

Lignin-Based Nanomaterials and Their Applications

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Abstract: Lignin is the second most abundant natural renewable biopolymer on Earth, after cellulose, and the most abundant byproduct of the pulp and paper industry. Nanomaterials, tiny particles typically ranging in size from 1 to 100 nm, have extensive applications across various industries, including food and pharmaceuticals. Notably, lignin stands out as a remarkable natural source due to its environmental friendliness, widespread availability, abundance, and cost-effectiveness. Recently, a number of literature reports have shown trends in the growth of studies, mainly on the use of lignin and its derivatives as renewable carbon sources and as relatively cheap precursors obtained from biomass. This review focuses on the many forms of technical lignin derived from different sources. Here, we present a thorough analysis of the latest developments in techniques for producing various types of lignin-based nanomaterials. We also investigate their use across a variety of fields, including tissue engineering, UV protection, the food industry, and cosmetics, as well as their antioxidant and antibacterial functions.

Keywords: lignin; sources of lignin; lignin extraction; lignin-based nanomaterial applications.

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1. Introduction

Lignocellulose, a renewable natural resource known for its environmentally friendly, cost-effective, and sustainable qualities, holds great promise as a viable alternative to traditional petrochemical resources in various applications [1]. Recent years have witnessed global attention toward harnessing bioenergy and valuable eco-friendly chemicals from lignocellulose, driven by concerns over resource availability, environmental impact, economic sustainability, and health considerations. Lignocellulose, sourced from plants and wood, primarily comprises cellulose, hemicellulose, and lignin. Current research efforts primarily concentrate on the utility of carbohydrates, particularly cellulose and hemicellulose. However, lignin, the Earth's second-most abundant biopolymer, remains underexplored, and its full potential for applications has yet to be realized [2].

Lignin is a complex organic polymer found in the cell walls of plants, primarily in woody and fibrous tissues. It plays a crucial role in providing structural support to plants and is a major component of wood. Lignin is a heterogeneous substance composed of phenolic compounds, and its presence in plant cell walls contributes to their rigidity and resistance to decay [3]. Lignin, characterized predominantly by its phenylpropane-derived components, namely p-coumaryl alcohol, sinapyl alcohol, and coniferyl alcohol, represents an amorphous

phenolic polymer, as illustrated in Figure 1. In addition to its structural function, lignin is a significant byproduct of various industrial processes, including paper and pulp production. Separating lignin from cellulose and hemicellulose is often necessary in these industries. Lignin can be used for various applications, including nanomaterial synthesis, biofuel production, and as a source of renewable chemicals; in some cases, it has potential value as a material for bioplastics and other advanced materials [4]. Lignin nanoparticles refer to nanoscale-sized particles or structures derived from lignin, a complex organic polymer found in plant cell walls. Lignin nanoparticles have attracted attention in recent years for their potential applications across materials science, nanotechnology, and environmental engineering. Lignin nanoparticles can be produced by mechanical milling, chemical modification, or enzymatic processes. These methods aim to reduce the size of lignin molecules to the nanometre range. Lignin nanoparticles offer advantages, including being renewable, biodegradable, and relatively low-cost compared to some other nanomaterials [5]. Despite their potential, lignin nanoparticles face challenges in controlling their size and properties and achieving consistent quality. Researchers are working to address these issues to enable broader adoption of lignin nanoparticles in industry.

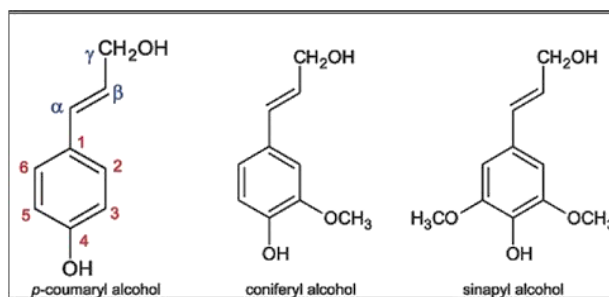


Figure 1. Key precursors of lignin.

2. Sources of Lignin

Lignin is a complex organic polymer found in plant cell walls. Lignin is widely available from various plant sources, with the primary sources being.

Wood: lignin is abundant and a major component of tree cell walls. Hardwood and softwood trees, such as oak, pine, maple, and spruce, are excellent sources of lignin. The pulp and paper industry often extracts lignin from wood during pulping. The lignin content of wood can vary depending on the type of wood, its age, and other factors. On average, lignin makes up about 20–30% of the dry weight of wood. However, this percentage can vary across different wood species. Hardwoods tend to have a lower lignin content, typically in the range of 20–25%, while softwoods may have a higher lignin content, often around 25–30% [6].

