Applications of Lignin in the Agri-Food Industry

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Abstract

Of late, valorization of agri-food industrial by-products and their sustainable utilization is gaining much contemplation world-over. Globally, 'Zero Waste Concept' is promoted with main emphasis laid towards generation of minimal wastes and maximal utilization of plant-based agri-food raw materials. One of the wastes/by-products in the agri-food industry are the lignin, which occurs as lignocellulosic biomass. This biomass is deliberated to be an environmental pollutant as they offer resistance to natural biodegradation. Safe disposal of this biomass is often considered a major challenge, especially in low-income countries. Hence, the application of modern technologies to effectively reduce these types of wastes and maximize their potential use/applications is vital in the present day scenario. Nevertheless, in some of the high-income countries, attempts have been made to efficiently utilize lignin as a source of fuel,

as a raw material in the paper industry, as a filler material in biopolymer based packaging and for producing bioethanol. However, as of today, agri-food industrial applications remains significantly underexplored. Chemically, lignin is heterogeneous, bio-polymeric, polyphenolic compound, which is present naturally in plants, providing mechanical strength and rigidity. Reports are available wherein purified lignin is established to possess therapeutic values; and are rich in antioxidant, anti-microbial, anti-carcinogenic, antidiabetic properties, etc.

This chapter is divided into four sub-categories focusing on various technological aspects related to isolation and characterization of lignin; established uses of lignin; proved bioactivities and therapeutic potentials of lignin, and finally on identifying the existing research gaps followed by future recommendations for potential use from agri-food industrial wastes.

Keywords: Lignin, Waste Valorization, Polymers, Bioactivities, Therapeutic Potential

Chapter outlook:

1. Introduction: Lignin-what are they?
2. Lignin structure, derivatives and modifications
3. Established uses of lignin
4. Established biological activities and therapeutic potential
5. Conclusions and future prospects

1. Introduction: Lignin-what are they?

Lignin is a highly valued inexpensive waste, which is finding wide applications in the agri-food sector. Lignin stands next to cellulose as a natural plant-based polymer and is localized mainly in the cell walls. Chemically, lignin is a heterogeneous, bio-polymeric, polyphenolic compound providing mechanical strength and rigidity to plants. In fact, lignin is designated as a major renewable resource of carbon (and a better alternative to fossil), and aromatic molecules next to cellulose (Awungacha Lekelefac, 2015; Buggand Rahmanpour, 2015). Naturally, as a polymer, lignin (a non-carbohydrate) is linked with cellulose and hemicellulose (carbohydrate polymers) via ester or ether or covalent bonds. As a polymer, the monomer units of lignin (rather precursor of lignin polymer) mainly comprises of phenyl-propane monomers (referred to as monolignol) encompassing sinapyl, p-coumaryl and coniferyl alcohol. Syringyl-guaiacyl type lignin is obtained from hardwoods, while it is guaiacyl type in softwoods, and with the presence of p-hydroxyphenyl lignin in both the types of woods. In Figures 1 and 2, schematic representation of lignocellulose in biomass and its composition, and precursors and basic-unit in lignin molecule are provided. Lignin accounts for up to 30% (by dry mass) in plants and ~40% of biomass as lignocellulose (cellulose, hemicellulose, and lignin) in agriculture residues (Lupoiet al.2015; Ragauskaset al. 2014). Nevertheless, lignin waste is produced in abundance in pulping, wood processing and paper industries (occurring as spent liquors). The most promising use of lignin has been generation of power (has a melting temperature of up to 160°C) and in production of value-added bio-chemicals, aromatic compound (like benzene, toluene, xylene), cement additives, and biofuel in bio-refineries (Rinaldi et al. 2016; Xu et al. 2014). This potential uses have been attributed to high carbon to oxygen ratio in lignin (Schutyseret al. 2018). Of late, lignin is explored to be used in cosmetics, agriculture and food industry applications. Irrespective of this, huge tons of lignin waste generated contributes to serious environmental pollution related issues. And, it is opined that ~2% of lignin to be effectively utilized for value addition (Lora et al. 2002).

2. Lignin structure, derivatives, and modifications

Due to the heterogeneity nature, the primary chemical structure, properties, and functionality of lignin remain unidentified. The coupling or bonding, as well as arrangement between macromolecules, is also quite complicated. Nevertheless, the extraction of lignin from the lignocellulosic biomass/plant debris is technically a challenging task. The microstructure variations and isolation techniques differ for lignin isolated from various plant/agriculture residues (hemp, straws, flax, stem, etc). Besides, isolation of lignin in pure form from agricultural wastes is tedious and expensive and in the majority of the instances, lignin offers resistance to enzymatic or chemical treatments. According to Kim et al. (2018), lignin valorization depends on efficient extraction and purification with minimal compressed structural arrangements from lignocellulose. Further, the lignin-carbohydrate complexes render the extraction of lignin to be complicated (Ragauskaset al. 2014). Of course, depolymerization of lignin via biocatalysts, and finding uses in the paper, detergent and food industries is well documented (Korbag et al. 2014; Wang et al. 2013, 2018). Till date, isolation, characterization, and evaluation of biosynthetic pathways of lignin have performed mainly in silages, woods and in selected vascular plants (Whetten and Sederof, 1995). As extraction of lignin is expensive, attempts are made to develop engineered plants (genetically modified) with less scope for lignin accumulation or those wherein degradation can be achieved easily via chemical treatments (Mansfield et al. 2009; Vanholme et al. 2008). Structure of lignin in lignocellulosic material and the typical linkages present in lignin is depicted in Figures 3 and 4.

Lignin extraction (delignification) is mainly undertaken via acid hydrolysis, alkaline hydrolysis, reduction and oxidation fractionation,steam explosion, hydroxyl-methylation, acetylation, epoxidation reaction (epoxides formation), precipitation procedures,bleaching, fermentation, etc(Castro et al. 2019; Galkinet al. 2016; Kim et al. 2016;Shi et al. 2019; Thomas et al. 2017). Thio-acidolysis coupled with reductive cleavage method has also been explored to evaluate the cereal lignin composition (Bunzel et al. 2004; Begum et al. 2004). Kraft processing and sulfite/chemical pulping are common processes used to produce kraft lignin, lignosulfonates and soda lignin (Figueiredo et al. 2018; Schutyseret al. 2018; Zhang et al.

