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Review

Lignin Biodegradation and Its Valorization

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Abstract: Lignin, a rigid polymer composed of phenolic subunits with high molecular weight and complex structure, ranks behind only cellulose in the contribution to the biomass of plants. Therefore, lignin can be used as a new environmentally friendly resource for the industrial production of a variety of polymers, dyes and adhesives. Since laccase was found to be able to degrade lignin, increasing attention had been paid to the valorization of lignin. Research has mainly focused on the identification of lignin-degrading enzymes, which play a key role in lignin biodegradation, and the potential application of lignin degradation products. In this review, we describe the source, catalytic specificity and enzyme reaction mechanism of the four classes of the lignin-degrading enzymes so far discovered. In addition, the major pathways of lignin biodegradation and the applications of the degradative products are also discussed. Lignin-degrading bacteria or enzymes can be used in combination with chemical pretreatment for the production of value-added chemicals from lignin, providing a promising strategy for lignin valorization.

Keywords: lignin; biodegradation; pathway; value-added chemicals; valorization

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1. Introduction

The phenolic polymer lignin is of great abundance in nature as a promising renewable energy resource, contributing about 30% of the weight and 40% of the energy of global lignocellulosic biomass (Figure 1a). An extraordinary structural diversity is caused by the varied monomer ratios and bond types of three monolignols [1]. The random structures and resistant linkages are considered to be the major obstacles for the industrial application of lignin compared. Although some enzymes related to lignin degradation have been found, challenges still exist in the process of lignin valorization [2,3]. First, it is difficult for enzymes to interact with lignin that consist of heterogeneous and amorphous structures. Second, it is hard to extract lignin from a lignocellulosic biomass. Two main strategies are designed to solve this challenge. The first strategy for the extraction of lignin is to keep lignin insoluble and make cellulose and hemicellulose to enter the liquid phase. Another diametrically opposite strategy is to hydrolyze or solubilize lignin but keep cellulose and hemicellulose insoluble (Figure 1a) [4]. The third challenge is to obtain chemical products from lignin processing with high yields and purities. During the depolymerization process, the depolymerized lignin fractions usually have high reactivity under depolymerization conditions, which can cause numerous uncontrollable side reactions, including repolymerization and condensation. These side reactions generate new compounds that might hinder

the direct conversion of lignin to target products [5,6]. With the discovery of more lignin-degrading enzymes and pathways, increasing attention will be paid to the value-added chemicals derived from lignin degradation.

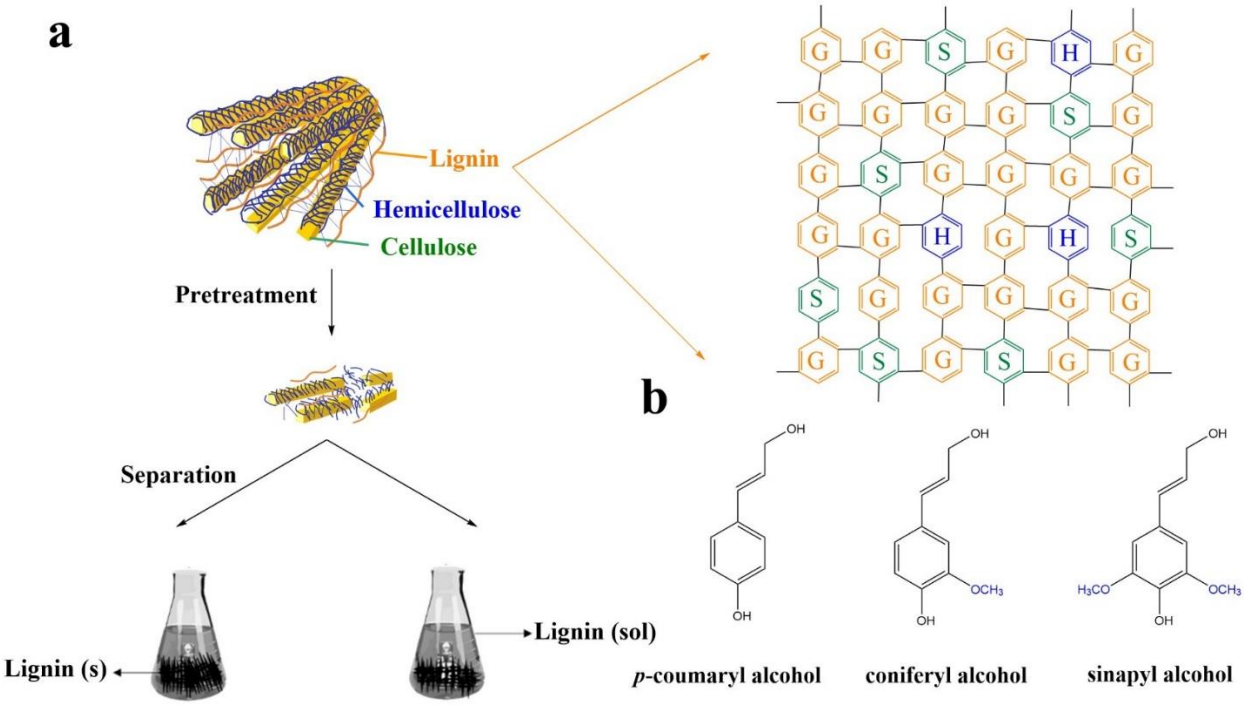

Figure 1. The structural formula and extraction methods of lignin. Lignin is a category of polymers composed of phenolic subunits, with three monolignols connected by ether bonds and carbon–carbon bonds. This figure gives a representative model for part of the structure of lignin. The circumjacent monolignols are linked with minolignols that are not displayed in the figure. Lignin is separated from lignocellulosic materials using two different strategies, making the lignin stay in the precipitate or enter the liquid phase (shows in ''s" and ''sol") (**a**). The *p*-coumaryl, coniferyl and sinapyl alcohols are the three monolignols found in lignin (**b**).

In this review, we summarize the enzymes for lignin depolymerization and the degradative pathways for lignin-derived aromatic compounds. In addition, the value-added chemicals produced from lignin have also been discussed to present the opportunities for lignin valorization. A better understanding of the enzymes and pathways involved in lignin degradation and valorization will contribute to the bioconversion of lignin to value-added products by creating more efficient artificial pathways.

2. Lignin

Coniferyl (G), sinapyl (S) and *p*-coumaryl (H) alcohols are the three categories of monolignols in lignin, which are divided into guaiacyl (G-type), guaiacyl-syringyl (GS-type) and grassy or guaiacyl-syringylp-coumaric (GSH-type) (Figure 1b). Figure 1a gives a representative example of the lignin structure to exhibit the three monolignols and the linkages in lignin; among which, the β-O-4 linkages are the most common ones. However, it needs to be noted that, in actual examples, other aromatic units are occasionally included in lignin, which is a common phenomenon. For example, Stewart et al. described the structure of the lignin polymers from poplar. The lignin from wild-type poplar contains *p*-hydroxybenzoate [7]. C-lignin, found in plants such as *Vanilla planifolia* and *Cleome hassleriana*, is wholly derived from caffeyl alcohol [8]. For sure, the GSH-type proportion and linkages proportion in these practical examples also varied from each other.

As a concept different from lignins in vivo, technical lignins (e.g. kraft lignin, soda lignin, lignosulfonates and organosolv lignin) are isolated lignins, most of which are

byproducts from the paper and pulp industry [1,9]. Kraft lignin, which is recovered from the black liquor, is generated from the paper and pulp industry as a by-product that is generated by treatment with Na_2S and NaOH [10]. However, the extraction of lignin from black liquor limits the commercial development of lignin until the emergence of the LignoBoost and LignoForce methods, which could also be applied for lignosulfonate and soda lignin. An economical benefit could be achieved as the extracted lignin has a high proportion of phenolic hydroxy groups [11].

Lignosulfonate is obtained as a by-product in the spent liquor of the pulping process by treating plant fiber as raw materials with an aqueous solution of sulfur dioxide and a calcium, magnesium, ammonium or sodium base [12]. The kraft lignins could also be used as raw metarials for lignosulfonate production. In the reviews provided by Ruwoldt [13] and Kienberger et al. [14], the lignin extraction processes and their dominant products, including commercialized lignosulfonates, were well-summarized. Membrane processes for the isolation and purification of lignosulfonates are also commercially available. In the meanwhile, fractionation of the lignosulfonates could obtain products with high quality. Recently, Demuner et al. elucidated two different processes for lignosulfonate production from eucalypt kraft lignin by sulfomethylation and acid sulfonation [15]. Varied pH levels can be applied in this process, for example, lignosulfonate production through neutral sulphite pulping was investigated [16]. It has the higher sulfur content and the lower price at the market when compared with kraft lignin [17].

Soda lignin is obtained from the soda or soda-anthraquinone pulping processes, in which 13–16% sodium hydroxide (pH 11–13) is used to extract lignin [18]. The chemical composition of soda lignin is closer to the natural lignin when compared with kraft lignin and lignosulphonate [19]. The major advantage of soda lignin is that it is obtained from wheat straw, an unwanted agricultural waste derived from the cropping of wheat.

Organosolv lignin is attained from the organosolv process, in which organic solvents are applied. Organosolv lignins, which are hydrophobic and water-insoluble, have several important characteristics: low molecular weight, high quality and high purity [20]. Nonetheless, the application of organic solvents may face the problem of environmental pollution [15]. However, organosolv lignin is sulfur-free, as is soda lignin, thus relieving the concern of environmental pollution from another perspective. In a review given by Wang et al., they well-summarized the chemical extraction methods for technical lignin [6].

Common derivatives such as vanillin, lipid and PHA could be produced via the lignin degradation process [21]. Multiple high value-added small molecules have been linked with lignin. Lignin, with a great amount of phenols, is considered to be a good candidate for producing phenolic resins. At present, products from lignin depend on sources besides the operating conditions [2]. Producing lignin-based resin with a high substitution rate of lignin to phenols is still a challenge. Recently, lignin with more S units was converted to desirable phenolic resins with a suitable viscosity and high substitution rate using chemical means with the beginning of methylolation [22]. Like phenolic resins, bio-oil generated by lignin can also broaden the application of lignin and thereby meet the new concept of carbon neutrality. Lignin can be transited to bio-oil via thermochemical methods (pyrolysis, gasification and liquefaction) [23]. However, these processes are usually energy-consuming and labor-intensive [24]. Problems like high energy demand and environment pollution encourage us to explore new ways for lignin degradation and valorization. The biodegradation of lignin could be an ideal choice. By exploiting enzymes by means such as cell-free systems, and taking advantage of the pathway of microorganisms to produce high value-added compounds, the biodegradation and valorization of lignin has a broad prospect.

3. Enzymes for Lignin Depolymerization

The enzymes involved in lignin depolymerization are mainly divided into four categories: laccase, lignin peroxidase (LiP), manganese peroxidase (MnP) and versatile peroxidase (VP).