Non-woody plants: lignin can also be found in non-woody plants, including agricultural residues and crop residues. For example, corn stover, wheat straw, and sugarcane bagasse contain lignin and are used as feedstocks for lignin extraction in some processes.

Grasses: some grasses, such as bamboo, switchgrass, and miscanthus, also contain lignin and can serve as renewable lignin sources for various applications.

Agricultural byproducts: certain byproducts, such as rice husks and corn cobs, contain lignin and can serve as sources for lignin extraction.

Industrial residues: lignin is a byproduct of various industrial processes, such as pulping and papermaking, where it is separated from cellulose and hemicellulose. This industrial lignin can be used for various applications, including biofuels and materials.

The choice of lignin source can depend on factors such as the intended application, availability, and sustainability considerations. Lignin from different sources may have variations in composition and properties, which can influence its suitability for specific applications. Table 1 lists the lignin contents of the different feedstocks. Researchers are continually exploring methods to efficiently extract and utilize lignin from various sources to develop sustainable and value-added products.

Table 1. Lignin content in various feedstocks.

Feedstocks	Percentage of lignin	References
Parthenium weed	23.26	[7]
Wheat straw	19.8	[8]
Sugarcane bagasse	24.83	[9]
Spruce	27.9	[10]
Rice straw	19.37	[11]
Pinewood	27.7	[12]
Cherry tree pruning	23	[13]

3. Extraction of Lignin Using Various Methods

Depending on the desired lignin type, purity, and application, lignin can be extracted from plant biomass using various methods. Here are some common methods for lignin extraction:

3.1. Alkaline pulping.

Kraft Process: This is the most widely used lignin extraction method in the pulp and paper industry. The Kraft pulping method is the prevailing technique for treating lignocellulose, accounting for roughly 85% of total lignin production [14]. Wood chips are cooked in a sodium hydroxide (NaOH) solution and sodium sulfide (Na₂S) under high pressure and temperature. Lignin dissolves and can be separated from cellulose fibers. To begin with, lignin can be made soluble by subjecting it to high pH levels, typically 13 to 14, and elevated temperatures, approximately 170°C. This process involves breaking the ether linkages in lignin, thereby increasing the number of phenolic-OH groups that can be ionized at this pH. This ionization is what enables lignin to become soluble [15,16]. Subsequently, an acid, such as H₂SO₄, can be used to precipitate lignin from the remaining alkaline solution, thereby reducing the pH to 5-7.5 [17].

For the commercial production of kraft lignin, LignoBoost Technology has been employed to extract lignin from pulp black liquor. This process uses CO₂ acidification to precipitate lignin [18]. Following precipitation, the lignin is then filtered through an initial chamber press filter. The resulting filter cake is redispersed, and additional acid is added to the mixture. Generally, kraft lignin contains only a small percentage of sulfur groups, typically 1-3% by weight. Most commercially available lignin is sulfonated to enhance its water solubility, as it is naturally soluble only at pH levels greater than 10.

Soda Process: Soda pulping is used to treat non-wood fibers such as hay, rice, and sugar cane bagasse, which account for 5% of total pulp production [15]. The lignin solubilization process is identical to the kraft process, which digests biomass at temperatures between 140 and 170°C in the presence of a 13–16% sodium hydroxide solution by weight. Anthraquinone, on the other hand, is used as a catalyst to reduce carbohydrate degradation and dissolve lignin. Due to the high content of -COOH, which is the product of oxidation of aliphatic-OH groups, the soda lignin extracted is not easy to recover by filtering and centrifugation [17]. Soda lignin

has a mean MW of 2400 Da, but depending on carbon content, it will range from 1000 to 3000 Da [15]. The Soda lignin, on the other hand, contains no sulfur, making it a good candidate for high-value chemical production [17].

3.2. Organosolv extraction.

This method extracts lignin using organic solvents, often ethanol, methanol, or acetone, under high-temperature, high-pressure conditions. To effectively remove lignin from certain types of plant-based biomass, it's essential to carefully select the optimal conditions. This selection should take into account factors such as the type and concentration of the solvent, the presence and concentration of a catalyst, the size of the biomass particles, temperature, the duration of delignification, and the ratio of solid to liquid components [19].

