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From lignin association to nano-/micro-particle preparation: extracting higher value of lignin

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As the most abundant source of renewable aromatic compounds on the planet, lignin is gaining growing interest in replacing petroleum-based chemicals and products. Value-added applications of lignin are also essential for the economic viability of future bio-refineries. It is however an under-utilized natural resource due to its structural heterogeneities. Lignin nanoparticles offer many opportunities for value-added applications of lignin. The solution structures of lignin were proposed as one of the key elements in controlling lignin nano-/micro-particle preparation. Fundamental understanding of solution structures of lignin aid in designing and better fabrication of lignin nanoparticles. A deeper understanding of the observed experimental results also points to the need for detailed studies of lignin in solution. This review consists of two major topics, the solution structures of lignin and lignin nano-/micro-particle preparation. Suggestions for future studies regarding these two topics were also put forward.

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Introduction

Lignocellulosic biomass is considered a renewable resource for production of biofuels or chemicals *via* different biorefining processes.¹ Lignocellulosic biomass consists primarily of cellulose, hemicellulose, and lignin as the major structural biopolymers. Lignin is of special interest since it contains aromatic structures, which offer the potential of replacing industrially relevant aromatic polymeric and fine chemicals.^{1–10} The primary structure of lignin is formed by the radical co-polymerization of three different phenylpropane monomer units, namely sinapyl alcohol, coniferyl alcohol and *para*-coumaryl alcohol (Fig. 1).¹ Co-polymerization during bio-synthesis leads to a variety of carbon–carbon and ether linkages in the lignin matrix with the β -O-4 linkage as the most abundant interunit linkage (Table 1).⁷ Lignin is isolated from wood and annual plants by different extraction processes which usually alters the native structure of lignin.² At an industrial scale, processed lignin is produced in pulp mills and it is traditionally divided into three distinct classes: kraft lignin, ligno-

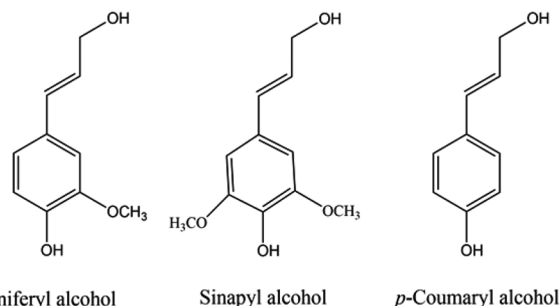


Fig. 1 Typical phenylpropanoid precursors of lignin.

sulfonate and soda lignin.⁶ In laboratories, lignin is also isolated by several other experimental procedures including those that impart minimal alterations to the native lignin in biomass. These include milled wood lignin, mild acidolysis lignin, cellulolytic lignin and enzymatic mild acidolysis lignin.^{2,11} Other techniques presently being used include organosolv pulping⁶ and ionic liquid-based biomass fractionation.¹² Structural analysis of isolated lignin suggests that it contains a number of functional groups such as aliphatic and phenolic hydroxyls, carboxylic, carbonyl and methoxyl groups.⁴ These functional groups, together with phenyl rings, confer upon lignin many unique properties as will be discussed below.

It was estimated that ~50 million tonnes of lignin were extracted annually by the paper and pulp industry from woody biomass, but only ~2% has been utilized commercially frequently as low-value chemicals such as dispersants, adhesives and surfactants.^{4,7,8} The major reasons for the

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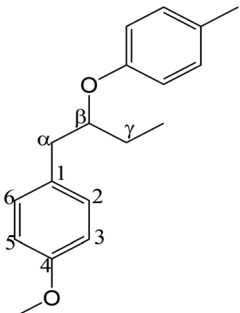
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Table 1 Typical abundance of inter-unit linkages in isolated lignin

Inter-unit linkage (%)	β -O-4	β -1	β - β	β -5	4-O-5	5-5	
	Poplar wood lignin	57.8	2.1	2.1	1.8	0.7	0.7
	Aspen steam exploded lignin	25.9	17.0	37.8	12.6	4.5	2.2
	Spruce wood lignin	46.0	1.0	2.0	9–12.0	3.5	9.5
	Birch wood lignin	60.0	7.0	3.1	6.0	7.5	4.5
	Wheat straw MWL	75.0	N.D.	4.0	3.0	2.0	3.0
	<i>Eucalyptus grandis</i> lignin	61.0	2.1	3.0	3	N.D.	3.0