3.1. Laccase (EC 1.10.3.2)

As a typical lignin oxidase, increasing attention has been paid to lignin depolymerization by laccase (EC 1.10.3.2). Laccase, a type of multi-copper oxidase (MCO), generally has four copper atoms (one type-1 copper, one type-2 copper and two type-3 coppers) in the catalytic site and oxidizes a variety of substrates by performing the single-electron transfer reaction four times. A O_2 molecule is reduced to two molecules of H_2O through the electron transfer pathway in laccase (Figure 2) [25,26]. The laccase-like activity could be detected by applying agar plates containing standard laccase substrates guaiacol or syringaldazine and then monitoring the dark colors coming from the oxidation of these substrates [27]. Chen et al. analyzed the binding mechanism of laccase from *Trametes versicolor* (formerly *Coriolus versicolor* or *Polyporus versicolor*) with lignin model compounds, and it turned out that hydrophobic contacts were necessary between laccase and the model compounds, but H-bonds were alternative [28]. In the reaction between laccases and lignins, the phenoxy radicals are first to be generated. The enzyme kinetics of lignin radical formation can be achieved by electron paramagnetic resonance (EPR) [29]. The formation of radicals could result in (1) depolymerization of the lignin [30], (2) polymerization of the lignin [31] or (3) the change of the functional group [32]. These potential outcomes could be effected by factors such as reaction conditions or whether the Laccase-Mediator System is involved in the reaction system.

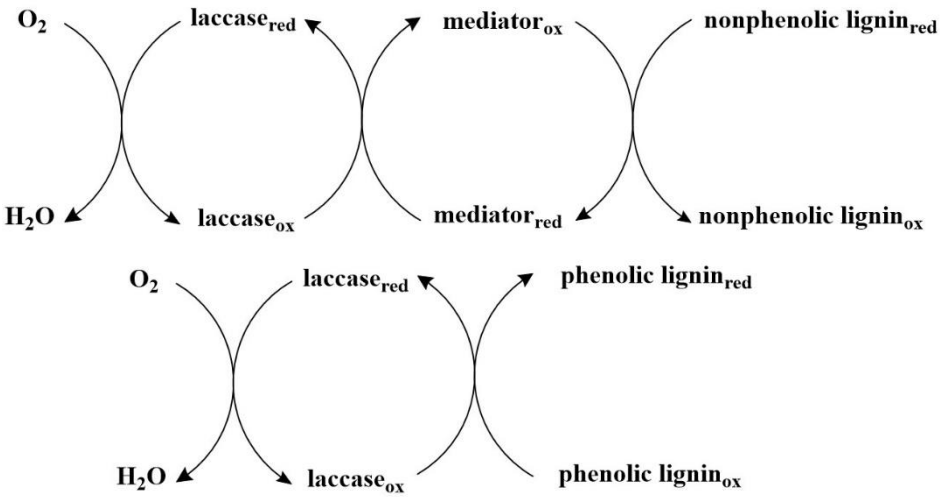

Figure 2. Schematic representation of the catalytic mechanism of laccase. Laccase catalyzes the oxidation of reduced substrates with molecular oxygen, with or without the participation of an electron transfer mediator. The ''ox" refers to oxidized compounds, while "red" represents reduced compounds.

The depolymerization of lignin requiring mediators is a common opinion [30,33]. Due to the relatively low redox potential of laccase for aromatic compounds, the Laccase–Mediator System (LMS) has been widely studied in order to expand the applications of laccases [34–38]. The mediators can be divided into three categories: natural mediators, synthetic mediators and other mediators. Some effective mediators have been widely used in industries, such as 1-hydroxybenzotriazole (HBT), methyl syringate and 2,2′-azino-bis(3-ethylbenzo thiazoline-6-sulfonic acid) (ABTS). In the LMS, the mediator is firstly oxidized by laccase and then undergoes a redox reaction with the substrate (Figure 2). This mechanism also implies that the laccase is a type of environment-friendly biocatalyst due to its lower requirements for factors such as heat for pyrolysis. Although mediators can tremendously accelerate the process of substrate oxidation by laccase [39], it also has significant influences on the stability of laccase. The free radicals generated from the oxidized mediator could attack laccase and then lead to its inactivation. To avoid the radical attack and improve the stability of laccase in LMS, it could be a promising strategy to find mediators that generate free radicals with lower activities.

According to the evolutionary tree created in this review, laccases from different organisms are highly homologous to each other, which suggests that their protein sequences are highly conserved. The identification of the specific amino acids responsible for the increase of the oxidation potential of laccase will contribute to the industrial application of laccase. Laccases from fungi, plants, insects and bacteria have been characterized. Laccases from white-rot fungi *Pycnoporus cinnabarinus* and *T. versicolor* have attracted wide attention since the last century [40]. *P. cinnabarinus* produces laccase in one isoform, and neither LiP nor MnP are detected. Thus by comparison between wild-type strains and laccase-less mutants, laccases from *P. cinnabarinus* are proven to be efficient for lignin degradation [41]. Kawai et al. reported that laccase from *T. versicolor* can catalyze various reactions of nonphenolic-O-4 lignin in the presence of HBT, such as β-ether cleavage, Cα-Cβ cleavage, aromatic ring cleavage and Cα-oxidation [42]. Compared with fungal laccases, laccases from bacteria have a higher thermostability and wider effective pH range [43–45]. Moreover, they are efficiently expressed in heterologous hosts such as *E. coli* with relatively high yields. All of these advantages render bacterial laccases great potential in energy and environmental biotechnology. Fungal laccases and bacterial laccases also tend to cause different effects on lignin; a study showed that fungi mineralized kraft lignin, while bacteria partially degraded and modified lignin [46]. In addition, due to their low substrate specificity, laccases have also been applied in many fields such as bioremediation, wood and paper industries [47,48]. The application of laccase is also reflected in the potential of small lignin production. With *Trametes villosa* laccase combined with HBT, the yield of glucose and ethanol were increased from lignocellulosic by Gutiérrez et al. [30] Through catalyzation of the above-mentioned enzymes, lignin enters the degradative pathways. To better understand the degradative pathways for lignin-derived aromatic compounds, it is necessary to summarize the products and effect of the enzymes in lignin depolymerization. The biodegradation of alkaline lignin by *Bacillus ligniniphilus* L1 resulted in the production of phenylacetic acid, 4-hydroxy-benzoicacid and vanillic acid [49]. Based on the whole-genome sequencing (with no LiP and MnP) and the decolorization experiment, laccase is expected to be responsible for the depolymerization of alkaline lignin in *B. ligniniphilus* L1.

3.2. Lignin Peroxidase (EC 1.11.1.14)

Lignin peroxidase (LiP) (EC 1.11.1.14), which belongs to the peroxidase-catalase superfamily, was firstly discovered in white-rot fungus *Phanerochaete chrysosporium* during the 1980s [50,51]. LiP is a heme peroxidase, which contains a protoporphyrin IX (heme) as the prosthetic group. Heme iron is responsible for the electron transfer and the high redox potential of LiP. Hydrogen peroxide (H_2O_2) functions as the electron acceptor in the catalytic site of LiP and drives the oxidation step. Two steps are required for the reduction of LiP. Compared with laccase, LiP has a higher reduction potential and requires no mediators [52]. However, previous studies found that the addition of veratryl alcohol (3,4-dime-thoxybenzyl alcohol; VA) can enhance the activity of LiP by transforming the electron between LiP and the substrates, thus promoting the rate of lignin depolymerization (Figure 3) [53]. LiP exhibits oxidative activity on a variety of compounds, such as phenolic compounds, amines, aromatic ethers and polycyclic aromatics [54,55]. Only two single-electron transfers are required for substrate oxidation. Though H_2O_2 plays an important role in the typical peroxidase catalytic cycle, excess H_2O_2 inhibits the activity of LiP [56]. To exploit the lignin degradation ability of LiP, explorations from different strategies were carried out. Majeke et al. reported the synergistic application of quinone reductase (QR) and LiP; this combination decreased the molecular weight (MW) of four different lignins [57] and showed the potential to benefit from the cooperation of different enzymes. On the other hand, considering LiP could be utilized in cell-free systems, the production of LiP can be improved. The effort for the large-scale production of LiP could boost the application of LiP for reasons such as cost reduction. Liu et al. achieved a maximum LiP activity of 1645 mU/L via multipulse-fed batch production [58]. Based on these paradigms, LiP will have larger application prospects.

Figure 3. Schematic representation of the catalytic mechanism of LiP, MnP and VP. LiP (**a**), MnP (**b**) and VP (**c**) require H_2O_2 for the oxidation of substrates, with veratryl alcohol and Mn^{2+} being used as facultative mediators for LiP and VP, respectively.

3.3. Manganese Peroxidase (EC 1.11.1.13)

Manganese peroxidase (MnP) (EC 1.11.1.13) was also discovered in *P. chrysosporium* [59]. MnP could be secreted by ligninolytic fungi into their microenvironment and, thus, be an ideal choice for cell-free systems. Similar to LiP, MnP is also a heme-containing enzyme, with disulfide bonds and Ca^{2+} maintaining the conformation of the active site [60]. When H_2O_2 binds to the ferric enzyme in a resting state, the reactions will be initiated by forming an iron–peroxide complex (Figure 3). MnP compound III, an inactive oxidation state, could be formed under excess H_2O_2 condition [61]. Therefore, first, Mn^{2+} is oxidized to Mn^{3+}; then, Mn^{3+} acts as the redox mediator to attack phenolic lignin structures

and results in the formation of instable free radicals, causing lignin degradation. One remarkable difference in the catalytic mechanism between LiP and MnP is that MnP, but not LiP, requires the conversion between Mn^{2+} and Mn^{3+} as an intermediate of the reaction. In the absence of mediators, one molecule of water will be produced in LiP's catalytic cycle, but the number of water is two for MnP's catalytic cycle [62]. By the treatment of milled wood with the MnP–, Mn^{3+}– or Fe^{2+}–linoleic acid system, MnP exhibited the most intense reactions, including transformation in the lignin structure and water-soluble low molar mass aromatic fragments releasing [63]. Base on the increase of the carboxyl content, the degradation of lignin was carried out via β-O-4 and Cα–Cβ cleavage and side-chain oxidation. In addition, besides the degradation of lignins, attention has been paid to the versatility of MnP. For example, MnP from *P. chrysosporium* could improve the efficiecy of cellulosic decomposing [64]. A manganese peroxidase-producing yeast consortium (MnP-YC4) has been developed to withstand lignin degradation inhibitors while degrading and detoxifying azo dye [65].

3.4. Versatile Peroxidase (EC 1.11.1.16)

Versatile peroxidase (VP) (EC 1.11.1.16), also belonging to the peroxidase-catalase superfamily, was firstly found in *Pleurotus eryngji*. Studies have revealed that VP is a "hybrid peroxidase", because its gene sequence contains the partial sequences of LiP and MnP (Figure 3). It integrates the substrate specificity and catalytic properties of LiP and MnP, respectively [66]. Therefore, VP can oxidize phenolic, nonphenolic and lignin derivatives without manganese ion or any mediator because of the high redox potential and broader substrate spectrum.

The high redox potential of VP results in a wide substrate specificity. For eample, VP can oxidize the LiP substrate veratryl alcohol; five molecules of water will be produced in the presence of veratryl alcohol (VA) [39,67]. In a previous study, VP showed oxidizing activity on hydroquinone in the absence of exogenous H_2O_2 but in the presence of Mn (II) [68]. When oxidizing phenolic compounds, VP uses a similar mechanism to MnP.

4. Degradative Pathways for Lignin-Derived Aromatic Compounds

Degradation of lignin-derived aromatic compounds provides microorganisms with carbon and energy resources and may contribute to the enhanced conversion of lignin to value-added chemicals. The β-O-4 linkages usually account for the largest proportion in lignin, making the β-Aryl ether (β-O-4) pathway play an important role in the depolymerization process of lignin. After the loss of the benzyl hydroxyl group in the β-aryl ether structural unit, the benzyl cation will form a new C–C cross-linkage. Through the biphenyl catabolic pathway, some benzene rings are disrupted to form mono-benzene or aliphatic compounds. The ring cleavage products are finally converted to organic acids that can enter the central carbon metabolism [69,70].

