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The cover picture shows that many efficient lignin fractionation processes are being developed to obtain specific molecular lignin fractions with defined properties.
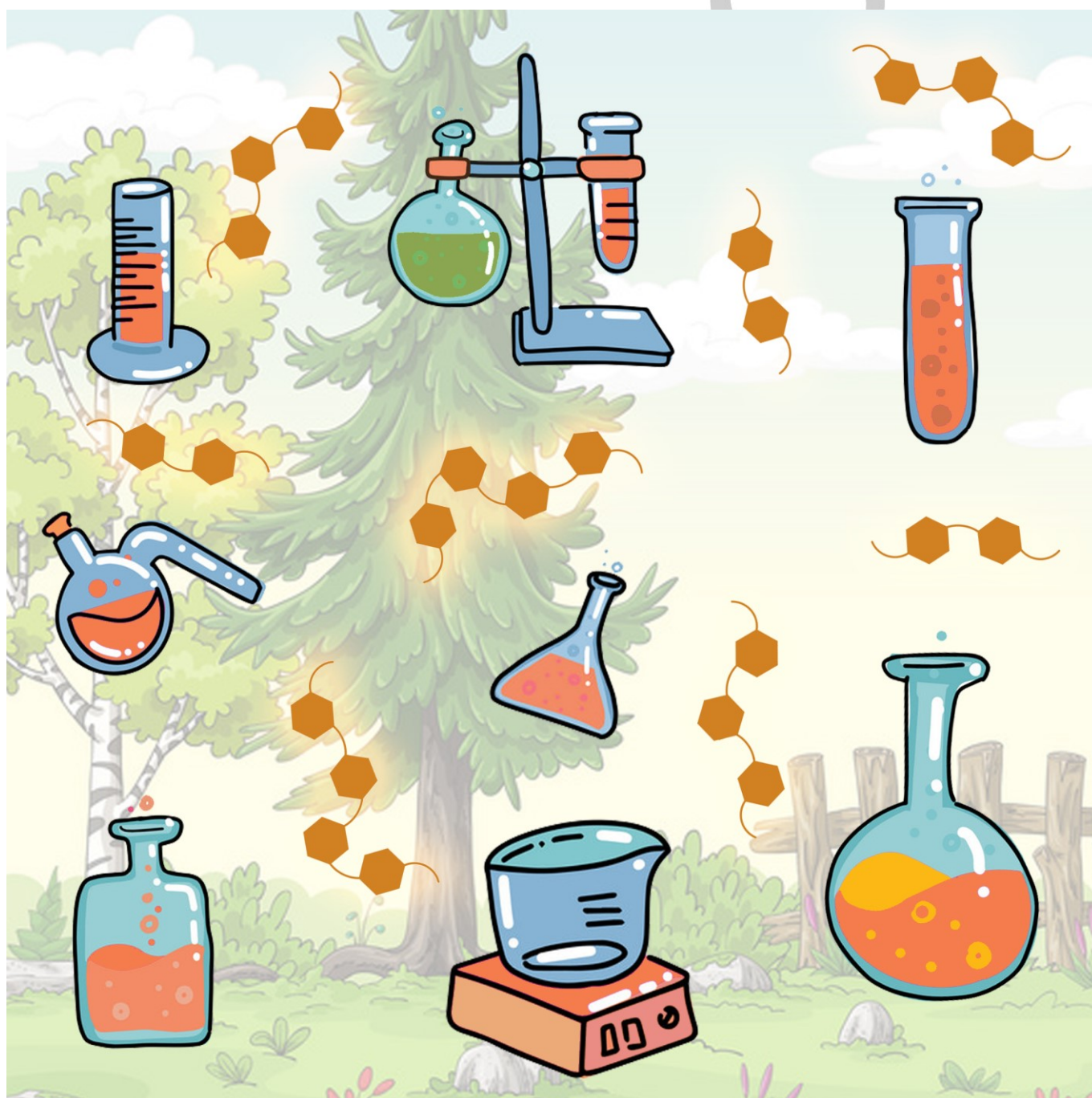
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Abstract: Lignin, as the most abundant aromatic biopolymer in nature, has attracted great attention due to the complexity and yet richness of its functional groups for value-added applications. The yield of production of lignin and the reactivity of prepared lignin are very important to guarantee the study and development of lignin-based chemicals and materials. Various fractionation techniques have been developed to obtain high yield and relatively high-purity lignin as well as carbohydrates (hemicelluloses and celluloses) and to reduce the condensed and degraded nature of conventional biorefinery lignin. Herein, novel and efficient biomass fractionation and lignin fractionation towards lignin valorization are summarized and discussed.

1. Introduction

Due to resource shortage and the energy crisis, biorefinery has attracted much attention. Lignin is the most abundant aromatic renewable resource in nature, accounting for 15% to 35% by weight of lignocellulosic biomass. [1] However, in the pulp and paper industry, lignin has long been treated as a waste byproduct and commonly burned to supply heat and energy for the pulping process or regenerate chemicals used for pulping due to its chemical recalcitrance and structural complexity. In recent years, with a better understanding of lignin physics and chemistry, more and more high performance materials are being developed from lignin resources,[2] which would open not only a new design for functional materials but also a promising way for biorefinery.[3]

Lignocellulosic biomass is a primary candidate for alternative energy due to its potential for green chemicals, biofuels, and bio-based products. The efficient fractionation strategies from lignocellulose for lignin is of great importance for the subsequent transformation into value-added products in the biorefinery platform.[4] The intricate relationship among lignin, cellulose, and hemicellulose and the similarity between some components of lignin and high glycan increases the difficulty of separation.[5] So, the harsh treatment was put to issue this question, which causes an irreversible degradation and condensation reactions of lignin during traditional carbohydrate first conception of lignocellulose biorefinery. Generally speaking, lignin presents the heterogeneous structure and broad molecular weight distribution which would severely affect its potential applications in materials.[6] In addition, the higher contents of phenolic hydroxyl groups in lignins could contribute to their chemical modification and physical interaction. Many studies showed that the contents of β-aryl ether (β-O-4) linkages closely related to valorize lignin for chemical production through subsequent depolymerization[7] and release monomeric phenols from lignin.[8] However, during the cleavage of ether bonds of lignin, the generation of reactive intermediates which are prone to subsequent formation the stable carbon-carbon (C-C) bonds instead of the hydroxyl, thus the lignin subunits exhibit lower reactivity than native lignin. That has brought up the difficulty of catalytic depolymerization of lignin in order to modify or functionalize lignin for downstream applications. The single target product, serious degradation of raw lignin, the presence of sulfur, and some other disadvantages of the traditional fractionation method seriously limit the wide and deep studies of lignin chemistry and applications.[9]

According to this philosophy, it is very important to obtain high purity lignin with commendable chemical reactivity. In addition, the exploitation of a lignin-based coproduct also depends on the inherent structures and chemical reactivity of the lignin polymers. Hence, numerous researches have been made to develop novel approaches of fractionation to isolate lignin from biomass and obtain economically valuable chemicals. Based on concept to utilize the entire lignocellulose substrate, many methods of fractionation with various solution systems, including alkali, organosolv, ionic liquids, and deep eutectic solvents, etc., are recently gradually developed and have received the attention among academia and industries. Enzymes can also be used to assist the separation of lignin by e.g. hydrolyzing carbohydrates. Moreover, several methods for further fractionation of lignin have been studied to obtain specific molecular lignin fractions with defined properties.

