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Complete List of Authors:	Li, Ruolin; Nanjing Forestry University Zheng, Yayue ; Nanjing Forestry University Zhao, Xiaoxue; Nanjing Forestry University, Chemical Engineering Yong, Qiang; Nanjing Forestry University Meng, Xianzhi; University of Tennessee Knoxville College of Engineering, Department of Chemical and Biomolecular Engineering Ragauskas, Arthur; University of Tennessee Knoxville College of Engineering, Department of Chemical and Biomolecular Engineering; ORNL; The University of Tennessee Knoxville Institute of Agriculture, Department of Forestry, Wildlife and Fisheries Huang, Caoxing; Nanjing Forestry University

Recent advances in biomass pretreatment using biphasic solvent system

Ruolin Li[a], Yayue Zheng[a], Xiaozue Zhao[a], Qiang Yong[a], Xianzhi Meng[b*], Arthur Ragauskas[b,c,d*], Caoxing Huang[a*]

[a] Co-Innovation Center for Efficient Processing and Utilization of Forest Products, College of Chemical Engineering, Nanjing Forestry University, Nanjing 210037, China

[b] Department of Chemical and Biomolecular Engineering, University of Tennessee, Knoxville, TN, 37996, USA

[c] Joint Institute for Biological Sciences, Biosciences Division, Oak Ridge National Laboratory (ORNL), Oak Ridge, TN 37831, USA

[d] Department of Forestry, Wildlife and Fisheries, Center for Renewable Carbon, The University of Tennessee, Institute of Agriculture, Knoxville, TN 37996-2200, USA

Corresponding authors:

Email address: aragausk@utk.edu (Art Ragauskas); hcx@njfu.edu.cn (Caoxing Huang); xmeng5@utk.edu (Xianzhi Meng)

Abstract

The complexity and recalcitrance of lignocellulosic biomass seriously hinder its subsequent conversion to liquid fuels. To achieve high-value utilization of lignocellulosic biomass, the physical-chemical barrier should be overcome through appropriate pretreatment techniques to improve the accessibility of cellulose for efficient enzymatic hydrolysis. With the rapid emergence of novel pretreatment solvents, biphasic solvent pretreatments represent a nascent and green pretreatment method that has shown outstanding advantages and broad application prospects in the biorefinery of lignocellulosic substrates due to its ability to provide an economically viable biomass upgrading, separation process for products in solvent phase, and reutilization of solvents. Herein, different types of biphasic solvents (e.g., 2-Methyltetrahydrofuran, methyl isobutyl ketone, 1-butanol, phenoxyethanol, ionic liquid, and deep eutectic solvent) were reviewed systematically, including the fundamental designs of biphasic solvents for biomass pretreatment, their effect on the fractionation of individual biomass components (e.g., carbohydrate and lignin) and the enzymatic hydrolysis performance, and the coproduction of furan and hydroxymethylfurfural. Finally, the main pros and cons of these different biphasic solvent systems are summarized, and the future development direction is also proposed. This review can provide a reference for designing and selecting effective biphasic pretreatment methods for various types of lignocellulosic biomass.

Keywords: biphasic solvent, pretreatment, enzymatic hydrolysis, biomass, solvent recycle

1. Introduction

The conversion of lignocellulosic biomass to liquid fuel such as bio-ethanol represents one way to shift humankind dependence on traditional fossil fuels.[1-3] The main chemical composition of lignocellulosic biomass includes cellulose, hemicellulose, lignin, and non-structural extractives (e.g., fats, waxes, and inorganics). Cellulose and hemicellulose are polysaccharides, while lignin is a 3D polyphenolic polymer.[4] Based on a dry basis, the plant cell wall of noon-wood lignocellulosics primarily comprises 30-45% cellulose, 20-35% hemicellulose, and 10-25% lignin.[5] Woody lignocellulosics mainly contains 40-45% cellulose, 25-35% hemicellulose, and 20-30% lignin. **Fig. 1** shows the chemical structure of the main components of lignocellulosic biomass at different length scales.[6] Specifically, cellulose is a linear polymer consisting of β-1,4-linked D-glucose residues, consisting of crystalline and amorphous regions. Hemicellulose is a branched complex carbohydrate whose structure consists of a variety of polysaccharides such as pentose, hexose, and sugar acid residues. Finally, lignin is an amorphous aromatic polymer synthesized from free radical polymerization of three types of building block monomers called monolignols, namely p-coumaryl alcohol (H), coniferyl alcohol (G), and sinapyl alcohol (S). These monolignols are connected via a variety of chemical interlinkages, including β-O-4, β-5, β-β, 5-5, and 4-O-5, forming a macromolecule containing different types of functional groups such as methoxyl, hydroxyl, and carboxylic acid.[7] The ether linkages (e.g., β-O-4 and α-O-4) are the primarily linkages which could be easily cleaved during acid-catalyzed pretreatment, while other types of C-C bonds are typically much more resistant to chemical degradation and potentially need high temperatures. Lignin provides structural support to plant cell wall, facilitate water transfer in tissues and organs, and protect plants against biotic stresses. Being an amorphous polyphenolic hydrophobic polymer, lignin is generally considered insoluble in pH neutral aqueous solution unless it is degraded via various chemical or biological routes.[8]

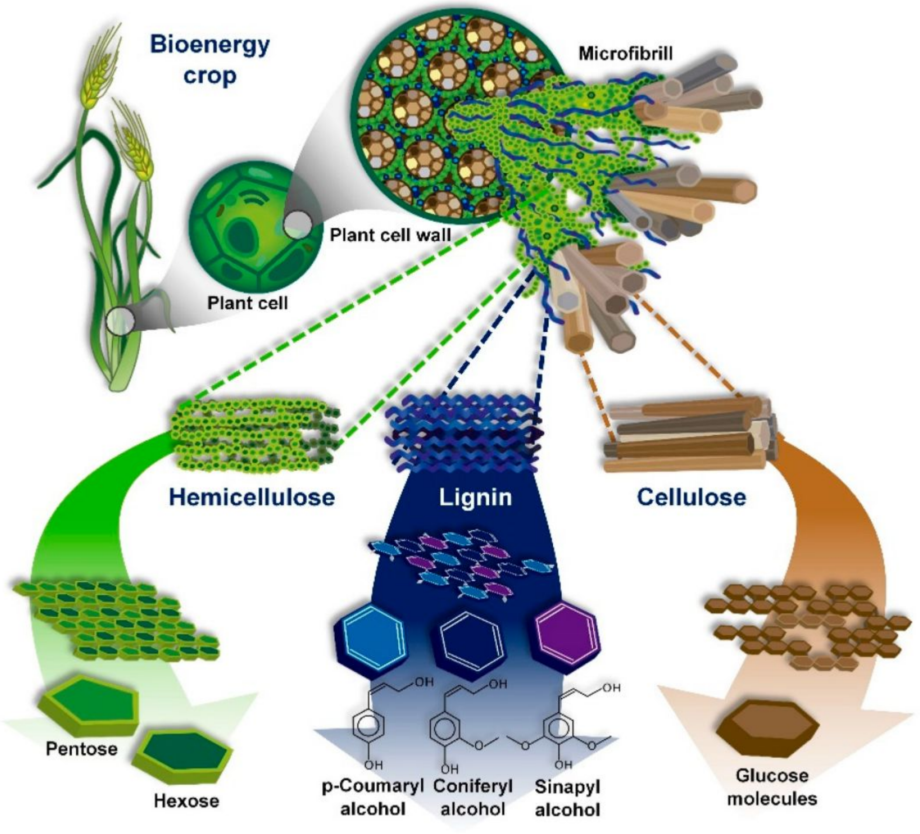

Figure 1. The basic structures of major components (cellulose, hemicellulose, and lignin) in the lignocellulosic biomass.[9]

In the cell wall of lignocellulosic biomass, each component is either chemically or physically entangled and bonded through a combination of covalent and non-covalent linkages.[10] This results in a complex structure of lignocellulosic biomass that is highly resistant to microbial or enzymatic degradation.[11] To effectively degrade polysaccharides into fermentable sugars using enzymes, raw lignocellulosic materials need to be pretreated to disrupt their native structures.[12, 13] As depicted in **Fig. 2**, the purpose of pretreatment is to depolymerize lignin, solubilize hemicellulose, and disrupt the crystalline domains of cellulose. This could result in an increase in the accessible surface area and a decrease in the degree of polymerization of cellulose, opening the lignin-carbohydrate matrix towards the efficient cellulose saccharification and other downstream conversions for the production of fermentable monosaccharide.[14]

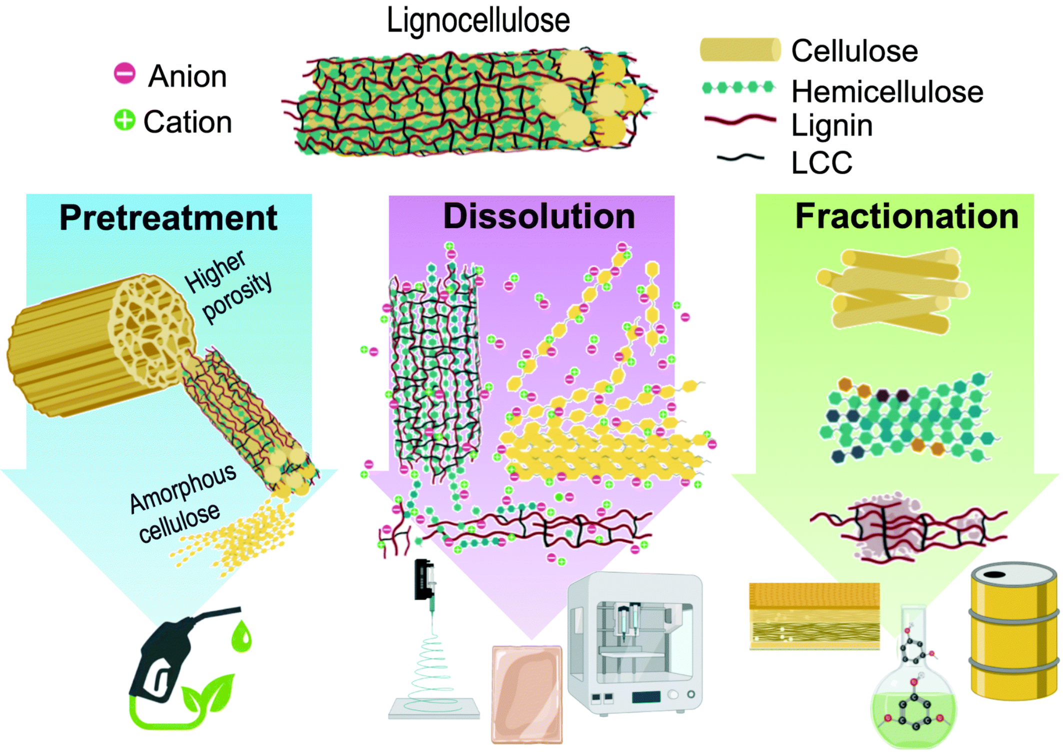

Figure 2. The effects of pretreatment on the changes of sub-structures and components of lignocellulosic biomass for efficient enzymatic hydrolysis.[15]