Adapted from ref. 7 and 10 with permission.

limited widespread use of lignin are: (1) the complexity of the lignin structure which is still not fully resolved;⁷ (2) variability of the structure of lignin isolated from different processes and different biomasses;² (3) broad molecular weight distributions and limited solubility;¹³ (4) propensity to re-polymerize after fragmentation;^{14,15} (5) incompatibility with host matrices due to self-association and differences in polarity.⁶ In spite of these hurdles, significant progress is being made in research for the applicability of lignin as a resource for chemicals and materials. Lignin has been utilized in a variety of applications which broadly include:^{6,8,9,16,17} (1) lignosulfonates, as dispersants, water reducers in concrete, additives in coal-water slurry or viscosity reducers; (2) use of lignin as a filler or additive in polymers and biopolymers (the lignin content is usually less than 20–30 wt%); (3) depolymerized lignin to produce chemicals and/or upgraded to fuels; (4) lignin-derived functional materials such as carbon fibers, activated carbon, adhesives and foams.

Lignin is being studied in the field of materials science owing to its abundance and relatively low cost, resistance to oxidation, resistance to water, UV absorbance, biocompatibility, biodegradability and sustainability.^{6,13,18,19} Lignin possesses multiple functional groups that can form inter- and intra-molecular hydrogen bonding which affects its compatibility with host matrices. The functional properties of lignin-containing blends largely depend on the compatibility of lignin with the host matrices.^{6,8,20} Improved thermal-oxidative and mechanical properties are often observed for miscible polymer/lignin blends.^{8,9} Synthetic polymers or biopolymers containing polar groups offer the possibility of creating intermolecular hydrogen bonds with lignin, showing better compatibility.^{6,8} However, strong association between lignin molecules²¹ decreases miscibility with the host matrix and it can lead to phase separation, which presents a challenge for the efficient utilization of lignin. Strategies to improve the compatibility of lignin with non-polar polymers have been summarized in several reviews.^{2,6} Chemical modification of lignin by oxyalkylation or hydroxyalkylation has been shown to minimize the association between lignin molecules and effectively improve their compatibility with the host matrices.^{21,22}

Kraft lignin has been reported to exhibit particle sizes ranging from 10 μm to greater than 100 μm , which have been demonstrated to be detrimental to the mechanical properties of the blends.²³ A new strategy to enhance lignin's blending properties with a host matrix is to use lignin nanoparticles. Improved dispersion for lignin nanoparticles (**8**, see Table 2) in polyvinyl alcohol was observed which resulted in enhanced thermal stability.²⁴ In addition, nanoparticles exhibit either improved or different properties compared to their parent materials. Lignin-based nanoparticles have been shown to exhibit higher anti-oxidant activity due to a higher surface-area-to-volume ratio.^{25,26} Another significant benefit of using lignin-based nanoparticles is that it offers morphological control in light of its structural heterogeneity.²⁷

It is expected that lignin nanoparticles will play a vital role in promoting lignin valorization, similar to what synthetic polymer nanoparticles contribute to the polymer industry.²⁸ In light of the renewed interest in promoting value-added applications of lignin, a survey of studies (patents not included) of lignin nanoparticle preparation and their potential applications is a timely report. Lignin nanoparticles are mainly prepared *via* solution-based processing where particles are prepared by controlled precipitation of lignin solutions. Their sizes range from tens to hundreds of nanometers with variable shapes. To this end, understanding solution structures of lignin is essential to prepare well-controlled lignin nanoparticles. In this short review, discussions on the association of lignin in solutions will be carried out followed by a summary of lignin nanoparticle preparation. This review is not meant to be comprehensive; it is focused on discussing possible associative forces present in lignin solutions. It is our intention that this review will generate attention to lignin nanoparticles for value-added applications.