In this review, we attempt to summarize the development in studying fractionation of lignin from biomass over the last decade. A summary of the raw materials/solvents and the results of each method for the fractionation of biomass and lignin are provided in **Table 1** and **2**, respectively. Emphasis will be on the evaluation of the yield of pristine lignin and molecular weight (Mw) and distribution of lignin fractions.
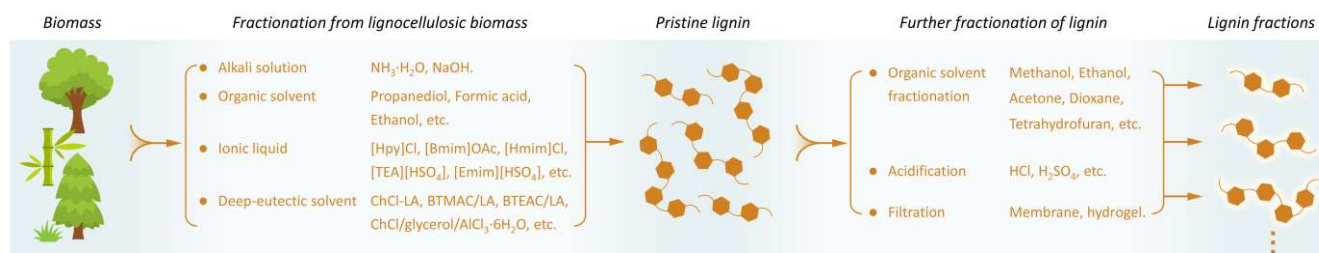
Figure 1. Schematic illustration of the approaches of fractionation of lignin.

2. Fractionation from lignocellulosic biomass

Figure 1 illustrates the main approaches of fractionation from lignocellulosic biomass.

2.1. Alkali-based fractionation

kraft pulping, and soda pulping are the traditional and the most widely used pulping processes. However, the pristine lignin obtained by the kraft pulping process containing the sulfur and the structure of the lignin was severely damaged after soda pulping, which can complicate lignin downstream valorization.

Alkali-based fractionation was investigated, which utilizes various kinds of alkaline (e.g., ammonia, NaOH, Ca(OH)$_2$, etc.). Typically, it can efficient to treat the graminaceous feedstocks due to its lower severity of the treatment compared to traditional soda pulping.[10] Obtaining the lignin from wood after alkali pretreatment may need harsher conditions that risk altering the lignin structure.[11] The common reagent used in alkali-based fractionation was the NaOH, followed by was ammonia which with several well-known benefits, such as the easy recovery of solvent, the preserve of lignin structure and alters cellulose crystalline structure.[12] Up to now, some ammonia-based extraction and isolation procedures are available, mainly including ammonia fiber explosion (AFEX),[13] anhydrous ammonia pretreatment (AAP)[14]and recycled aqueous ammonia expansion (RAAE).[15]

AFEX is a promising thermochemical pretreatment which only makes the cell walls changed to enhance cellulase accessibility without the lignin and hemicelluloses removal. The mechanism of AFEX was discussed by Chundawat et al., they found that the penetration process of ammonia through the cell walls would facilitate the cleavage of lignin–carbohydrate ester linkages, that that allows removal/redeposition of cell wall decomposition products onto outer wall surfaces and hence results in increased wall porosity. During the process, the biomass matrix cannot fractionate to the lignin fraction, but the following lignin extraction was benefiting a lot from AFEX, which can up to 50% removal of the AFEX-pretreated feedstocks by organic or alkaline solution.[16] Subsequently, the mechanism and the causes for improved digestibility of AFEX pretreated materials were further studied, the results show that it is the disruption of lignin-carbohydrate linkages of mainly polymeric lignin that contribute to the efficiency of AFEX pretreatment, and the process shows a minimum change to feedstocks which can preserve the lignin structure.[17] Another method is anhydrous ammonia pretreatment (AAP). Mittal et al.

use this method followed by a mild NaOH extraction (0.1 M NaOH, 25°C) to treat corn stover with the result of more than 65% lignin removal.[14] The extracts of lignin exhibit considerable antimicrobial and antioxidant activities, when the corn stover using by low-moisture anhydrous ammonia (LMAA), subsequently extracted the lignin by 4% (w/v) sodium hydroxide.[18] RAAE is a novel technology with the object to get high biomass digestibility under relatively low temperatures and short pretreatment time. After RAAE pretreatment, about 50-75% lignin was removed while most of the carbohydrates were preserved. Specifically, only by 11 min treatment at 85 °C, 80% water to dry corn stalks loading, and 1.5 L/min ammonia flow rate, up to 68.3% lignin was removed and 85.69% of glucan digestibility was achieved.[15]

In addition, a few modified aqueous ammonia-based fractionation were used in the pretreatment process of biomass. For example, the sugarcane bagasse treated by aqueous ammonia with glycerol (AAWG) at 120°C~180°C with 49.34%~77.46% delignification, which indicates that the level of fractionation is directly related to temperature.[19] A modified aqueous ammonia soaking (AAS) method was used to treat the eucalyptus, and the results show that the addition of H$_2$O$_2$ to the AAS could further promote the fractionation of the eucalyptus.[20] Wheat straw was treated by aqueous ammonia combined with hydrothermal pretreatment, and the results showed that the nitrogen-containing lignin fractions are good for dye adsorption with broad spectrum adsorption of anionic, cationic, and uncharged organic dyes from aqueous solutions.[21] The ammonia-based fractionation process is sustainable for large scale applications without containing carbon or release greenhouse gas (GHG) contain.[22] Although the ammonia-based fractionation is more preferable to limit ether bond cleavage due to milder treatment conditions, ammonia lignin residue had a higher cellulase adsorption affinity compared to organosolv lignin which reduced cellulose hydrolysis.[23]

2.2. Organosolv fractionation

Organosolv fractionation is a promising process using an organic solvent to dissolve lignin from the plant cell walls for effective separation of lignin. The lignin was separated in the recovery process to achieve the purpose of the comprehensive utilization of components, which fits well into the concept of sustainable biorefinery. Unlike impure lignin obtained by the traditional pulping process, e.g. kraft and sulfite process, the lignin obtained from organosolv fractionation shows low molecular weight and contains no sulfur element. Moreover, nontoxic reagent organic

Table 1. Approaches of fractionation from lignocellulosic biomass.