3.3. Enzymatic hydrolysis of lignocellulosic.

Enzymatic hydrolysis of lignin is derived from a process involving the use of cellulases and hemicellulases to break down cellulose and hemicellulose in biomass. This process results in lignin remaining as solid and insoluble residues. The entire process is advantageous due to its environmental friendliness and cost-effectiveness [20]. The resulting lignin products are primarily free from sulfur and exhibit very limited solubility in both water and certain organic solvents. Nevertheless, they maintain a closer structural resemblance to native lignin when compared to other forms of technical lignin. Enzymatic hydrolysis lignin typically comprises 65–80% lignin content, alongside other components like carbohydrates, proteins, and ashes. This type of lignin has numerous industrial applications, including use as a dispersant, binder, sorbent, emulsifier, and in the production of various polymeric chemicals [21].

3.4. Ionic liquids (ILs).

Ionic liquids are special organic salts that can dissolve lignin at room temperature. They offer a more selective and potentially milder way to extract lignin from biomass. Ionic liquids are proficient in disrupting cellulose's crystalline structure and segregating lignin and polysaccharide components into distinct fractions. Additionally, depending on the specific process conditions, it's possible to modify the functional properties of the extracted lignin, thereby enabling the production of high-value products with tailored characteristics. Nevertheless, several noteworthy challenges are associated with the use of ILs as a pretreatment method. These challenges encompass the high cost of ILs, the recuperation and recycling of ILs post-pretreatment, and the absence of efficient process technologies for IL utilization. Consequently, the incorporation of IL technology within a biorefinery presents formidable hurdles [22].

3.5. Steam explosion.

Biomass is exposed to high-pressure steam, followed by a sudden pressure release, which extracts lignin. This method can disrupt the biomass structure, making it more accessible for lignin removal. Steam explosion is a widely employed physicochemical pretreatment technique in woody biomass processing. In this process, lignocellulose powders are initially exposed to high-pressure steam at temperatures ranging from 160 to 270°C for a few seconds to several minutes, after which the pressure is abruptly released to return to atmospheric levels. Steam explosion typically induces a combination of both physical and chemical

transformations. On the one hand, intense water evaporation disrupts lignocellulosic fibers, while on the other hand, hydrolysis reactions break C-O-C bonds. As a result of this treatment, hemicellulose can be extracted and broken down into oligosaccharides or monosaccharides, while lignin can be separated from its original structure without significant alteration [23].

4. LNMs Characteristics

Different forms are typical characteristics of LNMs (Figure 2, Table 2). The shapes might be non-spherical or irregular, hollow spheres, quasi-spheres, cuboids, or well-defined spheres, alone or in structures such as clusters and aggregates. Furthermore, increased lignin concentrations often enable higher yields in the manufacture of LNPs [24].

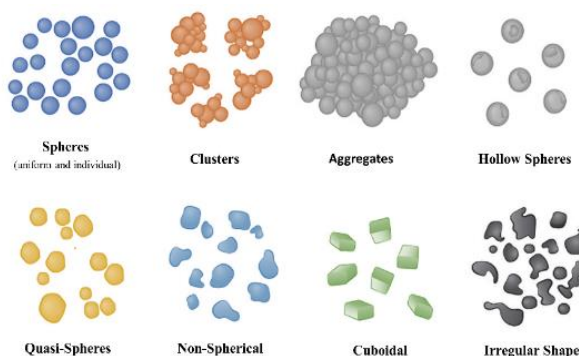


Figure 2. Illustrations of the various LNP forms. The lignin type used (i.e., the extraction method), the chemical, physical, or biological changes it undergoes, and the way in which the LNPs are made also directly affect the forms of these nanoparticles.

Table 2. An overview of the various techniques utilized to create LNPs and other lignin-based nanomaterials, along with a list of possible uses.

Morphology	Raw material	Method	Size (nm)	Yield (%)	Shape	Application	References
Nanoparticles	Alkali lignin	Heating and mechanical agitation	10-15	98	Spheres	Antibacterial, antifungal, antioxidant and antiplatelet activity	[26]
Nanoparticles	Kraft, alkali, and organosolv lignin	Aerosol flow reactor	230-1900	> 60	Spheres	Surfactant free-emulsification	[27]
Nanoparticles	Alkaline corn cob lignina	Solvent exchange (THF) + ultrasonication	100-800	82.3	Spheres	Sunscreen elaboration	[28]
Nanoparticles	Corn stover and switchgrass	Antisolvent precipitation (acetone + water) + ultrasonication	142-234	75-87	Spheres	Biorefineries	[29]
Nanoparticles	Soda coconut fibers	Microbial hydrolysis	22-207	58.4	Non-spherical	Useful in textile, biomedical, and environmental applications	[30]
Nanoparticles	Alkaline lignin	Antisolvent precipitation (APS + water)	80-230	Higher yields	Quasi-spheres and aggregates	Drug delivery carrier for hydrophobic compounds	[24]
Nanoparticles	Alkali lignin	Antisolvent precipitation (ethylene glycol) + Acid precipitation (HCl)	40-60	-	Uniform and flat	Removal of Safranin-O dye and Basic Red 2 dye	[31]

