Exploration of BioMat-X

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Functional lignin hydrogels for biosensors and biomedical therapy

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Abstract

Lignin, the second most abundant natural polymer after cellulose, has emerged as a promising renewable resource for developing functional biomaterials. Due to its aromatic structure and abundance of phenolic, hydroxyl, and methoxy groups, lignin exhibits intrinsic antioxidant, UV-blocking, antimicrobial, and biocompatible properties, making it an attractive candidate for hydrogel fabrication. This review provides a comprehensive overview of lignin-based hydrogel, focusing on their structural characteristics, extraction methods, and strategies used for hydrogel preparation, including crosslinking copolymerization, graft polymerization, interpenetrating polymer networks, and controlled polymerization techniques such as ATRP and RAFT. Particular emphasis is placed on recent advances in the application of lignin-based hydrogels in biosensing and biomedical fields, including wearable strain and pressure sensors, drug delivery systems, wound healing, and tissue engineering. The multifunctional properties of lignin contribute to enhanced mechanical strength, electrical conductivity, UV protection, and controlled drug release, enabling the design of smart and sustainable hydrogel systems. Despite these advantages, several challenges remain that limit large-scale translation, including lignin heterogeneity, limited solubility, variability in hydrogel performance, and potential impurities from industrial extraction processes. Addressing this limitation through improved lignin purification, chemical modification, and standardized synthesis approaches will be essential for advancing lignin-based hydrogels towards practical biomedical and sensing applications.

Keywords

lignin, hydrogel, biosensor, extraction methods, wound healing, tissue engineering

Introduction

Hydrogels are three-dimensional networks of either natural or synthetic polymers that can absorb large amounts of water without dissolving, while retaining a high degree of flexibility [1]. These systems are typically produced through chemical reactions involving one or more monomers and polymer chains, forming association links that enable them to absorb water up to hundreds or even thousands of times their original dry weight [2]. Based on the type of crosslinking, hydrogels are generally classified into chemical and physical hydrogels: covalent forces form chemical hydrogels, whereas weak secondary forces form physical hydrogels [3, 4]. Natural polymer hydrogels offer several advantageous properties, including biocompatibility and biodegradability [5].

Lignin is a natural polymer and the second most abundant plant-derived polymer after cellulose. It occurs in plants such as coconut fibre and wood and constitutes one of the three main components of the cell wall in lignocellulosic biomass. Recently, it has gained attention as a renewable resource for hydrogel formation [2, 6]. Lignin is an amorphous, highly branched biomacromolecule with a molecular weight typically ranging from 1,000 to 20,000 g/mol [7]. Generally, Lignin is of two types: natural and technical/industrial. Industrial lignin is made up of lignocellulose or recovered from industrial wastes. Industrial lignin is inexpensive to produce, costing approximately 200–500 USD/dry ton depending on its quality, compared with around 1,000 USD/dry ton for polyethylene, a commonly produced synthetic polymer. This cost advantage, combined with its renewability, makes lignin a potential substitute for both natural and synthetic polymers [6, 8].

This review highlights an updated overview of current advancements that are driving the development and innovation of lignin-based hydrogels. It explores the composition and structure of the lignin, followed by its types, different extraction methods, and preparation techniques of lignin-based hydrogels. Finally, the applications of lignin-based hydrogels in various biosensing and biomedical applications are discussed.

The key research gap addressed by this review is the limited availability of literature that critically links material design, synthesis strategies, and practical device-level applications of lignin-based hydrogels. Most of the existing reviews emphasize on material preparation but provide little discussion on how lignin's structural variability, processing methods, and crosslinking strategies influence hydrogel performance in biomedical and sensing applications. This review fills that gap by offering a comparative analysis of preparation methods and highlighting both opportunities and limitations, thereby providing clearer insights for the future development and translation of lignin-based hydrogel technologies.

Lignin composition and structure

The main elements of lignin are C, H, and O. Natural lignin consists primarily of three phenylpropanoid monomers: *p*-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol. These monomers give rise to *p*-hydroxyphenyl (H), guaiacyl (G), and syringyl (S) units. In softwoods, lignin is mainly composed of guaiacyl units linked by carbon–carbon and ether bonds, whereas hardwood lignin contains approximately equal amounts of syringyl and guaiacyl units, and grass lignin contains all three monolignols [2, 7, 9]. Figure 1 depicts the basic lignin structure and its three monolignol building blocks.

Although lignin has high potential in the polymer sector, its direct use is limited by certain drawbacks, including suboptimal mechanical properties and thermal degradation of the final product. Therefore, chemical modification is often necessary to enable its use as a starting material for novel materials such as composites or hydrogels [10].

Industrial types

It is important to distinguish between natural lignin, which is an integral component of the plant cell wall, and industrial (technical) lignin, which is isolated from woody biomass. It is mainly sourced from pulp, paper, and biorefinery processes and is categorized based on extraction methods. Based on extraction techniques, industrial lignin is classified into four major types: alkali lignin (produced via soda or kraft pulping), lignosulfonates, enzymatic hydrolysis lignin, and organosolv lignin [11], as illustrated in Figure 2.

Kraft lignin, generated from kraft pulping, exhibits a highly cross-linked structure with many phenolic hydroxyl groups and typically contains 1–3% sulphur. Lignosulfonates, obtained from sulphite pulping, incorporate sulfonic acid groups into the lignin chain and show higher sulphur levels (3.5–8%). Soda lignin is produced from the soda pulping process, where only sodium hydroxide (NaOH) is used as the pulping

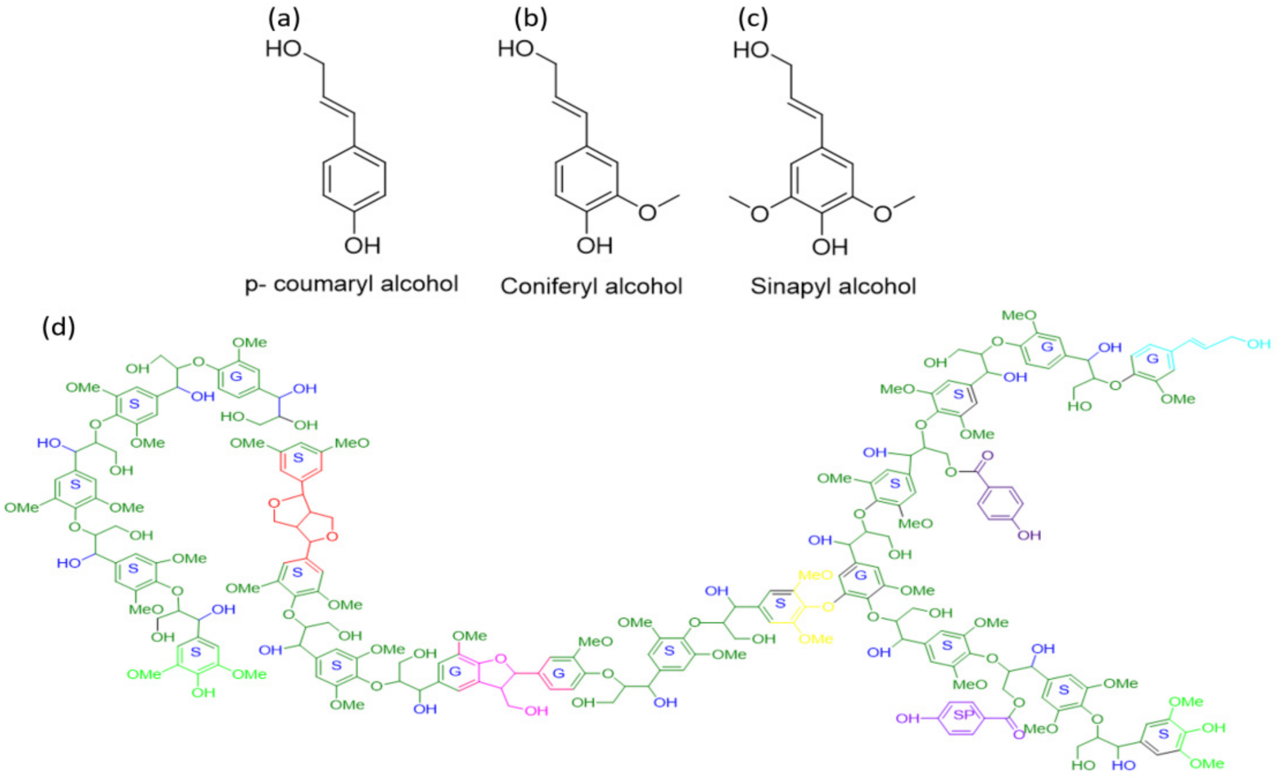


Figure 1. The three monomers of lignin. (**a**) *p*-coumaryl alcohol; (**b**) coniferyl alcohol; (**c**) sinapyl alcohol; (**d**) the chemical structure of lignin (*S* = syringyl, *G* = guaiacyl, SP = sinapyl *p*-hydroxybenzoate-derived). Dark green color: β–*O*–4, β-aryl ether. Pink color: β-5, phenylcoumaran. Yellow color: 4–*O*–5, biphenylether. Red color: β–β, resinol. Sky blue color: cinnamyl alcohol end group. Light green color: phenolic end group. The structures have been made using ChemDraw Software.

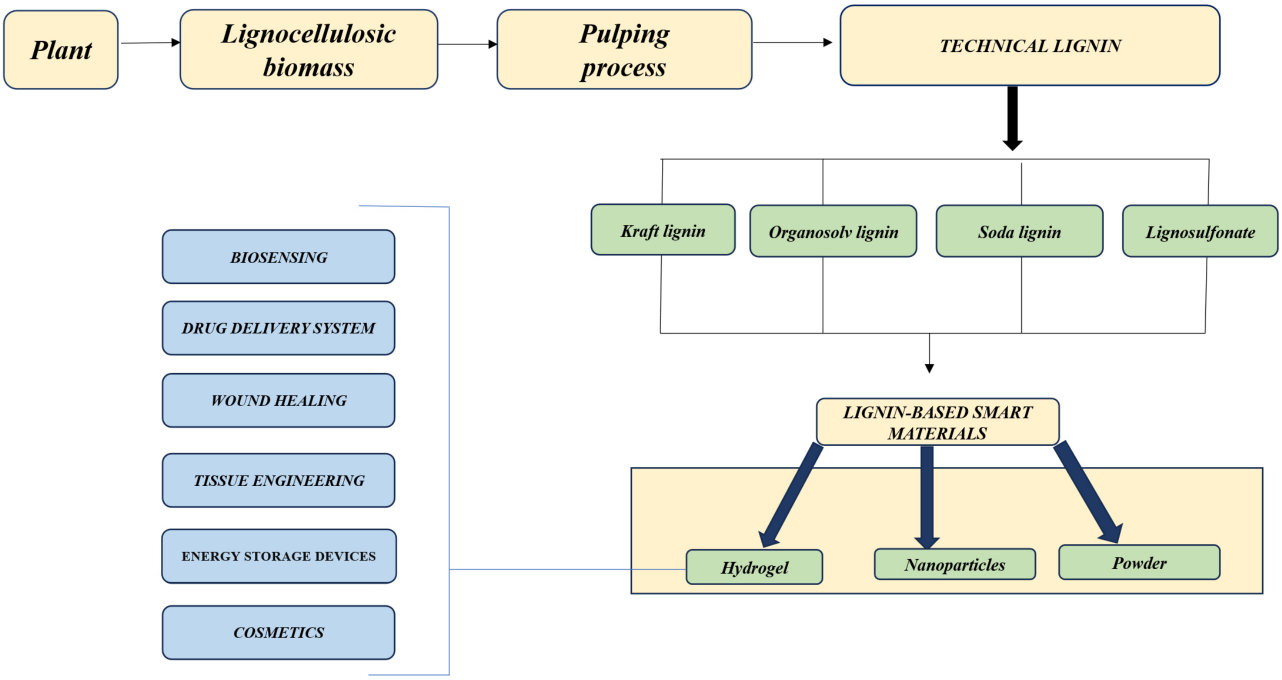


Figure 2. Schematic roadmap of technical lignin production and its applications. Lignocellulosic biomass derived from plants undergoes pulping processes to yield technical lignin, including kraft lignin, organosolv lignin, soda lignin, and lignosulfonates. These lignin types are further processed into lignin-based smart materials such as hydrogels, nanoparticles, and powders, which find applications in biosensing, drug delivery systems, wound healing, tissue engineering, energy storage devices, and cosmetics.

chemical. Organosolv lignin, isolated using organic solvents, undergoes minimal condensation reactions and therefore, preserves a structure similar to natural lignin. Kraft is most efficient for large-scale extraction, but organosolv lignin is the best-quality lignin for high-performance and biomedical applications [7].

Among the different lignin types, organosolv lignin generally exhibits the best biocompatibility compared to kraft lignin and lignosulfonates (sulfonated lignin, SL). Organosolv lignin is obtained using organic solvents without sulfur-containing chemicals, resulting in higher purity, lower toxicity, and fewer inorganic impurities, which makes it more suitable for biomedical and cosmetic applications such as hydrogels, drug delivery systems, and tissue engineering. In contrast, Kraft lignin contains residual sulfur (≈ 1.5–3%) and condensed structures formed during harsh alkaline pulping, which can reduce its biocompatibility and limit its use in sensitive biological systems. Lignosulfonates, although water-soluble due to sulfonate groups, often contain higher sulfur content and various impurities from sulfite pulping, which may cause cytotoxicity or interfere with biological interactions. Therefore, because of its sulfur-free composition, higher structural integrity, and cleaner chemical profile, organosolv lignin is considered the most biocompatible lignin type for biomedical and pharmaceutical applications [12].

A major research focus in lignin utilization is chemical valorization, particularly depolymerization. Because lignin has a complex and chemically stable polyphenolic structure, it is difficult to break down into low molecular weight compounds. Methods such as pyrolysis, enzymatic oxidation, hydrolysis, and hydrogenation have been explored, but they often require harsh conditions [7].

To overcome these limitations, researchers now emphasize on chemical modification of lignin to enhance its physicochemical properties and expand its applications. This usually involves modifying reactive hydroxyl groups (phenolic and aliphatic hydroxyl groups). Modifying groups can significantly improve the reactivity and solubility of lignin [13].