Approaches	Biomass type	Raw materials	Solvent[a]	Yield (%)	Delignification degree[b] (%)	Ref.
Alkali solution	Hardwood	Eucalyptus residues	80% ammonia aqueous /AAS		55	[20]
	herbaceous	Sugarcane bagasse	9.25% ammonia / 9.51% ammonia /AAWG		77.81 / 70.91	[19]
		Sugarcane bagasse	1.5% NaOH/3% H_2O_2		89.8	[24]
Organic solvents	Hardwood	Willow powder	2-PrOH/H_2O	61		[25]
		Beech	95% EtOH/water/0.18 M H_2SO_4		73	[26]
		White birch	70% GVL/0.1 M H_2SO_4	72	>95	[27]
		Birch wood	50-70% MA		24.6-55.4	[28]
		Poplar wood	67% p-TsOH	55.8		[29]
	herbaceous	Wheat straw	50% EtOH	84		[30]
		Wheat straw	62%-90% FA	20-68	63-86	[31]
Ionic liquids	Hardwood	Poplar	[Hpy]Cl / [Hmim]Cl	61.0 / 60.4		[32]
		Eucalyptus	[Bmim]OAc		29.7-43.3	[33]
	herbaceous	Corn stover	[Hmim]Cl	60.48		[34]
		Wheat straw	58.7%[Emim][HSO_4]/alkaline	42.6		[35]
		Miscanthus x giganteus	10% [TEA][HSO_4]	82	88	[36]
		Bamboo	[Hpy]Cl / [Hmim]Cl	51.7 / 50.3		[32]
Deep-eutectic solvents	Hardwood	Poplar wood powder	ChCl/glycerol/$AlCl_3$·$6H_2O$	96	95.46	[37]
		Poplar wood	ChCl-LA	58		[38]
		Eucalyptus sawdust	ChCl-LA (1:10)	64		[39]
	Softwood	Douglas fir	ChCl-LA	78		[38]
	herbaceous	Wheat straw	ChCl-LA	5-80		[40]
		Corncobs	BTMAC/LA (1:2) / BTEAC/LA (1:2)	52 / 70		[41]

[a] AAWG—aqueous ammonia with glycerol, AAS—aqueous ammonia soaking, H-AFEX—the hydrogen peroxide presoaking prior to ammonia fiber expansion. 2-PrOH—2-propanediol, EtOH—ethanol, FA—formic acid, [Hmim]Cl—1-*H*-3-methy-limidazolium chloride, [Emim][HSO_4]—1-ethyl-3-methylimidazolium hydrogen sulfate, [TEA][HSO_4]—triethylammonium hydrogen sulfate, [Hpy]Cl—Pyridinium chloride, [Bmim]OAc—1-butyl-3-methylimidazolium acetate, ChCl—choline chloride, LA—lactic acid, BTMAC—benzyltrimethyl-ammonium chloride, BTEAC—benzyltriethylammonium chloride, GVL—γ-valerolacton, MA—maleic acid, p-TsOH—p-toluenesulfonic acid.

[b] Delignification degree = (1-the lignin recovery after precipitation/lignin present in the raw materials)×100%, lignin recovery after precipitation are given as % w/w of the amount of lignin present in the raw materials

solvent can be recovered during organosolv fractionation. A wide range of organic solvents, mainly including organic alcohols (i.e., methanol, ethanol), organic acids (i.e., acetic acid, formic acid), esters, and combined solvents with and without acid or alkaline catalysts are used in biomass fractionation. The catalysts used are acid, a base, or a salt.

These solvents providing selective solubilization of lignin from various lignocellulosic biomass including poplar wood, wheat straw, and eucalyptus, etc. The excellent solubility to dissolve lignin results in slight chemical modification and the mechanisms are considered as the cleavage of aryl ether bonds. During the organosolv fractionation, the β-O-4 linkages are more hardly broken than the α-O-4 linkages which normally need more severe conditions, especially at elevated acid concentrations.[42]

Despite organosolv fractionation or pulping has been utilized for more than a hundred years, the application is still not widely used in industrial production due to considering high equipment requirements and the dangers, toxic, and costs-increase posed by the use of solvents.[43] In addition, organosolv fractionation for non-wood feedstocks (e.g., corn stover, wheat straw, rice straw, bamboo, etc.) exhibit better effect relative to woody feedstocks.

These feedstocks represent a small fraction of the global chemical pulping market but may represent a significant feedstock for biorefining processes. Up to now, several organosolv fractionations based on extraction and isolation procedures are available. The main fractionations including alcohols-based fractionation and organic acid-based fractionation.

Alcohols-based fractionation. Ethanol pulping is the earliest and the most widely studied approach of alcohols-based fractionation. Generally, the process of ethanol fractionation is carried out under elevated temperatures without or with the addition of the acidic or alkaline catalysts. Temperatures used in this process can be as high as 200 °C. Lower temperatures can also be used depending on the type of biomass and the addition of a catalyst. For example, wheat straw can be fractionated by using autocatalytic and acid-catalyzed ethanol organosolv, and the lignin yield of 84% was reached without the use of a catalyst (organosolv at 210 °C, 50% w/w aqueous EtOH). Similar results were obtained at 190 °C using 30 mM H_2SO_4 as the catalyst and 60% w/w aqueous EtOH.[30] The process produces three main fractions of biomass, including high purity lignin, pure cellulose fibers, and hemicellulose-derived products (mainly xylose).

