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Review

Deep eutectic solvents for improved biomass pretreatment: Current status and future prospective towards sustainable processes

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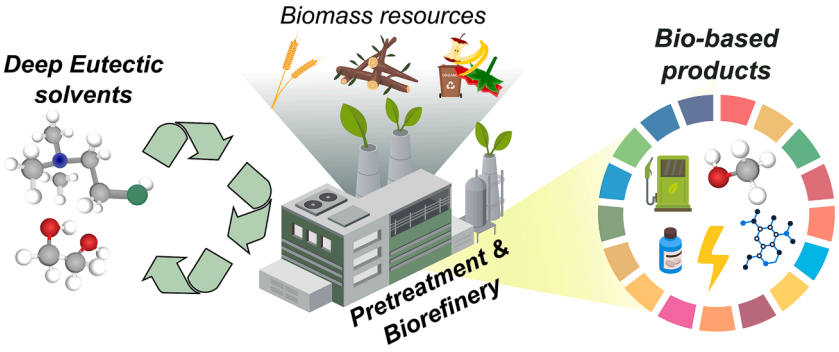
HIGHLIGHTS

- Pretreatment is a key step for biomass conversion.
- Deep Eutectic Solvents have shown compare favorably with other pretreatment methods.
- Biorefinery approach based on DES pretreated materials is reviewed.
- Tecno-economic and environmental issues dealing with DES application are considered.
- Updated state-of-the-art and barriers to improvement are discussed in this review.

GRAPHICAL ABSTRACT



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ABSTRACT

Pretreatment processes — recognized as critical steps for efficient biomass refining — have received much attention over the last two decades. In this context, deep eutectic solvents (DES) have emerged as a novel alternative to conventional solvents representing a step forward in achieving more sustainable processes with both environmental and economic benefits. This paper presents an updated review of the state-of-the-art of DES-based applications in biorefinery schemes. Besides describing the fundamentals of DES composition, synthesis, and recycling, this study presents a comprehensive review of existing techno-economic and life cycle assessment studies. Challenges, barriers, and perspectives for the scale-up of DES-based processes are also discussed.

1. Introduction

Transitioning to a sustainable economy requires deep transformations and alternatives replacing fossil resources with renewable ones. Biorefineries will be central players in converting biomass resources into bio-based products (energy, fuels, chemicals, and materials), contributing to climate change mitigation and reducing the dependency on unsustainable fossil resources. Hence, switching from

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first-generation biomass resources to higher generations is crucial to balance the pressure on food markets (Shams Esfandabadi et al., 2022) and move closer to achieving sustainable development goals.

Despite its versatility for multiple uses, biomass resources must be adequately treated to separate it into its main components, and make them available in acceptable forms and purity for subsequent conversion processes. Hence, the use of Deep Eutectic Solvents (DES) for biomass pretreatment in biorefinery schemes has received increased attention in the last decade (Kim et al., 2018a; Y. Wang et al., 2021a). The momentum builds from the idea that DES are deemed as alternative "green" and "environmentally friendly" solvents and more economical than other neoteric solvents such as ionic liquids (ILs) (Y. Wang et al., 2021a). Moreover, DES show desirable and unique properties. They can be easily prepared and customized for particular applications, show high-efficiency in various biomass treatments, and are cost-effective (Ijardar et al., 2022). They also can exhibit low toxicity and be recycled, offering a great alternative to improve the sustainability of biomass conversion processes (Procentese et al., 2015a). All these features make DES attractive in numerous applications focused on converting biomass resources into energy and valuable products through tailored extraction and pretreatment, physico-chemical and biochemical transformations (Mbous et al., 2017).

Notwithstanding previous research and reviews on the topic (Sharma et al., 2022; Hansen et al., 2021), this contribution presents a comprehensive appraisal of state-of-the-art knowledge of DES-based biomass pretreatment and refining, focusing on assessing technical feasibility, economic viability, and environmental implications at an industrial scale. First, a description of the composition, functional characteristics, and fractionation capabilities of DES is presented. Then, most relevant studies on the use of DES to produce renewable chemicals and recycling are explored and discussed. Techno-economic and life cycle assessment studies of DES-based biorefineries are next critically examined. Finally, the review highlights the benefits and challenges or gaps and identifies opportunities for future work. This review opens new perspectives on the research of DES-based biorefineries and provides background to promote the large-scale deployment of DES processes for improved biomass refining.

2. Composition and functional characteristics of DES

2.1. Basic composition

The term "eutectic mixture" refers to a combination of at least two components, i.e., Lewis or Brønsted acids and bases containing various anionic and/or cationic species besides other molecular compounds. These can act as hydrogen bond donor (HBD) and hydrogen bond acceptor (HBA) species, decreasing the lattice energy of the system and hence promoting a melting point depression lower than the values of the individual components. As explained by Martins et al., the use of the word "deep" is dependent on a significant negative deviation (ΔT_2) of the melting temperature of the mixture (Fig. 1 – blue line) when compared to the melting temperature of an ideal eutectic mixture (Fig. 1 – red line) (Martins et al., 2019). Therefore, phase diagrams and thermodynamic calculations must be considered to determine whether a eutectic mixture is "deep" or not. Although this distinction is essential to understand the physicochemical properties of DES systems, it is frequently less relevant from an application standpoint (Da Costa Lopes, 2021).

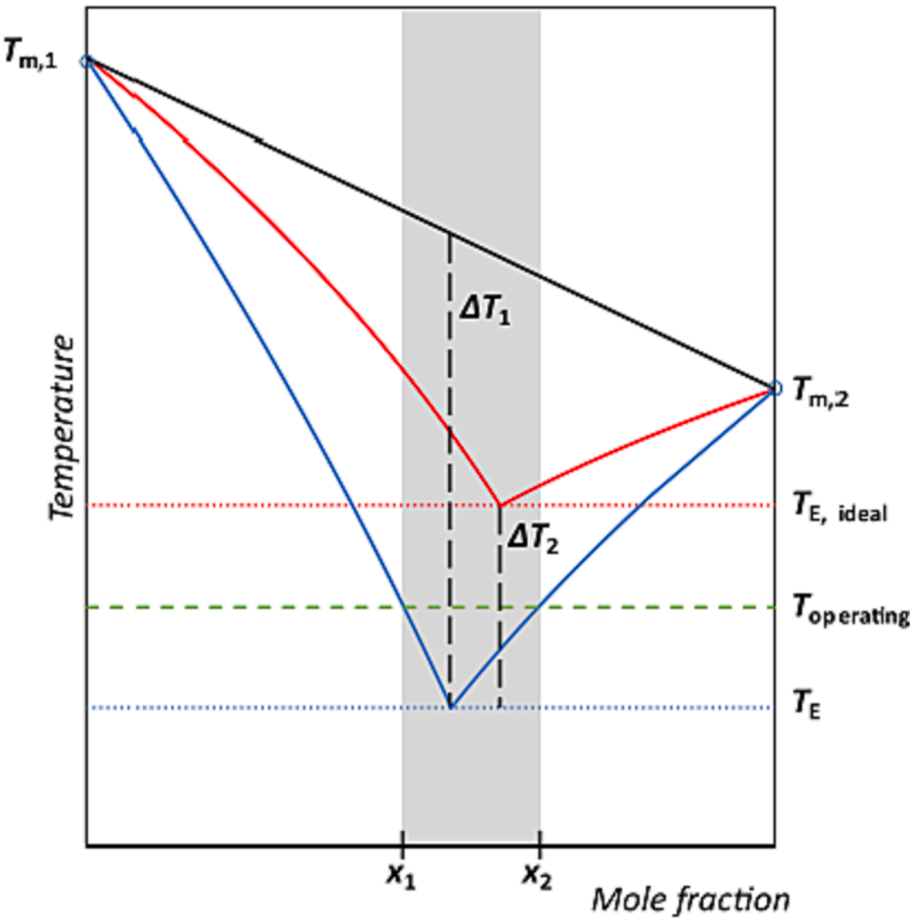

Fig. 1. Schematic representation of the comparison of the solid-liquid equilibria of an eutectic mixture (red line) and a deep eutectic mixture (blue line). Reprinted with permission from (Martins et al., 2019). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

DES can be described by the general formula $Cat^+X^-Y_z$. Cat^+ is typically an ammonium, phosphonium, or sulfonium ion; X^- is a Lewis base, typically a halide anion; Y is a Lewis or Brønsted acid; and z is the number of Y species interacting with X^- (El Achkar et al., 2021). Due to the plethora of compounds at variable ratios that can be successfully used in their formation, DES can be designed or tailor-made to a specific application. By changing the nature and molar ratios of the HBA and/or HBD, a wide range of physicochemical properties, including density, viscosity, acidity, and polarity, can be fine-tuned (Ijardar et al., 2022).

DES can be classified into five types based on the nature of the components used. Type I and Type II are usually prepared by combining a quaternary ammonium salt (e.g., choline chloride – ChCl) with a metal chloride (e.g., $ZnCl_2$) or a metal chloride hydrate (e.g., $FeCl_3{\cdot}6H_2O$), respectively. Type III usually relies on ChCl as HBA and amides, carboxylic acids, or alcohols as HBDs. Type IV is formed with a metal chloride hydrate and HBDs such as amides and polyols; while Type V comprises non-ionic components, especially molecular HBAs and HBDs (Abranches et al., 2019).

Apart from the DES categories mentioned above, other terminology can be adopted depending on the components' nature. DES can be prepared from substances found in nature, particularly primary metabolites, such as organic acids, amino acids, and sugars. In these particular cases, they are also called "natural deep eutectic solvents" (NADES or NDES) (Liang et al., 2020). More recently, hydrophobic deep eutectic solvents (HDES) composed of hydrophobic compounds, such as tetrabutylammonium bromide, menthol, thymol, and fatty acids as HBAs, together with long alkyl chain alcohols and carboxylic acids as HBDs have also been studied (Florindo et al., 2019a). Also, a new type of supramolecular deep eutectic solvent (SUPRADES), including as HBA cyclic oligosaccharides such as cyclodextrins, have been developed (El Achkar et al., 2020).

2.2. Physicochemical and functional properties of DES

As mentioned before, DES properties can be tailored for particular applications by choosing different HBA and HBD combinations and proportions. Yet, the structure and properties of individual components making up DES are not entirely responsible for the physicochemical properties of the final mixture. The nature of intermolecular interactions between HBA and HBD is also a crucial factor influencing the physicochemical properties (Rente et al., 2021). Hydrogen bonding has been reported as the major interaction between DES components. This is particularly true for Type V DES; however, when organic or inorganic salts are present in the DES (Types I to IV), ionic interactions are also relevant (Da Costa Lopes, 2021).

These intermolecular interactions, especially hydrogen bonding, greatly impact the viscosity of DES, a key physicochemical property of a solvent that determines its fluidity and mass transfer in a particular chemical process. For these reasons, low-viscosity solvents are frequently preferred. In this regard, viscosity is one of the main drawbacks of applying DES, since most of them disclose high viscosity values.

Another relevant physicochemical property of a solvent and essential for the design of a chemical process is density, which is related to the activity and molecular mobility of the solvent. DES densities are often temperature-dependent and have higher values than water (Biernacki et al., 2020). Furthermore, the density values are highly dependent on the structure of DES components and their molar ratio (Shafie et al., 2019).

Other physicochemical properties of DES can also vary significantly. For instance, due to their high viscosity, most DES tend to have poor ionic conductivities ($\kappa < 2$ mS cm^{-1} at room temperature). The surface tension of DES can also be affected by their viscosity, and the reported values generally vary between 35 and 75 mN m^{-1} at 25 °C, which are higher than most molecular organic solvents (Hansen et al., 2021). In addition to these properties, DES solvation properties can also change according to DES composition and need to be evaluated, normally by using solvatochromic probes or, more recently, through quantum chemistry and molecular simulation (Florindo et al., 2018).

Although DES-based technologies are promising for many applications, the challenges mentioned above still impede faster development and implementation. Increasing temperature and adding suitable co-solvents, such as water, have been suggested as promising strategies to overcome some challenges (Gabriele et al., 2019). Adding water may significantly alter the physicochemical properties of DES due to strong hydrogen bonding interactions which, in turn, can positively affect the DES ability to interact/solubilize target compounds (Nolasco et al., 2022).

Given a large number of possible HBA and HBD combinations, DES may disclose high to low biodegradability and toxicity. DES can be hazardous due to the precursor molecules, or synergistic interaction between the components can influence its toxicity and biodegradability (Radošević et al., 2015). Hence, the complete recyclability of the solvent becomes extremely important to reduce the environmental impact of the process, and particularly when DES exhibit toxicity or limited biodegradability (Da Costa Lopes, 2021).

3. Primary biomass fractionation processes based on DES

The tunable feature of DES and their delignification ability and hemicelluloses removal capability make them appealing to fractionate biomass. The following sections briefly discuss the fractionation ability of DES, including the removal properties of extractives and amorphous cellulose.