The various motifs with different linkages found in lignin are also strongly linked to the synthesis of LNMs and their morphology. The distance between the links can also determine the size and shape of the LNMs. Lignin's molecular weight is another important component. When lignin is dissolved in solvents that break certain bonds between aromatic rings, the molecular weight decreases, and the particles get smaller [25]. The morphology of LNMs plays an important role in determining their efficacy. For example, amorphous lignin and LNPs with rough shapes and sharp edges can make them harder to interact with other substances, especially when forming hybrid nanocomposites. LNMs that have a more spherical shape are well-suited for Pickering stabilization and biological applications. They are highly effective in transporting hydrophobic compounds to specific cells. Furthermore, smaller particles are less cytotoxic than larger particles [25].

Characterizing lignin after extraction and purification is essential, as these processes can induce structural alterations in its macromolecular framework. Due to its complex nature as an aromatic biopolymer bound to carbohydrates, lignin characterization poses challenges and requires the integration of multiple techniques [32]. The assessment of the physical and chemical properties of lignin involves a combination of wet-chemical, spectroscopic, chromatographic, thermal, and mechanical analyses [32,33]. In brief, wet chemistry techniques include conventional approaches to lignin chemistry, encompassing elemental analysis, quantification of functional groups (such as O-methyl, total and phenolic hydroxyls, carbonyl, and carboxyl groups), and degradation methods to assess inter-unit linkages (e.g., nitrobenzene oxidation or thioacidolysis). Structural characterization relies on spectroscopic methods, including ¹H, ¹³C, and ³¹P nuclear magnetic resonance (NMR) spectroscopy, two-dimensional (2D) NMR with heteronuclear single-quantum coherence, Fourier transform infrared spectroscopy (FTIR) analysis, Raman spectroscopy, and surface analysis using X-ray photoelectron spectroscopy (XPS). Chromatographic techniques are employed to determine molecular weight and polydispersity through gel permeation chromatography. Thermal properties are evaluated by thermal gravimetric analysis and differential scanning calorimetry, while dynamic mechanical properties assess lignin's mechanical characteristics [21]. Figure 3 shows the experimental techniques used to characterize lignin nanomaterials.

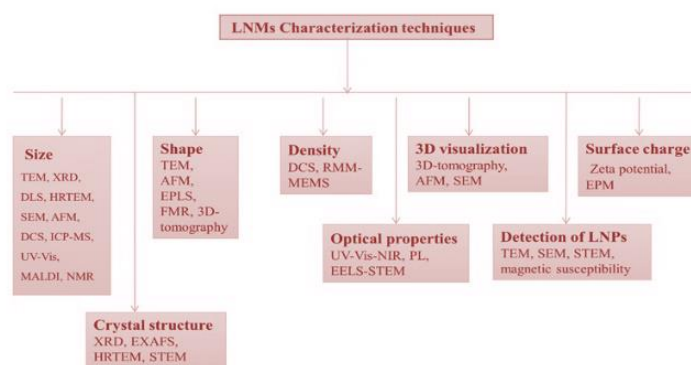


Figure 3. Experimental techniques used to characterize lignin nanomaterials. **Abbreviations:** (TEM: Transmission Electron Microscope; XRD: X-ray Diffraction; DLS: Dynamic Light Scattering; SEM: Scanning Electron Microscope; HRTEM: High-resolution Transmission Electron Microscope; AFM: Atomic Force Microscopy; DCS: Differential scanning calorimetry; ICP-MS: Inductively Coupled Plasma Mass Spectrometry; UV-vis: Ultraviolet-visible Spectrophotometry; MALDI: Matrix-assisted laser Desorption/Ionization; NMR: Nuclear Magnetic Resonance; STEM: Scanning Transmission Electron Microscopy; EXFAS: Extended X-ray Absorption Fine Structure; EELS: Electron Energy Loss Spectroscopy).