Currently, a large number of pretreatment methods have been performed for biomass to achieve its high enzymatic digestibility, which can be roughly classified into physical pretreatment, chemical pretreatment, and biological pretreatment.[16] Physical pretreatment includes mechanical processes as well as ultrasonic and microwave pretreatment.[17, 18] Mechanical treatment such as chipping, grinding, ball milling, and extrusion could reduce the particle size of raw materials and increase the specific surface area of cellulose.[19] This kind of physical treatment is generally applied to biomass prior to chemical pretreatment to improve the pretreatment efficiency of cellulose. Chemical pretreatments typically include dilute acid,[20] alkaline,[21] organosolv,[22] ionic liquid,[23] DES, and H_2O_2 pretreatment.[24] During the pretreatment process, lignin and hemicellulose in the lignocellulosic biomass can be degraded/removed by the solvents employed, which will reduce the barrier of the cell wall for improving the enzymatic digestibility of cellulose. Biological pretreatment involves the use of biological enzymes to degrade specific components of lignocellulosic materials to remove the physical barrier for enzymatic hydrolysis caused by lignin and hemicellulose. Some commonly used pretreatment technologies are listed in **Table 1**, which includes their major mode of actions as well as typical advantages and disadvantages. Organosolv pretreatment mainly targets lignin in the lignocellulosic biomass. It can depolymerize the large molecular weight of lignin into small molecular weight phenolic fragments that could be solubilized in the liquid phase. Currently, various acids have been coupled with organosolv solvent during pretreatments that are performed at a relatively mild condition, which can not only achieve the goal of co-removal of lignin and hemicellulose but also can minimize the formation of hydrolysis inhibitory byproducts from hemicellulose (such as FF and HMF) and avoid possible lignin condensation at the same time.[25] It has been reported that the recovered lignin fractions from organosolv pretreatment frequently has fewer structural changes compared to other treatments such as acid treatment and steam explosion.[26, 27] Most existing organosolv pretreatment methods also use water as a co-solvent to further enhance the lignin solubility.[28] Overall, it can significantly improve the enzymatic hydrolysis efficiency of raw materials by removing hemicellulose and lignin.

Table 1. Mechanisms of action, advantages, and disadvantages of different pretreatment technologies.

Pretreatment method	Major mode of action	Advantage	Disadvantage	Reference
Mechanical milling	Reduce the particle size and crystallinity of lignocellulosic materials	Control of final particle size to ease handling	High energy consumption	19
Extrusion	Shortening of fiber and defibrillation	Operate at high solids loadings, limited production of inhibitory compounds, short time	High energy consumption, effect is limited when no chemical agents are used, mostly effective on herbaceous type biomass	29
Acid	Hemicellulose and lignin fractionation	removal of hemicellulose and limited delignification	High cost of the reactors, chemicals are corrosive and toxic, formation of inhibitory by-products	20
Alkaline	Hemicellulose and lignin fractionation	Effective delignification	Formation of inhibitors	21
Organic solvent	Hemicellulose and lignin fractionation	Produce low residual lignin substrates that reduce unwanted adsorption of enzymes and allow their recycling and reuse	High capital investment, formation of inhibitory by-products	22
Oxidation	Destruction of lignin and hemicellulose	Lower production of by-products	Cellulose is partly degraded, and high reagent and processing cost	30

Ionic liquid	Cellulose crystallinity reduction and partial hemicellulose and lignin removal	Low vapor pressure designer solvent, working under mild reaction conditions	Costly reagents with complex workup, toxicity, poor biodegradability, inhibitory effects on enzyme activity	23
Hydrothermal	Hemicellulose and lignin fractionation	Residual lignin content remains inhibitory toward enzymatic hydrolysis	High water consumption and energy input	31
Ammonia fiber expansion	Lignin removal	High efficiency and selectivity for reaction with lignin	Less effective for softwood, costly ammonia, environmental concerns	32
Sulfite	Lignin removal and modification with SO_3^- group	Effective for woody materials, energy-efficient	Necessary for pretreatment to be preceded by biomass size-reduction	33
Biological	Lignin removal	Low cost, simple equipment	The hydrolysis rate is very low, and it is difficult to be used in industrial production	34

Currently, lignin-first fractionation of biomass has been receiving increasing interest because the approach can be tuned to protect lignin structure from severe recondensation for further application.[35, 36] Meanwhile, significant amount of lignin could be also removed from the cell wall, leading to the production of a cellulose-rich solid residue that is highly digestible by enzymatic hydrolysis. Therefore, integration of lignin-first fractionation and biphasic pretreatment for biomass can realize the effective depolymerization/modification of lignin during the fractionation process and facilitate subsequent lignin valorization.[37] Organic aqueous solvents such as water/ethanol,[37] water/acetone,[37] and water/γ-valerolactone (GVL),[38] water/glycerol have been investigated for monophasic organosolv pretreatment processes because they have a great ability to dissolve lignin.[39] Furthermore, some organic solvents (e.g., Cyrene[40] and dimethyl isosorbide[40]) can also be derived from biomass resources, therefore utilizing those renewable solvents in biomass pretreatment paves the way for realizing a closed-loop environmentally friendly process for future lignocellulosic biorefineries. Although these monophasic pretreatments solvent system can realize the solubilization and fractionation of lignin and hemicelluloses after the pretreatment, they still face efficiency hurdles due to product separation and retrievability of solvent issues. The biphasic pretreatment system has been widely studied, aiming to better recover dissolved lignin/hemicellulose and extract products in solvent phase with higher purity. After the co-dissolving of lignin and hemicellulose from cell wall of biomass by biphasic pretreatment, a good enzymatic digestibility of cellulose in the pretreated solid can be achieved to release fermentable sugars. In addition, the used solvents in the biphasic system after pretreatment can be easily recovered for recycling by ordinally standing and filtration. Hence, biphasic pretreatment may produce fewer chemical pollutants, which is considered as the environment-friendly technology for the bio-refinery.[41, 42] As a nascent and green pretreatment method, biphasic pretreatment has gradually shown outstanding advantages and broad application prospects in the biorefinery. The analysis of core papers published papers in WOS (Web of Science) with keywords of "Biphasic " and " Pretreatment" showed that the numbers of articles in this field are gradually increased from 2001 to 2022, indicating the biphasic pretreatment is becoming a hot research topic (**Fig. 3A**). Using the Co-Occurrence 9.9 (COOC) software to analyze the hierarchical cluster analysis of high-frequency phrases in the published papers, it can be seen from the two-mode matrix figure (**Fig. 3B**) that the high frequency words were “biomass”, “lignin”, “cellulose”, “glucose” and “enzymatic hydrolysis”. Biphasic pretreatment is a relatively new developing technology, and various works about this topic in biorefinery have been published, while there are few reviews to summarize and evaluate the pros and cons of this particular pretreatment system.

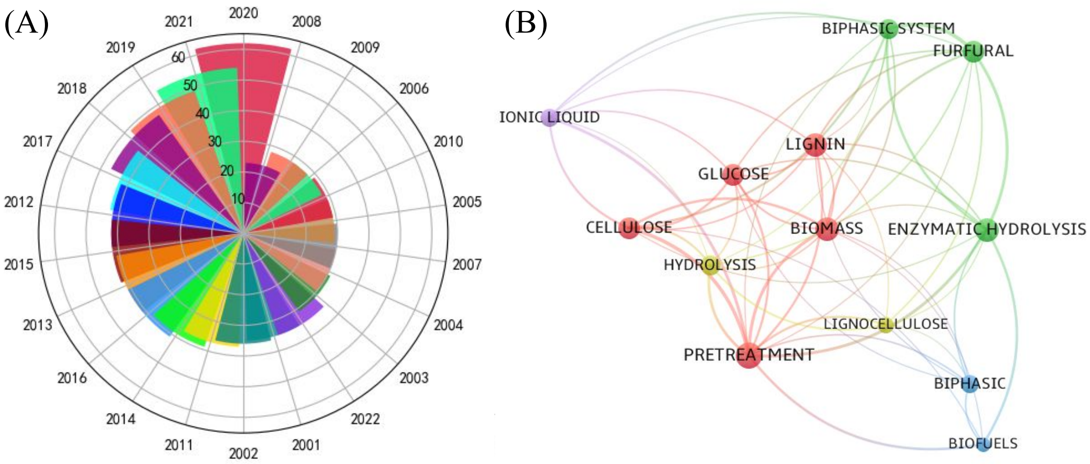

Figure 3. The accordingly published papers from 2008 to 2022 (A); The keyword network of biphasic biomass pretreatment (B).

In this review, some commonly used biphasic solvent pretreatments developed in recent years are summarized and compared, which provides a reference for developing a more effective biphasic pretreatment to recover the different fractions of lignocellulosic biomass. In addition, the future development of these different biphasic solvent systems are also proposed.

2. *Application and types of biphasic solvent pretreatments*

Biphasic solvent systems used in biomass pretreatment are typically composed of two partially or fully immiscible phases, commonly an organic solvent and water or occasionally two immiscibly organic solvents. Commonly, the employed organic solvent that could be used to form a biphasic pretreatment solvent system include 2-Methyltetrahydrofuran (2-MeTHF),[43] Methyl isobutyl ketone (MIBK),[44] butanol,[45] phenol,[46] phenoxyethanol,[47] cyrene,[48] and γ-valerolactone (GVL).[49] Currently, the main principle for the selection of these solvents in the biphasic pretreatments is considering their relative energy difference (RED) values with lignin. In 1967, Charles proposed the concept of Hansen solubility parameters (HSP), which was aimed to predict if one material will be dissolved in another and form a solution. The RED concept was originated from the combining the three parameters (δ_d, δ_p, and δ_h) with the interaction radius. It is pointed out that if RED < 1 indicates that the molecules are alike and will dissolve; RED = 1 means the system will partially dissolve; RED > 1 means the system will not dissolve. Hence, the physical properties, Hansen solubility parameters (HSP) and green solvent rating of the common biphasic solvents are summarized in Table 2.

Table 2. Physical properties, solubility parameters and green solvent ratings for selected organic solvents.

Solvent	Boiling point (°C)	Flash point (°C)	HSP (Mpa$^{1/2}$) δ_D	δ_P	δ_H	RED*	Green solvent rating[a] Safety	Health	Environment	Ranking[b]
Butanol	118	35	16.0	5.7	15.8	1.06	3	4	3	Recommended
2-MeTHF	80	-11	16.9	5.0	4.3	1.35	6	5	3	Problematic
GVL	205	81	19.0	16.6	7.4	0.83	1	5	7	Problematic
MIBK	118	14	15.3	1.4	2.0	1.46	4	2	3	Recommended
Toluene	111	4	18.0	5.9	14.9	1.54	5	6	3	Problematic
Cyrene	226	108	18.8	10.5	7.0	0.89	1	2	7	Problematic

[a] Value obtained from CHEM21 selection guide of organic solvents.[50]

[b] Recommended: solvents to be tested first in a screening exercise, if of course there is no chemical incompatibility in the process conditions; Problematic: these solvents can be used in the lab, but their implementation in the pilot plant or at the production scale will require specific measures, or significant energy consumption.