3.1. Extractives

Biomass extractives are non-structural biomass constituents that can be divided into water and ethanol-soluble fractions. Extractives can be inorganic cations, anions, and/or organic materials such as phenolic compounds, fatty acids, triglycerides, sterols, terpenic compounds, alkaloids, among others (Doménech et al., 2021; Gómez-Cruz et al., 2021a). From a biorefinery perspective, the interest in this fraction is growing for two main reasons. First, this fraction may contain high added-value compounds e.g., essential oils, pigments, bioactive compounds like some phenolic compounds and triterpenic acids, etc. (Doménech et al., 2021). Another reason is that their pre-extraction can improve subsequent polysaccharides recovery and their conversion into fermentable sugars, as some of these compounds (e.g., organic acids and phenolic compounds) are inhibitory products in the fermentation processes (Doménech et al., 2021). Therefore, DES could be applied to extract these compounds from biomass like olive- and grape-derived biomasses (Contreras et al., 2022, Contreras et al., 2020). For example, Pan et al., using ChCl:urea, observed a reduction of the content of extractives in the pretreated solids from rice straw, as it occurs with other lignocellulose components (M. Pan et al., 2017a). Yu et al. (2020) showed a reduction between 76 % and 91 % of water soluble extractives in preterated solids using ChCl-based DES pretreatment (ChCl:OA, ChCl:urea, ChCl:glycerol).

Nonetheless, the removal rate of extractives was not generally reported (or determined) in most of the studies overviewed in the present review. In other cases, the extractives were obtained with other solvents before DES pretreatment, e.g. (Li et al., 2019, 2017; Sun et al., 2022), which clearly highlights the need of further development of integrated strategies that would allow using DES for that purpose and to break the biomass recalcitrance through the fractionation of the structural components of biomass.

3.2. Lignin

In recent years, biomass delignification and lignin valorization has attracted increased attention. The application of DES for delignification (lignin extraction) favors decreasing cellulose crystallinity and

generates microvoids and cracks in the pretreated solids improving the downstream conversion (Ling et al., 2020). DES pretreatment can favor the penetration of DES from the cell lumen to the cell wall, making lignin accessible in the secondary wall (Hong et al., 2022). Notably, DES can be tailored based on their composition to increase lignin solubilization. Hence, ChCl, betaine, acetamide, urea, among others, have been tested as HBA with different types of HBDs (Bai et al., 2022; C. Y. Ma et al., 2021b). The combination of ChCl and organic acids has resulted in higher delignification rates than those achieved with other HBAs like betaine and acetamide (Ling et al., 2020). Moreover, ChCl is cheaper than other HBAs. A wide range of organic acids has been applied for delignification, such as formic acid (FA), acetic acid, glycolic acid, propionic acid, lactic acid (LA), tartaric acid, citric acid, oxalic acid (OA), levulinic acid, and their combinations (Bai et al., 2022; Fernandes et al., 2021; Ling et al., 2020; Lynam et al., 2017) (some relevant examples are in Table 1). For this type of DES, delignification takes place mostly by acidic clevage of β-*O*-4 lignin bonds yet with an important role of the HBA (da Costa Lopes et al., 2020). Furthermore, lignin solubilization has been correlated with the Kamlet–Taft parameters (in particular, α-value) and pKa values of the DES (Mankar et al., 2022). Other crucial factors for delignification using ChCl-based DES are the pretreatment severity and the characteristics of the HBD like polarity, alkyl chain length, capacity to form hydrogen bonds, and the molar ratio of HBD to ChCl (Xu et al., 2021).

In general, the pretreatment by DES requires relatively mild severe conditions to get effective delignification; i.e., up to 175 °C and between a few min to several hours when using microwave and conventional heating, respectively (Fernandes et al., 2021; Wang and Lee, 2021). This is an advantage compared to conventional pretreatments, such as organosolv-based delignification. The operating conditions are in the same range (Gómez-Cruz et al., 2021b; Gómez-Cruz et al., 2022), while harsher conditions are often applied when using other types of pretreatment, e.g., using dilute acids (~0.1 %) pretreatment, higher temperatures are required (>200 °C). In any case, using a relatively higher temperature in DES pretreatment improves DES activity and reduces viscosity and surface tension. This favors the fractionation of lignocellulosic components and the accessibility of protons to facilitate the release of lignin. Therefore, this factor and time should be tested for each DES and biomass type to aid effective solubilization and delignification, but limiting lignin condensation (Bai et al., 2022).

Water addition to DES media is another possibility to reduce viscosity and increase mass transfer (New et al., 2019), with similar performance up to ~20 % (H. Li et al., 2022a). Moreover, tuning aqueous DES solutions with catalytic mineral acids (e.g., HCl and H_2SO_4) or strong organic acids (e.g., *p*-toluenesulfonic acids), can also help to achieve high delignification yields at a temperature below 100 °C (Soares et al., 2021).

Lignin extraction using DES is considered a cost-effectiveness pretreatment with high or similar yields to conventional thermo-chemical pretreatments (Lynam et al., 2017; Mankar et al., 2022). Nonetheless, using acidic DES to solubilize lignin can lead to equipment corrosion effects during processing. Compared with other types of HBDs, Wang and Lee (2021) suggested that the use of glycerol (Gly)-based DES instead of organic acids can reduce this effect (Wang and Lee, 2021).

Table 1
Performance of different deep eutectic solvnts and conditions of biomass pretreatments expressed in terms of of removal of lignin, hemicelluloses and cellulose.

Feedstock	DES type	Molar Ratio	T (°C), t (min)	Lignin (%)	Hemice-llulose (%)	Cellulose (%)	Reference
Willow trunk	ChCl:LA	1:10	120 °C, 12 h	91.8	>70 %[1]	14.1[2]	(Li et al., 2017)
Coconut coir	ChCl:LA	1:4	150 °C, 20 min (MW)	82	NR	NR	(Mankar et al., 2022)
Poplar wood	ChCl:Gly	1:2	120 °C, 4 h	0.04	NR	NR	(Xia et al., 2018)
Poplar wood	ChCl:Gly:$AlCl_3{\cdot}6H_2O$	1:2:0.28	120 °C, 4 h	95.5	NR	NR	(Xia et al., 2018)
Maritime pine sawdust	ChCl:LA:TA	1:4:1	175 °C, 1 h	94.9	NR	NR	(Fernandes et al., 2021)
Maritime pine sawdust	ChCl:LA:TA	1:4:1	150 °C, 2 h	86.2	NR	NR	(Fernandes et al., 2021)
Maritime pine sawdust	ChCl:LA	1:5	150 °C, 2 h	81.3	NR	NR	(Fernandes et al., 2021)
Maritime pine sawdust	ChCl:LA	1:2	150 °C, 2 h	76.7	NR	NR	(Fernandes et al., 2021)
Rice straw	ChCl:acetic acid	1:3.6	126 °C, 2.5 h	83.1	82.1	NR	(Maibam and Goyal, 2022)
Pinus bungeana wood	ChCl:LA	1:10	120 °C for 8 min (MW)	42.8	74.7[1]	10.12	(Li et al., 2019)
Pinus bungeana wood	ChCl:LA	1:10	120 °C for 4 h	66.6	74.9[1]	19.02	(Li et al., 2019)
Mosso bamboo	ChCl:levulinic acid	1:2	120 °C for 2 h	28.9	–	–	(Ling et al., 2020)
Mosso bamboo	ChCl:malonic acid	2:1	160 °C, 10 min (MW)	11.7	69.4	44.5	(Ling et al., 2021)
Mosso bamboo	ChCl:succinic acid	2:1	160 °C, 10 min (MW)	6.2	86.4	44.8	(Ling et al., 2021)
Mosso bamboo	ChCl:OA	2:1	160 °C, 10 min (MW)	42	58.6	48.2	(Ling et al., 2021)
Raw poplar sawdust	$ZnCl_2$:LA	1:10	140 °C, 3 h	97.5	NR	NR	(Bai et al., 2022)
Oil palm fronds	ChCl:urea-30 vol% water	1:2	120 °C, 4 h	16.3	NR	NR	(New et al., 2019)
Bamboo residues	ChCl:oxalic acid	1:1	130 °C, 6 h	21.2	91.1	9.67	(N. Li et al., 2022b)
Poplar wood	Cholinium lysine:urea-5 wt% water	1:2	90 °C, 6 h	NR	35.3	62.13	(Wang et al., 2022)
Poplar wood	ChCl:EG mixed with 0–20 wt% water and 0–4 wt% NaOH	1:2	100–140 °C, 2–4 h	18.7–62.2	6.0–35.3[4] 26.7–93.3[5]	10.8–26.4	(H. Li et al., 2022a)
Miscanthus	ChCl:Gly	1:2	110 °C, 12 h	17.8	25.9	62.2	(Hassan and Mutelet, 2022)
Miscanthus	ChCl:EG	1:2	110 °C, 12 h	16.7	25	53.1	(Hassan and Mutelet, 2022)

ChCl, Choline chloride; EG, ethylene glycol; Gly, glycerol; LA, lactic acid; MW, microwave; NR, not reported: OA, oxalic acid; TA, tartaric acid. [1]Referred to hemicellulosic sugars. [2]Referred to glucans.[3]The yield was 59.2%.[4]Referred to xylans.[5]Referred to mannans.

However, acidic-ChCl based DES exhibit better performance in lignin removal (Mankar et al., 2022) related to higher acidity (Mankar et al., 2021).

Applying adequate antisolvents, part of the lignin can be isolated from the DES media (Fernandes et al., 2021; Provost et al., 2022). In some cases, the isolated lignin preserves most functional groups (Mankar et al., 2022), although it seems to depend on the delignification conditions and on the nature of the pristine biomass, considering the results reported by other authors (Bai et al., 2022; Fernandes et al., 2021).

3.3. Hemicelluloses

Removal of lignin is generally linked to hemicelluloses depletion, whose magnitude depends on the conditions applied. DES can effectively extract hemicelluloses from biomass (Liang et al., 2020; Morais et al., 2018). Under neutral conditions this can be achieved with limited depolymerization and deacetylation (Morais et al., 2018). Although acidic DES are more efficient on breaking ether and ester bonds between hemicelluloses and lignin to favor their solubilization (Maibam and Goyal, 2022), they can also induce extensive hemicelluloses degradation (Morais et al., 2020). Nonetheless, depending on the pretreatment purpose, DES can be designed to increase hemicellulose's solubilization and removal rate (compared to lignin) if required, as illustrated with some key examples in Table 1. For example, using cholinium lysine-urea based DES or ChCl:OA at mild temperature conditions, hemicelluloses were removed from poplar wood chips and bamboo residues to a greater extent than lignin (H. Li et al., 2022a; N. Li et al., 2022b; Wang et al., 2022). Higher removal rate of hemicelluloses from corncob was also achieved when betaine and histidine were mixed with water (Liang et al., 2020).

Notably, the heating technology applied in the pretreatment can also improve the efficiency of the fractionation processes. As an example, Li and coauthors combined microwave-assisted heating (MWAH) (120 °C, ~8 min) with ChCl:LA (1:10) on *Pinus bungeana* wood pretreatment, observing a significantly higher removal rate of hemicelluloses (75 %) compared to lignin (43 %) (Zulkefli et al., 2017). However, the results using conventional heating (120 °C, 4 h) were different (Table 1) (Li et al., 2019). Microwave irradiation efficiently heats the biomass-DES and creates 'hotspots' with an explosive action on the recalcitrant structure of lignocellulose, causing rapid dissolution of lignin and xylan. Hence, MWAH was highly efficient in removing non– or low-substituted xylan and synergistically MWAH-DES solubilized high-substituted xylan and lignin. However, in other cases, the hydrolysis of this polymer hinders its recovery from the pretreatment liquor (Liang et al., 2020; Wang et al., 2022).

3.4. Cellulose

Cellulose presents intense cohesive energy that prevents the dissociation and reorganization of the hydrogen bonding and its solubilization in DES. For example, ChCl can stabilize the DES-cellulose system due to forming a strong hydrogen bonding network (Mankar et al., 2021).

Therefore, most studies using DES take advantage of the removal of lignin and hemicelluloses by acidic DES for fractionation (see reviews by (Mankar et al., 2021; Wang and Lee, 2021)), but there are some exceptions. For example, ChCl combined with glycerol was preferred vs urea and EG to increase *Miscanthus* biomass fractionation towards cellulose isolation, providing a 38.2 % cellulose-rich fraction with 68 % purity (Table 1) (Hassan and Mutelet, 2022). According to the authors this was related to the lower acidity and polarity of glycerol compared to the other HBDs, which favored the solution to remove amorphous cellulose. Temperature also influenced the biomass fractionation with maximum cellulose recovery, grade, and regeneration rates around 107 °C. In this line, several studies have shown that amorphous cellulose can be released from herbaceous biomass using DES to different extents depending on the DES type and conditions, along with hemicelluloses or the ensuing sugars and lignin (Okoufo et al., 2022; Yu et al., 2020). This fact has been exploited, for example, to loosen the fiber structure of ramie for nanofibrilation combining ChCl-based DES pretreatment and ball milling (W. Yu et al., 2019b).