Solution structures of lignin

The solution structures of lignin are often characterized by a wide distribution of sizes and molecular weights.^{29–31}

Table 2 Preparation of lignin nano-/micro-particles

Entry number	Morphology	Methods	Diameter (nm)	Shape	Brief description of preparation
1	Nanoparticles ⁵⁴	Anti-solvent precipitation	30 to 175 (size can be controlled)	Not specified	Lignin (indulin AT) dissolved in EG, precipitated by HNO ₃
2	Nanoparticles ⁵³	Anti-solvent precipitation	154 to 762	Not specified	Lignin (protobind-1000) dissolved in EG, precipitated by HCl
3	Nanoparticles ²⁶	Anti-solvent precipitation	104 ± 60, 80 ± 27	Spheres	Lignin (dioxane, alkali) dissolved in acetone/water mixture (9 : 1, v/v), precipitated in water
4	Nanoparticles ²⁵	Solvent evaporation	144 ± 30	Spheres	Lignin (organosolv) dissolved in acetone, carried away by super critical CO ₂
5	Nanoparticles ⁵⁵	Self-assembly	120	Spheres	Lignin (alkali) dissolved in dioxane, aggregation induced by adding cyclohexane
6	Nanoparticles ⁵⁶	Self-assembly	110	Spheres	Acetylated lignin (alkali) dissolved in THF, association induced by adding water
7	Nanoparticles ⁵⁹	Self-assembly	200–500	Spheres	Lignin (kraft) dissolved in THF, association induced by adding water <i>via</i> dialysis
8	Nanoparticles ²⁴	Mechanical shearing	10 to 30	No regular shape	Lignin (kraft) dissolved in water, treated using a high shear homogenizer for 4 h
9	Nanoparticles ⁵⁸	Sonication	100 to 500	No regular shape	Aqueous lignin (alkali) solution was sonicated for 1 h
10	Microcapsules ¹⁹	Interfacial crosslinking	300 to 1400, depending on the experimental conditions		(Kraft) crosslinking at the interface of oil droplets
11	Nanocapsules ¹³	Interfacial crosslinking	311 to 390 in water; 162 to 220 in cyclohexane		(Sodium lignosulfonate) crosslinking at the interface of water nano-droplets
12	Nanotubes ⁵⁷	Polymerization	Diameter determined by the size of the nano-pores in the template		Polymerization onto walls of the nano-pores

Individual lignin molecules (also called “discrete components”,³² “subunits”^{30,33,34} and “building blocks”³⁵) have been referred to the entity with the lowest molecular weight as determined by gel permeation chromatography (GPC)^{31,32,36} or the smallest size measured by light scattering, small angle X-ray and neutron scattering (SAXS, SANS).^{29,30,34,35,37}

Scattering studies have shown the presence of processed lignin molecules with sizes of a few nanometers in solution.^{30,34,35,37} This is consistent with molecular weight measurements where extracted lignin typically has number-averaged values less than 10 000 g mol⁻¹.^{11,38} A scanning electron microscopy study of the molecular organization of the enzymatically polymerized dehydrogenation polymer (DHP) of coniferyl alcohol on a cellulose substrate showed a globular structural unit (subunit) with a diameter of 5 nm.³³ It is not clear whether these entities exist naturally in plant cell walls or are just fragments of larger lignin macromolecules produced during isolation processes. It is likely that there exist lignin subunits in plant cell walls with sizes of just a few nanometers. These lignin subunits are hypothesized to further assemble into supramolecular structures through either polymerization or association.^{39,40}

In principle, interactions between lignin molecules and solvents can be quantified by multi-angle light scattering, SAXS and SANS *via* the Flory–Huggins interaction parameter and the second virial coefficient.⁴¹ Analogous to polymer solutions, solvent quality can be classified as “poor”, “0” and “good”, depending on the solvent-mediated monomer interactions.⁴¹ This has been rarely reported for lignin solutions due to the strong association of lignin molecules that complicates the

data analysis.²⁹ SANS and SAXS studies of solution structures of lignin were recently summarized in a review.³⁸ These studies suggest that individual lignin molecules are compact particles with non-spherical shapes (ellipsoids, cylinders or discs)^{35,38} and self-assemble into larger fractal objects in solutions.