Lignin condensation is the unavoidable reaction during acidic or alkaline ethanol fractionation process. It is formed *via* the formation of the reactive benzyl carbocations or benzyl-linked oxygen atoms since it easily forms a bond with an electron-rich carbon atom in the aromatic ring of another lignin units.[44] The obtained solid residues are separated by filtration and washed with warm organosolv solvent avoiding dissolved lignin redeposition. Then, the lignin was obtained by precipitation with water. The treatment of willow use 2-propanediol (2-PrOH)/H$_2$O (7:3) at 190 °C for 10 h which show that the obtained lignin yield can reach 61% with high purity (93%).[25] Obviously, ethanol fractionation yields relatively clean and impurity-free lignin that can be directly used for the production of value-added materials. But there are some factors limiting the application, such as limited degree of fractionation (high kappa number), high temperature, and high pressure.

Organic acid-based fractionation. Because of effective hydrolysis and extensive fractionation, organic acids, primarily acetic acid, and formic acid (FA), have been extensively employed in the biomass fractionation process. DapíA et al. demonstrated that beech wood could be fractionated using 80% formic acid at a temperature from 110 °C to 130 °C.[45] Moreover, the ash content is lower than traditional pulping, for example, approximately 64% of ash or 83% of silica in wheat straw remained in the pulp after atmospheric acetic acid (AcOH) pulping,[46] lower impurities (ash 0–0.1%) in FA-lignin (FAL).[47] Due to a lower boiling point than acetic acid, FA had been recognized as a promising agent for organosolv pulping and fractionation. As a volatile weak organic acid, FA can be converted directly from the fraction of lignocelluloses or directly recycled for fractionation.[48]

Chempolis and CIMV processes involve using formic acid for the treatment of non-wood fibre sources in a single-stage process. Zhang et al. obtained the FA-lignin (FAL) with high guaiacyl content by using one-step mild formic acid pretreatment, and FAL fraction exhibited a loose structure which is prominent for its further catalytic conversion into chemicals and energy.[49] Similarly, after one-step FA hydrolysis (85 °C, 5 h), about 80% of lignin was removed from corn husk, and the obtained lignin with high-purity (>99%) would have the potential for phenol-formaldehyde resin and concrete water-reducer applications.[50]

In order to realize fractionation, severe experimental conditions were needed such as increasing temperature and pressure. So, the β-O-4 linkages are broken during the FA-based fractionation, which resulted in the increasing content of phenol hydroxyl, the formation of C-C condensation structure, and the side chain formylation of lignin. Although the yield of lignin separated by this method is high, the high value potential use of lignin is greatly limited due to a large number of β-O-4 broken. For example, the bamboo is fractionated using FA under high pressure (at 145 °C for 45 min, 0.3 MPa), presents a quick and efficient fractionation method by enhancing the cleavage of interunitary bonds in lignin (β-O-4′, β-β, and β-5′), and dissolved lignin also occurred condensation reaction.[51]

FA-based fractionation can also be conducted under low temperatures and at atmospheric pressure[48], but it still needs more treatment or long reaction time to avoid lignin condensation, e.g. 60 °C for 8 h[52], 105 °C for 3 h.[53] Li et al. reported bamboo using the Milox method at 101 °C for 2 h achieved the highest fractionation (88.9%).[47] After acetic and formic acid treatment, *M. x giganteus* showed a low S/G ratio (0.7), and the disappeared β-

O-4 linkages during organosolv fractionation up to 21% and 32%, respectively.[54] It can conclude that extensive degradation of lignin occurred as a result of long reaction time as indicated by a significant reduction of aryl-ether linkages.

Based on the biorefinery concept, numerous novel fractionation technologies have developed to separate structural constituents of lignocellulose for subsequent product upgrading. For example, γ-valerolactone (GVL), as a green non-toxic solvent, was introduced into biomass fractionation[55]. About 50–60% of the extracted lignin can be precipitated by the addition of water after GVL/water treatment at 180°C and the lignin shows high phenolic content, relatively low dispersity and low molecular mass.[56] Alonso et al. processed white birch wood chips using GVL/water (70:30, mass ratio) fractionation at 125°C and low pressure (<3 bar) for 3 h. By adding 0.1 M sulfuric acid to serve as a catalyst, resulting in the removal of >95% of the lignin, and the lignin can be used to produce carbon foam material. Although GVL can be recovered after fractionation, managing solvent losses is challenging during the process.[27] In addition, hydrotrope was also introduced into biomass fractionation in order to enhance lignin dissolution at low-temperature. As a hydrotrope, *p*-toluenesulfonic acid (*p*-TsOH) shows good performance which can be able to dissolve a substantial (approximately 90%) amount of wood lignin at 80°C or lower and within a short 20 min period.[57] The β-O-4 linkages were well preserved (43% retention) even under severe condition (67wt% *p*-TsOH, 70 °C for 30 min).[58] Recently, Zhu and his co-workers used maleic acid hydrotropic fractionation (MAHF) to treat the birch wood at mild condition (atmospheric pressure, ≤100°C), the results showed that the dissolved lignin with a low degree of condensation and very light color which is dispersible due to carboxylation making it amenable to a variety of applications.[28] In order to improve the reactivity of lignin for the following valorization, a novel method, the sequential organosolv fragmentation approach (SOFA) using ethanol plus different-stage catalysts, was developed to selectively dissolve lignin for producing multiple uniform lignin streams by Liu et al., and they fabricated lignin nanoparticles (LNPs) with desired quality features using the fractionated lignin by tailing its chemistry and reactivity.[59]

2.3. Ionic liquid (IL)-assisted fractionation

Ionic liquids (ILs) have received considerable attention and have been extensively exploited for biomass fractionation due to their excellent ability to destroy the crystalline structure of cellulose or remove lignin/hemicelluloses. ILs are mainly composed of cations (generally organic) and anions (organic or inorganic).[60] The use of ILs as biomass processing solvents started with the discovery of cellulose dissolving ILs.[61]

ILs can selectively break the bond between cellulose, hemicellulose, and lignin. In terms of the difference of their selectivity, the methods of extract lignin from lignocellulosic biomass by ILs including partial and full dissolution systems. The former IL-based system, only lignin and hemicellulose can be extracted by ILs while the cellulose fraction remains in the form of a solid pulp, then the lignin can be precipitated by antisolvent.[34] In the latter system, the entire lignocellulose substrate can be dissolved, then cellulose and lignin were precipitated respectively from the product mixture by the addition of an antisolvent (organic or aqueous–organic solution).[62]

Among numerous ILs, 1-ethyl-3-methylimidazolium acetate ([C_2mim]-[OAc]) was demonstrated to effectively extract lignin from lignocellulose raw material, such as wood,[63] wheat straw, etc. Bogel-Lukasik et al. investigated the fractionation process of the wheat straw in 1-ethyl-3-methylimidazolium acetate ([Emim][CH_3COO]) and reported that 87wt% purity of the carbohydrate-free lignin-rich fraction can be recovered.[64] And the chemical transformations involved in the [C_2mim]-[OAc] pretreatment was more deeply investigated.[65]