According to the application intended to be given to LNMs, the respective characterization approaches are applied. In the field of hybrid nanocomposites and tissue engineering development, evaluations using X-ray photoelectron spectroscopy (XPS), Fourier-transform infrared (FT-IR) spectroscopy, differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and thermomechanical analysis (TMA) are important. Conversely, in cosmetic formulation, delivery systems, and other biomedical applications, in addition to measuring absorbance and transmittance in UV spectrometers, radical scavenging is assessed using 2,2-diphenyl-1-picrylhydrazyl (DPPH) assays. Also, in specific scenarios, such as with drug delivery for cancer cells, *in vitro* and *in vivo* toxicity trials are necessary. If these LNMs are modified or used with other materials, cytotoxicity testing must be repeated and reviewed to demonstrate their safety.

5. Lignin Nanomaterials

Several types of nanomaterials can be derived from lignin, including:

Lignin nanoparticles are produced from lignin and can vary in size and shape depending on the processing method. These are nanoparticles, typically 1 to 100 nanometres in size, produced by techniques such as nanoprecipitation, solvent evaporation, or emulsification. They can be further categorized by source (e.g., hardwood, softwood, grasses) and processing method.

Lignin nanofibers are long, thin nanomaterials with a high aspect ratio, making them suitable for various applications, including reinforcement. Lignin nanofibers are elongated nanostructures with diameters in the nanometer range and lengths extending to micrometers. They can be produced via processes such as electrospinning or mechanical fibrillation. Lignin nanofibers have potential applications in materials such as nanocomposites, membranes, and tissue engineering scaffolds.

Lignin nanospheres: these are spherical nanomaterials derived from lignin and are often used in drug delivery and encapsulation applications.

Lignin nanocomposites: various nanomaterials can be incorporated into lignin matrices to create nanocomposites, including nanocellulose, often derived from the same biomass as lignin. Nanocellulose can form strong and lightweight composites. Graphene and graphene oxide can enhance electrical conductivity and mechanical strength. Clay nanoparticles are used to improve barrier properties and thermal stability. Metal Oxide Nanoparticles: Such as titanium dioxide (TiO₂) and zinc oxide (ZnO), which can impart photocatalytic and antimicrobial properties.

Lignin nanotubes: lignin nanotubes are a special form of lignin nanomaterial that combines the structural qualities of nanotubes with the natural benefits of lignin. These nanotubes feature a tubular nanostructure and offer unique properties that can be useful across applications in materials science, biology, and environmental engineering. Several methods can be used to produce lignin nanotubes, including electrospinning, a technique in which a lignin solution is electrically charged to form fine fibers, which can be further processed into nanotubes. Self-assembly: lignin molecules can self-assemble into nanotubular structures under specific conditions, typically incorporating surfactants or other templating agents. Template-assisted synthesis: using templates such as anodic aluminum oxide (AAO) membranes, lignin can be deposited, then the template is removed, leaving nanotubes.

These lignin-based nanomaterials offer a range of possibilities for environmentally friendly, sustainable alternatives across industries such as packaging, biomedical, and materials science.

6. Applications of Lignin Nanomaterial

Lately, nanomaterials derived from lignin have gained widespread use as biomaterials across a broad range of applications, including antimicrobial effects, food and cosmetic applications, UV absorption, tissue engineering, and antioxidant functionality. In the upcoming section, we will provide an overview of the primary applications of nanomaterials based on lignin (Figure 4).

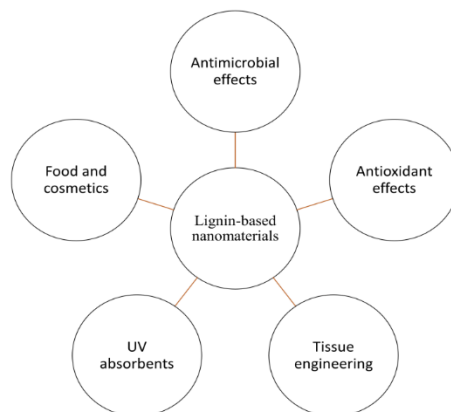


Figure 4. Different applications of lignin-based nanomaterials.