[*] RED of lignin-solvent interaction was calculated using Hansen solubility sphere radius of lignin (~13.7).

Novel ionic liquid and deep eutectic solvent (DES) can also form a biphasic solvent system with water or organic solvent to facilitate biomass processing. For example, it has been hypothesized that apolar solvents have a higher capacity than poplar solvents in terms of extracting furans from the aqueous solution.[51] On the other hand, solvents like GVL and Cyrene have great solvent power dissociating lignin as indicated their relatively low relative energy difference (RED <1), therefore they could be used to directly target lignin, and overcome biomass recalcitrance.

Depending on the HSPs and physicochemical properties of the solvent, these different biphasic systems could primarily remove the lignin in the cell wall of biomass. Depending on the co-solvents used in biphasic systems, such as acid solution or alkaline solution, the hemicelluloses in the cell wall of biomass can also be partially or total extracted alongside with lignin. The simultaneous removal of lignin and hemicellulose from biomass will endow the cellulosic residue excellent enzymatic digestibility. In addition, the acid-based biphasic system could extract furan (FF) and hydroxymethylfurfural (HMF) products from the reactive phase (e.g., dehydration in aqueous) and prevent possible overreactions. It is well documented that FF and HMF can be obtained from carbohydrates (e.g., cellulose and hemicellulose) in lignocellulosic biomass (Fig 4A and 4B). They are versatile platform biorenewable chemicals that could be used to make a broad array of other important chemicals and fuel products.[52,53] Due to the ability of some organic solvents to stabilize the reactive intermediates and extract the final product, the biphasic organosolv pretreatment has the advantage of promoting FF formation and slowing its degradation with prolonged reaction times commonly employed with aqueous only solvent systems[5] Hence, the application and types of biphasic solvent pretreatments for the achievement of excellent enzymatic digestibility of biomass and co-production of FF/HMF will be systematically reviewed in the following sections.

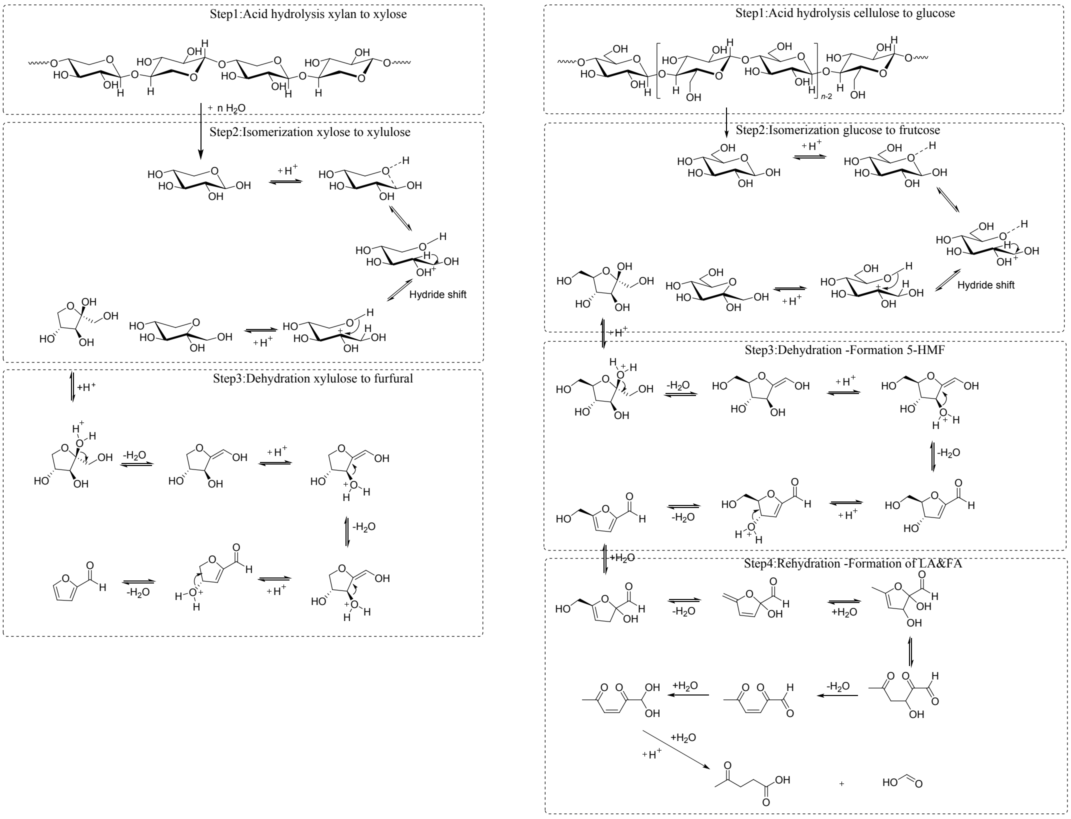

Figure 4. Key steps of reaction pathway involved in xylan and cellulose conversion to FF (A) and HMF (B), respectively.[54]

2.1. Methyl isobutyl ketone (MIBK) biphasic pretreatment system

Methyl isobutyl ketone (MIBK), a derivative of acetone, could be also generated from glucose and thus is considered a renewable bio-solvent.[55] The biphasic pretreatment system it formed with water is known for its ability to improve the FF and HMF selectivity during acid pretreatment, comparing to that for other organic solvent such as toluene or cyclohexanol (**Fig. 5A**). Zhang et al. showed that FF yield increased from 65 to 85% when the MIBK/water biphasic system was used compared to single-phase systems.[56] This study also showed that sulfuric acid is a better catalyst than hydrochloric acid in terms of maximizing furfural yields. Similarly, a butanol modified MIBK/water biphasic system converted over 90% fructose at high concentrations to HMF at 80% selectivity, with the help of DMSO to suppress undesired side reactions.[57] The addition of a salt, such as NaCl, into the biphasic system could increase the partition coefficient of furans into the organic phase, therefore improving the yields. For example, addition of NaCl into the MIBK/water biphasic system significantly increased the FF yield from 8.7 to 42.5%.[58] Effect of MIBK/H_2O ratio on the FF and HMF yield has also been investigated, and results showed that a 6:4 organic-to-aqueous ratio gave maximum FF yield around ~65%, while relatively low HMF yields (from 2 to 5%) were obtained.[59] FF and HMF possess an excellent selectivity and distribution coefficient with MIBK. These products in the MIBK phase can be easily separated by vacuum evaporation or distillation which accompanied with the purpose of solvent recovery.[58] For example, it has been reported that the vacuum evaporation technology could separate 99.5% of MIBK and 97.5% of HMF at conditions of 13 mbar and 70 °C.[60] Recently, Qi et al. proposed MIBK/water system with synthesized magnetic carbon-based solid acid catalyst (MMCSA) to achieve a highest FF yield of 79.04% from xylose (**Fig. 5B**).[61] This suggested that MIBK/H_2O biphasic system had a much more pronounced effect on the degradation of hemicellulose than cellulose.

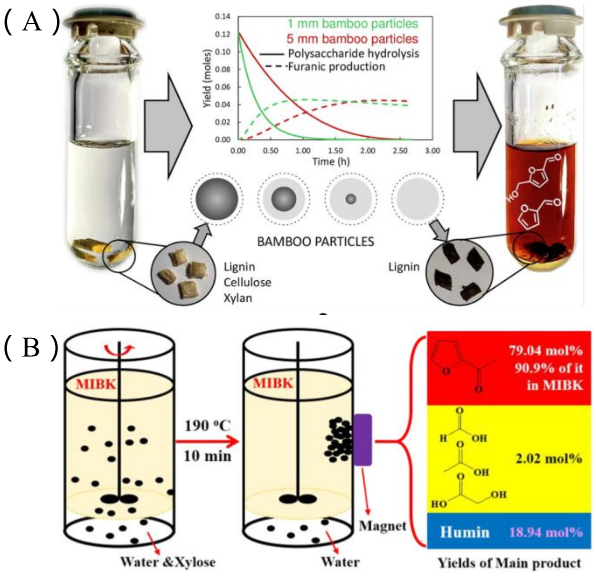

Figure 5. (A) Simultaneous production of 5-HMF and FF from bamboo in a MIBK/H_2O biphasic system;[62] (B) Schematic diagram of MIBK/water biphasic system with synthesized magnetic carbon-based solid acid for the production of FF.[61]

It has been shown that the MIBK/water pretreatment system possesses the ability to degrade xylose or xylan from biomass. Hence, this pretreatment is also used to overcome biomass recalcitrance to some extent by dramatic solubilization of hemicellulose, alternation of cellulose crystallinity, and change of biomass surface morphology.[5, 61] For example, it has been reported that the biphasic system of MIBK/water showed good performance to remove of hemicellulose, which can yield pretreated biomass with a enzymatic digestibility of 70.7% for *Eucalyptus*[58] and 80% for *Miscanthus*.[63] When aluminum nitrate was used as catalyst in the MIBK/water biphasic pretreatment system, 97% of hemicelluloses in *Eucalyptus* could be solubilized, and the enzymatic hydrolysis of the pretreated biomass reached 85.5%.[58] In addition, a kinetic study has shown that a near complete acid hydrolysis of cellulose to glucose in the MIBK/water biphasic system could be achieved using HCl as catalyst.[61]

A kinetic study has shown that the MIBK/water biphasic system didn't change the fundamental kinetics of the xylose dehydration reactions in the aqueous phase; instead the organic phase's ability to serve as "storage" for the formed FF products played an essential role in maximizing the final product yield.[64] The production of HMF from cellulose could also benefit from the MIBK aqueous biphasic system.[65] For a more elaborate discussion on the advances in HMF production from biomass in the biphasic solvent, the reader is referred to the following review.[60] In-situ microwave-assisted hydrolysis of biomass to both FF and HMF was also reported.[54, 62] Overall, the key advantages of this biphasic system are 1) significantly mitigating the recalcitrance of biomass for improving its enzymatic digestibility by removing hemicellulose and lignin from cell wall, 2) suppression of unwanted side reactions due to the in-situ extraction of HMF and furfural into the MIBK phase, and 3) an easy recovery of HMF and furfural from the reaction system.

2.2. 2-Methyltetrahydrofuran biphasic pretreatment system

2-Methyltetrahydrofuran (2-MeTHF) is a renewable liquid with similar properties to MIBK, and it can be directly produced from renewable resources such as furfural, γ-valerolactone, and levulinic acid.[43] It is relatively stable in an acidic environment and is highly immiscible with water, so its aqueous solution could form a two-phase system that could potentially be used to pretreat lignocellulosic biomass.

