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Can Multiple Ions in an Ionic Liquid Improve the Biomass Pretreatment Efficacy?

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ABSTRACT

Over the last few decades, efforts to transition the global production of fuels and chemicals towards renewable carbon feedstocks has accelerated. A large portion of these efforts have focused on valorization of one of the most abundant renewable carbon sources, lignocellulose. Pretreatment of lignocellulose is the first critical step in this process. In this study, novel ionic liquid (IL) systems consisting of multiple ions known to be effective at biomass pretreatment were tested on woody and grassy biomass. Molecular simulations and experimental results established the synergistic advantages of combining specific individual components in these systems. For pine (woody) biomass, pretreatment with the combination of imidazolium, cholinium, acetate, and lysinate ions achieved 80% glucose and 70% xylose yields at high biomass loading. For sorghum biomass, an IL system comprising of cholinium, lysinate, and palmitate ions not only enabled a 98% glucose yield but was also found to be biocompatible in a one-pot configuration, producing the biofuel precursor bisabolene using an engineered strain of the yeast *Rhodosporidium toruloides*.

KEYWORDS

lignocellulosic biomass, pretreatment, one-pot, double salt ionic liquids, Rhodosporidium toruloides, pine, sorghum, biofuel, bisabolene

Continuous efforts have been made over the last decades to transition from the use of fossil fuels as sources of chemicals and energy to renewable carbon resources. Among these, carbon-neutral lignocellulosic biomass including human-inedible agricultural, forest, and herbaceous lignocellulose has been identified as a promising alternative for both chemicals, biomaterials, and energy.[1] The main constituents of lignocellulosic biomass, namely cellulose, hemicellulose, and lignin, are held together by covalent and strong hydrogen bonds forming a complex matrix recalcitrant to enzymatic or chemical depolymerization.[2] The development of cutting-edge technologies to deconstruct this rigid structure into readily processable components is therefore necessary to overcome the structural complexity of the biomass and promote its efficient utilization. One of the most essential steps in this process is biomass pretreatment. Several chemical pretreatment methods involving hot water, dilute acid, ionic liquid, alkali, organic solvent (organosolv), ammonia fiber expansion, etc. have been demonstrated.[3-5]

Pretreatment with ionic liquids (ILs, salts possessing organic cations with a melting point below 100 °C)[6] is an attractive approach owing to their outstanding ability to dissolve, fractionate, and convert biopolymers.[7-9] In particular, IL-based pretreatments are known to reduce cellulose crystallinity, enhance surface accessibility to (bio)catalysts, and facilitate lignin removal.[7,8,10-14] Research efforts from our group and others have established that both the cation and anion in the IL are active agents in the pretreatment process. For example, acetate ions ($[\mathrm{Ace}]^-$) have been observed to enhance the accessible surface area and porosity in herbaceous and woody biomass without any significant delignification.[10-11] In another study, the alkyl chain length and the aromaticity of the IL cations were found to have a profound effect on the solubility of the biomass biopolymers, while the anions affect the intra- and intermolecular interactions in these biopolymer(s).[8,12-13] Notably, imidazolium-based ILs have been widely investigated for biomass pretreatment and were found to be most effective on various types of biomass. However, their high cost and limited compatibility with enzymes and microorganisms commonly used for lignocellulose deconstruction and conversion have led to the use of cholinium cation as a greener and more economical alternative.[14] It is important to highlight that these IL mixtures are distinct from the IL-solvent mixtures, where usually a room temperature IL is diluted with a non-ionic solvent (e.g. water) for the pretreatment of biomass.[15-16] This study is focused on the former.

Interestingly, minimal efforts have been made to integrate the respective advantageous properties of various ions in one IL to afford a clean, viable, energy-efficient, and economical biomass pretreatment method. For example, the dissolution of Avicel® cellulose in a mixture of imidazolium-based ILs was recently investigated using two mechanistically similar anions, namely chloride and acetate.[17] The solubility of cellulose was improved when compared to the pure ILs, probably as a result of synergy among anions with distinct characteristics. These promising results laid the foundation for this study using multi-component ionic liquids tailored for pretreatment of specific types of lignocellulose.

