low temperatures (150 °C), the prevailing linkage remains the β -O-4' ether even after 8 h of treatment, while increasing the temperature causes the abundance of this linkage to decrease quickly (Figure 14).¹⁸⁰

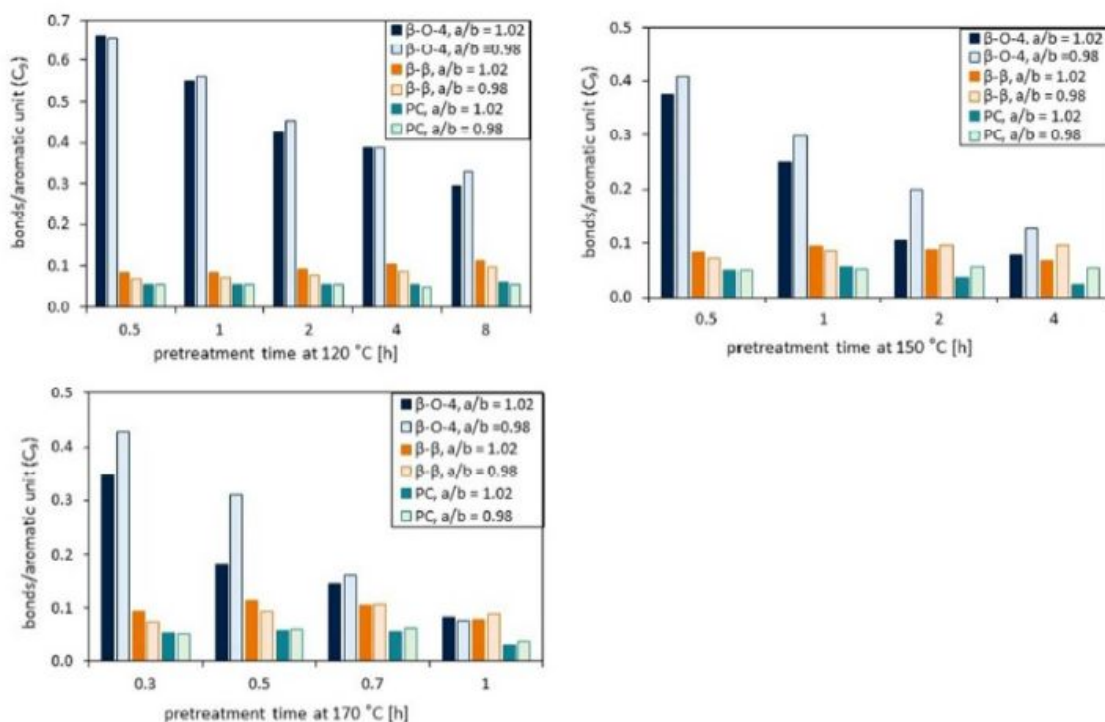


Fig. 14. Analysis of linkages (β -O-4' ether linkage, β - β' (resinol) linkage and phenylcoumaran (PC) linkage) in lignin isolated after pretreatment with $[\text{N}_{2220}]\text{HSO}_4$ at different acid/base ratios ($a/b=1.02$ and 0.98) and different temperatures. Top left: $120\text{ }^\circ\text{C}$, top right: $150\text{ }^\circ\text{C}$ and bottom left: $170\text{ }^\circ\text{C}$.¹⁸¹

An acid/base ratio of 0.98 tends to preserve the β -O-4 bond, especially for more harsh pretreatment conditions, long reaction times or high temperatures. The molar weight (MW) of the recovered lignin varied depending on the conditions employed: a strong decrease was detected with increasing pretreatment times, from approx. $25\ 000\text{ g/mol}$ after 30 min to approx. $13\ 000\text{ g/mol}$ after 2 hours at $120\text{ }^\circ\text{C}$. Under these conditions, differences in the acid/base ratio (1.02 and 0.98) had no significant effects. In contrast, at $170\text{ }^\circ\text{C}$ and using short pretreatment times, a significant increase of MW was observed with the 0.98 acid/base ratio medium, leading to a higher molecular weight lignin if compared with the 1.02 ratio.¹⁸⁰ This study highlighted how the process is highly tunable, although recondensation of the recovered lignin can easily occur, in contrast to what was observed for $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$.

Recently, the performance of the Ionosolv process based on 1-methylimidazolium chloride ($[\text{HC}_1\text{im}]\text{Cl}$) and of the Organosolv process based on a 60% (w/w) ethanol/water mixture were compared.¹⁸² Although the Ionosolv process was carried out under milder conditions than the Organosolv process ($120\text{-}150\text{ }^\circ\text{C}$ vs $185\text{-}215\text{ }^\circ\text{C}$ respectively) the former was found to be more effective in terms of lignin removal. On the other hand, the lignin recovered after the Ionosolv process showed a high number of C-C bonds indicating a high degree of recondensation. In contrast, the lignin produced by the Organosolv process was characterised by a higher content of C-O linkages with no signs of recondensation.¹⁸²

A valuable solution to lignin condensation problems is the mixed Ionosolv-Organosolv process based on the *N,N*-dimethyl-*N*-butylammonium hydrogen sulfate $[\text{N}_{1140}]\text{HSO}_4$ -ethanol mixture.¹⁸³ The $[\text{N}_{1140}]\text{HSO}_4$ system proved to be more efficient than $[\text{N}_{2220}]\text{HSO}_4$ in the treatment of softwood.¹⁸⁴ This process allows for high delignification yields, typical of the Ionosolv process, while at the same time obtaining high quality lignin. Indeed, studies conducted on the yielded lignin showed that the presence of alcohol induced α -alkoxylation during lignin fractionation and turned β -O-4' ether units into α -alkoxylated ether units. This modification not only increased the solubility of lignin, but also inhibited the onset of condensation reactions. This hybrid process makes it possible to obtain both high quality cellulosic and lignin material that is optimal for a biorefinery process.¹⁸³

In order to compare the three main classes of ILs capable of extracting lignin, Dutta et al.¹⁶⁵ reported a comparative study focused on dissolving Kraft lignin with $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$, $[\text{N}_{2220}]\text{HSO}_4$, and $[\text{Ch}]\text{Lys}$. The $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$ pretreatment showed little change in β -aryl ether content together with a strong decrease in molecular weight due to reduced recondensation phenomena. In contrast, PIL $[\text{N}_{2220}]\text{HSO}_4$ showed the highest degree of β -O-4' chain breakage and the highest number of dehydration and recondensation reactions resulting in the smallest decrease in molecular weight. Additionally, $[\text{Ch}]\text{Lys}$ showed an intermediate effect on the treated lignin, with a moderate depolymerization, dehydration, and relative recondensation observed on the produced material.¹⁶⁵

The type of IL also influences the composition of the soluble fraction. An analysis of the composition after treatment at $140\text{ }^\circ\text{C}$ for 1 h showed that $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$ exhibited the highest yield of monomeric lignin depolymerization products. Some products such as vanillin and acetovanillinone, which are commonly present in the $[\text{Ch}]\text{Lys}$ and $[\text{N}_{2220}]\text{HSO}_4$ fractions, were only observed in low concentration

(Figure 15). Under severe pretreatment conditions (160 °C for 1, 2, and 3 h), treatment with [Ch][Lys] produced mainly guaiacol, while treatment with [N₂₂₂₀][HSO₄] produced guaiacylacetone as the main product. Finally, pretreatment with [C₂C₁Im][OAc] furnished almost equivalent amounts of guaiacylacetone and guaiacol.¹⁶⁵

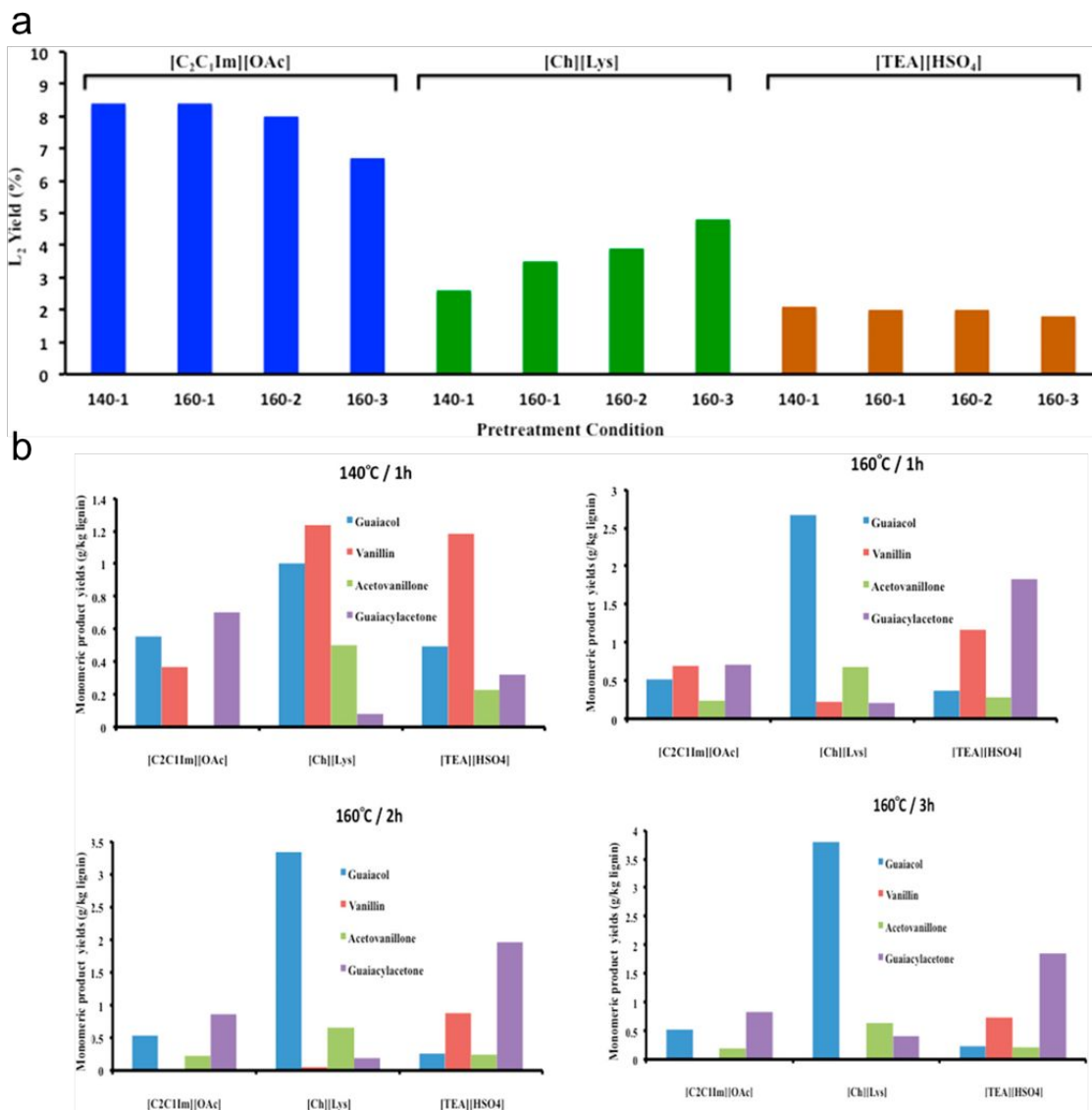


Fig. 15 a) Overall yield (%) of soluble depolymerized lignin products as a function of pretreatment conditions and IL categories. b) Composition of lignin depolymerization fraction expressed in g/Kg lignin as a function of pretreatment conditions and IL categories. Adapted with permission from Dutta et al.¹⁶⁵ Copyright 2017 American Chemical Society.

DESs are certainly a viable alternative to ILs for the dissolution of lignin. This is reflected by a large number of publications where DESs are used profitably in the extraction of lignin from biomass. Amongst this body of work, the systems that use metals as additives/catalysts,^{185,186} ILs or synthetic ammonium salts^{187,188} as HBAs components are of minor interest. Indeed, the use of these materials greatly reduces the usually acknowledged benefits of DESs with a frequent increase in costs.

As mentioned in the previous section, DESs with acidic HBDs are the most studied and those that showed the best lignin removal performance (Figure 16).

