Three-Dimensional Printing of Wood-Derived Biopolymers: A Review Focused on Biomedical Applications

Wenyang Xu,*†‡ Xiaoju Wang,† Niklas Sandler,‡ Stefan Willför,† and Chunlin Xu*†§

†Johan Gadolin Process Chemistry Centre, c/o Laboratory of Wood and Paper Chemistry, Åbo Akademi University, Turku FI-20500, Finland
‡Laboratory of Pharmaceutical Sciences, Åbo Akademi University, Turku FI-20500, Finland
§Kemira Oyj, Espoo FI-02270, Finland

ABSTRACT: Wood-derived biopolymers have attracted great attention over the past few decades due to their abundant and versatile properties. The well-separated three main components, i.e., cellulose, hemicelluloses, and lignin, are considered significant candidates for replacing and improving on oil-based chemicals and materials. The production of nanocellulose from wood pulp opens an opportunity for novel material development and applications in nanotechnology. Currently, increased research efforts are focused on developing 3D printing techniques for wood-derived biopolymers for use in emerging application areas, including as biomaterials for various biomedical applications and as novel composite materials for electronics and energy devices. This Review highlights recent work on emerging applications of wood-derived biopolymers and their advanced composites with a specific focus on customized pharmaceutical products and advanced functional biomedical devices prepared via three-dimensional printing. Specifically, various biofabrication strategies in which woody biopolymers are used to fabricate customized drug delivery devices, cartilage implants, tissue engineering scaffolds and items for other biomedical applications are discussed.

KEYWORDS: Wood-derived biopolymers, 3D printing, Biomedical applications, Customized drug delivery device, Tissue engineering scaffold, Cellulose, Cellulose ether, Cellulose ester, Cellulose nanofibrils, Cellulose nanocrystals, Hemicellulose, Lignin

INTRODUCTION

The scarcity of oil resources and the resulting gradual shortage of oil-based materials encourage society to strive for more environmental sustainability. Renewable materials are “green” alternatives that minimize waste generation.1 Trees provide us with a vast volume of sustainable and renewable materials. Wood from trees has long been used in daily life in various forms, including in construction, furniture, paper, food additives, and medical supplies.2 More recently, novel and creative ways of utilizing wood-derived lignocellulosic materials have increasingly contributed to sustainable development in biotechnology, bioengineering, and the bioeconomy.3–5

Wood naturally has a hierarchical structure composed of three major components: cellulose, lignin, and hemicelluloses.6 Recently, many green and sustainable fractionation technologies have been developed in the context of biorefineries to make these biopolymers industrially available in large quantities as well as in high purities.7 First, cellulose is the most abundant natural polymer on earth and, at the macro- or microscale, is composed of chains of glucose compacted together as fibrils and microfibrils oriented with specific angles, forming both crystalline and amorphous regions. Both cellulose nanofibrils (CNFs) and cellulose nanocrystals (CNCs)8 have been widely exploited as a new generation of nanomaterials in various disciplines, mainly but not exclusively limited to biomaterials in hydrogel form and nanofillers in advanced composite materials. Lignin, with its cross-linked and complex phenolic structure, is the second most abundant component after to cellulose.9,10 Lignin has mainly been treated as a waste stream for energy production. Currently, due to improved understanding of the aromatic structure of lignin at the molecular level, a large library of modifications and uses of lignin has been developed.11,12 For example, lignin has shown great potential as a sustainable platform for the production of biobased aromatic chemicals, to prepare environmentally friendly as well as low cost lignin-reinforced polymer composites for various engineering applications.10 Hemicelluloses, known as xylans in hardwoods and glucomannans in softwoods, are the second most abundant polysaccharides in plant cell walls and form a complex bonding network by linking cellulose fibers into microfibrils and cross-linking with lignin to provide the plant with structural strength. During the past decade, some biorefinery approaches, e.g., pressurized hot water extraction, have made it possible to fractionate hemicelluloses from wood in economic and eco-friendly processes. Hemicelluloses have been increasingly investigated from various perspectives as feedstocks for

Received: October 27, 2017  
Revised: March 20, 2018  
Published: March 27, 2018
bioethanol, biopolymers, emulsion stabilizers, and possible health applications. There are several excellent reviews discussing the fundamental properties of the three components in wood, including their chemistry, structures, and potential applications.

3D printing is a popular type of additive manufacturing (AM) that provides the ability to rapidly prototype a wide range of object geometries. AM is a family of technologies that includes extrusion, direct energy deposition, ink solidification, and photopolymerization. Various types of materials, including powders, epoxy resins, thermal plastics, and certain gel-like biomaterials, can be rapidly prototyped using computer-aided design (CAD). Owning to the biodegradability, biocompatibility, and noncytotoxicity of wood-derived biopolymers, increasing interest has been shown in using 3D printing techniques to apply them as biomaterials for versatile biomedical applications, such as customized and controlled drug delivery and tissue engineering.