Lignin association is a common phenomenon that not only takes place in a solid matrix but also in aqueous and organic solutions.^{29,42,43} Most of the studies of lignin solutions have focused on kraft lignin, which represents the greatest amount of industrially processed lignin produced, and lignosulfonate, which is the most commercialized source of lignin. Kraft lignin becomes soluble in alkaline solutions by ionization of phenolic groups. With the presence of high concentrations of sodium chloride in alkaline solutions, increasing temperature leads to phase separation of lignin due to the decreased degree of ionization.^{39,44} Lignosulfonate is water-soluble due to the introduction of sulfonate groups into lignin during chemical pulping. Both kraft lignin and lignosulfonate present surface active⁴⁵ and amphiphilic properties and they share a polyelectrolyte character.^{3,46}

In 1979, Lindström studied the association and precipitation of kraft lignin (Indulin ATR, 11037-2, Westvaco Co., Charleston, SC., USA) in aqueous solutions varying in pH from 8.6 to 3.7.⁴⁷ It was found that the degree of association between lignin molecules increased with decreasing ionization of the carboxylic group in the lignin. He suggested that the hydrogen bonding between carboxylic groups and various ether oxygens and hydroxylic groups was responsible for the

inter-molecular association of lignin.⁴⁷ Later, McCarthy *et al.* studied the association of kraft lignin, isolated from the black liquor of Douglas fir, in aqueous NaOH solutions.^{31,32} Lignin molecules adopted an expanded random coil conformation in dilute alkaline solutions at pH 9.5 as determined by the relationship between the radius of gyration and molecular weight.³¹ Association between lignin molecules increased with increasing lignin concentration under aqueous conditions of pH 13 and 14.³² Hydrogen bonding was not considered as the driving force for the association of lignin molecules at higher concentrations because acetylation of these lignin samples did not appreciably affect the proportion of higher molecular weight complexes in *N,N*-dimethylformamide. Hydrophobic interactions alone were believed to be not strong enough to overcome the repulsion between charged lignin molecules. It was thus proposed that non-bonded orbital interactions between aromatic moieties of the lignin molecules were responsible for the association.³²

More recently, Qiu *et al.* investigated the mechanism of kraft lignin association in tetrahydrofuran (THF) using iodine as a probe.⁴⁸ The results suggested that the non-bonded orbital interactions (π - π interactions) of the aromatic groups caused the association of lignin molecules. Zhou *et al.* reported the association of sodium lignosulfonate in water with lignin concentrations varying from 10 to 2500 mg L⁻¹.⁴⁹ The analysis suggested that individual lignin molecules started to associate to form hollow micelles which further clustered into larger loose aggregates with increasing lignin concentration. It was proposed that lignin molecules associated *via* hydrogen bonding and intermolecular van der Waals forces. The electrostatic repulsion between lignin molecules made the aggregates rather loose.⁴⁹ Vainio *et al.* discovered that the lignosulfonate molecules assumed a flat shape and the charged groups were mostly located at the flat surfaces.⁵⁰ Lignosulfonate molecules were shown to aggregate along the edges of the flat particles.⁵⁰

The kinetics of kraft lignin (Indulin AT, lot 123H0189, Aldrich) association under alkaline conditions was studied by Norgren *et al.*³⁹ The association was induced by adding sodium chloride at pH 10.5 and 70 °C. At a sodium concentration of 1.5 M, samples were phase-separated (salting out effect) at room temperature. Individual lignin molecules associated to form colloidal particles that further agglomerated into fractal clusters in the presence of sodium chloride (Fig. 2). The fractal nature of lignin clusters in solutions has also been discussed by Yurii *et al.*⁵¹ It was hypothesized that the supramolecular structure of lignin *in situ* is an infinite network composed of fractal clusters linked to one another. When isolated from the plant tissue, the inhomogeneous fractal network is destroyed and its fragments pass into the solution as fractal clusters.⁵¹ Interestingly, the supramolecular structure of kraft lignin in solutions was compared to the organization of native lignin in cell walls.³⁹ Both reaction-limited cluster-cluster aggregation regimes and diffusion-limited cluster-cluster aggregation regimes were observed, with the former characterized by more compact aggregates and

a higher mass fractal dimension and the latter by loose ones and a lower mass fractal dimension.³⁹ This aggregation behavior was similar to that of monodisperse polystyrene colloids.³⁹