6.1. Antimicrobial effects.

Lignin-based metallic nanoparticles have attracted attention for their potential antimicrobial effects, combining lignin's inherent properties with those of metallic nanoparticles. Metallic nanoparticles, such as silver (Ag), copper (Cu), and zinc oxide (ZnO), have well-documented antimicrobial properties. The antibacterial activity of lignin-based nanoparticles can be attributed to several mechanisms: Lignin can enhance ROS formation, which can damage microbial cell membranes, proteins, and DNA. Lignin and its derivatives can interact with microbial cell membranes, causing structural damage and leakage of cell contents. Lignin-based nanomaterials sometimes contain metal nanoparticles (such as silver or copper), which release toxic metal ions that are harmful to bacteria. The phenolic groups in lignin can denature proteins and enzymes in microbial cells, resulting in cell death. Types of lignin-based nanomaterials with Antimicrobial Properties: Lignin can be converted into nanoparticles, improving its surface area and reactivity. LNPs have demonstrated antibacterial activity against a broad spectrum of bacteria and fungi. Nanoparticles, such as silver or zinc oxide, can be coated with lignin to combine the antibacterial properties of both materials. The lignin coating can enhance the stability and dispersion of metal nanoparticles. Combining lignin with other polymers or nanomaterials can form composites with synergistic antibacterial properties. For instance, lignin-polyvinyl alcohol (PVA) composites have shown significant antibacterial activity. Lignin may be electrospun into nanofibers, which can then be used as antimicrobial mats for wound dressings or air filters. Applications: Lignin-based nanoparticles can be utilized to cover medical equipment or as components in wound dressings to prevent infections. Incorporating lignin nanoparticles into packaging can help extend the shelf life of

food products by limiting microbial growth. Lignin-based nanomaterials can be used to filter and disinfect water, removing microbiological pollutants.

Lignin nanoparticles can be incorporated into fabrics to develop antibacterial textiles for medical and consumer applications. When incorporated into either pure or grafted polylactic acid matrices, lignin nanoparticles and cellulose nanocrystals have exhibited antibacterial properties, reducing the growth of the plant pathogenic bacterium *Pseudomonas syringae* pv. tomato (Pst). Findings from studies involving polylactic acid (PLA) nanocomposite films containing lignin nanoparticles have particularly underscored how this environmentally friendly attribute can lead to innovative defenses against harmful infections. This underscores its potential utility, especially within the food packaging sector [34]. An important aspect of lignin is its intrinsic antibacterial activity, which positions it as a promising, eco-friendly agent effective against pathogenic microorganisms. Its inherent biocidal properties offer the potential to address environmental concerns associated with the use of silver nanoparticles while also enhancing the controlled release of active ingredients in agriculture [35].

6.2. Food and cosmetics.

Lignin-based metallic nanomaterials have the potential to find applications in both the food and cosmetics industries due to their unique properties and versatility. Lignin-based metallic nanomaterials can be incorporated into food packaging to enhance its antimicrobial properties [36]. This can help extend the shelf life of perishable food products by inhibiting the growth of spoilage microorganisms and pathogens. These nanomaterials can also provide a barrier against oxygen and moisture, reducing food spoilage and maintaining product freshness. They can be used as antimicrobial coatings for food-contact surfaces and equipment in food processing facilities, reducing the risk of microbial contamination and foodborne illness. Metallic nanoparticles, such as zinc oxide (ZnO) and titanium dioxide (TiO₂), are commonly used in sunscreens for their broad-spectrum UV protection [37]. Lignin-based metallic nanoparticles can be incorporated into sunscreen formulations to enhance UV protection while potentially reducing the whitening effect associated with some sunscreens. Lignin-based metallic nanoparticles can be used in various skin care products, such as creams, lotions, and serums. They may offer antioxidant properties and help protect the skin from oxidative stress and environmental damage. These nanoparticles can be used in anti-aging formulations due to their potential to promote collagen production and skin elasticity. They may also have anti-inflammatory properties, which can help reduce redness and irritation.

Lignin's natural ability to protect plants against pathogenic attacks underlies its antibacterial properties. Essentially, lignin acts as a barrier, preventing bacteria and fungi from breaking down carbohydrates and accessing the plant's internal environment. Technical lignins isolated from lignocellulosic biomass have demonstrated antibacterial, antifungal, and antiviral properties in biological and medical research contexts [38]. While it's widely recognized that phenols and polyphenols possess antibacterial properties, the precise underlying mechanism remains unclear. The effectiveness of lignin's antibacterial activity depends on both the type of lignin and the bacterial strain. For instance, kraft lignin extracted from maize has proven effective against Gram-positive bacteria such as *Staphylococcus aureus* and *Listeria monocytogenes*, but less so against Gram-negative bacteria and bacteriophages.