Herein, we employed 1-ethyl-3-methyl-imidazolium acetate ([C_2mim][Ace]) and cholinium lysinate ([Ch][Lys]) in combination for the pretreatment of pine (*Pinus radiata*), a challenging softwood biomass. A 20 wt% biomass loading of pine was suspended in a 1:1 (w/w) mixture of [C_2mim][Ace] and [Ch][Lys] to afford a total IL loading of 80 wt%. The pine-IL slurry was then heated at 140 °C for 3 h. Pine was also pretreated with the individual pure ILs as a control. Effective pretreatment of biomass with most ILs have been reported at temperatures between 120 and 160 °C,[7-8] and thereby we chose 140 °C for our experiments. The pretreated biomass was washed extensively with water to obtain IL-free pretreated pine solids. After washing, yields of solids corresponding to 81.4%, 77.1% and 77.2% were recovered from pretreatments using [C_2mim][Ace], [Ch][Lys], and 1:1 mixture of ILs, respectively (see Figure S1).

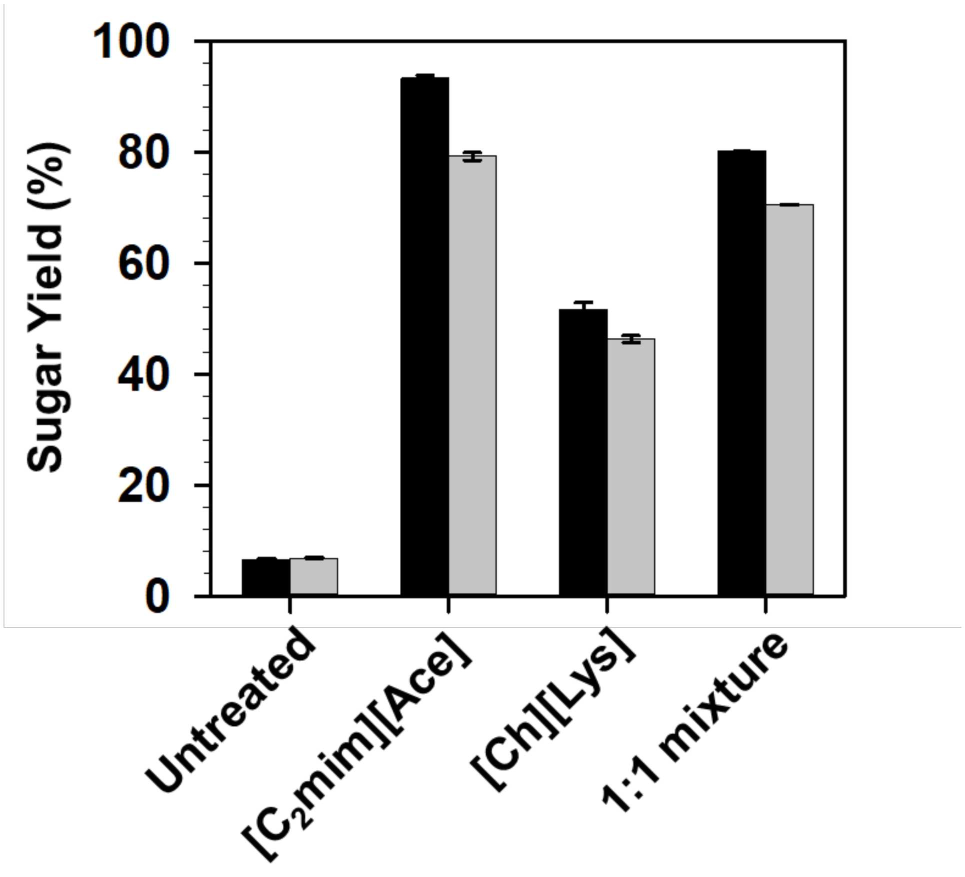
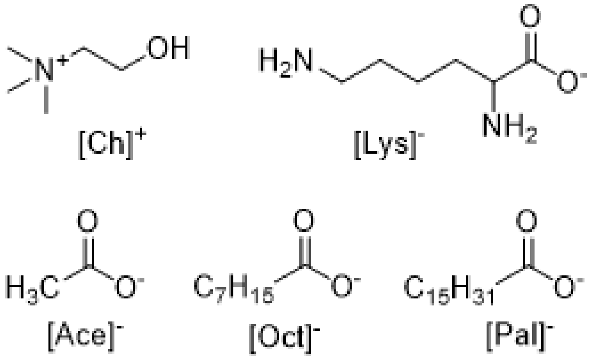