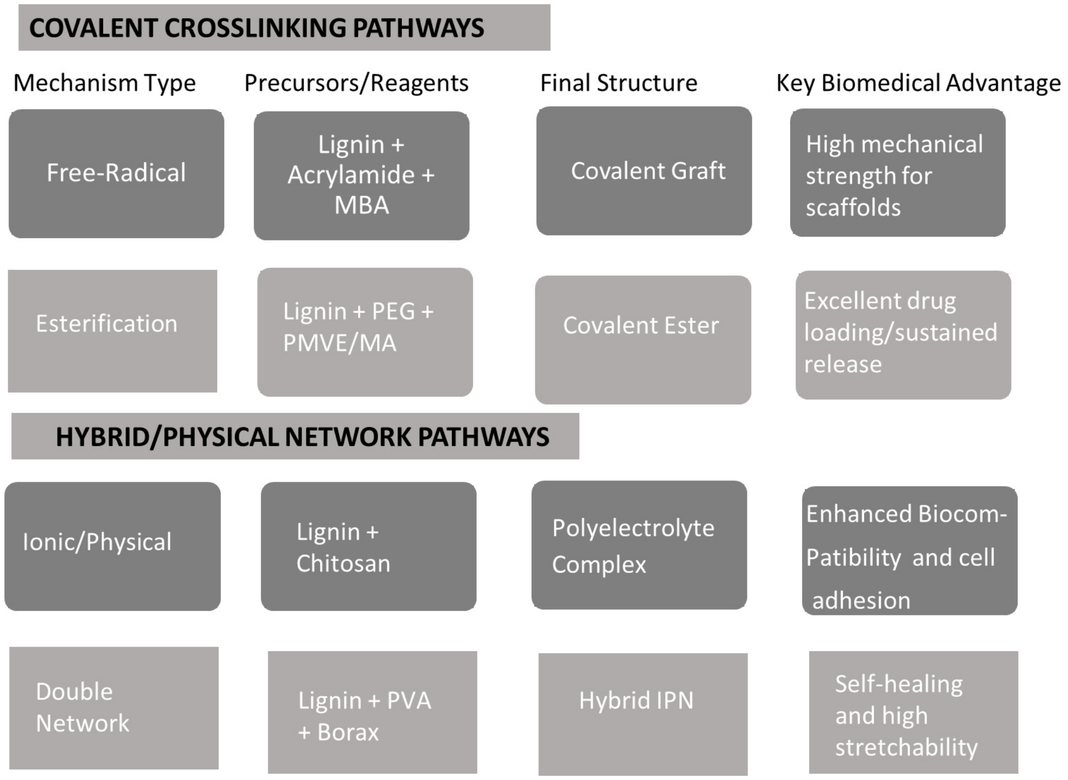
Accurate structural characterization is essential to predict or tailor its properties for smart hydrogel applications. Specific linkages such as β–*O*–4, β–β, and β–5(2) enhance flexibility and generally reduce the glass transition temperature, thereby facilitating chemical modification. In contrast, linkages such as β–5(1), β–β(1), 5–5, and 4–*O*–5 increase rigidity, resulting in higher thermal stability but lower elasticity [14].

Functional groups such as carboxyl (C=O), hydroxyl (–OH), methoxy ($-OCH_3$), and phenolic (C_6H_5OH) can be readily modified using chemical reactions (amination, sulfonation, oxidation, esterification, etc.), enabling the design of hydrogels with properties tailored to specific applications such as enhancing water solubility, reactivity, compatibility and thermal stability [15]. To enhance its performance in hydrogels, chemical modification strategies such as graft polymerisation [16], crosslinking [10], and atom transfer radical polymerisation [17] have been explored. Figure 3 summarizes the pathways and functional outcomes of lignin-based hydrogel crosslinking.

Although lignin is already used in the polymer industry, it can only be added in small amounts due to limitations related to thermal degradation and mechanical properties. Therefore, chemical modification is considered the most promising strategy to transform lignin into a valuable raw material for advanced materials like composites and hydrogels [7].

One of the major challenges in translating lignin-based materials from laboratory research to clinical and industrial use is the inherent heterogeneity of lignin. Unlike synthetic polymers, lignin is a natural biomacromolecule whose structure varies significantly depending on the plant source (hardwood, softwood, or agricultural residues) and the extraction method. These variations lead to differences in molecular weight, functional group composition, and impurity content, which ultimately influence the physiochemical properties and biological performance of lignin-based formulations. As a result, the same lignin material may exhibit inconsistent behaviour between batches, affecting drug loading capacity, release profile, antioxidant activity, and biocompatibility [13].

The lignin heterogeneity is a major challenge due to its variable composition. It can be practically reduced by controlling how different fractions separate based on real physicochemical behaviour. In fractional precipitation, adding a non-solvent like hexane or water gradually forces lignin out of solution; high molecular weight fractions precipitate first, while low molecular weight fractions remain dissolved. This method can produce very uniform cuts with a polydispersity index (PDI ≤ 1.5), and tuning the solvent ratio directly controls properties. For example, increasing hexane lowers molecular weight and increases



COVALENT CROSSLINKING PATHWAYS

Mechanism Type	Precursors/Reagents	Final Structure	Key Biomedical Advantage
Free-Radical	Lignin + Acrylamide + MBA	Covalent Graft	High mechanical strength for scaffolds
Esterification	Lignin + PEG + PMVE/MA	Covalent Ester	Excellent drug loading/sustained release

HYBRID/PHYSICAL NETWORK PATHWAYS

Mechanism Type	Precursors/Reagents	Final Structure	Key Biomedical Advantage
Ionic/Physical	Lignin + Chitosan	Polyelectrolyte Complex	Enhanced Biocom-Patibility and cell adhesion
Double Network	Lignin + PVA + Borax	Hybrid IPN	Self-healing and high stretchability

Figure 3. Schematic categorization of lignin modification into two primary branches.

aromatic –OH and carboxylic groups, making the fraction more reactive. In pH-dependent precipitation, lignin precipitates when phenolic groups are protonated (pKa ~9–11). At pH ≤ 2–3, it becomes insoluble, giving lower molecular weight, more functionalized fractions, but with limited control. In solvent extraction, a polar solvent like methanol selectively dissolves low-molecular-weight lignin (< 500 Da), leaving behind higher-molecular-weight fractions (> 500 Da) [18].

From a regulatory perspective, agencies such as the FDA and EMA require clearly defined Critical Quality Attributes (CQAs) and a robust Chemistry, Manufacturing, and Controls framework to ensure that each batch of a product maintains consistent quality, safety, and efficacy. However, the structural variability of lignin makes it difficult to establish standardized characterization protocols and reliable quality benchmarks. Consequently, this lack of uniformity complicates regulatory approval and clinical translation, as regulators require predictable material behaviour and well-documented safety profiles. Therefore, addressing lignin heterogeneity through standardized extraction methods, improved purification strategies, and advanced analytical characterization is essential to ensure reproducibility, facilitate regulatory compliance, and support the successful development of lignin-based biopharmaceutical systems. [12, 19].

Lignin-based hydrogels

In recent years, bio-based hydrogels made from environmentally friendly natural polymers have gained significant interest. Materials such as lignin, chitosan, collagen, and hyaluronic acid are commonly used, each offering unique characteristics and application potential. Chitosan hydrogels, known for their strong biocompatibility and water affinity, are widely utilized in wound healing and drug delivery. Collagen- and hyaluronic acid-based hydrogels possess high biological activity, making them valuable in medical and tissue engineering applications [7]. Lignin is preferred over other lignocellulosic components like cellulose and hemicellulose, and even many synthetic polymers, because it offers unique multifunctionality rooted in its aromatic and phenolic structure. Mechanistically, its phenolic –OH groups enable antioxidant and antimicrobial activity, while its aromatic network provides UV absorption and rigidity, allowing lignin to act as both a structural and functional additive in hydrogels, compared to cellulose and chitosan [20].

Unlike many synthetic polymers, such as poly(vinyl alcohol), which often require toxic chemical crosslinkers, lignin can be used in physically crosslinked systems, enabling greener and more cost-effective synthesis. Moreover, lignin is the most abundant aromatic biopolymer and is widely available as a low-cost byproduct of the pulp and paper industry, whereas biopolymers require dedicated extraction or cultivation. The complex phenolic structure of lignin also confers better radical-scavenging ability and enhanced stability. Additionally, lignin contributes to sustainability and circular economy goals by utilizing waste biomass (such as almond and walnut shells), while many synthetic polymers contribute to environmental pollution [7].

Lignin-based hydrogels exhibit excellent transport capabilities, as they can accommodate both hydrophilic and hydrophobic drugs due to their diverse functional groups [6]. Recent studies also demonstrate that lignin-based hydrogels can exhibit smart properties, such as electrical conductivity and stimuli-responsiveness, making them suitable for applications in biosensors [21], wearable electronics [22], supercapacitors [23], tissue engineering [24], and drug delivery [25].

Electrical conductivity in hydrogels is achieved by incorporating conductive components such as conductive polymers, nanoparticles, or ionic species into their 3D network. This enables charge transport while retaining flexibility and high-water content, making them suitable for applications like biosensors, flexible electronics, and energy storage [26].

Stimuli-responsive lignin-based hydrogels are smart materials that change their swelling or properties in response to stimuli like temperature, pH, or mechanical stress. Their responsiveness is often enhanced by adding functional monomers, though it may be limited by the structural complexity of lignin. These hydrogels show potential in applications such as drug delivery and biomedical systems [1, 7].

However, these advantages come with some limitations. Lignin has a complex and irregular structure, meaning it is not uniform like many other polymers. Its molecular weight can vary widely (around 1,000–20,000 g/mol), which can make its behaviour less predictable and more difficult to control in formulations. This leads to variability in performance, along with processing difficulty and inconsistent thermal properties. In contrast, cellulose offers uniformity and strength but lacks functionality. Synthetic polymers provide consistency but are non-biodegradable and often lack intrinsic activity [7].

The composition of lignin varies widely depending on its source and extraction method, leading to inconsistent hydrogel performance. Native lignin is poorly soluble and has low reactivity, often requiring chemical modification to achieve effective crosslinking. Industrial lignin may also contain impurities such as ash, carbohydrates, or sulphur, which can affect biocompatibility. Additionally, lignin's dark color and characteristic odor may restrict applications in cosmetics or clinical settings. These factors collectively hinder standardization, reproducibility, and large-scale adoption of lignin-based hydrogel in biomedical applications [7].

Properties of lignin

Biodegradability and biocompatibility

Lignin is a potential initiator molecule for the hydrogel synthesis and has several biological applications, such as tissue engineering and wound treatment, since it is less toxic and biocompatible [15].

The degradation of lignin is caused by certain fungi and bacteria. In nature, it is mainly broken down by fungi, which are more effective than bacteria, which tend to be slower and less extensive. These microorganisms rely on specialized enzyme systems that degrade lignin through radical-based oxidative processes. They can produce a variety of enzymes (including different isoenzymes and isoforms) depending on environmental conditions such as nutrient supply, oxygen levels, and temperature, which helps in the effective breakdown of lignin into biomass [7]. Denser pore architectures created by highly crosslinked hydrogels make them less accessible to microorganisms that break down lignin, such as actinomycetes and fungi. Fungal attack is further limited by reducing phenolic substructures because many fungi depend on enzymes that target these groups [26].

Although research on bacterial lignin degradation is more limited compared to fungi, certain bacteria are known to degrade lignin, mainly belonging to actinomycetes, α-proteobacteria, and γ-proteobacteria groups [27].

Lignin shows good biocompatibility when combined with many polymers such as chitosan, polyethylene glycol (PEG), collagen, etc., making it useful for biomedical applications like drug delivery and tissue engineering. In many studies, lignin-based composites have shown minimal cytotoxicity and good cell viability, indicating that lignin is a safe and effective component. This has been demonstrated by Ravishankar and coworkers [28], they prepared hydrogel and cross-linked films by mixing chitosan solution with alkali lignin solution. The MTT assay results suggest that the gels showed low cytotoxicity with cell viability of 99 ± 3% for chitosan-alkali lignin xerogels comparable to pure chitosan (99 ± 2%) and alkali lignin (114 ± 0.2%), confirming good biocompatibility [28]. In another study, Li and team [29] prepared lignin amine (LA) by modifying sodium lignosulfonate and then developed LA- PVA (lignin amine-poly vinyl alcohol) hydrogel. The cytotoxicity testing using L929 cells (CCK-8 assay) showed that cells proliferated well in the presence of hydrogel. Although cell viability decreased by about 25% compared to control, it was still considered low, indicating acceptable biocompatibility with maintained bacterial activity [29].

Organosolv lignin shows the best biocompatibility because it contains very low sulfur and fewer impurities, making it more suitable for biomedical hydrogels. Purified kraft lignin can also be used but may contain residual sulfur. Lignosulfonates are generally less preferred due to their higher sulfur content and ionic nature. Biocompatibility must always be confirmed with specific *in-vitro* (Cytotoxicity assay) and *in-vivo* studies to ensure safety, cell compatibility, and predictable biological response [7].

Mechanical properties

The content of the lignin-based hydrogel directly affects its mechanical properties, including tensile strength, rheological properties, storage modulus, and loss modulus. An increase in the content of lignin may result in a higher degree of crossing as well as the storage and loss modulus, which indicate energy dissipation and stiffness of the hydrogel, and so will the tensile strength [15].

The mechanical properties of lignin-based hydrogels depend mainly on the type and amount of crosslinking in their three-dimensional network. If the network is formed by weak particle attractions, it is unstable and easily damaged. Hydrogen-bonded networks are more stable and elastic due to higher liquid content and particular and partial molecular alignment. The strongest and most stable hydrogels are formed through chemical (covalent) bonds, making them suitable for mechanical and thermal applications. For instance, Belgodere and team [30] developed collagen-based 3D hydrogels combined with lignin materials, specifically sodium lignosulfonate (SLS) and alkali-extracted lignin, to enhance the mechanical properties and functionality of the collagen matrices. SLS significantly increases stiffness by strongly interacting with collagen fibres. Transmission Electron Microscopy (TEM) showed that collagen-SLS fibril bundles exhibited a tighter and more compact structure than collagen-only fibril bundles. This indicates that specific chemical structure and interactions of lignin, rather than just its presence, are crucial for enhancing stiffness in a collagen-based composite [30].