2016). Further, organosolv processing (organic solvent + water+ acid/base catalyst) is also recommended wherein pure lignin devoid of fsulfur and hemicellulose can be obtained (Paszner and Cho, 1989, Li et al. 2017 Zhang et al. 2017). Use of solvents like ethanol, methanol, acetone, and others with low boiling temperature is common in organosolv processes, and these solvents can effortlessly recuperated via distillation method (Rodríguez and Jiménez, 2008).

In obtaining aromatic compounds/aldehydes, the lignin oxidation process is recommended via the use of copper catalysts. Modification of lignin via various processes leads to cleavage in intra- molecular bonds or in covalent linkages (mainly attached to the polysaccharides) leading to variations in the lignin fragments. Besides, the pulping process contributes to variations in the functional group (i.e., sulfonate carboxyl or phenolic hydroxyl groups) of extracted lignin. The extraction process of lignin from lignocellulosic biomass is always undertaken cautiously to ensure that slowly break down occurs to obtain lignin or their products with lower molecular weight ([illegible] and Weckhuysen, 2014). However, extraction methods and original source of lignin can significantly influence physico-chemical properties of the extracted products (Upton and Kasko, 2016). Once lignin is obtained in pure form, their characterization can be performed by various accessible techniques like NMR (31P NMR, 13C NMR), Fourier-Transform Infrared Spectroscopy, Gel Permeation Chromatography and other reliable analytical techniques, which are based on molecular weight determination. Some of the major components of lignin-derived extracts include p-hydroxybenzoic acid, ferulic acid, hydroxyphenyl acids, syringic acid, coumaric acid, vanillic acid, vanillin, p-hydroxybenzaldehyde and syringaldehyde (Cruz et al. 2001).

3. Established uses of lignin

The major use of lignin is their use as fuel to generate energy. Production of biofuels is one the major area of application lignocellulosic materials (Crestini et al. 2010; Lou et al. 2013, 2014; Ro et al. 2019). Value addition in bio-refineries via conversion into economically valued chemicals has generated much interest (Abo et al. 2019; Chen and Wan, 2017). The major phenolic compounds and their derivatives obtained as intermediates during lignin biosynthesis holds much value and are used as a base material in cosmetics (e.g. moisturizing cream, sunscreen), bioplastics, resins, pharmaceuticals, food, and agriculture fields (as herbicides). Wood adhesives and lignin-epoxy resins are prepared from lignin owed to their polyphenolic structure. Lignosulfonates also find potential usage as slurry dispersants, dye-stuff dispersants, oil well dispersant, and surfactants (Qian et al. 2015; Stephen 1981; Wu et al. 2012). Promising use of lignin and their composites for developing functional materials with a wide range of applications as aerogels, nanofibers, and hydrogels has been detailed (Chen et al. 2011; Fernandes et al. 2013; Kai et al. 2015). In addition, depending on the source material, lignin can exhibit hydrophobic as well as hydrophilic nature, display good viscoelasticity and rheological features (Doherty et al. 2011). However, polyphenolic compounds in lignin and the action type of their derivatives can directly be linked with modification modes employed and on composition (Popa et al. 2008). Polyphenolic compounds along with ketones not only provides protection against UV light but also perform the role of natural antioxidants (hence used in cosmetic industries like in sunscreens) (Qian et al. 2015;Zimniewska et al. 2012). Recently Lee et al. (2019) reported on the synergistic effects of lignin isolated from *Miscanthussacchari florus,* which on addition to sunscreen, significantly enhanced the protective effects against UV radiation. Besides, with oxidation leading to the formation of aromatic compounds and/or aldehydes, lignin is valued in the perfume industry too (Priefert et al. 2001; Qu et al. 2017).

Of late, in modern agriculture system, lignin-based products are gaining popularity towards controlled/slow-release of herbicides, pesticides, and fertilizers (e.g. urea granules) (Pereira et al. 2003; Mulder et al. 2011, Wang and Zhao, 2013).Du et al. (2014) have reported 'layer-by-layer' self-assembly method for controlled herbicide and pesticides release via the use of microcapsules. Nevertheless, it is well established that lignin-based microcapsules do not exhibit any type of cytotoxicity and can be easily incorporated into cells (Tortora et al. 2014). Furthermore, for delivery of hydrophobic molecules, the same authors (Tortora et al. 2014) have reported on the use of ultrasound-assisted kraft lignin for micro-capsulation. However, there is a word of caution, wherein controlled release to the soil can face wide challenges in the agriculture field wherein natural processes like bio-leaching/bio-degradation/photo-degradation/volatilization, and other chemically induced degradations can occur, thus limiting the efficacy of the controlled release technique. Moreover, owing to high resistance offered to salt contamination, lignosulfonates is recommended to be used as a water-oil emulsion stabilizer in various field of applications like in asphalt stabilization, paper gluing, etc (Browning, 1955; Cateto et al. 2014). By use of selective solvents and by precipitating lignin, nanoparticles were developed which were environmentally friendly, safe and non-toxic (Frangville et al. 2012). These nanoparticles were recommend to find practical applications in heavy metals absorption as well as in drug delivery. Further, lignin-based complexes/nanoparticles are synthesized to explore their potential use in biomedical industrial applications (Figueiredo et al. 2017). So also, several other potential application of lignin-based nanoparticles have been reported (Chen, 2019; Mishra and Ekielski, 2019; Zikeli et al. 2019).

Richter et al. (2016) have demonstrated the ability of lignin nanoparticles (precursors used was kraft lignin and organosolv lignin) to fulfill the purpose of producing novel biodegradable colloids with modifiable surface properties. According to the authors, the lignin-based nanoparticles are expected to perform the role of a biodegradable carrier and also had biocidal actives. Authors have opined that the new lignin-based nanoparticle formulation can be an effective base for future uses for sustainable transfer of nano-vehicles as pesticides, fungicides, antimicrobials, and drugs.