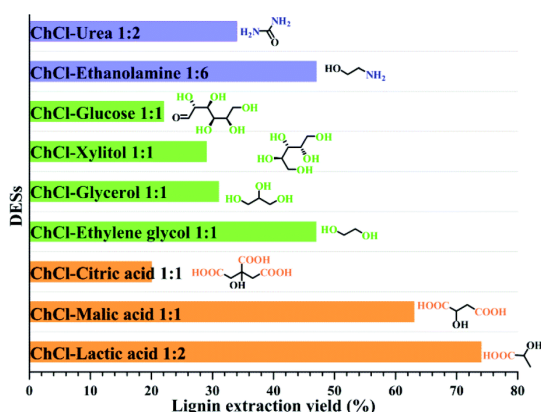


Fig. 16 Effect of HBD type on lignin extraction yield.¹⁸⁹

From the perspective of an integrated biorefinery process, the efficiency of lignin removal cannot be any longer the only parameter taken into consideration. In the evaluation of DESs as tools in biomass valorization, the effect of the pretreatment on lignin structure is also of primary importance. In a seminal paper, Alvarez-Vasco et al.¹⁹⁰ described how the quality of lignin extracted from hardwood (poplar) and softwood (*D. fir*) changes depending on which DES is employed in the process. The system investigated were based on ChCl combined with a selection of four HBDs: acetic acid, LA, levulinic acid and Gly. Since then, numerous studies have been carried out on the mechanism of lignin dissolution in acidic, basic and neutral environment. The findings described in the literature reveal that basic DESs lead to a less pure and highly recondensed lignin with small particle size compared to the material recovered with acidic DESs.¹⁹¹ Among the acidic HBDs, LA is certainly the most commonly used, and its effect on lignin structure was evaluated under different conditions and on different biomasses. The techno-economic benefits of this medium have already been described and highlighted.¹⁶⁸ Shen et al.¹⁹² studied the extraction capacity of ChCl:LA (1:10) in the temperature range 90–130 °C and with a reaction time of 6 h. Under the optimised conditions of 110 °C for 3 h, the delignification yield increased to 80 % and the recovery of the removed lignin to 44 %. When employing this protocol, the obtained lignin showed good purity, homogeneous molecular weight and the β -O-4' and β - β linkages resulted preserved. These results were partly confirmed by Shen et al.¹⁹³ in a following work. Indeed, an in-depth analysis of the recovered lignin provided interesting data not only on the depolymerization reaction products but also on the structural modification caused by dehydration and subsequent condensation reactions, consistent with a mechanism similar to that previously observed with $[N_{2220}]\text{HSO}_4$. In addition, LA component of the DES was found to react with the -OH groups of lignin forming the corresponding esters (Figure 17).

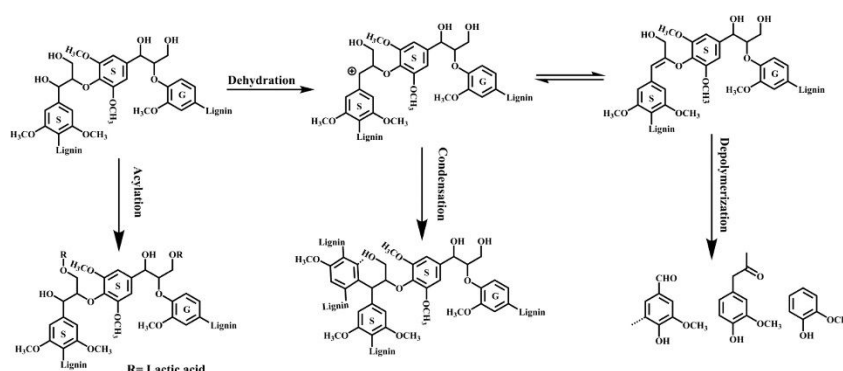


Fig. 17 Reaction pathways during the pretreatment process with ChCl:LA (1:10). Reprinted with permission from Shen et al.¹⁹³ Copyright 2020 American Chemical Society.

Some of the same authors of the previous reference confirmed the presence of γ -acetylated groups in the regenerated alkali lignin (AL) isolated from poplar also at low temperatures.¹⁹⁴ However, the presence of the esters was not observed after treatment with cholinium chloride:oxalic acid (ChCl:OA, 1:1). This is attributed to the larger steric hindrance of OA compared to LA. However, treatment with ChCl:OA (1:1) seems to favor condensation reactions. In addition, the presence of S- and G-derived diketones on the depolymerized lignin fraction (lignin oil) in ChCl:LA (1:10) was observed for the first time. The mechanism proposed to account for this reactivity pattern involves the cleavage of β -O-4' linkages, the removal of C_α hydroxy groups to form benzylic carbocations and finally oxidation of the alcoholic groups to obtain C_α ketones.¹⁹⁴

The effect of ChCl:LA (1:10) was compared with that of propionic acid:U (PA:U, 2:1) and cholinium chloride:p-toluenesulfonic acid (ChCl:pTSA, 1:1) using 2-phenoxy-1-phenylethanol (PPE) as a model substrate for the more complex lignin.¹⁹⁵ The tests confirmed that ChCl:LA was capable of breaking down PPE and at the same time producing PPE lactic acid ester and lactic acid oligomers. In contrast, PA:U (2:1) was not able to degrade the PPE bonds despite it being able to dissolve lignin. Finally, the high acidity of ChCl:pTSA (1:1) made it the most effective system in breaking down PPE, leading, however, to the condensation of cleaved products with prolonged reaction times. This result highlights the important role of the acidity of the HBD partner, both in the dissolution and in the occurrence of side reactions of lignin. In the same work, it was observed that the addition of water decreased the cleavage of PPE bonds and strongly suppressed undesired side reactions.¹⁹⁵

The presence and the nature of the halide anion also play an important role in the dissolution process. da Costa Lopes et al. evaluated the properties of cholinium bromide (ChBr) by replacing ChCl in the ChCl:pTSA system. The kinetic study performed with ChCl:pTSA (1:1) and ChBr:pTSA (1:1) demonstrated that PPE-halogenide intermediates are important in increasing the rate of cleavage reactions. The results obtained are in line with DFT calculations attributing to the β -O-4 ether bond cleavage a pivotal role.¹⁹⁵ Previously, the role of the chloride anion had been investigated in an industrial application concerning milled wood from *Eucalyptus globulus*, in this case by following lignin cleaving reactions carried out in a ChCl:LA (1:10).¹⁹⁶ The DES was compared with the NaCl:LA mixture and showed similar results in terms of lignin dissolution.¹⁹⁶ This behaviour highlights the importance of the chloride anion in the dissolution process but raises at the same time some concern as to whether the cholinium portion is actually needed. However, further studies are certainly required to further elucidate this aspect.

As noted in the previous section, the use of ChCl:LA has serious limitations in terms of recyclability. In addition to the cholinium ester formation, lactide formation and LA oligomerization as well as formation of LA esters on both the cellulosic and lignin portions are all encountered issues. These side reactions actually lead to the consumption of the LA HBD component, raising serious doubts as to the real applicability of this DES in the pretreatment of lignocellulosic biomass. Hence, the identification of DESs alternative to ChCl:LA and with fewer limitations is of the highest interest, especially in view of the full utilization of lignin in an economically sustainable manner.

The use of low melting mixtures with boric acid (BA) as HBD component is a viable alternative. Cholinium chloride:boric acid (ChCl:BA) showed good delignification performance of softwood

sawdust at 90 °C while avoiding condensation of the solubilized lignin.¹⁹⁷ The observed results are attributed to the formation of a cyclic ester between boric acid and the hydroxy functionalities situated at position α and γ . Similarly, the DES composed of ChCl, BA, and polyethylene glycol-200 (PEG-200) in a 1:1:1.5 ratio showed excellent lignin and hemicellulose dissolution capabilities when used on wheat straw biomass.¹⁹⁸ The recovered lignin displayed a low molecular weight, a narrow polydispersity index and good retention of the β -O-4', β - β' , β -5' bonds present in pristine lignin. Another possible option is the use of DESs with polyalcoholic HBDs partners which would overcome the problems associated with the use of carboxylic acids. However, their effectiveness is reduced due to the reduced acidity. For this reason, Chen et al.¹⁹⁹ employed cholinium chloride:ethylene glycol (ChCl:EG, 1:2 and 3:2) with the addition of 0.5 or 1.0 wt% H₂SO₄ for switchgrass fractionation. The lignin properties such as molecular weight, number of ether bonds as well as degree of condensation were modulated by controlling the DES composition and the pretreatment conditions. In general, the obtained lignin exhibited low condensation degree, well preserved β -O-4' linkages, and high volatility similar to that of cellulolytic enzyme lignin (CEL). Similar results were obtained using ChCl:Gly (1:2) with 0.9 wt% H₂SO₄.²⁰⁰ Although the lignin obtained is undoubtedly of excellent quality, the use of H₂SO₄ represents a limitation, due to corrosion issues, that can be eliminated by mechanical means. As described in the previous section, ChCl:Gly (1:2) was successfully used in the pretreatment of sorghum bagasse using co-rotating twin-screw extruders. The analysis of the recovered lignin after pretreatment with two different biomass loadings (30 and 50 wt%) showed a decrease in molecular weight by 50% and a slight increase in the polydispersity index.²⁰¹ The decrease in the ratio of S/G units suggested that some condensation reactions, albeit moderately, occurred even during the extrusion process. Furthermore, the data highlighted the decrease of H units in the lignin after extrusion, while analysis of the ether linkages showed that only limited cleavage occurred during the extrusion that followed pretreatment. The quality of the recovered lignin, together with the excellent delignification performance, make of this pretreatment one of the most innovative and interesting reported in the literature.

A comparison of ILs and DESs in lignin solubilisation process does not reveal a clear winner. The choice of the most suitable system depends on the biomass of interest and the type of lignin to be obtained. The use of DESs requires on average longer pretreatment times (6 h vs. 1-2 h for DESs and ILs, respectively) while a wide variety of different lignins can be obtained with both media. The only direct comparison between ILs and DESs present in the literature is between ChCl:LA (1:9) and 1-allyl-3-methylimidazolium chloride [AC₁im]Cl.²⁰² However, the unfortunate choice of a poorly efficient IL for lignin dissolution such as [AC₁im]Cl makes this analysis undeservedly unfair for ILs. Anyway, even the comparison of the best performing ILs and DESs, although of interest, would remain confined to the specific case selected, as each process must be evaluated according to many parameters and possible effects on other biomass components must also be considered.

5.4. Cellulose purification

Full utilisation of cellulose relies on its dissolution, processing and transformation into new materials or chemicals. Transformation of cellulose into low molecular weight products has been reviewed elsewhere and will only be partially discussed in this critical review.²⁰³⁻²⁰⁵ Cellulose solubilisation is at the basis of many of its industrial manipulations. Indeed, unlike commonly used polymers, this polysaccharide cannot be melted prior to processing. For this reason, interest in cellulose

solubilisation has been longstanding and many unsolved challenges still remain in this area, which hamper the use of this material. One well known process for dissolving cellulose is based on the LiCl/*N,N*-dimethylacetamide (DMAc) system,²⁰⁶ although many other systems have been developed such as molten salt hydrates, aqueous NaOH,²⁰⁷ NaOH/U²⁰⁸ and lithium hydroxide (LiOH)/U solutions.²⁰⁹ Although the LiCl/DMAc system is capable of dissolving up to 15 wt% of cellulose, it requires high dissolution times and temperatures (up to 150 °C and 48 h) and is extremely water-sensitive.²¹⁰ On top of these aspects, the reduced availability of lithium due to its limited nature and increasing use in battery manufacture has led to a sharp increase in price.²¹¹ Base/U systems can also solubilise up to 4 wt% of cellulose at -10 °C and in the presence of water.²¹² However, the need to work with cryogenic systems increases energy demand and plant costs considerably.

In the industrial context, the most used process is the so-called Lyocell process, which uses *N*-methylmorpholine-*N*-oxide monohydrate (NMMO·H₂O) as the solvent and is capable of solubilising up to 30 wt% of cellulose (depending on the type of cellulose used).^{213,214} However, the process shows significant limitations due to the occurrence of side reactions. These phenomena have detrimental effects on the structure of the cellulose with consequent loss of mechanical properties and a temporary or permanent discoloration of the fibers. In parallel, a pronounced decomposition of NMMO is observed, leading to an increased need for stabilisers, like isopropyl gallate.²¹⁵

As a way to respond to the shortages of the technologies described above, ILs were proposed as an alternative medium for performing cellulose-based transformations. Since 2002, after the first work by Swatloski et al.²¹⁶ on cellulose dissolution with ILs, the number of publications and patents in this area has grown exponentially and the field has matured very quickly.^{213,217,218}

Nowadays, there are three pilot scale processes and one commercial scale process which use ILs for cellulose transformation. Natural Fiber Welding, Inc. has developed a commercial scale process that uses [C₂C₁im]OAc to turn natural fibers into welded materials.²¹⁹ Thanks to this technology, it is possible to recycle and even upcycle existing natural materials to create new high-performance textiles.

Metsä Spring, a corporate venturing arm of the Metsä Group is building a IL-based, closed-loop pilot plant capable of producing 40 Kg of fiber per hour for a total budget of EUR 40 million.²²⁰ Similarly, the German Institutes of Textile and fiber Research Denkendorf (DITF) has developed a spinning process, called HighPerCell®, for the production of hemp-based cellulose fibers. In the process, the cellulose pulp from hemp is dissolved in ILs and then spun in a special wet spinning system.²²¹ Sticking to cellulose fibers, Aalto University in Finland has developed the closed-loop Ioncell® process, a new dry-jet wet spinning process for cellulose fibers production based on a PIL, 1,5-diazabicyclo[4.3.0]non-5-enium [DBNH]OAc (Figure 18).^{222,223}

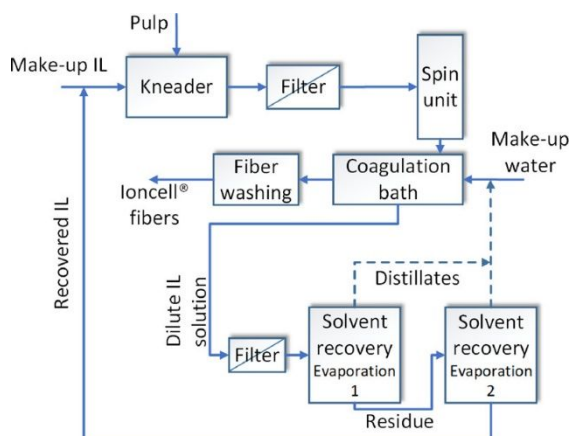


Fig. 18. Scheme of the Ioncell-Lyocell process revealing dissolution, fiber spinning, and solvent recovery steps Reprinted with permission from Elsayed et al.²²⁴. Copyright 2020 American Chemical Society.