Lignin content plays a key role in mechanical performance. Increasing lignin improves rheological properties, including storage modulus (G’) and loss modulus (G”), with G’ generally higher due to the rigid phase within the hydrogel, which further enhances mechanical strength [26].

Additionally, the tensile strength of lignin-based hydrogels can vary from 0.5 to 4 MPa according to the type of lignin and its cross-linking density. In comparison, tensile strength of conventional chitosan hydrogels ranges between 0.1 and 2 MPa, while alginate systems often remain below 1 MPa [31].

Water uptake and retention

The hydrophilic network structure of lignin- based hydrogels is due to the presence of hydrophilic groups, such as hydroxyl, amino, carboxyl, and sulfonate functional groups in lignin, that form strong connections with water molecules, which allow these systems to absorb and hold large volumes of water. Additionally, the greater swelling ratios are associated with a less dense pore size distribution. This has been observed in a hydrogel prepared by Mondal et al. [32], using SL, polyacrylic acid (PAA), and $NiCl_2$. Results suggested that water retention is strongly enhanced by SL due to its hydrophilic functional groups and network-forming ability. SL contains phenolic hydroxyl and sulfonate groups, which can form H-bonds with water molecules and hold water within the hydrogel matrix. Also, lignin forms crosslinking (via H-bonding and coordination with Ni^{2+}), creating a dense and compact polymer network that physically restricts water evaporation. Additionally, the charged sulfonate groups attract and stabilize water through electrostatic interaction, reducing water loss [32].

Moreover, the type and density of crosslinking determine the amount of water absorbed, as physical crosslinks enable more responsive action, while chemical crosslinks improve structural integrity and prolonged swelling. Their characteristic of responding to external stimuli like temperature, pH, and ionic strength makes them useful for regulated water retention. Hence, they are excellent options for use in biomedical domains, personal care goods, and agriculture, where moisture control is essential [26, 33]. The moderate swelling of the lignin system is attributed to π–π interactions and hydrogen bonding within the polymer network, which restricts excessive water uptake while maintaining structural integrity [34].

UV blocking ability

Lignin is a complex aromatic polymer made of H, G, and S units with various linkages and functional groups that generate chromophore (unsaturated group responsible for electron absorption) such as quinoids, catechols, conjugated carbonyls and auxochromes (saturated groups with nonbonding electrons) such as phenolic hydroxyl, methoxy, amino, –CO, –SH, and $-SCH_3$ groups that enhance UV absorption by donating electrons to the aromatic ring of chromophore. These structures absorb UV light through electronic transitions, giving lignin excellent UV-shielding properties. However, its practical use is limited by its dark color, which reduces its aesthetic and commercial value [20, 35]. This has been demonstrated by Li and team [36], who developed lignin-based model compounds and incorporated them into sunscreen formulations to systematically study UV-shielding behaviour and synergy with ethylhexyl methoxycinnamate (EHMC). Lignin enhances UV protection due to the chromophore groups (C=C, carbonyl, quinone) that absorb UV radiation through π→π and n→π electronic transitions. While auxochromes increase electron density and reduce the HOMO-LUMO energy gap, resulting in stronger and red-shifted absorption in the UVA-UVB region. Lignin exhibits a synergistic effect with EHMC through π–π stacking interactions, forming charge-transfer complexes that further lower the energy gap and increase absorption intensity and SPF [36].

Pore structure

The pore structure plays a crucial role in controlling the diffusion, absorption, and release characteristics of active ingredients such as drugs, proteins, and nanoparticles in lignin-based hydrogels. The accessibility and mobility of these entities within the hydrogel system are determined by the mesh size (ξ) of the lignin-based hydrogel, which refers to the average distance between cross-linked polymer chains. Typically, lignin-based hydrogels exhibit a rougher surface morphology. Compact pores are observed in hydrogels containing up to 5% (w/w) lignin, whereas lignin concentrations above 5% (w/w) result in larger, more irregular pores and defects in the hydrogel texture [26].

Lignin can be combined with polymers such as PVA, PEG, or acrylic acid to achieve variable crosslinking densities, owing to its complex aromatic structure and abundance of functional groups (hydroxyl, carboxyl, and methoxyl). Consequently, the network mesh size can be tuned from nanometres to micrometres, depending on the degree of swelling and the crosslinking technique employed [37].

Zerpa and team prepared lignin-based hydrogels via free radical polymerization using a fixed lignin content (7–10% w/w) with varying amounts of NIPAAM, and MBAAm with AIBN as an initiator. The incorporation of lignin significantly reduced structural parameters (lower porosity and smaller pores), where the control hydrogel (without lignin) showed higher surface area, pore volume, and pore size. As a result, the swelling capacity of lignin-based hydrogel decreased, while thermal stability improved, with major degradation occurring at ∽420°C (while ∽415°C for the control). Hence, lignin addition led to a more compact structure with reduced swelling but enhanced rigidity and thermal resistance [38], as shown in Table 1.

Table 1. Lignin-based hydrogels versus natural polymer hydrogels.

Hydrogel	Tensile strength	Swelling ratio (%)	Conductivity	Degradation time	UV- Shielding	References
Lignin-hydrogel	~0.5–4 MPa	~200–5,000%	~10^{-3}–10 S/m	~2–6 weeks (depending on crosslinking)	~90–99% UV blocking	[39–41]
Chitosan	~0.2–2 MPa	200–350%	~10^{-5}–10^{-3} S/m	~1–4 weeks	~40–60% UV blocking	[42, 43]
PVA	~0.1–3 MPa	~100–500%	~0.38 mS/cm to 2.8 mS/cm	~3–8 weeks	~20–40% UV blocking	[44, 45]
PEG	~0.05–1.5 MPa	~200–1,500%	~10^{-6} to 10^{-3} S/m	~days to weeks	Negligible UV shielding	[46, 47]

Preparation of lignin-based hydrogels

Crosslinking copolymerization, interpenetrating polymer networks, and crosslinking grafted lignin and monomers are the usual steps in the synthesis of hydrogels from lignin [2].

Interpenetrating polymer network and polymerization method

A physical mixture involves dispersing or blending lignin with different polymers, where lignin functions as a natural biomass embedded within the polymer matrix. The insertion of lignin into the hydrogel structure through interpenetration or semi-interpenetration is known as the interpenetrating network structure approach. The primary mechanism is the polymerization of free radicals. In the presence of initiators, the phenolic hydroxyl groups in lignin generate free radicals that react with monomer and/or polymer chains to create graft structures [26]. For example, Xia and coauthors [48] prepared thermo-sensitive semi-IPN hydrogels using poly(*N*-isopropylacrylamide) (PNIPAAm) and lignocellulose with lignin. FTIR confirmed the presence of both amide (PNIPAAm) and hydroxyl (lignocellulose/lignin) groups, indicating successful incorporation and interaction, while scanning electron microscopy (SEM) showed a porous network structure affected by lignin content [48].

IPN systems are advantageous for improving mechanical strength, stability, and multifunctionality because two independent polymer networks are formed without covalent bonding between them. This was demonstrated in hydrogels prepared by Oveissi et al. [49], by incorporating lignin into polyurethane hydrogel as a physically crosslinking component. The abundant polar sites present on the backbone of lignin form a secondary network within the polymer matrix through hydrogen bonding and ionic interactions, thus resulting in a semi-interpenetrating structure. This dual network system improves Young's modulus, tensile strength, toughness, and elongation at break [49].

They are moderately scalable but usually require multi-step synthesis and sometimes organic solvents. Control over the exact network architecture is limited compared to controlled polymerization techniques. IPNs are widely used in biomedical and drug delivery applications due to their tunable swelling and biocompatibility, but the synthesis complexity can limit precise structural design [50].

Crosslinking copolymerization

Crosslinked copolymerization, in which carboxymethylated lignocellulosic materials are grafted with hydrophilic monomers like acrylic acid, is a typical method for creating lignin-based hydrogels. As a natural cross-linker, lignin strengthens the hydrogel's structural integrity by creating covalent bonds with polysaccharides. To stabilize the network, artificial cross-linkers such as MBAAm may also be employed. Water retention and swelling capacity of the hydrogel are greatly influenced by the lignin concentration and crosslinking density; optimal absorbency is achieved with moderate crosslinking. Superabsorbent hydrogels that are environmentally benign and biodegradable can be developed using this technique [51, 52].

Munguía-Quintero and coworkers [53] developed a lignin-graft-(poly(acrylamide-co-*N*,*N*'-methylenebisacrylamide)) hydrogel/copolymer via free radical crosslinking copolymerization. FTIR confirmed successful grafting. SEM analysis showed that raw lignin had an irregular, fragmented surface, whereas the modified lignin exhibited a more uniform and larger morphology, confirming structural modification. The incorporation of lignin provided active functional groups and a stable backbone, which enhanced thermal stability and adsorption performance (high Pb^{2+} removal). Hence, lignin influenced the hydrogel by improving mechanical stability, functional group availability, and performance, while also contributing to a more robust and crosslinked network structure [53].

This is one of the simplest and most scalable methods, where monomers and crosslinkers polymerize simultaneously to form a hydrogel network. It is widely used in industrial hydrogel production because it requires straightforward reaction setups. However, it often uses radical initiators and chemical crosslinkers that may introduce toxicity concerns, limiting its suitability for sensitive biomedical applications. The control over network structure is moderate compare with controlled radical polymerization techniques [54].

Crosslinking grafted lignin and monomers

Grafting on the backbone of lignin with unsaturation monomers or other functional compounds increased its reactivity. Grafted lignin can copolymerize with hydrophilic monomers in the presence of a crosslinker to produce a variety of hydrogels for use in a range of applications. Further copolymerization may be possible in most cases when a double bond is introduced into the lignin structure using an unsaturated monomer [55].

Grafted crosslinking involves attaching side polymer chains onto a backbone polymer and then forming a crosslinked network [50]. For example, Rajan et al. [56], prepared lignin-based methacrylate copolymer hydrogels using modified organosolv lignin and hydroxyethyl methacrylate (HEMA). The interaction between lignin and polymer occurs through covalent grafting (HEMA onto lignin) along with additional hydrogen bonding and hydrophobic interaction, which together form a more rigid and stable network. Infrared spectroscopy (FTIR) confirmed covalent bonding and successful copolymerization between lignin and HEMA. Glass transition temperature and increased stiffness indicate formation of a crosslinked, uniform polymer network rather than a physical mixture [56].

This method often uses relatively mild reaction conditions and can incorporate natural polymers, making it attractive for biomedical and environmental applications. However, controlling grafting density and uniformity is difficult, which can lead to heterogeneous network structures. Scalability is moderate, and reproducibility can sometimes be an issue [50].

ATRP and RAFT for lignin-based hydrogels

RAFT (reversible addition-fragmentation chain transfer polymerization) and ATRP (atom transfer radical polymerization) were two popular techniques for creating polymers with controlled and engineered architectures. To create lignin-based hydrogels with well-aligned structures, ATRP and RAFT have both been employed. With respect to ATRP and RAFT polymerizations, "graft-from" and "graft-onto" were two fundamental methods for creating hydrogels. Creating polymers from active areas found on the backbone polymer was known as the "graft-from strategy." Lignin often functioned as the backbone polymer, allowing the grafted polymers to form from the protein's active sites. To integrate synthetic polymers with lignin using the "graft-onto" approach, covalent connections are formed between the lignin backbone and the graft polymers' terminal groups [57–59]. Click chemistry is the most widely utilized reaction to graft guest polymers onto lignin because of its great efficiency and ease of usage [58, 59].

ATRP offers excellent control over molecular weight, polymer architecture, and functional group placement, allowing precise design of hydrogel networks. This makes it highly suitable for advanced functional materials and responsive biomedical systems. However, ATRP typically requires transition metal catalysts (such as copper as residual Cu must be reduced to ppm levels (< 10–50 ppm for biomedical use) due to cytotoxicity) and strict reaction conditions, which may raise toxicity concerns and complicate purification, especially for biomedical uses. Scalability can also be limited due to catalyst removal requirements [58]. This has been depicted by Liu et al. [60], they prepared lignin-based gene delivery copolymers by converting lignin into macroinitiator through esterification of lignin's hydroxyl groups using 2-bromoisobutyryl bromide and then grafting PDMAEMA chains via ATRP. The resulting copolymers formed DNA-loaded nanoparticles and showed efficient gene delivery. NMR and FTIR confirmed successful synthesis, results showed that shorter PDMAEMA chains gave lower toxicity and better transfection, demonstrating controlled structure-performance behaviour [60].

RAFT polymerization provides high control over polymer structure similar to ATRP, but it does not require metal catalysts. This reduces toxicity issues and makes RAFT more suitable for biomedical and sensing applications. It also allows versatile monomer selection and precise functionalization. However, RAFT requires specific chain transfer agents and may involve longer reaction times, which can affect cost and industrial scalability [58]. For instance, Xu and coresearcher [61] developed a lignin-based methyl methacrylate (MMA)-*co*-butyl acrylate (BA) hybrid acrylic resin by first synthesizing lignin-graft-polyacrylamide (lignin-g-PAM) as macromolecular chain transfer using RAFT polymerization, and then using it in RAFT mini-emulsion polymerization to copolymerize MMA and BA. NMR and FTIR confirmed the successful formation of the graft copolymer. The results further showed high monomer conversion (~86–90%), stable latex particles, and increased glass transition temperature (~58.6°C) compared to pure resin (−1.3°C), confirming successful incorporation of lignin [61].

There is no single universally best method; the choice depends on the application. Crosslinking copolymerization is best for large-scale and simple hydrogel synthesis, ATRP and RAFT are best for precise structural control, while RAFT is generally considered the most suitable for biomedical applications due to better control and lower toxicity compared to ATRP. IPN systems are preferred when enhanced mechanical strength and multifunctionality are required (Table 2).

Lignin-based hydrogels for sensing

Biosensing

A biosensor is an electronic device capable of detecting, transmitting, and recording changes in physiological data [62]. It uses a biological component to detect specific substances and a transducer to convert the detection into an electrical signal. Biosensors offer an inexpensive, extremely sensitive, selective, real-time, and compact method for assessing biomarker changes compared to existing benchtop analytic techniques [63].