On the other hand, kraft lignin from eucalyptus can deactivate both gram-positive (e.g., *Bacillus cereus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*) and gram-negative (e.g.,

Escherichia coli, *Salmonella enteritidis*) bacteria [39]. Lignin can serve as a standalone antibacterial agent, be combined with other antibacterial agents, or be integrated into more complex systems. For instance, wrapping lignin around a core of silver nanoparticles enhances its antibacterial activity against *S. aureus* and *E. coli* without releasing harmful silver ions into the environment [40].

Lignin possesses significant potential as a UV-absorbing material due to its exceptional oxidation resistance. In a study by Qian *et al.* [41], they employed a self-assembly process to create lignin reverse micelles (LRMs). This transformation of lignin into reverse colloidal spheres significantly enhanced its hydrophobicity, improving compatibility between LRMs and high-density polyethylene (HDPE). Importantly, as LRMs retained lignin's phenolic hydroxyl groups, the resulting HDPE/LRM composite materials exhibited remarkable UV-absorbing capabilities. Furthermore, using the self-assembly approach, the researchers generated three different sizes of conventional lignin colloidal spheres (large, midsize, and small). To create lignin-based sunscreens, these colloidal spheres were subsequently combined with pure skin lotions. The findings demonstrated that creams containing lignin colloidal spheres exhibited enhanced sunscreen performance compared to those with unmodified lignin.

Additionally, the size of the colloidal spheres played a crucial role in determining sunscreen performance, with larger spheres showing reduced effectiveness. In the sun-blocking process, the presence of phenolic hydroxyl groups was found to be pivotal. Acetylating lignin to shield these groups significantly decreased sun protection factor (SPF) values. Conversely, an increase in the content of phenolic hydroxyl groups corresponded to higher SPF values. For instance, the addition of 10 wt% small-sized organosolv lignin colloidal spheres with a higher phenolic hydroxyl group content resulted in an SPF value as high as 15.03. This study thus provides a straightforward approach for creating natural lignin-based sunscreens with excellent UV-blocking properties Qian *et al.* [42].

6.3. Tissue engineering.

Tissue engineering is a multidisciplinary field that integrates cells, growth factors, and advanced scaffolds to restore, enhance, replace, or maintain a tissue or organ that is not functioning optimally due to chronic conditions or sudden injuries. The ideal scaffolds should possess qualities such as biocompatibility, biodegradability, a well-connected porous structure, and exceptional rheological properties. Research in biomaterials for tissue engineering and regenerative medicine encompasses a wide range of interdisciplinary considerations. Tissue engineering scaffolds are synthetic, three-dimensional constructs that replicate the extracellular matrix of tissues. They provide structural reinforcement and direct three-dimensional tissue development to facilitate tissue regeneration. Scaffolds facilitate cell adhesion, migration, differentiation, and proliferation. The specific requirements for scaffolds vary depending on their intended applications, often necessitating a delicate balance of different and at times conflicting characteristics. For instance, scaffolds used in bone regeneration must possess adequate mechanical strength for implantation, controlled degradability, and the ability to be replaced by natural bone tissue, all while avoiding the generation of toxic degradation byproducts. Currently, bone replacement materials include autologous transplants (sourced from areas like the chin, retro-molar region, iliac crest, or trabecular bone), allogeneic transplants (obtained from bone banks), xenogeneic transplants (subjected to temperature or chemical pretreatment), and alloplastic materials (such as hydroxyapatite, tri-calcium phosphate, ceramics, and polymers based on α -hydroxyl acid). Emerging stem cell-based