Investigations of lignin association in solutions are complicated by the variability of the structure of lignin isolated from different processes and different biomasses, the solvents used to prepare the solutions and the age of the solutions.^{11,36,42,52} The solution structure may become stabilized over a period of several days or even weeks that presents a challenge for the reproducible characterization of lignin solutions.^{36,42} Argyropoulos *et al.* reported that association forces and the propensity of different types of lignin to associate in various solvents are not the same.^{42,52} Lignin molecules can associate in the absence of hydrogen bonding.⁴² Therefore, hydrogen bonding, intermolecular van der Waals forces, non-bonded orbital interactions, hydrophobic interactions and ionic interactions can all contribute to the association of lignin molecules. The propensity of lignin to associate is essentially determined by its chemical structure. The presence of large amount of phenyl rings and multiple functional groups dictates the interactions between lignin molecules and the solvents. In addition, conformation of lignin molecules may also play a role in its association through entropic effects.⁵² A more recent study demonstrates that the amount of methoxy groups which is related to the degree of branching in the individual lignin molecules affects their association in dimethyl sulphoxide.³⁵ Environmental factors such as temperature, pH, and ionic strength strongly affect the solution structures of lignin and thus offer an effective way to control lignin association. Chemical modifications of extracted lignin, such as acetylation, also dramatically change its association in solutions.

Nanoparticle preparation

Nanoparticles with controllable sizes, narrow size distributions and desired shapes are often required for industrial applications.²⁸ Lignin nanoparticles can be readily modified chemically due to the presence of multiple functional groups, thus significantly expanding their potential applications. Biocompatibility makes them an attractive candidate for drug and gene delivery. However, the lack of well-defined structures of lignin poses a serious challenge for medical applications. Lignin nanoparticles (including capsules and tubes) have been prepared by anti-solvent precipitation,^{25,26,53,54} self-assembly,^{55,56} interfacial polymerization/crosslinking,^{13,19} using nanopore alumina membranes as a template,⁵⁷ mechanical shearing²⁴ and sonication.⁵⁸ A survey of literature studies of lignin nanoparticles is summarized in Table 2.

Velev *et al.* prepared negatively charged lignin nanoparticles (1) with controllable sizes ranging from 30 to 175 nm by an anti-solvent precipitation method. Kraft lignin was first dissolved in ethylene glycol that was followed by addition of HNO₃. Lignin nanoparticles were then infused with silver ions by absorption and coated with a polydiallyldimethylammonium chloride layer.⁵⁴ The obtained nanoparticles were

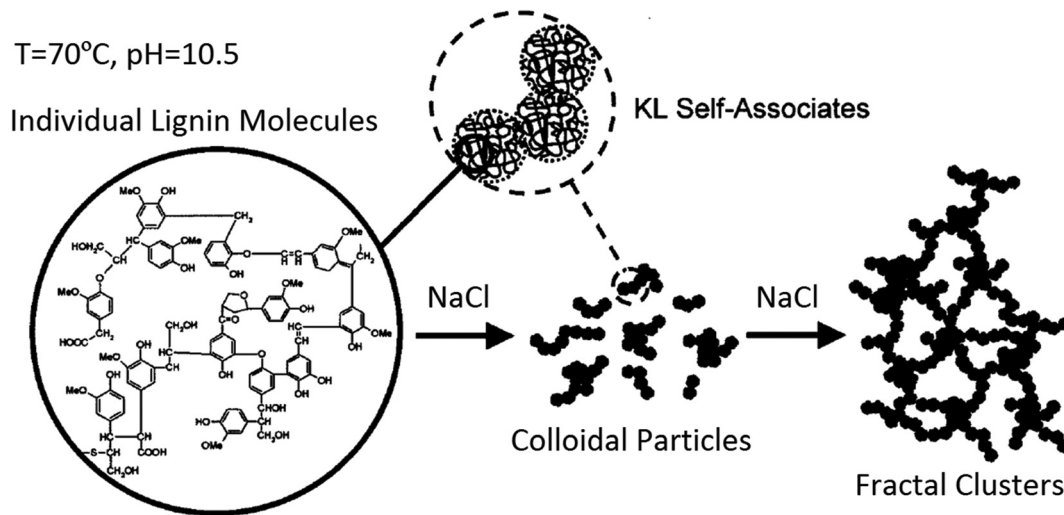


Fig. 2 Hierarchical structures formed by individual lignin molecules in solutions (reproduced from ref. 39 with permission from the American Chemical Society).