Various process parameters would affect the dissolution of lignocellulosic material, such as the effect of IL anion or cation, solvation properties of ILs, and viscosity, etc. These relevant parameters were summarized by Badgujar and Bhanage [66] and pointed IL should in the context of green sustainable chemistry, IL properties should be optimized for biomass processing. A key example is the high viscosity of most ionic liquids, so several studies try to solve this issue. For example, increasing the temperature may be a method to reduce IL viscosity.[67] In addition, the currently popular ionic liquids in lignocellulosic biomass treatment such as the imidazolium-based ionic liquids are likely to remain expensive and their preparation is often very difficult. Therefore, the recyclability of ionic liquids is necessary. Up to now, numerous investigations of the use of IL have focused on the cost and recyclable problems. Xu et al. found that [Amim]Cl still retains well fundamental nature after sequential pretreatments.[33] The ILs could be synthesized only *via* one step for the fractionation of biomass resulted in considerable lignin extraction yields of 61.0% and 60.4% from poplar with [Hnmp]Cl and [Hmim]Cl pretreatments, respectively.[32] Up to 85% of the lignin can be solubilized into the IL solution and 80% lignin recovery can be achieved by using the low-cost ionic liquid triethylammonium hydrogen sulfate [TEA][HSO_4] at mild temperature (120 °C).[36] The lignin-rich solid fractions were obtained with distinct purities and yields by aqueous ionic liquid solution ([Emim][HSO_4]/H_2O), and the IL was successfully separated, recovered, and reused.[35]

2.4. Deep eutectic solvents (DESs) fractionation

Issues such as toxicity, poor biodegradability, and high cost have nevertheless restricted the implementation of ILs. In order to overcome these problems, new solvents-deep eutectic solvents (DESs, also known as the third generation of ionic liquids) have entered the field of vision of researchers. The term DESs was coined by Abbott and co-workers in 2003.[68] It has important significance as a substitute for traditional ionic liquids for the isolation and extraction of lignin. DESs are solvents that are synthesized in a liquid state at room temperature by at least one hydrogen bond donor (HBD) usually quaternary ammonium salts and one hydrogen bond acceptor (HBA) such as alcohols or carboxylic acids.

Francisco et al. reported that DESs have high lignin solubility and very poor or negligible cellulose solubility, [69] and the properties of DESs can be easily tuned by changing the HBDs and HBAs.[70] Mechanism investigation revealed that the functional groups in the DESs significantly affected their ability to dissolve lignin[71], and it can evaluate the potential of DESs for lignin processing more closely. Jablonsky et al. found the best fractionation of wheat straw based on the selectivity of lignin removal was the DESs composed of ChCl with lactic acid (1:10) compared with choline chloride with urea (1:2), malonic acid (1:1), lactic (1:9; 1:10), malic acid (1:1).[72] During the fractionation

process, the mass transfer rate significantly affect the lignin extraction under 90 °C while elevating the temperature more than 120 °C, the temperature becomes the dominant factor.[39] In addition, DESs viscosity plays a role in the fractionation of lignocellulosic components by DESs. DESs viscosity could decrease with increasing temperature[73], but higher temperature against the lignin structure protection. Chen et al. found that the molar ratio of ChCl–PCA (1:1) would allow the formation of more hydrogen bonds which is helpful for the stability of the solvents and lignin removal.[74] Jablonsky et al found the fractionation efficiency could be improved by the addition of a third component to classical two-component DESs due to a decrease of density and viscosity.[75]

The LCCs linkage could be cleaved when $AlCl_3 \cdot 6H_2O$ in ChCl/glycerol DES which also leads to fractionation efficiency improvement.[37] Several notable studies have highlighted the benefits of DESs for the preparation of lignin. Yu et al. have demonstrated that both the hydrogen bonds and ether bonds in lignin–carbohydrate complexes could be cleaved during DESs pretreatment, thereby facilitating the selective extraction of lignin.[76] The lignin yield by ChCl and HBD (acetic acid, lactic acid, levulinic acid, and glycerin) could reach 78% and 58% from poplar and Douglas fir respectively, and the extracted lignin has high purity (95%) with unique structural properties.[38] Good performance with considerable lignin yield can still be achieved through DES recycling.[39] Although the main fractionation mechanism employed by DESs treatment is the cleavage of ether linkages, the condensation of lignin fragments little occurred. Singh et al. use lignin-derived compounds as potential raw materials for DESs preparation from biomass processes and the lignin removal (60.8%) provided by ChCl-PCA.[77] Higher lignin yield (up to 80%) could obtain from prairie cordgrass (PCG) and switchgrass (SWG) biomass.[78]

Generally speaking, there is still much room for development in the fractionation of lignocellulosic biomass and the extraction of lignin using DESs. The homogeneous molecular weight lignin could be obtained using novel DESs including benzyltrimethylammonium chloride (BTMAC)/lactic acid (LA) in a short time (2 h) at 140 °C.[41] The integration of DESs pretreatment with other technologies show good results. For example, the lignin removal can reach 65–80% using acidic ChCl:lactic acid pretreatment with ultrafast 45 s microwave heating at 800 W and the purity reach 85–87%.[79] Recently, the green processing of lignocellulosic biomass and its derivatives in the DESs system has been comprehensively and critically reviewed. The authors pointed out that DESs are attractive solvents for the fractionation of lignocelluloses and the valorization of lignin.[80] Another review stressed three key parts: performance of varying types of DESs and pretreatment schemes for biopolymer fractionation, properties, and conversion of fractionated saccharides, as well as DESs, extracted lignin.[81]

In spite of the rapid development in the past ten years, some drawbacks still restricted the practical applications of these solvent systems, such as the thermal instability, susceptibility to contaminants.[80] In another aspect, the ideal DESs type for biomass conversion is still uncertain, and the studies about the application using the DESs lignin are still not enough. There is still much research to be done for the DESs fractionation technology.