A biosensor operates on two main principles: biological recognition and signal sensing. It consists of three key components: A bioreceptor (such as an enzyme, antibody, or DNA) that specifically interacts with the target analyte, a transducer that converts this interaction into a measurable signal (usually electrical or optical), and a signal processing system that amplifies and displays the results. When the analyte binds to or reacts with the biological element, it produces changes such as electron transfer, heat, or ion release, which are then detected by the transducer. Biosensors are designed to provide rapid, accurate, and real-time detection, making them highly useful in healthcare, environmental monitoring, and food safety [64, 65].

As lignin and its derivatives are biocompatible and biodegradable, lignin-based conductive hydrogels are used as biomaterials for bioelectronic sensors that monitor blood pressure, heartbeat, pulse, and human mobility [26]. As lignin is inexpensive and works well with various polymeric materials, it has been used to create biosensor electrodes. Enzymes and non-catalytic peptides that resemble biomolecules have been incorporated into lignin-based biosensors [8]. Lignin-based biosensors, often combined with enzymes, can detect biomolecules such as glucose by producing measurable changes, such as pH or electrical conductivity. Table 3 presents various biosensor applications of lignin-based hydrogels. Lignin-based biosensors operate via well-defined signal transduction mechanisms, where the interaction between a

Table 2. A comparative table for the preparation methods of lignin-based hydrogels.

Method	Principle/Mechanism	Advantages	Limitations	Scalability	Applications	References
Interpenetrating Polymer Network (IPN/ semi-IPN)	Formation of two independent networks; lignin incorporated via physical interpenetrating or semi-IPN; free radical polymerization	Improves mechanical strength, toughness, and stability; multifunctional properties’ enhanced swelling behaviour	Multi-step synthesis; may require organic solvents	Moderate	Drug delivery, biomedical hydrogels, responsive materials	[26, 50]
Crosslinking copolymerization	Simultaneous polymerization of monomers with lignin acting as crosslinker	Simple method; cost-effective; high swelling and water retention; biodegradable material possible	Use of chemical crosslinkers and initiators may cause toxicity; less precise structure	High (industrial friendly)	Superabsorbent hydrogels, agriculture, wastewater treatment	[52, 54]
Crosslinking grafted lignin and monomers	Grafting functional monomers onto lignin backbone followed by crosslinking	Enhanced reactivity; stronger and more stable network; tunable properties; mild reaction conditions	Difficult to control grafting density; heterogeneity; reproducibility issues	Moderate	Biomedical materials, coatings, controlled drug release	[50, 55]
ATRP/RAFT (controlled radical polymerization)	Controlled/living radical polymerization using “graft-from” or “graft-onto” strategies for precise architecture	Excellent control over molecular weight, structure, and functionality; advanced material design	ATRP: requires metal catalysts (toxicity, purification); RAFT: requires special agents, longer time, higher cost	Low to moderate	Advanced drug delivery systems, smart hydrogels, sensors	[57–59]

Table 3. Lignin-based hydrogels in biosensor applications

Hydrogel composition	Lignin type	Synthesis	Properties	References
Amino-grafted sodium lignosulfonate, polyvinyl alcohol (PVA), *in situ* grown silver nanoparticles (AgNPs)	Lignosulfate	Grafting amino groups onto lignosulfonate, crosslinking with PVA, followed by *in situ* AgNP growth	Strong antibacterial activity (against *Staphylococcus aureus*, *Escherichia coli*), good mechanical strength and elasticity, porous network	[29]
Water/glycerol, PEDOT: sulfonated Lignin (PEDOT:SL), PAA	Sulfonated lignin	*In-situ* radical polymerization of acrylic acid with PEDOT:SL in water/glycerol	High electrical conductivity, soft, elastic, self-wrinkling, anti-freezing capability, biocompatible (non-toxic to skin and cells)	[66]
Fe-sulfonated lignin (SL), Polyacrylic acid (PAA), Lignin-based nanoparticles–Fe^{3+} chelates, ammonium persulfate (APS)	Sulfonated lignin	Redox/coordination-initiated polymerization using SL–Fe^{3+} complex and APS at room temperature	High stretchability (1,680%), strong adhesion (36.4 kPa), good conductivity (7.0 × 10^{-2} S/m), UV-blocking (99.7%), excellent self-healing (up to 85.7% stretch recovery, 98.5% conductivity recovery)	[67]
Poly (acrylic acid), poly (vinyl alcohol), lignosulfonate, and LiCl	Lignosulfate	Redox polymerization via LS/Fe^{3+}/APS system at room temperature, no external stimulus	Mechanical strength (1.04 MPa), stretchability (758%), and conductivity (9.81 S/m)	[68]
Top layer: quaternary hydroxyethyl cellulose (QHEC), bottom layer: lignosulfonate sodium (LS)–borax	Lignosulfonate sodium	Layer-by-layer assembly forming a double-layer hydrogel with oppositely charged polymers enabling ionic crosslinking	Top layer: strong (Young’s modulus ~101.3 kPa), non-adhesive (2.2 kPa), bottom layer: soft (14.2 kPa), adhesive (18.7 kPa), mechanical adaptability, skin compatibility, antimicrobial, biodegradable	[69]
Sodium lignosulfonate-silver (Ls-Ag), cellulose nanocrystals, poly(acrylamide), ammonium persulfate (APS)	Lignosulfate	APS radical polymerization catalyzed by Ls-Ag, forming cellulose-PAM composite hydrogel.	High tensile strength (406 kPa), ultra-stretchability (1,880%), self-recovery, robust adhesion, conductivity (~9.5 mS/cm), UV shielding, and antibacterial activity (> 98%)	[70]
Aminated lignin (AL), polydopamine (PDA), polyacrylamide (PAM), and biomass carbon aerogel (C-SPF)	Animated lignin- lignin extracted from corncob	Dual-network polymerization combining PAM with AL/PDA and biomass carbon aerogel reinforcement	High elasticity and self-adhesion, stable over 500 cycles, ultrahigh sensitivity (170 kPa^{-1}), quick response, mechanical strength, Biocompatible and antibacterial	[71]

Table 3. Lignin-based hydrogels in biosensor applications (*continued*)

Hydrogel composition	Lignin type	Synthesis	Properties	References
Ca^{2+}-adsorbed tannic acid–sulfonated lignin (Ca^{2+}–TA@SL) and polyacrylamide (PAM)	Sulfonated lignin	Sulfonated lignin doped with tannic acid, Ca^{2+}-adsorbed, then polymerized with PAM	Excellent conductivity, Strong adhesion, UV resistance, antioxidant and antibacterial activity, real-time ECG/EMG sensing	[72]

target analyte and a bioreceptor (enzyme, antibody, or peptide) is converted into a measurable signal [26]. Electrochemical biosensors combine biological recognition (such as glucose oxidation) to generate electrons that alter the current, voltage, or impedance [8].

Evaluating the performance of a biosensor is crucial to ensure its reliability and practical applicability. Biosensor performance is typically assessed using key metrics such as sensitivity (ability to detect small changes in analyte concentration), detection range (span over which the response is reliable and linear), signal intensity and signal-to-noise ratio, selectivity (specific response to target molecules), and throughput (efficiency in screening large sample sizes). As illustrated in a study by Ho and coworkers on the optimized lignin-based biosensor with increased signal intensity ~1.5-fold, a wider limit detection ranges up to 640 μM, and higher sensitivity detection, confirming enhanced overall efficiency and reliability [65].

Wang and coworkers [66] created a multipurpose organo-hydrogel sensor using water/glycerol as the dispersion medium, poly (3,4-ethylenedioxythiophene): sulfonated lignin (PEDOT:SL) as conductive fillers, and PAA as the skeleton. The organo-hydrogel sensor sensed neck vibrations, a faint pulse, and limb movement. It also exhibited conductive, self-wrinkling, soft, elastic, and anti-freezing qualities. Physiological signals needed for electromyography (EMG) and electrocardiography (ECG) detection could be transmitted via this conductive hydrogel, as described in Figure 4. The organo-hydrogel is non-toxic and may shield skin from frostbite, according to animal studies and cell culture tests [66].

As a catalyst for hydrogel-based bio-electronic sensors, industrial lignin is also employed. For instance, SL, ferric ions (Fe^{3+}), and PAA were the building blocks of a multifunctional hydrogel that was quickly created by Wang and team [68] at room temperature employing a dynamic redox and coordination mechanism (Figure 5). The SL–Fe^{3+} complex speeds up polymerization and permits gelation in a matter of minutes by starting ammonium persulfate (APS) to generate semiquinone and hydroxyl radicals. Excellent mechanical and functional qualities are also imparted by the physically crosslinked network formed by the reversible coordination between Fe^{3+} and SL. The resultant hydrogel has exceptional UV-blocking ability (99.7% at 2 mm thickness), great stretchability (up to 1,680%), conductivity (7.0×10^{-2} S/m), robust adhesion (up to 36.4 kPa), and high transparency (81%). It also has exceptional self-healing capabilities, recovering up to 85.7% of its stretch and 98.5% of its conductivity after damage. This hydrogel is a very promising platform material for the creation of wearable, flexible, and self-healing biosensors as well as electrical interfaces in human–machine systems, even though it is not a biosensor in and of itself [68].

Strain sensor

Flexible strain sensors based on hydrogels can be firmly affixed to the human body and convert mechanical signals (bending, stretching) into electrical ones (resistance, conductivity) due to their unique advantages of flexibility, biocompatibility, and lightweight. This allows for the capture of both large-scale (e.g., joint bending, body movement) and tiny-scale (e.g., pulse, heartbeat, breathing, throat vibration) human body action. Such transduction approaches often involve capacitance, piezo-resistivity, and piezo-electricity [62]. Table 4 shows lignin-based hydrogels in strain sensor applications.

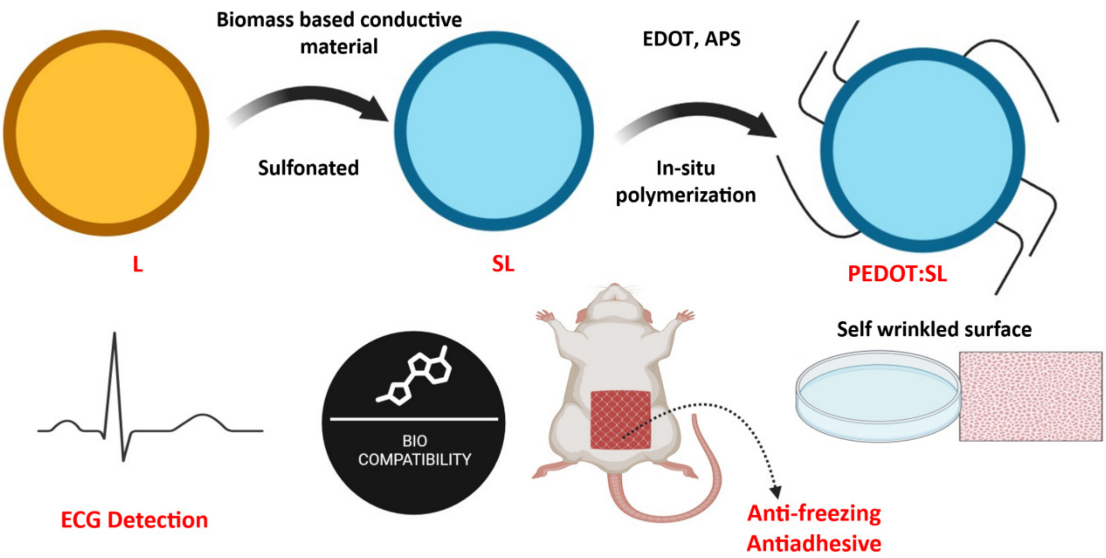


Figure 4. Diagram describing the synthesis, characteristics, and uses of PEDOT:SL-PAA organo-hydrogel.

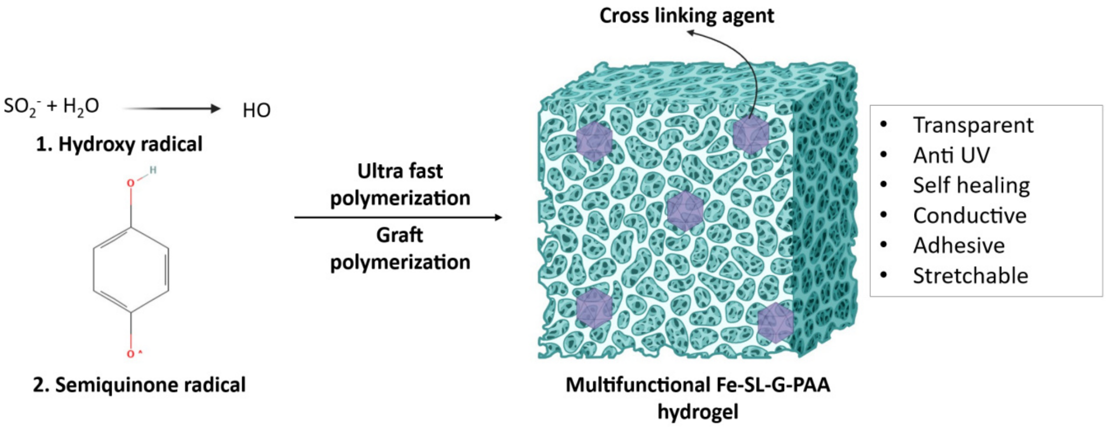


Figure 5. Schematic representation of many fast monomer polymerization processes triggered by free radicals and multifunctional hydrogels made of SL/metal ion chelate crosslinked polymer chains.

An exceptionally flexible and conductive hydrogel was developed by Zhao et al. [75] for advanced strain sensing through the incorporation of sulfonated lignin-coated silica nanoparticles (LSNs), polyacrylamide (PAM), and ferric ions (Fe^{3+}) (Figure 6). Ultrafast gelation within 60 seconds was achieved via the dynamic redox interaction between the catechol groups on the LSNs and Fe^{3+}, resulting in the formation of a robust three-dimensional network. The optimized hydrogel (containing 1.5 wt% LSNs) exhibited outstanding mechanical properties, including an elongation of approximately 1,100%, a tensile strength of ~180 kPa, a compressive strength of ~480 kPa, and a low hysteresis ratio (< 15%), ensuring precise strain recovery. In addition, the abundant catechol groups provided effective UV protection (~95.1%) and excellent self-adhesion to a variety of surfaces, including human skin. The hydrogel demonstrated remarkable repeatability and high-fidelity response as a strain sensor over a broad strain range (10–200%), making it highly promising for long-term, skin-conformal wearable electronics for human motion tracking [75].