The use of PILs results in highly oriented cellulosic fibers with a higher tenacity than commercial viscose and NMMO-based Lyocell fibers.²²³ In 2020, a pilot plant capable of producing 10 Kg of fiber per day was launched and is estimated to reach the commercial scale by 2025.²²⁵ All these processes have a Technology Readiness Level (TRL)²²⁶ in the range from 7 to 9, clearly demonstrating how this field of application is technologically advanced.²²⁰

In the last twenty years, a huge number of ILs capable of solubilising cellulose has been developed by varying the structure of the cation and the type of anion.^{213,227} Alongside, the mechanism of dissolution has been studied and the effects of the ILs' structural changes on their dissolving power have been documented.^{218,227,228} A valuable tool for describing and predicting the solvent ability of ILs towards cellulose is based on the Kamlet-Taft parameters. At first, the solvent capacity was attributed mainly to the HBA strength of the anion, hence to the β parameter. In particular, it was reasoned that ILs with β values greater than 0.8 would be the most suitable for dissolving cellulose (acetate and chloride anions).²²⁹ Later, the role of the cation was reconsidered thanks to some key observation concerning the behaviour of imidazolium-based ILs. In these systems, the IL establishes hydrogen bonds with cellulose hydroxyl groups via the C-2 of the imidazole ring and at the same time interacts with the hydrophobic portions of the cellulose chains.²³⁰ Consequently, ILs with high α -values, which are typical for imidazole cations without electronegative groups (oxygen and/or nitrogen) and poorly hindered (short alkyl chains) around the C-2 position, perform best in cellulose dissolution.²³¹ The effect of the π^* parameter is less pronounced than that of α and β parameters. A high π^* value denotes a high cation-anion interaction thus reducing the possibility of ions to interact with the hydroxyl groups of cellulose. In summary, high α and β values and low π^* values promote cellulose dissolution.²³² In this context, Hauru et al.²³³ introduced the concept of net basicity, $\beta-\alpha$. This parameter more reliably describes both the dissolution and the regeneration of cellulose by ILs as well as by NMMO-H₂O. By plotting the $\beta-\alpha$ and β parameters of neat ILs, the range $0.35 < \beta-\alpha < 0.9$ and $0.80 < \beta < 1.20$ were identified as the optimal ranges for cellulose dissolution. This type of correlation between Kamlet-Taft parameters and solvent capacity proves effective not only for neat ILs, but also for their mixtures with polar co-solvents.²³³ Indeed, polar molecular solvents are widely used in combination with ILs in cellulose dissolution processes. The use of co-solvents expands the portfolio of possible solvent systems for cellulose, lowering the overall cost of the medium and at the same time modulating the viscosity of ILs and IL/cellulose solutions. In this framework, Rinaldi et al.²³⁴ introduced the concept of organic electrolyte solutions (OES), composed of mixtures of ionic species and molecular solvents, and showed their ability to instantaneously dissolve cellulose. In particular, low mole fractions of [C₂C₁im]Cl or [C₂C₁im]OAc (χ_{IL} = 0.08-0.4) in polar solvents (e.g. dimethyl sulfoxide (DMSO), sulfolane, 1,3-dimethyl-2-imidazolidinone, and γ -valerolactone (GVL)) were able to solubilize up to 10 wt% of cellulose in far less time (few minutes) than when used in neat form.²³⁴ As OES, even ILs not capable of dissolving cellulose in pure form become potential new options to be tested.²³⁵⁻²³⁷ In addition, Holding et al.²³⁸ showed how acetate amphiphilic phosphonium ILs, which are poor solvents for the polysaccharide, become suitable solvents for cellulose when mixed with DMSO, dissolving up to 19 wt% cellulose. Furthermore, an additional benefit of this latter series of ILs stems from their poor solubility in water, which allows for their recovery at the end of the cellulose water-based coagulation process, with a clear energy and material-saving advantage.²³⁶

PILs are also a valuable option for dissolving cellulose, as they can be easily and inexpensively prepared (please see section 5.7.2). Moreover, one of the most promising processes in the scale-up phase is based on amidinium PILs. The originating Ioncell process employs a [DBNH]OAc IL, which performs very well as it can dissolve up to 17 wt% of cellulose at temperatures around 80 °C in a few minutes.²²³ [DBNH]OAc possesses a net basicity β - α of 0.57 and a β of 1.1, which makes for an excellent cellulose solvent.²³⁹ Similar net basicity parameters are also observed for other guanidinium and amidinium acetate PILs, β - α of 0.75 for 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-enium acetate ([mTBDH]OAc) and β - α of 0.41 for 1,5-diaza-bicyclo[4.3.0]undec-5-enium acetate ([DBUH]OAc), all effective solvents for cellulose.²⁴⁰ Unfortunately, many works promoting the use of ILs in processing tend to underestimate potential issues arising from their use in a continuous process. Although PILs have a lower cost than AILs, a key feature for their use in a commercial setting is the ability to efficiently undergo recycling. However, the latter process is sometimes hindered by the presence of by-products in the raw pulp, while this accumulation of impurities can lower the solvent capacity and change the viscosity of the solution. For example, in a continuous spinning process such as Ioncell, these aspects result in a continuous modification of the operating conditions in an attempt to keep the properties of the resulting fibres constant.²²⁴ Furthermore, for PILs the recovery process from the coagulation bath is hampered by the fact that the [DBNH] and the [mTBDH] acetate ILs form with water non-stoichiometric azeotropic mixtures with acid-base ratios of 5:3 (acetic acid:[DBN]) and 3:2 (acetic acid:[mTBD]), respectively.²⁴¹ In addition, amidinium and guanidinium ILs have been shown to be subjected to hydrolysis when used in media with water contents higher than 20 wt%.^{240,242} The presence of varying amounts of these impurities reduces the dissolving power of ILs and is the main hurdle to the industrial development of this process. Based on these considerations, the recyclability of [DBNH]OAc from aqueous media was analysed and an average recovery rate of 95.6 wt% was observed.²⁴³ With water content of 4.1-5.4 wt% (6.0-13.6 mol%) per cycle, up to a maximum of 41.5-54.9 mol% of hydrolysis product was observed. The recycling of the IL did not change the chemical composition or degree of polymerisation of the recovered cellulose, but the colour of the regenerated material gradually darkened as the number of recycling cycles increased.²⁴³ Replacing [DBNH]OAc with [mTBDH]OAc allowed the number of recycles to be increased to five without a refill of fresh IL.²³⁹ This is attributable to the higher stability towards hydrolysis of mTBD compared to DBN.^{240,242} In addition, the higher basicity of mTBD compared to DBN ($pK_a = 25.4$ and 23.4 , respectively, in acetonitrile)²²⁴ leads to a higher ΔpK_a value and thus to an increased thermal stability of the PIL.²⁴⁴ From the perspective of increasing the hydrolytic stability of [mTBDH]OAc, it was observed that small stoichiometric excesses of acetic acid significantly reduced the kinetics of hydrolysis.²⁴⁰ At the same time, the effect of this addition on the ability to dissolve 12 wt% cellulose was tested for [mTBDH]OAc.²²⁴ In a direct dissolution comparison with 3 wt% of water, [mTBDH]OAc could withstand the presence of 20 wt% of hydrolysis products and an acid/base ratio of 1.3, while the dissolution capacity of [DBNH]OAc was already compromised at 5 wt% of hydrolysis products and an acid/base ratio of 1.1 (Figure 19).²²⁴

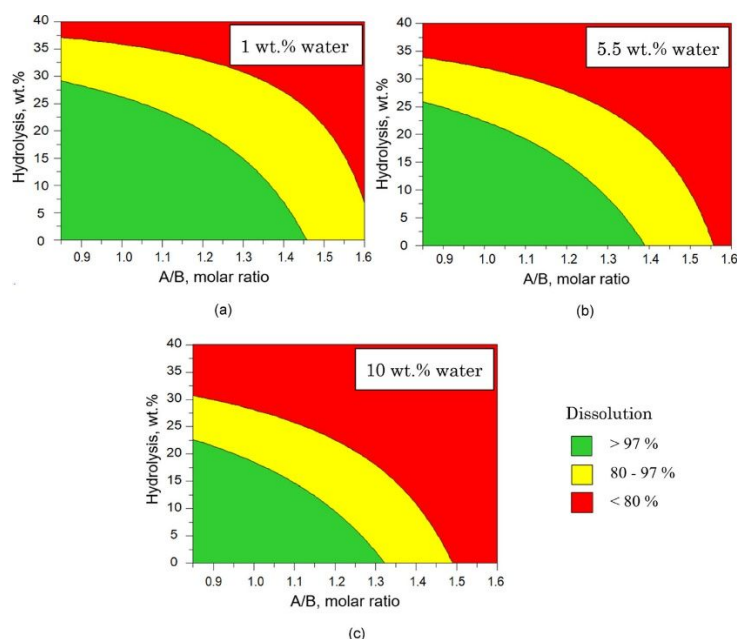


Fig. 19. Dissolution contours for 13 wt% cellulose in [mTBDH]OAc in different A/B ratios and hydrolysis product compositions at (a) 1 wt% water, (b) 5.5 wt% water, and (c) 10 wt% water. Reprinted with permission from Elsayed et al.²²⁴. Copyright 2020 American Chemical Society.

These data show a higher tolerance of [mTBDH]OAc compared to [DBNH]OAc towards impurities, making the process based on [mTBDH]OAc much more robust in view of its commercialisation. However, a question arises concerning the effective nature of this solvent system. Indeed, from a formal point of view it is no longer a PIL, but a mixture of mTBD:acetic acid in a molar ratio of 1:1.3. This type of solvent system together with the OESs, described above, could be considered as the “transition zone” between ILs and DESs. It is worth stressing that the potential “deep” nature of the above mixtures has never been verified. Likewise, there are systems capable of dissolving cellulose and defined as “DES” in the literature whose phase diagrams have not been reported, nor do they possess the often vaunted DES properties of low toxicity, low volatility, and ease of preparation. This is the case for instance of “DESs” systems whose HBAs are imidazole zwitterions²⁴⁵ or allylammonium chlorides,²⁴⁶ which require a preparation process similar to that of ILs. Another controversial example is represented by the DBU/methylthiourea mixture reported by Fu et al.,²⁴⁷ a system capable of dissolving cellulose and whose dissolution mechanism was investigated by quantum mechanical calculations. Apart from the nature of the mixture, which was not investigated, it is important to emphasise that both the strong basicity of DBU and even more the toxicity of methylthiourea are far from the concept of sustainable solvent design.

The first example of cellulose dissolution with solvents with recognised DES nature was reported by Sharma et al. and dates back to 2013.²⁴⁸ In this work, different combinations of ChCl, ChBr, chlorocholinium chloride (ClChCl), and betaine hydrochloride (BetHCl) mixed with U, Gly, and EG in a 1:2 molar ratio were tested in cellulose dissolution processes using microwaves and ultrasound as alternative heating sources. The study showed that DES ChCl:U (1:2) was the best performing system as dissolved up to 8 wt% of microcrystalline cellulose (MW 3.12×10^5 Da) at 100 °C.²⁴⁸ The other U-based DESs, ClChCl:U (1:2) and BetHCl:U (1:4), were also able to dissolve cellulose although in reduced amounts, while performances of DESs with alcoholic HBDs were reported to be much less promising.²⁴⁸ A further DES capable of dissolving cellulose was cholinium chloride:imidazole (Im) ChCl:Im (3:7), which was capable of dissolving 2.48 wt% of cellulose in 1 h.²⁴⁹ Conversely, the solvent

properties of DESs with an acidic HBD such as OA, citric acid and malic acid (MA) were proven not satisfactory and the effect of the acidity on the structure of the treated cellulose was often even not investigated.²⁵⁰ However, to confirm the potential of these materials, it is worth stressing that acid-based DESs are widely used with high efficiency in the preparation of nanocellulose by erosion of the amorphous part of the cellulose.^{251–253}

The application of U-based DESs as media for cellulose processing has been studied by different research groups.^{248,254,255} However, these efforts resulted in conflicting data as some papers mention their reaction media as solutions,^{248,255} while in the majority of the cases the obtained mixtures are described as swollen cellulose suspensions.^{256,257} These discrepancies are likely due to the different types of cellulose processed in terms of molecular weight and crystallinity. However, a detailed analysis of the literature shows that cellulose often undergoes preliminary treatments before being subjected to DES, such as sonication in saturated CaCl_2 solutions²⁴⁹ or exposure to solution containing Na^+ ions and subsequent washing with acetone.²⁵⁷ These pretreatments often place a significant burden on the sustainability of the whole protocol and partly compromise the benefits of using DESs. Conversely, an application of DESs in cellulose processing that can lead to interesting industrial developments was proposed by Nguyen et al.²⁵⁸ The NADES $\text{ChCl}:\text{MA}$ was used as an additive in the Lyocell process with $\text{NMMO} \cdot \text{H}_2\text{O}$ as the main solvent. In the study, the effect of different molar ratios of the NADES components (1:1, 1.5:1, 2:1, 1:1.5, 1:2) and of different additive percentages in $\text{NMMO} \cdot \text{H}_2\text{O}$ were investigated. The mixture consisting of $\text{NMMO} \cdot \text{H}_2\text{O} + 15\text{wt}\% \text{ChCl}:\text{MA}$ (1.5:1) was found to be the best performing system as it showed a higher dissolving power than the pure solvent (12 wt% versus 17 wt%).²⁵⁸

Furthermore, the use of the additive allowed for expanding the working window of the Lyocell process to room temperature, well below the melting temperature of NMMO (70 °C). The reduction of the working temperature has the dual benefit of lowering energy consumption and reducing solvent and cellulose degradation reactions. In a preliminary recyclability study, under laboratory conditions, the system was found to be recyclable five times, with a recovery rate of more than 95%.²⁵⁸ As noted above for the PIL $[\text{mTBDH}]\text{OAc}$, this system also falls outside the formal definitions of DESs. Indeed, giving the intimate interactions between all components, this system is likely better described as a ternary mixture of $\text{NMMO}/\text{ChCl}/\text{MA}$ with peculiar properties rather than $\text{NMMO} \cdot \text{H}_2\text{O}$ in combination with NADES as additive. The exact nature of the ternary mixture has not been investigated, but this does not detract from the quality of the whole system which showed great potential for industrial application.