approaches offer the potential for personalized, patient-specific solutions. Biomaterials must adhere to specific criteria, including biocompatibility as per ISO standards, which includes long-term studies, stability when exposed to physiological conditions (pH, temperature), mechanical robustness tailored to the intended application (e.g., stress/strain, elongation, impact moduli), corrosion resistance for metallic components, residue-free metabolization for biodegradable materials, and functional appropriateness for their intended use. The initial step in the interaction between cells and scaffolds involves cell adhesion processes, which hinge on intensive interactions at the cell-biomaterial interface. These interactions are strongly influenced by surface characteristics, including polarity (hydrophilic vs. hydrophobic), surface roughness, and topography. The development of scaffolds begins with polymer synthesis using advanced polymerization techniques to achieve well-defined porous structures that facilitate cell ingrowth. The polymer's bulk and surface properties must be tailored to mimic the natural environment. Scaffold surface characteristics, including polarity and topography, must align with cell shape to support adhesion, proliferation, and growth [43,44]. While many materials have been explored for stem-cell-based tissue engineering, only a few have originated from lignocellulose feedstock or its derivatives. In 2009, Rekola *et al.* [45] reported on the osteoconductivity of heat-treated wood bone implants. They found that heat treatment of wood enhanced the biological properties of these implants, with higher temperatures resulting in improved *in vitro* osteoconductivity, although lignin was not specifically investigated. Quraishi and colleagues [46] created an alginate-lignin composite aerogel by blending alginate and lignin solutions, employing CO₂-induced gelation and foaming to produce aerogels with micro-sized interconnected pores. These aerogels exhibited low stiffness, similar to that of fibrous tissue, and did not exhibit cytotoxic effects on mouse fibroblast-like L929 cells *in vitro*. Farhat *et al.* [47] manufactured various polysaccharide-based composites using a reactive extrusion process. They crosslinked starch, hemicellulose, or lignin with citric acid and characterized the resulting hydrogels for swelling, mechanical strength, and degradability. The swelling behavior was influenced by pH and the quantity of citric acid used as a cross-linker. Degradation rates were studied under physiological conditions for 15 days, and degradation could be controlled by introducing additional catalysts during polymer extrusion. Dynamic mechanical analysis revealed a significant reduction in the compressive modulus as the hydrogel degraded.

6.4. Antioxidant effects.

The intricate chemical structure of lignin, which includes aromatic rings bearing methoxy and hydroxyl groups, enables its incorporation into various materials to produce antioxidant products suitable for multiple applications. These functional groups play a crucial role in preventing oxidative reactions by donating hydrogen [48]. In one study, researchers Lu *et al.* [49] generated lignin nanoparticles (LNPs) with an average size of around 144nm using a supercritical anti-solvent precipitation method. They employed nanoscale lignin at a concentration approximately 12.4 times that of bulk lignin, resulting in LNPs with enhanced antioxidant and free radical-scavenging properties and improved reducing power. Consequently, these nanoscale lignin products have potential applications in the food processing and pharmaceutical industries. In another investigation, Yearla and Padmasree [50] produced dioxane LNPs with an average size of approximately 104nm through an anti-solvent precipitation method. In this process, a lignin solution was prepared by dissolving lignin in a mixture of acetone and water (9:1 v/v), then adding it to water. These LNPs exhibited superior antioxidant and UV-protection properties compared to bulk lignin, as evidenced by increased

survival rates of *Escherichia coli* under UV-induced stress. The resulting LNPs have promising prospects in the food, pharmaceutical, and cosmetic industries due to their beneficial properties.

7. Conclusions

Lately, there has been growing interest in scientific investigations concerning lignin particles. Lignin possesses a multifaceted molecular structure featuring various functional groups, making it a valuable resource for crafting distinctive particles. This review article aims to consolidate the latest developments in the use of lignin-based nanomaterials. Among the noteworthy potential applications of lignin, a particularly promising avenue is its incorporation into drug delivery systems. There is a growing demand for environmentally friendly biomaterials, driven by their cost-effectiveness and ecological benefits, including their compatibility with living organisms and their natural breakdown. Consequently, lignin has emerged as a promising component for these new sustainable materials thanks to its notable attributes. These qualities, such as its antioxidant, antimicrobial, and stabilizing properties, position this biopolymer as a favorable choice for various practical applications. The growing interest in using lignin in the chemical and pharmaceutical research sectors is a significant catalyst for developing high-value products, including chemicals and biopolymers, derived from a sustainable, renewable source of aromatic compounds. While research in this area is still relatively limited, lignin shows significant promise in the creation of various medical products, including hydrogels, micro- and nanoparticles, fibers, capsules, scaffolds, fibrous mats, membranes, webs, and more. This potential stems from its advantageous attributes, such as biodegradability and biocompatibility, as well as its antioxidant, antibacterial, thermal, and mechanical properties. However, several challenges hinder the advancement of lignin-based medical materials. These challenges include lignin's complex and heterogeneous nature, technical constraints in the synthesis processes, and legal and regulatory considerations for medical applications. Anticipated technological advancements are expected to address these issues, enabling the development of lignin-based biomaterials that can yield higher-value products tailored to specific shapes, sizes, and performance requirements.

Author Contributions

Conceptualization, N.K., D.Y., S.K.; methodology, N.K., D.Y., S.K.; investigation, N.K., D.Y., S.K.; resources, N.K., D.Y., S.K.; data curation, N.K., D.Y., S.K.; writing—original draft preparation, N.K., D.Y., S.K.; writing—review and editing, N.K., D.Y., S.K. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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