Pressure sensor

Pressure sensors are force-sensitive devices that undergo structural changes when physical pressure is applied. These sensors operate by converting, detecting, and quantifying pressure into electrical signals, enabling their use in various electronic applications [82]. The three primary types of pressure sensors are piezoelectric (generate an electrical signal when mechanical stress is applied), capacitive (detect changes in capacitance due to deformation or pressure), and piezoresistive (change electrical resistance in response to applied mechanical strain) sensors. For wearable healthcare monitoring, next-generation piezoresistive

Table 4. Lignin based hydrogels in strain sensor applications.

Hydrogel composition	Lignin kind	Synthesis	Properties	Applications	References
Polyvinyl alcohol (PVA), carboxymethyl chitosan (CMC), cellulose nanofibrils (CNF), lignin-based carbon (LC) nanoparticles	Lignin-derived carbon (LC)	Dispersed lignin-based carbon (LC) was combined with PVA, CMC, and CNF that had been dissolved in water. Several freeze-thaw cycles were used to the mixture in order to create a physically crosslinked conductive hydrogel (PSH)	Tensile strength: 133 kPa, compression stress: 37.7 kPa, excellent stretchability and fatigue resistance	Monitoring palm clutching, finger bending, elbow flexion, wearable flexible strain sensors	[73]
Enzymatic hydrolysis lignin (DEL), poly (vinyl alcohol) (PVA), silver nanoparticles (AgNP)	Enzymatic hydrolysis lignin (DEL)	*In situ* reduction of Ag^+ with sodium citrate in DEL-PVA matrix; promotes nanophase separation and AgNP formation	Strain at break: 1,220%, tensile strength: 13.3 MPa, toughness: 78.1 MJ/m^3, electrical conductivity: ~1.0 S/m	Flexible and wearable strain sensors, motion-responsive electronic devices	[74]
Sulfonated lignin-coated silica nanoparticles (LSNs), polyacrylamide (PAM), ferric ions (Fe^{3+})	Sulfonated lignin	Rapid gelation in ~60 seconds via self-catalytic redox reaction between Fe^{3+} and catechol groups on LSNs	Elongation: ~1,100%, tensile strength: ~180 kPa, compressive strength: ~480 kPa, hysteresis ratio: < 15%	Strain sensors for wearable electronics, human motion tracking	[75]
Lignin-graft-poly(acrylic acid) (LPAA), acrylamide (AM), sodium chloride (NaCl)	Lignin-graft-poly (acrylic acid) (LPAA)	By adding LPAA to an AM/NaCl solution, composite conductive hydrogels were created, creating a hydrogen-bonded crosslinked network without the need for outside stimuli	Excellent UV shielding: 99.95%, good transparency, strain sensing: gauge factor = 2.51 (100–500% strain range), tensile strength: 96 kPa, compressive strength: 0.54 MPa	Wearable strain sensors for physical activity monitoring, flexible and transparent electronics, UV-protective wearable devices	[76]
Gelatin, polypyrrole, sodium lignosulfonate	Sodium lignosulfonate	Simple fabrication via dynamic noncovalent interactions	Biocompatibility, conductivity, high strain sensitivity: GF = 6.08, fast response: 107 milliseconds, strong adhesion: 23.88 kPa to pig skin	Wearable flexible strain sensors, real-time monitoring of human physiological activities	[77]
Lignin–Fe^{3+} self-catalytic system, 2-hydroxyethyl acrylate (HE-AA), [2-(methacryloyloxy) ethyl] dimethyl-(3-sulfopropyl) ammonium hydroxide (DMAPS), water–ethylene glycol (EG) mixture	Lignin–Fe^{3+}	Rapid redox polymerization of lignin–Fe^{3+} with HE-AA and DMAPS in EG solution	Fracture stress: 236.15 kPa, elongation at break: 556.8%, self-adhesion: ~110 ± 3.1 kPa on paper, water retention: 73.7% (non-drying), antifreezing: stable from −60°C to 60°C, sensor performance-gauge factor: 6.044, response time: 198 ms	Strain sensors for skin-mounted flexible electronics, wearable health monitoring and motion tracking	[78]
Poly (acrylic acid) (PAA), liquid metal (LM), TEMPO-oxidized lignin	TEMPO-oxidized lignin	The hydrogel was created by polymerizing acrylic acid with free radicals at room temperature. TEMPO-oxidized lignin was used to stabilize the liquid metal and start the gel formation process	High conductivity, self-healing, strong adhesion, high tensile strength, antibacterial activity (due to lignin), strain sensing accuracy, stable electrical output	Flexible and wearable sensors, electronic skin (e-skin), health monitoring devices, soft robotics	[79]
Lignosulfonate (LS), ferric ions (Fe), nanocellulose	Lignosulfonate (LS)	By combining lignosulfonate, Fe^{2+} ions, and nanocellulose, the hydrogel was quickly created at ambient temperature in 63 seconds without the requirement for UV light or additional heating	Rapid gelation (as fast as 63 seconds with 8 wt% LS), high tensile strength: 227 kPa, excellent elongation at break: 515%, self-supporting and flexible structure	Wearable strain sensors for monitoring human joint movement, flexible electronics, potential for biomedical and motion detection devices	[80]
Sulfonated lignin–silica nanoparticles (LSNs), iron ions (Fe^{3+}), polyacrylamide (PAM), MXene (Ti_3C_2 Tx)	Sulfonated lignin	SNs, Fe^{3+}, and MXene were combined at room temperature to synthesize the hydrogel.	Tensile strength: ~76 kPa, elongation at break: ~700%, self-adhesion: ~19.9 kPa	Flexible and wearable strain sensor electronics, human motion sensing and health monitoring	[81]

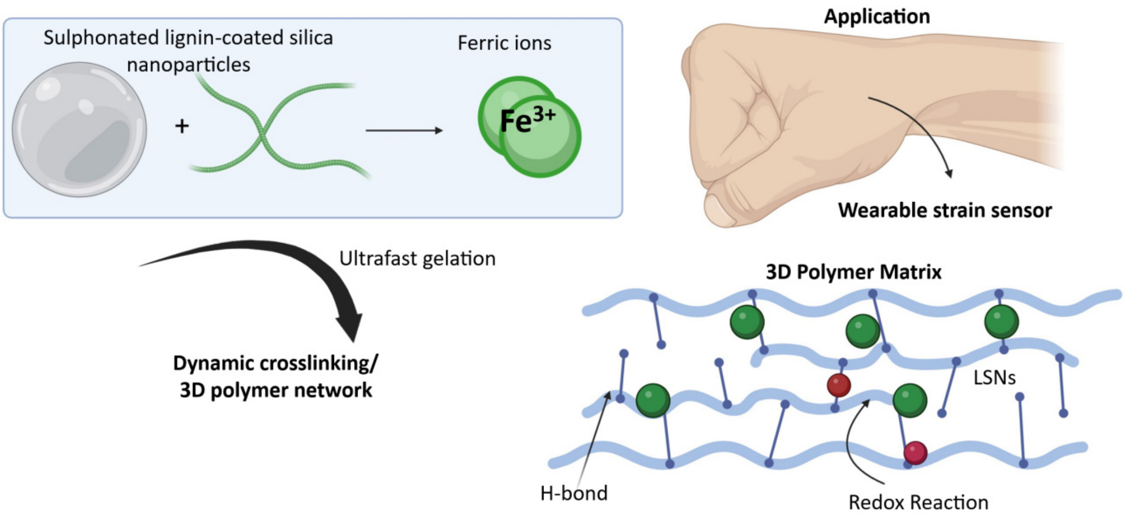


Figure 6. Diagrammatic representation of the manufacture and multipurpose use of a hydrogel based on lignin-coated silica nanoparticles for wearable electronics and strain detection.

sensors should combine high sensitivity with excellent flexibility, compressibility, stretchability, and bending capability, features that are often lacking in traditional piezoresistive sensors made from brittle metals or fabricated on rigid substrates [83]. Pressure sensors, as a subset of tactile sensors, have gained significant attention due to their potential in applications such as precision surgery and diagnostic health monitoring. Hydrogel-based pressure sensors with mechanosensory capabilities can be fabricated from natural polymers rich in functional groups, allowing them to transform pressure input into electrical conductivity output, similar to the mechanism of strain sensors [62]. Table 5 summarizes the various roles of lignin-based hydrogels in pressure sensor applications.

Limitations and challenges in sensor applications

Lignin-based hydrogel sensors generally exhibit good signal stability owing to their crosslinked polymer networks formed through hydrogen bonding, ionic interactions, or metal coordination bonds. These networks help maintain structural integrity during repeated mechanical deformations, such as bending, stretching, or compression, enabling reliable detection of human motion over long periods. However, long-term use may still lead to signal drift because of gradual structural relaxation, hydrogel dehydration, or conductive pathway degradation. Repeated mechanical cycling and environmental exposure can weaken the network, potentially reducing the sensing sensitivity and long-term stability [87].

For wearable and biomedical sensing applications, hydrogels must remain stable under physiological conditions, such as body temperature, sweat exposure, and varying pH. However, continuous exposure to biological fluids, enzymes, and physiological electrolytes can alter the hydrogel network structure, thereby affecting its mechanical strength and conductivity. Over time, swelling, hydrolysis, or partial degradation may occur, which can influence the durability and reliability of the sensing signals [88].

In addition, interference from moisture, salts, and competing ions present in biological fluids can influence the sensing performance. Lignin-based hydrogel sensors often operate through ionic conductivity or resistance changes within hydrated polymer networks. Their performance can be affected by environmental moisture and ions present in sweat or the surrounding media. Water uptake can change the swelling degree of the hydrogel and modify the conductive pathways, leading to variations in the electrical signal. Similarly, ions such as Na^+, K^+, or Cl^- can influence ion transport within the hydrogel matrix, causing fluctuations in resistance to moisture, and ionic interference remains an important challenge for practical sensor deployment. This highlights the need for improved structural design and protective strategies for stable sensing performance [89].

Moisture may change the electrical conductivity or swelling behavior of lignin-based composites, whereas ions such as metal cations or electrolytes can interact with the functional groups of lignin (e.g.,

Table 5. Lignin-based hydrogels in pressure sensor applications.

Hydrogel composition	Lignin type	Synthesis	Properties	Applications	References
Polyvinyl alcohol, lignin-silver hybrid nanoparticles (Lig-Ag NPs)	Alkaline lignin	Alkaline lignin and $AgNO_3$ combine to form Lig-Ag NPs, which are then implanted in a PVA matrix to create a porous hydrogel by dynamic hydrogen bonding and ammonia release	Porous structure (from NH_3 release), exceptional compressibility, high pressure sensitivity, steady and fast signal response	Piezoresistive pressure sensors	[82]
Poly (acrylic acid), lignosulfonate sodium (LS), ferric ions (Fe^{3+}) for asymmetric adhesion	Lignosulfonate sodium (LS)	LS was incorporated into PAA to form a hydrogel, followed by Fe^{3+} ion soaking on the upper surface to induce asymmetric adhesion	Conductivity: ~0.45 S/m, stretchability: ~2,250%, compressive modulus: ~20 kPa (very soft), wearable comfort, anti-interference in sensors	Wearable pressure sensors, skin-adherent but anti-adhesive tissue dressings	[84]
Poly (acrylic acid) (PAA), 3-allyloxy-2-hydroxypropyl lignin (AHP-lignin)	AHP-lignin	Free-radical polymerization was used to create multifunctional hydrogels by combining AHP-lignin with PAA	Self-adhesion, conductivity, UV shielding capacity, pressure sensitivity to small forces, biocompatibility	Wearable pressure sensors, body motion monitoring	[85]
Sodium lignosulfonate–silver, SBMA ([2-(methacryloyloxy) ethyl] dimethyl-(3-sulfopropyl) ammonium hydroxide)	Sodium lignosulfonate	Using sodium lignosulfonate–silver nanoparticles and SBMA as functional monomers, hydrogel was created at room temperature through redox-triggered polymerization	Excellent mechanical strength and flexibility, antimicrobial activity (from silver), antioxidant activity (from lignosulfonate), electrical conductivity (suitable for sensors), anti-freezing ability (due to SBMA), rapid gelation at room temperature	Pressure/strain sensors, wound dressings	[86]

phenolic or carboxylic groups), potentially altering the sensing signal. These interactions may lead to signal drift, reduced selectivity, and decreased reproducibility in complex biological environments [90].

Biomedical applications of lignin-based hydrogel

Hydrogels derived from lignin exhibit significant potential for biomedical applications. Combining lignin with other polymers improves the rigidity, mechanical strength, stability, water uptake, viscoelasticity, and controlled-release properties of hydrogels, making them suitable for tissue engineering, wound healing, drug delivery, and 3D bioprinting [50]. Hydrogel applications are often divided into two distinct categories: biomedical and environmental [15].

Lignin-based hydrogel in a drug delivery system

Drug delivery systems aim to enhance the therapeutic efficacy and disease-targeting properties of a drug molecule at a controlled rate, along with reducing severe adverse effects [50]. Currently, lignin-based drug transporter systems, such as hydrogels, have been employed for efficient drug delivery. Active pharmaceutical ingredients (API) can be incorporated into lignin-based carriers via inclusion, adhesion, encapsulation, and chemical modification. Lignin can (i) safeguard light-sensitive compounds, (ii) facilitate the dispersion of the active components in either liquid or solid composites, (iii) prevent the unintentional loss of volatile and potentially harmful active ingredients, and (iv) substitute synthetic polymers currently employed in these applications [9].