Overall, the use of DESs in the solubilisation and processing of cellulose has severe limitations as the maximum solubilities achieved are rather low. Furthermore, the different data found in the literature for the same DES indicate a strong variability, which is due to the type of cellulose employed and to the pretreatment carried out on the starting materials. Not surprisingly, most of the applications of DES in cellulose technology are related to those areas where actual dissolution is not required.^{259–262} Prominent among these is the preparation of cellulose nanocrystalline (CNC)^{252,263–266} and cellulose nanofiber (CNF)^{253,267–269}, where the lower cost of DESs compared to ILs plays in their favour. From the point of view of sustainability, the synergistic use of ILs and DESs would be certainly desirable. Indeed, this would expand the fields of application and reduce potential drawbacks by exploiting the best features of each medium. In this context, the work reported by Wang et al.,²⁷⁰ where ILs and DESs were used for the preparation of plasticized cellulosic films, represents an inspiring example. $[\text{C}_4\text{C}_1\text{im}]\text{Cl}$ was used to solubilise cotton linters and subsequently form a cellulosic

gel. The IL was then washed away with water and recovered, while the DES ChCl:U (1:2) was added to the cellulosic gel. The cellulosic film obtained after drying at 55 °C was completely transparent and colorless, with an improvement in mechanical properties in terms of increase in elongation and decrease in tensile strength.²⁷⁰ The effect of the DES on the quality of the end product was compared with that of Gly and sorbitol, both already used as plasticizers, and showed a similar effect as additive albeit at lower dosages. Furthermore, with ageing, the sorbitol-plasticized film became opaque and weakened due to crystallisation of the plasticiser. Conversely, this phenomenon was not observed when ChCl:U (1:2) was used.²⁵⁸ This example combines the advantages of both class of solvents, namely the excellent solvent and gel-forming capabilities of [C₄C₁im]Cl and the low cost and low toxicity of ChCl:U (1:2) for the preparation of plasticized cellulose films.

5.5. Hemicellulose dissolution

The most undervalued component of lignocellulosic biomass is hemicellulose. Although it represents 15-35 wt% of biomass, its exploitation at industrial level remains very limited.²⁷¹ Therefore, within the perspective of an environmentally and economically sustainable biorefinery, this fraction must be better exploited and valorised. Currently, hemicellulose is mainly employed as additive in the food and pharmaceutical industries,^{272,273} while its use as barrier enhancement in polymer films is of potential interest.²⁷⁴⁻²⁷⁶ A further field of application for hemicellulose is in the tissue paper industry, where it can function as an additive to increase the biomechanical properties of cellulose products.²⁷⁷ The factors limiting the use of hemicellulose are both its heterogeneous and amorphous nature. The first aspect is related to the high variety of forms that this material can have: hemicellulose is a branched polysaccharide composed of hexose sugars (mannose, galactose) and pentose sugars (xylose and arabinose). The structure of hemicellulose varies depending on its source in terms of the type of saccharide units, degree of polymerisation, and presence of functionalities such as acetyl and methyl groups, cinnamic, glucuronic and galacturonic acids.¹³³ Hardwood hemicellulose consists mainly of O-acetyl-4-O-methylglucuronoxylan backbone chains with 8-17 % acetyl groups and side groups such as 4-O-methylglucuronic and galacturonic acids. The latter increase the stability of hemicellulose in acidic and basic environments. The average degree of polymerisation is in the range of 100-200.²⁷¹ Softwood hemicellulose is composed of partially acetylated O-acetyl-galactoglucomannans linear chain (around 6%) with an average degree of polymerisation between 40 and 100. The lower degree of polymerisation of softwood hemicellulose makes it more soluble in water.²⁷¹ The non-woody or switchgrass hemicellulose is similar to hardwood hemicellulose but with the presence of arabinose, lower degree of acetylation and low degree of polymerisation (DP 50-185).²⁷¹ Thus, the high structural variability requires the development of very flexible industrial processes, which limits its diffusion and applicability. The second factor that limits the valorisation of hemicellulose is related to its amorphous nature which reduces its stability against hydrolysis.¹³³ For this reason, under the pulping and pretreatment conditions mentioned above, hemicellulose is mainly depolymerised and degraded into the respective sugars and furan derivatives such as furfural.²⁷⁸ Although the process stream resulting from the removal/degradation of the hemicellulose is already recovered and exploited, the sugars obtained are poorly fermentable and the by-products obtained, mainly furans, strongly inhibit enzymatic processes.²⁷¹ Research aimed at finding fractionation processes that eliminate or at least reduce the degradation of hemicellulose is therefore of primary importance. Once more the utilisation of DESs and ILs represent a viable alternative to conventional industrial processes of hemicellulose removal, which are based on drastic

treatments with dilute acids, bases, or alternatively hydrothermal conditions, supercritical fluid, and steam explosion.^{271,279}

As mentioned above, the excellent dissolution capacity of halide- and acetate-based AILs towards cellulose and hemicellulose enables extremely efficient processes. Using this technology, it is possible to recover the cellulose by reprecipitation with water and further the hemicellulose with the addition of ethanol.²⁸⁰ However, the primary limitation of this approach remains the associated loss of crystallinity of the resulting cellulose, the high sensitivity to water, and the cost of the medium. The use of AILs/water mixtures has proven successful and widespread as it allows the selective solubilisation of the hemicellulose, while keeping the cellulose intact. Unlike Ionosolv processes that commonly employ acidic AILs or PILs, the use of ILs with basic acetate anion avoids degradation of the hemicellulose during the extraction processes. Among the various systems reported in the literature, ILs/water mixtures are the most widely used. Based on this knowledge, Froschauer et al.²⁸¹ developed the IONCELL-P(ulp) process using $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$ /water, which proved efficient in the selective removal of hemicellulose. The same authors also investigated the effect of water in the interaction between five different ILs and wood polymers.²⁸² Regarding hemicellulose removal, 1-ethyl-3-methylimidazolium dimethyl phosphate $[\text{C}_2\text{C}_1\text{im}]\text{DMP}$ was found to be superior to its chloride and acetate counterparts but also to PILs 5-methyl-1,5-diazabicyclo[4.3.0]non-5-enium dimethylphosphate $[\text{mDBN}]\text{DMP}$, $[\text{DBNH}]\text{OAc}$, and 1,5-diazabicyclo[4.3.0]non-5-enium propionate $[\text{DBNH}]\text{EtCOO}$. However, PILs showed greater removal of hemicellulose than AILs at pulp loadings above 10 wt% (Figure 20).

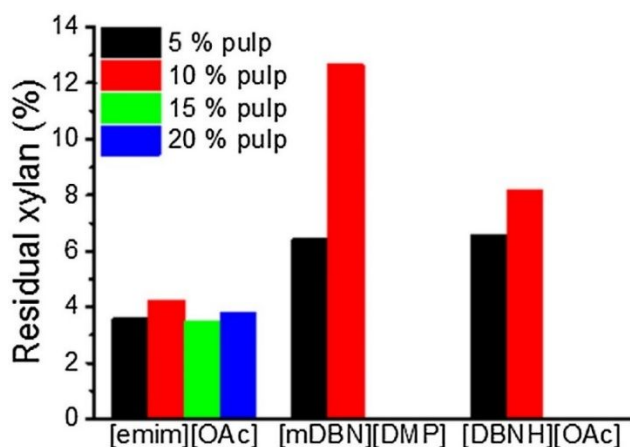


Fig. 20 The effect of pulp load on the xylan removal efficiency.²⁸²

The IONCELL-P process has been widely used for the separation of Kraft pulp (originated from different biomasses) from hemicellulose, with the aim of increasing its quality to dissolving grade.^{283,284}

A further interesting system is the organic electrolyte solution (OES) consisting of $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$ and the biobased solvent GVL, in turn derived from cellulose processing. This system performs well in the presence of water, as the GVL/ $[\text{C}_2\text{C}_1\text{im}]\text{OAc}$ /water mixture in a 2:1:1 ratio transforms hardwood Kraft pulp into dissolving grade material under mild conditions.²⁸⁵ In addition, GVL was used to develop a hybrid Organosolv/IONCELL-P process for the fractionation of birch wood and subsequent purification of the resulting cellulose.²⁸⁶ The first step involved the use of the GVL/water mixture to

obtain paper grade pulp, while the IONCELL-P process was used to remove the hemicelluloses and to obtain a GVL-IONCELL pulp. This material was of a significantly higher quality compared to pulp obtained with the more impacting commercial processes.²⁸⁶

A biobased alternative to $[C_2C_1im]OAc$ is cholinium acetate ($[Ch]OAc$). In fact, Cheng et al.²⁸⁷ reported the benefits of treating ground bagasse and Southern yellow pine with $[Ch]OAc$, which can solubilize the hemicellulose and the lignin while retaining the cellulose unchanged. In this study, the authors evaluated the solvent capability of $[Ch]OAc$ and $[Ch]OAc$ /water (5:1 in mass) for single biomass components using MCC for cellulose, xylan for hemicellulose, and Kraft lignin for lignin. Neat $[Ch]OAc$ and $[Ch]OAc$ /water are both able to solubilize up to 13 wt% of xylan.²⁸⁷ This system is appealing because the IL used is derived from renewable sources and is highly recyclable compared to the more expensive $[C_2C_1im]Cl$ and $[C_2C_1im]OAc$.²⁸⁸ A similar system was used by Sun et al.²⁸⁹ for switchgrass fractionation, but the information on the hemicellulosic fraction was not disclosed.

$[Ch]OAc$ has been successfully used as HBD component in the preparation of DESs. Dugoni et al.²⁹⁰ reported the preparation of three different DESs with $[Ch]OAc$ as HBA and levulinic acid, glycolic acid, and imidazole (Im) as HBD moieties, respectively. The three DESs showed very good solvent capabilities towards xylan from beechwood, which was used as a model for hemicellulose. The addition of water to the DESs increased the solvent capacity, which reached an optimum balance with the DES $ChOAc:Im$ (1:1) + 15wt% water being able to dissolve a considerable 45 wt%. The use of $[Ch]OAc$ in DES systems brought a significant increase in performance compared to pure $[Ch]OAc$ (Figure 21).²⁹⁰

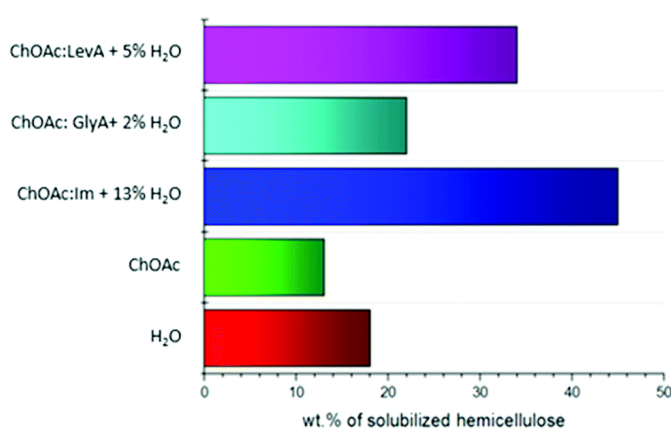


Fig. 21 Comparison of the maximum values of hemicellulose solubility obtained in $[Ch]OAc$ -based DESs + wt% water, $[Ch]OAcIL$ and water.²⁹⁰

In addition, $[Ch]OAc$ -based DESs have also proven to be markedly better performing than their $ChCl$ -based analogues. Furthermore, a cost analysis showed that the high price of $[Ch]OAc$ -based DESs is purely due to the limited commercialization of $[Ch]OAc$ compared to the more widespread component $ChCl$ (3.44-1.39 euro/Kg for $ChCl$ -based DES vs 3.58-1.67 euro/Kg for $[Ch]OAc$ -based DES).²⁹⁰

The number of papers dealing with hemicellulose solubilization using DESs is very limited. These include works that use DESs comprising toxic chemicals, such as thiourea²⁹¹, or acid DESs^{292–294} that degrade the hemicellulose structure with similar issues to those reported for ILs.