For example, Vom Stein et al. first proposed a 2-MeTHF/water two-phase solvent system with oxalic acid as a catalyst, also known as the OrganoCat approach, for the effective depolymerization of hemicellulose in the aqueous phase under mild conditions.[66, 67] Meanwhile, lignin was depolymerized and solubilized into the organic phase and could be directly separated from the pulp and the soluble carbohydrates by *in situ* extraction. Stiefel et al. showed that an alkaline solution of pH 13-14 could completely extract lignin from the organic phase into the aqueous phase accompanied by a decrease in molecular weight (**Fig. 6**).[68] In another study, Li et al. showed that after 2-MeTHF/water pretreatment, the recovered bamboo lignin was sugar-free, exhibited a typical natural lignin structure and functionality, and had a medium molecular weight ranging from ~2240-3730 g/mol.[69] Due to the removed lignin, the resulting pretreated solid residue mostly contained cellulose and could be directly converted to glucose via enzymatic hydrolysis. Enzymatic hydrolysis of MeTHF/water pretreated bamboo showed a 6.7-fold increase in glucose release compared to the untreated bamboo.[69] Grande et al. further showed that biomass with a loading of 100 g/L could be effectively fractionated within 3 h, and no significant amount of by-products such as furan was produced due to the mild applied pretreatment temperature (<140 ^{o}C).[70] The pretreatment was scaled-up to a 3L reactor, and biomass flexibility was also demonstrated. Meanwhile, the yield of cellulose hydrolysis of the pretreated bamboo residue reached 92.9%, suggesting this approach is a promising way to convert biomass to biofuels. Overall, the proposed work represents an energy-efficient strategy for the pretreatment and fractionation of lignocellulosic biomass, which can not only achieve the goal of improving enzymatic digestibility of biomass but also for the valorization of lignin and hemicellulose in biomass during pretreatment.

In addition, the biphasic 2-MeTHF/water pretreatment could also be catalyzed with acids (such as Lewis acids, H_2SO_4, and oxalic acid) in the water phase, which is aimed to increase the degradation performance of hemicellulose. For example, Morone et al. performed the 2-MTHF biphasic system containing oxalic acid with straw at 148 ℃ for 25 min, which could achieve 74.69% removal yield of hemicellulose and 60.87% degree of delignification. The enzymatic digestibility of pretreated straw was 42.12%.[71] In the work of Sun et al., a highest furfural yield (68.1%) and glucose yield (78.9%) could be obtained from corn stalks pretreated by 2-MeTHF/H_2O biphasic system with 0.05 M H_2SO_4 at 170 ℃ for 60 min.[72] When coupling a Lewis acid catalyst, such as $AlCl_3$ with this pretreatment system for birch wood at 180 ℃ for 1 h, an excellent degradation of hemicellulose (100%) endowed the pretreated birch with the maximum enzymatic hydrolysis yield of 77%, which is 7.4 fold improved compared to raw material. The above system ultimately achieved a similar one-pot transformation of lignocellulosic biomass to biofuel precursors along with a clean lignin stream with high valorization potential.[73]

Overall, the 2-MeTHF/water co-solvent pretreatment system mainly has the following advantages over other types of acid-catalyzed organosolv pretreatment: 1) compared with sulfuric acid, formic acid, and other acid catalysts, oxalic acid is less corrosive; 2) 2-MeTHF is environmentally friendly because it is biomass-derived and easy to recycle, and 3) a good enzymatic digestibility of pretreated biomass can be achieved with relatively mild pretreatment conditions. Compared with other biphasic solvent systems, 2-MeTHF showed limited ability to remove majority of lignin from the plant cell wall, thus the enzymatic hydrolysis of pretreated biomass typically requires high enzyme loading which significantly added extra cost to the bioconversion process.

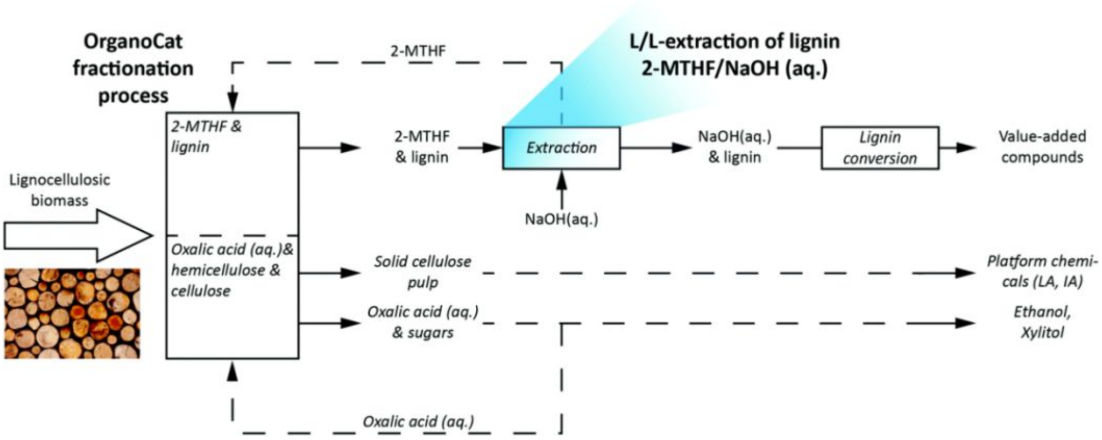

Figure 6. The OrganoCat process for the fractionation of lignocellulosic biomass with the subsequent alkaline extraction of lignin.[68]

2.3. 1-butanol biphasic pretreatment system

1-Butanol and water can form a biphasic solvent system in the range of 1.6–19.0 mol/mol at a treatment temperature of 200 °C, simultaneously providing a Hildebrand solubility parameter (δ) of 28.5 and 42.0 Mpa$^{1/2}$ representing the organic and aqueous phase, respectively.[45] This indicated that both hemicellulose and lignin could be effectively solubilized by the butanol/water biphasic system due to the similarity between δ of the solvent system and the δ values of lignin and hemicellulose. Kawamata et al. demonstrated the advantages of this butanol/water biphasic system over conventional ethanol organosolv pretreatment by showing that a much greater level of lignin and hemicellulose removal could be achieved in the butanol/water system (as shown in **Fig. 7A**).[45] The pretreated hardwood possessed an excellent enzymatic digestibility. In addition, it also demonstrated that lignin could also be catalytic depolymerized and cracked to phenols in this novel butanol/water biphasic system in a series of studies. [74-76] To investigate the versatility of the butanol/water biphasic system, Schmetz et al. applied this biphasic pretreatment on biomass of various compositions and origins (e.g., eucalyptus, beech, Japanese cedar, sugar cane bagasse, beet pulp, sugar beet pulp and tall fescue) and subsequently assessed the efficiency of pretreatment in terms of delignification, pulp/lignin purity, lignin molecular weight, and enzymatic digestibility of pretreated materials.[77] These reported results showed that this type of biphasic pretreatment is more effective when applied on hardwood and herbaceous plant. Excellent enzymatic hydrolysis yields could be achieved with 96% sugar release for sugar cane bagasse and 100% for sugar beet pulp and tall fescue. While softwoods, such as Japanese cedar was too recalcitrant for this pretreatment to achieve acceptable enzymatic digestibility, which is due to the high quantity of lignin composed mostly of G-units, leading to only 12% delignification. Conversion of cellulose to HMF in butanol/water biphasic system catalyzed by metal chloride was also reported with promising yields, which could achieve the HMF yields of 90%.[78] In addition, it is found that a furfural yield with 77.5% could be achieved from corncob with 99.7% of xylose conversion.[79] Hence, 1-butanol can be regarded as a promising biphasic pretreatment system to not only remove hemicellulose/lignin for achieving good enzymatic hydrolysis but also co-produce the valuable HMF and FF from the degraded products.

Lignocellulosic reductive catalytic fractionation (RCF) is an emerging chemocatalytic biomass conversion technology that integrates biomass pretreatment (i.e. delignification) with lignin depolymerization and stabilization. After RCF, a cellulose-rich pulp and a lignin-derived bio-oil comprising phenolic monomers in close-to-theoretical yields are obtained.[80] Hence, this concept has been also introduced in the butanol biphasic pretreatment system. For example, Renders et al. showed that RCF of *Eucalyptus* could be achieved in a butanol/water biphasic system at 200 ^{o}C by using Ru/C as the catalyst, ultimately converting biomass into a cellulose-rich pulp, a lignin-derived bio-oil, and a hemicellulose-derived polyols (**Fig. 7B**).[81] The produced cellulose-rich pulp can be sustainable used to produce the fermentable sugars by enzymatic hydrolysis. In addition, the cooling-induced phase separation of butanol and water offers a facile way to separate the aromatic component (organic phase) from polyols products (aqueous phase). Currently, the Ru/C-catalyzed RCF process in butanol/water has been performed on different types of biomass, such as eucalyptus,[82] and poplar sawdust,[83] which is aimed to firstly degrade the lignin into aromatic monomers and obtain the lignin-rare solid for further enzymatic hydrolysis. In addition, coupling sodium dithionite with butanol/water biphasic system has been examined with birch sawdust, which also produces a cellulosic pulp for enzymatic hydrolysis with yield of 91.4%.[84, 85] The high enzymatic digestibility of pretreated biomass by butanol/water biphasic system with co-solvent is due to the obviously structural changes occurring in the pretreatment.

In summary, 1-butanol can be produced from biomass and is suitable for pretreatment as an organic solvent just like ethanol. While, the 1-butanol/water system only presents a two-phase at certain temperatures and concentration conditions, and the lignin removal rate for softwood is very low, so this system is not suitable for all conditions of pretreatment. In addition, the recovery of the solvent system is also a challenge yet to be resolved. On the other hand, the high alcohol content of pretreatment (e.g., 95% butanol) could only form one phase solution with water, but is capable of suppressing lignin degradation reactions and thus is typically applied on biomass to isolate lignin with high integrity or β-O-4 linkages and high yields.[86] Such lignin are ideal substrates for depolymerization to mono-aromatic chemicals.