4.1. β-Aryl ether (β-O-4) Catabolic Pathway

Aromatic oligomers and monomers commonly found in lignin have been used to study how lignin-derived aromatic compounds are degraded [71,72]. Whatever the proportion of S, G and H, the β-O-4 linkage is dominant in lignins. A higher ratio of syringyl alcohol to guaiacyl alcohol (S/G) leads to an increased β-O-4 linkage. Therefore, the β-aryl ether degradative pathway plays a key role in the degradation of lignin-derived aromatic compounds, thus receiving a lot of research attention for the production of various phenolic chemicals. β-etherase is a promising candidate for the cleavage of β-O-4 bonds. The multiple GST family member β-etherases from *Sphingobium* sp. strain SYK-6 (formerly *Sphingomonas paucimobilis* SYK-6) include several etherases (eg. ligE, ligF and ligP) [73]. In the β-aryl ether degradation process, LigE, LigF and LigP catalyze a nucleophilic attack on the Cβ atom of the substrates by GSH. All three Lig GSTs produced β-S-glutathionyl-α-veratrylethanone from the achiral side chain-truncated model substrate β-guaiacyl-α-veratrylethanone (Figure 4). However, LigE- or LigP-catalyzed reactions

could yield only one of the two potential products, which might benefit in producing valuable chiral products from individual stereoisomers of -aryl substrates [74]. Marinovic et al. characterized the first functionally characterized fungal GSH-dependent β-etherase Ds-GST1 from the white-rot fungus *Dichomitus squalens* [3]. Ds-GST1 selectively cleaved the β-O-4 aryl ether bond and showed an accumulation of guaiacol with lignin model compound 2-(2-methoxyphenoxy)-3-oxo-3-(4-hydroxy-3-methoxyphenyl)propan-1-ol as the substrate. Apart from β-etherase, β-O-4 ether cleavage could also be achieved by the laccase/mediator system treatment (LMS). Under the condition of highly concentrated buffers at pH 6, Hilgers et al. obtained 80% ether cleavage with laccase from *T. versicolor*, in contrast to the result of <10% using the conventional buffer [75]. This study reveals the relation and competition between ether cleavage and Cα-oxidation. There have been reports that the reduction of the β-O-4 groups could improve the efficiency of lignin to convert to value-added product PHA [76]. With the development of synthetic biology, the β-aryl ether pathway can be engineered to improve the production of more value-added compounds from lignin.

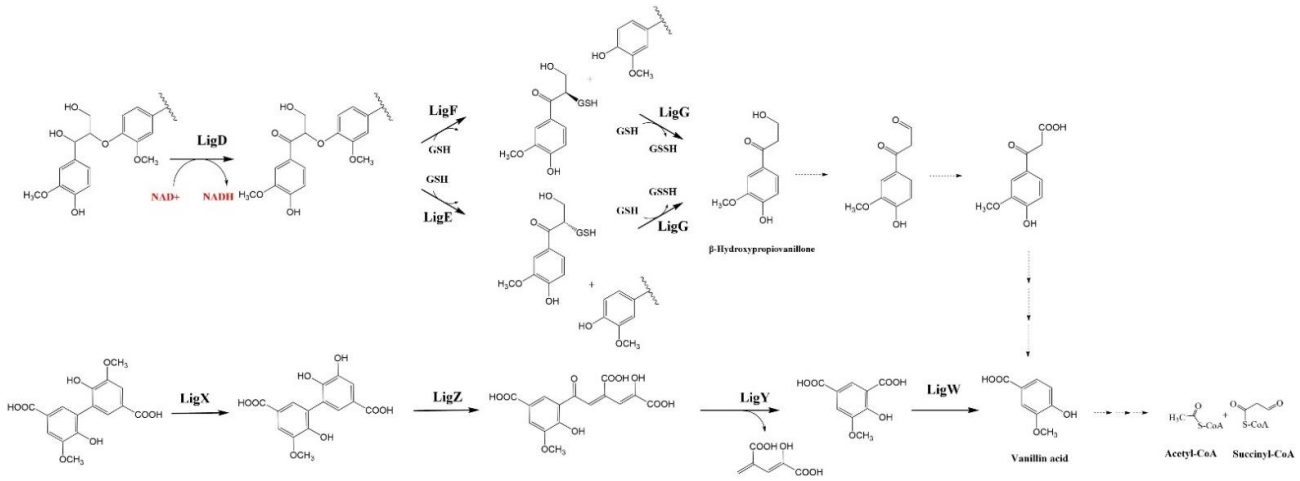

Figure 4. The β-Aryl ether (β-O-4) catabolic pathway and biphenyl linkage catabolic pathway. The enzymes involved in the β-Aryl ether (β-O-4) catabolic pathway and the biphenyl linkage catabolic pathway are from *Sphingobium* sp. SYK6 [73,77]. The β-Hydroxypropiovanillone and vanillin acid, which are produced from β-O-4 catabolic pathway and biphenyl linkage catabolic pathway, could be utilized for further valorization (showed in dotted arrows) [78,79].

4.2. Biphenyl Catabolic Pathway

A pathway for the degradation of the biphenyl component of lignin has been found in *Sphingobium* sp. strain SYK-6 (Figure 4) [80,81]. With the formation of 2,2′-dihydroxy-3,3′-dimethoxy,-5,5′-dicarboxybiphenyl by cleavage of the C3 side chain attached to biphenyl, pyruvic acid was eventually obtained. Although biphenyl linkages only account for about 10% of the total linkages in lignin, the biphenyl catabolic pathway also plays an important role in the degradation of lignin-derived aromatic compounds and even the highly toxic polychlorinated biphenyls (PCBs), which is a huge concern for many years. To remove the PCB pollutants in soil, a number of bacteria were isolated from the contaminated soil and were screened to verify the capability for degrading biphenyl compounds [82,83], and the PCB-degrading bacterial strains were varied within the genera *Stenotrophomonas*, *Pseudomonas* and *Rhodococcus*. The research on the degradation of PCBs provides a new theoretical basis for studying the biphenyl catabolic pathway. Coculturing of the PCB- and lignin-degrading microorganisms may further improve the lignin degradation.

4.3. β-ketoadipate Pathway

β-ketoadipate is a typical intermediate produced by microorganisms in the process of decomposing phenols, benzene and other aromatic compounds. It can be produced

from protocatechuate, which is derived from phenolic compounds, including *p*-cresol, 4-hydroxybenzoate and numerous lignin monomers (Figure 5). In addition, catechol generated from various aromatic compounds can also enter the β-ketoadipate pathway for degradation. However, not all β-ketoadipate comes from the β-ketoadipate pathway. 2-hydroxy-4-carboxy-butanyl-CoA (HCB-CoA) could be converted to β-ketoadipyl-CoA through the phenylacetic acid pathway (Figure 6) [84,85]. Niu et al. analyzed the biodegradation of lignin (coniferous and broad-leaved trees as raw materials after a sodium sulfite treatment) by *Brevibacillus thermoruber*. After the depolymerization of lignin is conducted by MnP, laccase and LiP, the biodegradation of the lignin G and H monomers were mainly proceeded via the β-ketoadipate pathway. By the analysis of the degradation products, one of the degradation products of benzoic acid is *cis*, *cis*-muconate, which is a β-ketoadipate pathway intermediate [86].

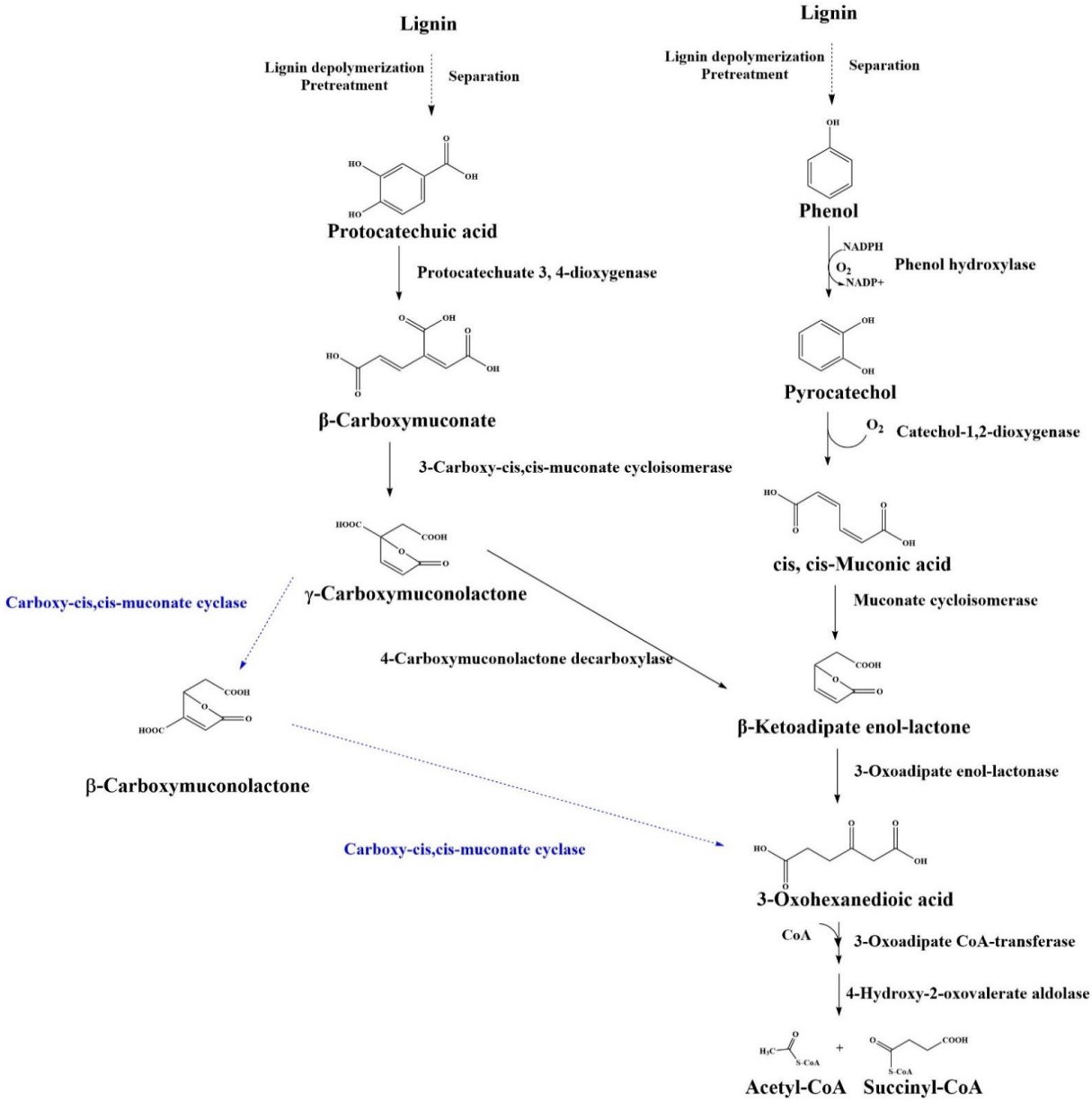

Figure 5. The degradative pathways of protocatechuic acid and phenol through β-ketoadipate. The lignin-derived aromatic compounds are degraded to central metabolites via these pathways for biosynthesis and energy. The enzymes are from *Sphingobium* sp. strain SYK-6, with the exception of carboxy-cis, cis-muconate cyclase from eukaryotes [91].