The unique properties of hydrogels, such as their ability to retain water, biocompatibility, and controllable swelling behavior, have made them increasingly valuable in drug delivery systems. The gel matrix can be easily manipulated by adjusting the type and quantity of crosslinking agents because they are porous. In addition, drugs can be loaded into the gel matrix more easily. The drug is released in a rate-dependent manner based on the diffusion coefficient of the drug molecules through the gel network [91]. For example, Preet and coworkers prepared lignin–chitosan–chondroitin sulphate–PVA hydrogel. The results showed controlled and pH-dependent drug release (higher at pH 7.4), indicating a diffusion-based release owing to the porous lignin network [92]. Similarly, Morales and coinvestigators [93] prepared lignin-based hydrogels using PVA and different types of modified lignin (alkaline and organosolv lignin from almond and walnut shells). The hydrogel followed the Korsmeyer-Peppas model and exhibited Fickian diffusion behavior ($n < 0.5$), indicating that the drug diffused out mainly through the hydrogel matrix [93].

Hydrogels can be administered via various routes, including systemic distribution by intravenous infusion, local needle injection, topical administration, and surgical implantation. The choice of delivery route is based on the dose size and patient compliance [91]. Lignin-based hydrogels can deliver both water-soluble and lipid-soluble drugs because of the presence of hydrophobic and hydrophilic groups in the lignin backbone, making them suitable for drug delivery applications [8].

Lignin possesses a highly aromatic structure composed of phenylpropane units, which enables strong π–π stacking interactions with drug molecules that contain aromatic rings [94]. These interactions occur when the delocalized π-electron systems of the aromatic rings of lignin align with the π-electron clouds of aromatic drug molecules, creating stable non-covalent associations. Such stacking interactions help enhance the drug loading capacity and stabilize the drug within lignin-based carriers, including lignin-derived metal–organic frameworks (MOFs) and covalent organic frameworks (COFs) [95]. For instance, Zhou and coworkers [96] developed lignin hollow nanoparticles (LHNPs) from renewable lignin using a self-assembly method as a carrier for doxorubicin (DOX) (an anticancer drug). They found that LHNPs exhibited a good drug loading capacity (~60%). The drug loading mechanism involves H-bonding, electrostatic attraction, and π–π interactions between lignin and DOX [96].

Drug release from lignin-based systems generally follows diffusion- or swelling-controlled mechanisms. Commonly applied release kinetics models include the zero-order (constant release rate), first-order (concentration-dependent release), Higuchi (diffusion-controlled release proportional to the square root of time), and Korsmeyer-Peppas models, which help determine whether the release mechanism is Fickian diffusion, anomalous transport, or polymer relaxation-controlled. In many lignin-based hydrogels and nanoparticles, the release behavior fits the Higuchi or Korsmeyer-Peppas models, indicating that drug diffusion through the porous polymer matrix is the dominant mechanism [97].

In lignin-based materials, π–π stacking not only facilitates the efficient encapsulation of hydrophobic or aromatic drugs but also contributes to controlled and sustained drug release, as the drug molecules remain temporarily bound to the lignin matrix. Environmental factors, such as pH, solvent polarity, and ionic strength, can influence these interactions, enabling responsive drug release under physiological conditions [98]. Farhat et al. [99] developed pH-responsive hydrogels using natural polymers, such as lignin, starch, and hemicellulose. Drug release was controlled by swelling-dependent diffusion, where higher swelling (at higher pH) led to a faster release of molecules. The release mechanism follows anomalous transport ($0.5 < n < 1$), indicating that both diffusion and polymer relaxation control drug release. Lignin influences drug release by contributing to the crosslinked structure, where increased crosslinking reduces swelling and slows down the release. Its natural structure helps to form stable, controlled-release hydrogels [99].

Importantly, lignin-based carriers are often stimulus-responsive in physiological environments. Under different pH conditions (such as acidic tumor microenvironments or gastric fluid), ionizable groups in lignin (e.g., phenolic and carboxyl groups) undergo protonation or deprotonation. At low pH, protonation can weaken electrostatic interactions and hydrogen bonding, thereby accelerating drug release. At neural or basic pH, deprotonation may increase swelling and electrostatic repulsion within the hydrogel network, thereby enhancing drug release. Additionally, lignin is susceptible to enzymatic degradation, particularly by oxidative enzymes (e.g., peroxidases and laccases), which can gradually break down the polymer matrix and promote controlled drug release. This enzyme responsiveness supports biodegradability and reduces long-term accumulation in the body [6, 19].

Zhu and coworkers [25] developed a pH-responsive sprayable hydrogel using carboxymethyl chitosan combined with trans-resveratrol-loaded lignin-based nanoparticles as the drug carrier. The drug release mechanism depended on pH, it followed Fickian/non-Fickian diffusion at neutral and alkaline pH and showed zero-order release at skin-like pH (∽6.0). Lignin-based nanoparticles controlled the release via pH-sensitive solubility and thus enabled tunable drug release behaviour [25]. Recent developments in lignin-based hydrogels for drug delivery are summarized in Table 6.

Lignin based hydrogel in wound healing

Wound healing is a normal physiological mechanism associated with tissue structural injury, usually divided into four stages: homeostasis, inflammation, proliferation, and remodelling, involving various cells and endogenous substances [50].

To speed up and to provide complete wound healing, several types of wound dressing have been identified such as gauze, hydro fibres, film, foam, hydrocolloids and hydrogels. Although, several currently utilized wounds dressings exhibit limitations, for example, they may obstruct the circulation of gases between the wound and its surroundings, thereby making it challenging for both nutrients and oxygen to pass through the wounded area. Furthermore, some dressings are difficult to remove, may not offer appropriate protection against microbiological invasions or preserve sterility, and can provoke allergic reactions [107].

Hydrogels offer several advantages, such as they have the ability to absorb and hold a considerable amount of water in the network, allowing it to keep a humid environment in the wound region, thereby improving wound therapy and management [108]. Moreover, hydrogels offer a flexible framework for incorporating other substances, including medications, antimicrobial and antibacterial agents, as well as additional biomolecules, which increases their overall effectiveness in accelerating wound healing [109]. Microbes can contaminate wounds and adhere to dressings, increasing infection risk, as most wound infections are caused by bacteria. Lignin, a natural biopolymer, is an excellent agent for wound dressing as it possesses various functional groups in its structure, which are responsible for the antimicrobial, antioxidant, and anti-inflammatory activity as described in Figure 7.

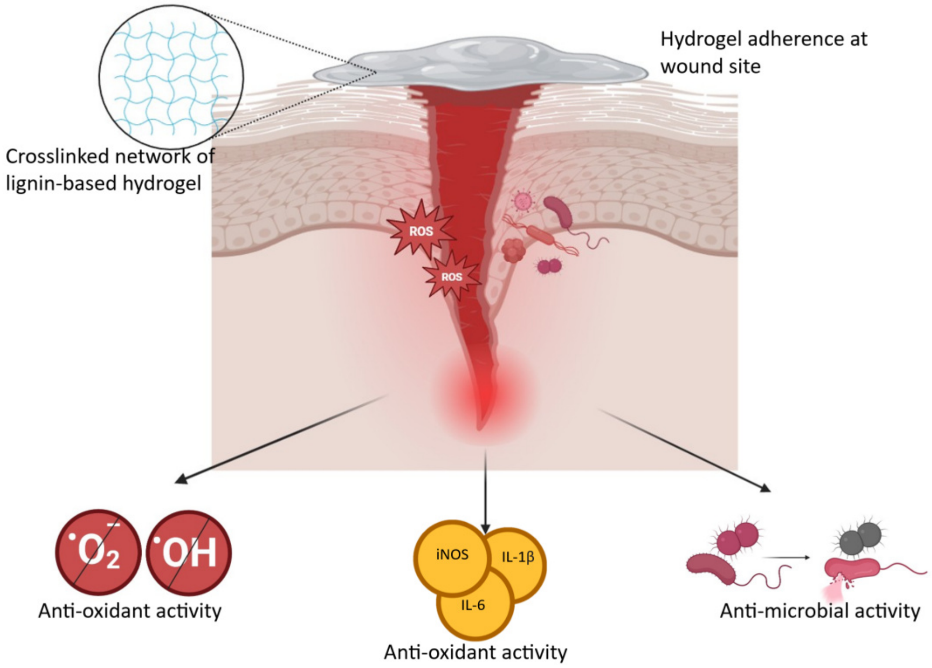


Figure 7. Schematic illustration of a lignin-based hydrogel applied at a wound site.

Table 6. Applications of lignin-based hydrogel as a drug delivery carrier

Material	Drug used	Method	Properties	Application	Reference
Cellulose/lignin hydrogel (95:05 ratio)	Paracetamol	Mixture of cellulose and lignin in NaOH/urea, freeze-thaw, addition of epichlorohydrin as crosslinker, freeze-dry	Pore size:100–160 μm, swelling dec slightly. Diffusion: 1.1 × 10^{-4} cm^2/s. Mechanical strength: high compressive. Modulus (~11 kPa) achieved	Enhance release of paracetamol (~50%) than pure cellulose hydrogel	[100]
Lignin/β-cyclodextrin (LCD) matrix	Ketoconazole (K) & Piroxicam (P)	β-Cyclodextrin crosslinked with lignin using epichlorohydrin, followed by loading of drugs into the matrix	*In vitro* release studies (Korsmeyer-Peppas model) revealed that the LepCD-based materials released medicines at a slower rate (k = 1.117–1.789) compared to LCD-based materials with a constant release rate (k = 2.210–4.824)	Used as drug carrier	[101]
Gelatin/lignin hydrogel using EDC as cross linker	Ribavirin	Lignin + NaOH solution, to which gelatin is added. Magnetically stirred & left overnight at 80°C to obtain an aqueous solution. EDC is used to crosslink the gelatin/lignin sample	Higher lignin concentration (3%) in gelatin/lignin hydrogels resulted in greater cumulative ribavirin release i.e., 68% higher as compared with gelatin hydrogel after 270 min	For antiviral drug delivery	[102]
Lignocellulose nanofibril-poly(vinyl alcohol) hydrogel	Tetracycline hydrochloride	Crosslinking	high compression modulus (3.92 MPa) and significant sustained-release effect with a release rate of 80.73% after 336 h	Potential for controlled drug delivery system	[103]
M-HPMC/M-SLS hydrogel (methacrylate hydroxypropyl methylcellulose (M-HPMC) and methacrylate lignin (M-SLS) hydrogel)	Alpha-pinene (α-pinene)	Preparation of nanostructured lipid carriers (NLCs) and loading of α-pinene into NLCs. α-pinene-loaded NLCs (0, 18, 38, and 50 wt%) were encapsulated in M-HPMC/M-SLS hydrogel	Controlled α-pinene release for up to 96 h, shows significant antioxidant activity. Increased adhesive strength (113.5 ± 7.5 kPa) to bovine buccal mucosa	Buccal mucoadhesive hydrogel for the potential application in the treatment of oral ulcers	[104]
Cotton stalk lignin hydrogel	Curcumin, naringenin, α-lactalbumin	Lignin + HEC polymerization in the Prescence of PEG400 (2–4%) & 1–3% glycerol. Addition of actives by mixing at 50–80°C at 2,000 rpm to form hydrogel	Pore size: 283 nm (ocular). Swelling ratio: high (about 385%). Mechanical strength: tensile strength: 0.63 MPa. Elasticity modulus: 0.52 MPa	For topical ocular treatment of diabetic retinopathy	[105]
CP loaded lignin based PVA hydrogel	Ciprofloxacin	–	Cumulative drug release found to be 88.2 ± 3.2% after 10 h. CP-loaded hydrogel exhibits antibacterial activity towards *Staphylococcus aureus*, *Bacillus subtilis*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*	Can be used as pharmaceutical carrier. Useful for sustained release applications	[106]

The antioxidant activity of lignin is primarily attributed to its abundant phenolic and oxygen-containing functional groups, which are capable of neutralizing reactive free radicals. Phenolic hydroxyl groups present in lignin can denote hydrogen atoms or electrons to reactive radicals through single-electron transfer and hydrogen atom transfer mechanism, thereby terminating oxidative chain reactions. This radical scavenging ability enables lignin to reduce the accumulation of reactive oxygen species (ROS) that are responsible of oxidative stress in biological systems [110]. From a clinical perspective, controlling oxidative stress is particularly important in wound healing and tissue regeneration, where excessive ROS can damage cellular membranes, proteins, and DNA, ultimately delaying tissue repair. By scavenging free radicals, lignin-based materials can help protect surrounding tissues, reduce inflammation, and promote a favorable environment for cell proliferation and healing [111]. As showed by the lignin–chitosan–chondroitin sulphate–PVA hydrogel made by Preet et al. [92], which showed antioxidant activity by effectively neutralize free radicals and reduce oxidative stress. This activity is mainly due to lignin’s phenolic hydroxyl groups, which donate hydrogen atoms or electrons to stabilize free radicals, thereby preventing cellular damage [92].

In addition to antioxidant effect, certain functional groups in lignin, such as methoxy and epoxy groups, contribute to antibacterial activity by disrupting bacterial cell membranes and inducing cell death [111]. For instance, Ciolacu and team [112] developed cellulose-modified lignin (CLE) hydrogels using cellulose and chemically modified lignin, cross-linked with epichlorohydrin. Antibacterial activity was tested against *Escherichia coli* and *Staphylococcus aureus*, showing increased effectiveness with higher lignin content. Lignin inhibits bacteria by its hydroxyl and methoxyl groups interacting the cell membrane of bacteria, causing membrane disrupting and leakage of cellular contents, making them suitable for wound healing application [112].

Lignin naturally acts as a defence barrier and can inhibit bacteria, fungi, and viruses, making it a promising natural antimicrobial material. The antibacterial activity of lignin is mainly associated with its phenolic hydroxyl groups, which can damage bacterial cell membranes and lead to cell lysis. Lignin has been reported to inhibit certain fungal species, although the exact mechanism of fungal suppression is not yet clearly understood [113].

The anti-microbial effectiveness largely depends on the source of lignin and the extraction method used, as these factors influence its chemical structure and functional groups. For instance, Kraft lignin has been reported to effectively inhibit gram-positive bacteria such as *Listeria monocytogenes* and *Staphylococcus aureus*, while other lignin types extracted from eucalyptus have shown activity against both gram-positive bacteria (*Bacillus cereus*, *Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli*, *Salmonella enteritidis*). Research has reported that kraft lignin can inhibit the growth of fungi such as *Aspergillus niger*, *Mucor circinelloides*, and *Penicillum solitum* [113]. However, kraft lignin derived from eucalyptus has demonstrated particularly strong antifungal activity against *Aspergillus niger* compared to other lignin types [114].