shown to kill a broad spectrum of bacteria. These nanoparticles were believed to have higher antimicrobial activity and smaller environmental impact than metallic silver nanoparticles.⁵⁴ Mohanty *et al.* prepared lignin nanoparticles (2) using a similar acid precipitation technique.⁵³ Nano-composites consisting of lignin nanoparticles, poly(trimethylene terephthalate) (PTT) and vapor-grown carbon fibers were fabricated and improved thermal and water-resistance properties were observed. Hydrogen bonding between aliphatic -OH groups of lignin and carbonyl groups of PTT was confirmed by FTIR.⁵³ Padmasree *et al.* manufactured lignin nanoparticles (3) by adding lignin/acetone/water solutions into water under constant stirring.²⁶ The nanoparticles exhibited higher antioxidant activity and UV protectant potential compared to their parent lignin. In another process, super critical CO₂ was used to carry away the acetone from lignin/acetone solutions and lignin nanoparticles (4) were precipitated out.²⁵ Enhanced antioxidant properties were also observed for these lignin nanoparticles.

By adding water into a lignin/THF solution the hydrophobic to hydrophilic balance was changed and uniform colloidal spheres (6) were prepared from acetylated lignin.⁵⁶ The segregation of hydrophilic groups and the hydrophobic skeleton was induced by water, and lignin molecules were observed to associate with hydrophilic groups residing on the surface of the nanoparticles. The association process was determined to be complete at a water content of 67 vol%.⁵⁶ Lignin colloids were formed in water after evaporating the THF that was stabilized by electrostatic repulsion from the ionized groups residing on the surface.⁵⁶ In a more recent study, softwood kraft lignin without acetylating was dissolved in THF and spherical lignin nanoparticles (7) were obtained by subsequently introducing water into the system through dialysis.⁵⁹ Conversely, lignin nanoparticles (5) with improved surface hydrophobicity were fabricated by adding cyclohexane into a lignin/dioxane

solution.⁵⁵ In this case, alkali lignin is completely dissolved in dioxane. Addition of cyclohexane drives the association of lignin molecules with more hydrophobic segments present on the surface. The miscibility of acquired lignin nanoparticles with high-density polyethylene (HDPE) was significantly improved and the UV-absorbing and mechanical properties of the lignin/HDPE blends were also enhanced.⁵⁵ It is interesting to note that the mechanical shearing²⁴ or sonication⁵⁸ of aqueous lignin solutions also produced lignin nanoparticles (8 and 9). These processes do not utilize hazardous solvents and are thus attractive.

Emulsion and interfacial polymerization are important techniques for preparing polymer nanoparticles.⁶⁰ In one work, sodium lignosulfonate was dissolved in water which was then mixed with cyclohexane containing a surfactant polyglycerol-polyricinoleate.¹³ Stable aqueous nano-droplets were formed in cyclohexane. Lignin molecules were crosslinked by toluene-diisocyanate solubilized in cyclohexane where the reaction was assumed to only take place at the interface of aqueous nano-droplets. The obtained nanocapsules (11) have diameters in the range of 311–390 nm in water and a shell thickness of about 10–20 nm.¹³ In another work, a high-intensity ultrasonic technology was used to emulsify an oil phase in a lignin aqueous solution and subsequently cross-link lignin at the interface of oil droplets.¹⁹ The stability of the lignin shells can be further improved by addition of a cross-linking agent.¹⁹ The water- or oil-filled lignin nano-/micro-capsules (10) can be used to encapsulate hydrophilic or hydrophobic drugs, creating novel avenues for the utilization of lignin.

Lignin nanotubes (12) were prepared using nanopore alumina membranes as a template and they were tested as vehicles for gene delivery into human cells.⁵⁷ In this approach, pore walls of alumina membranes were first coated with a base layer of lignin by reacting lignin with amino groups attached to the surfaces of the nanopores. Multiple layers of DHP were

deposited onto the base layer following the polymerization of model monolignols catalyzed by horseradish peroxidase. The templates were then dissolved in phosphoric acid and the lignin nanotubes were obtained.⁵⁷

Preparation of lignin nanoparticles with well-defined sizes is essential to promote its widespread application. Solution-based lignin nanoparticle preparation is essentially based on dissolution of lignin that is followed by changes in solvent quality. This switch in solvent quality is controlled by many parameters such as temperature, mixing speed, rate of solvent removal and the amount of anti-solvent used. Lignin exists as individual molecules and fractal clusters in solutions. It is believed that the solution structure is one of the factors that influence lignin nanoparticle preparation; however, a correlation between them is missing from literature studies and will be addressed in future studies. The internal structures of prepared lignin nanoparticles, for example, the porosity, and their correlation with nanoparticle properties also need to be investigated.