The lignin demethylation process formed by the O-demethylases, which will be discussed later, could convert lignin into pyrocatechol-enriched products by specifically removing the O-methyl/methoxyl groups of kraft lignin and releasing methanol [87]. On the other hand, as an important product of chemical depolymerization, phenol is differcult to be produced by enzymatic catalysis [88,89]. However, phenol could be converted to catechol (pyrocatechol) by enzymes such as phenol hydroxylase (PH) in *Pseudomonas stutzeri* OX1 [90].

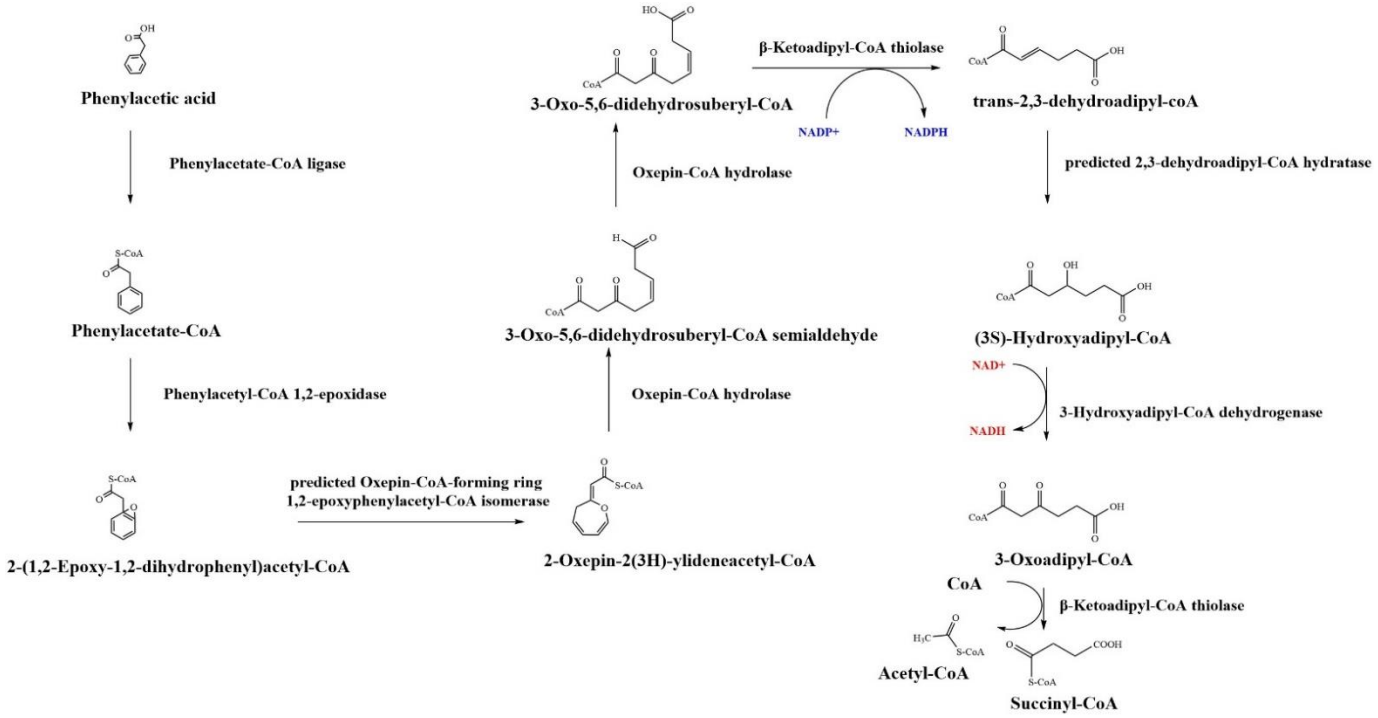

Figure 6. The degradative pathways of phenylacetic acid. Phenylacetate is degraded into tricarboxylic acid (TCA) cycle intermediates through the central metabolic pathway [84,85].

5. Auxiliary Pathways

5.1. β-oxidation-like Pathway

Many aromatic compounds can be degraded to obtain TCA cycle intermediates through the β-oxidation-like pathway, providing microorganisms with carbon and energy sources. Benzoate, coming from the degradation of lignin, can be further degraded to TCA cycle intermediates through the β-oxidation-like pathway [70]. In addition, the side chains of aromatic compounds such as *p*-coumaryl alcohol are degraded gradually, along with the release of acetyl-CoA in the meanwhile (Figure 7) [92]. A shorter side chain decreases the degree of cross-linking of lignin and thus increases its utilization efficiency. The released acetyl-CoA enters the central metabolism for biosynthesis or for energy.

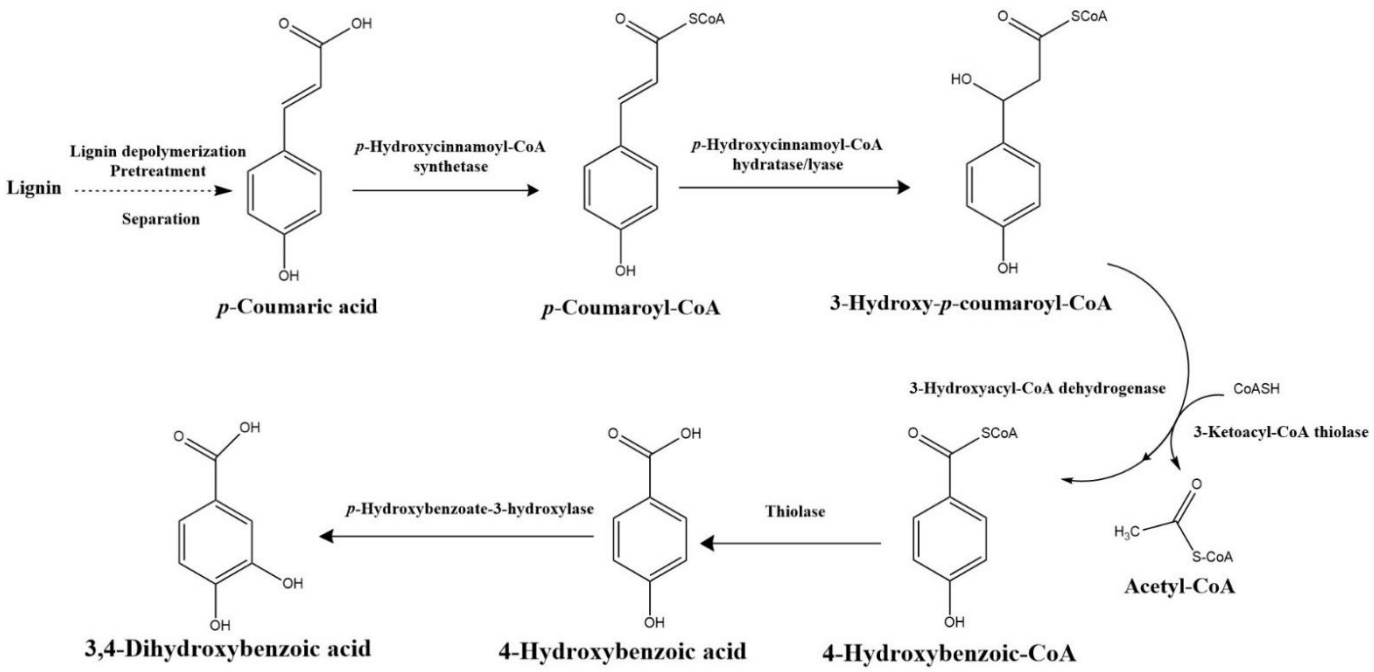

Figure 7. 3,4-dihydroxybenzoic acid is obtained via the β-oxidation-like pathway. The side chain of *p*-coumaric acid is firstly activated and then gradually degraded, with the release of acetyl-CoA for biosynthesis through the central metabolism or for energy [92].

5.2. Fenton Reaction

The Fenton reaction is an inorganic chemical reaction; the mixed solution of hydrogen peroxide (H_2O_2) and divalent iron ion Fe^{2+} oxidizes organic compounds such as carbox-ylic acids, alcohols and esters. The generated hydroxyl radical, which has a high redox potential of about 2.73V, can directly attack aromatic compounds [93]. Peroxidase en-zymes include LiP and MnP, containing ferric heme when they are at the resting state, catalyzing a cycle similar to the Fenton reaction (Figure 8a). In this cycle, H_2O_2 initiates the reaction by combining with Fe^{3+} to form an iron peroxide complex. The phenol substrate oxidizing activity is then activated after the generation of the Fe^{4+}–oxygen–porphyrin complex, with a concomitant reduction of H_2O_2 to H_2O. Therefore, the Fenton reaction can be used to attack lignin-derived aromatic compounds by generating a hydroxyl radical, which is formed by the reduction of Fe^{3+} and O_2 to Fe^{2+} and H_2O_2 with 2,5-dimethoxyhydroquinone (2,5-DMHQ) to 2,5-dimethoxy-1,4-benzoquinone (2,5-DMBQ) [94,95] (Figure 8b). In addition, there is evidence that the Fenton reaction facilitates the degradation of PCBs [96]. However, more investigations are still needed to further confirm whether the combination of the Fenton reaction and the biphenyl catabolic pathway can promote the degradation of lignins or not. Iron plays a key role in the reactivity of the Fenton reaction. The consumption of H_2O_2 in the Fenton reaction explains the reason why Fe^{2+} shows inhibition of the activity of laccase [97]. However, research also shows that iron can enhance the activity of laccase, and laccase, in turn, promotes the association of organic matter with iron, assisting the stabilization of soil organic matter [98,99]. Therefore, the influence of iron on lignin degradation is much more complicated.

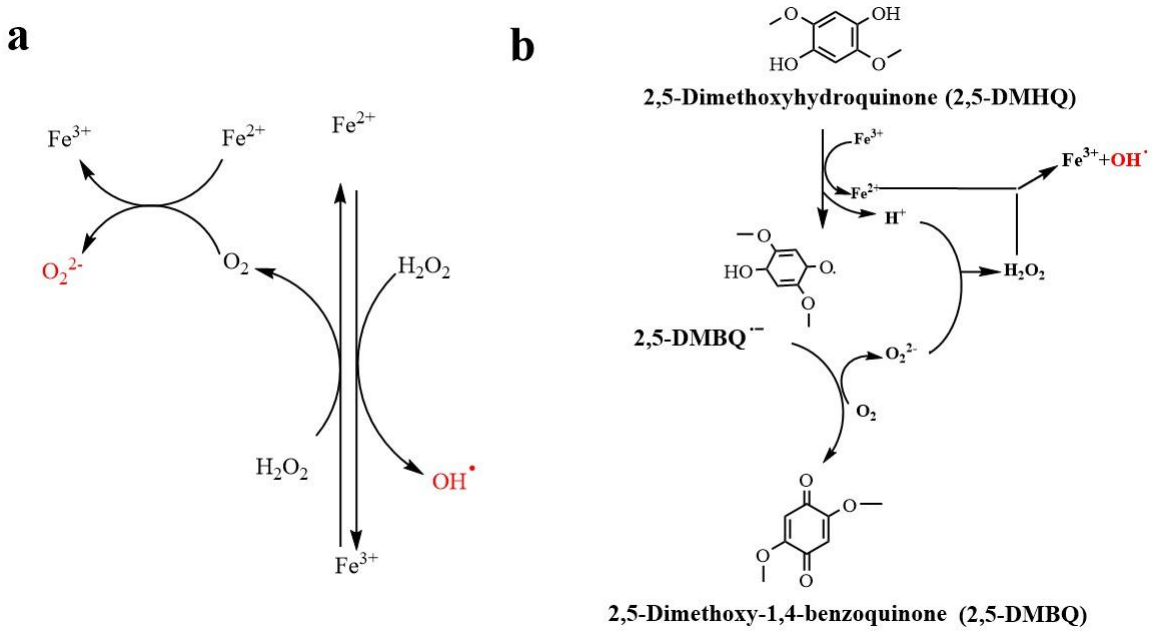

Figure 8. The mechanism of the Fenton reaction and its application. The hydroxyl radical (OH·) obtained from the Fenton reaction has a redox potential of more than 2.73 V, making it capable of directly attacking aromatic compounds [93] (**a**). The hydroxyl radical, which is capable of attacking lignin derivative 2,5-dimethoxyhydroquinone (2,5-DMHQ), is formed by the reduction of Fe^{3+} and O_2 to Fe^{2+} and H_2O_2 with 2,5-dimethoxy-1,4-benzoquinone (2,5-DMBQ) [94,95] (**b**).