Figure 1. Glucose (black) and xylose (gray) yields after enzymatic hydrolysis of untreated or pretreated pine with 1-ethyl-3-methylimidazolium acetate ([C_2mim][Ace]), cholinium lysinate ([Ch][Lys]) and 1:1 (w/w) mixture of [C_2mim][Ace] and [Ch][Lys]. *Pretreatment conditions:* pine (20 wt%), IL (80 wt%), 140 °C, 3 h. *Saccharification conditions:* pine (5 wt%), 10 mg enzyme (CTec3:HTec3, 9:1 v/v) per g sorghum, 50 °C, 72 h.

The pretreatment efficacy was measured in terms of holocellulose digestibility using commercial enzyme cocktails (Novozymes Cellic® CTec3 and HTec3) and plotted as Figure 1. The enzymatic hydrolysis was carried out at a protein loading of 10 mg per g of biomass at 50 °C for 72 h. All IL pretreatments resulted in significantly faster saccharification rates compared to the untreated pine (6.6% glucose and 6.8% xylose). Consistent with previous reports, [C_2mim][Ace] could effectively pretreat softwood yielding 93.2% glucose and 79.2% xylose; possibly by enhancing the accessible surface area.10 [Ch][Lys], on the other hand, released only 51.6% and 46.3% glucose and xylose, respectively. These values are considerably lower than those typically obtained when using this IL with grassy biomass, demonstrating the importance of developing new approaches to deconstruct feedstocks such as pine.[18] Interestingly, 80.1% glucose and 70.5% xylose was obtained with a 1:1 w/w mixture of [C_2mim][Ace] and [Ch][Lys] under identical conditions. It must be highlighted that strong molecular bases are known to deprotonate acidic proton of imidazolium ILs forming carbenes and adducts,[19] which consequently render such ILs ineffective for pretreatment. This was not observed in our case when [C_2mim][Ace] was used in combination with a stronger IL base, [Ch][Lys].

The incorporation of multiple ions with known distinct pretreatment mechanisms in an IL paves the path to develop new strategies to boost the pretreatment efficiency while reducing the cost associated with the pretreatment step. In order to further explore the concept, here we use a unique tool called “double salt ionic liquids” (DSILs; systems containing three or more ions often possessing unexpected physicochemical properties), developed by the IL community.[20-21] In this study, we have synthesized cholinium ($[Ch]^+$)-based DSIL employing lysinate, acetate, octanoate ($[Oct]^-$), and palmitate ($[Pal]^-$) anions (Scheme 1), since the anions have been known to play a predominant role in biomass pretreatment.[8,10] Lysinate has been observed to selectively dissolve lignin during biomass pretreatment, while acetate is a stronger base known to effectively disrupt intermolecular H-bonding.[18] We anticipate palmitate (C_{16} acid-derived anion) to have higher lignin interactions due to the hydrophobicity of the longer alkyl chain. Also, the hydrophobicity that is being imparted to the IL might facilitate its recycling. Octanoate, a C_8 acid-derived anion is believed to possess properties unique to both acetate and palmitate.



Scheme 1. Cholinium cation in combination with various anions used in this study.