The intention of the current review is to explore the applications of using wood-derived biopolymers in 3D printing techniques. It begins with a brief introduction to the fundamentals of 3D printing systems, which is essential for the following discussion on the required properties of woody biopolymers used as feedstock materials, either in the form of filaments or hydrogels, for various 3D printing techniques. In the core portion of the Review, the utilization—properties—application relationships of wood-derived biopolymers as feedstock materials in 3D printing will be further discussed.
with respect to the subsystems of cellulose, hemicellulose, or lignin. With a narrow focus on biomedical applications, we aim to summarize the current state-of-the-art approaches utilizing wood-derived biopolymers in fabricating personalized pharmaceutical products or functional medical devices via 3D printing techniques. This Review will increase the interest of researchers globally in the AM of woody biopolymers and the development of new ideas in this recently emerging field.

### 3D Printing Technique Overview

Currently, 3D printing techniques are classified into extrusion, direct energy deposition, powder bed fusion, binder jetting, vat photopolymerization, and sheet lamination. During the process of bioprinting, the 3D printing technique that has emerged in the tissue engineering field, complex tissues are incorporated with living cells. The properties of the abundant and widely applicable wood-derived biopolymers, including their high thermal degradation stability, intrinsic gelation, and easy chemical modification, make them suitable as the feedstock materials for 3D printing techniques in the form of solid powders, synthetic photocurable resins, solid filaments, nanomaterial hydrogels, etc. In this section, only techniques currently suitable for wood-derived biopolymers are described.

#### Solid Powder-Driven Technique: 3DP Printing Technique

The 3DP printing technique, which is based on powder binding, is one type of AM, as shown in Figure 1a. Initially, the powder is bound with inorganic or organic binders by inkjet printing to build up individual layers. Subsequently, the powder reservoir is lifted, and the printing platform is lowered one layer before deposition of the next layer. A roller spreads the powder while removing excess powder into an overflow box. More binder is applied to build up the new layer. The above-mentioned steps are repeated to manufacture the 3D object as designed.

#### Liquid Resin-Driven Technique: Stereolithography

Stereolithography, abbreviated as SLA, was the first 3D printing technique when it was developed in 1984 by Charles (Chuck) Hull et al. SLA is a laser-assisted printing technique, as shown in Figure 1b. It uses light to selectively cure and solidify the liquid ink in a layer-by-layer process with an ultraviolet (UV) light projector. The surface of the UV-curable monomer bath is scanned into patterns by UV light representing the slice cross-section and undergoes photoinduced polymerization. The cured layer is formed within 2D cross sections, while the uncured monomer remains in the bath. Thus, the printer only needs to move in the vertical direction.

#### Hydrogel Extrusion: Direct Ink Writing

Direct ink writing (DIW) is also called robocasting. Hydrogels and slurries are used as inks for the DIW system, as shown in Figure 1c. This additive manufacturing technique requires feed inks with an adequate rheological modulus and shear-thinning properties. Most of the time, the hydrogel is stored in a syringe-like reservoir connected to a dispensing nozzle on the printer head. The displacement of the syringe piston and the flow of ink through the nozzle result in stress inside the nozzle on the printer head, causing the viscosity of the hydrogel to decrease and the ink to start to flow. As the hydrogel is deposited and the stress disappears, the hydrogel relaxes and forms a solid gel, resulting in the successful buildup of 3D objects.

The preparation of the hydrogel serving as the printing ink is critical to achieve good printability in DIW. Many excellent existing reviews have focused on the hydrogel preparation, their chemo-mechanical properties, and the relevant applications. In general, inks must be properly formulated such that they can (i) easily and rapidly be gelated, (ii) easily flow through tiny nozzles with low resistance and show shear-thinning properties, (iii) show a high zero viscosity and have enough stiffness to steadily maintain the filament structure after extrusion, (iv) have sufficiently high yield stress and rapidly recover elasticity to prevent viscous flow of the ink and the collapse of the wet printed object, (v) have sufficient solid content after drying to avoid large deformations, (vi) be easily cured with good fidelity by rapid cross-linking methods such as ionic, thermal, and UV-induced curing, and (vii) be compatible, biodegradable, durable and noncytotoxic when aiming at biomedical applications.

#### Solid Filament-Driven Technique: Fused Deposition Modeling

Fused deposition modeling (FDM), which is based on material melting flow-solidification, is a simple and cost-effective approach to 3D object manufacturing (Figure 1d). The hot melt extrusion technique is used for filament manufacturing before printing. As the well-shaped filament goes through the feeding roller, heater, and nozzle, the melt paste is printed layer-by-layer on a printing platform. The successive layer is deposited on the top of the previous layer, and the two are fused together when the material cools and solidifies. Additionally, a cooling fan is attached to the extrusion head to accelerate the cooling and solidification.