Moving ahead, lignin finds its application in development of food packaging films, bioplastics development, polymer production and bio-degradability. Besides, lignin finds potential usage in textile and fabric industries (as protector or a barrier against intense UV light), in electro-chemical uses, as heavy metals adsorbents, as a plasticizer, binder, dispersants and much more (Bhat et al. 2013; Fierro et al. 2013; He et al. 2013; Klapiszewski et al. 2013; Lee 2014; Luo et al. 2018;Nagaraju et al. 2014; Stewart et al. 2008; Zimniewska et al. 2008). Another interesting field of lignin application is its potential use as a basic raw material for the fabrication of cheap and economically feasible carbon fiber (Baker et al. 2012). It is expected that in the near future, these carbon fiber (nanofibers) can find wide applications as a replacement for poly-acrylonitrile in industries linked with aerospace, automation, sports equipment production, capacitor, and batteries, etc.

Vanillin (4-hydroxy-3-methoxybenzaldehyde), a much appreciated and expensive flavouring compound originally isolated from vanilla beans can be produced from black liquor wastes of paper industry (like kraft lignin) or from lignosulfonates obtained from softwood of coniferous plants. Apart from food industrial use, vanillin also finds its applicability in the pharmaceutical and cosmetic industry (as an ingredient in perfume, lotion, sun protective cream, etc).

Use of lignin as a natural biopolymer and as a filler material (cross-linking agent) in the development of novel packaging films has been studied in detail by various researchers. Owing to its stable inter- and intra- molecular bonding, coupled with thermoplastic nature and behaviour, lignin has been a polymer in demand (Nimz, 1974; Kubo and Kadla, 2005; Ugartondo, 2008). According to Stewart (2008), chemical-based modification of lignin nanomaterials opens up the possibilities to develop novel, tailored multicomponent polymer system with desirable properties, which can be used for producing bioplastics for agricultural purposes (e.g. lignin- mulch films). Vengal and Srikumar (2005) extracted lignin from wood chips waste (obtained from paper industry) and blended this with starch and gelatin to produce lignin-starch and lignin-gelatin biodegradable polymeric films. Calgeris et al. (2012) reported developing lignin-starch biodegradable films and studied their drug release properties. Their results revealed a faster drug release rate of ciprofloxacin (< 1hour) from biofilms, with the drug release mechanism being pH dependent.

Further, Bhat et al. (2013) have developed a low cost, environmental friendly novel food packaging films from sago palm starch (as the film matrix), and lignin (as a reinforcing material) obtained from oil palm black liquor waste (with 30% w/w glycerol used as plasticizer). Packaging films developed exhibited good thermo-mechanical properties, barrier properties and seal strength with improved water resistance. Besides, there are several reports focusing on the potential use of lignin in combination with their biopolymers (e.g. blending of starch/gelatin with lignin) and with chemical modifications (for polypropylene films) to produce packaging films for wider food industry applications (Baumberger et al. 1997).

Recently, Liu et al. (2019) have proposed bioconversion of kraft lignin to poly-hydroxyalkanoate by using *Pandoraea* sp. B-6 (Gram-negative bacterium). Depolymerization of kraft lignin followed characterization revealed 24.7% to be amassed in B-6 (grown in 6 g/L kraft lignin mineral medium). Further, it was observed that the monomer 3-hydroxybutyrate to be present as a single major component, with PHA comparable to commercial bioplastics.

Lignin being a natural component of fiber, a strong bonding exists between the lignin matrix and fiber component (Naegele et al. 2016). Natural composite films produced from this combination are always strong and displays good mechanical properties. Besides, food packaging films developed from fiber/lignin-based materials can always be a good replacement for oil/petroleum-based polymers. Lignin used in different forms as a filler material (e.g. organosolv, kraft, soda lignin) is reported to exhibit better mechanical properties (Pucciariello et al. 2010). The electro-spinning of C-lignin (devoid of chemical treatments obtained from vanilla seeds) into fibers was successful and was foreseen to find wide industrial applications (Nar et al. 2016).

Hydrogels, which are either monomer or polymers suspended in aqueous solution (water-based medium) have a wide range of medical applications (wound healing properties, providing relief against burns, drug delivery, tissue engineering, etc) (Curvello et al. 2019; Mishra and Wimmer, 2017). Of late, lignin-based hydrogels are gaining popularity owing to superior water absorption and retention properties, tissue imitating abilities, low toxicity, bio-compatibility as well as controlled diffusion of desirable materials (Thakur and Thakur, 2015; Zamboni et al. 2018). In agriculture fields, lignin-based hydrogels can be valuable to be utilized for reducing drought stress and to increase irrigation productivity where low water retention is a challenge. Hydrogels have been reported (Peng and Chen, 2011) to be effective for slow release and movement of fertilizers too.

Lignin-based hydrogels have been prepared by graft copolymerization (El-Zawawy, 2005). It was noticed that hydrogel prepared from alkaline lignin to exhibit higher swelling ratio with and slow water uptakes compared with kraft lignin, and this was assigned to the internal structural network (El-Zawawy, 2005).

4. Biological activities and therapeutic potential

Available research articles and database clearly indicates plant derived lignin to possess rich biological activities and therapeutic potential. Some of these include antioxidant properties, antimicrobial activity, anti-cancer/anti-tumour activity, anti-thrombosis, anti-HIV properties and much more. The main compounds responsible for these activities are assigned to polyphenolic compounds, guaiacol and guaiacyl units, 4-hydroxy-3-methoxy-cinnamic acid and ferulic acid (Azadfar et al. 2015; Sadeghifar et al. 2015;Ou and Kwok, 2004). However, compared to other macro-molecules and bioactive compounds, research on identifying potential pharmaceutical benefits of lignin still remains in the infant stage. In **Table 1,** a summary on the some biological properties and uses of lignin in agri-food industry is depicted. In the preceding text, some reported activities are being discussed:

4.1. Antioxidant activity

The main contributing factor for the exhibited antioxidant properties/radical scavenging activities of lignin is the presence of natural polyphenols. The effectiveness of polyphenolic components in lignin as a major contributing factor as an antioxidant (Barapatre et al. 2016; Hasnaoui et al. 2014; Zhu and Xu, 2013) as well as providing protection against UV is well established in the cosmetic industry. The effective antioxidant activity of using lignin (and their linked mono- and dimeric compounds) has been tapped in dietary and medicinal products as well as in other soft materials like rubber and pulp (Barclay et al. 1997; Satoh et al. 1999).