Cholinium-based ILs and DSILs were synthesized by acid-base reactions of cholinium hydroxide in methanol and appropriate acid or mixture of acids (see Supporting Information). [Ch][Lys], cholinium acetate ([Ch][Ace]), cholinium octanoate ([Ch][Oct]), and cholinium palmitate ([Ch][Pal]) were obtained by treating one equivalent of cholinium hydroxide with one equivalent of lysine, acetic, octanoic, and palmitic acids, respectively. For DSIL synthesis, cholinium hydroxide was reacted with a 1:1 mixture of two acids (added at once) with the total molar amount of the acids being equal to that of the hydroxide to yield DSILs with a general formula, $[Ch][A1]_{0.5}[A2]_{0.5}$, where A1 and A2 are the anions from two different acids. DSILs synthesized were cholinium lysinate acetate ($[Ch][Lys]_{0.5}[Ace]_{0.5}$), cholinium lysinate octanoate ($[Ch][Lys]_{0.5}[Oct]_{0.5}$), cholinium lysinate palmitate ($[Ch][Lys]_{0.5}[Pal]_{0.5}$), cholinium acetate octanoate ($[Ch][Ace]_{0.5}[Oct]_{0.5}$), cholinium acetate palmitate ($[Ch][Ace]_{0.5}[Pal]_{0.5}$), and cholinium octanoate palmitate ($[Ch][Oct]_{0.5}[Pal]_{0.5}$). The identity and purity of the synthesized ILs and DSILs was established by NMR, FT-IR, and thermal analysis (see Supporting Information).

COnductor like Screening MOdel for Real Solvent (COSMO-RS) calculations have been embraced on several occasions to explore the viability of a new solvent candidate in biomass pretreatment. Most of the previous studies have concluded that logarithmic activity coefficient ($\ln(\Upsilon)$) is a dominant parameter in predicting dissolution properties of the solute, while others have also considered the excess enthalpy (H^E) along with $\ln(\Upsilon)$.[22-23] Herein, we predicted the $\ln(\Upsilon)$ of lignin in various cholinium-based IL/DSIL to test the hypothesis through studying the intra- and intermolecular interactions between lignin and IL/DSIL (Figure 2). Typically, lower logarithmic activity coefficients ($\ln(\Upsilon)$) implies stronger interactions (i.e., higher dissolution) of the solute with the solvent. Based on these predictions, palmitate-containing ILs/DSILs were pronounced better pretreatment solvents as far as lignin dissolution was concerned.