4. Production of renewable chemicals from biomass using DES

4.1. High value extractable compounds

DES have been employed to recover a wide range of added-value extractives components from biomass such as antioxidants, pigments, and bioactive compounds with pharmacological potential (Abdallah et al., 2022; Fernández-Prior et al., 2020; Lazzarini et al., 2022). Moreover, the extraction of these compounds can be performed before subsequent pretreatment steps; reducing the effects of contamination of the major biomass fractions or they can be degraded and/or lost in downstream biomass operations, which generally implies high-severity conditions. The extraction of these compounds is attractive when looking for target molecules to formulate "clean label" ingredients with antioxidant, color, or functional properties. In this case, NADES are especially attractive due to their natural origin and biocompatible formulations that can be directly used in food, pharmaceutical, and cosmetic ingredients (Abdallah et al., 2022). This also opens the possibility to directly apply NADES-based extracts in product formulations without the need for intensive purification steps to separate extracted compounds from NADES.

Different DES combinations have been applied to recover added-value compounds, including the combination of ChCl and betaine with organic acids, urea or carbohydrates; carbohydrates combined with organic acids; and mixtures of carbohydrates (Alam et al., 2021; Fanali et al., 2020; R. Wang et al., 2021a) (Table 2).

The use of ternary DES (e.g., ChCl:levulinic acid:N-methyl urea) has also revealed successful results when an extraction target is a diverse group of phenolic compounds with different polarities (Xu et al., 2019). The effect of polarity can be explained by the rule "like dissolves like", meaning that DES with moderate polarity will solubilize weak and medium polar phenolic compounds (Xu et al., 2019). The water content in DES can be adjusted to modulate these properties and to change the polarity index to render higher extraction efficiency if required. Since hydrogen bonding interactions between the DES with the hydroxyl groups of phenolic compounds favor solubilization (Che Zain et al., 2021), high water contents can impair the interactions between the DES and the target compounds and, in turn, reduce the extraction yield (Fanali et al., 2020; Rico et al., 2021). Furthermore, it was demonstrated that polymeric phenolic compounds, such as tannins with high industrial value (Neto et al., 2020a), can be more efficiently extracted using quaternary eutectic solvents composed of ChCl, glycerol, ethanol and water (Neto et al., 2020b). This DES extraction process can still be improved, in terms of extraction time reduction, yield improvement and selectivity through the combination of DES with microwave irradiation heating (Neto et al., 2022).

DES can also be applied to extract less polar compounds, like carotenoids and triterpenoids from different type of wastes, for example, combining ChCl, tartaric acid and methanol (instead of water) as co-solvent (Koutsoukos et al., 2019), ethyl acetate:ethyl lactate mixture (Lazzarini et al., 2022) and hydrophobic DES based on natural terpenes (Silva et al., 2020) (Table 2).

4.2. Reducing sugars

To recover reducing sugars, biomass pretreatments based on DES can be mainly addressed through lignin and/or hemicelluloses fractionation. Meanwhile, the cellulose-rich solid is separated by filtration (or centrifugation) from the liquor, which will contain the solubilized fractions

Table 2
DES and extraction conditions applied to extract bioactive compounds from biomass.

Compound type	Feedstock	Conditioning	DES extraction	Extraction yield	Reference
Hyaluronic acid	Tuna eyes	Separation of the vitreous humor and freeze-drying	1 % w/w solid loading with lactic acid:fructose (5:1), at 50 °C for 24 h	10.7 μg/mL Precipitated extract by ethanol: 0.3 μg/mL	(Abdallah et al., 2022)
Phenolic compounds	Olive pomace		1:1 solid loading, ChCl:glycolic acid:oxalic acid (1:1.7:0.3) at 120 °C for 60 min	Hydroxytyrosol (85.8 mg/g)	(Fernández-Prior et al., 2020)
Phenolic compounds	Oil palm leaves	Cutting, freeze-drying, milling and sieving 0.3 mm)	1 % w/w solid loading in ChCl:glycerol (1:3)-43 % w/w water, 25 °C for 30 min (ultrasonic bath)	Luteolin and apigenin content (152.6 mg/g)	(Che Zain et al., 2021)
Phenolic compounds	Spent coffee grounds	Drying	7 % w/v solid loading in betaine:triethylene glycol (1:2)-30 % water at 65 °C for 20 min (ultrasonic bath)	Chlorogenic acids (~4.7 mg/g)	(Fanali et al., 2020)
Phenolic compounds	Citrus peel	Freeze-drying and milling (80 mesh)	2 % w/v solid loading in ChCl:levulinic acid:*N*-methyl urea (1:1.2:0.8) at 50 °C for 25 min	Polymethoxylated flavonoids (18.8 mg/g); glycosides of flavonoids (47.1 mg/g)	(Xu et al., 2019)
Carotenoids	Apricot waste	Freeze-drying	2.2 % w/v soalding loading in ChCl:tartaric acid-20 % methanol at 120 W, 70 °C for 20 min, 120 W	β -carotene (0.8 mg/g)	(Koutsoukos et al., 2019)
Carotenoids	Shrimp head	Freeze-drying	10 % w/v solid loading in ChCl:tartaric acid-20 % methanol at 30–35 °C for 5 min (ultrasound, 600 W, pulsed mode)	Astaxanthin (0.08 mg/g)	(Koutsoukos et al., 2019)
Carotenoids	Shrimp head	Freeze-drying	5 % w/v solid loading in ChCl:tartaric acid-20 % methanol, 30 W at 52 °C for 7 min (microwave)	Astaxanthin (0.3 mg/g)	(Koutsoukos et al., 2019)
Carotenoids	Tomato pomace	Non-thermal air-drying	1 % w/v solid loading in ethyl acetate:ethyl lactate (30:70 v/v) at 60 °C for 20 min (ultrasonic bath)	Lycopene (0.08 mg/g); β -carotene (3.9 mg/g)	(Lazzarini et al., 2022)
Triterpenic acids	*Eucalyptus globulus* outer bark	Drying, milling and sieving (40–60 mesh)	15 % w/w solid loading in menthol:thymol (1:2) at room temperature or 90 °C for 4 h	Ursolic acid (18–20 mg/g); oleanolic acid (8.4–10 mg/g); betulinic acid (3–4 mg/g)	(Silva et al., 2020)

ChCl, Choline chloride.

such as lignin, hemicelluloses and degradation products thereof (Hassan and Mutelet, 2022; Maibam and Goyal, 2022). Afterward, enzymatic hydrolysis is applied to produce glucose from cellulose.

DES with acid-based HBDs are usually applied to remove lignin and hemicelluloses, improving the subsequent cellulose saccharification step and obtaining high glucose yields (Isci et al., 2020; Wang and Lee, 2021; Ling et al., 2021). Besides LA, DES with shorter chain length organic acids, as FA and acetic acid, have been applied to promote the cellulose conversion into glucose, with yields up to 92 % (Isci et al., 2020; Maibam and Goyal, 2022).

DES pretreatment can decrease the content of surface lignin and its condensation, favoring cellulose accessibility by enzymes (H. Li et al., 2022a). Although most studies used conventional heating in the pretreatment by DES, the application of MWAH can lead to enhanced enzymatic conversion with energy requirements (Ríos-González et al., 2021). Another example was reported by Ma et al. (2022a), achieving enzymatic saccharification of 95.4 % when combining MWAH and the ternary DES ChCl:ethylene glycol:$AlCl_3$. In other cases, ultrasound assisted DES pretreatment to favor delignification and enzymatic hydrolysis yield (Ong et al., 2021). Since DES viscosity can prevent the cavitation disruptive effect associated with ultrasound irradiation, water or alkaline aqueous solutions can be added as modifiers to favor the production of sugars (Ong et al., 2021).

4.3. Biofuels

Several approaches have been described in the literature to obtain alcohol biofuels by using mainly glucose. The production of reducing sugars for conversion into biofuels depends on the approach followed (section 4.2). As an example of application, *Miscanthus* pretreated with 20 % dimethyl sulfoxide and 80 % ChCl:glycerol (1:2) at 100 °C for 6 h enabled to get a cellulose-rich solid, which was then hydrolyzed and fermented by *Saccharomyces cerevisiae* for 72 h yielding an ethanol yield close to 72 % (Hassan and Mutelet, 2022). Alternatively, Isci et al. applied MWAH and the acidic DES ChCl:FA (1:3), removing mainly hemicelluloses. Then, the solid fraction was simultaneously saccharified and co-fermented using Cellic Ctec2 and *Escherichia coli KO11*, which can ferment both hexoses and pentoses, yielding 82 % of bioethanol (26 % dry biomass) (Isci et al., 2020).

Another liquid biofuel is biodiesel, and for its production, some microalgae biomasses are attractive sources of lipids that do not compete with food supply chains. It presents the common bottleneck of downstream biomass processing, showing high energy demand disruption, especially microalgae (Lu et al., 2016). The production of biodiesel using microalgae lipids can be performed conventionally in two steps or in one step based on DES-methanol media catalyzed with sulfuric acid (Y. Pan et al., 2017b). In both cases, acidic-based DES enhanced biomass fractionation and lipid recovery. Concerning both strategies, the last approach enabled the direct conversion of lipids from wet biomass into fatty acid methyl esters (FAMEs), overcoming the hydrolysis reaction due to the presence of water. It also led to an increased FAMEs content.

Biomass fractionation using DES can also be applied to produce gas fuels, e.g., biogas and biohydrogen (Basak et al., 2022; Jing et al., 2022; Yu et al., 2019a). As an example, Basak et al. used a cascading fractionation based on hydrothermal and DES pretreatments to remove hemicelluloses and lignin, respectively. Then, a methane production of 467.8 mL/g $VS_{initial}$ was achieved by anaerobic digestion of the hemicellulosic sugars and cellulose fraction, which were more accessible to efficiently promote the anaerobic process (Basak et al., 2022). Ethanolamine has been tested as HBD as an alternative to the aforementioned ChCl-based DES, enabling delignification, while removing hemicelluloses (Jing et al., 2022). In this study, corncob was pretreated using ChCl:ethanolamine to convert sugars into biohydrogen (yield 151 mL/g) by enzymatic hydrolysis and photofermentation with mixed bacteria (*Rhodospirillum* spp. and *Rhodobacter sphaeroides*).

4.4. Other sugar based products

Pectins and oligosaccharides (obtained from the partial hydrolysis of hemicelluloses), which owe bioactive and techno-functional properties, are also targeted macromolecules to be obtained using DES at mild thermal conditions (Contreras et al., 2020; Rico et al., 2021). In another

context, DES can work as a green media to provide cellulose nanocrystals (CNC) and to functionalize this type of cellulosic material. CNCs (or nanowhiskers) present low density, high crystallinity, and mechanical strength, making it possible to find high value applications in sectors like electronics, food packaging, and biomedical materials (Tang et al., 2022).

Producing sugar derived building blocks such as furfural from renewable biomasses is also a topic of extreme interest in the biorefinery context, given the enormous potential to be converted into other value-added chemicals and materials (Contreras et al., 2020; Tang et al., 2022). DES can be applied to produce furfural under mild thermal conditions (Lee and Wu, 2021; Morais et al., 2021). For example, in a recent study, a furfural yield of 55 % was achieved using a biphasic system formed by ChCl:LA (1:2) and 2-methyltetrahydrofuran with 0.2 M $Al_2(SO_4)_3$ and 0.075 M H_2SO_4 to pretreat *Eucalyptus grandis* biomass at 150 °C for 30 min (Sun et al., 2022). Crucial factors to increase furfural yield and minimize its degradation are time, temperature, viscosity, density, melting point, and the addition of catalysts, which will address the workup process (Lee and Wu, 2021). Moreover, DES media has also been demonstrated to be very promising for carrying out the efficient one-pot conversion of DES pre-extracted hemicelluloses (Morais et al., 2018) into C-5 sugars and their subsequent conversion into furfural (Morais et al., 2021) and xylitol (Romaní et al., 2020). The furfural and xylitol yields reported in these studies are amongsts highest reported in the literature.

4.5. Lignin derivatives

Lignin valorization should be a part of any integrated biorefinery that aims to maximize the utilization of renewable biomass. Lignin is the primary aromatic polymer forming part of the lignocellulosic biomass and constitutes above 30 % of the world's organic carbon (Provost et al., 2022). Notably, in second-generation biorefineries, lignin is traditionally burned to produce electricity and heat. However, it can also be marketed in different sectors. Lignin itself can also serve to obtain polymers, carbon fibers, adhesives, etc., but it depends on the lignin quality (Fernandes et al., 2021). Another use is the production of monomeric phenolic compounds such as 2-methoxy-4-propylphenol to be used in diesel engines (Zhang et al., 2021).