5.3. Demethylation

The low reactivity of lignin hinders the direct utilization of lignin, so the modification of lignin has been developed as an alternative strategy to improve the lignin application [100,101]. The most widely used methods include demethylation [102,103], methylolation [104,105], phenolation [106,107], oxidative degradation and hydrothermal depolymerization/liquefaction [108,109]. Fungi and bacteria have been used for decades to carry out the demethylation of lignin, with advantages of less investments and shorter processing times. Demethylation has been validated to be the most effective method to enhance the reactivity of lignin by removing the methoxyl group. The demethylated guaiacyl-type synthetic lignin showed higher tannin-like properties and transformed into a useful precursor for lignin-based epoxy resin [110]. By demethylation, followed by catalytic hydrogenolysis, Kim et al. obtained a selective production of catechols, which are an important catabolic node in the β-ketoadipate pathway, from milled wood lignin [111] and could be further processed by the β-ketoadipate pathway. The demethylation process could be catalyzed by enzymes. The catalyzation by O-demethylase results in the formation of phenolic hydroxyls groups. O-demethylases from fungus and bacteria have been reported, such as *Aspergillus* sp., *Galerina autumnalis* [112] and *Desulfitobacterium hafniense* DCB-2 [113].

It is still not clear if laccase is responsible for the process of losing a methyl group from aryl methoxyl, since the role that laccases play in these processes might not be the same. The terms of demethylation and demethoxylation imply different reaction mechanisms, which refer to the removal of the methyl group and the methoxyl group, respectively. The "demethylation" process by laccase could be the combining of demethoxylation and addition of a phenolic hydroxyls group, rather than a direct demethylation process. By detecting the increase of the concentration of pyrocatechol structures in lignin, the demethylation reaction catalyzed by laccase from *Botryosphaeria rhodina* was confirmed, with methanol and ABTS as the final product and mediator, respectively [114,115]. Blue laccase from *Galerina* sp. HC1 was also reported for the demethylation of kraft lignin [116]. The sequences of internal peptides from this blue laccase were highly similar to the reported laccase. It needs to be noted that the optimal pH for this blue laccase is 3.0, which is relatively low, implying

the effects of laccase under different pH could be varied, providing new strategies for lignin valorization.

There has been reported that the demethylation of lignin causes side-chain ether bond breakage during lignin pyrolysis [117]. However, the contents of the phenolic hydroxyl groups and carboxyl groups increased after demethylation [118,119]. Therefore, the reactions of repolymerization and condensation also occur during the process of lignin degradation. Overall, the conversion of -OCH_3 into hydroxyl groups could significantly improve the lignin reactivity, and therefore, the demethylation caused by fungi and bacteria, or the secreted enzymes could provide alternatives for chemical means.

6. Value-Added Chemicals Produced from Lignin

The value-added products can be obtained in two ways, one of which is the pretreatment of lignin from raw materials, and the other one of which is to enter the metabolic pathways.The pretreatment of lignin could be chemical or enzymatic, aiming to obtain aromatic compounds derived from lignin, following by the conversion of these compounds by the metabolism pathway. Through the relatively similar degradative pathways, metabolic nodes such as catechol and the central metanolism pathway, multiple value-added products could be obtained by different hosts [79].

Strains from *Rhodococcus opacus* have been widely used for the production of lipids from lignin [120,121], Liu et al. achieved a high lipids titer (1.83 g/L), with corn stover as the raw metarial [122]. The combinatorial pretreatment increased the lipid concentration by 12.8–75.6%, reflecting the effect of the pretreatment.

Besides the pretreatment, genetic engineering could also be used to obtain the value-added products. By employing the *Sphingobium* SYK-6 *ligAB* genes and *Paenibacillus praA* gene, *Rhodococcus jostii* RHA1 has been used as chassis cells to produce 2,4-pyridine-dicarboxylic and 2,5-pyridine-dicarboxylic from vanillic acid or wheat straw lignocellulose [123]. Similarly, the *Pseudomonas putida* KT2440 expressing exogenous O-demethylase from *Amycolatopsis* sp. could process a variety of lignin-derived monomers, such as converting guaiacol to catechol [124]. Up to 4.5 g/L PHA was obtained by the engineered *P. putida* KT2440, with the design of "plug-in processes of lignin (PIPOL) " and corn stover as the raw material [125]. It suggests the combination of designed pretreatment and genetic engineering could further improve the yield of value-added products from lignin. An engineered *E. coli* strain could use protocatechuate as the sole carbon and energy source by expressing a heterologous pathway from *P. putida*, providing a good strategy for the enhanced bioconversion of lignin-derived aromatics to value-added chemicals [126].

Some useful compounds could be treated as products of the valorization process. On the other hand, these compounds could also be supplied as a substrate for valorization. The deletion of vanillin dehydrogenase resulted in the vanillin accumulation in *Amycolatopsis* sp. ACTT 39116 when ferulic acid was used as the substrate [127]. Vanillin can also be used as a substrate for the production of catechol and vanillic acid in engineered *E. coli* [128]. Vanillic acid was then converted to PHA in *P. putida* [129]. It is crucial to select appropriate substrates and chassis cells for the successful valorization of lignin. The *cis*, *cis*-muconate, is an important intermediate in lignin degradation. An engineered *C. glutamicum* MA-2 strain produced 85 g/L and 1.8 g/L *cis*, *cis*-muconate from catechol and hydrothermal pretreated softwood lignin, respectively [130]. This study demonstrates that valorization requires a comprehensive consideration to reduce the production costs of value-added chemicals.

Besides vanillin, bioplastics and lipids, oleogels that are potentially applicable as biolubricating greases were also produced with wheat straw soda lignins, which were obtained by the solid-state fermentation (SSF) of wheat straw supplemented with *Streptomyces* sp. MDG147 [131]. The combination of chemical process and microbial fermentation provides another strategy for the production of value-added products from lignin. The pretreated lignin and metabolic intermediates such as vanillin and vanillic acid could be used as substrates for valorization. To further reduce the production costs, engineering of the

extremophiles, such as the energy and fresh water saving halophilic bacteria, could be a promising strategy.

7. Conclusions

Depolymerization plays a central role in the degradation of lignin, providing a prerequisite for the production of value-added chemicals from lignin-derived aromatic compounds. However, the heterogeneous and amorphous structures of lignin present a big challenge to the biological utilization of lignin mildly and sustainably. Though laccase and other lignin-degrading enzymes have been discovered to be able to degrade lignin, it is still difficult to produce lignin-derived chemicals with high purities and yields. With the fast development of enzyme engineering and synthetic biology, more efficient enzymes and pathways will be created to greatly improve the degradation of lignin and economically produce value-added chemicals.

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References

1. Abdelaziz, O.Y.; Brink, D.P.; Prothmann, J.; Ravi, K.; Sun, M.; García-Hidalgo, J.; Sandahl, M.; Hulteberg, C.P.; Turner, C.; Lidén, G. Biological valorization of low molecular weight lignin. *Biotechnol. Adv.* **2016**, *34*, 1318–1346. [CrossRef] [PubMed]
2. Ren, T.; Qi, W.; Su, R.; He, Z. Promising techniques for depolymerization of lignin into value-added chemicals. *ChemCatChem* **2019**, *11*, 639–654. [CrossRef]
3. Marinović, M.; Nousiainen, P.; Dilokpimol, A.; Kontro, J.; Moore, R.; Sipilä, J.; De Vries, R.P.; Mäkelä, M.R.; Hildén, K. Selective cleavage of lignin β-O-4 aryl ether bond by β-etherase of the white-rot fungus Dichomitus squalens. *ACS Sustain. Chem. Eng.* **2018**, *6*, 2878–2882. [CrossRef] [PubMed]
4. Dashtban, M.; Maki, M.; Leung, K.T.; Mao, C.; Qin, W. Cellulase activities in biomass conversion: Measurement methods and comparison. *Crit. Rev. Biotechnol.* **2010**, *30*, 302–309. [CrossRef]
5. Wang, Z.; Li, N.; Pan, X. Transformation of ammonia fiber expansion (AFEX) corn stover lignin into microbial lipids by Rhodococcus opacus. *Fuel* **2019**, *240*, 119–125. [CrossRef]
6. Wang, H.; Pu, Y.; Ragauskas, A.; Yang, B. From lignin to valuable products–strategies, challenges, and prospects. *Bioresour. Technol.* **2019**, *271*, 449–461. [CrossRef]
7. Stewart, J.J.; Akiyama, T.; Chapple, C.; Ralph, J.; Mansfield, S.D. The effects on lignin structure of overexpression of ferulate 5-hydroxylase in hybrid poplar1. *Plant Physiol.* **2009**, *150*, 621–635. [CrossRef]
8. Wang, X.; Zhuo, C.; Xiao, X.; Wang, X.; Docampo-Palacios, M.; Chen, F.; Dixon, R.A. Substrate specificity of LACCASE8 facilitates polymerization of caffeyl alcohol for C-lignin biosynthesis in the seed coat of Cleome hassleriana. *Plant Cell* **2020**, *32*, 3825–3845. [CrossRef]
9. Ayuso-Fernández, I.; Rencoret, J.; Gutiérrez, A.; Ruiz-Dueñas, F.J.; Martínez, A.T. Peroxidase evolution in white-rot fungi follows wood lignin evolution in plants. *Proc. Natl. Acad. Sci. USA* **2019**, *116*, 17900–17905. [CrossRef]
10. Wang, C.; Kelley, S.S.; Venditti, R.A. Lignin-based thermoplastic materials. *ChemSusChem* **2016**, *9*, 770–783. [CrossRef]
11. Kazzaz, A.E.; Feizi, Z.H.; Fatehi, P. Grafting strategies for hydroxy groups of lignin for producing materials. *Green Chem.* **2019**, *21*, 5714–5752. [CrossRef]