2.5. Enzyme assisted fractionation

Usually, milled wood lignin (MWL) was prepared for the studies of lignin structural characterization, which was considered to be the most similar to native lignin.[82] The obtained MWL has low yield, which maybe half that of the crude preparation and its residual carbohydrate content is about 4%. Subsequently, enzyme assisted extraction to obtain lignin was developed which mainly uses cellulase to hydrolyze cellulose aiming to remove carbohydrates. The assistant function of enzyme improves the yield of lignin and the obtained lignin was named as cellulolytic enzyme lignin (CEL). There is no reason not to acknowledge that the enzymatic treatment has successfully assisted in lignin extraction, such as mild reaction conditions, the use of renewable and biocatalysts, reduction in the use of toxic chemicals. Enzymatic hydrolysis was applied after mild alkaline treatments in situ to the ball-milled swollen cell wall and the yield of swollen residual enzyme lignin can reach 95%.[83] The novel method combined the alkaline treatment and enzymatic hydrolysis, which not only has little change on the lignin structures but also obtain the syringyl-rich lignin macromolecules as compared to CEL.

The addition of enzymes into lignin fractionation would reduce the use of toxic chemicals with economic and environmental protection advantages. However, it may extend treat time, so enzymatic mild acidolysis lignin (EMAL), one modified method was investigated to improve lignin recovery and purity.[84] This strategy is usually used in laboratory research. Li et al compare the pyrolysis of wood and herbaceous EMAL find that high phenolics yield can obtain at mild pyrolysis temperature of 450 °C to 650 °C.[85] The enzyme also uses in further fractionation of the lignin. For example, two common lignin (alkaline lignin: AL, and hydrolysis lignin: HL) were treated with laccase, and the results show that the structure, especially the Ph-OH contents and molecular weight of lignin could be effectively controlled which benefits for the antioxidant application.[86]

3. Semi-continuous or continuous biomass fractionation

During fractionation, ether bonds are cleaved and a new stable carbon-carbon (C-C) bonds are formed, which is an undesirable reaction, limiting the achievement of excellent lignin monomer yield *via* depolymerization. It is well acknowledged that the use of acid/alkaline and/or high temperatures during fractionation leads to severe and irreversible condensation, so some strategies were developed to avoid condensation. A simple but effective strategy to preserve lignin structures by employing rapid flow-through fractionation was applied over the last few decades. The diffusive flux remains high in a flow-through setup and the lignin concentration is relatively low, as a fresh solvent is constantly added to the system. The increased flow rate could enhance the lignin removal[87] and cellulose digestibility[88]. In a batch system, the lignin concentration is increased during the extraction, resulting in a decrease in diffusive flux as a function of time. In another word, when operating in flow-through mode, the dissolved lignin fragments are removed from the heating zone, which limits the extent of structural alteration and redeposition.

Almost 100% lignin could remove with the temperature and/or dilute acid elevated,[89] but the lignin structures were destroyed under harsh conditions by flow-through treatment. For example, Zhang et al. used only 0.05% (w/w) H_2SO_4 at temperatures of 200 to 270 °C by flow-through fractionation, and they found that β-O-

4 linkages had significant cleavage and β-5 linkages slight repolymerization[90]. The organosolv process under relatively low temperatures may have benefits for lignin utilization. With ethanol, water and sulfuric or formic acid as catalyst under 140-195 °C by flow-through fractionation, the lignin fractions yield up to 86%.[91] To confirm that the produced lignin is suitable for further utilization, the lignin conversion was combined with semi-continuous organosolv fractionation to obtain Lignin-to-Liquid (LtL)-oils which shows high conversion yields at up to 94% based on lignin mass input.[92] Under mild temperature (130 °C), Wang et al. use 72wt% aqueous formic acid by flow-through fractionation of biomass which shows similar lignin yields compared to batch extractions but retains high β-O-4 ether bond (76% retention).[31] During the process, the formylation appeared at α-position was also found, which makes lignin soluble in formic acid and accelerates the delignification process.[93] Using acidic alcohol-water mixtures (120°C) by flow-through fractionation show the similar results that extraction efficiencies of over 55% were achieved, yielding lignin with good structural quality in terms of β-O-4 linking motifs.[26] The acid-hydrotrope-dissolved lignin (AHL) yield was exceptionally good at 81.9% with high β-O-4 linkages (80% retention) using *p*-TsOH (2.5 mol/L) by flow-through reaction under 98 °C for 40 min[58]. In addition, sequential extraction (SF) of hemicellulose and lignin to avoid excessive degradation of them have been described.[94] The second step of SF was characterized by mild conditions of 100 °C, 40wt% *p*-TsOH for one hour, and achieved 83% lignin dissolution with a well-preserved structure.

In addition, in order to avoid condensation, one strategy to prevent structural degradation is the direct hydrogenolysis of native lignin in biomass (i.e. reductive catalytic fractionation or catalytic upstream biorefining). However, there are still several important obstacles, such as catalyst recovery and mass transfer limitations in traditional batch reactors, which have nevertheless restricted the large-scale implementation of this method. Currently, moving from batch to flow-through reactors has become one of the research hotspots.[95] The flow-through RCF reactors enhance the mass transfer resulting in a very good yield of monophenolic compounds 37wt%.[96] Compared with traditional batch reactors, data acquired from the flow-through RCF reactors helps to understand the kinetic and mechanistic reactions during the processes.[97]

The above discussion showed that even if the cleavage of β-O-4 ether bond could not be prevented during the fractionation, further C-C bonds condensation reaction could be prevented by appropriate methods.

4. Further fractionation of lignin

Although numerous studies have shown to obtain the lignin for further application, the lignin presents a broad molecular weight distribution that limits the comprehensive and efficient utilization. Usually, the lignin with low Mw may with high antioxidant performance due to its highly reactive functional group content.[98] The lignin with high Mw has good performance to use as materials for carbon fiber.[99] Therefore, the further fractionation of lignin seems to be a preferential way as it can achieve specific molecular lignin fractions with defined properties. Until now, various approaches for fractionation of lignin have been reported, which mainly including membrane-assisted filtration, acidification,

Table 2. Approaches of fractionation from lignocellulosic biomass.