More interesting is the work of Morais et al.²⁹⁵ where DES ChCl:U was used for the removal of hemicellulose from *Eucalyptus globulus* hardwood. The dissolving power of the DES at different molar ratios, neat and in the presence of water, was evaluated in the solubilization of xylan from beechwood (Figure 22a). The remarkable value of 310 mg of xylan per g of DES was obtained with ChCl:U 1:2 + 50 wt% water at 90 °C. Under these conditions, the DES is able to solubilize the hemicellulose without significant changes in the degree of polymerization (Figure 22b).²⁹⁵

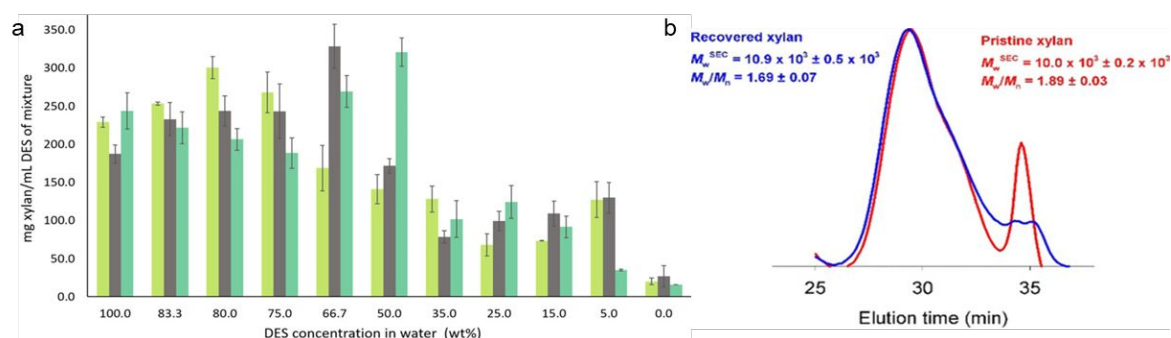


Fig. 22 a) Solubility of xylan in aqueous ChCl/U (1:2) at different concentration and different temperatures (70 °C, 80 °C and 90 °C). b) SEC profiles of the pristine and recovered xylans.²⁹⁵

Considering the excellent results obtained, the use of DES for the solubilisation of hemicellulose seems to be superior to the use of ILs in terms of efficiency, cost and residual toxicity. In particular, the systems developed by Morais et al. and Dugoni et al. are complementary to each other. The first one, based on ChCl:U (1:2, at 50 wt% of water) demonstrated excellent results in the pretreatment of *Eucalyptus globulus* while the second one, based on ChOAc:levulinic acid, exhibited a very good purification capacity on Kraft cellulose. For both systems, it is important to note the excellent DESs' recyclability after hemicellulose extraction.

5.6. ILs and DESs toward chitin

Recently, the use of ocean biomass as a source of raw material has attracted enormous interest both at academic and industrial level.²⁹⁶ Among the various marine biopolymers, chitin is undoubtedly the most interesting in terms of its potential applications, but primarily because it is biologically produced in huge quantities. Indeed, chitin is used as a structural material by the majority of invertebrate organisms and is thus the second most abundant polysaccharide biopolymer in nature after cellulose. It has been estimated that between 10^{12} and 10^{14} tons of this compound are annually produced in nature as the main component of marine shells (for example α -chitin in the shell of crustaceans and β -chitin in squid pens),²⁹⁷ but it is also found in mushrooms and insects.

Chemically, chitin is a polysaccharide only composed of β -1,4-linked 2-(acetylamino)-2-deoxy-D-glucose units. The structure of this polysaccharide is more complex than those reported above for other polysaccharides because, as well as different molecular weights and crystallinity degrees, chitin may present three polymorphic forms (α , β , and γ chitin) and different degrees of acetylation (DA).²⁹⁸ Each of these structural parameters has a strong effect on the mechanism and the difficulty of chitin dissolution. On the other hand, this structural variability makes of this natural polymer an exceptional material with unique properties^{299,300} like biocompatibility, non-toxicity and

antimicrobial power. These features ensures that chitin and its derivative chitosan are considered excellent materials for use in the biomedical field.³⁰¹ Only in this sector, chitin market size was valued at \$42.29 billion in 2020 and is projected to reach \$69.29 billion in 2028.³⁰² In addition, chitin is one of the few nitrogen-containing biopolymers, making it an excellent precursor for the synthesis of organonitrogen biochemicals.^{303,304}

Despite this potential, chitin remains underutilized at industrial level, mainly on account of its low solubility in common solvents. Indeed, chitin dissolves at low concentrations in LiCl/DMAc, CaCl₂/methanol and hexafluoroisopropanol (HFIP) but these treatments cause considerable changes in the biopolymer structure such as degree of crystallinity and crystal form, molecular weight, and DA.^{305,306} In addition to these media, solvent systems based on aqueous solutions of acids, bases or salts such as phosphoric acid, LiSCN, NaOH/U, and KOH/U were reported to dissolve chitin.²⁹⁸ Although the base/U systems show great solvent capabilities, they require energy-consuming freezing/thawing cycles, which make them less suitable for industrial applications. For chitin, as for other polysaccharides, the development of solvent systems capable of solubilising a high load without changing the structural characteristics is essential for efficient and cost-effective use.

In this context, ILs are the main tool for the industrial exploitation of chitin. In fact, they are able to solubilise large quantities of chitin while minimising structural changes. For this reason, since the first report by Rogers et al. in 2001, numerous research papers, technical reports and reviews on this subject have appeared in the literature. Rogers and co-workers founded the company 525 Solution and more recently Mari Signum with the aim of obtaining and using chitin for industrial applications. However, which IL works best with respect to chitin dissolution is not entirely clear. In fact, even the literature values for the same ILs present inconsistencies. This discrepancy is undoubtedly due to the different types of chitin used and to the different operating conditions. As a result, although it is clear that dissolution of chitin in ILs is possible, an in-depth comparison is difficult. Nevertheless, some general considerations about the dissolution of chitin in ILs are possible to be advanced.

AILs are undoubtedly those capable of dissolving larger quantities of chitin, and among these, the imidazolium-based ones are the best performing media.³⁰⁷ The best result reported in the literature was obtained using [C₂C₁im]OAc, which solubilises 16 wt% of pure chitin at 100 °C in 19 h.³⁰⁸ Differently from what was observed for cellulose dissolution, where only the anion strongly influences the performance, for chitin the combined effect of cation and anion seems to be crucial and predominant over the contribution of the individual ion. For example, for [AC₁im]-based ILs, bromide shows higher solvent capacity than chloride (4.8-5 wt% for Br⁻³⁰⁹ compared with 0.5 wt% for Cl⁻³¹⁰), whereas for the [C₂C₁im]-based ILs, only chloride is able to dissolve chitin (10 wt%).³¹¹ It is also interesting to note that ILs containing a dimethylphosphate anion, which have a high solvent capacity towards cellulose, do not act as solvent in the case of chitin.³¹⁰ By analysing the solubilisation performance of various ILs for different types of chitin, Shamshina identified and ranked by increasing ability 5 ILs: [AC₁im]Cl < [C₄C₁im]Cl < [C₂C₁im]Cl < [C₄mim]OAc < [C₂C₁im][OAc].³¹² In selecting the proper IL to be used in a process scale-up, the solvent power is certainly important, but the cost of the medium and its recyclability are likewise relevant. Acetate ILs are very efficient in the dissolution of chitin, but they are also costly and raise some concerns about their recyclability due to the low thermal stability. Nevertheless, Sun et al. reported that [C₂C₁im][OAc] can be efficiently recycled by using pervaporation systems without significant loss due to degradation.³¹³

Optimising the cost of ILs remains an open issue and the use of "statistical mixtures" of ILs OAc instead of pure ILs has been proposed as a way to considerably reduce their cost and synthetic impact. In fact, the 2:1:1 mixture of $[\text{C}_2\text{C}_1\text{im}]\text{OAc}:[\text{C}_2\text{C}_2\text{im}]\text{OAc}:[\text{C}_1\text{C}_1\text{im}]\text{OAc}$ can be sourced at low cost, without passing through halide intermediates, from the reaction between glyoxal, formaldehyde, a combination of ethyl- and methylamine and acetic acid at 70 °C for a total time of 13 h.³¹⁴ This mixture was found to have a solvent power toward lignin 1.6 times higher than the corresponding pure ILs.³¹² Interestingly, $[\text{HN}(\text{CH}_2\text{CH}_2\text{OH})_3]\text{OAc}$ and $[\text{HN}(\text{CH}_2\text{CH}_2\text{OH})_3]\text{MeSO}_3$, which were unable to dissolve chitin when tested in pure form, became working solvents for this polysaccharide even at room temperature when mixed with ethylenediamine (EDA) at different molar ratios (between 1:0.5 and 1:2).³¹⁵ These two latter systems presumably represent examples of eutectic mixtures capable of dissolving chitin.

The literature about the use of DESs for chitin dissolution is far less vast than that for ILs. The first work in this area was published by Prasad et al. in 2013³¹⁶ and describes that cholinium chloride:thiourea (ChCl:thiourea, 1:2) dissolves 9 wt% of α -chitin in 6 h of heating at 100 °C. In this study, the dissolution capability of ChCl:U (1:2), cholinium bromide:U (ChBr:urea, 1:2), ClChCl:U (1:2), and BethCl:U (1:4) using conventional heating, microwave and ultrasound were tested. The authors claim that the use of DES was favourable compared to ILs due to their lower cost and lower toxicity.³¹⁶ Although DESs are often less expensive than the majority of ILs, any generalisation regarding their low toxicity should be avoided. Thiourea is indeed a toxic compound (category 4) displaying carcinogenicity (category 2), reproductive toxicity (category 2) as well as long-term aquatic hazard (category 2)³¹⁷ and therefore DESs containing thiourea are likely toxic. Thiourea was used as HBD also in the preparation of DESs with ILs as HBA ($[\text{AC}_1\text{im}]\text{Cl}$, $[\text{C}_4\text{C}_1\text{im}]\text{Br}$, $[\text{C}_2\text{C}_1\text{im}]\text{Cl}$, $[\text{C}_2\text{C}_1\text{im}]\text{Br}$).³¹⁸ Although this class of solvents is capable of solubilising chitin (2-5 wt%), their real "deep eutectic nature" was not verified. Therefore, the work of Prasad et al.³¹⁶ is the only study concerning the dissolution of chitin in DES which however does not investigate the dissolution mechanism nor the rheological properties of the solution. Moreover, their investigation only highlights the decrease of the molecular weight of the regenerated chitin, while no effect on DA was observed. In contrast, the literature available on chitin dissolution in ILs provides information on the solubilisation mechanism, the characteristics of the polymer in solution and the effects of the dissolution process on chitin structure. These studies, which have been reported in several papers^{319–321} and reviews,^{298,322} will not be discussed in detail in this critical review.

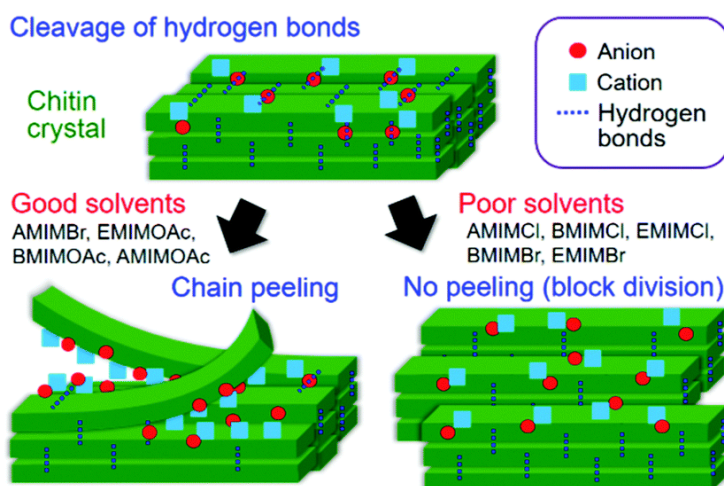


Fig. 23 Dissolution mechanism of chitin crystal models in imidazolium-based ILs.³¹⁹

As a general rule, inter- and intramolecular hydrogen bond networks need to be destroyed for chitin dissolution (Figure 23). For ILs, as in the case of cellulose dissolution, a correlation between the α and β Kamlet-Taft parameters and the ability to solubilise chitin was observed. Shimo et al.³¹⁵ found that only ILs with β values > 0.5 , typically attributable to basic anions, were able to dissolve chitin. Conversely, the α value which is ascribable to the cation nature seems to be less important. These findings, which are surely valid for the ILs under consideration, were in conflict with what was previously reported for ILs and especially with what experimentally observed for DESs. Indeed, ChCl:EG and ChCl:Gly, which display β values > 0.5 (0.57 and 0.52 respectively),³²³ were unable to solubilise chitin. These inconsistencies indicate that the dissolution mechanism is a rather complex process, which cannot be correlated solely to acidity or basicity of the IL's ions.

The number of publications describing the use of ILs in chitin technology is substantially larger than that concerning DESs. The main reason for this trend is time-related, as the first reports involving ILs were from 2001,³²⁴ while as mentioned above the first study about the same use of DESs was published 12 years later.³¹⁶ In addition, the limited number of DESs capable of dissolving chitin and the rather low maximum load reached strongly limited the use of DESs in all applications which require the solubilisation of this polysaccharide. Therefore, applications such as wet- and electrospinning,^{325–327} preparation of hydro and ionogels,^{328,329} production of porous chitin microbeads,³³⁰ membrane fabrication³³¹ as well as enzymatic and chemical transformation of chitin in homogeneous phase^{332–336} are at the moment prerogative only of ILs. On the other hand, DESs are mainly used in the preparation of nanofibres³³⁷ and nanocrystals^{338,339} through the exploitation of the acidity of the HBD component, which leads to the degradation of the amorphous part of chitin and leaves the crystalline portions intact.