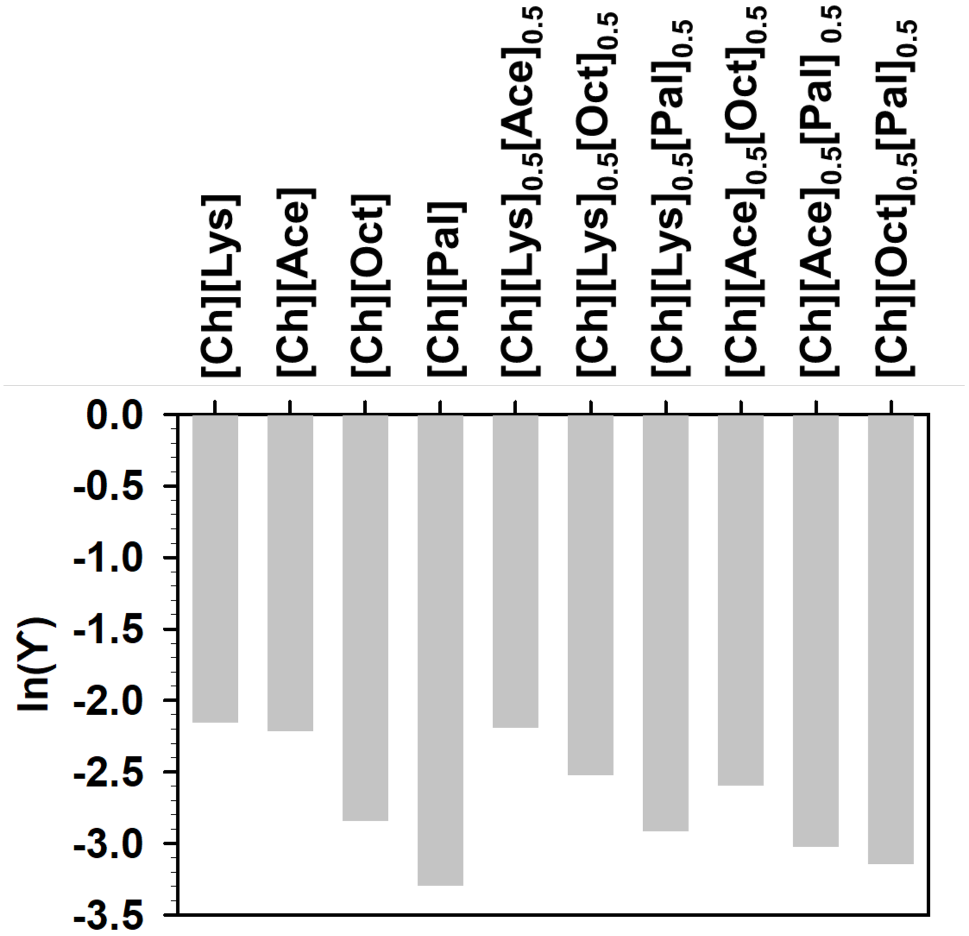


Figure 2. COSMO-RS predicted logarithmic activity coefficients (ln(ϒ)) of lignin in various cholinium-based ILs/DSILs.

A very recent study pointed out that the use of grass as a feedstock over woody biomass could potentially assuage the effects of global warming.[24] Considering this fact, the pretreatment effectiveness of the aforementioned DSILs and their respective individual ILs was evaluated on sorghum (*Sorghum bicolor*; grass) rather than pine. Sorghum was pretreated under the same conditions as pine; 20 wt% sorghum was mixed with IL (or DSIL) and heated at 140 °C for 3 h.

The resulting slurry was washed with water-ethanol (1:1 v/v) to remove IL/DSIL from the biomass.