Several available reports have indicated the potential antioxidant activities of lignin extracted from various plant resources like rice husk, hybrid poplar, apple tree, sugar cane, wheat straw, stover (Azadfar et al. 2015; Bhat et al. 2010; Faustino et al. 2010; Pan et al. 2006; Vinardell et al. 2008; Salantiet al. 2010). Apart from being a potential free radical scavenger, lignin can stabilize various oxygen and free radical species induced reactions (Sakagamiet al. 1992).

Vinardell et al. (2008) evaluated antioxidant activity in cosmetic or topical application of industrial lignin obtained from bagasse, curan, lignosulfonate and by steam explosion. Among all, lignin obtained from bagasse was observed to be comparable with epi-catechin, a well-established antioxidant compound. Further, the authors concluded that all the lignin were safe on testing for eye and skin irritation leading the way for commercial exploitation in topical formulations and cosmetics. The antioxidant properties of lignin are also known to provide resistance against thermo-oxidation protection (Pouteau et al. 2003). Nevertheless, the efficacy of lignin antioxidants effects as stabilizers is well studied (Barana et al. 2016; Spinoza-Acosta et al. 2016). Presence of non-etherified phenolic hydroxyl groups serving as peroxyl radical scavengers is well demonstrated (García et al. 2010; Sadeghifar et al. 2015). So also, Azadfar et al. (2015) have linked hydroxycinnamic acids and guaiacyl monomers (in pre-treated wheat straw with ozone and soaked in aqueous ammonia) with antioxidant activities and have concluded that lignin can be a good feedstock of 4-vinylguaiacol and guaiacol as antioxidants.

Lignin extracted from sugarcane has been studied for their biological activity and health benefits including that of antioxidant activity (Mitjans and Vinardell, 2005). Kaur et al. (2017) via chemical modification (viz., acetylation, epoxidation and hydroxymethylation) of sugarcane bagasse obtained lignin, and reported unmodified lignin and hydroxymethyl lignin to exhibit high antioxidant activity. Antioxidant activity of lignin from 'corn stover' residues is reported to exhibit strong antioxidant activity, which was measured by employing Folin-Ciocalteureagent method and hydrophilic oxygen radical absorbance capacity (Dong et al. 2011).

Combination of gelatin and lignin for producing films was reported to enhance the oxidative stability, appearance and of protein quality in 'salmon fillets' which were pre-exposed to high-pressure processing (Ojagh et al. 2011). Further, Núñez-Flores et al. (2013) used lignin as an active food packaging material (to tap antioxidant potentiality) for developing fish gelatin films (85% gelatin and 15% lignin: w/w) with antioxidant capacity (via the use of sulfur-free water-insoluble lignin powders L- 1000 and 2400) at non-cytotoxic concentrations. Warm water species extracted fish gelatin used with glycerol and sorbitol as a plasticizer. On visual examination at the macroscopic level, lignin incorporation led to dark brownish color with reduced transparency and acceptable levels of miscibility. Further, at micro- level, results of the structural evaluation indicated lignin to inhibit gelatin molecule interaction. Films developed exhibited good plasticizing nature and light barrier properties, with negligible impact on water solubility. It was also reported that at non-cytotoxic concentration, lignin proves to be an effective antioxidant. The authors concluded by recommending the use of lignin-based composite films in food applications wherein UV induced lipid oxidation needs to be prevented.

Li and Ge (2012) investigated lignin extracted from sugarcane bagasse by employing ethanol and alkaline solutions. After characterizing, alkaline lignin was found to have large molecular mass with a higher number of phenolic hydroxyl and methoxyl groups offering good thermal stability than ethanol-extracted lignin. Further, their studies revealed the radical scavenging activity of alkaline lignin to be much higher than alcohol extracted lignin. Overall, in food industries, lignin's antioxidant capacity and radical scavenging ability is tapped for use in bio-packaging films as well as to enhance the compatibility of lignin with another polymer matrix. Lignin also finds application to be used as a stabilizer for food-stuff and livestock feed- owed to their antioxidant and antimicrobial properties. However, due to the complexity in the structure, high molecular weight, presence of other polymers (admixture)and poly-dispersity, the efficacy of antioxidant and free radical scavenging activities can be significantly compromised/decreased (Dizhbite et al. 2004;Pouteau et al. 2005;Sederoff et al. 1999).

4.2. Antimicrobial effects

Lignin has been explored for its potential antimicrobial activities against human and plant pathogens. The main compounds responsible for the activity has been assigned to the presence of polyphenols, sinapyl and coniferyl alcohol (Zemek et al. 1979). Polyphenolic compounds have been shown to interact with the microbial cell membrane and disrupt their cell structure leading to cell component leakage (Gyawali and Ibrahim, 2014; Yang et al. 2016). Lignin obtained from pulp by-products (liquor) has been revealed to exhibit rich anti-bacterial activity against Gram-positive bacteria like *Bacillus subtilis* and *B. mycoids*. However, lignin had not exhibited any activities against Gram-negative bacteria or fungi (Nada et al. 1989). Oh-Hara et al. (1990) have shown antimicrobial activities exhibited by commercial lignin to be significantly low when compared with lignin fractions obtained via alkaline extracted pine cone.

Slavikova and Kosikova (1994) report anti-microbial activity against yeasts from lignin isolated from soft and hardwoods. Dizhbite et al. (2004) have demonstrated kraft lignin to be effective against phyto-pathogenic microorganisms. Dong et al. (2011) have reported antimicrobial activities of lignin extracted from corn stover residues against *Listeria monocytogenes* and *Staphylococcus aureus* (Gram-positive bacteria) and *Candida lipolytica* (yeast). However, authors reported that no activity to exist for Gram-negative bacteria (bacteriophage MS2, *Escherichia coli* O157:H7 or *Salmonella enteritidis*).