Essentially, ILs are used in processes where chitin requires solubilisation, whereas DESs are used in processes where chitin merely needs to be swelled but not solubilised. This is in line with a similar trend already observed for cellulose, despite DESs possessing a higher solvent capability towards chitin. The process wherein this different behaviour is most evident is the "pulping" of chitin, where ILs and DESs act in an opposite fashion. Indeed, chitin can be extracted through two different approaches: i) selective dissolution of the biopolymer, which allows for its separation from the inorganics and protein fractions by filtration, ii) chemical "erosion" of the inorganic fraction and simultaneous solubilisation/degradation of the protein portion, which permits recovery of the chitin without prominent modification of the chemical structure. Both alternatives are valid and can be followed depending on the end use of the extracted chitin. By using ILs, it is possible to selectively solubilise chitin and then recover it by precipitation, spinning or directly by conversion into the product of interest. Alternatively, the use of DESs is more suitable for the second approach since, by judicious selection of HBA and HBD, it is possible to decompose the inorganic and protein fraction, which are consequently removed. Using DESs would allow raw chitin to be obtained at an overall lower cost. An interesting approach that has not yet been investigated to date is the combined use of DESs and ILs in chitin pulping. Indeed, the use of acid DESs in the pretreatment would allow for the inorganic part (mainly CaCO_3) to be effectively removed and the protein part to be degraded. This approach would be particularly interesting in the treatment of 'hard', highly mineralised biomasses (e.g. crab shells) with a high CaCO_3 content. The resulting material, highly enriched in chitin, would contain part of the degraded protein fraction and could only be considered 'technical

grade chitin'. To further purify this chitin, making it suitable for instance for biomedical use, the consecutive selective dissolution in ILs followed by filtration could be pursued. This process would be particularly suitable in terms of efficiency and cost-effectiveness, as it exploits the synergistic effects of DESs and ILs while maximising their benefits and minimising their drawbacks.

5.7. Beyond dissolution and fractionation performances

5.7.1 Recycle of ILs and DESs

A critical aspect which needs to be considered for a proper evaluation of impact and potential of a given new medium is its recovery and reuse. In the case of ILs, the recycle at the end of a process has always been deemed as a mandatory step to counterbalance their high costs. However, the recycling step is nowadays of fundamental importance for whatever application and media, irrespective of economic evaluations, in view of the zero waste production goals. Practically, disposal of the medium should be considered the last resort, rather than the option of choice when designing a process. Recycling should be evaluated both in terms of energy consumption of the process and of wt% and quality of the medium recovered. These parameters quantify the ability of a medium to be inexpensively used in consecutive cycles while retaining the initial performance.

Most works which deal with this subject both for ILs and DESs describe these solvents' performances on different cycles, while in depth analysis of energy costs and quality of the medium recovered are less studied. In the case of ILs, a few different recycling options have been analysed and the results are summarized in dedicated reviews.^{340,341} Conversely, limited data have been gathered thus far for DESs and further investigations are needed.³⁴² It is also worth stressing that some reports on DESs recycling could be hidden in the literature on account of misleading titles, as it is the case for the pressure driven membrane processes, nanofiltration, reverse osmosis and pervaporation studies performed on ChCl:EG (1:2) by Haerens et al.³⁴³ In the case of biomass treatment, the addition of antisolvents to DES-lignin/hemicellulose mixtures to precipitate the polysaccharides and recover the DES after evaporation of water/ethanol/acetone is the strategy described in most reports. The DES thus obtained is often used in following runs and performances are evaluated without an in-depth study of the DES composition, possible degradation and of the presence of contaminants. Indeed, low molecular weight molecules soluble in the DES are likely to be extracted from the biomass and contaminate the DES.

Overall, it is not trivial to state which of the two media (ILs or DESs) is the most amenable to recycling. This question is further complicated by the fact that the application of interest plays an important part in assessing the medium's performance. Within the biomass treatment research area, a comparison could be attempted according to the works by Chang et al, who reported the recovery both of an IL ([AC₁im]Cl)³⁴⁴ and a DES (ChCl:EG, 1:2)³⁴⁵ by electrodialysis. The authors treated the same biomass (*Eucalyptus globulus* wood) and then studied the recovery with the two media. The schematic electrodialysis process both for IL and DES is reported in Figure 24.

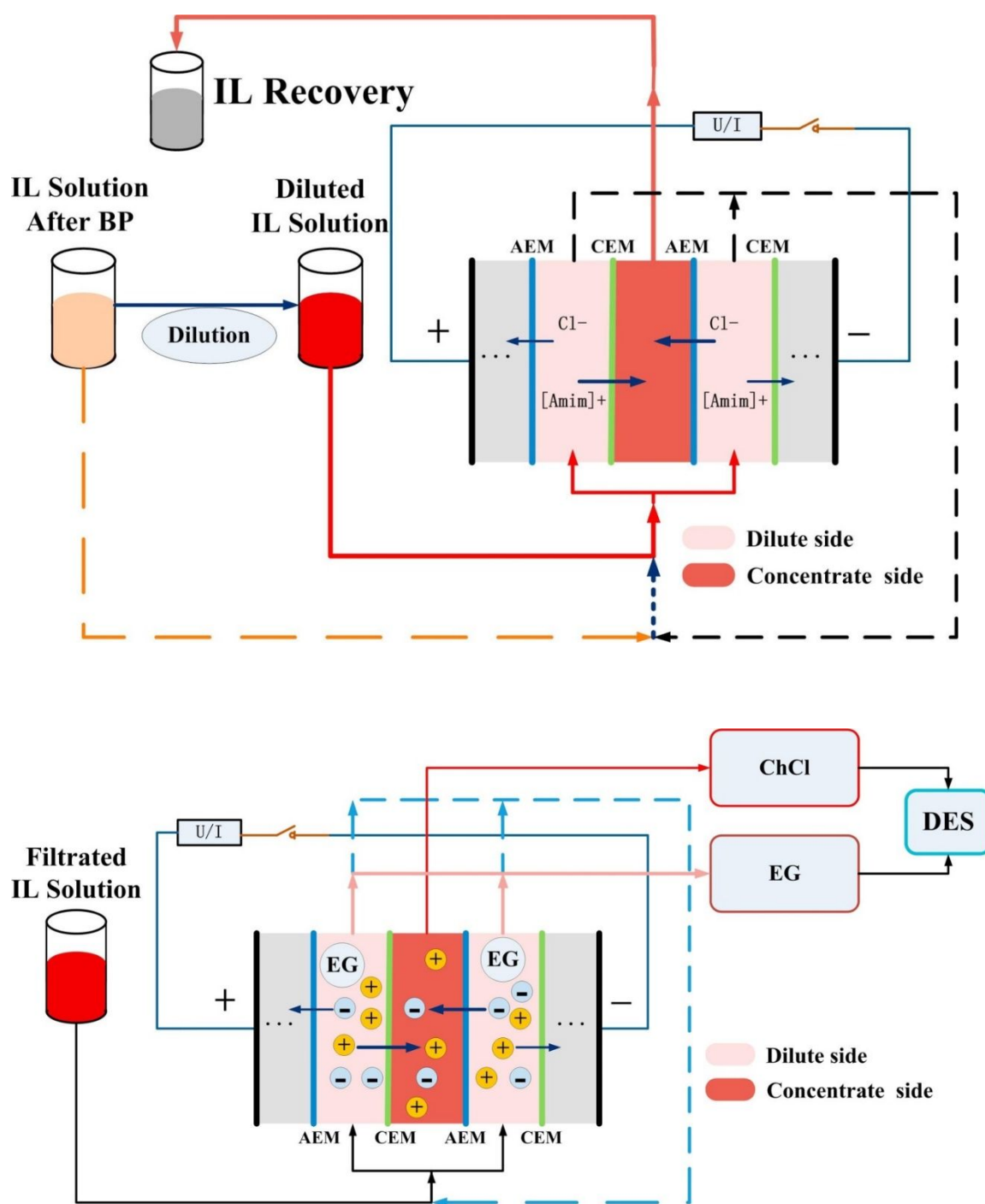


Fig. 24 IL (top) and DES (bottom) recovery process with electrodialysis treatment.

The main difference between the two schemes stems from the nature of the two media. In particular, the presence of the non-charged species (EG) in the DES case determines the separation of the HBA and HBD during the electrodialysis process and the need to reconstruct the DES system at the end of the process before its further use.

For $[\text{AC}_1\text{im}]\text{Cl}$, the recovery ratio was 66-71% with a specific energy consumption as high as 429-467 g/KWh in a single electrodialysis treatment (at 15 V applied voltage and 5 L/min solution flow rate). An improvement of performances was observed with the semi-continuous process, where the recovery ratio increased to 93% with a slight drop of the specific energy consumption in the case

studied. For ChCl:EG (1:2), under the same applied voltage and solution flow rate, recovery ratios of 84% for ChCl and of 96% for EG with the specific energy consumption lower than 300 g/KWh were obtained in a single electrodialysis treatment. In the semi-continuous process, enhancement of ChCl recovery was observed (up to 92%) together with a slight decrease of the EG recovery and beneficial effects on the energy consumption when compared to the single recovery process. On the basis of these results, one could be tempted to claim ChCl:EG (1:2) as a more convenient solvent than [AC₁im]Cl in the biomass treatment, at least from the recovery perspective.

However, it is worth stressing again that focusing on a partial picture could bring to wrong conclusions. Indeed, the two biomass processes are substantially different: the DES treatment is carried out on a lower biomass loading and more importantly it is combined with a previous hydrothermal treatment. This latter removes hemicellulose and low molecular weight molecules, thus preventing DES contamination and making its recycling easier (especially in the case of the non-charged EG). Even more worrying is the observation that the recovered IL and DES act differently in repeated runs. While recycled [AC₁im]Cl provided almost the same efficiency of the fresh IL, the reconstituted ChCl:EG (1:2) displayed a worse efficiency than the fresh DES.

In conclusion, it is difficult to have a clear-cut indication of which systems is more amenable to efficient recycling, even when the same technique and biomass is employed. Further investigations and more innovative approaches in the recycling of both ILs and DESs are needed for designing industrially feasible processes based on these non-conventional media.

5.7.2. Techno-economic analysis

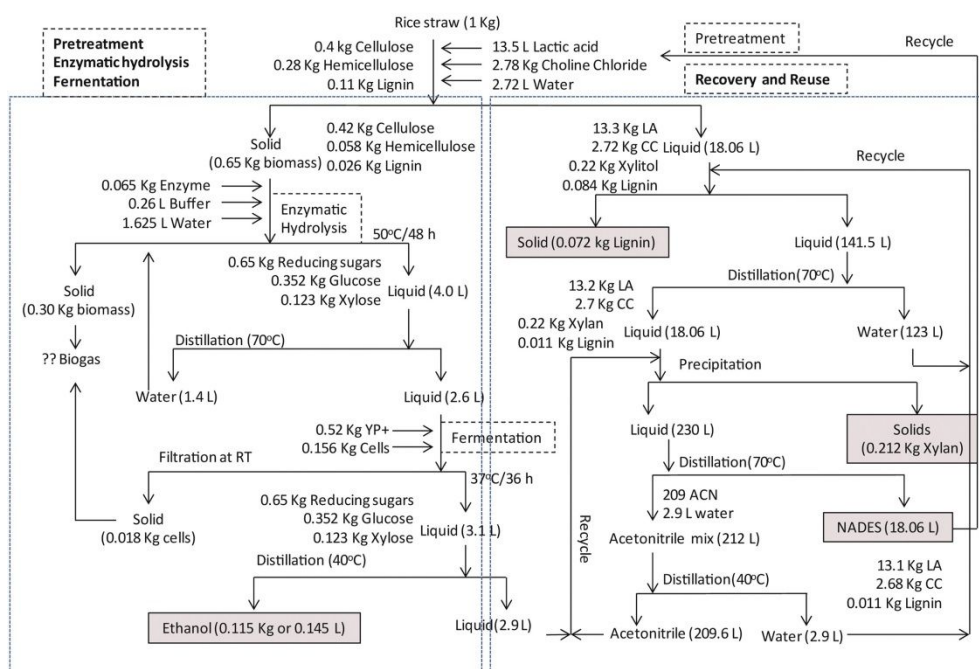
The main criticism directed at ILs is related to their cost, which hampers their real industrial applicability. The high price of ILs mostly derives from the synthetic efforts required for their synthesis and purification. Conversely, and in contrast to ILs, one of the most praised DESs features is the ease of preparation, which just involves the mixing of the two DES components. However, these oversimplified views need to be contextualized, as the end-application of interest should be considered as well. ILs have already reached relatively widespread application at the industrial level and are nowadays exploited in several commercial processes.²²⁰ The widespread use especially of imidazolium ILs is witnessed by the fact that some of them obtained the REACH registration by Proionic.²¹³ Although it is reasonable and commonly accepted that the price of ILs would drop substantially with the advent of large-scale production, the preparation of these materials is undoubtedly a critical aspect, which needs to be considered carefully. Optimization of the synthetic strategies is still a matter of intense research and advancement within this specific area will contribute to the overall reduction of cost and environmental impact of ILs preparation. This aspect was recently highlighted in a report on continuous counter-current in a mixer-settler strategy used in the context of a metathesis reaction.³⁴⁶ It is also worth highlighting the publication of an analysis focused on cost and impact of ILs considering both production and use.³⁴⁷ On the basis of per-weight efficiency of the desulfurized-fuel process, the use-cost of [C₄C₁im]BF₄ obtained via traditional metathesis reaction became comparable to acetonitrile and lower than DMF, while the halide-free mixture of imidazolium ILs prepared through the statistical reaction of formaldehyde, amines and glyoxal, became the cheapest option.