Concerning this latter application, DES can be designed to solubilize lignin and isolate lignin-rich fractions by precipitation using adequate antisolvents. The yield and purity of the isolated fractions depend on the DES type and temperature, among other factors (Fernandes et al., 2021). In the case of the use of acidic DES is the delignification and dissolution steps, the co-solvent addition (e.g. water), and temperature influence the lignin molecular weight (Provost et al., 2022) and purity (Fernandes et al., 2021). Globally, using DES formed by ChCl and LA at 80 °C provided a guaiacyl (G)-type lignin with 61 % of β-*O*-4 bonds from softwood chips powder of spruce and pine, while brewer's spent grain yielded lignin with 35 % G units and 53 % β -*O*-4 bonds. The lignin recovered by acidic DES processes and more severe thermal conditions (100 °C) showed a marked reduction of β -*O*-4 units as in lignin acidolysis, while C—C bonds were the main interunit linkages. Nevertheless, this lignin could have applications for the synthesis of soluble derivatives. In this line, using acidic DES, Hong et al. (2020) obtained lignin oil with syringyl (S)- and G-derived diketones from poplar. The obtainment of lignin nanoparticles (<100 nm) by DES and its use for mixing with cream to improve sunscreen performance has also been suggested (Ma et al., 2022a).

5. DES recycling

Besides the tunability of DES for specific applications, their easier recyclability compared to other solvents makes them very attractive. Hence, the recovery and reuse of DES after biomass pretreatment, fractionation, and conversion into added-value components are equally important to their ability to disrupt the biomass matrix. After biomass pretreatment, the first step in DES recovery is the removal of the compounds extracted from biomass, particularly lignin and hemicelluloses (Isci and Kaltschmitt, 2022), but also extractives. Typically, macromolecular fractions can be recovered from the liquor by adding an anti-solvent, such as water, ethanol, or acetone in adequate amount. The anti-solvents break the hydrogen bonding network between the HBA and HBDs, changing the media's polarity, and causing the precipitation of the solubilized components. Then, the most common strategy for DES recovery is the evaporation/distillation of the anti-solvent after removing the precipitated compounds (Isci and Kaltschmitt, 2022). This method allows recovering the DES free of macromolecular/unsoluble compounds but does not remove soluble impurities and degradation products generated, as well as extractives that will remain dissolved in DES (Procentese et al., 2015) and build up in the process upon DES reuse. Thus, removing impurities to keep the performance of DES in new pretreatment runs is yet a big challenge to overcome, as impurities can compromise the whole biomass conversion process (Chen et al., 2018a; Satlewal et al., 2019; Yan et al., 2022).

A selection of studies exploring the recycling and reusability of DES is summarized in Table 3. Although some of the studies demonstrated the effect of DES recycling on the efficacy of the systems toward biomass processing, many of those studies (Cheng et al., 2022; Kim et al., 2018; Mankar et al., 2022; Zhong et al., 2022) have not clearly evaluated the impact of the recycling on DES composition (HBA:HBD ratio and total DES content), nor on the presence of low molecular weight soluble components. For instance, the decrease in the pretreatment efficacy of recycled DES, especially acid-based DES, can be explained by losses of the HBA and/or HBD during the DES regeneration, which can impact the overall acidity of the solvent. This has been reported by some authors in studies applying different types of acidic DES and biomass feedstocks (Bai et al., 2022; Mankar et al., 2022; Yang et al., 2022; Yao et al., 2022; Zhong et al., 2022). For example, Shen et al. showed that the pH of ChCl:LA (1:10) after the fourth recycling step was 12.7 % higher than that of the pristine DES (Shen et al., 2019). In another work, Chen et al. showed an increase in the pH value from 0.16 to 1.78 between fresh and second recycled ChCl:Gly (1:2) (Chen et al., 2018b).

A reduction of delignification performance has also been shown for alkaline DES which have been recycled through acidification with CO_2 to precipitate extracted lignin from DES on diluted acid pretreated corncob (hemicelluloses free), yet 89.6 % delignification was still achieved after three recycling steps (Ma et al., 2022b). In another study, the DES recovery yields were at least 90 % in each cycle of re-use of alkaline-based cholinium lysinate:urea (1:2) with 5 wt% water, after pretreatment of poplar wood. The composition and proportion of DES components were maintained after the treatment, as confirmed by ^{1}H and ^{13}C NMR. Nonetheless, the hemicelluloses yield decreased from 59.2 % to 40.5 % after three recycling steps, along with a gradual decrease in the molecular weights of extracted hemicelluloses (Wang et al., 2022). In both studies, the decreased capability after several recycling steps could be attributed to the decrease in the alkalinity, increase in the viscosity, decrease of hydrogen bonding ability, and accumulation of lignin fragments on the recovered DES.

From another perspective, Zhao et al. studied the recyclability of $ZnCl_2$:LA (1:10) after the pretreatment of corn stover and the hydroxymethylfurfural conversion yield. They observed that there is a cost and environmental benefit in the recovery and reuse of DES, while the volume of acetone/water applied for washing and precipitation of lignin can exhibit a high economic impact associated with distillation costs (size of equipment and operational efforts) (Zhao et al., 2022).

6. DES-based integrated biorefinery approaches

6.1. Examples of DES application in biorefinery schemes and bioproducts

As clearly shown above, DES are very appealing for integrated

Table 3
Selected reports on recycling and reusability of DES.

Feedstock	DES	Main results	Reference
Switchgrass	ChCl:*p*-coumaric acid	DES recovery yield of 95 %, slightly affected by impurities	(Kim et al., 2018)
Poplar	ChCl:*p*-hydroxybenzoic acid	Acetic acid impurities coming from hemicelluloses	(Y. Wang et al., 2020)
Eucalyptus wood	ChCl:EG	A membrane-based methodology combining ultrafiltration with electrodialysis reduced favors the purity of the recycled DES	(Liang et al., 2019)
Corn cob	Benzyltrimethylammonium chloride:LA	Decrease of approx. 5 % in the enzymatic digestibility of cellulose-rich residues with the increasing number of DES recovery steps	(Guo et al., 2019)
Moso bamboo	Three levulinic acid-based DES combined with acetamide, betaine and ChCl	Enzymatic hydrolysis performance decreased the glucose yield from 48 to 79 % to 24–39 % after the third reuse cycle; the removal of lignin was 28.9 %, 20.6 % and 11.9 %	(Ling et al., 2020)
Eucalyptus wood	ChCl:urea:acetic acid	Xylans could be effectively extracted and routed to other valorization strategies in DES media	(Morais et al., 2018)
Beechwood xylan	ChCl:malic acid in the presence of γ-valerolactone (GVL)	The simultaneous recovery of furfural and recycling of DES/GVL was performed by liquid–liquid extraction with 2-methyltetrahydrofuran followed by distillation.	(Morais et al., 2020)
Beechwood xylan	ChCl:malic acid with LiBr	Recyclability of the acid-based DES in the presence of alkali metal halide salt (LiBr)	(Morais et al., 2021)
Hybrid *Pennisetum*	ChCl:Gly:$FeCl_3$	The cellulose saccharification yield after fourth recycling step was maintained at 99.5 %	(Z. K. Wang et al., 2020b)
Sugarcane bagasse	ChCl:EG:$NiCl_2{\cdot}6H_2O$	After the third recycling step, the delignification yield decreased from 84 % to 76.2 %, when compared to pristine DES and the glucan enzymatic hydrolysis decreased from 66.5 % to 49.8 %	(Chourasia et al., 2022)
Moso bamboo culms	ChCl:1,4-butanediol:$AlCl_3$	After seven recycling steps, DES recovery yields was 90 %, lignin removal dropped from 80 % to 42.78 %; the glucan enzymatic hydrolysis was still 100 %	(Cheng et al., 2022)
Coconut coir	ChCl:LA	Lignin removal yield decreased from 82 to 68.5 % in four recycling steps	(Mankar et al., 2022)
Castor stalk	Guanidine hydrochloride:LA	The delignification yield decreased with the increase of the recycling steps. The enzymatic hydrolysis efficiency was not affected after three times of DES recycling, remaining around 90 % glucose yield	(Zhong et al., 2022)

ChCl, Choline chloride; EG, ethylene glycol; LA, lactic acid; Gly, glycerol.

biorefineries processes, delivering simultaneously several bio-based products (i.e., chemicals and biofuels). Some diagrams of integrated biomass conversion using DES for lignocellulosic biomass, and oilseeds and their derived cakes (based on Grudniewska et al., 2018) and Wongsirichot et al., 2019) are exemplified in Fig. 2. Moreover, Table 4 summarizes some recent scientific studies on the topic, most relying on residual biomasses starting materials. Biomass should be conditioned before the extraction and pretreatment and most studies apply drying

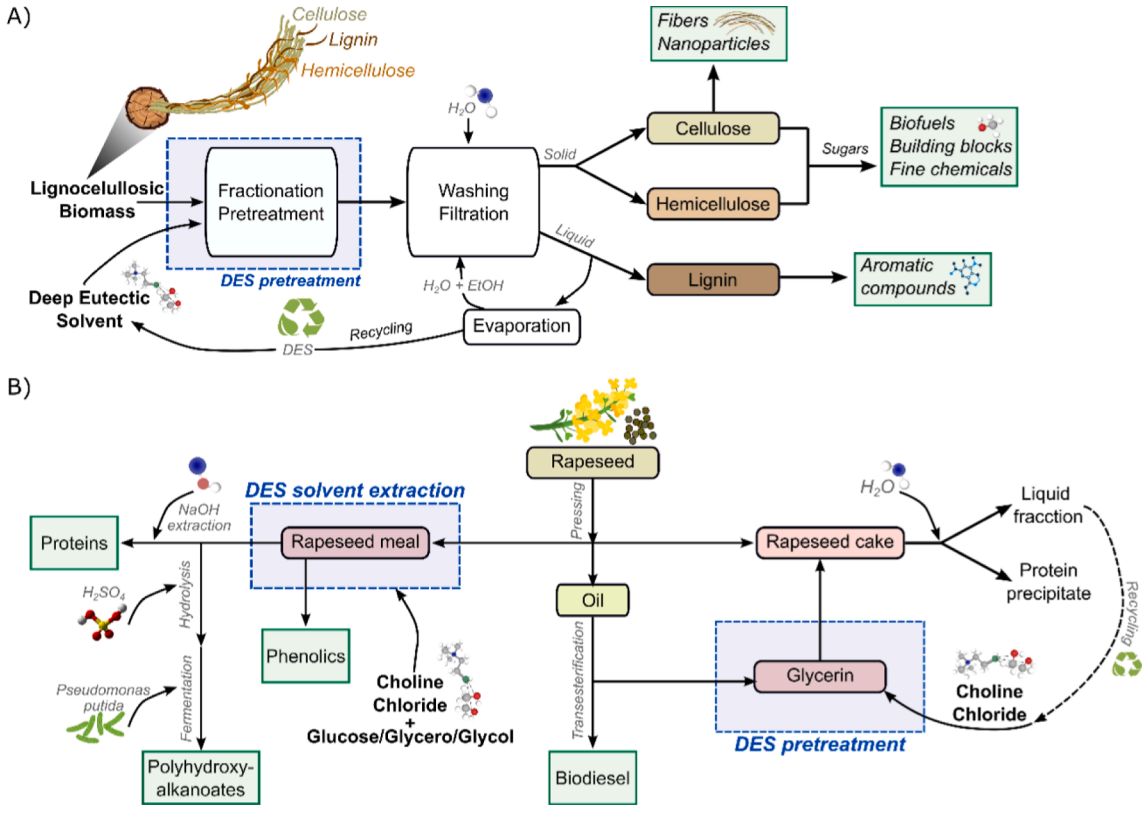

Fig. 2. General diagrams exemplifying cascading processes and bio-based products that can be obtained from a) lignocellulosic biomass and b) oilseeds and derived defatted cakes calling upon the use of deep eutectic solvents.

Table 4
Relevant examples of DES pretreatments applied in biorefinery schemes.

Feedstock	DES	Process conditions	Main results	Reference
Poplar wood	ChCl:EG:$AlCl_3$	$AlCl_3$-catalyzed hydrothermal pretreatment + DES pretreatment + enzyme hydrolysis	Glucose, lignin, xylooligosaccharides are obtained as main products	(C.-Y. Ma et al., 2021a)
Wet olive pomace	ChCl, glycolic and oxalic acid	Combination of thermal and DES treatment at different temperatures, time and sample/solvent ratios.	Temperature of thermal treatment could be reduced from 180 °C to 120 °C. The concentration of acid sugars increased by six times and the concentration of hydroxytyrosol by 30 times	(Fernández-Prior et al., 2020)
Rice straw	ChCl:LA	Different solid loading and enzymatic hydrolysis conditions along with1 atm pressure and 121 °C for 15 min	129 L ethanol per ton of raw material and 90 % lignin recovery. 98 % of the DES was recovered and reused three times	(Kumar et al., 2018)
Engineered sorghum bagasse	ChCl:*p*-hydroxybenzoic acid (PA)	ChCl and PA were mixed at different molar ratios. Biomass (10 wt%) was loaded to the DES and allowed to react at 120 °C for 3 h	Fermentable sugars were increased by 190 % compared to untreated material. Production of phenolic compounds was demonstrated by hydrogenolysis of the fractionated lignin	(Y. Wang et al., 2021b)
Orange peel waste	ChCl:EG	Seven different NADES checked. The solution with 50 % water was selected as the best performing		(Panić et al., 2021)
Switchgrass	ChCl:Gly	1.5 g switchgrass mixed with 15 g pretreatment solvent at 120 °C for 1 h. The solid fraction was enzymatically hydrolyzed. Lignin was separated from pretreatment liquor, which was in turn fermented by *Rhodotorula toruloides*	Efficient fractionation of biomass. The oleaginous yeast *R. toruloides* produced 18.7 g/L biomass with 8.1 g lipids/L and 15.0 mg carotenoids. 89 % glucose yield from solids	(Chen et al., 2018b)
Rapeseed cake and evening primrose cake	ChCl:Gly	Oilseed cakes (5 g) mixed with DES (45 g) and treated at 60, 100, and 140 °C for 2 h in an oil bath	Process is oriented to obtain vegetable-derived proteins, improving the results compared to untreated materials	(Grudniewska et al., 2018)

ChCl, Choline chloride; EG, ethylene glycol; LA, lactic acid; Gly, glycerol.

and milling for that purpose. Then, if there are valuable extractable compounds, they can be isolated before pretreatment (Table 2). At the same time, pretreatment generally requires more severe conditions to break the lignocellulosic structure of biomass and promote fractionation for the production of bio-based products (Table 1). Nonetheless, as deduced from the information shown, the use of DES improves operational conditions, for example, by reducing thermal requirements (Fernández-Prior et al., 2020) or increasing fractionations efficiency (Chen et al., 2018b). In other cases, product concentration or yield results were also improved compared to conventional fractionation processes.