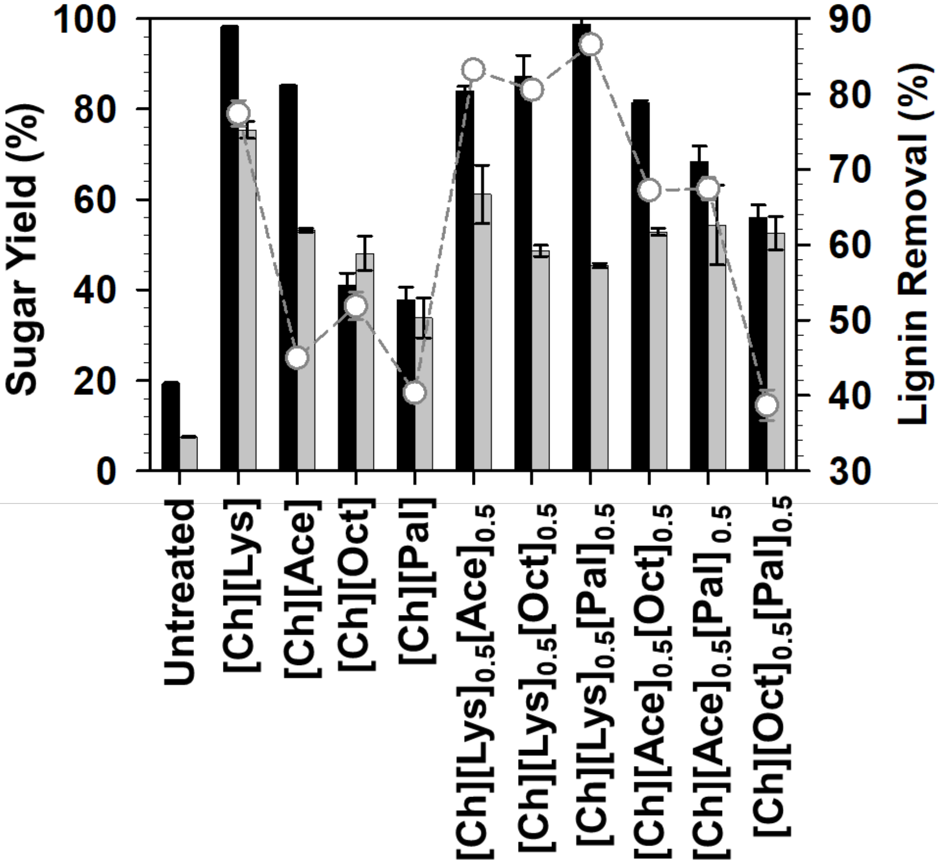


Figure 3. *Left Y-axis.* Glucose (black bars) and xylose (gray bars) yields after enzymatic hydrolysis of untreated or IL/DSIL pretreated sorghum. *Right Y-axis.* Lignin removal efficiency (○) after pretreatment with cholinium-based IL/DSIL. *Pretreatment conditions:* sorghum (20 wt %), IL/DSIL (80 wt%), 140 °C, 3 h. *Saccharification conditions:* sorghum (5 wt%), 10 mg enzyme (CTec3:HTec3, 9:1 v/v) per g sorghum, 50 °C, 72 h.

The change in holocellulose and lignin content was monitored before and after pretreatment to understand the effect of different anions (Figure S2). No glucan or xylan loss was observed for any of the DSIL under study. Significant lignin loss (>65%) was recorded for most of the DSIL systems with a maximum of 86.6% for $[Ch][Lys]_{0.5}[Pal]_{0.5}$ (Figure 3). Discrepancies were observed in the predicted and experimental values in terms of lignin dissolution. For instance, [Ch][Lys] and [Ch][Ace] were predicted to dissolve lignin similarly, however, [Ch][Lys] and [Ch][Ace] distinguished with 77.4% and 45% delignification, respectively, after pretreatment under identical conditions. The disagreement between the COSMO-RS predictions and experimental values could be accounted for by considering the viscosity of the employed ILs, a critical factor in biopolymer dissolution. An increase in viscosity is known to restrict mass transfer, hindering the solute dissolution.[25-26] Similarly, higher viscosities of [Ch][Oct] and [Ch][Pal] can explain the lower lignin removal efficiencies observed. The introduction of a second anion to form a DSIL improved the lignin removal capability through synergy. A 77.4% delignification degree achieved by [Ch][Lys] was promoted to 83.2%, 80.6%, and 86.6% by $[Ch][Lys]_{0.5}[Ace]_{0.5}$, $[Ch][Lys]_{0.5}[Oct]_{0.5}$, and $[Ch][Lys]_{0.5}[Pal]_{0.5}$, respectively. Remarkably, up to 49% enhancement in delignification was achieved for acetate-based DSILs containing octanoate or palmitate as second anion when compared to single anion containing [Ch][Ace]. Overall, the extent of delignification was observed in the following order: $[Ch][Lys]_{0.5}[Pal]_{0.5}$ > $[Ch][Lys]_{0.5}[Ace]_{0.5}$ > $[Ch][Lys]_{0.5}[Oct]_{0.5}$ > [Ch][Lys] > $[Ch][Ace]_{0.5}[Pal]_{0.5}$ > $[Ch][Ace]_{0.5}[Oct]_{0.5}$ > [Ch][Oct] > [Ch][Ace] > [Ch][Pal] > $[Ch][Oct]_{0.5}[Pal]_{0.5}$.

Enzymatic hydrolysis of untreated and pretreated sorghum was performed (as described earlier) to evaluate the pretreatment efficiency of the cholinium-based IL/DSIL (Figure 3). Pretreatment with these systems accelerated the enzyme activity compared to untreated sorghum (19.2% glucose and 7.5% xylose). $[Ch][Lys]_{0.5}[Pal]_{0.5}$ afforded maximum glucose release among all DSILs. The glucose release from the pretreated sorghum was in the following order: $[Ch][Lys]_{0.5}[Pal]_{0.5}$ (98.8%) ~ [Ch][Lys] (98.2%) > $[Ch][Lys]_{0.5}[Oct]_{0.5}$ (87.2%) > [Ch][Ace] (85.2%) > $[Ch][Lys]_{0.5}[Ace]_{0.5}$ (84.0%) > $[Ch][Ace]_{0.5}[Oct]_{0.5}$ (81.4%) > $[Ch][Ace]_{0.5}[Pal]_{0.5}$ (68.4%) > $[Ch][Oct]_{0.5}[Pal]_{0.5}$ (56.0%) > [Ch][Oct] (41.1%) > [Ch][Pal] (37.9%). The efficiency of sugar release was correlated with the extent of lignin removal for most ILs/DSILs. Higher delignification correlated with greater cellulose digestibility in the case of lysinate or palmitate containing DSILs.