It is also worth stressing that in the case of PILs, the synthetic strategy is as simple as the one commonly employed for DESs and requires a simple mixing step, as mentioned above. An illustrative

case is that reported by Hallett et al.,³⁴⁸ who carried out a techno-economic evaluation of PILs used in biomass processing, namely $[\text{N}_{2220}]\text{HSO}_4$ and 1-methylimidazolium hydrogen sulfate $[\text{HC}_{1\text{im}}]\text{HSO}_4$. The cost prices were estimated as $\$1.24 \text{ Kg}^{-1}$ and $\$2.96\text{--}5.88 \text{ Kg}^{-1}$, respectively, with the cost of the former comparing positively with the price of acetone and ethyl acetate. This comparative analysis was further refined by also taking into account the indirect costs such as human health, resources and environmental impact.³⁴⁹ $[\text{N}_{2220}]\text{HSO}_4$ was found to have the lowest total cost followed by acetone, as an example of a traditional solvent from fossil resources, and Gly, as a representative of solvents from renewable resources. Gly displayed the highest production cost due to the cost of its precursors (rapeseed oil and soybean oil) and considerably higher indirect costs than the other solvents analyzed in terms of human health and environmental impact. This work clearly emphasizes the importance of evaluating the cost of any chemical species from a wider perspective, where direct production costs, although fundamental, are just one of the many factors.³⁴⁹ Furthermore, in the context of the present ILs/DESs comparison, it is of interest to stress that Gly, which is one of the most commonly used HBD of NADESs, presents the highest total cost within the series.

Of the few papers dealing with techno-economic evaluations of processes involving DESs, three are related with the subject of this analysis.^{350–352} Specifically, these reports describe the treatment of rice straw and switchgrass either with $\text{ChCl}:\text{LA}$ or $\text{ChCl}:\text{EG}$ with 1 wt% of H_2SO_4 for the production of low molecular weight products. Two major conclusions can be drawn from these studies: a) the development of multi-product biorefineries should be targeted in view of profitable and sustainable processes instead of a single, high volume-low value compound and b) the biomass/DES ratio should be as high as possible to reduce the costs of solvents required for the recovery of the biomass fractions from the DES system and for the overall DES recycling. In the case studied, solid loadings were in the region of 10–27 wt%, which differ from the usual amounts tested in the vast majority of lab-scale studies reported in the literature to date for DESs. To further highlight the importance of the biomass/DES ratio on the overall reactors size and process costs of a DES-based biorefinery, and thus recommend paying attention to this parameter even at an early stage in an investigation, the comparison of the pretreatment process flow steps at 5 wt% and 10 wt% solid loading reported by Kumar et al.³⁵³ are summarized in Figure 25. The amounts of water and acetonitrile required for treating 1 Kg of rice straw increased from 53 to 123 liters and from 110 to 210 liters, respectively by halving the biomass loading.

Set-II: Pretreatment at 5% solids loading and hydrolysis at 25% solids loading



Set-IV: Pretreatment at 10% solids loading and hydrolysis at 25% solids loading

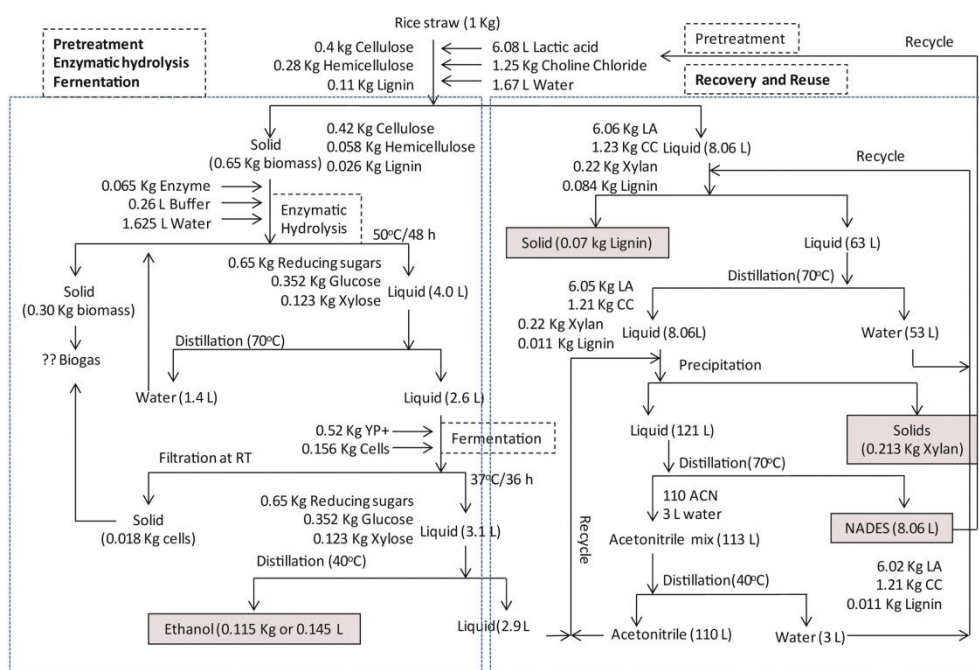


Fig. 25 Pretreatments process flow steps of 5 wt% (set-II, up) and 10 wt% (set-IV, bottom) solid loading, adjusted from reference ³⁵³.

In the above techno-economic analyses, the potential issues related to DES recycling and diminishing performances over time are almost completely overlooked. This is despite the problems reported by Morais et al.³⁵⁴ concerning the esterification of cellulose, degradation of xylan, and polymerization of LA using ChCl:LA (1:10) as medium and the drastic reduction in furfural production when the recycled DES is used, in the case of ChCl:EG (1:2) with 1 wt% of H₂SO₄.³⁵⁵ Therefore, further studies are needed to thoroughly unveil the actual cost contribution of DESs in biorefineries, beyond the simple cost of raw material for their initial preparation. In the case of ILs, a few more techno-

economic analyses of different processes have been carried out,³⁵⁶ which span from biogas upgrading³⁵⁷ and CO₂ capture,³⁵⁸ to production of fuel grade *tert*-butyl alcohol³⁵⁹ and synthesis of platinum nanoparticles.³⁶⁰

Within the specific theme of the review, Blanch et al highlighted already in 2011³⁶¹ how reduction of ILs cost, reduction of ILs loading and increase of ILs recycling were key areas to be tackled for increasing the profitability of a lignocellulosic ethanol biorefinery based on IL pretreatment. Furthermore, the authors studied the effect of selling lignin-derived products to reduce the minimum selling price of the ethanol product. Overall, the IL-based processes share the same issues of the DESs-based processes, with the additional concern of the IL price. The potential impact on profitability of the IL/biomass ratio, followed by the other criticalities mentioned above, was further corroborated by the analysis presented by Ferrari et al³⁶² for a biorefinery designed to transform sugarcane into ethanol. In this work, the biomass pretreatment process is carried out with a mixture of [H₃N(CH₂CH₂OH)]OAc and of [H₃N(CH₂CH₂OH)]OHex. Of note is also the recent comparative techno-economic analysis of *Eucalyptus globulus* wood pretreatment carried out either with [C₂C₁im]OAc or [Ch]OAc.³⁶³ In particular, the amount of water needed to remove residual IL from dissolved cellulose during the washing step, the effect on the subsequent enzymatic hydrolysis and the IL recycling step all indicate the possibility of lower operating costs for the imidazolium containing IL. Despite these findings, additional features such as the potential environmental footprints and the overall toxicity should be considered in future developments.

The most informative case study is, however, represented by the Ionosolv process and its development over time. Indeed, its evolution well exemplifies the potential of ILs in biomass pretreatment in conjunction with the need to thoroughly study each step and the necessity to devise or consider even hybrid options when solving problems or increasing efficiency. The Ionosolv process proposed by Hallet et al. is summarised in Figure 26 and is based on PILs. As mentioned previously, the cost of PILs is often comparable to and in some cases lower than conventional organic solvents.^{348,349} The first study on the Ionosolv process entailed the use of [N₂₂₂₀]HSO₄ plus 20 wt% of water at 120 °C and a 1:10 solid loading.³⁶⁴ This setting allowed for the complete dissolution of hemicellulose and of 85 wt% of lignin in the fractionation process of the grass *Miscanthus x giganteus*, leaving behind a cellulose rich pulp. Studies on the saccharification step and on the quality of the lignin recovered were also performed as well as an assessment of the recovery of the IL (ca. 98% for each cycle).³⁶⁴ The potential effect of inorganic salts brought in by the biomass on the IL quality was also investigated, an aspect often almost completely overlooked, and finally the presence of IL degradation products was ascertained. The preliminary techno-economic analysis identified the solid loading and water usage during lignin recovery as the critical aspects.

Intensification and diversification strategies and an in-depth analysis were then carried out to further investigate pro and cons of the Ionosolv process. In particular, the effect of higher loading (20 wt% solid loading), time, temperature³⁶⁵ as well as particle size and scaling up from 10 mL to 1 L³⁶⁶ were assessed. It is worth stressing that the scaling up required optimization of the washing protocols and agitator design, with the latter not required at the bench scale stage.

A different PIL, *N,N*-dimethylbutylammonium hydrogen sulfate, [N₁₁₄₀]HSO₄, was also employed in the Ionosolv process and was proved to be effective. It actually outperformed [N₂₂₂₀]HSO₄ in the

pretreatment of recalcitrant softwood pine with a remarkable 1:2 solid loading at 170 °C during 30 minutes.³⁶⁷

As a further possible variation, the hybrid combined Ionosolv-Organosolv strategy, which entails the use of a PILs, $[N_{2220}]HSO_4$ or $[N_{1140}]HSO_4$, and selected organic solvents (ethanol, butanol or acetone), was also explored in the pretreatment of two representative feedstocks, *Miscanthus* and pine.³⁶⁸ Beneficial effects were found in terms of higher loading, up to 1:2 solid loading with 60 wt% IL and 40 wt% ethanol at 120 °C, and lower energy consumption for the IL regeneration step, especially at high organic solvent concentration. Both aspects have direct implications for the economic profitability of the process.

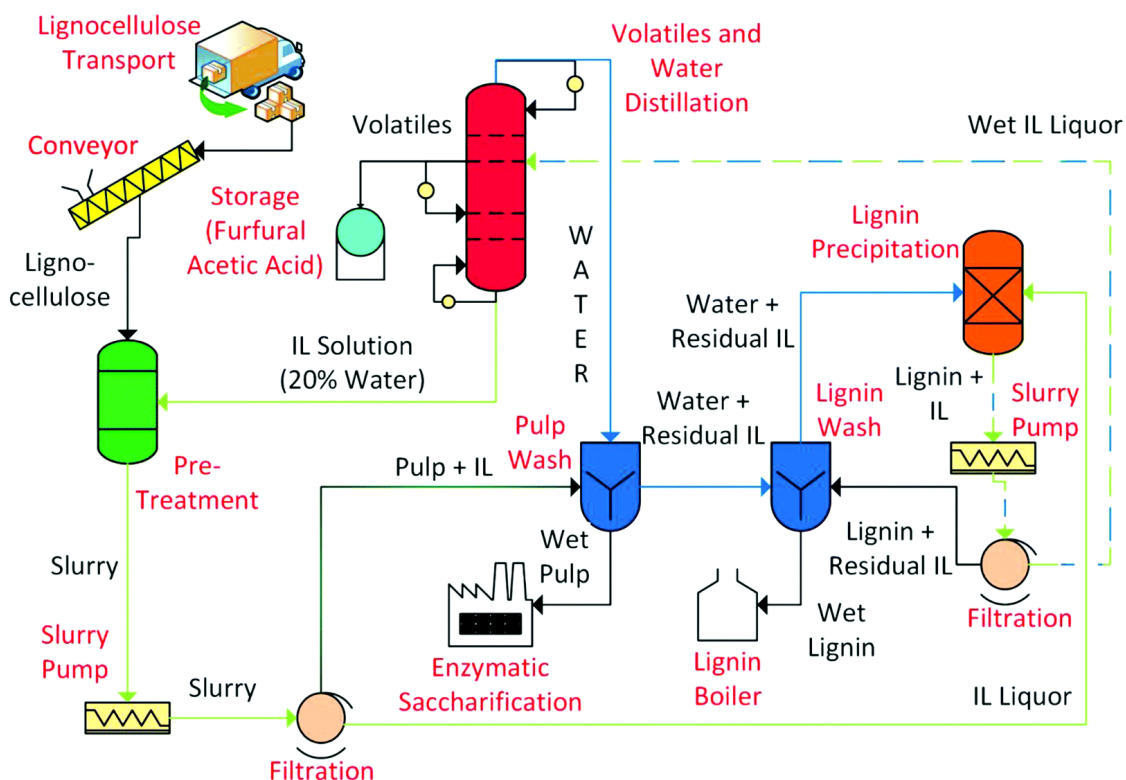


Fig. 26 Process flow diagram for the Ionosolv process taken from reference ³⁶⁴ .