6.2. Sustainability of DES based biorefinery processes

The green, environmentally friendly and sustainability labels of DES are often only attributed based on their biodegradability and low toxicity properties (Radošević et al., 2015). However, this claim is poorly justified or incomplete, as, introducing any novel technology or change in biorefinery processes, may induce new direct or indirect environmental impacts that cannot be overlooked. Hence, at least two key aspects should be considered to determine whether DES may truly help transition towards more sustainable bioprocesses. First, the DES themselves should be aligned with the sustainability principles and outperform existing solvents. Since DES are prepared by simple mixing of their components, they are not subjected to the limitations often raised to ionic liquids synthesis, yet, some hurdles could arise from the eventual nonsustainable origin of their components (HBAs or HBDs). Hence, bio-based DES, i.e., those prepared from chemical compounds sustainably obtained from renewable resources, may fully fulfill this criterion (Y. Wang et al., 2021a). Secondly, the overall sustainability of the whole value chain relying on DES should improve compared to the conventional treatments. The latter is particularly relevant as DES usage may affect the process conditions (temperature, residence time, energy requirements) and other upstream and downstream activities (Osman et al., 2021), ultimately determining the final environmental performance. This critical issue is called burden-shifting, which could lead to undesirable and even irreversible environmental problems that should be avoided to protect the environment thoroughly.

For this reason, whether a particular biomass conversion process relying on DES for biomass pretreatment is environmentally friendly or not can only be concluded by following a life cycle perspective, i.e., by considering the complete value chain (Ubando et al., 2020).

7. Environmental and techno-economic assessment of DES-based biorefineries

Whether DES can contribute to more sustainable biorefining processes can only be concluded by carrying out a techno-economic assessment (TEA) and environmental analysis through life cycle assessment (LCA). This is particularly relevant for emerging DES treatments that are still at the early stages of deployment (low technology readiness levels or TRL). To be sustainable, DES-based biorefineries should be technically scalable at the industrial level and economically and environmentally appealing compared with alternative processes.

For the technical viability and economic profitability of emerging technologies such as DES, TEA are often conducted. These analyses consist of computer-aided simulation scaling-up exercises using modeling tools such as Aspen Plus, Aspen HYSYS, or SuperPro. Capital and operational expenditures, net present value, and payback period are economic indicators often evaluated using simulation mass and energy balance results.

TEA studies applied to DES-based biorefineries are very scarce, although they are fundamental to reach the commercial scale. Kumar and coauthors presented the first TEA of different designs for a NADES-based biorefinery (Kumar et al., 2020). TEAs relying on process simulation in Aspen Plus software were applied for the production of bioethanol (Peng et al., 2021) and the co-production of butanediol, furfural, and lignin (Zang et al., 2020). Recently, a TEA of DES-IL catalyst system for lignin and 5-hydroxymethylfurfural production was performed (Zhao et al., 2022). Overall, all these studies of DES-based biorefineries found the DES recycling time is critical to the operating costs but showed economic advantages in using DES.

For the environmental assessment, LCA constitutes a powerful methodology to support sustainable decision-making by quantifying impacts considering the entire life cycle of the systems. Comprehensive information on the challenges and recommendations of applying LCA to biorefinery systems can be found in many previous works (Yang Liu et al., 2021; Zhou et al., 2021).

The goal of an LCA-based biorefinery study using DES might be to compare the environmental impacts of different technologies, process configurations, or biomass feedstocks. The system boundaries depend on the study's goal. However, *cradle-to-gate* and *cradle-to-grave* system

boundaries are the most used. The former starts from raw material acquisition (including biomass cultivation and the synthesis of the DES) to the factory gate before the bioproduct is transported to the final consumer, while the latter includes the use phase, end life, recycling (if any), and final disposal (Fig. 3). The functional unit of the study —reference magnitude to which all the impacts to deliver the system's function will be evaluated— may refer to the use of feedstock (quantity of biomass feedstock or land), the production of a single bioproduct, or multifunctional systems delivering more than one bio-based product. Hence, biorefinery studies often face the allocation issue of distributing impacts among various co-products, which greatly influences the results (Vance et al., 2022). Moreover, completing the life cycle inventory (LCI) analysis —all inputs and outputs of the system— might also be challenging because DES are a new kind of solvent, and no information is available in databases. Hence, lab-scale experimental primary data synthesizing DES and process simulation tools could be us as a proxy for those data gaps (Ioannou et al., 2021).

Regarding the life cycle impact assessment (LCIA), impacts beyond climate change should be considered as often environmental trade-offs arise in biorefinery studies (e.g., eutrophication and water and land use). Finally, in the interpretation phase, analyzing the data quality regarding the biomass feedstock and novel DES might be necessary due to data gaps and low TRL.

LCA has been widely used to assess the sustainability of biorefineries using solvents other than DES (e.g., organic solvents, ILs) (Ioannidou et al., 2022). However, LCA studies on DES in biomass pretreatment are still very scarce (Sharma et al., 2022). This research gap was identified in many articles analyzing DES for biomass pretreatment (Hessel et al., 2022; Ho and Wu, 2020; Zhong et al., 2022), but the knowledge gap remains mainly unexplored to date.

Only a handful of studies have conducted LCA to evaluate the impacts of bioresources technologies using DES. For example, laboratory-scale LCA showed that the application of DES to extract valuable bioactive compounds from different bio-based feedstocks could reduce waste and environmental impacts compared with traditional methods (Bisht et al., 2021; Guo et al., 2021). Alternatively, in another study, the use of ethanol lead to lower environmental impacts under categories such as global warming, acidification, and fossil resources attributed to the higher heating requirements for the extraction with DES (Murugan et al., 2021). Concerning other bio-based products, a recent study compared the LCA impacts of a process synthesizing 2,5-dihydroxymethylfuran based on different green solvents, including DES (Hessel et al., 2022). The environmental benchmarking showed that the process based on DES performed better in global warming category than those using ILs, but worse than those relying on supercritical CO_2 and theriomorphic solvents. Notably, the process relying on DES showed the highest impact in toxicity categories such as freshwater ecotoxicity and human non-carcinogenic toxicity.

Recently, Zargar et al. investigated the impacts of producing lignin-containing cellulose nanocrystals using DES pretreatment to produce nanomaterials at a lab scale. The evaluation was conducted through a *cradle-to-gate* scope, and the results revealed the manufacturing of DES as the predominant contributor to the impact on global warming potential, acidification, and cumulative energy demand (Zargar et al., 2022). Similar conclusions were obtained by Xia et al. (Xia et al., 2021) in a study producing bioplastics from lignin-cellulose slurry using DES for deconstructing the natural wood powder. Again, the DES preparation was found to be the major driver of fossil fuel depletion, smog formation, global warming potential, and acidification.

In another study, Guo *et al.* investigated the use of DES for biomass pretreatment in processing pellets. The feedstock employed was residual agricultural biomass (wheat straw), and the results indicate significant environmental savings compared with traditional alkali or acid methods (Guo et al., 2022).

8. Challenges and outlook

DES and NADES have demonstrated to be promising and effective alternatives solvents in several biomass pretreatment processes. However, several aspects still require further research and development. According to the Strengths, Weaknesses, Opportunities, Threats (SWOT) analyses performed by Panić et al. (2021), a major weakness includes the lack of scale-up initiatives using DES and mass transfer issues along with high energy consumption (Panić et al., 2021). For example, the viscosity of DES is a critical parameter for industrial applications, particularly when DES establish strong hydrogen bonding networks

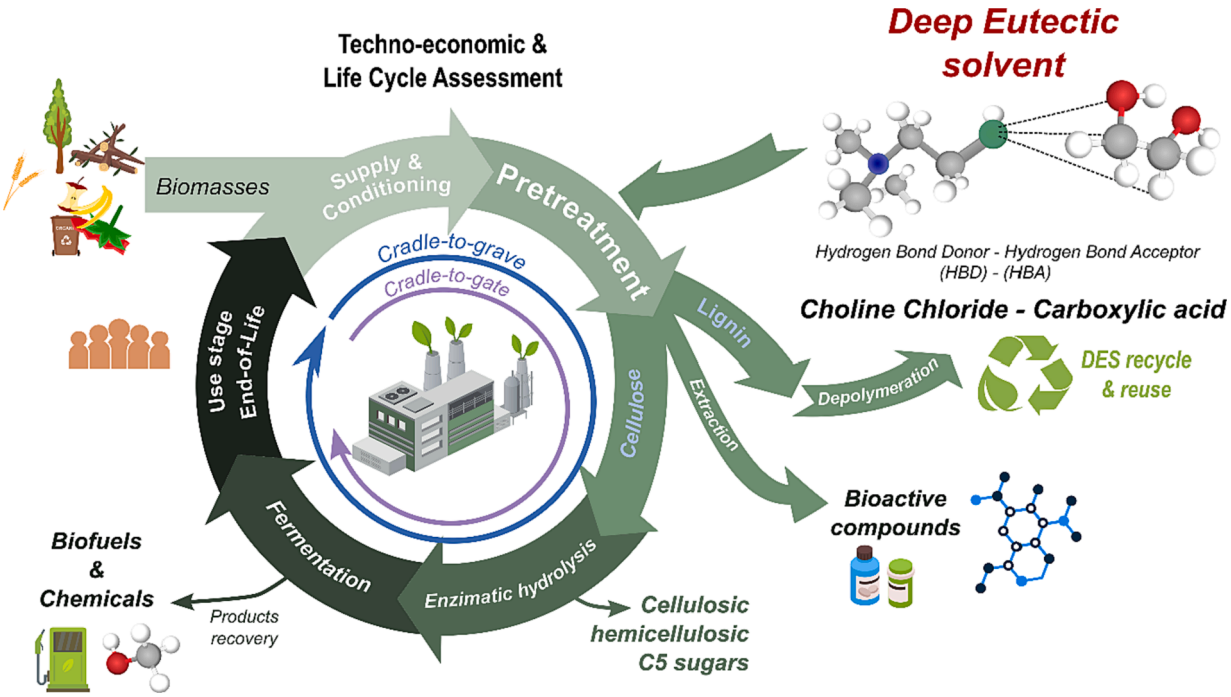

Fig. 3. General scope of an illustrative life cycle study of a biomass valorization route using deep eutectic solvents in the pretreatment.

(Stefanovic et al., 2017). The same for density, surface tension, etc. The quintessential green solvent, i.e. water, can be added as an opportunity to modify these properties.

Moreover, some biomass components can be co-extracted using DES media, which could be useful if taking advantage from this situation, but if not, it could threaten the efficacy and usability cycles of the DES. Other issues are the potential losses of DES components and the change of DES properties during the workup process (Mankar et al., 2022). Therefore, developing new recycling methods to manage these issues (or opportunities in the former case) will be mandatory, especially considering the positive benefit for the economics of the process.

As the main threat to use DES in biorefinery processes, new developments may be slowed down because of alternative conventional pretreatment methods preference (e.g., using organic solvents, inorganic alkali and acids, etc.). Nonetheless, DES, particularly NADES, can be combined with new green emerging technologies (e.g., microwave or ultrasound irradiation) to develop energy efficient biomass deconstruction and valorization processes. However, and despite looking highly promising, in most cases, the scaling up of these technologies is in its infancy (Kumar et al., 2019).

Another threat is the cost of DES because they are relatively more expensive than the typical acid and alkali used in pretreatment processes (New et al., 2019). Their efficient recycling and reuse may help to overcome the economic barrier. New processes for chemical and biochemical/enzymatic conversion of isolated compounds/extracts in the same DES media (one-pot or sequentially) or developing final formulations that take advantage of the presence of the DES need to be explored. The potential direct application of some NADES as a vehicle of bioactive compounds for food, cosmetics, and pharmaceutical applications is an opportunity to address in extraction studies as the first step of biorefinery processes and to reduce costs regarding purification.