Cruz et al. (2001) evaluated the antioxidant and antimicrobial activities of different lignocellulosic materials (barley bran, eucalyptus globulus wood, corn-cobs, corn-leaves) obtained from acid hydrolysates as ethyl acetate extracts. Their results revealed eucalyptus wood extracts to have better inhibition among all of the extracts against yeasts and bacteria, with minimum inhibition concentration ranging between 10^2-5×10^3 μg/ml and minimum bactericide concentration being 10^3-10^5μg/mL.

Antimicrobial activity against *Escherichia coli* was evaluated in cellulose fiber coated with chitosan and lignosulfonate (Hui and Lincai, 2015). Alternated immersion technique was employed and results revealed chitosan to exhibit better antimicrobial activity compared to the lignosulfonates coated layer. Nanocomposite films produced by using poly(lactic acid) incorporated with 2 types of bio-based nano-fillers viz., cellulose nanocrystals and lignin nanoparticles have been reported to exhibit antimicrobial activity against pathogenic Gram-negative bacteria like *Xanthomonasaxonopodis* pv. vesicatoria and *X. arboricola*pv. pruni (Yang et al. 2016). Yearla et al. (2016) by employing nanoprecipitation technique produced dioxane lignin nanoparticles and alkali lignin nanoparticles from two different sources of lignin (hardwood di-oxane lignin obtained from the subabul stem and softwood alkali lignin obtained from a commercial source). Results of this study revealed that on exposure to UV at a different time interval, dioxane lignin nano-particles to offer enhanced protection for Escherichia coli against UV. Crude lignin extract obtained from sugarcane bagasse has been testified to exhibit anti-bacterial effects against *Staphylococcus epidermidis* (DMST 15505; Minimum Inhibition Concentration being 4,096 µg/mL) (Sunthornvarabhas et al. 2017). Kaur et al. (2017) on comparing unmodified and modified lignin from sugarcane bagasse, reported epoxy lignin to be highly effective against pathogenic bacteria like *Bacillus* sp. and *Klebsiella* sp. Additionally, antibacterial activity against pathogenic *Staphylococcus aureus* (a Gram-positive bacteria)is reported from hydrotropic lignin obtained from birch wood (Gabov et al. 2017). Besides, antibacterial and antifungal activity of lignin capped silver nanoparticles against human pathogenic *E. coli, S. aureus, and A. niger*is also being reported (Marulasiddeshwara et al.2017).

Jonglertjunya et al. (2014) coated limes in different combinations with lignin to evaluate their efficacy in retention of quality as well as for potential antifungal activities. The formulations employed for the investigations comprised of: 0.8% xanthan gum + 1.5% lignin extracted with 40% NaOH; 0.4% xanthan gum & 1.5% lignin extracted with 40% NaOH in 50% ethanol and 0.8% xanthan gum + 1.5% lignin extracted from 40% NaOH in 50% ethanol. Results of this study showed 0.8% xanthan gum +1.5% lignin extracted in 40% NaOH to sustain weight loss and changes in color along with exhibiting good antifungal activities.

Further, on overall comparison, limes coated with lignin had better antifungal activity compared to those without coated with commercial lignin.

Additionally, several studies have reported on the anti-viral properties (e.g. anti-HIV) activity of lignin extracted from different sources. High levels of anti-HIV activities of lignin fractions on comparison with zhydrolyzable and condensed tannins vehave been reported by Nakashima et al. (1992). Lee et al. (2011) have established antiviral activities against HSV 1 and HSV 2 in the lignin-carbohydrate-protein complex in aniseed plant (*Pimpinellaanisum*). Matsuhisa et al. (2015) report strong inhibition of hep[illegible] virus in cultured cells by alkaline hydrolysate lignin. Andrei et al. (2011) described strong anti-HSV activity of lignin-sulfonic acid under *in vivo* (in HSV-2 infected mice) and *in vitro* conditions. On the other note, lignin application as an ultraviolet protectant against for the beet armyworm nucleopolyhedrovirus and baculovirus is reported (Salamouny et al., 2002, 2009).

Baurhoo et al. (2008) in one of their review papers have discussed the effectiveness of alcell lignin (purified lignin), which exhibited [illegible] prebiotic effects in 'monogastric' animals by encouraging beneficial bacterial growth as well as enhancing the intestinal morphological structure (measured by villi height and goblet cell numbers). Further, lignin fragments have been accounted for inducing bactericidal effects and managing microbial pathogens in the intestine.

4.3. Anticancer/anti-tumour activity

There are a couple of studies reporting on strong anti-cancer/anti-tumor activities of lignin isolated from various sources. Plant based dietary fibers (encompassing oligosaccharides, lignin, etc) are already established to provide protection against various types of cancers. Protection against colon cancer by plant-based dietary fiber rich in lignin is reported (Meister, 2007). Lu et al. (1998) have illustrated protective effects of alkali-lignin against colorectal cancer. These authors indicated the protective property against colon cancer to be dependent on the levels of lignin present in dietary fiber and on the free radical-scavenging ability of lignin. Siddiqui et al. (2018) have reported using utilizing an environmentally friendly, cost-effective, biocompatible nano-particulate carrier composed of lignin formulations filled with an anti-cancer agent, P-gp modulator, functionalized with ligand for CD44 receptors expressed on colon cancer cells.

Carboxylated lignin nanoparticles were used for anticancer therapy. Low water-soluble cytotoxic agents were loaded into carboxylated lignin nanoparticles which showed improved release, (was pH-sensitive) and exhibited increased anti-proliferative effects in various types of cancer cells on comparison with normal endothelial cell lines (Figueiredo et al. 2017).

In one of the studies by Ugartondo et al. (2008), lignin has been presented to exhibit rich antioxidant properties (at lower concentrations) along with with exhibiting cytotoxic effects (at high concentrations). The authors established this via their studies on antioxidant activity and cytotoxic effects of different types of industrial lignin by using human keratinocyte HaCaTcell membrane and murine fibroblast 3T3 cells. Further, Lu et al. (1998) have attributed anticancer activity (growth and reduction in viable cancer cells) of lignin for their capability to inhibit enzyme activity, which was linked with superoxide anion radical generation. On the other note, inhibition of UV induced mutagenicity in *Euglena gracilis*(a single-celled flagellate eukaryote) is reported by Belicová et al. (2000).