Approaches	Raw materials[a]	Solvent[b]/membrane*	M_w (g mol⁻¹)	Dispersity (Đ)	Ref.	Mw determination methods
Organosolv	KL	EtOH/H₂O	1500-7600	1.36-2.54	[100]	PSS MCX1000 & 100000 Å columns, 0.1 M NaOH eluent (pH 13) 25°C, 0.5 ml/min, polystyrene sulphonate standards
		DMK/H₂O	1600-18900	1.44-5.62		
		PEGME/H₂O	1700-4300	1.43-2.24		
	EHL	GL-EtOH	13300-30100	1.49-1.53	[101]	
	EHL	DCM	3814	2.21	[102]	G3000PWxl column, tris-acetate buffer (20 mmol/L, pH 7.4), 25°C, 0.5 mL/min, polyethylene glycol standards
		EtOAc	6748	2.35		
		NBA	7325	1.80		
	EHL	60% - 5% GVL	11135-4235	1.56-1.86	[103]	
	EHL	EtOH-H₂O (19:1 - 4:1 v/v)	6818-15352	1.68-1.39	[104]	
	SKL	MeOH	2040	3.52	[105]	GRAM PreColumn and two GRAM 1000 analytical columns, DMSO/0.5% (w/w) LiBr, 60°C, 0.5 mL/min, pullulan standards
		EtOH	1400	3.04		
		1-propanol	790	2.82		
		iso-propanol	760	2.62		
		tert-butanol	780	3.00		
		DMK	2450	3.95		
		MEK	1300	4.06		
		EtOAc	710	2.37		
	KL	EtOAc	1000	1.5	[106]	PSS column 100 Å and PSS GRAM 10000 Å analytical columns, DMSO/0.5% (w/w) LiBr, 60°C, 0.5 mL/min, pullulan standards
		EtOH	2100	1.9		
		MeOH	3200	2.0		
		acetone	5400	2.0		
	SL	EtOAc	1200	1.6	[107]	
		EtOH	2280	1.9		
		MeOH	3080	2.0		
		acetone	6360	2.1		Waters UltraStyragel HR4, HR2 and HR0.5 4.6 × 300 mm solvent efficient columns, THF eluent, 35°C, 0.3 ml/min, polystyrene standards
	HL	EtOAc	950	1.5	[107]	
		EtOH	1390	1.6		
		MeOH	2170	1.8		
		acetone	3150	2.0		
	Alder soda lignin	[Bmim]Cl	5751	3.6	[108]	
		[Bmim]Me₂PO₄	3730	2.8		
		[Bmim]OAc	2533	3.3		
		[Bmim]OTs	2844	3.5		
	SKL	THF	2300	1.7	[109]	THF eluent, 30°C, 0.5 ml/min, polystyrene standards
		MeOH	2900	1.8		
		MEK	1680	1.5		
	SKL	MeOH/DMK (7:3)	10244	3.02	[110]	Styragel HR 1 7.8 × 300 mm and Styragel HR 5E 7.8 × 300 mm column, THF eluent, 35°C, 0.7 ml/min, polystyrene standards
		EtOAc/PE (9:1)	2468	1.50		
		PE	770	1.23		
	Acetone lignin	60% - 30% DMK/H₂O	12500-1200	4.8-1.2	[111]	Styragel HR 2 and Styragel HR 5E column, THF eluent, 30°C, 0.7 ml/min, polystyrene standards
	KL	90% - 70% MeOH/H₂O	5016-5143 (dissolved) 11364-14870 (undissolved)	1.63-1.86 (dissolved) 2.13-2.46 (undissolved)	[112]	PL1110-6300 and PL1110-6530 columns, THF eluent, 40°C, polystyrene standards
	MWL	EtOAc/MEK/MeOH/DMK/DIOX-H₂O	2410-10640	1.3-2.1	[113]	THF eluent
	OL		1470-10490	2.3-1.9		
	CELF lignin	35% - 20% THF	1366-560	1.3-1.8	[114]	THF eluent, 1.0 ml/min, polystyrene standards
Acidification	HKBL	HCl pH 9 to 1	5316-3630	8.39-14.08	[115]	Two Supelco TSK-HXL columns (G2000 and G1000) and a G1000Hxl-G4000Hxl guard column, THF eluent, 40°C, 0.8 ml/min, polystyrene standards
	SKBL	HCl pH 9 to 1	13859-3464	16.48-5.09		
	SIBL	6 M H₂SO₄ pH 2.5 pH 5.0 pH 10.5	788-798 1008-1072 1347-1508	3.0-4.4 2.9-3.2 4.1-5.5	[116]	Suprema 1000 and Suprema 100, columns, DMSO/0.1% (w/w) LiBr, 80°C, 1.0 mL/min, pullulan standards
Filtration	*E. globulus* IKL	50 kDa* 15 kDa* 5 kDa*	12029 9576 9641	1.126 1.15 1.13	[117]	OligoPore column 300 × 7.5 mm, MesoPore column 300 × 7.5 mm, and a guard column Oligopore 50 × 7.5 mm, an isocratic mobile phase of dimethylformamide (DMF) with 0.5% w/v of lithium chloride (LiCl), 70°C, 0.8 mL/min, pullulan standards
	AL	Cell-AL hydrogel*	499 1054 1220	1.13 1.43 1.21	[118]	PL-gel 10 mm Mixed-B 7.5 mm ID column, THF eluent, 1.0 ml/min, polystyrene standards

[a] KL—kraft lignin, SKL—softwood kraft lignin, EHL—enzymatic hydrolysis lignin, MWL—milled wood lignin, OL—organosolv lignin, CELF—co-solvent enhanced lignocellulosic fractionation, SL-softwood lignin, HL-hardwood lignin, HKBL—hardwood Kraft black liquors, SKBL—softwood Kraft black liquors, SIBL—softwood industrial black liquor, IKL—industrial kraft liquor, AL—alkaline lignin. [b] MeOH—methanol, EtOH—ethanol, PEGME—propyleneglycol monomethyl ether, GL—glycerol, DMK—acetone, MEK—methyl ethyl ketone, THF—tetrahydrofuran, EtOAc—ethyl acetate, PE—petroleum ether, DCM—dichloromethane; DIOX—dioxane, GVL—γ-valerolactone.

and organic solvent fractionation. **Table 2** highlights the major fractionation conditions, Mw determination methods, distribution, and dispersity.

After further fractionation of lignin, the differences in their chemical structure were investigated. The lignin obtained by ultrafiltration present narrow molecular weight distribution in the results of the size exclusion chromatography. After the ultrafiltration, the obtained lignin fractions can be used as a biobased component in blends with polyethylene due to low molecular weight and a high quantity of phenolic hydroxyl groups.[119] As mature technology is widely used in industry, but there are some disadvantages, for example, the existence of partial polysaccharides, fouling of the membranes, and expensive instrumentation. The ceramic membrane was used to fractionate the LignoBoost kraft lignin for enhancing membrane performance over time, and the lignin fractions with low molecular weights were obtained with the molecular weight cut-off of 1 kDa which showed better antioxidant activity due to higher proportion of non-condensed phenolic hydroxyl groups.[120] The high molecular weights lignin with the higher content of carbohydrates and inorganics usually isolated from the relatively high cut-offs membrane.[117] Compare to ultrafiltration, acidification was an simpler and less energy consuming technique. Labidi et al. divided kraft lignin into three fractions by precipitation at different pH conditions with various acids (sulphuric acid and hydrochloric acid), and the effect of the process and the precipitation technique on lignin composition were analyzed. The fractions of lignin with higher molecular weights were precipitated at higher pH due to this fraction is easier to destabilize.[121] Subsequently, sequential acid precipitation method also proved this,[115] and the lignin fractions precipitated at higher pH exhibited higher purity due to the relatively low content of polysaccharides.[116] Although this fractionation method was easily used, the existence of polysaccharides makes the lignin fractions still with relatively low purity limiting its application.