In this line, the DES as media for the direct carbohydrolases application could also conduct future studies to take advantage of this opportunity. In a recent opinion, Florindo and coworkers suggested that some properties of DES, like hydrophobicity and low viscosity, can improve enzyme activity and stability (Florindo et al., 2019b; Florindo et al., 2019a), while the presence of lignin derivatives and the acid conditions, when acidic DES are applied, could not be well tolerated by enzymes (e.g. inhibition and adsorption effects on enzymes). In contact with fermentative microorganisms, DES could disintegrate cells (Jamaldheen et al., 2021), limiting their use for direct hemicellulosic sugars conversion with non-conventional microorganisms. Hence, some studies are moving in this direction and, for example, Romaní et al. showed that ChCl:urea did not affect the production of xylitol from xylan by S. cerevisiae PE-2 GRE3 (Romaní et al., 2020).

Overall, integrating TEA and LCA of biorefineries is prime and of utmost importance to fully understand the economic and environmental implications at the industrial scale. For this, process system engineering tools can be coupled with LCA methodologies providing a robust framework to promote technologies (Ioannou et al., 2021). Only by ensuring biorefineries' technical and economic viability and demonstrating their positive impacts on the environment will be possible to succeed in scale-up technologies with low TRL.

The scarce TEA and LCA studies show the importance of assessing DES-based biorefineries *via* its combined approach to make informed decisions ensuring their sustainable large-scale deployment. The main challenge for TEA is that DES properties are unavailable in simulation software databases and should be defined manually. Concerning LCA, the scope of studies should be expanded to *cradle-to-grave*, which is suitable for comparative assessments but also sheds light on the environmental implications of introducing bio-based products in the market (including final use and disposal). Moreover, LCA studies should consider a comprehensive set of impacts beyond climate-change-related impacts — today's primary environmental concern — to analyze potential trade-offs and avoid burden-shifting to other environmental impacts. Challenges remain regarding the LCI data due to DES are very novel chemical compounds. To overcome it, most studies simplified it by considering the energy requirements at the lab scale. Here, standardized methods, transparency, and sensitivity analysis to make all studies comparable would be recommended to assess the robustness of the TEA and LCA results.

9. Conclusions

Transforming the current economical model of development into a fully sustainable economy requires replacing fossil-based products with renewable counterparts, calling upon fully sustainable production processes. Due to their highly tunable and green properties, DES have emerged among the most promising solvents in biorefinery processes to achieve that goal. Although much research and development are still needed, DES can already be key players in biorefinery systems for sustainable development. Upcoming laboratory studies on DES-based biorefineries should complement TEA scaling-up exercises and LCA analysis. Only this integrated approach will help make informed decisions and guide the sustainable development of biorefinery processes.

Declaration of Competing Interest

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

Data availability

The authors do not have permission to share data.

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References

Abdallah, M.M., Leonardo, I.C., Krstić, L., Enríquez-de-Salamanca, A., Diebold, Y., González-García, M.J., Gaspar, F.B., Matias, A.A., Bronze, M.R., Fernández, N., 2022. Potential Ophthalmological Application of Extracts Obtained from Tuna Vitreous Humor Using Lactic Acid-Based Deep Eutectic Systems. Foods 11, 342.

Abranches, D.O., Martins, M.A.R., Silva, L.P., Schaeffer, N., Pinho, S.P., Coutinho, J.A.P., 2019. Phenolic hydrogen bond donors in the formation of non-ionic deep eutectic solvents: The quest for type v des. Chem. Commun. 55, 10253–10256.

Alam, M.A., Muhammad, G., Khan, M.N., Mofijur, M., Lv, Y., Xiong, W., Xu, J., 2021. Choline chloride-based deep eutectic solvents as green extractants for the isolation of phenolic compounds from biomass. J. Clean. Prod. 309, 127445.

Bai, Y., Zhang, X.F., Wang, Z., Zheng, T., Yao, J., 2022. Deep eutectic solvent with bifunctional Brønsted-Lewis acids for highly efficient lignocellulose fractionation. Bioresour. Technol. 347, 126723.

Basak, B., Patil, S., Kumar, R., Ha, G.-S., Park, Y.-K., Khan, M.A., Yadav, K.K., Fallatah, A. M., Jeon, B.-H., 2022. Integrated hydrothermal and deep eutectic solvent-mediated fractionation of lignocellulosic biocomponents for enhanced accessibility and efficient conversion in anaerobic digestion. Bioresour. Technol. 351, 127034.

Biernacki, K., Souza, H.K.S., Almeida, C.M.R., Magalhã, A.L., Gonç, M.P., 2020. Physicochemical Properties of Choline Chloride-Based Deep Eutectic Solvents with Polyols: An Experimental and Theoretical Investigation. Cite This ACS Sustain. Chem. Eng 8, 18712–18728.
Bisht, M., Martins, M., Dias, A.C.R.V., Ventura, S.P.M., Coutinho, J.A.P., 2021. Uncovering the potential of aqueous solutions of deep eutectic solvents on the extraction and purification of collagen type I from Atlantic codfish (Gadus morhua). Green Chem. 23, 8940–8948.
Che Zain, M.S., Yeoh, J.X., Lee, S.Y., Shaari, K., 2021. Physicochemical Properties of Choline Chloride-Based Natural Deep Eutectic Solvents (NaDES) and Their Applicability for Extracting Oil Palm Flavonoids. Sustainability 13, 12981.
Chen, Z., Bai, X., Lusi, A., Wan, C., 2018a. High-Solid Lignocellulose Processing Enabled by Natural Deep Eutectic Solvent for Lignin Extraction and Industrially Relevant Production of Renewable Chemicals. ACS Sustain. Chem. Eng. 6, 12205–12216.
Chen, Z., Reznicek, W.D., Wan, C., 2018b. Deep eutectic solvent pretreatment enabling full utilization of switchgrass. Bioresour. Technol. 263, 40–48.
Cheng, J., Huang, C., Zhan, Y., Han, S., Wang, J., Meng, X., Yoo, C.G., Fang, G., Ragauskas, A.J., 2022. Effective biomass fractionation and lignin stabilization using a diol DES system. Chem. Eng. J. 443, 136395.
Chourasia, V.R., Bisht, M., Pant, K.K., Henry, R.J., 2022. Unveiling the potential of water as a co-solvent in microwave-assisted delignification of sugarcane bagasse using ternary deep eutectic solvents. Bioresour. Technol. 351, 127005.
Contreras, M.d.M., Romero, I., Moya, M., Castro, E., 2020. Olive-derived biomass as a renewable source of value-added products. Process Biochem. 97, 43-56.
Contreras, M.d.M., Romero-García, J.M., López-Linares, J.C., Romero, I., Castro, E., 2022. Residues from grapevine and wine production as feedstock for a biorefinery. Food Bioprod. Process. 134, 56-79.
Da Costa Lopes, A.M., 2021. Biomass delignification with green solvents towards lignin valorisation: Ionic liquids vs deep eutectic solvents. Acta Innov. 40, 64–78.
Da Costa Lopes, A.M., Gomez, J.R.B., Coutinho, J.A.P., Silvestre, A.J.D., 2020. Novel insights into biomass delignification with acidic deep eutectic solvents: a mechanistic study of β-*O*-4 ether bond cleavage and the role of the halide counterion in the catalytic performance. Green Chem. 22, 2474–2487.
Doménech, P., Duque, A., Higueras, I., Fernández, J.L., Manzanares, P., 2021. Analytical Characterization of Water-Soluble Constituents in Olive-Derived By-Products. Foods 10, 1299.
El Achkar, T., Moura, L., Moufawad, T., Ruellan, S., Panda, S., Longuemart, S., Legrand, F.X., Costa Gomes, M., Landy, D., Greige-Gerges, H., Fourmentin, S., 2020. New generation of supramolecular mixtures: Characterization and solubilization studies. Int. J. Pharm. 584, 119443.
El Achkar, T., Greige-Gerges, H., Fourmentin, S., 2021. Basics and properties of deep eutectic solvents: a review. Environ. Chem. Lett. 19, 3397–3408.
Fanali, C., Della Posta, S., Dugo, L., Gentili, A., Mondello, L., De Gara, L., 2020. Choline-chloride and betaine-based deep eutectic solvents for green extraction of nutraceutical compounds from spent coffee ground. J. Pharm. Biomed. Anal. 189, 113421.
Fernandes, C., Melro, E., Magalhães, S., Alves, L., Craveiro, R., Filipe, A., Valente, A.J.M., Martins, G., Antunes, F.E., Romano, A., 2021. New deep eutectic solvent assisted extraction of highly pure lignin from maritime pine sawdust (Pinus pinaster Ait.). Int. J. Biol. Macromol. 177, 294–305.
Fernández-Prior, M.Á., Charfi, A., Bermúdez-Oria, A., Rodríguez-Juan, E., Fernández-Bolaños, J., Rodríguez-Gutiérrez, G., 2020. Deep eutectic solvents improve the biorefinery of alperujo by extraction of bioactive molecules in combination with industrial thermal treatments. Food Bioprod. Process. 121, 131–142.
Florindo, C., McIntosh, A.J.S., Welton, T., Branco, L.C., Marrucho, I.M., 2018. A closer look into deep eutectic solvents: exploring intermolecular interactions using solvatochromic probes. Phys. Chem. Chem. Phys. 20 (1), 206–213.
Florindo, C., Branco, L.C., Marrucho, I.M., 2019a. Quest for Green-Solvent Design: From Hydrophilic to Hydrophobic (Deep) Eutectic Solvents. ChemSusChem 12 (1549–1559), 7.
Florindo, C., Lima, F., Ribeiro, B.D., Marrucho, I.M., 2019b. Deep eutectic solvents: Overcoming 21st century challenges. Curr. Opin. Green Sustain. Chem. 18, 31–36.
Gabriele, F., Chiarini, M., Germani, R., Tiecco, M., Spreti, N., 2019. Effect of water addition on choline chloride/glycol deep eutectic solvents: Characterization of their structural and physicochemical properties. J. Mol. Liq. 291, 111301.
Gómez-Cruz, I., Romero, I., Contreras, M. del M., Labidi, J., Hernández-Ramos, F., Roseiro, L.B., Duarte, L.C., Castro, E., Carvalheiro, F., 2022. Combined Extraction and Ethanol Organosolv Fractionation of Exhausted Olive Pomace for Bioactive Compounds. Adv. Sustain. Syst. 6, 2100361.
Gómez-Cruz, I., Contreras, M.d.M., Romero, I., Castro, E., 2021a. Sequential extraction of hydroxytyrosol, mannitol and triterpenic acids using a green optimized procedure based on ultrasound. Antioxidants 10, 1781.
Gómez-Cruz, I., Contreras, M.d.M., Romero, I., Castro, E., 2021b. A biorefinery approach to obtain antioxidants, lignin and sugars from exhausted olive pomace. J. Ind. Eng. Chem. 96, 356–363.
Grudniewska, A., De Melo, E.M., Chan, A., Gniłka, R., Boratyński, F., Matharu, A.S., 2018. Enhanced Protein Extraction from Oilseed Cakes Using Glycerol-Choline Chloride Deep Eutectic Solvents: A Biorefinery Approach. ACS Sustain. Chem. Eng. 6, 15791–15800.
Guo, Y., Li, Y., Li, Z., Yan, W., Chen, P., Yao, S., 2021. Extraction assisted by far infrared radiation and hot air circulation with deep eutectic solvent for bioactive polysaccharides from Poria cocos (Schw.) wolf. Green Chem. 23, 7170–7192.
Guo, T., Yu, Y., Wan, Z., Zargar, S., Wu, J., Bi, R., Sokhansanj, S., Tu, Q., Rojas, O.J., 2022. Energy pellets from whole-wheat straw processed with a deep eutectic solvent: A comprehensive thermal, molecular and environmental evaluation. Renew. Energy. 194, 902–911.
Guo, Z., Zhang, Q., You, T., Zhang, X., Xu, F., Wu, Y., 2019. Short-time deep eutectic solvent pretreatment for enhanced enzymatic saccharification and lignin valorization. Green Chem. 21, 3099–3108.
Hansen, B.B., Spittle, S., Chen, B., Poe, D., Zhang, Y., Klein, J.M., Horton, A., Adhikari, L., Zelovich, T., Doherty, B.W., Gurkan, B., Maginn, E.J., Ragauskas, A., Dadmun, M., Zawodzinski, T.A., Baker, G.A., Tuckerman, M.E., Savinell, R.F., Sangoro, J.R., 2021. Deep Eutectic Solvents: A Review of Fundamentals and Applications. Chem. Rev. 121, 1232–1285.
Hassan, E.-S.-R.-E., Mutelet, F., 2022. Evaluation of miscanthus pretreatment effect by Choline chloride based Deep Eutectic solvents on bioethanol production. Bioresour. Technol. 345, 126460.
Hessel, V., Tran, N.N., Asrami, M.R., Tran, Q.D., Long, N.V.D., Escribà-Gelonch, M., Tejada, J.O., Linke, S., Sundmacher, K., 2022. Sustainability of green solvents–review and perspective. Green Chem. 24, 410–437.
Ho, M.C., Wu, T.Y., 2020. Sequential pretreatment with alkaline hydrogen peroxide and choline chloride: copper (II) chloride dihydrate–Synergistic fractionation of oil palm fronds. Bioresour. Technol. 301, 122684.
Hong, S., Shen, X.-J., Pang, B., Xue, Z., Cao, X.-F., Wen, J.-L., Sun, Z.-H., Lam, S.S., Yuan, T.-Q., Sun, R.C., 2020. In-depth interpretation of the structural changes of lignin and formation of diketones during acidic deep eutectic solvent pretreatment. Green Chem. 22, 1851–1858.
Hong, S., Li, H.-Y., Shen, X.-J., Sun, S.-N., Sun, Z., Yuan, T.-Q., 2022. Unveiling the migration and transformation mechanism of lignin in eucalyptus during deep eutectic solvent pretreatmen. ChemSusChem 15, e202200553.
Ijardar, S.P., Singh, V., Gardas, R.L., 2022. Revisiting the Physicochemical Properties and Applications of Deep Eutectic Solvents. Molecules 27, 1368.
Ioannidou, S.M., Filippi, K., Kookos, I.K., Koutinas, A., Ladakis, D., 2022. Techno-economic evaluation and life cycle assessment of a biorefinery using winery waste streams for the production of succinic acid and value-added co-products. Bioresour. Technol. 348, 126295.
Ioannou, I., D'Angelo, S.C., Galán-Martín, Á., Pozo, C., Pérez-Ramírez, J., Guillén-Gosálbez, G., 2021. Process modelling and life cycle assessment coupled with experimental work to shape the future sustainable production of chemicals and fuels. React. Chem. Eng. 6, 1179–1194.
Isci, A., Erdem, G.M., Bagder Elmaci, S., Sakiyan, O., Lamp, A., Kaltschmitt, M., 2020. Effect of microwave-assisted deep eutectic solvent pretreatment on lignocellulosic structure and bioconversion of wheat straw. Cellulose 27, 8949–8962.
Isci, A., Kaltschmitt, M., 2022. Recovery and recycling of deep eutectic solvents in biomass conversions: a review. Biomass Convers. Biorefinery 12, 197–226.
Jamaldheen, S.B., Kurade, M.B., Basak, B., Yoo, C.G., Oh, K.K., Jeon, B.-H., Kim, T.H., 2021. A review on physico-chemical delignification as a pretreatment of lignocellulosic biomass for enhanced bioconversion. Bioresour. Technol. 346, 126591.
Jing, Y., Li, F., Li, Y., Jiang, D., Lu, C., Zhang, Z., Zhang, Q., 2022. Biohydrogen production by deep eutectic solvent delignification-driven enzymatic hydrolysis and photo-fermentation: Effect of liquid–solid ratio. Bioresour. Technol. 349, 126867.
Kim, K.H., Dutta, T., Sun, J., Simmons, B., Singh, S., 2018. Biomass pretreatment using deep eutectic solvents from lignin derived phenols. Green Chem. 20, 809–815.
Koutsoukos, S., Tsiaka, T., Tzani, A., Zoumpoulakis, P., Detsi, A., 2019. Choline chloride and tartaric acid, a Natural Deep Eutectic Solvent for the efficient extraction of phenolic and carotenoid compounds. J. Clean. Prod. 241, 118384.
Kumar, N., Muley, P.D., Boldor, D., Coty IV, G.G., Lynam, J.G., 2019. Pretreatment of waste biomass in deep eutectic solvents: conductive heating versus microwave heating. Ind. Crops Prod. 142, 111865.
Kumar, A.K., Sharma, S., Shah, E., Patel, A., 2018. Technical assessment of natural deep eutectic solvent (NADES) mediated biorefinery process: A case study. J. Mol. Liq. 260, 313–322.
Kumar, A.K., Sharma, S., Dixit, G., Shah, E., Patel, A., Boczkaj, G., 2020. Techno-economic evaluation of a natural deep eutectic solvent-based biorefinery: Exploring different design scenarios. Biofuels. Bioprod. Biorefining 14, 746–763.
Lazzarini, C., Casadei, E., Valli, E., Tura, M., Ragni, L., Bendini, A., Gallina Toschi, T., 2022. Sustainable Drying and Green Deep Eutectic Extraction of Carotenoids from Tomato Pomace. Foods 11, 405.
Lee, C.B.T.L., Wu, T.Y., 2021. A review on solvent systems for furfural production from lignocellulosic biomass. Renew. Sustain. Energy Rev. 137, 110172.
Li, H., Li, X., Li, D., Zhang, J., Nawaz, H., You, T., Xu, F., 2022a. Highly-efficient pretreatment using alkaline enhanced aqueous deep eutectic solvent to unlock poplar for high yield of fermentable sugars: Synergistic removal of lignin and mannan. Bioresour. Technol. 351, 126993.
Li, T., Lyu, G., Liu, Y., Lou, R., Lucia, L.A., Yang, G., Chen, J., Saeed, H.A.M., 2017. Deep eutectic solvents (DESs) for the isolation of willow lignin (Salix matsudana cv. Zhuliu). Int. J. Mol. Sci. 18, 2266.
Li, N., Meng, F., Yang, H., Shi, Z., Zhao, P., Yang, J., 2022b. Enhancing enzymatic digestibility of bamboo residues using a three-constituent deep eutectic solvent pretreatment. Bioresour. Technol. 346, 126639.
Li, P., Zhang, Q., Zhang, X., Zhang, X., Pan, X., Xu, F., 2019. Subcellular dissolution of xylan and lignin for enhancing enzymatic hydrolysis of microwave assisted deep eutectic solvent pretreated Pinus bungeana Zucc. Bioresour. Technol. 288, 121475.
Liang, Y., Duan, W., An, X., Qiao, Y., Tian, Y., Zhou, H., 2020. Novel betaine-amino acid based natural deep eutectic solvents for enhancing the enzymatic hydrolysis of corncob. Bioresour. Technol. 310, 123389.
Liang, X., Fu, Y., Chang, J., 2019. Effective separation, recovery and recycling of deep eutectic solvent after biomass fractionation with membrane-based methodology. Sep. Purif. Technol. 210, 409–416.