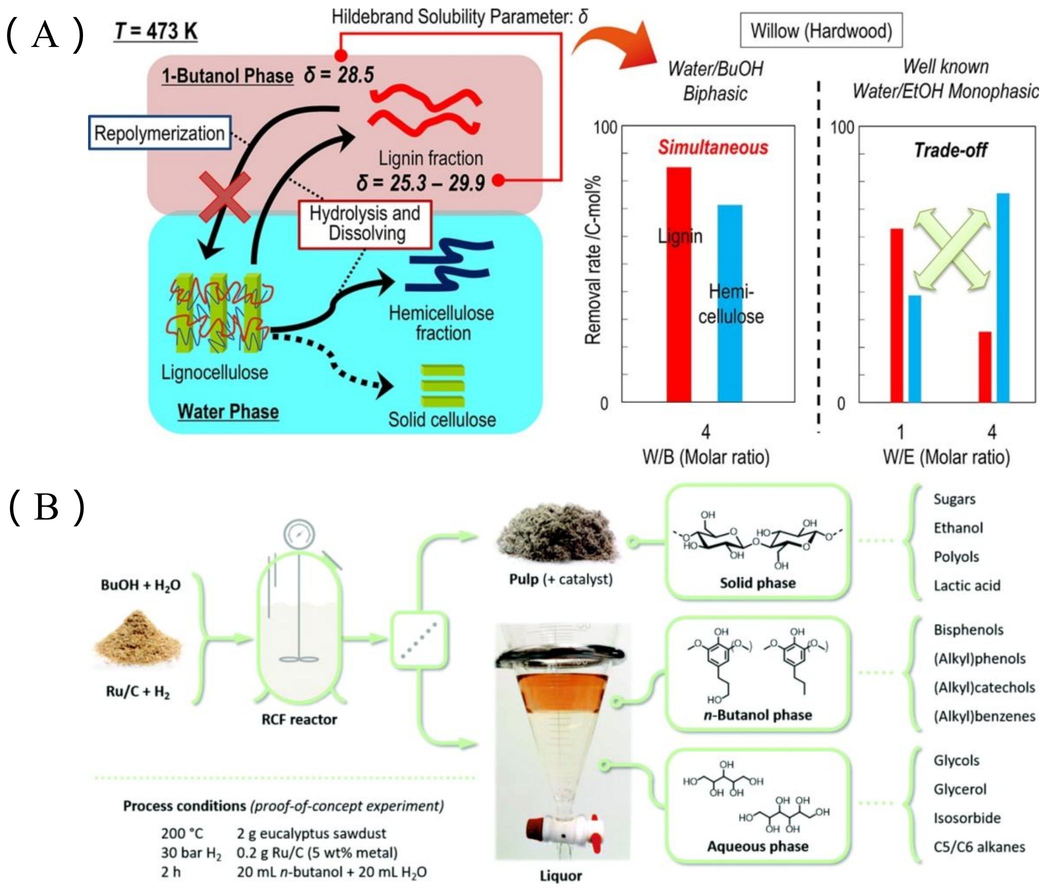

Figure 7. (A) Water/1-butanol pretreatment with appropriate δ values for the dissolution of lignin and hemicellulose;[45] (B) Schematic diagram of butanol/water biphasic RCF process to produce a cellulosic pulp, lignin-derived phenolic monomer, and hemicellulose-derived polyols.[81]

2.4. Phenoxyethanol biphasic pretreatment system

Phenoxyethanol is considered a green, non-toxic organic solvent with a RED value of 0.94 with respect to lignin, suggesting it is a good lignin solvent.[47] It is a biocompatible and biodegradable solvent that is used in different commercial products, such as cosmetics, skincare products, vaccines, and preservatives for medicine.[87] Lastly, phenoxyethanol and water are almost completely immiscible, thus offering a great opportunity to prepare a two-phase solvent pretreatment system that mainly targets lignin.

Currently, biphasic fractionation of rice straw under mild conditions (e.g., 130 °C, 0.05 M sulfuric acid, and 2 h) in acidified phenoxyethanol/water system has been reported.[88] After pretreatment, the majority of cellulose (>85%) was retained in the solid residue, and more than 90% and 60% of hemicellulose and lignin were removed from the native rice straw, resulting in an ~80% cellulose conversion after enzymatic hydrolysis. Actually, the phenoxyethanol/acid ratio plays an essential role in governing the extent of delignification, which can linearly affect the enzymatic digestibility of pretreated. It is reported that more than 90% of lignin could be removed from bamboo when 75% of phenoxyethanol was mixed with 25% water, resulting in >90% of enzymatic digestibility.[89] The pretreatment liquor could be recycled/reused and the pretreated biomass still showed relatively high enzymatic digestibility ranging from 67 to 77%. The phenoxyethanol/water biphasic system could also be performed under alkaline conditions, which demonstrated superior delignification performance (82.16% lignin removal) at 80 °C to achieve a good enzymatic digestibility (>80%) for rice straw.[90] Except for acid/alkaline solutions, acetone has also been proposed in the phenoxyethanol/water system to pretreat the different biomass, which could result an excellent delignification (>92%) for the satisfying enzymatic digestibility (>80%) for bagasse and corncob.[91] All of the above references demonstrate that phenoxyethanol/water biphasic system has the advantages of being green, environment-friendly, and recyclable, which can achieve high lignin and hemicellulose removal and enzyme digestibility. While, the airtight pretreatment equipment should be applied for the phenoxyethanol based pretreatment. As the safety hazards for human with stomach upset, dizziness, nausea, respiratory problems, and headaches may be occurred when they inhale a large amounts of exposed phenoxyethanol in the industrial operating environment.

2.5. Ionic liquid biphasic pretreatment system

Ionic liquid (IL), known as room temperature molten salt, has the physicochemical properties of non-flammability, extremely low vapor pressure, and high chemical stability due to the strong electrostatic forces between ions.[92] IL has excellent hydrogen bond coordination ability, which can break the hydrogen bonds of carbohydrates and lignin in lignocellulosics and make the plant cell wall structure loose and porous. Thus, it could provide more substrate binding sites that are beneficial to the solubilization and separation of lignocellulose components.[93] ILs could be designed by a different combination of selected anions and cations. The common anions of ILs include Cl^-, Br^-, BF_4^-, PF_6^-, $CF_3SO_3^-$, and CH_3COO^-, while IL cations are typically organic compounds including imidazolium, ammonium, pyridinium, and phosphonium. Some common cations and anions in ILs used in the pretreatment process are shown in **Fig. 8**. The application of ILs in biorefinery has expanded to the biomass pretreatment and characterization, and it has been reported that some ILs could solubilize the entire plant cell wall for NMR characterization and selectively remove lignin or hemicellulose during biomass pretreatment.[94, 95]

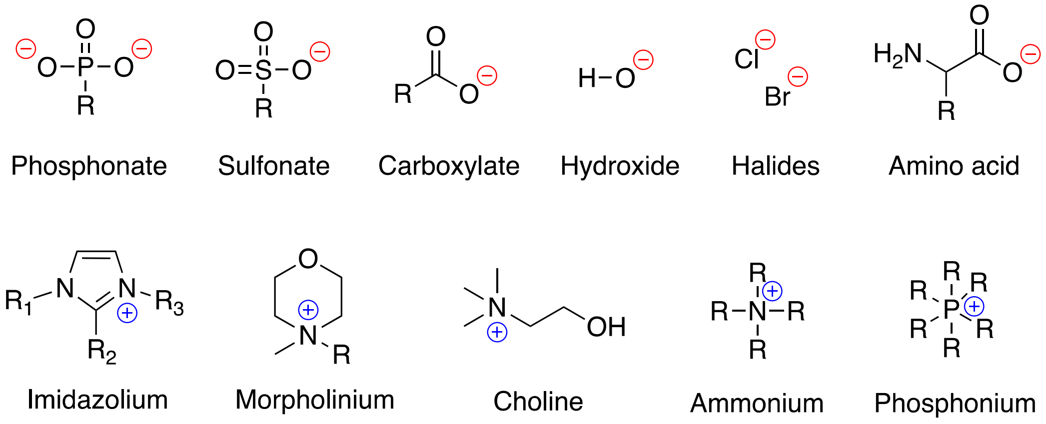

Figure 8. Typical anions and cations in ILs.

The majority of IL pretreatments in the literature target lignin and is performed in a single-phase system (i.e., neat IL); water is often used as an antisolvent to precipitate the carbohydrate-rich and highly digestible cellulosic material, which can achieve the good enzymatic digestibility with yield over 80%. Aqueous ILs could also be potentially utilized as a biphasic system to pretreat lignocellulosic biomass for enzymatic hydrolysis. First of all, the addition of water could decrease the viscosity of the IL system, thus increasing the mass transfer of solvent into the cell wall of lignocellulose during biomass pretreatment as well as increasing the lignin solubility by altering the solubility parameter of the solvent. The increased removal of lignin from the cell wall of biomass by IL pretreatment endow the solid residue with good enzymatic sugar release properties, such as 95% enzymatic hydrolysis yield for wheat straw pretreated by cholinium argininate ([Ch][Arg]),[96] 93.1% yield for wheat straw and 82.9% yield for eucalyptus pretreated by [emim][HSO4],[97] 81.7% yield for corn stalk pretreated by [Bmim]BF4/water,[98] and 99.0% for pussy willow pretreated by [EMIM]Ac/DMSO.[99] In addition, various co-solvents, such as glycol, imidazolium, and $FeCl_2$, have also been proposed to be added in the IL system to improve the pretreatment efficiency to achieve satisfying enzymatic digestibility of biomass (over 90%).[100-102] Generally, lignin solubility in IL aqueous solution has been investigated in different pretreatment systems, and results showed that HSP theory could be used to assess the range of IL content in the IL-water mixture, and maximum lignin solubility could be achieved at 70 wt% IL content in the dialkylimidazolium based IL system.[103] In addition, IL/water biphasic system also showed some promises for recovering the IL, which plays an essential role in the industrial application of ILs as the pretreatment for the biorefinery of different lignocellulosic biomasses.[104-106] One of the challenges is how to effectively separate the sugar products from the IL system as well as recovery and reuse of the expensive IL. Acid hydrolysis of pure cellulose or cellulose in pretreated biomass to produce the sugars could be performed in an imidazolium-based IL system, and sodium hydroxide could be added into the IL system to induce a biphasic system that can achieve simultaneous extraction of glucose product and recycling of the IL.[107, 108] Electrolytes, such as, $AlCl_3$, $MgCl_2$, NaCl and KCl could also be used to induce the formation of the biphasic system and promote the formation of HMF from cellulose.[109] Besides adding an electrolyte to induce the formation of a biphasic system after the hydrolysis reaction, acid hydrolysis of cellulose directly in IL/water biphasic system was also reported.[110] After the reaction, an aqueous phase that is rich in glucose and an IL phase that is rich in HMF were obtained. The above-mentioned alkaline solution of the imidazolium-based IL system is also capable of serving as a biphasic pretreatment liquid, achieving up to 82% delignification.[111]

In general, compared with traditional organic reagents, ionic liquids not only have a variety of excellent properties, such as thermal stability, designability, and non-volatility, but also have stronger delignification performance. The biphasic system formed with water could enable facile recycling of IL and easy recovery of the hydrophilic sugar-derived products from the reaction system. The IL/water biphasic system could also facilitate high-efficiency acid hydrolysis of lignocellulosic biomass. Compared to traditional IL pretreatment followed by enzymatic hydrolysis, the consolidated pretreatment and acid-hydrolysis process offer a promising route to produce sugar monomers from native biomass without the utilization of enzymes. While, ionic liquids are costly to produce on a large scale, which makes it difficult to apply them as the commercial pretreatment technology.