In contrast, lignosulfonates display broad antimicrobial activity, which is mainly attributed to their anionic surfactant nature due to presence of sulfonate groups. These charged structures enable lignosulfonates to interact with cellular components such as lipids and proteins, disrupting normal microbial cell functions and inhibiting growth. Soda lignin has been reported to shown moderate antibacterial activity, particularly against gram-positive bacteria such as *Staphylococcus epidermidis* and *Bacillus* species. However, it has shown little or no activity against microorganisms, such as *Escherichia coli* and *Aspergillus niger*. The anti-microbial effectiveness of soda lignin can also vary depending on processing conditions such as extraction temperature and biomass source [115]. Thus, lignin-based hydrogels offer numerous advantages in wound healing applications in Table 7.

Lignin-based hydrogel in cosmeceuticals

Because of its outstanding antioxidant activity and remarkable ability to absorb UV radiation, lignin hydrogel has been proposed as a suitable alternative for cosmetic applications [122]. The UV absorption property of lignin is due to the presence of UV chromophore groups such as phenolics, hydroxyl groups (OH), conjugated double bonds, and carbonyl groups (C=O) [123]. However, limited studies have been conducted on the development and use of lignin hydrogels in cosmetic formulations. For example, Darmawan et al. [124] developed a natural sunscreen formulation using *tengkawang butter* (as the base) combined with different types of lignosulfonates (Ca, Mg, and Na forms) at varying concentrations (1–10% *w*/*w*). The SPF evaluation showed a significantly higher UV protection, with sodium lignosulfonate due to lignin's chromophore structure; additionally, π–π stacking increases light absorption efficiency. However, the study has key limitations such as poor solubility and dispersion of lignin in lipid-based systems, leading to stability issues, time-consuming formulation, and inconsistent SPF behaviour. Moreover, results are limited to *in-vitro* studies, requiring further *in vivo* testing and compatibility assessment before practical cosmetic application [124].

Wang and team [125] produced a natural hair conditioner with a micellar lignin hydrogel emulsion system that has 26% lignin and 6% coconut oil as triglycerides. The results showed that the lignin gel emulsion remains stable after one year of storage; this suggests a longer shelf life for possible commercial use. Compared to the commercial product, the lignin gel-based conditioner effectively smooths damaged

Table 7. The various applications of lignin-based hydrogels in wound healing.

Material	Preparation method	Function/activity	Target pathogen	Findings	Reference
Lignin-graft polyoxazoline conjugated triazole	Polymerization & covalent modification	Anti-biofilm activity, anti-inflammatory	*Pseudomonas aeruginosa*	Biofilm activity: reduction in thickness of biofilm structure from 30 nm to 8 nm (treated) after 12 h incubation; anti-inflammatory: inhibits LPS-induced iNOs, IL-1β, TNF-alpha α	[116]
Lignin-based hydrogel	Solid state esterification with PEG and poly (methyl vinyl ether-*co*-maleic acid)	Anti-microbial	*Staphylococcus aureus*, *Proteus mirabilis*	Significant reduction in bacterial adherence observed (up to 5-log)	[117]
Ag-Lignin NPs-PAA-pectin hydrogel	Formulation of Ag-lignin nanoparticles followed by polymerization with pectin and acrylic acid	Anti-bacterial, wound healing	*Staphylococcus epidermidis*, *Escherichia coli*	Bactericidal ratio of hydrogel for *Staphylococcus epidermidis* and *Escherichia coli* was found to be 98% and 97%, respectively. Healing ratio found to be 90%	[118]
AgNPs-lignin hydrogel	Crosslinking and *in-situ* gelation	Anti-microbial	*Staphylococcus aureus*, *Escherichia coli*	Complete bactericidal inhibition at high concentration (up to 10^8 cfu/mL)	[29]
Lignin-MA/SBMA double network hydrogel	Free radical polymerization of SBMA and lignin-MA	Antimicrobial, anti-fouling	*Staphylococcus aureus*, *Escherichia coli*	40% lignin -MA hydrogel showed 94.8% reduction of *Escherichia coli* and 95.7% reduction of *Staphylococcus aureus*	[119]
Lignosulfonate-PVC composite hydrogel	Covalent interaction (hydrophobic) induced gelation (i.e., physical crosslinking)	Self-wound healing, tissue adhesiveness	–	Rat liver bleeding model: bleeding decreased from 196.7 mg to 29.4 mg (treated) within 60 s. Strong adhesion of 41.3 kPa to liver tissue	[120]
OTC-loaded lignin chitosan bio composite hydrogel	Freeze thaw method (5 cycles)	Antibacterial, wound healing, antioxidant	*Staphylococcus aureus*, *Escherichia coli*	Strong antibacterial activity: zone of inhibition found to be 2 mm (*Escherichia coli*) and 24.5 mm (*Staphylococcus aureus*). Antioxidant activity: 39.3% RSA (at 50 mg)	[92]
PVA-CS-EGCG hydrogel	–	Anti-bacterial, wound healing	*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Salmonella Typhimurium*	Antibacterial (MIC/MBC): effective inhibition and bactericidal effect at 0.22–0.88 mg/mL against pathogens	[121]

hair, as shown by a 13% reduction in wet combing force. Additionally, due to its phenolic component, lignin offers natural UV protection and significant antioxidant activity. These findings indicate that developing a completely natural hair conditioner with lignin gel emulsions could help advance sustainable personal care products [125].

Another study demonstrated the use of a lignin hydrogel patch in the treatment of Atopic dermatitis, a chronic skin disease. Trinh and co-workers prepared a therapeutic antioxidant lignin hydrogel patch using lignin powder and the cross-linker poly (ethylene glycol) di-glycidyl ether (PEG-DGE). The study includes the AD mouse model and the results demonstrate that the hydrogel patch successfully reduced the thickness of the epidermis, inhibited inflammation, and reduced oxidative damage to DNA, which helped to regulate oxidative stress in cellular functions. The results of these studies suggest that lignin hydrogels can significantly reduce the inflammatory immunological response associated with atopic dermatitis due to their inherent ROS-scavenging characteristics. Thus, the study shows that the potential application of lignin hydrogel patches in the treatment of various skin diseases associated with inflammation and oxidative stress in the skin [126].

Despite the promising antioxidant, UV-protective, and antimicrobial properties of lignin, its translation into commercial cosmetic formulation remains limited due to several scientific and regulatory challenges. One major limitation is the intrinsic dark brown color of lignin. Most technical lignin, such as kraft and soda lignin, possesses a dark to black coloration. When incorporated into cosmetic formulations such as creams, lotions, or sunscreens, this color can significantly alter the appearance of the final product. Since cosmetic products are highly dependent on visual appeal and consumer perception, the strong pigmentation of lignin may limit its use or require additional purification and modification processes to produce lighter or color-controlled derivatives [127, 128].

Restu and team [129] developed a natural cream-based sunscreen using lignin as the active UV-protection ingredient. The SPF study showed a maximum SPF ≈ 15 at 2% lignin, indicating effective UV-protection. However, a key drawback of the study was its intrinsic dark brown color, which negatively affects the aesthetic acceptability of cosmetic products, along with poor solubility and dispersion issues in cream formulation. As a potential solution, the study implies that reducing particle size, improving purification, or modifying lignin chemically can enhance dispersion and performance. Additionally, formulation strategies (better emulsification system) may help overcome these limitations, although further optimization and research are still required for practical cosmetic use [129].

Another important challenge is the unpleasant odor associated with technical lignin, particularly kraft lignin, which arises from volatile organic compounds such as guaiacol, acetic acid, and sulfur-containing molecules generated during pulping processes. This odor can negatively affect the sensory quality of cosmetic formulations and requires additional purification or chemical modification steps [130].

In addition, lignin exhibits poor solubility, dispersion, and compatibility with conventional cosmetic bases, which can lead to aggregation, phase separation, and instability in emulsions or gels. These formulation difficulties arise mainly from the highly heterogeneous and complex aromatic structure of lignin [131].

Lignin is still considered a novel bio-based cosmetic ingredient, and therefore requires extensive toxicological evaluation, skin irritation testing, and regulatory approval before commercialization. The lack of comprehensive long-term safety data and standardized quality specifications for cosmetic-grade lignin further delays its regulatory acceptance and industrial adoption [127].

Lignin-based hydrogel in tissue engineering

Tissue engineering is a multidisciplinary science that aims to repair and rejuvenate diseased and deteriorated tissues and organs using appropriate and biocompatible substances that imitate native and original tissues, resulting in the restoration and enhancement of tissue function [132].

Various techniques can be used to generate tissues or organs. The common strategy associated with the concept of tissue engineering is the utilization of healthy cells seeded on a natural or fabricated extracellular matrix (known as a scaffold) to construct implantable segments of the organism [133], as illustrated in Figure 8. Scaffolds serve the following primary purposes: (a) transport the propagated cells to the intended location within the patient's body; (b) stimulate interactions between the cells and the biomaterial; (c) encourage cell adhesion; and (d) allow for the proper passage of gases and growth factors to assure survival, development, and differentiation of cells [134].

Recently, hydrogels have been most widely used as scaffolds due to their high swelling capacity, ability to mimic the extracellular matrix, and desirable mechanical properties. It has been demonstrated that scaffolds made of lignin are effective in stimulating the production of new bone. This is because lignin has the ability to promote osteogenic cell proliferation, which is a necessary step in the process of bone formation. Furthermore, additional findings indicated that lignin might rectify aberrant bone remodelling by suppressing osteoclast differentiation [135]. For bone regeneration, the scaffold should possess high mechanical strength. Lignin-based hydrogels illustrated excellent mechanical properties. It has been shown that the stiffness, tensile strength, and storage modulus of hydrogels all rise substantially with an increase in the concentration of lignin, thereby making them suitable for bone regeneration applications [136].

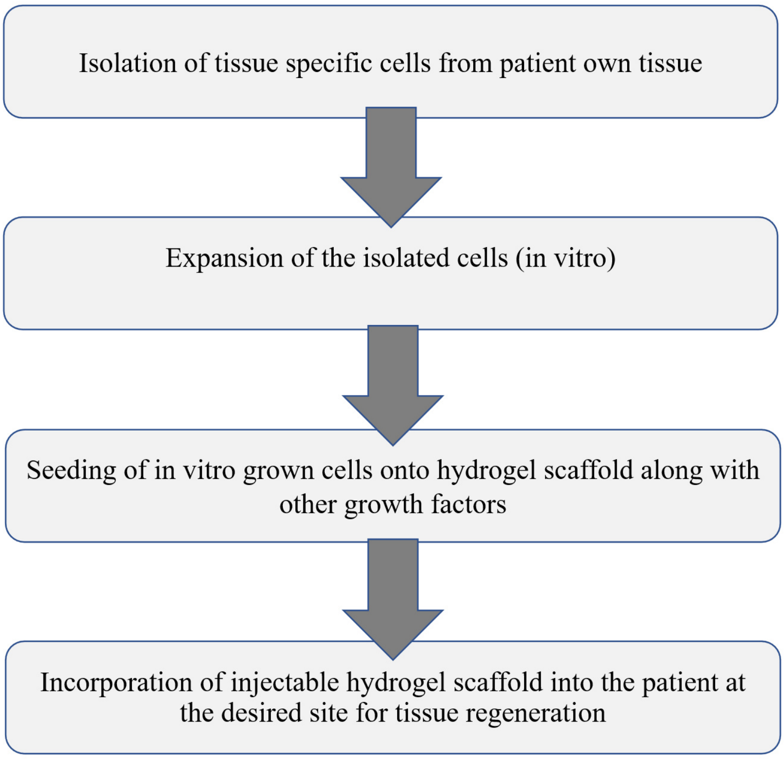


Figure 8. Diagrammatic representation of a typical injectable hydrogel scaffold-based tissue engineering approach, illustrating cell isolation, *in-vitro* cell expansion, cell seeding onto the hydrogel scaffold with growth factors, and subsequent injection into the patient.

Wang and coworkers [137] developed a biomimetic bone scaffold using electrospun lignin/polycaprolactone nanofibers, which were mineralized in simulated body fluid to form bone-like hydroxyapatite (Hap). The phenolic and hydroxyl groups of lignin chelate Ca^{2+} ions and promote nucleation and growth of Hap through co-precipitation with PO_4^{3-}, mimicking natural bone mineralization. This Hap-coated surface enhances osteogenic cell proliferation, promoting osteoblast adhesion, which strengthens cell-matrix interactions and supports bone-like tissue development. However, limitations include restricted cell penetration due to dense nanofiber structure and the study being limited to *in-vitro* evaluation, requiring *in-vivo* validation and scalability assessment for clinical application [137].

Zheng and team [138] developed a bone-protective therapeutic system using lignin-carbohydrate complexes (LCC) isolated from wheat straw. These materials help to protect bones. Lignin part (LCC-A) involves strong anti-oxidant/ROS scavenging activity, and carbohydrate part (LCC-B) acts by promoting osteogenic cell proliferation and differentiation by activating natural cell defence pathways. The limitations are that the exact working mechanism is not fully clear, and it is still in the early research stage [138].

Here, Table 8 demonstrates the potential of lignin-based hydrogel applications in tissue engineering.

Stimuli-responsive applications of lignin-based hydrogels

Stimuli-responsive hydrogels are hydrogels that react rapidly to slight variations in chemical or physical conditions. They are also referred to as *intelligent*, *smart*, or *environmentally sensitive* hydrogels [140]. These systems can respond to a variety of stimuli, including chemical factors (e.g., pH, ions) and physical factors such as temperature, light, or magnetic fields [141].

For developing lignin-based hydrogels that respond to stimuli, it is useful either to directly synthesize sensitive molecules within the hydrogel matrix or to incorporate such molecules into preformed lignin hydrogels [142]. For example, the most common approach for producing thermo-responsive lignin-based hydrogels is to introduce temperature-sensitive monomers into the lignin hydrogel network [7]. Similarly, pH-responsive polymers, a subset of stimuli-responsive polymers, can alter their structure and functional properties in response to the pH of the surrounding medium. Due to the presence of hydroxyl and carboxyl

Table 8. The various uses of lignin-based hydrogels in tissue engineering.