12. Meister, J.J. Modification of lignin. *J. Macromol. Sci. Part C Polym. Rev.* **2002**, *42*, 235–289. [CrossRef]
13. Ruwoldt, J. A critical review of the physicochemical properties of lignosulfonates: Chemical structure and behavior in aqueous solution, at surfaces and interfaces. *Surfaces* **2020**, *3*, 622–648. [CrossRef]
14. Kienberger, M.; Maitz, S.; Pichler, T.; Demmelmayer, P. Systematic review on isolation processes for technical lignin. *Processes* **2021**, *9*, 804. [CrossRef]
15. Demuner, I.F.; Gomes, F.J.B.; Gomes, J.S.; Coura, M.R.; Borges, F.P.; Carvalho, A.M.M.L.; Silva, C.M. Improving kraft pulp mill sustainability by lignosulfonates production from processes residues. *J. Clean. Prod.* **2021**, *317*, 128286. [CrossRef]
16. Hanhikoski, S.; Niemelä, K.; Vuorinen, T. Biorefining of Scots pine using neutral sodium sulphite pulping: Investigation of fibre and spent liquor compositions. *Ind. Crops Prod.* **2019**, *129*, 135–141. [CrossRef]
17. Tribot, A.; Amer, G.; Alio, M.A.; de Baynast, H.; Delattre, C.; Pons, A.; Mathias, J.-D.; Callois, J.-M.; Vial, C.; Michaud, P. Wood-lignin: Supply, extraction processes and use as bio-based material. *Eur. Polym. J.* **2019**, *112*, 228–240. [CrossRef]
18. Guadix-Montero, S.; Sankar, M. Review on catalytic cleavage of C–C inter-unit linkages in lignin model compounds: Towards lignin depolymerisation. *Top. Catal.* **2018**, *61*, 183–198. [CrossRef]
19. Wörmeyer, K.; Ingram, T.; Saake, B.; Brunner, G.; Smirnova, I. Comparison of different pretreatment methods for lignocellulosic materials. Part II: Influence of pretreatment on the properties of rye straw lignin. *Bioresour. Technol.* **2011**, *102*, 4157–4164. [CrossRef] [PubMed]
20. Vishtal, A.G.; Kraslawski, A. Challenges in industrial applications of technical lignins. *BioResources* **2011**, *6*, 3547–3568. [CrossRef]
21. Chen, Z.; Wan, C. Biological valorization strategies for converting lignin into fuels and chemicals. *Renew. Sustain. Energy Rev.* **2017**, *73*, 610–621. [CrossRef]
22. Pang, B.; Lam, S.S.; Shen, X.J.; Cao, X.F.; Liu, S.J.; Yuan, T.Q.; Sun, R.C. Valorization of technical lignin for the production of desirable resins with high substitution rate and controllable viscosity. *ChemSusChem* **2020**, *13*, 4446–4454. [CrossRef]
23. Qian, Y.; Zuo, C.; Tan, J.; He, J. Structural analysis of bio-oils from sub-and supercritical water liquefaction of woody biomass. *Energy* **2007**, *32*, 196–202. [CrossRef]
24. Kloekhorst, A.; Heeres, H.J. Catalytic hydrotreatment of alcell lignin using supported Ru, Pd, and Cu catalysts. *ACS Sustain. Chem. Eng.* **2015**, *3*, 1905–1914. [CrossRef]
25. Morpurgo, L.; Graziani, M.; Finazzi-Agro, A.; Rotilio, G.; Mondovi, B. Optical properties of japanese-lacquer-tree (Rhus vernicifera) laccase depleted of type 2 copper (II). Involvement of type-2 copper (II) in the 330nm chromophore. *Biochem. J.* **1980**, *187*, 361–366. [CrossRef]
26. Claus, H. Laccases and their occurrence in prokaryotes. *Arch. Microbiol.* **2003**, *179*, 145–150. [CrossRef]
27. Mandic, M.; Djokic, L.; Nikolaivits, E.; Prodanovic, R.; O'Connor, K.; Jeremic, S.; Topakas, E.; Nikodinovic-Runic, J. Identification and characterization of new laccase biocatalysts from Pseudomonas species suitable for degradation of synthetic textile dyes. *Catalysts* **2019**, *9*, 629. [CrossRef]
28. Chen, M.; Zeng, G.; Lai, C.; Li, J.; Xu, P.; Wu, H. Molecular basis of laccase bound to lignin: Insight from comparative studies on the interaction of Trametes versicolor laccase with various lignin model compounds. *RSC Adv.* **2015**, *5*, 52307–52313. [CrossRef]
29. Perna, V.; Agger, J.W.; Andersen, M.L.; Holck, J.; Meyer, A.S. Laccase induced lignin radical formation kinetics evaluated by electron paramagnetic resonance spectroscopy. *ACS Sustain. Chem. Eng.* **2019**, *7*, 10425–10434. [CrossRef]
30. Gutiérrez, A.; Rencoret, J.; Cadena, E.M.; Rico, A.; Barth, D.; José, C.; Martínez, Á.T. Demonstration of laccase-based removal of lignin from wood and non-wood plant feedstocks. *Bioresour. Technol.* **2012**, *119*, 114–122. [CrossRef]
31. Braunschmid, V.; Binder, K.; Fuerst, S.; Subagia, R.; Danner, C.; Weber, H.; Schwaiger, N.; Nyanhongo, G.S.; Ribitsch, D.; Guebitz, G.M. Comparison of a fungal and a bacterial laccase for lignosulfonate polymerization. *Process Biochem.* **2021**, *109*, 207–213. [CrossRef]
32. Mattinen, M.-L.; Maijala, P.; Nousiainen, P.; Smeds, A.; Kontro, J.; Sipilä, J.; Tamminen, T.; Willför, S.; Viikari, L. Oxidation of lignans and lignin model compounds by laccase in aqueous solvent systems. *J. Mol. Catal. B: Enzym.* **2011**, *72*, 122–129. [CrossRef]
33. Kawai, S.; Iwatsuki, M.; Nakagawa, M.; Inagaki, M.; Hamabe, A.; Ohashi, H. An alternative β-ether cleavage pathway for a non-phenolic β-O-4 lignin model dimer catalyzed by a laccase-mediator system. *Enzym. Microb. Technol.* **2004**, *35*, 154–160. [CrossRef]
34. Hilgers, R.; Vincken, J.-P.; Gruppen, H.; Kabel, M.A. Laccase/mediator systems: Their reactivity toward phenolic lignin structures. *ACS Sustain. Chem. Eng.* **2018**, *6*, 2037–2046. [CrossRef]
35. Bujanovic, B.; Ralph, S.; Reiner, R.; Hirth, K.; Atalla, R. Polyoxometalates in oxidative delignification of chemical pulps: Effect on lignin. *Materials* **2010**, *3*, 1888–1903. [CrossRef]
36. Rencoret, J.; Pereira, A.; del Río, J.C.; Martínez, A.N.T.; Gutiérrez, A. Delignification and saccharification enhancement of sugarcane byproducts by a laccase-based pretreatment. *ACS Sustain. Chem. Eng.* **2017**, *5*, 7145–7154. [CrossRef]
37. Rencoret, J.; Pereira, A.; Del Río, J.C.; Martínez, A.T.; Gutiérrez, A. Laccase-mediator pretreatment of wheat straw degrades lignin and improves saccharification. *BioEnergy Res.* **2016**, *9*, 917–930. [CrossRef]
38. Xie, B.; Tobimatsu, Y.; Kamitakahara, H.; Takano, T. Reaction Selectivity in Electro-oxidation of Lignin Dimer Model Compounds and Synthetic Lignin with Different Mediators for the Laccase Mediator System (PZH, NHPI, ABTS). *ACS Sustain. Chem. Eng.* **2022**, *10*, 6633–6641. [CrossRef]
39. Kumar, A.; Chandra, R. Ligninolytic enzymes and its mechanisms for degradation of lignocellulosic waste in environment. *Heliyon* **2020**, *6*, e03170. [CrossRef]

40. Guo, M.; Lu, F.; Du, L.; Pu, J.; Bai, D. Optimization of the expression of a laccase gene from Trametes versicolor in Pichia methanolica. *Appl. Microbiol. Biotechnol.* **2006**, *71*, 848–852. [CrossRef]
41. Eggert, C.; Temp, U.; Eriksson, K.-E.L. Laccase is essential for lignin degradation by the white-rot fungus Pycnoporus cinnabarinus. *Febs Lett.* **1997**, *407*, 89–92. [CrossRef]
42. Kawai, S.; Nakagawa, M.; Ohashi, H. Degradation mechanisms of a nonphenolic β-O-4 lignin model dimer by Trametes versicolor laccase in the presence of 1-hydroxybenzotriazole. *Enzym. Microb. Technol.* **2002**, *30*, 482–489. [CrossRef]
43. Arias, M.; Blánquez, A.; Hernandez, M.; Rodriguez, J.; Ball, A.; Jiménez-Morillo, N.; González-Vila, F.; González-Pérez, J. Role of a thermostable laccase produced by Streptomyces ipomoeae in the degradation of wheat straw lignin in solid state fermentation. *J. Anal. Appl. Pyrolysis* **2016**, *122*, 202–208. [CrossRef]
44. Guan, Z.-B.; Shui, Y.; Song, C.-M.; Zhang, N.; Cai, Y.-J.; Liao, X.-R. Efficient secretory production of CotA-laccase and its application in the decolorization and detoxification of industrial textile wastewater. *Environ. Sci. Pollut. Res.* **2015**, *22*, 9515–9523. [CrossRef]
45. Shi, X.; Liu, Q.; Ma, J.; Liao, H.; Xiong, X.; Zhang, K.; Wang, T.; Liu, X.; Xu, T.; Yuan, S. An acid-stable bacterial laccase identified from the endophyte Pantoea ananatis Sd-1 genome exhibiting lignin degradation and dye decolorization abilities. *Biotechnol. Lett.* **2015**, *37*, 2279–2288. [CrossRef]
46. Asina, F.; Brzonova, I.; Voeller, K.; Kozliak, E.; Kubátová, A.; Yao, B.; Ji, Y. Biodegradation of lignin by fungi, bacteria and laccases. *Bioresour. Technol.* **2016**, *220*, 414–424. [CrossRef] [PubMed]
47. Colao, M.C.; Lupino, S.; Garzillo, A.M.; Buonocore, V.; Ruzzi, M. Heterologous expression of lcc1 gene from Trametes trogii in Pichia pastoris and characterization of the recombinant enzyme. *Microb. Cell Factories* **2006**, *5*, 31. [CrossRef] [PubMed]
48. Bo, W.; Yan, Y.; Xu, J.; Fu, X.; Han, H.; Gao, J.; Li, Z.; Wang, L.; Tian, Y.; Peng, R. Heterologous expression and characterization of a laccase from Laccaria bicolor in Pichia pastoris and Arabidopsis thaliana. *J. Microbiol. Biotechnol.* **2018**, *28*, 2057–2063. [CrossRef]
49. Zhu, D.; Zhang, P.; Xie, C.; Zhang, W.; Sun, J.; Qian, W.-J.; Yang, B. Biodegradation of alkaline lignin by Bacillus ligniniphilus L1. *Biotechnol. Biofuels* **2017**, *10*, 44. [CrossRef] [PubMed]
50. Kirk, T.K.; Croan, S.; Tien, M.; Murtagh, K.E.; Farrell, R.L. Production of multiple ligninases by Phanerochaete chrysosporium: Effect of selected growth conditions and use of a mutant strain. *Enzym. Microb. Technol.* **1986**, *8*, 27–32. [CrossRef]
51. Leisola, M.; Kozulic, B.; Meussdoerffer, F.; Fiechter, A. Homology among multiple extracellular peroxidases from Phanerochaete chrysosporium. *J. Biol. Chem.* **1987**, *262*, 419–424. [CrossRef]
52. Fujii, K.; Uemura, M.; Hayakawa, C.; Funakawa, S.; Kosaki, T. Environmental control of lignin peroxidase, manganese peroxidase, and laccase activities in forest floor layers in humid Asia. *Soil Biol. Biochem.* **2013**, *57*, 109–115. [CrossRef]
53. Sayadi, S.; Ellouz, R. Roles of lignin peroxidase and manganese peroxidase from Phanerochaete chrysosporium in the decolorization of olive mill wastewaters. *Appl. Environ. Microbiol.* **1995**, *61*, 1098–1103. [CrossRef]
54. Wang, X.; Yao, B.; Su, X. Linking enzymatic oxidative degradation of lignin to organics detoxification. *Int. J. Mol. Sci.* **2018**, *19*, 3373. [CrossRef] [PubMed]
55. Calvo-Flores, F.G.; Dobado, J.A. Lignin as renewable raw material. *ChemSusChem* **2010**, *3*, 1227–1235. [CrossRef] [PubMed]
56. Sung, H.J.; Khan, M.F.; Kim, Y.H. Recombinant lignin peroxidase-catalyzed decolorization of melanin using in-situ generated H2O2 for application in whitening cosmetics. *Int. J. Biol. Macromol.* **2019**, *136*, 20–26. [CrossRef]
57. Majeke, B.; Collard, F.-X.; Tyhoda, L.; Görgens, J. The synergistic application of quinone reductase and lignin peroxidase for the deconstruction of industrial (technical) lignins and analysis of the degraded lignin products. *Bioresour. Technol.* **2021**, *319*, 124152. [CrossRef] [PubMed]
58. Liu, E.; Segato, F.; Wilkins, M.R. Fed-batch production of Thermothelomyces thermophilus lignin peroxidase using a recombinant Aspergillus nidulans strain in stirred-tank bioreactor. *Bioresour. Technol.* **2021**, *325*, 124700. [CrossRef]
59. Kuwahara, M.; Glenn, J.K.; Morgan, M.A.; Gold, M.H. Separation and characterization of two extracelluar H2O2-dependent oxidases from ligninolytic cultures of Phanerochaete chrysosporium. *FEBS Lett.* **1984**, *169*, 247–250. [CrossRef]
60. Wariishi, H.; Valli, K.; Gold, M.H. Oxidative cleavage of a phenolic diarylpropane lignin model dimer by manganese peroxidase from Phanerochaete chrysosporium. *Biochemistry* **1989**, *28*, 6017–6023. [CrossRef]
61. Wang, Y.; Vazquez-Duhalt, R.; Pickard, M.A. Purification, characterization, and chemical modification of manganese peroxidase from Bjerkandera adusta UAMH 8258. *Curr. Microbiol.* **2002**, *45*, 77–87. [CrossRef] [PubMed]
62. Hofrichter, M. Lignin conversion by manganese peroxidase (MnP). *Enzym. Microb. Technol.* **2002**, *30*, 454–466. [CrossRef]
63. Masarin, F.; Norambuena, M.; Ramires, H.O.; Demuner, B.J.; Pavan, P.C.; Ferraz, A. Manganese peroxidase and biomimetic systems applied to in vitro lignin degradation in Eucalyptus grandis milled wood and kraft pulps. *J. Chem. Technol. Biotechnol.* **2016**, *91*, 1422–1430. [CrossRef]
64. Min, K.; Kim, Y.H.; Kim, J.; Kim, Y.; Gong, G.; Um, Y. Effect of manganese peroxidase on the decomposition of cellulosic components: Direct cellulolytic activity and synergistic effect with cellulase. *Bioresour. Technol.* **2022**, *343*, 126138. [CrossRef] [PubMed]
65. Ali, S.S.; Al-Tohamy, R.; Khalil, M.A.; Ho, S.-H.; Fu, Y.; Sun, J. Exploring the potential of a newly constructed manganese peroxidase-producing yeast consortium for tolerating lignin degradation inhibitors while simultaneously decolorizing and detoxifying textile azo dye wastewater. *Bioresour. Technol.* **2022**, *351*, 126861.