2.6. Deep eutectic solvents (DESs) biphasic pretreatment system

Deep eutectic solvents (DESs), a eutectic mixture composed of a hydrogen bond donor (HBD) and hydrogen bond acceptor (HBA) at a specific molar ratio, are considered a green alternative solvent than ILs. The common salts as hydrogen bond HBA and HBDs used in DESs system are listed in **Fig. 9.**[112] The research on DESs has escalated in recent years due to their low cost, environmental friendliness, and ease of preparation. Compared with ILs, DESs have favorable characteristics such as non-flammability, biocompatibility, and biodegradability.[113, 114] DES have been found to be an effective pretreatment technique that mainly targets for lignin dissolving and degrading, which can generate cellulose-rich pulp materials with highly enzymatic digestible capacity. For example, excellent enzymatic digestibility after pretreatment has been reported for various types of biomass including *Eucalyptus* (94.3%),[10] bamboo (81.3%-96.0%),[13, 115] and corn stover (70%)[116] using DES system including lactic acid and choline chloride, lactic acid and betaine, and xylitol and choline chloride.

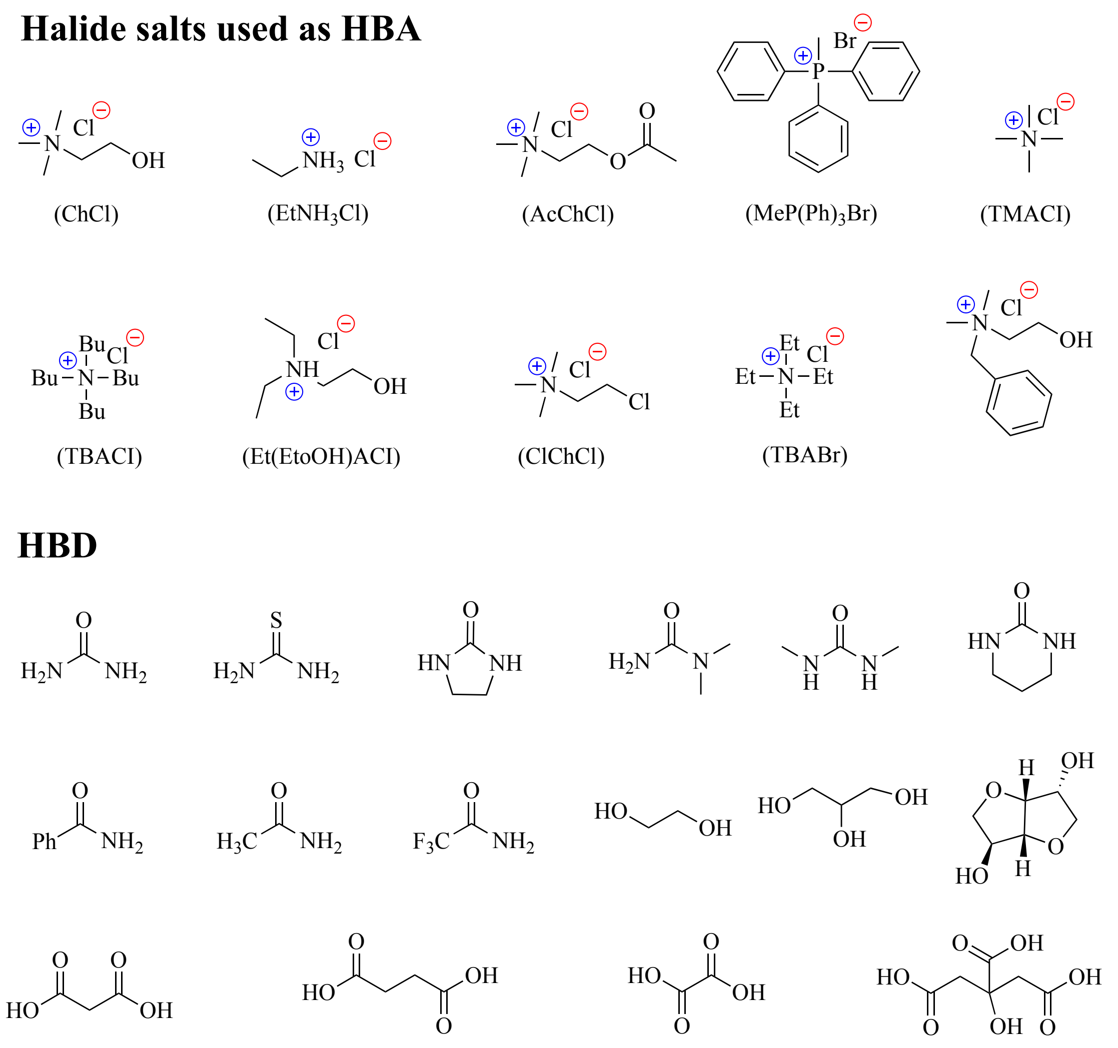

Fig. 9 Common salts as hydrogen bond HBA and HBDs used in DESs system.[112]

The single-phase DES pretreatment and its effect on lignin extraction and saccharification enhancement has been extensively studied and reviewed.[117, 118] However, research on biphasic DES pretreatment is still in its infancy. Currently, choline chloride (ChCl) based DES system is known to be a good reaction media for xylose dehydration.[119] An aqueous DES comprising ChCl and ethylene glycol as HBA and HBD could form a biphasic system with acetone (serve as extraction phase), in which xylose could be effectively converted to FF with 75% yield and selectively (>90%) partitioned into the acetone phase.[120] By this traditional choline chloride (ChCl) based DES pretreatment, an excellent enzymatic digestibility could be achieved for pretreated Eucalyptus with 94.3% yield,[10] pretreated rice straw with 87.1% yield,[121] pretreated corncob with 96.4% yield,[122] and pretreated switchgrass with 93.8% yield.[123] In addition, a ChCl-based DES/MIBK biphasic pretreatment was developed for the co-production of FF and fermentable glucose.[124] The DES served as both a Brønsted acid catalyst and pretreatment solvent, and Lewis acids such as $AlCl_3$ and $Al_2(SO4)_3$ could also be used as a co-catalyst to facilitate the formation of FF. Besides achieving a high FF yield (~50-70%), the glucose yield of pretreated *Eucalyptus* could reach ~80%. Higher sugar release could not be obtained due to the presence of lignin (nearly 10%) in the pretreated solid residue. A near 100% conversion of cellulose to glucose in pretreated *Eucalyptus* was reported in a biphasic system comprising choline chloride-based DES and 2-MeTHF.[125] This is mainly due to the increase of cellulose accessible surface area caused by the significant removal of hemicellulose (100%) and lignin (91%). Another study showed that DES system could remove 88% of lignin from rice straw, which facilitated the enzymatic hydrolysis of cellulose.[126] DMSO and GVL are typically miscible with ChCl-based DES and therefore unsuitable for biphasic application, and solvents like butanol could react with DES components like oxalic acid forming dibutyl oxalate. While, solvents like ethyl acetate, anisole, MIBK, 2-MeTHF, Ethyl N-Butyrate, and 1,2-dimethoxybenzene could all form a second phase with ChCl-based DES to form the biphasic system.[127-129] DES could also form a biphasic system with water. However, the integrity of DES system could be destroyed by the disruption of the DES hydrogen-bond complex with water, which will reduce its ability to fractionate the components in lignocellulose.[130]

The presence of an organic phase could also improve the recycle ability of DES. For example, a biphasic system comprising ChCl and acetonitrile (MeCN) or butyrate was developed to convert carbohydrates to HMF.[131] After the reaction, both the HMF product and ChCl were in-situ solubilized in the MeCN phase and could be recovered, and the recycled DES system showed high HMF yield (from 88-92%) within 5 consecutive runs. Overall, utilization of the second organic phase in the DES system could improve the yield of biomass degradation products such as FF and HMF while facilitating their recovery. Meanwhile, since DES pretreatment is also an effective lignin-target pretreatment, it could also facilitate delignification, therefore improving the enzymatic hydrolysis yield. Compare to the aforementioned solvent systems, DES pretreatment system is characterized by low cost, safe composition, environmental friendliness, and simple preparation. Although DES has an ideal effect on cellulase hydrolysis, it is inferior to the MIBK biphase system in terms of FF and HMF production.

2.7. Others chemical solvents based biphasic pretreatment system

Besides organic solvents, CO_2 can also be coupled with water to fabricate the biphasic pretreatment for various types of biomass.[132] At high pressure (>200 bar) of CO_2 with operating temperature from 150 to 250 ^{o}C, a biphasic mixture containing CO_2-rich supercritical phase and an aqueous phase could be formed and used as a pretreatment liquid to pretreat switchgrass, corn stover, and woody biomass.[133] After high solid loading (20-40%) pretreatment, 73, 81, and 85% of glucose yield was achieved from woody biomass, switchgrass, and corn stover, respectively. The hydrolysis yield of hardwood could be further increased by over 80% by using a two-temperature stage biphasic CO_2/H_2O pretreatment at high solid loadings (~40%).[134, 135] During the pretreatment process, the polysaccharides in the cell wall of biomass can be degraded by the dissolved CO_2 (acts as an acid catalyst) in liquid water. In addition, the CO_2 phase possessing high diffusivities can swell the cellulose in the cell wall of biomass.[136] For the biphasic CO_2-H_2O pretreatment, the CO_2 is immiscible in water under atmospheric conditions, which allows the CO_2 to be easily separated and recycled without environmental pollution. The proposed schematic reactors to provide CO_2 and recycle CO_2 are shown in Fig. 10. Hence, this biphasic pretreatment can be considered a green pretreatment technology.