The mismatch of the polarity and hydrophilicity of lysinate and palmitate in $[Ch][Lys]_{0.5}[Pal]_{0.5}$ could be pivotal for the observed pretreatment efficiency as reported earlier for other systems.[27] However, this conclusion is speculative at this stage. Biomass pretreated with acetate-containing systems, on the other hand, resulted in better cellulose digestibility, although the delignification ability was poor. This could be a result of the reduced cellulose crystallinity and increased surface area accessibility effects caused by acetate-based systems. $[Ch][Ace]_{0.5}[Oct]_{0.5}$ or $[Ch][Ace]_{0.5}[Pal]_{0.5}$ containing soft and hard anions in single composition is especially interesting in this regard because it may potentially promote two distinct mechanisms of pretreatment. This paves the way for further studies on biomass pretreatment using DSILs with varied molar ratios or multiple ions to meet the desired properties and go beyond the shortcomings of IL.

A one-pot biomass conversion technology comprising pretreatment, enzymatic hydrolysis, and fermentation was recently introduced by our research group.[28-29] This process eliminates the need for a water-wash step after pretreatment providing noteworthy economic and environmental advantages. The one-pot process, however, requires a biocompatible ionic liquid such as [Ch][Lys] to enable facile downstream processing. We investigated the viability of using [Ch][Lys]$_{0.5}$[Pal]$_{0.5}$ in a one-pot process. To do so, 20 wt% sorghum was mixed with 10 wt% [Ch][Lys]$_{0.5}$[Pal]$_{0.5}$ and 70 wt% DI water and heated at 140 °C for 3 h. The pH of the slurry was 8.4 after the pretreatment and it was adjusted to 5 using concentrated HCl before performing enzymatic saccharification as previously described. 63.9% glucose and 42.3% xylose yields were obtained in a one-pot configuration with [Ch][Lys]$_{0.5}$[Pal]$_{0.5}$. The lower yields here could be attributed to diluted IL pretreatment (sorghum to IL 2:1 w/w) compared to IL pretreatment without water (Figure 3, sorghum to IL 1:4 w/w).

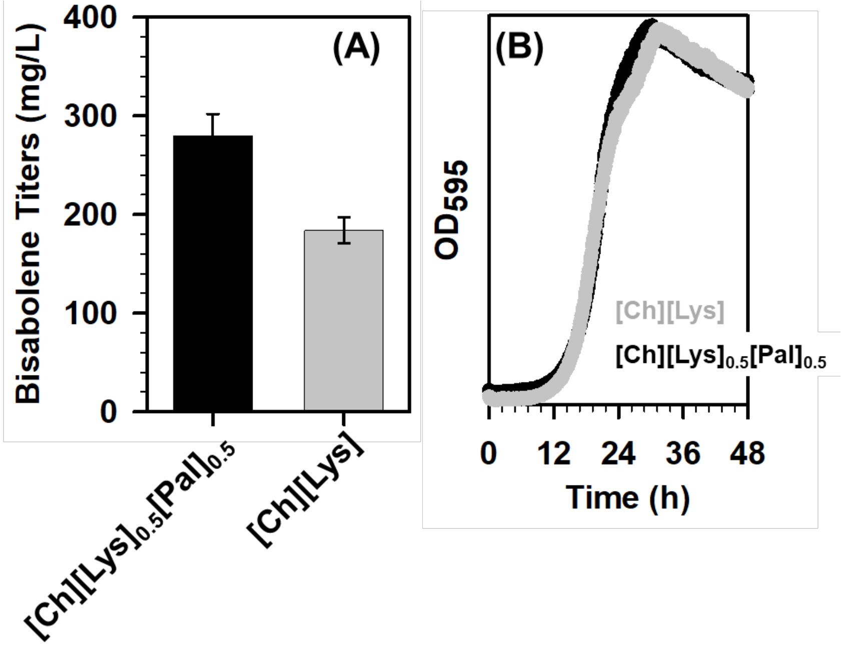


Figure 4. (A) Bisabolene titers after a 4-day incubation, and (B) growth curves of *Rhodosporidium toruloides* during a 2-day incubation in hydrolysate obtained using [Ch][Lys]$_{0.5}$[Pal]$_{0.5}$ (black) and [Ch][Lys] (gray) as pretreatment solvents.