4.4. Anti-coagulant, Anti-emphysema, Anti-diabetic, and Anti-obesity

A wide range of research activities are being concentrated towards finding other potential therapeutic applications of lignin in medicinal field. Controlled release concept proposed in agriculture fields (for fertilizers and herbicides) has been extended for release of various drugs used in human medicine. Some of these include evaluating the anti-coagulant, anti-emphysema, anti-diabetic and anti-obesity activities. Reports available indicate the inhibition potential of thrombin by sulfated low molecular weight lignin (Henry et al. 2014; Mehta et al. 2016).Novel anticoagulants(exhibiting dual anionic properties and hydrophobicity was produced by using sulfated low molecular weight lignin which accomplished the role of practical mimetics compared to low molecular weight heparin (Monien et al. 2006).

Lignin's anti-nociceptive and anti-inflammatory properties have been assigned to the presence of sinapyl alcohol, a lignin precursor. Anti-proliferative activity of water-soluble fractions of carbohydrate-lignin metabolites (obtained from chaga mushroom) is reported (Song et al. 2008).

Barapatre et al. (2015) have reported antidiabetic activity of alkali lignin by *in vitro*alfa-amylase inhibition. Further, Hasegawa et al. (2015) by employing *in vivo* (rat) and *in vitro* experiments (alfa-glucosidase inhibition) reported the efficacy of lignosulfonic acid to show antidiabetic activity, wherein the mechanism of action include inhibition of alfa-glucosidase and decreased levels of glycaemia in blood.

Anti-obesity properties of ligno-phenols have been shown to manage obesity in HepG2. Norikura et al. (2010) by employing *in vitro* models showed a decrease in oleate-induced apo-B secretion. Further, ligno-phenols has been linked with obesity control under in vivo conditions wherein rats which were fed with a high-fat diet showed decreased plasma triglyceride level (Sato et al. 2009).

On another note, Zhang et al. (2013) have reported on the formation of a new activator of α-amylase and lignin, which significantly enhanced α-amylase activities. Their results showed lignin to interact with α-amylase forming a 1:1 lignin/α-amylase complex. As per the authors, this result is useful to understand lignin as a dietary fiber component and was envisaged to contribute as an activator of α-amylase, in food industries.

Pancreatic enzymes activity is linked with human health helps as it helps in hydrolyzing fat molecules, helps in active digestion and adsorption of micro nutrients). Any disturbances of this enzyme can lead to diabetic conditions and adiposity. Zhang et al. (2014) have studied the effects of lignin on pancreatic lipase and reported a pancreatic lipase -lignin complex to be formed with enhanced enzyme activity. As per the authors, generated results helps in understanding the activation effects and interaction between lignin and pancreatic lipase, and this is expected to find wide applications in both food and pharmaceutical industries.

5. Conclusion and future prospects

In the present review, we have summarized information from the currently available databases on the potentiality of plant-derived lignin. The prospective uses and application of lignin, which remains significantly underutilized as a plant by-products discussed in detail. Though many interesting research works have been initiated and have been reported in recent years, still there is a wide gap which exists relevant to tapping lignin's potentiality, and valorization of lignin for agri-food industry applications. Though reports indicate highly value-added products (as bio-fuel, biopolymers, chemicals, aromatic monomers, cosmetic and medicinal uses) to be produced, lignin's application remains in infancy, especially in agri-food and pharmaceutical sectors. The structural complexity of lignin isolated from differed sources has been considered to be a major hindrance for practical exploitation. Some of the common challenges incurred on purification has been overcome and available reports indicate lignin's efficacy to be useful in drug delivery; microencapsulation for controlled release of desired materials in food industry (release of bioactive compounds in bio-packaging films) and agricultural fields (release of fertilizers or pesticides) and cosmetics applications (as in sunscreen). Lignin's use as a filler material in packaging films and as composites in hydrogels (eco-friendliness) offers much scope in pharmaceuticals and agri-food industries, and this gap needs to be filled at the earliest.

Use of lignin/carbon as a bio-sorbent for *in situ* treatment of agriculture and food industry waste water is another arena that needs to be explored. Nano-composites/nano-particles/nanostructured material from lignin as well as developing carbon nanofibres are still in initial stages. Further, proved antioxidant potential can be a boon for the food industry to use lignin as a natural preservative. Whereas, proved antimicrobial activities can also be beneficial for application of lignin and their products for safe storage of foods (active food packaging material) or in agriculture field (as antimicrobial coating agent) to provide protection against plant pathogens. Owed to lignin's natural biodegradability and being devoid of cytotoxicity, they can be a good basic raw material in food packaging industries.

Future research needs to focus on developing low-cost technologies for easy conversion of lignin biomass to obtain purity and identification techniques to ensure the structural components/integrity. The scope is also there for utilizing lignin in livestock and pets food as well as to those related to pharma-cosmetic-food applications. Attempts can also be made to offer genetic modification of lignin to obtain higher amounts of biomass to be exclusively used in agri-food industry. Even though a wide range of opportunities coexists, newer challenges can also be expected, especially considering the purity and safety issues. Finally, sustainable approaches/green technology concepts need to be adopted for tapping the potentiality of lignin for agri-food industrial applications.

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Legend to figures:

Fig. 1. Lignocellulose in biomass and its composition (reproduced with permission from Elsevier publishers, License Number4556500933093 dated Mar 26, 2019, Source; Chio et al. 2019, Journal: Renewable and Sustainable Energy Reviews).

Fig. 2. The precursors and basic-unit in lignin molecule (reproduced with permission from Elsevier publishers, License Number 4556511362424 dated Mar 26, 2019, Source; Chio et al. 2019, Journal: Renewable and Sustainable Energy Reviews).

Fig. 3. Structure of lignin in lignocellulosic material (reproduced with permission from Elsevier publishers, License Number 4556530848259 dated Mar 26, 2019, Source; Agarwal et al. 2018, Journal: Fuel Processing Technology).