66. Camarero, S.; Sarkar, S.; Ruiz-Dueñas, F.J.; Martínez, M.J.; Martínez, A.T. Description of a versatile peroxidase involved in the natural degradation of lignin that has both manganese peroxidase and lignin peroxidase substrate interaction sites. *J. Biol. Chem.* **1999**, *274*, 10324–10330. [CrossRef] [PubMed]
67. Sáez-Jiménez, V.; Acebes, S.; Guallar, V.; Martínez, A.T.; Ruiz-Dueñas, F.J. Improving the oxidative stability of a high redox potential fungal peroxidase by rational design. *PLoS ONE* **2015**, *10*, e0124750. [CrossRef]
68. Chan, J.C.; Paice, M.; Zhang, X. Enzymatic oxidation of lignin: Challenges and barriers toward practical applications. *ChemCatChem* **2020**, *12*, 401–425. [CrossRef]
69. Bugg, T.D.; Rahmanpour, R. Enzymatic conversion of lignin into renewable chemicals. *Curr. Opin. Chem. Biol.* **2015**, *29*, 10–17. [CrossRef]
70. Beckham, G.T.; Johnson, C.W.; Karp, E.M.; Salvachúa, D.; Vardon, D.R. Opportunities and challenges in biological lignin valorization. *Curr. Opin. Biotechnol.* **2016**, *42*, 40–53. [CrossRef] [PubMed]
71. Ma, H.; Li, T.; Wu, S.; Zhang, X. Effect of the interaction of phenolic hydroxyl with the benzene rings on lignin pyrolysis. *Bioresour. Technol.* **2020**, *309*, 123351. [CrossRef] [PubMed]
72. Yamaguchi, A.; Mimura, N.; Shirai, M.; Sato, O. Effect of metal catalysts on bond cleavage reactions of lignin model compounds in supercritical water. *Waste Biomass Valorization* **2020**, *11*, 669–674. [CrossRef]
73. Reiter, J.; Strittmatter, H.; Wiemann, L.O.; Schieder, D.; Sieber, V. Enzymatic cleavage of lignin β-O-4 aryl ether bonds via net internal hydrogen transfer. *Green Chem.* **2013**, *15*, 1373–1381. [CrossRef]
74. Gall, D.L.; Kim, H.; Lu, F.; Donohue, T.J.; Noguera, D.R.; Ralph, J. Stereochemical features of glutathione-dependent enzymes in the Sphingobium sp. strain SYK-6 β-aryl etherase pathway. *J. Biol. Chem.* **2014**, *289*, 8656–8667. [CrossRef]
75. Hilgers, R.; Van Dam, A.; Zuilhof, H.; Vincken, J.-P.; Kabel, M.A. Controlling the competition: Boosting laccase/HBT-catalyzed cleavage of a β-O-4′ linked lignin model. *ACS Catal.* **2020**, *10*, 8650–8659. [CrossRef]
76. Liu, Z.-H.; Olson, M.L.; Shinde, S.; Wang, X.; Hao, N.; Yoo, C.G.; Bhagia, S.; Dunlap, J.R.; Pu, Y.; Kao, K.C. Synergistic maximization of the carbohydrate output and lignin processability by combinatorial pretreatment. *Green Chem.* **2017**, *19*, 4939–4955. [CrossRef]
77. Peng, X.; Egashira, T.; Hanashiro, K.; Masai, E.; Nishikawa, S.; Katayama, Y.; Kimbara, K.; Fukuda, M. Cloning of a Sphingomonas paucimobilis SYK-6 gene encoding a novel oxygenase that cleaves lignin-related biphenyl and characterization of the enzyme. *Appl. Environ. Microbiol.* **1998**, *64*, 2520–2527. [CrossRef] [PubMed]
78. Higuchi, Y.; Aoki, S.; Takenami, H.; Kamimura, N.; Takahashi, K.; Hishiyama, S.; Lancefield, C.S.; Ojo, O.S.; Katayama, Y.; Westwood, N.J. Bacterial catabolism of β-hydroxypropiovanillone and β-hydroxypropiosyringone produced in the reductive cleavage of arylglycerol-β-aryl ether in lignin. *Appl. Environ. Microbiol.* **2018**, *84*, e02670-17. [CrossRef]
79. Liu, H.; Liu, Z.-H.; Zhang, R.-K.; Yuan, J.S.; Li, B.-Z.; Yuan, Y.-J. Bacterial conversion routes for lignin valorization. *Biotechnol. Adv.* **2022**, *60*, 108000. [CrossRef]
80. Peng, X.; Masai, E.; Katayama, Y.; Fukuda, M. Characterization of the meta-cleavage compound hydrolase gene involved in degradation of the lignin-related biphenyl structure by Sphingomonas paucimobilis SYK-6. *Appl. Environ. Microbiol.* **1999**, *65*, 2789–2793. [CrossRef]
81. Peng, X.; Masai, E.; Kasai, D.; Miyauchi, K.; Katayama, Y.; Fukuda, M. A second 5-carboxyvanillate decarboxylase gene, ligW2, is important for lignin-related biphenyl catabolism in Sphingomonas paucimobilis SYK-6. *Appl. Environ. Microbiol.* **2005**, *71*, 5014–5021. [CrossRef]
82. Mohn, W.W.; Westerberg, K.; Cullen, W.R.; Reimer, K.J. Aerobic biodegradation of biphenyl and polychlorinated biphenyls by Arctic soil microorganisms. *Appl. Environ. Microbiol.* **1997**, *63*, 3378–3384. [CrossRef] [PubMed]
83. Shuai, J.; Yu, X.; Zhang, J.; Xiong, A.-s.; Xiong, F. Regional analysis of potential polychlorinated biphenyl degrading bacterial strains from China. *Br. J. Microbiol.* **2016**, *47*, 536–541. [CrossRef]
84. Li, C.; Chen, C.; Wu, X.; Tsang, C.-W.; Mou, J.; Yan, J.; Liu, Y.; Lin, C.S.K. Recent advancement in lignin biorefinery: With special focus on enzymatic degradation and valorization. *Bioresour. Technol.* **2019**, *291*, 121898. [CrossRef] [PubMed]
85. Li, X.; He, Y.; Zhang, L.; Xu, Z.; Ben, H.; Gaffrey, M.J.; Yang, Y.; Yang, S.; Yuan, J.S.; Qian, W.-J. Discovery of potential pathways for biological conversion of poplar wood into lipids by co-fermentation of Rhodococci strains. *Biotechnol. Biofuels* **2019**, *12*, 60. [CrossRef]
86. Niu, J.; Li, X.; Qi, X.; Ren, Y. Pathway analysis of the biodegradation of lignin by Brevibacillus thermoruber. *Bioresour. Technol.* **2021**, *341*, 125875. [CrossRef] [PubMed]
87. Venkatesagowda, B.; Dekker, R.F. Enzymatic demethylation of Kraft lignin for lignin-based phenol-formaldehyde resin applications. *Biomass Convers. Biorefinery* **2020**, *10*, 203–225. [CrossRef]
88. Cao, L.; Iris, K.; Liu, Y.; Ruan, X.; Tsang, D.C.; Hunt, A.J.; Ok, Y.S.; Song, H.; Zhang, S. Lignin valorization for the production of renewable chemicals: State-of-the-art review and future prospects. *Bioresour. Technol.* **2018**, *269*, 465–475. [CrossRef] [PubMed]
89. Jiang, C.; Cheng, Y.; Zang, H.; Chen, X.; Wang, Y.; Zhang, Y.; Wang, J.; Shen, X.; Li, C. Biodegradation of lignin and the associated degradation pathway by psychrotrophic Arthrobacter sp. C2 from the cold region of China. *Cellulose* **2020**, *27*, 1423–1440. [CrossRef]
90. Cafaro, V.; Izzo, V.; Scognamiglio, R.; Notomista, E.; Capasso, P.; Casbarra, A.; Pucci, P.; Di Donato, A. Phenol hydroxylase and toluene/o-xylene monooxygenase from Pseudomonas stutzeri OX1: Interplay between two enzymes. *Appl. Environ. Microbiol.* **2004**, *70*, 2211–2219. [CrossRef]