Summary and outlook

Despite the continuous development of commercial operations of the cellulosic ethanol industry, conversion of lignin streams to value-added components still remains a challenge, which casts a shadow over the fate of future biorefineries.^{61,62} In general, lignin conversion is being actively explored by two different routes: controlled depolymerization into small molecules^{63–67} or as a building block to synthesize new functional materials.^{68,69} Lignin is considered as a natural polymer and can be presented as nanoparticles which further expand the scope of its application. This is in analogy to polymer nanoparticles. Polymer nanoparticles have been playing a vital role in a wide range of areas including electronics, photonics, nanomedicine, *etc.*^{70,71} Methods for preparation of lignin nanoparticles are essentially adopted from those used in manufacturing polymer nanoparticles.^{70,71} However, lignin possesses many unique properties as described in this paper which can be harnessed for particular applications. Unlike most synthetic polymers, lignin has a very complex structure, which makes characterization and processing a challenge.

This short review summarizes the current understanding of lignin solution structures, preparation and application of lignin nanoparticles. Literature studies on the preparation, functionalization and application of lignin nanoparticles are still limited. Fundamental understandings of lignin solution structures, their relation to nanoparticle preparation and properties, nanoparticles stability and dispersion will certainly lead to advancement in synthesizing lignin-based functional materials. It is believed that this short review provides a perspective that would prompt the development of new processes for manufacturing lignin nanoparticles with designed properties.

The propensity of lignin to associate in solutions and in solid matrices is determined by its chemical structure and molecular architecture. It is important to characterize the

supramolecular structure of lignin in different media in order to fully explore its value-added applications. GPC,¹¹ light scattering, SAXS and SANS^{35,72} have contributed greatly to our understanding of lignin association in solutions. However, more systematic studies are still needed in light of the complexity of the structure of lignin.

SANS and SAXS are powerful techniques in revealing the size, shape and interactions of lignin individual molecules as well as aggregates in solutions. Previous scattering studies show that lignin individual molecules assumed an elongated shape with sizes of a few nanometers. They further associate to form larger aggregates whose dimensions are often beyond the measurable range of typical SANS/SAXS setups. Ultra small angle neutron and X-ray scattering are complementary techniques to cover the larger length scale although there might be a problem with the low scattering intensity of lignin solutions. Neutron and X-ray scattering studies of lignin are still scarce due to the limited neutron beam time and special expertise and extensive training required for such measurements. More studies on lignin are needed using SANS/SAXS to reveal, for example, lignin/solvent interactions, the kinetics of lignin association, and the fractal nature of lignin and to characterize the prepared nanoparticles.

Studies of the relationship between lignin nanoparticle surface functional groups and their stability and dispersion properties need to be carried out; this will enable better control of nanoparticle preparation.⁷³ Lignin nanoparticles hold promise in manufacturing composite materials with pre-designed properties. They can act as carriers for drugs and genes with proven biocompatibility which is a vital property in nanomedicine.⁷⁴ Lignin's biodegradability is very attractive considering its minimized environmental impact.⁷⁵ Atom transfer radical polymerization (ATRP) and ring opening polymerization techniques have been successfully applied to make functional lignin-based materials.⁶⁸ Introduction of functional groups onto the surface of lignin nanoparticles provides new possibilities for high value applications.^{68,73,76} For example, CO₂-responsive lignin nanoparticles have been successfully prepared by ATRP grafting of 2-(diethylamino)ethyl methacrylate.⁷⁶

Although lignin nanoparticles offer many opportunities for high value applications, they are currently under-exploited. It is anticipated that lignin-based materials with designed nano-/micro-structures are of particular interest in the field of lignin applications. Many of the processes of manufacturing lignin nanoparticles involve hazardous solvents. From an industrial point of view, it is desirable to minimize the utilization of hazardous solvents or to replace them with green solvents such as water,²⁴ supercritical CO₂²⁵ and room temperature ionic liquids (RTILs). Some RTILs can readily dissolve lignin⁶³ which offers a possibility of preparing nanoparticles by controlled precipitation. Therefore, there is a need to develop new processes for the efficient and cost effective preparation of lignin nanoparticles under minimized environmental impact conditions with the desired structures and properties suitable for particular applications.

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