Fig. 4. Typical linkages present in lignin (reproduced with permission from Elsevier publishers, License Number 4556530848259 dated Mar 26, 2019, Source; Agarwal et al. 2018, Journal: Fuel Processing Technology).

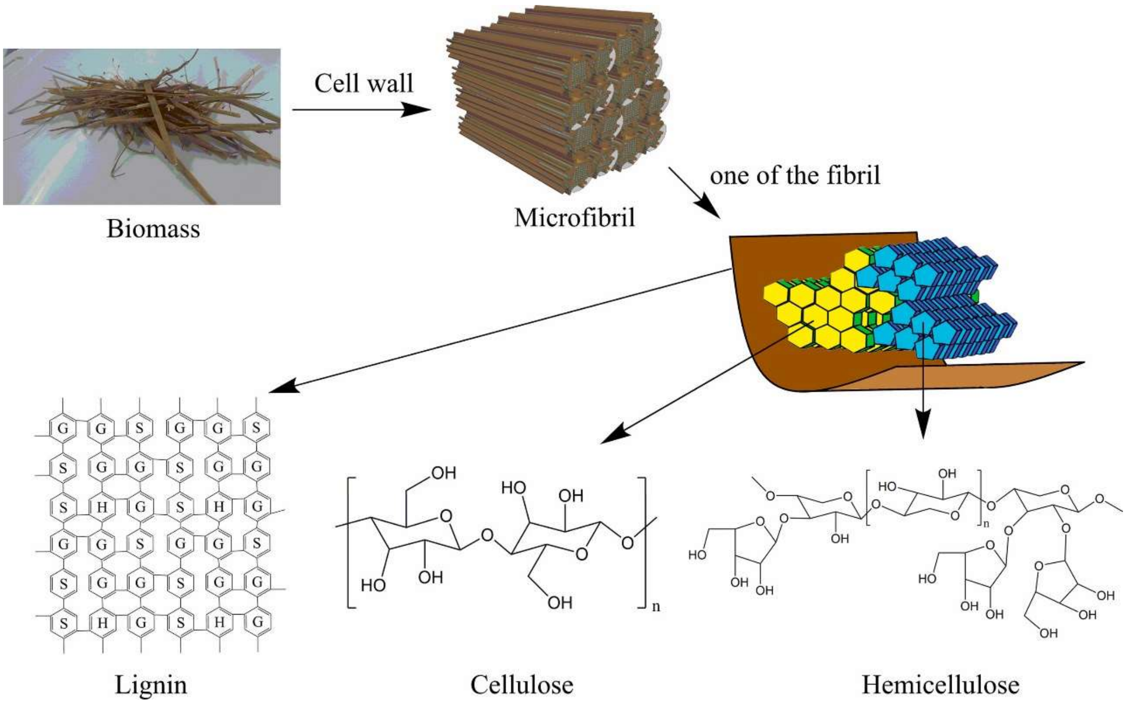
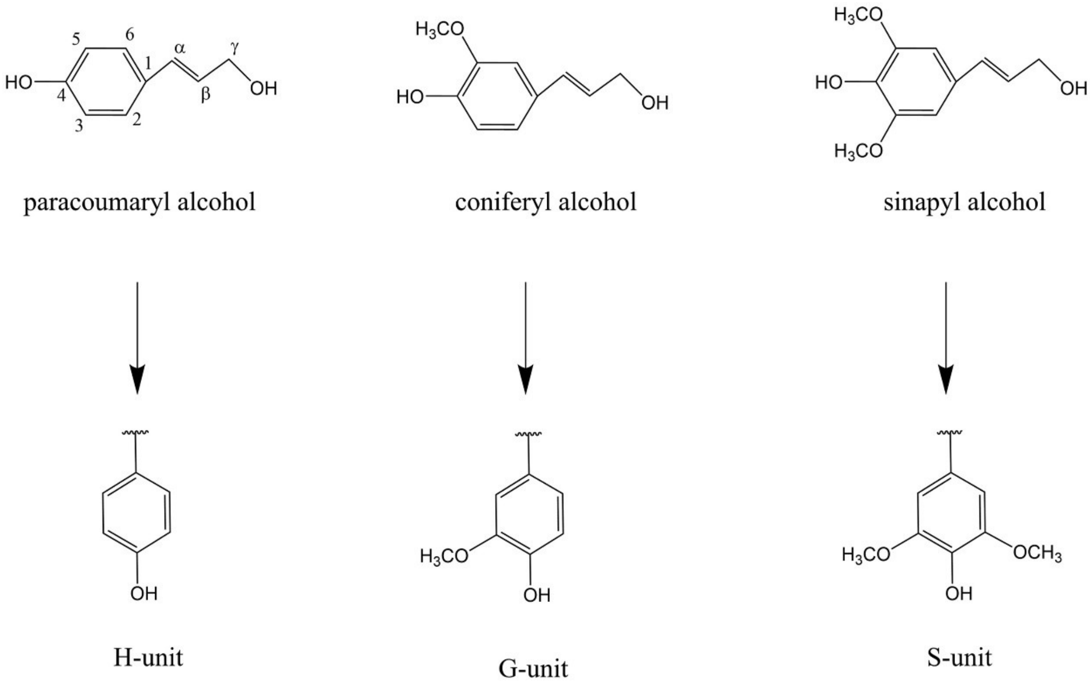
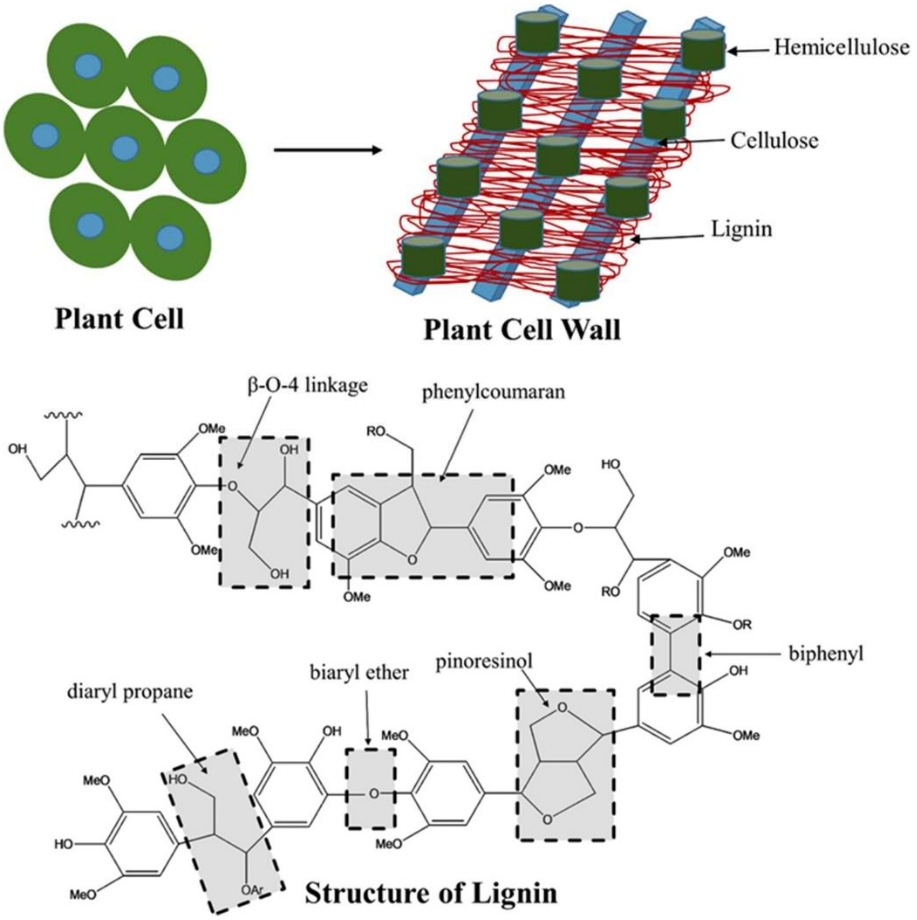