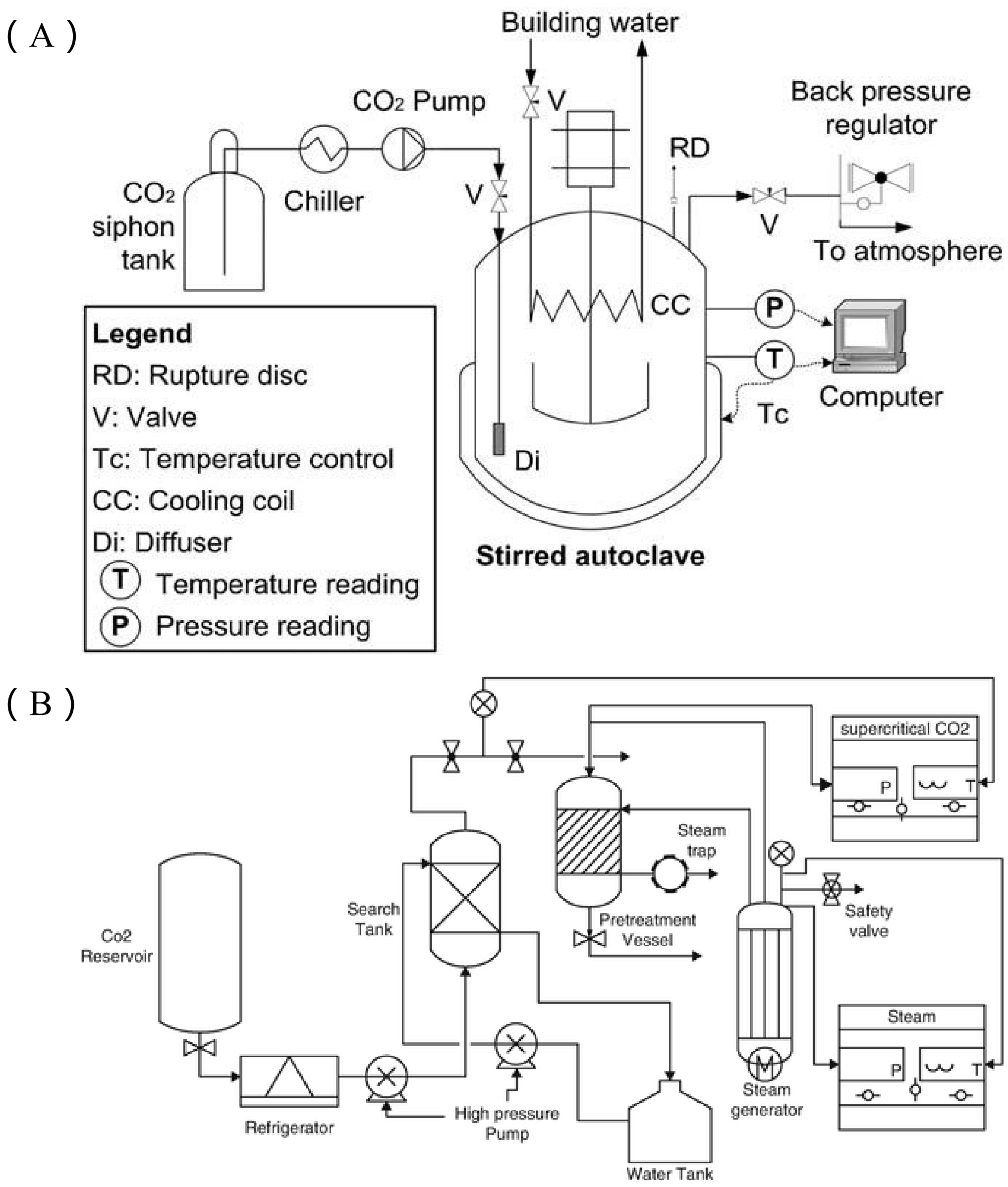

Figure 10. The proposed schematic reactors to provide CO_2 and recycle CO_2 using (A) stirred autoclave[135] and (B) none-stirred autoclave[137] during Biphasic CO_2-H_2O pretreatment

GLV and water are miscible at room temperature, so GVL aqueous pretreatment is generally considered a single-phase pretreatment technology. For example, Shuai et al. reported the pretreatment of hardwood by γ-valerolactone/water system under the catalysis of sulfuric acid could achieved the pretreated solids retained 96-99% of the original cellulose and 80% degree of delignification, resulting the enzymatic hydrolysis yield with 99%.[138] Luterbacher et al. demonstrated an approach for upgrading lignin using γ-valerolactone (GVL) as a solvent (consisting of 80 wt% GVL and 20 wt% water) was an effective pretreatment system, which could be attracted extensive attention for biorefinery due to its environmental protection, safety, and sustainable characteristics.[139] However, in the presence of lignin, a biphasic system could be formed between GLV and water at a GVL concentration between 30 to 50 wt%.[49] The liquid-liquid phase split leads to the formation of an aqueous top and organic bottom phase containing low and high molecular weight lignin, respectively, and could be used to suppress the growth of lignin agglomerates. Another way to create aqueous biphasic system for water miscible solvent such as GVL and THF is by the addition of NaCl or the use of seawater to induce the "salting-out" effect. Acid-free conversion of cellulose into HMF could be achieved with a yield of ~48.6% in a THF/seawater biphasic system.[140] The chloride ion was found to facilitate the isomerization of glucose to fructose and subsequently accelerate its dehydration to HMF. In the same biphasic solvent system, the RCF solid residue that is rich in carbohydrate was converted to HMF and FF with a total yield of up to 24.5 wt%.[141] Up to a 75% yield of FF could be obtained from xylose in the THF/NaCl biphasic medium under microwave heating at 140 ^{o}C catalyzed by $AlCl_3$.[142]

Lignin solubilized in 2-MeTHF or MIBK biphasic system typically has low molecular weight and few β-O-4 interunit linkages due to the significant depolymerization of lignin. Such lignin substrates have low valorization potential in terms of aromatic monolignol production; thus these biphasic systems are generally considered cellulose-centered pretreatment. To enable lignin-first biorefinery, a pentanol-water biphasic pretreatment technique was developed to suppress lignin degradation and condensation during acid-catalyzed pretreatment.[143] Due to the pentoxylation of the α-OH group in lignin side chain, over 40% of vulnerable aryl ether linkages were preserved, and low amounts of C-C linkages were detected. Organic solvents such as toluene,[144] phenol,[46] and o-sec-butylphenol[145] could all form a biphasic solvent system with water to enhance the biomass components' processability.

Organic solvents could form a biphasic solvent system with each other as well. It was reported that the Cyrene/*p*-toluenesulfonic acid biphasic system was capable of fractionating bamboo into lignocellulosic xylooligosaccharides (67.7% yield), fermentable sugars (22.9% yield), and lignin nanoparticles (99.% purity).[48] Molten lithium bromide hydrate solution could also form a biphasic solvent system with an organic solvent such as dichloromethane, toluene, benzene, and cyclohexane. The biphasic solvent system could efficiently convert cellulose and lignocellulosic biomass into furan-based chemicals, including FF and bromomethylfurfural (BMF).[146] Over 90% yield of BMF could be obtained via pure cellulose conversion, while ~70 and 85% yield of FF and BMF could be produced from real biomass.

In summary, biphasic solvent pretreatment could improve the enzymatic hydrolysis efficiency of raw materials by effectively removing lignin and hemicellulose and increasing the recovery of biomass degradation products (e.g., FF and HMF). The aforementioned biphasic pretreatments for various biomass to enhance cellulose digestibility and convert the products of HMF /FF are summarized in **Table 3** and

Table 4, respectively. Compared with the conventional aqueous phase pretreatment, one of the advantages of the biphasic solvent pretreatment is that the solvent can be recycled through simple distillation and the products could be easily separated via simple phase separation, thereby greatly reducing the solvent consumption in the pretreatment process. It meets the concept of green development and is a pretreatment technique with great prospects.

Table 3. Biphasic solvent system for biomass pretreatment to enhance cellulose digestibility.

Solvent system	Biomass substrates	Acid catalyst	Pretreatment condition	Delignification	Cellulose digestibility	Reference
2-MeTHF/H_2O	Bamboo	Oxalic acid	120 ^{o}C, 20 min	~24%	~20%	69
2-MeTHF/H_2O	Bamboo	Oxalic acid	140 ^{o}C, 20 min	~35%	~50%	
2-MeTHF/H_2O	Bamboo	Oxalic acid	160 ^{o}C, 20 min	~45%	~88%	
2-MeTHF/H_2O	Bamboo	Oxalic acid	180 ^{o}C, 20 min	~56%	~93%	
2-MeTHF/H_2O	Birch wood	$AlCl_3$	180 ^{o}C, 60 min	~75%	~77%	73
MIBK/H_2O	Eucalyptus	HCl	150 ^{o}C, 60 min	trace	~60%	59
MIBK/H_2O	Corn stalk	$Al(NO_3)_3$	160 ^{o}C, 60 min	27.8%	85.5%	147
MIBK/H_2O	Eucalyptus	Formic acid	160 ^{o}C, 60 min	~36%	~30%	58
MIBK/H_2O	Eucalyptus	Formic acid	180 ^{o}C, 60 min	~44%	57.7%	
MIBK/H_2O	Eucalyptus	Formic acid	200 ^{o}C, 60 min	~73%	70.7%	
MIBK/H_2O	Beechwood	H_2SO_4	175 ^{o}C, 60 min	~49%	~29.3%	148
Butanol/H_2O	sugarcane bagasse	N/A	200 ^{o}C, 120 min	~67%	N/A	45
Butanol/H_2O	sugarcane bagasse	H_2SO_4	180 ^{o}C, 45 min	~87%	96%	77
Butanol/H_2O	Tall fescue	H_2SO_4	180 ^{o}C, 45 min	~87%	100%	
Phenoxyethanol/H_2O	Rice straw	H_2SO_4	130 ^{o}C, 2 h	~63.2%	80.9%	88
Phenoxyethanol/H_2O	Rice straw	H_2SO_4	130 ^{o}C, 3 h	~53.7%	N/A	
Phenoxyethanol/H_2O	Rice straw	H_2SO_4	150 ^{o}C, 3 h	~26.0%	N/A	
Phenoxyethanol/H_2O	Bamboo	H_2SO_4	100 ^{o}C, 60 min	73.5%	48.5%	89
Phenoxyethanol/H_2O	Bamboo	H_2SO_4	120 ^{o}C, 60 min	91.6%	91.3%	
Phenoxyethanol/H_2O	Rice straw	NaOH	55 ^{o}C, 120 min	78.2%	80.1%	90
Phenoxyethanol/H_2O	Rice straw	NaOH	80 ^{o}C, 30 min	82.2%	82.5%	

ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	100 ^{o}C, 90 min	17.9%	30.3%	124
ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	120 ^{o}C, 90 min	34.2%	57.3%	
ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	140 ^{o}C, 90 min	52.5%	77.0%	
ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	160 ^{o}C, 90 min	66.4%	80.8%	
ChCl:LA/MeTHF	Eucalyptus	H_2SO_4+Al_2(SO4)$_3$	130 ^{o}C, 30 min	82.0%	70.0%	125
ChCl:LA/MeTHF	Eucalyptus	H_2SO_4+Al_2(SO4)$_3$	150 ^{o}C, 30 min	91.0%	97.0%	
ChCl:LA/MeTHF	Eucalyptus	H_2SO_4+Al_2(SO4)$_3$	170 ^{o}C, 30 min	92.0%	52.0%	
Pentanol/H_2O	*Acacia Confusa*	H_2SO_4	170 ^{o}C, 60 min	70.3%	92.2%	143
Phenol/H_2O	*Populus*	H_2SO_4	120 ^{o}C, 60 min	80.0%	~80%	149
Phenol/H_2O	*Populus*	H_2SO_4	120 ^{o}C, 120 min	84.7%	~80%	
Phenol/H_2O	*Populus*	H_2SO_4	150 ^{o}C, 60 min	93.7%	87.7%	
Cyrene/TsOH	Bamboo	TsOH	120 ^{o}C, 60 min	79.4%	90.6%	48

Table 4. Biphasic solvent system for biomass conversion to HMF and FF.