Solvent fractionation is based on partial solubility of polymers into solvents. Generally, the ability of fractionation lignin by the solvent is correlated with hydrogen bonding capacity. Increasing the hydrogen bonding capacity of the solvent can extract relative higher molecular weights lignin fractions.[109] Numerous articles on the topic of lignin solvent fractionation have been investigated. For example, softwood kraft lignin was fractionated by ethyl acetate, ethanol, methanol, and acetone to five fractions with dispersity reduced below 2, and more carbohydrate content was found in the high Mw lignin fractions compared with the unfractionated lignin.[105] The low Mw lignin fractions showed higher antioxidant activities due to higher resistances to oxidative degradation compared with high Mw fractions.[107] The relatively high phenolic hydroxyl (-OH) existing in low fractions could also easily form hydrogen bond between lignin and the other two components containing abundant -OH groups.[122] Meanwhile, it is reported the homogeneity and narrow dispersity of lignin is beneficial for synthesizing the tunable thermosetting epoxies.[106] Jiang et al. fractionated softwood kraft lignin via a sequential extraction method using methanol, acetone, ethyl acetate, and petroleum ether to four lignin fractions with different molecular weight and dispersities.[110] Utilizing three different solvents (dichloromethane, acetic ether, butyl alcohol) sequentially, the antioxidant performance of four lignin fractions was investigated by An et al., and antioxidant performance can be remarkably enhanced in some of the fractions.[102] But, the use of multiple

solvents complicated the fractionation process, a single solvent is suitable to issue this problem. Sadeghifar et al. fractionated the organosolv lignin into different fractions via a simple approach using aqueous acetone followed by adding water. a simple approach only using one organic solvent.[111] A similar approach was applied to fractionate the kraft lignin. Three different aqueous solvents (ethanol, acetone, and propylene glycol monomethyl ether) were used to dissolve kraft lignin, and the precipitated lignin fractions can be obtained by tuning water addition into a system with constant quality and high purity.[100] The suitable lignin fractions with lower molecular weight contain progressively higher phenolic and carboxylic acid -OH groups can be acquired by similar methods.[114]

Recently, γ-valerolactone (GVL) is arousing the interest of researchers, due to its better stability, harmlessness, biodegradability, and recyclability. Wang et al. fractionated enzymatic hydrolysis lignin (EHL) into three parts only by GVL/water solvent, the GVL subsequent reuse for lignin fractionation, and they found that the obtained fractions presented significantly low Mw dispersity and structural heterogeneity.[103] Another renewable solvent, ethanol-water solution, was successfully used to fractionate EHL. The high-molecular-weight lignin obtained by 80% ethanol-water (v/v) fractionation of EHL and its antioxidant activity improved followed by depolymerization.[123] Also, the antimicrobial activity of EHL was improved after the ethanol-water fractionation.[104]

Based on the concept of green environmental protection, glycerol was applied with ethanol for lignin fractionation and the results showed that this approach could realize the efficient fractionation of EHL with relatively narrow dispersity.[101] As a novel solvent, the ionic liquid was also investigated to fractionate technical lignin with high purity.[108] In addition, Dai et al. developed a novel hydrogel-assisted fractionation approach using lignin-containing cellulose (Cell-AL) hydrogel to fractionate lignin to produce uniform lignins.[118] Depending on the future use of the lignin, the right technique to obtain the fractions has to be chosen.

5. Status and outlook

Lignin is the most abundant aromatic biopolymer in nature, and lignin valorization becomes one of the hot topics recently due to its critical for integrated biorefineries. To scaled-up valorization, effective lignin fractionation is a critical step since fractionation can overcome the recalcitrance of lignocelluloses or broad molecular weight distribution of lignin producing functionally distinct lignin.

First, it has now been widely demonstrated that a higher quantity of phenolic hydroxyl of lignin in favor of their chemical modification and physical interaction, higher β-O-4 linkages of lignin would be beneficial for carbon fiber production and production of monomers or aromatics through subsequent depolymerization, narrow dispersity and purity of lignin would be facilitative for as a polymer in composites for lignin valorization. With this in mind, we sought to further improve the quality of fractionated lignin by using novel solvents, mild conditions, or novel technologies. Future research will continue to develop efficient fractionation to yield lignin fractions that can be suitable for lignin valorization. Aiming to avoid lignin condensation during fractionation progresses still a significant direction due to the stable carbon-carbon (C-C) bonds are formed once β-O-4

linkages break which can influence the activities of lignin. Next, diverse materials with different fractionation methods show different effects on lignin fractions. Although, recently researches are focus on the structures change of lignin during processes, applying the fractionation technologies on a large scale limiting by understanding the lignin chemistry in deep due to the intrinsic heterogeneity of its complex structures. Further studies are needed to define the ideal fractionation of lignin for tailing each type of value-added applications. A techno-economic analysis is also needed to constantly evaluate the progress of developed technology and scale-up production and application. In addition, although lignin fractionation from lignocelluloses and further fractionation based on obtaining high quality lignins have been greatly enhancing its application. The combination of fractionation and application may be a choice to simplify the biorefinery progresses.

Overall, the efficient lignin fractionation could play a critical role in the lignin valorization which can lead to higher profits for pulp and paper industries and second-generation biorefineries as well as better understanding lignin chemistry. Most importantly, fractionation is for better lignin valorization, but not for bringing greater waste such as the solvent recovery.

Acknowledgements

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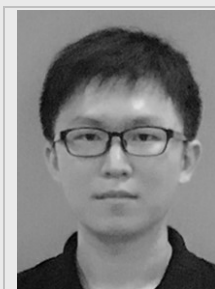
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Keywords: lignin • fractionation • lignocellulosic biomass • valorization • biorefinery

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Entry for the Table of Contents

The efficient fractionation strategies for lignin are the key and basis for the subsequent transformation into value-added products. Xu et al. review the approaches of lignin fractionation towards lignin valorization.