Components of hydrogels	Method of preparation	Properties achieved	Target tissue/cell	Application	References
Lignin nanoparticles + polyacrylamide	Ultrasonic dispersion of lignin nanoparticles and *in-situ* free radical polymerization	High cell viability was observed; the cells retained the ability to proliferate	Esophageal squamous carcinoma cells	Cancer-related tissue modelling	[136]
Gelatin + 2% lignin	Crosslinking of lignin with gelatin to form cryogels	Compression modulus: increases 1.8 times compared to neat gelatin gel; compression stress increases 7 times; supports bone cell differentiation	Bone cell	Bone tissue engineering scaffolds	[139]
Chitosan + alkali lignin	Inotropic crosslinking of chitosan with lignin (crosslinker)	Support cell adhesion (confirmed by HR SEM and fluorescence microscopy); porosity of hydrogel was found to be 72.53%; no cytotoxicity at 50 μg/mL concentration	Fibroblast/stem cell	Stem cell support scaffold tissue engineering	[28]

groups, lignin is naturally susceptible to pH changes. As a result, pH-responsive polymers can be coupled with lignin to create pH-sensitive lignin-based functional materials [143].

Light-responsive (or photo-responsive) hydrogels are another type of stimuli-responsive system and are generally categorized into two types: photodynamic therapy (PDT) and photothermal therapy (PTT). PDT can be applied in antimicrobial photodynamic therapy (APDT) and as antimicrobial coatings for treating wounds, acne, and other microbial infections. Upon exposure to an appropriate wavelength of light, the photosensitive substance becomes excited, and during relaxation, oxygen molecules are converted into ROS, which destroy bacterial cells. PTT, on the other hand, uses photothermal agents (PTAs) to generate heat in order to damage or kill abnormal cells or tissues. Both approaches act through direct structural damage rather than metabolic interference, resulting in minimal bacterial tolerance [144]. A key challenge in antimicrobial light therapy is the aggregation and uncontrolled release of photosensitive or photothermal agents. This limitation can be addressed by incorporating these agents into compatible hydrogels, which enable stable encapsulation and efficient delivery [145].

Additionally, lignin-based hydrogels offer distinct advantages in terms of sustainability, intrinsic antioxidant activity, and UV-blocking capacity in comparison to synthetic smart polymers such as PNIPAM, PEG-based systems, and other engineered stimuli-responsive networks. Lignin-based hydrogels and synthetic polymer hydrogels differ significantly in terms of their origin, structural characteristics, functionality, and performance. Lignin-based hydrogels are derived from lignin (natural source) as compared to synthetic polymer hydrogels produced through polymerization of synthetic monomers such as PEG, PVA, polyacrylamide (PAAm), and poly(*N*-isopropylacrylamide) (PNIPAM). Due to their natural origin, lignin-based hydrogels are considered more sustainable and environmentally friendly [35, 36].

Unlike many petroleum-based synthetic polymers, lignin shows low toxicity, natural antioxidant activity, UV resistance, and enzymatic degradation, which make it attractive for biomedical and environmental applications. In terms of swelling behaviour, lignin-based hydrogels typically exhibit swelling ratios around 500–900%, and in some lignocellulosic composites even above 1,000%, which is comparable to many synthetic polymer systems. However, synthetic superabsorbent polymers such as poly (acrylic acid)-based systems can reach much higher swelling capacities, up to 2,000%. Mechanically, lignin improves rigidity and increases storage modulus (G’ > G”) due to its aromatic and nano-aggregated structure, but synthetic double-network hydrogels can achieve superior tensile strength (often 1–10MPa) and very high elongation (> 1,000%), making them more flexible and mechanically tunable [146].

However, the major limitation of lignin is its complex, heterogeneous, and source-dependent structure (e.g., kraft, orhanosolv, lignosulfonate), which leads to variability and lower reproducibility compared to precisely engineered synthetic polymers. Moreover, while lignin-based hydrogels show pH and moderate temperature responsiveness due to hydroxyl and carboxyl groups, synthetic smart polymers can be designed with highly controlled stimuli responsiveness, such as exact lower critical solution temperature (e.g., ~32°C in PNIPAM). Therefore, hybrid systems combining lignin with synthetic polymers are often considered the most promising strategy to balance environmental sustainability with high-performance material properties [147]. The various applications of stimuli-responsive lignin-based hydrogels are summarized in Table 9.

Energy-based applications of lignin-based hydrogel

Conductive hydrogel-based devices have drawn a lot of interest in the fields of wearable devices, physical activity, and personalized drug therapy. Hydrogel devices require strong conductivity to convert external mechanical inputs into feasible electrical signals. These systems require a consistent electric supply of external energy more significantly, when employed as strain sensors or electronic patches/skin [69]. This external energy may be accomplished via a variety of techniques, including thermal, battery-based, electrochemical, and supercapacitor devices, although supercapacitors receiving popularity due to their widespread uses and higher performance [152]. Supercapacitors, a category of electrochemical energy storage systems, offers a feasible solution for energizing wearable bioelectronics and implantable healthcare devices. Wearable and implantable electronics (WIEs) are primarily made up of circuits, power units, and sensors or conducting electrodes. Since they are often affixed to the human body either internally (implanted) or outwardly, each component must be small, thin, flexible, secure, and comfortable. Numerous WIEs have been created to track physiological responses including blood pressure, heart rate, glucose levels, and neurological activity, allowing for rapid and precise diagnosis and therapy implementation, as well as evaluation of treatment effectiveness [153]. Also, supercapacitors provide a secure and reliable energy source for implantable medical devices, including drug delivery system, pacemakers, and neurological implants [154]. In the supercapacitor, hydrogels can be used as an electrode, electrolyte, or both functions simultaneously [152]. Electrolytes, a key component of capacitors, batteries, and other electronic items, are vital carrier of ions as they move during charging and discharging and have been widely employed in energy storage devices and flexible sensing. In comparison to conventional electrolytes, such as pure solid and liquid electrolytes, hydrogel electrolytes have received a lot of attention due to their high mechanical properties, rigidity, and excellent environmental adaptability [143]. Generally, lignin has been employed exclusively as an electrolyte and electrode material. It is a strongly crosslinked aromatic polymer with a considerable number of carbonyls and phenolic or phenolate groups. Due to these unique physicochemical features, lignin is regarded as a potential candidate for the development of efficient electrodes and electrolytes [26]. Currently, the most common lignin-based electrolytes are hydrogels used to build solid-state supercapacitors. At present, there are limited techniques for turning lignin into electrolytes for supercapacitors, thus more straightforward preparation techniques need to be investigated [155]. Table 10 demonstrates recent advancements related to lignin-based hydrogel electrolytes in the field of energy storage devices.

Conclusion

Lignin-based hydrogels emerge as a promising class of sustainable and multifunctional biomaterials combining biodegradability, inherent anti-oxidant activity, UV-shielding ability, and tunable physicochemical properties. Lignin is not merely a passive filler but an active functional component as its aromatic structure, phenolic groups, and linkage chemistry directly influence hydrogel performance by affecting mechanical strength, swelling behaviour, drug release, and biosensing capability. Chemical modification strategies (such as grafting, crosslinking, and controlled polymerization like ATRP/RAFT) play a crucial role in overcoming lignin’s inherent heterogeneity and poor processability, enabling better control over network architecture and functionality.

Table 9. The various types of stimuli responsive lignin-based hydrogels and their applications.

Material	Stimuli response type	Agent	Properties	Application	References
Lignosulfonate-NIPAM-IA hydrogels	Temperature sensitive + pH sensitive (dual stimuli response)	*N*-isopropylacrylamide (NIPAM) for and itaconic acid (IA) as temperature and pH sensitive components, respectively	The temperature-sensitive behaviours of LNIH-3.7%, LNIH-5.7%, and LNIH-6.9% hydrogels have been observed at around 35°C, which is relatively close to the physiological temperature of 37°C. Each LNIH hydrogel demonstrated pH sensitivity ranging from 3.0 to 9.1	Controlled release of drugs or pesticide	[148]
Ag-SLS/PPy-PDA@PEGDA hydrogel	Photothermal response	–	Under near-infrared irradiation (808 nm), the temperature of the hydrogel system increased up to 52.9°C within 3 min, validating high photothermal effect. Also demonstrated excellent antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*	Therapeutic dressing for infected wound healing, tissue engineering	[149]
LigHyd-RB@L AgNCs (lignin hydrogel doped RB-conjugated lignin-Ag nanocomposites)	Photodynamic + pH responsive release (dual stimuli response)	Rose Bengal	The survival rate of *Candida tropicalis* colonies declined to about 14%. In the presence of green laser (525 nm, 2.5 mW for 3 min), the IC50 value of LigHyd-RB@L AgNCs decreased by ~2 fold when compared to dark circumstances	Wound dressing, drug delivery of antimicrobial PDT	[150]
LPC-MWCNT (lignin–chitosan/multiwalled carbon nanotube) hydrogels	Photothermal	Carbon nanotubes	The LPC-MWCNTs1.5 hydrogel reached about 57°C after being exposed to an 808 nm NIR laser (1.5 W/cm^2, 5 min), which successfully killed 99% *Escherichia coli* and 97.8% *Staphylococcus aureus* by thermal denaturation	Antibacterial wound dressing	[151]

Table 10. The different types of applications of lignin-based hydrogels for energy.

Material	Electrode material	Device type	Properties	Application	References
Lignosulfonate functionalized graphene hydrogel (LSGH) fabricated with H_2SO_4 polyvinyl alcohol gel electrolyte	Metal free flexible LSGH electrode	Flexible supercapacitor	Specific capacitance of 432 Fg^{-1} in aq. Electrolyte as compared to pure graphene hydrogel (238 Fg^{-1}). Also, exhibit high mechanical stability	Flexible energy device	[156]
Chemical crosslinked lignin hydrogel electrolytes	Electrospun lignin/polyacrylamide nanofiber electrodes	Flexible supercapacitor	High capacitance of 129.23 Fg^{-1}. Delivers a maximum energy & power density of 4.49 $Wh·kg^{-1}$ & 2.63 $kW·kg^{-1}$ respectively	Energy storage devices	[157]
Double crosslinked lignin hydrogel electrolyte	PANI-deposited carbon cloth	Flexible supercapacitor	Exhibit high mechanical strength (4.74 MPa) and ionic conductivity (0.088 cm^{-1})	Compression-resistant electronics	[158]
GAC-2 nitrogen-doped activated carbon/graphene hydrogel electrode	Graphene oxide	Flexible supercapacitor	Show high mechanical flexibility & exhibit energy density of 26.9 $Wh·kg^{-1}$	Energy storage electrical devices	[159]

As compared to conventional polymers, lignin offers unique multifunctionality and sustainability advantages over synthetic systems (which provide uniformity but lacks bioactivity) and other natural polymers like cellulose (which offer strength but limited functionality). However, there are some limitations of lignin such as batch-to-batch variability, structural complexity, and impurity-related concerns, which hinders reproducibility and large-scale translation. Different types of industrial lignin on the basis of method of preparation are available, among which organosolv lignin stands or for biomedical use due to its higher purity and biocompatibility, whereas kraft and lignosulfonates are less attractive due to high sulfure content and structural condensation limitations. The real-world application of lignin depends on the overcoming key limitations related to structural variability and reproducibility.

Future perspective

Lignin is an abundant by-product of the pulp and paper industry, driving strong interest in lignin-based materials. Lignin-based hydrogels show promise in sensors and flexible energy storage. However, commercialization remains limited due to processing and performance challenges. Advances in scalable synthesis, functionalization, and interdisciplinary research are essential.

The transition of lignin-based hydrogels from laboratory research to industrial production presents significant challenges alongside their promising potential. Large-scale manufacturing is hindered by reliance on batch polymerization processes that require precise control of parameters such as temperature, pH, and radical initiation, which are difficult to replicate consistently at scale. Additionally, variability in lignin feedstocks from different industrial sources complicates reproducibility, highlighting the need for standardized processing methods. Economic feasibility is another key concern, as lignin hydrogels must compete with petroleum-based materials by leveraging lignin's low-cost and abundant availability.

Regulatory requirements further add complexity, particularly for biomedical applications such as drug delivery, wound healing, and tissue engineering. Compliance with strict safety standards necessitates extensive evaluation of biocompatibility, cytotoxicity, degradation behavior, and long-term stability, along with assurance of batch-to-batch consistency and safe degradation products. Even environmental applications require validation of biodegradability and absence of ecotoxicity.

Despite these barriers, lignin hydrogels remain highly promising due to advances in chemical modifications (e.g., esterification, sulfonation, etherification) and the development of hybrid and nanocomposite systems with materials like chitosan, cellulose nanofibers, graphene oxide, and metal nanoparticles. These strategies enhance mechanical, functional, and antibacterial properties, enabling applications in biosensing, soft electronics, and biomedical scaffolds. Furthermore, stimuli-responsive lignin hydrogels offer innovative opportunities in smart drug delivery and responsive biomedical devices.

Overall, the future of lignin-based hydrogels depends on integrating advancements in material design, scalable processing technologies, regulatory compliance, and cost optimization, enabling their transformation into sustainable and commercially viable materials for diverse environmental and biomedical applications.

Abbreviations

ATRP: atom transfer radical polymerization

BA: butyl acrylate

DOX: doxorubicin

EHMC: ethylhexyl methoxycinnamate

Hap: hydroxyapatite

LCC: lignin-carbohydrate complexes

LHNPs: lignin hollow nanoparticles

LSNs: lignin-coated silica nanoparticles

MMA: methyl methacrylate

PAA: polyacrylic acid

PDT: photodynamic therapy

PEG: polyethylene glycol

PNIPAM: poly(*N*-isopropylacrylamide)

PTT: photothermal therapy

PVA: polyvinyl alcohol

RAFT: reversible addition-fragmentation chain transfer polymerization

ROS: reactive oxygen species

SEM: scanning electron microscopy

SL: sulfonated lignin

SLS: specifically sodium lignosulfonate

WIEs: wearable and implantable electronics

Declarations

Author contributions

HK: Conceptualization, Visualization, Data curation, Writing—review & editing, Writing—original draft. Disha: Data curation, Writing—review & editing. KS: Data curation, Writing—review & editing. OS: Project administration, Supervision, Writing—review & editing. BS: Conceptualization, Investigation, Project administration, Supervision, Writing—review & editing. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

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