Ling, Z., Guo, Z., Huang, C., Yao, L., Xu, F., 2020. Deconstruction of oriented crystalline cellulose by novel levulinic acid based deep eutectic solvents pretreatment for improved enzymatic accessibility. Bioresour. Technol. 305, 123025.
Ling, Z., Tang, W., Su, Y., Shao, L., Wang, P., Ren, Y., Huang, C., Lai, C., Yong, Q., 2021. Promoting enzymatic hydrolysis of aggregated bamboo crystalline cellulose by fast microwave-assisted dicarboxylic acid deep eutectic solvents pretreatments. Bioresour. Technol. 333, 125122.
Liu, Y., Lyu, Y., Tian, J., Zhao, J., Ye, N., Zhang, Y., Chen, L., 2021. Review of waste biorefinery development towards a circular economy: From the perspective of a life cycle assessment. Renew. Sustain. Energy Rev. 139, 110716.
Lu, W., Alam, M.A., Pan, Y., Wu, J., Wang, Z., Yuan, Z., 2016. A new approach of microalgal biomass pretreatment using deep eutectic solvents for enhanced lipid recovery for biodiesel production. Bioresour. Technol. 218, 123–128.
Lynam, J.G., Kumar, N., Wong, M.J., 2017. Deep eutectic solvents' ability to solubilize lignin, cellulose, and hemicellulose; thermal stability; and density. Bioresour. Technol. 238, 684–689.
Ma, C.Y., Gao, X., Peng, X.P., Gao, Y.F., Liu, J., Wen, J.L., Yuan, T.Q., 2021b. Microwave-assisted deep eutectic solvents (DES) pretreatment of control and transgenic poplars for boosting the lignin valorization and cellulose bioconversion. Ind. Crops Prod. 164, 113415.
Ma, C.-Y., Xu, L.-H., Zhang, C., Guo, K.-N., Yuan, T.-Q., Wen, J.-L., 2021a. A synergistic hydrothermal-deep eutectic solvent (DES) pretreatment for rapid fractionation and targeted valorization of hemicelluloses and cellulose from poplar wood. Bioresour. Technol. 341, 125828.
Ma, C.Y., Xu, L.H., Sun, Q., Shen, X.J., Wen, J.L., Yuan, T.Q., 2022a. Tailored one-pot lignocellulose fractionation to maximize biorefinery toward controllable producing lignin nanoparticles and facilitating enzymatic hydrolysis. Chem. Eng. J. 450, 138315.
Ma, C.Y., Xu, L.H., Sun, Q., Sun, S.N., Cao, X.F., Wen, J.L., Yuan, T.Q., 2022b. Ultrafast alkaline deep eutectic solvent pretreatment for enhancing enzymatic saccharification and lignin fractionation from industrial xylose residue. Bioresour. Technol. 352, 127065.
Maibam, P.D., Goyal, A., 2022. Approach to an efficient pretreatment method for rice straw by deep eutectic solvent for high saccharification efficiency. Bioresour. Technol. 351, 127057.
Mankar, A.R., Pandey, A., Modak, A., Pant, K.K., 2021. Pretreatment of lignocellulosic biomass: A review on recent advances. Bioresour. Technol. 334, 125235.
Mankar, A.R., Pandey, A., Pant, K.K., 2022. Microwave-assisted extraction of lignin from coconut coir using deep eutectic solvents and its valorization to aromatics. Bioresour. Technol. 345 (126528), 8.
Martins, M.A.R., Pinho, S.P., Coutinho, J.A.P., 2019. Insights into the Nature of Eutectic and Deep Eutectic Mixtures. J. Solution Chem. 48, 962–982.
Mbous, Y.P., Hayyan, M., Hayyan, A., Wong, W.F., Hashim, M.A., Looi, C.Y., 2017. Applications of deep eutectic solvents in biotechnology and bioengineering—Promises and challenges. Biotechnol. Adv. 35, 105–134.
Morais, E.S., Mendonça, P.V., Coelho, J.F.J., Freire, M.G., Freire, C.S.R., Coutinho, J.A.P., Silvestre, A.J.D., 2018. Deep Eutectic Solvent Aqueous Solutions as Efficient Media for the Solubilization of Hardwood Xylans. ChemSusChem 11, 753–762.
Morais, E.S., Freire, M.G., Freire, C.S.R., Coutinho, J.A.P., Silvestre, A.J.D., 2020. Enhanced Conversion of Xylan into Furfural using Acidic Deep Eutectic Solvents with Dual Solvent and Catalyst Behavior. ChemSusChem 13, 784–790.
Morais, E.S., Freire, M.G., Freire, C.S.R., Silvestre, A.J.D., 2021. Enhanced furfural production in deep eutectic solvents comprising Alkali metal Halides as additives. Molecules 26, 4.
Murugan, M.D., Tee, L.H., Oh, K.S., 2021. Evaluation of the environment impact of extraction of bioactive compounds from Darcyodes rostrata using Deep Eutectic Solvent (DES) using Life Cycle Assessment (LCA), in. Journal of Physics: Conference Series. IOP Publishing 12005.
Neto, R.T., Santos, S.A.O., Oliveira, J., Silvestre, A.J.D., 2020a. Biorefinery of high polymerization degree proanthocyanidins in the context of circular economy. Ind. Crops Prod. 151, 112450.
Neto, R.T., Santos, S.A.O., Oliveira, J., Silvestre, A.J.D., 2020b. Tuning of proanthocyanidin extract's composition through quaternary eutectic solvents extraction. Antioxidants 9, 1–17.
Neto, R.T., Santos, S.A.O., Oliveira, J., Silvestre, A.J.D., 2022. Impact of Eutectic Solvents Utilization in the Microwave Assisted Extraction of Proanthocyanidins from Grape Pomace. Molecules 27, 1–15.
New, E.K., Wu, T.Y., Lee, C.B.T.L., Poon, Z.Y., Loow, Y.-L., Foo, L.Y.W., Procentese, A., Siow, L.F., Teoh, W.H., Daud, N.N.N., 2019. Potential use of pure and diluted choline chloride-based deep eutectic solvent in delignification of oil palm fronds. Process Saf. Environ. Prot. 123, 190–198.
Nolasco, M.M., Pedro, S.N., Vilela, C., Vaz, P.D., Ribeiro-Claro, P., Rudić, S., Parker, S.F., Freire, C.S.R., Freire, M.G., Silvestre, A.J.D., 2022. Water in Deep Eutectic Solvents: New Insights From Inelastic Neutron Scattering Spectroscopy. Front. Phys. 10 https://doi.org/10.3389/fphy.2022.834571.
Ong, V.Z., Wu, T.Y., Chu, K.K.L., Sun, W.Y., Shak, K.P.Y., 2021. A combined pretreatment with ultrasound-assisted alkaline solution and aqueous deep eutectic solvent for enhancing delignification and enzymatic hydrolysis from oil palm fronds. Ind. Crops Prod. 160, 112974.
Osman, A.I., Mehta, N., Elgarahy, A.M., Al-Hinai, A., Al-Muhtaseb, A.H., Rooney, D.W., 2021. Conversion of biomass to biofuels and life cycle assessment: a review. Environ. Chem. Lett. 19, 4075–4118.
Pan, Y., Alam, M.A., Wang, Z., Huang, D., Hu, K., Chen, H., Yuan, Z., 2017b. One-step production of biodiesel from wet and unbroken microalgae biomass using deep eutectic solvent. Bioresour. Technol. 238, 157–163.
Pan, M., Zhao, G., Ding, C., Wu, B., Lian, Z., Lian, H., 2017a. Physicochemical transformation of rice straw after pretreatment with a deep eutectic solvent of choline chloride/urea. Carbohydr. Polym. 176, 307–314.
Panić, M., Andlar, M., Tišma, M., Rezić, T., Šibalić, D., Cvjetko Bubalo, M., Radojčić Redovniković, I., 2021. Natural deep eutectic solvent as a unique solvent for valorisation of orange peel waste by the integrated biorefinery approach. Waste Manag. 120 (340–350), 2.
Peng, J., Xu, H., Wang, W., Kong, Y., Su, Z., Li, B., 2021. Techno-economic analysis of bioethanol preparation process via deep eutectic solvent pretreatment. Ind. Crops Prod. 172, 114036.
Procentese, A., Johnson, E., Orr, V., Campanile, A.G., Wood, J.A., Marzocchella, A., Rehmann, L., 2015. Deep eutectic solvent pretreatment and subsequent saccharification of corncob. Bioresour. Technol. 192, 31–36.
Provost, V., Dumarcay, S., Ziegler-Devin, I., Boltoeva, M., Trébouet, D., Villain-Gambier, M., 2022. Deep eutectic solvent pretreatment of biomass: Influence of hydrogen bond donor and temperature on lignin extraction with high β-O-4 content. Bioresour. Technol. 349, 126837.
Radošević, K., Bubalo, M.C., Srček, V.G., Grgas, D., Dragičević, T.L., Redovniković, I.R., 2015. Evaluation of toxicity and biodegradability of choline chloride based deep eutectic solvents. Ecotoxicol. Environ. Saf. 112, 46–53.
Rente, D., Paiva, A., Duarte, A.R., 2021. The role of hydrogen bond donor on the extraction of phenolic compounds from natural matrices using deep eutectic systems. Molecules 26, 2336.
Rico, X., Nuutinen, E.-M., Gullón, B., Pihlajaniemi, V., Yáñez, R., 2021. Application of an eco-friendly sodium acetate/urea deep eutectic solvent in the valorization of melon by-products. Food Bioprod. Process. 130, 216–228.
Ríos-González, L.J., Medina-Morales, M.A., Rodríguez-De la Garza, J.A., Romero-Galarza, A., Medina, D.D., Morales-Martínez, T.K., 2021. Comparison of dilute acid pretreatment of agave assisted by microwave versus ultrasound to enhance enzymatic hydrolysis. Bioresour. Technol. 319, 124099.
Romaní, A., Morais, E.S., Soares, P.O., Freire, M.G., Freire, C.S.R., Silvestre, A.J.D., Domingues, L., 2020. Aqueous solutions of deep eutectic systems as reaction media for the saccharification and fermentation of hardwood xylan into xylitol. Bioresour. Technol. 311, 123524.
Satlewal, A., Agrawal, R., Das, P., Bhagia, S., Pu, Y., Puri, S.K., Ramakumar, S.S.V., Ragauskas, A.J., 2019. Assessing the Facile Pretreatments of Bagasse for Efficient Enzymatic Conversion and Their Impacts on Structural and Chemical Properties. ACS Sustain. Chem. Eng. 7, 1095–1104.
Shafie, M.H., Yusof, R., Gan, C.Y., 2019. Synthesis of citric acid monohydrate-choline chloride based deep eutectic solvents (DES) and characterization of their physicochemical properties. J. Mol. Liq. 288, 111081.
Shams Esfandabadi, Z., Ranjbari, M., Scagnelli, S.D., 2022. The imbalance of food and biofuel markets amid Ukraine-Russia crisis: A systems thinking perspective. Biofuel Res. J. 9, 1640–1647.
Sharma, V., Tsai, M.-L., Chen, C.-W., Sun, P.-P., Patel, A.K., Singhania, R.R., Nargotra, P., Dong, C.-D., 2022. Deep eutectic solvents as promising pretreatment agents for sustainable lignocellulosic biorefineries: A review. Bioresour. Technol. 360, 127631.
Shen, X.-J., Wen, J.-L., Mei, Q.-Q., Chen, X., Sun, D., Yuan, T.-Q., Sun, R.-C., 2019. Facile fractionation of lignocelluloses by biomass-derived deep eutectic solvent (DES) pretreatment for cellulose enzymatic hydrolysis and lignin valorization. Green Chem. 21, 275–283.
Silva, N.H.C.S., Morais, E.S., Freire, C.S.R., Freire, M.G., Silvestre, A.J.D., 2020. Extraction of high value triterpenic acids from Eucalyptus globulus biomass using hydrophobic deep eutectic solvents. Molecules 25, 210.
Soares, B., Lopes, C., Silvestre, A.J.D., Rodrigues, P.C., Freire, C.S.R., Coutinho, A.P., 2021. Wood delignification with aqueous solutions of deep eutectic solvents. Ind. Crops Prod. 160, 113128.
Stefanovic, R., Ludwig, M., Webber, G.B., Atkin, R., Page, A.J., 2017. Nanostructure, hydrogen bonding and rheology in choline chloride deep eutectic solvents as a function of the hydrogen bond donor. Phys. Chem. Chem. Phys. 19, 3297–3306.
Sun, L.-L., Yue, Z., Sun, S.-C., Sun, S.-N., Cao, X.-F., Yuan, T.-Q., Wen, J.-L., 2022. Exploration of deep eutectic solvent-based biphasic system for furfural production and enhancing enzymatic hydrolysis: Chemical, topochemical, and morphological changes. Bioresour. Technol. 352, 127074.
Tang, Y., Yang, H., Vignolini, S., 2022. Recent Progress in Production Methods for Cellulose Nanocrystals: Leading to More Sustainable Processes. Adv. Sustain. Syst. 6, 2100100.
Ubando, A.T., Felix, C.B., Chen, W.-H., 2020. Biorefineries in circular bioeconomy: A comprehensive review. Bioresour. Technol. 299, 122585.
Vance, C., Sweeney, J., Murphy, F., 2022. Space, time, and sustainability: The status and future of life cycle assessment frameworks for novel biorefinery systems. Renew. Sustain. Energy Rev. 159, 112259.
Wang, Y., Kim, K.H., Jeong, K., Kim, N.-K., Yoo, C.G., 2021b. Sustainable biorefinery processes using renewable deep eutectic solvents. Curr. Opin. Green Sustain. Chem. 27, 100396.
Wang, W., Lee, D.J., 2021. Lignocellulosic biomass pretreatment by deep eutectic solvents on lignin extraction and saccharification enhancement: A review. Bioresour. Technol. 339, 125587 https://doi.org/10.1016/j.biortech.2021.125587.
Wang, Z.K., Li, H., Lin, X.C., Tang, L., Chen, J.J., Mo, J.W., Yu, R.S., Shen, X.J., 2020b. Novel recyclable deep eutectic solvent boost biomass pretreatment for enzymatic hydrolysis. Bioresour. Technol. 307, 123237.
Wang, R., Zhang, W., He, R., Li, W., Wang, L., 2021a. Customized deep eutectic solvents as green extractants for ultrasonic-assisted enhanced extraction of phenolic antioxidants from dogbane leaf-tea. Foods 10, 2527.