Fig. 1.



paracoumaryl alcohol
coniferyl alcohol
sinapyl alcohol
H-unit
G-unit
S-unit

Fig .2.



Hemicellulose
Cellulose
Lignin
Plant Cell
Plant Cell Wall
β-O-4 linkage
phenylcoumaran
biphenyl
pinoresinol
biaryl ether
diaryl propane
Structure of Lignin

Fig. 3.

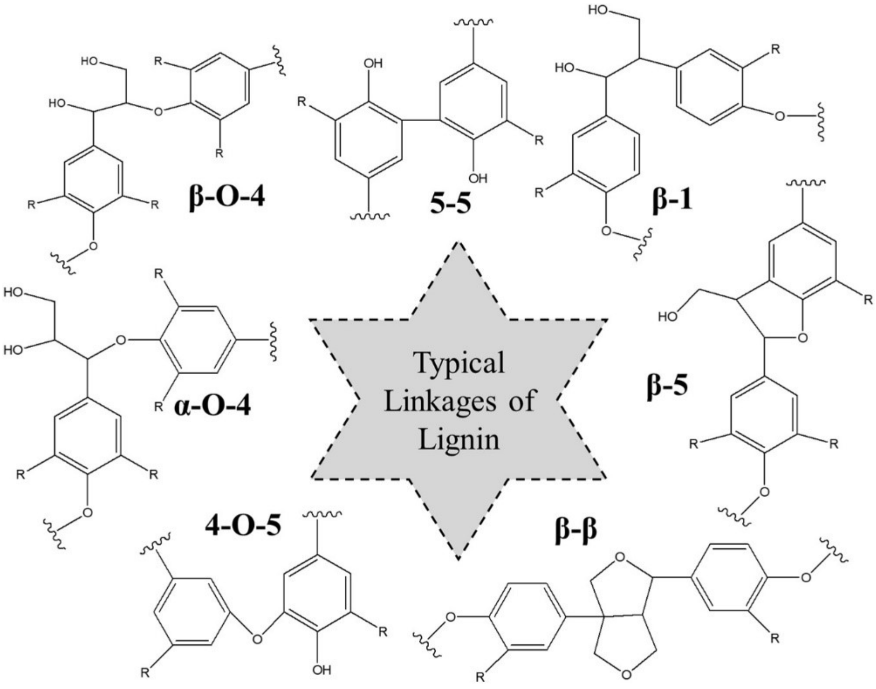


Fig.4.

Table 1: Summary on the some biological properties and uses of lignin in agri-food industry

Active chemicals	Sources	Biological properties	References
Podophyllotoxin derivatives: etopside, teniposide, etopophos	Rhizome of *Podophyllum emodi* L (Berberidaceae)	Anti-cancers (colon, lung, testicle cancer) leukaemia	Gong et al. (2019)
Podophyllotoxin derivatives: Deoxypicropodophyllin, thuriferic acid deoxypodophyllotoxin	Leaves of *Juniperus thurifera* Linne (Cupressaceae)	Analgesic; Anti-inflammatory	Guerrero et al (2013)
organosolv ethanol lignin (OEL)	Corn stalk	Tyrosinase inhibitor	Wang et al (2019)
Alkali and Organosolv lignins	Wheat straw	Antioxidant	Gil-Chavez et al. (2019)
Lignin–carbohydrate complexes	Bamboo	Antioxidants or immune-stimulants	Huang et al. (2018)
Biocomposite lignin-chitosan lignin-inspired bisguaiacol F (BGF),	*Artocarpus heterophyllus*	Wound healing and dressing materials Estrogenic activity	Jaganathan et al. (2018) Peng et al. (2018)
poly (lactic acid)/lignin biocomposites	beech wood		Spiridon & Tanase (2018)
Lignocellulosic	Oil palm empty fruit bunches	Antibacterial	Medina et al. (2016)
Lignosulfonic acid tannins	cacao husk	Anti-viral (Anti-HIV)	Sakagami et al. (2008)
Avermectin encapsulated with acetylated lignin and benzoylated lignin	pulp-making black liquor	Slow release of pesticides	Zhou et al. (2019)