Next, an engineered strain of the yeast *Rhodosporidium toruloides* able to produce the biofuel precursor bisabolene was cultivated in this hydrolysate and compared with a hydrolysate generated with [Ch][Lys]. The growth rates (μ) and substrate utilization yields obtained with [Ch][Lys]$_{0.5}$[Pal]$_{0.5}$ (μ = 0.16 h-1, 100% glucose and xylose utilization) were very similar to those obtained with [Ch][Lys] (μ = 0.16 h-1, 100% glucose and 96% xylose utilization), although the bisabolene titer was higher in the presence of [Ch][Lys]$_{0.5}$[Pal]$_{0.5}$ (Figure 4). These results indicate that the [Ch][Lys]$_{0.5}$[Pal]$_{0.5}$ hydrolysate obtained with a one-pot process can be used as cultivation media for *R. toruloides* and justify performing a more extensive characterization of the effects that DSILs may have over the biomass deconstruction process and the physiology of the biofuel producing strain.

In summary, we have developed unique DSIL systems consisting of ions with distinctive pretreatment mechanisms to improve the pretreatment efficiency of lignocellulose. The existing global knowledge on pretreatment will provide insights on how to develop and control the physicochemical properties of novel combinations of mechanistically different ions in an IL that are also compatible with the downstream processes. We would like to emphasize that this work demonstrates a single example of the large number of combinations that one can design and apply not only for fractionation of biomass but also for downstream processing, enabling an overall lower environmental and economic impact.

ASSOCIATED CONTENT

Supporting Information. Materials and methods, biomass compositional analyses, COSMO-RS details, IL/DSIL characterization (FT-IR, NMR, and thermal gravimetric analysis) are presented in the supplementary information along with this manuscript. The following files are available free of charge.

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Author Contributions

HC, JMG, and BAS conceived and supervised the project. AY, HC, HDM, and AR performed the experiments and analyzed the data. JGP recorded the NMR spectra. MM carried out the COSMO-RS calculations. HC and AY wrote the manuscript. All authors edited the manuscript. All authors have given approval to the final version of the manuscript.

Notes

The authors declare the following competing financial interest(s): HC, HDM, BAS, and JMG are named inventors on at least one related patent application. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. No writing assistance was utilized in the production of this manuscript.

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26. Also see Figure S3 in the Supporting Information.

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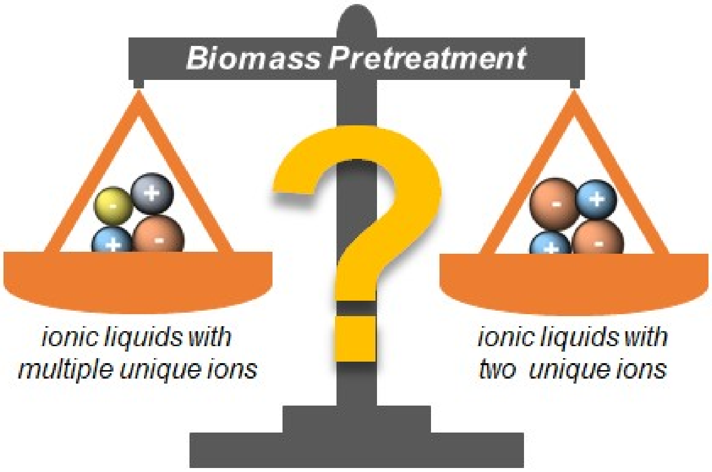

SYNOPSIS

Double salt ionic liquids facilitate enhanced pretreatment efficacies along with other advantages including biocompatibility and possibly cost efficiency.