Wang, Y., Zhang, W.J., Yang, J.Y., Li, M.F., Peng, F., Bian, J., 2022. Efficient fractionation of woody biomass hemicelluloses using cholinium amino acids-based deep eutectic solvents and their aqueous mixtures. Bioresour. Technol. 354, 127139.
Wongsirichot, P., González-Mique, M., Winterburn, J., 2019. Holistic valorization of rapeseed meal utilizing green solvents extraction and biopolymer production with *Pseudomonas putida*. J. Clean. Prod. 230, 420–429.
Xia, Q., Liu, Y., Meng, J., Cheng, W., Chen, W., Liu, S., Liu, Y., Li, J., Yu, H., 2018. Multiple hydrogen bond coordination in three-constituent deep eutectic solvents enhances lignin fractionation from biomass. Green Chem. 20, 2711–2721.
Xia, Q., Chen, C., Yao, Y., Li, J., He, S., Zhou, Y., Li, T., Pan, X., Yao, Y., Hu, L., 2021. A strong, biodegradable and recyclable lignocellulosic bioplastic. Nat. Sustain. 4, 627–635.
Xu, H., Kong, Y., Peng, J., Song, X., Liu, Y., Su, Z., Li, B., Gao, C., Tian, W., 2021. Comprehensive analysis of important parameters of choline chloride-based deep eutectic solvent pretreatment of lignocellulosic biomass. Bioresour. Technol. 319, 124209.
Xu, M., Ran, L., Chen, N., Fan, X., Ren, D., Yi, L., 2019. Polarity-dependent extraction of flavonoids from citrus peel waste using a tailor-made deep eutectic solvent. Food Chem. 297, 124970.
Yan, G., Zhou, Y., Zhao, L., Wang, W., Yang, Y., Zhao, X., Chen, Y., Yao, X., 2022. Recycling of deep eutectic solvent for sustainable and efficient pretreatment of corncob. Ind. Crops Prod. 183, 115005.
Yang, J., Zhang, W., Wang, Y., Li, M., Peng, F., Bian, J., 2022. Novel, recyclable Brønsted acidic deep eutectic solvent for mild fractionation of hemicelluloses. Carbohydr. Polym. 278, 118992.
Yao, L., Cui, P., Chen, X., Yoo, C.G., Liu, Q., Meng, X., Xiong, L., Ragauskas, A.J., Yang, H., 2022. A combination of deep eutectic solvent and ethanol pretreatment for synergistic delignification and enhanced enzymatic hydrolysis for biorefinary process. Bioresour. Technol. 350, 126885.
Yu, W., Wang, C., Yi, Y., Zhou, W., Wang, H., Yang, Y., Tan, Z., 2019. Choline chloride-based deep eutectic solvent systems as a pretreatment for nanofibrillation of ramie fibers. Cellulose 26, 3069–3082.
Yu, Q., Qin, L., Liu, Y., Sun, Y., Xu, H., Wang, Z., Yuan, Z., 2019a. In situ deep eutectic solvent pretreatment to improve lignin removal from garden wastes and enhance production of bio-methane and microbial lipids. Bioresour. Technol. 271, 210–217.
Yu, W., Wang, C., Yi, Y., Wang, H., Zeng, L., Li, M., Yang, Y., Tan, Z., 2020. Comparison of Deep Eutectic Solvents on Pretreatment of Raw Ramie Fibers for Cellulose Nanofibril Production. ACS Omega 5, 5580–5588.
Zang, G., Shah, A., Wan, C., 2020. Techno-economic analysis of co-production of 2, 3-butanediol, furfural, and technical lignin via biomass processing based on deep eutectic solvent pretreatment. Biofuels. Bioprod. Biorefining 14, 326–343.
Zargar, S., Jiang, J., Jiang, F., Tu, Q., 2022. Isolation of lignin-containing cellulose nanocrystals: life-cycle environmental impacts and opportunities for improvement. Biofuels. Bioprod. Biorefining 16, 68–80.
Zhang, Z., Kouris, G.D., Kouris, P.D., Hensen, E.J.M., Boot, M.D., Wu, D., 2021. Investigation of the combustion and emissions of lignin-derived aromatic oxygenates in a marine diesel engine. Biofuels. Bioprod. Biorefining 15, 1709–1724.
Zhao, J., Lee, J., Wang, D., 2022. An integrated deep eutectic solvent-ionic liquid-metal catalyst system for lignin and 5-hydroxymethylfurfural production from lignocellulosic biomass: Technoeconomic analysis. Bioresour. Technol. 356, 127277.
Zhong, L., Wang, C., Yang, G., Chen, J., Xu, F., Yoo, C.G., Lyu, G., 2022. Rapid and efficient microwave-assisted guanidine hydrochloride deep eutectic solvent pretreatment for biological conversion of castor stalk. Bioresour. Technol. 343, 126022.
Zhou, X., Huang, T., Liu, J., Gao, H., Bian, H., Wang, R., Huang, C., Sha, J., Dai, H., 2021. Recyclable deep eutectic solvent coupling sodium hydroxide post-treatment for boosting woody/herbaceous biomass conversion at mild condition. Bioresour. Technol. 320, 124327.
Zulkefli, S., Abdulmalek, E., Rahman, M.B.A., 2017. Pretreatment of oil palm trunk in deep eutectic solvent and optimization of enzymatic hydrolysis of pretreated oil palm trunk. Renew. Energy 107, 36–41.