Solvent system	**Biomass substrates**	**Acid catalyst**	**Reaction condition**	**HMF yield (% or g/L)**	**FF yield (% or g/L)**	**Reference**
2-MeTHF/H_2O	Birch wood	$AlCl_3$	140 ^{o}C, 60 min	0.08 g/L	0.04 g/L	73
2-MeTHF/H_2O	Birch wood	$AlCl_3$	160 ^{o}C, 60 min	0.13 g/L	0.11 g/L	
2-MeTHF/H_2O	Birch wood	$AlCl_3$	180 ^{o}C, 60 min	0.10 g/L	0.09 g/L	
2-MeTHF/H_2O	Birch wood	$CuCl_2$	180 ^{o}C, 60 min	0.075 g/L	0.075 g/L	
2-MeTHF/H_2O	Birch wood	$FeCl_3$	180 ^{o}C, 60 min	0.10 g/L	0.13 g/L	
2-MeTHF/H_2O	Birch wood	$NiCl_2$	180 ^{o}C, 60 min	0.15 g/L	0.12 g/L	
2-MeTHF/H_2O	Beech wood	Oxalic acid	140 ^{o}C, 3 h	N/A	6.8 wt%	150
2-MeTHF/H_2O	Beech wood	FDCA	140 ^{o}C, 3 h	N/A	4.2 wt%	
2-MeTHF/H_2O	Beech wood	FDCA	160 ^{o}C, 1 h	N/A	4.2 wt%	
2-MeTHF/H_2O	Beech wood	FDCA	160 ^{o}C, 2 h	N/A	12.2 wt%	
2-MeTHF/H_2O	Beech wood	FDCA	160 ^{o}C, 3 h	N/A	17.7 wt%	
MIBK/H_2O	Eucalyptus	HCl	160 ^{o}C, 60 min	<5 wt%	65.6 wt%	59
MIBK/H_2O	Corn stalk	$Al(NO_3)_3$	160 ^{o}C, 30 min	Trace	29.8 wt%	147
MIBK/H_2O	Corn stalk	$Al(NO_3)_3$	160 ^{o}C, 60 min	Trace	52.0 wt%	
MIBK/H_2O	Corn stalk	$Al(NO_3)_3$	160 ^{o}C, 120 min	Trace	46.5 wt%	
MIBK/H_2O	Cellulose/xylan	HCl	177 ^{o}C, 60 min	33.6 wt%	33.3 wt%	54
MIBK/H_2O	Bamboo	HCl	177 ^{o}C, 60 min	30.6 wt%	34.2 wt%	
MIBK/H_2O	Eucalyptus	Formic acid	180 ^{o}C, 30 min	16.7 mol%	65.6 mol%	
MIBK/H_2O	Eucalyptus	Formic acid	180 ^{o}C, 60 min	15.9 mol%	82.0 mol%	

MIBK/H_2O	Eucalyptus	Formic acid	200 ^{o}C, 30 min	40.1 mol%	56.7 mol%	58
MIBK/H_2O	Eucalyptus	Formic acid	200 ^{o}C, 60 min	23.7 mol%	45.1 mol%	
MIBK/H_2O	Straw	Sulfanilic acid	150 ^{o}C, 60 min	41 mol%	50 mol%	151
MIBK/H_2O	Barley husk	Sulfanilic acid	150 ^{o}C, 60 min	41 mol%	41 mol%	
MIBK/H_2O	Corn stover	$ChH_2PW_{12}O_{40}$	140 ^{o}C, 8 h	27.6 mol%	N/A	152
MIBK/H_2O	Pinewood	$ChH_2PW_{12}O_{40}$	140 ^{o}C, 8 h	11.6 mol%	N/A	
MIBK/H_2O	Bagasse	Zeolite H-USY	170 ^{o}C, 6 h	N/A	52 mol%	153
MIBK/H_2O	Bamboo culm	HCl	177 ^{o}C, 40-60 min	37 mol%	35 mol%	62
MIBK/H_2O	Bamboo leaf	HCl	177 ^{o}C, 40-60 min	35 mol%	34 mol%	
MIBK/H_2O	Corn stover hydrolyzate	H_2SO_4	170 ^{o}C, 10 min	N/A	69.1 mol%	53
MIBK/H_2O	Corn stover hydrolyzate	H_2SO_4	170 ^{o}C, 20 min	N/A	80.1 mol%	
MIBK/H_2O	Corn stover hydrolyzate	H_2SO_4	170 ^{o}C, 30 min	N/A	76.1 mol%	
MIBK/H_2O	Maple wood	HCl	170 ^{o}C, 30 min	32.4 wt%	56.2 wt%	56
MIBK/H_2O	Maple wood	H_2SO_4	170 ^{o}C, 30 min	13.5 wt%	58.3 wt%	
MIBK/H_2O	Fructose	Zeolite H-USY	120 ^{o}C, 5 h	65%	N/A	51
MIBK/H_2O	Xylose	$CrPO_4$	160 ^{o}C, 60 min	N/A	86%	154
MIBK/H_2O	Xylose-rich hydrolyzate	Sulphated carbon	175 ^{o}C, 3 h	N/A	64.8 mol%	155
MIBK/H_2O	Fructose	Sulphated carbon	150 ^{o}C, 3 h	26.6 mol%	N/A	
Butanol/H_2O	Fructose	Nb_2O_5	160 ^{o}C, 50 min	89 mol%	N/A	156
Butanol/H_2O	Glucose	Nb_2O_5	160 ^{o}C, 110 min	49 mol%	N/A	
Butanol/H_2O	Inulin	Nb_2O_5	160 ^{o}C, 80 min	74 mol%	N/A	
Butanol/NaCl	Cellulose	$FeCl_3$	220 ^{o}C, 20 min	73.2 wt%	N/A	78
Butanol/NaCl	Cellulose	$RuCl_3$	220 ^{o}C, 30 min	83.3 wt%	N/A	
Butanol/NaCl	Cellulose	VCl_3	220 ^{o}C, 40 min	71.3 wt%	N/A	
Butanol/NaCl	Cellulose	$TiCl_3$	220 ^{o}C, 40 min	72.4 wt%	N/A	

Butanol/NaCl	Cellulose	None	210 ^{o}C, 60 min	6.31 wt%	N/A	157
Butanol/NaCl	Cellulose	$CuCl_2$	190 ^{o}C, 60 min	Trace	N/A	
Butanol/NaCl	Cellulose	$FeCl_3$	190 ^{o}C, 60 min	6.31 wt%	N/A	
Butanol/NaCl	Cellulose	$CuCl_2 + FeCl_3$	190 ^{o}C, 45 min	49.1 wt%	N/A	
ChCl:EG/Acetone	Switchgrass	H_2SO_4	180 ^{o}C, 30 min	N/A	75%	120
ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	100 ^{o}C, 90 min	1.9 mol%	5.1 mol%	124
ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	120 ^{o}C, 90 min	5.8 mol%	45.4 mol%	
ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	140 ^{o}C, 90 min	18.7 mol%	70.3 mol%	
ChCl:OA/MIBK	Eucalyptus	$AlCl_3$	160 ^{o}C, 90 min	25.7 mol%	30.2 mol%	
ChCl:Fruc./MeCN	Fructose	HCl	100 ^{o}C, 4 h	90.3 mol%	N/A	131
ChCl:Fruc./MeCN	Glucose	HCl	100 ^{o}C, 4 h	3.1 mol%	N/A	
ChCl:Fruc./MeCN	Glucose	$CrCl_3$	150 ^{o}C, 30 min	60.3 mol%	N/A	
ChCl:Fruc./MeCN	Inulin	HCl	100 ^{o}C, 4 h	61.5 mol%	N/A	
ChCl:Fruc./MeCN	Sucrose	$CrCl_3$	150 ^{o}C, 30 min	69.8 mol%	N/A	
ChCl:LA/MeTHF	Eucalyptus	$H_2SO_4+Al_2(SO4)_3$	130 ^{o}C, 30 min	N/A	35.0 wt%	125
ChCl:LA/MeTHF	Eucalyptus	$H_2SO_4+Al_2(SO4)_3$	150 ^{o}C, 30 min	N/A	54.7 wt%	
ChCl:LA/MeTHF	Eucalyptus	$H_2SO_4+Al_2(SO4)_3$	170 ^{o}C, 30 min	N/A	49.7 wt%	
ChCl:CA/MIBK	Xylose	$AlCl_3$	140 ^{o}C, 25 min	N/A	73.1 mol%	158
ChCl:CA/MIBK	Xylose	$FeCl_3$	140 ^{o}C, 35 min	N/A	71.4 mol%	
ChCl:CA/MIBK	Xylan	$AlCl_3$	140 ^{o}C, 35 min	N/A	68.6 mol%	
ChCl:OA/EA	Corn husk	Oxalic acid	100 ^{o}C, 2 h	13 mol%	37 mol%	159
ChCl:OA/MIBK	Corn husk	Oxalic acid	100 ^{o}C, 2 h	9 mol%	52 mol%	
ChCl:OA/anisole	Corn husk	Oxalic acid	100 ^{o}C, 2 h	6 mol%	52 mol%	
ChCl:OA/DB	Corn husk	Oxalic acid	100 ^{o}C, 2 h	7 mol%	50 mol%	
Butyl phenol/H_2O	Starch	$YbCl_3$	170 ^{o}C, 80 min	42.0 mol%	N/A	

Butyl phenol/H_2O	Cellobiose	$YbCl_3$	170 ^{o}C, 80 min	40 mol%	N/A	46
Butyl phenol/H_2O	Maltose	$YbCl_3$	170 ^{o}C, 80 min	31 mol%	N/A	
Butyl phenol/H_2O	Cellulose	$YbCl_3$	170 ^{o}C, 360 min	21 mol%	N/A	
LiBr/DCM	Corn stover	HBr	125 ^{o}C, 126 min	N/A	69.4 mol%	146
LiBr/DCM	Switchgrass	HBr	125 ^{o}C, 126 min	N/A	51.2 mol%	
LiBr/DCM	Poplar	HBr	125 ^{o}C, 126 min	N/A	61.9 mol%	
LiBr/DCM	Aspen	HBr	125 ^{o}C, 126 min	N/A	83.9 mol%	
LiBr/DCM	Douglas fir	HBr	125 ^{o}C, 126 min	N/A	57.3 mol%	

3. Conclusion

Although pretreatment technologies have advanced significantly over the past few decades, energy consumption, processing difficulty, product yield, and production cost of many state-of-art pretreatment technologies have not met the requirements for the economic feasibility of carbohydrate-centered biorefinery processes. Considering the concept of a green chemical industry and cleaner production, it is significant to use biphasic pretreatment methods that can enable a full fractionation of lignocellulosic biomass to simple sugars, FF, HMF, and lignin in a single process unit.

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