The Ionosolv example thus highlights the need of an in-depth investigation of multiple variables before claiming the potential profitability of a biomass pretreatment/biorefinery process on the basis of limited lab-scale results. This important reminder must be kept in mind when assessing both IL-based and DESs-based processes.

6. Outlook and future perspective

The intention of this review is to highlight, without providing an exhaustive survey of the present literature, that there is no winner or loser between ILs and DESs, and none should even be searched. The possible cation-anion combinations for preparing ILs is almost limitless and the number of new mixture of compounds that yield DESs systems is constantly increasing (hydrophobic DESs were disclosed in recent years too).³⁶⁹ It is, thus, logical that some systems will be better suited for a given application and others for a different one. It could even be possible that one among the mixtures of

ILs (which could also give rise to DES systems in some cases), ILs with co-solvents/water, DESs with water or ILs-HBD mixtures will be the ideal matching medium for a given application, considering the whole life cycle of the process. Ultimately, since ILs and DESs are distinct classes of solvents, each one of them with distinct properties, they should be seen as options to choose from in the design and development of environmentally friendly process, both as alternatives to volatile organic solvents rather than alternatives to each other.

The dynamic research in the DESs field in recent years should avoid repeating the same mistakes made initially in the ILs area, in which a deleterious tendency to generalise behaviours and properties observed for specific cases took place. This generated frustration and misplaced expectations of ILs over time. It seems nowadays that DES research area is following the same path by claiming their superiority over ILs. The urge to define DESs as a viable alternative to ILs probably arises from the need to overcome the initial misleading classification of DESs as a new family of ILs. The main aim of this review is to defend the DESs field from future “scientific recriminations” by placing them in the correct place within the green media context. This should pave the way for an objective evaluation of their pro and cons, under specific situations.

From the same point of view stems also the need to reevaluate eutectic solvents (ESs) and low melting mixtures (LMMs) as other alternative media to VOCs endowed with the same potential as DESs and ILs to achieve more sustainable processes and systems. Nowadays, the term “DES” has an undeniable appeal within the scientific community and far too often new eutectic systems are just presented as DESs although their phase diagrams is not known. It is thus desirable that researchers working in the field will encourage a further understanding of the nature of DESs, through thermodynamic studies and the molecular and laboratorial scale, which will help to categorize the actual nature of the systems. Ultimately, it will always be impossible to decide *a priori* if a DES is more suited for a certain application than an IL, an ES or an LMM or even a bio-based solvent.

What is also clear from the above discussed examples is that further investigation is needed both at the fundamental and the applied levels. In the former case, it is not a surprise that the ILs field is more mature given that for instance the first studies of polysaccharides dissolution date back to 1934,³⁷⁰ while for DESs, some features still need to be defined such as the amount of water tolerated by each system. On the other hand, process-oriented studies which involve for instance techno-economic evaluations, system recycling efforts and life cycle assessments are urgently needed for both ILs and DESs and would provide invaluable data for further conscious development.

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Acronyms list

Acronyms	Name
[AC ₁ im]Cl	1-Allyl-3-methylimidazolium chloride
[BEMPH]NTf ₂	2-tert-Butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorinium bis(trifluoromethane)sulfonimide
[C ₁₀ C ₁ IM]FeCl ₄	1-Decyl-3-methylimidazolium tetrachloroferrate
[C ₁₀ C ₁ IM]NTf ₂	1-Decyl-3-methylimidazolium bis(trifluoromethane)sulfonimide
[C ₁₀ C ₁ IM]PF ₆	1-Decyl-3-methylimidazolium hexafluorophosphate
[C ₁₀ C ₁ im]Phe	1-Decyl-3-methylimidazolium phenolate
[C ₁₀ DABCO]Br	1-Decyl-1,4-diazabicyclooctane bromide
[C ₁₄ C ₁ im]Cl	1-Tetradecyl-3-methylimidazolium chloride
[C ₁₄ Qn]Br	1-tetradecylquinolinium bromide
[C ₁₆ C ₁ im]Cl	1-Hexadecyl-3-methylimidazolium chloride
[C ₁₆ C ₁ im]NTf ₂	1-Hexadecyl-3-methylimidazolium bis(trifluoromethane)sulfonimide
[C ₁ C ₁ im]OAc	1,3-Dimethylimidazolium acetate
[C ₁ C ₄ mor]Br	4-Butyl-4-methylmorpholin-4-ium bromide
[C ₁ C ₄ mor]CF ₃ SO ₃	4-Butyl-4-methylmorpholin-4-ium trifluoromethanesulfonimide
[C ₁ C ₄ mor]N(CN) ₂	4-Butyl-4-methylmorpholin-4-ium dicyanamide
[C ₁ C ₄ mor]NTf ₂	4-Butyl-4-methylmorpholin-4-ium bis(trifluoromethane)sulfonimide
[C ₂ C ₁ im]Br	1-Ethyl-3-methylimidazolium bromide
[C ₂ C ₁ im]Cl	1-Ethyl-3-methylimidazolium chloride
[C ₂ C ₁ im]DMP	1-ethyl-3-methylimidazolium dimethyl phosphate
[C ₂ C ₁ im]OAc	1-Ethyl-3-methylimidazolium acetate
[C ₂ C ₁ im]Phe	1-Ethyl-3-methylimidazolium phenolate
[C ₂ C ₂ im]OAc	1,3-Diethylimidazolium acetate
[C ₂ DABCO]Br	1-Etyl-1,4-diazabicyclooctane bromide
[C ₄ C ₁ im]BF ₄	1-Butyl-3-methylimidazolium tetrafluoroborate
[C ₄ C ₁ im]Br	1-Butyl-3-methylimidazolium bromide
[C ₄ C ₁ im]Cl	1-Butyl-3-methylimidazolium chloride
[C ₄ C ₁ im]OAc	1-Butyl-3-methylimidazolium acetate
[C ₄ C ₁ im]Phe	1-Butyl-3-methylimidazolium phenolate
[C ₄ DABCO]Br	1-Butyl-1,4-diazabicyclooctane bromide
[C ₆ C ₁ im]OAc	1-hexyl-3-methylimidazolium acetate
[C ₆ C ₁ im]Phe	1-hexyl-3-methylimidazolium phenolate
[C ₆ DABCO]Br	1-Hexyl-1,4-diazabicyclooctane bromide
[C ₈ C ₁ im]Cl	1-Octyl-3-methylimidazolium chloride
[C ₈ C ₁ im]OAc	1-Octyl-3-methylimidazolium acetate
[C ₈ C ₁ im]Phe	1-Octyl-3-methylimidazolium phenolate
[C ₈ DABCO]Br	1-Octyl-1,4-diazabicyclooctane bromide
[C ₉ (C ₁ im) ₂][NTf ₂] ₂	1,9-Bis(3-methylimidazolium-1-yl)nonane bis(trifluoromethane)sulfonimide
[Ch]Arg	Cholinium arginate
[Ch]Gl	Cholinium glycolate
[Ch]Lev	Cholinium levulinate

[Ch]Lys	Cholinium lysinate
[Ch]Mal	Cholinium malonate
[Ch]OAc	Cholinium acetate
[DBNH]OAc	1,5-diaza-bicyclo[4.3.0]non-5-enium
[DBNH]OPr	1,5-diazabicyclo[4.3.0]non-5-enium propionate
[DBUH]OAc	1,5-diaza-bicyclo[4.3.0]undec-5-enium acetate
[H ₂ N(CH ₂ CH ₂ OH) ₂]OAc	Bis(2-hydroxyethyl)methylammonium acetate
[H ₂ N(CH ₂ CH ₂ OH) ₂]OBut	Bis(2-hydroxyethyl)methylammonium butanoate
[H ₂ N(CH ₂ CH ₂ OH) ₂]OEt	Bis(2-hydroxyethyl)methylammonium etanoate
[H ₂ N(CH ₂ CH ₂ OH) ₂]OiBut	Bis(2-hydroxyethyl)methylammonium isobutyrate
[H ₂ N(CH ₂ CH ₂ OH) ₂]OPent	Bis(2-hydroxyethyl)methylammonium pentanoate
[H ₃ N(CH ₂ CH ₂ OH)]OHex	2-Hydroxyethylammonium hexanoate
[H ₃ N(CH ₂ CH ₂ OH)]NO ₃	2-Hydroxyethylammonium nitrate
[H ₃ N(CH ₂ CH ₂ OH)]OAc	2-Hydroxyethylammonium acetate
[H ₃ N(CH ₂ CH ₂ OH)]OBut	2-Hydroxyethylammonium butanoate
[H ₃ N(CH ₂ CH ₂ OH)]OF	2-Hydroxyethylammonium formate
[H ₃ N(CH ₂ CH ₂ OH)]OPr	2-Hydroxyethylammonium propanoate
[HC ₁ im]Cl	1-Methylimidazolium chloride
[HC ₁ im]HSO ₄	1-Methylimidazolium hydrogen sulfate
[HC ₁ im]OAc	1-Methylimidazolium acetate
[HC ₁ im]OEt	1-Methylimidazolium etanoate
[HC ₁ im]OF	1-Methylimidazolium formate
[HC ₁ im]OPr	1-Methylimidazolium propanoate
[HC ₄ im]HSO ₄	1-Butylimidazolium hydrogen sulfate
[HN(CH ₂ CH ₂ OH) ₃]MeSO ₃	Tris(2-hydroxyethyl)methylammonium methanesulfonate
[HN(CH ₂ CH ₂ OH) ₃]OAc	Tris(2-hydroxyethyl)methylammonium acetate
[HN(CH ₂ CH ₂ OH) ₃]OBut	Tris(2-hydroxyethyl)methylammonium butanoate
[HOC ₂ C ₁ im]Cl	1-hydroxyethyl3-methylimidazolium chloride
[HOC ₂ C ₁ im]ClO ₄	1-hydroxyethyl3-methylimidazolium perchlorate
[HOC ₂ C ₁ im]N(CN) ₂	1-hydroxyethyl3-methylimidazolium dicyanamide
[HOC ₂ C ₁ im]NO ₃	1-hydroxyethyl3-methylimidazolium nitrate
[HOC ₂ C ₁ im]NTf ₂	1-hydroxyethyl3-methylimidazolium bis(trifluoromethane)sulfonimide
[HOC ₂ C ₁ im]PF ₆	1-hydroxyethyl3-methylimidazolium hexafluorophosphate
[mDBN]DMP	5-methyl-1,5-diazabicyclo[4.3.0]non-5-enium dimethylphosphate
[mTBDH]NTf ₂	7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-enium bis(trifluoromethane)sulfonimide
[mTBDH]OAc	7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-enium acetate
[N ₁₁₄₀]HSO ₄	N,N-dimethyl-N-butylammonium hydrogen sulfate
[N ₂₀₀₀]Gl	Ethylammonium glycolate
[N ₂₀₀₀]NO ₃	Ethylammonium nitrate
[N ₂₀₀₀]OAc	Ethylammonium acetate
[N ₂₀₀₀]OF	Ethylammonium formate
[N ₂₂₀₀]OF	Diethylammonium formate
[N ₂₂₂₀]HSO ₄	Triethylammonium hydrogensulfate
[N ₂₂₂₂]Cl	Tetraethylammonium chloride
[N ₃₃₃₃]Cl	Tetrapropylammonium chloride

[N ₄₀₀₀]OF	Butylammonium formate
[N ₄₄₄₄]Br	Tetrabutylammonium bromide
[N ₄₄₄₄]Cl	Tetrabutylammonium chloride
[N ₅₀₀₀]OF	Pentylammonium formate
[N ₈₈₈₀]TfO	Trioctylammonium triflate
[P ₄₄₄₀]MsO	Tributylphosphonium mesilate
[P ₄₄₄₀]NO ₃	Tributylphosphonium nitrate
[P ₄₄₄₀]NTf ₂	Tributylphosphonium bis(trifluoromethane)sulfonimide
[P ₄₄₄₀]TfO	Tributylphosphonium triflate
[P ₄₄₄₄]Br	Tetrabutylphosphonium bromide
[P ₈₈₈₀]TfO	Tetraoctylphosphonium
[Ph ₃ NH]TfO	Triphenylammonium triflate
AILs	Aprotic Ionic Liquids
AL	Alkali lignin
BA	Boric acid
Bet	Betaine
BetHCl	Betaine hydrochloride
ChBr	Cholinium bromide
ChCl	Cholinium chloride
ChI	Cholinium Iodide
ChOAc	Cholinium acetate
ClChCl	Chlorocholinium chloride
CNC	Cellulose nanocrystalline
CNF	Cellulose nanofiber
DA	Degrees of acetylation
DMAc	N,N-Dimethylacetamide
DMSO	Dimethyl sulfoxide
EG	Ethylen glycol
G	Guaiacyl lignin subunit
Gly	Glycerol
GVL	γ-valerolactone
H	p-Hydroxyphenyl lignin subunit
H ₂ SO ₄	Sulfuric Acid
HFIP	Hexafluoroisopropanol
Im	Imidazole
LA	Lactic acid
MA	Malic acid
NMMO-H ₂ O	N-methylmorpholine-N-oxide monohydrate
OA	Oxalic acid
OES	Organic electrolyte solutions
PA	Propionic acid
PEG-200	Polyethylene glycol-200
PILs	Protic Ionic Liquids
pTSA	p-toluenesulfonic acid
S	Syringyl lignin subunit
U	Urea

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