91. Wells, T., Jr.; Ragauskas, A.J. Biotechnological opportunities with the β-ketoadipate pathway. *Trends Biotechnol.* **2012**, *30*, 627–637. [CrossRef] [PubMed]
92. Dikshit, P.K.; Jun, H.-B.; Kim, B.S. Biological conversion of lignin and its derivatives to fuels and chemicals. *Korean J. Chem. Eng.* **2020**, *37*, 387–401. [CrossRef]
93. Prousek, J. Fenton chemistry in biology and medicine. *Pure Appl. Chem.* **2007**, *79*, 2325–2338. [CrossRef]
94. Jensen, K.A., Jr.; Houtman, C.J.; Ryan, Z.C.; Hammel, K.E. Pathways for extracellular Fenton chemistry in the brown rot basidiomycete Gloeophyllum trabeum. *Appl. Environ. Microbiol.* **2001**, *67*, 2705–2711. [CrossRef] [PubMed]
95. Cohen, R.; Jensen, K.A.; Houtman, C.J.; Hammel, K.E. Significant levels of extracellular reactive oxygen species produced by brown rot basidiomycetes on cellulose. *FEBS Lett.* **2002**, *531*, 483–488. [CrossRef]
96. Sahni, M.; Finney, W.C.; Locke, B.R. Degradation of aqueous phase polychlorinated biphenyls (PCB) using pulsed corona discharges. *J. Adv. Oxid. Technol.* **2005**, *8*, 105–111. [CrossRef]
97. Zhou, C.; Dong, A.; Wang, Q.; Yu, Y.; Fan, X.; Cao, Y.; Li, T. Effect of common metal ions and anions on laccase catalysis of guaiacol and lignocellulosic fiber. *BioResources* **2017**, *12*, 5102–5117. [CrossRef]
98. Zhao, Y.; Xiang, W.; Ma, M.; Zhang, X.; Bao, Z.; Xie, S.; Yan, S. The role of laccase in stabilization of soil organic matter by iron in various plant-dominated peatlands: Degradation or sequestration? *Plant Soil* **2019**, *443*, 575–590. [CrossRef]
99. Niladevi, K.N.; Jacob, N.; Prema, P. Evidence for a halotolerant-alkaline laccase in Streptomyces psammoticus: Purification and characterization. *Process Biochem.* **2008**, *43*, 654–660. [CrossRef]
100. Kim, S.; Oh, S.; Lee, J.; Roh, H.-g.; Park, J. Changes of lignin molecular structures in a modification of kraft lignin using acid catalyst. *Materials* **2016**, *9*, 657. [CrossRef]
101. Lai, C.; Jia, Y.; Zhou, C.; Yang, C.; Shen, B.; Zhang, D.; Yong, Q. Facilitating enzymatic digestibility of larch by in-situ lignin modification during combined acid and alkali pretreatment. *Bioresour. Technol.* **2020**, *311*, 123517. [CrossRef] [PubMed]
102. Ferhan, M.; Yan, N.; Sain, M. Bark depolymerization during submerged fermentation using monofloral honey, a natural mediator substitute, and integration between laccases vs. bark biopolymers, characterized by Py-GC-MS. *RSC Adv.* **2015**, *5*, 14937–14952. [CrossRef]
103. Zou, L.; Ross, B.M.; Hutchison, L.J.; Christopher, L.P.; Dekker, R.F.; Malek, L. Fungal demethylation of Kraft lignin. *Enzym. Microb. Technol.* **2015**, *73*, 44–50. [CrossRef] [PubMed]
104. Zhang, W.; Ma, Y.; Wang, C.; Li, S.; Zhang, M.; Chu, F. Preparation and properties of lignin–phenol–formaldehyde resins based on different biorefinery residues of agricultural biomass. *Ind. Crops Prod.* **2013**, *43*, 326–333. [CrossRef]
105. Zhang, W.; Ma, Y.; Xu, Y.; Wang, C.; Chu, F. Lignocellulosic ethanol residue-based lignin–phenol–formaldehyde resin adhesive. *Int. J. Adhes. Adhes.* **2013**, *40*, 11–18. [CrossRef]
106. Zhao, M.; Jing, J.; Zhu, Y.; Yang, X.; Wang, X.; Wang, Z. Preparation and performance of lignin–phenol–formaldehyde adhesives. *Int. J. Adhes. Adhes.* **2016**, *64*, 163–167. [CrossRef]
107. Yang, Z.; Peng, H.; Wang, W.; Liu, T. Crystallization behavior of poly (ε-caprolactone)/layered double hydroxide nanocomposites. *J. Appl. Polym. Sci.* **2010**, *116*, 2658–2667. [CrossRef]
108. Zhang, Y.; Yuan, Z.; Mahmood, N.; Huang, S.; Xu, C.C. Sustainable bio-phenol-hydroxymethylfurfural resins using phenolated de-polymerized hydrolysis lignin and their application in bio-composites. *Ind. Crops Prod.* **2016**, *79*, 84–90. [CrossRef]
109. Cheng, S.; Wilks, C.; Yuan, Z.; Leitch, M.; Xu, C.C. Hydrothermal degradation of alkali lignin to bio-phenolic compounds in sub/supercritical ethanol and water–ethanol co-solvent. *Polym. Degrad. Stab.* **2012**, *97*, 839–848. [CrossRef]
110. Sawamura, K.; Tobimatsu, Y.; Kamitakahara, H.; Takano, T. Lignin functionalization through chemical demethylation: Preparation and tannin-like properties of demethylated guaiacyl-type synthetic lignins. *ACS Sustain. Chem. Eng.* **2017**, *5*, 5424–5431. [CrossRef]
111. Kim, K.H.; Jeong, K.; Zhuang, J.; Jeong, H.J.; Kim, C.S.; Koo, B.; Yoo, C.G. Tandem conversion of lignin to catechols via demethylation and catalytic hydrogenolysis. *Ind. Crops Prod.* **2021**, *159*, 113095. [CrossRef]
112. Venkatesagowda, B. Enzymatic Kraft lignin demethylation and fungal O-demethylases like vanillate-O-demethylase and syringate O-demethylase catalyzed catechol-Fe^{3+} complexation method. *J. Microbiol. Methods* **2018**, *152*, 126–134. [CrossRef]
113. Studenik, S.; Vogel, M.; Diekert, G. Characterization of an O-demethylase of Desulfitobacterium hafniense DCB-2. *J. Bacteriol.* **2012**, *194*, 3317–3326. [CrossRef] [PubMed]
114. Bashtan-Kandybovich, I.; Venkatesagowda, B.; Barbosa, A.M.; Malek, L.; Dekker, R.F. Modification of Kraft lignin by biological demethylation. *J-FOR* **2012**, *2*, 16–27.
115. Venkatesagowda, B. Enzymatic demethylation of lignin for potential biobased polymer applications. *Fungal Biol. Rev.* **2019**, *33*, 190–224. [CrossRef]
116. Ibrahim, V.; Mendoza, L.; Mamo, G.; Hatti-Kaul, R. Blue laccase from *Galerina* sp.: Properties and potential for Kraft lignin demethylation. *Process Biochem.* **2011**, *46*, 379–384. [CrossRef]
117. Ma, H.; Li, T.; Wu, S.; Zhang, X. Demethylation of a methoxy group to inhibit repolymerization during alkaline lignin pyrolysis. *Fuel* **2021**, *286*, 119394. [CrossRef]
118. Song, Y.; Wang, Z.; Yan, N.; Zhang, R.; Li, J. Demethylation of wheat straw alkali lignin for application in phenol formaldehyde adhesives. *Polymers* **2016**, *8*, 209. [CrossRef]
119. Wang, H.; Eberhardt, T.L.; Wang, C.; Gao, S.; Pan, H. Demethylation of alkali lignin with halogen acids and its application to phenolic resins. *Polymers* **2019**, *11*, 1771. [CrossRef]

120. Wei, Z.; Zeng, G.; Huang, F.; Kosa, M.; Huang, D.; Ragauskas, A.J. Bioconversion of oxygen-pretreated Kraft lignin to microbial lipid with oleaginous Rhodococcus opacus DSM 1069. *Green Chem.* **2015**, *17*, 2784–2789. [CrossRef]
121. Kosa, M.; Ragauskas, A.J. Lignin to lipid bioconversion by oleaginous Rhodococci. *Green Chem.* **2013**, *15*, 2070–2074. [CrossRef]
122. Liu, Z.-H.; Xie, S.; Lin, F.; Jin, M.; Yuan, J.S. Combinatorial pretreatment and fermentation optimization enabled a record yield on lignin bioconversion. *Biotechnol. Biofuels* **2018**, *11*, 21. [CrossRef]
123. Spence, E.M.; Calvo-Bado, L.; Mines, P.; Bugg, T.D. Metabolic engineering of Rhodococcus jostii RHA1 for production of pyridine-dicarboxylic acids from lignin. *Microb. Cell Factories* **2021**, *20*, 15. [CrossRef] [PubMed]
124. Mallinson, S.J.; Machovina, M.M.; Silveira, R.L.; Garcia-Borràs, M.; Gallup, N.; Johnson, C.W.; Allen, M.D.; Skaf, M.S.; Crowley, M.F.; Neidle, E.L. A promiscuous cytochrome P450 aromatic O-demethylase for lignin bioconversion. *Nat. Commun.* **2018**, *9*, 2487. [CrossRef] [PubMed]
125. Liu, Z.-H.; Hao, N.; Wang, Y.-Y.; Dou, C.; Lin, F.; Shen, R.; Bura, R.; Hodge, D.B.; Dale, B.E.; Ragauskas, A.J. Transforming biorefinery designs with 'Plug-In Processes of Lignin'to enable economic waste valorization. *Nat. Commun.* **2021**, *12*, 3912. [CrossRef]
126. Clarkson, S.M.; Giannone, R.J.; Kridelbaugh, D.M.; Elkins, J.G.; Guss, A.M.; Michener, J.K. Construction and optimization of a heterologous pathway for protocatechuate catabolism in Escherichia coli enables bioconversion of model aromatic compounds. *Appl. Environ. Microbiol.* **2017**, *83*, e01313-17. [CrossRef]
127. Contreras-Jácquez, V.; Rodríguez-González, J.; Mateos-Díaz, J.C.; Valenzuela-Soto, E.M.; Asaff-Torres, A. Differential activation of ferulic acid catabolic pathways of Amycolatopsis sp. ATCC 39116 in submerged and surface cultures. *Appl. Biochem. Biotechnol.* **2020**, *192*, 494–516. [CrossRef]
128. Wu, W.; Liu, F.; Singh, S. Toward engineering E. coli with an autoregulatory system for lignin valorization. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, 2970–2975. [CrossRef]
129. Wang, X.; Lin, L.; Dong, J.; Ling, J.; Wang, W.; Wang, H.; Zhang, Z.; Yu, X. Simultaneous improvements of Pseudomonas cell growth and polyhydroxyalkanoate production from a lignin derivative for lignin-consolidated bioprocessing. *Appl. Environ. Microbiol.* **2018**, *84*, e01469-18. [CrossRef]
130. Becker, J.; Kuhl, M.; Kohlstedt, M.; Starck, S.; Wittmann, C. Metabolic engineering of Corynebacterium glutamicum for the production of cis, cis-muconic acid from lignin. *Microb. Cell Factories* **2018**, *17*, 115. [CrossRef]
131. Borrero-López, A.M.; Blánquez, A.; Valencia, C.; Hernández, M.; Arias, M.a.E.; Eugenio, M.E.; Fillat, Ú.; Franco, J.M. Valorization of soda lignin from wheat straw solid-state fermentation: Production of oleogels. *ACS Sustain. Chem. Eng.* **2018**, *6*, 5198–5205. [CrossRef]