Thermoplastics such as polylactic acid (PLA), poly-caprolactone (PCL), ethylene-vinyl acetate (EVA), and acrylonitrile butadiene styrene (ABS) have been typically used as filament feedstock materials. Furthermore, materials having a thermal glass transition and a melting temperature below the temperature used for FDM printing can also be used as composites with these thermoplastics for filament manufacturing. However, factors such as the filament size, printing speed, printing temperature, and mechanical properties of both the filaments and the 3D objects need to be fully understood and adjusted for new material development.

#### Inkjet Printing

In this method, droplets of inks are jetted with the aid of thermal or piezoelectric actuators in a predefined pattern (Figure 1e). The dispersed materials are then polymerized by cross-linking methods such as UV light, chemical, and ionic cross-linking. A wide range of biomaterials can be utilized as the inks for inkjet printing, such as poly(ethylene glycol) dimethacrylate (PEGDMA), sodium alginate, and other hydrogels. A large number of studies have been published to demonstrate the applicability of different bioinks to inkjet printing for the fabrication of drug delivery systems. Inkjet printing is a fabrication method with a high printing speed (up to 10 000 droplets per second) and a wide spatial resolution range of approximately 50–300 μm. Moreover, the modification of commercially available inkjet printers allows their use for 3D bioprinting.

### 3D Printing of Cellulose

Cellulose is a linear homopoly saccharide consisting of β-(1→4) linked D-anhydroglucopyranose sugar units. Cellulose is hydrophilic but insoluble in water and most common organic solvents, mainly due to the presence of multiple intra- and intermolecular hydrogen bonds between the hydroxyl groups of the cellulose chains. The cellulose chains firmly hold together side by side and form microfibrils with high tensile strength. In the context of the direct application of cellulose to 3D printing, cellulose in the form of a dry powder, together with aqueous dextrose as the binder, was initially applied using the 3DP technique to fabricate...
technology has opened new and exciting horizons for applying these cellulose nanomaterials with their natural renewability and sustainable performance in high-value-added applications. In this section, 3D printable wood-derived cellulose materials are reviewed with a narrow focus on biomedical applications.

**Cellulose Ethers.** Cellulose ethers of different varieties are produced on an industrial scale by substituting the hydroxyl groups in cellulose with methyl, hydroxyethyl, hydroxypropyl, and other similar groups. This family includes ethylcellulose (EC), methylcellulose (MC), hydroxyethylcellulose (HEC), hydroxypropyl cellulose (HPC), and carboxymethylcellulose (CMC). Depending on the degree of substitution, cellulose ethers are soluble in alkaline aqueous phases or in different types of organic solvents. With the aid of 3D printing techniques, these cellulose ethers have found applications in personalized drug dosage formulations and in controlled drug release. Ethyl cellulose (EC) and hydroxypropyl methylcellulose (HPMC) were utilized with the 3DP system to design a doughnut-shaped, multilayered drug delivery device (DDD) to provide a linear release profile of acetaminophen as a model drug. In this type of DDD, the hydrophobic EC is not swellable, so it acts as a coating layer to retard the initial rapid release of the drug, while HPMC serves as the inner drug matrix and swells into a gel after contact with the dissolution medium, releasing the drug over a prolonged period by hydrophilic polymer erosion (Figure 2a). The 3DP system offers flexible and easy-to-apply strategies for developing such DDds with complex design features to obtain the desired drug release profile. In the HME process, the drug can also be blended into cellulose materials to fabricate drug-loaded filaments, which can then be further processed via layer-by-layer FDM 3D printing into pills with CAD-designed shapes and thicknesses for personalized drug dosages as shown in Figure 2b. HPMC can be used as a binder in direct extrusion to manufacture controlled release pharmaceutical bilayer tablets, in which MCC is also used as the disintegrant for an immediate release layer, as shown in Figure 2c.

Recently, the fabrication of DDds via FDM 3D printing using cellulose etherified derivatives, i.e., EC, hydroxypropyl methylcellulose acetate succinate (HPMCAS), HPMC, and hydroxypropyl cellulose (HPC) has also been demonstrated with the aim of controlled drug release for 3D constructs for tissue engineering applications. Meanwhile, the infiltration of lysine ethyl ester disocyanate has been employed to improve the mechanical strength after solidification. Microcrystalline cellulose (MCC) can be prepared by the depolymerization of cellulose (degree of polymerization (DP) less than 400) using enzymes or chemical treatments such as steam explosion or acid hydrolysis to remove the amorphous regions in the cellulose microstructure. The particle size of MCC varies within the range of tens of micrometers depending on the sources and preparation methods. MCC has been applied as a valuable additive in cosmetics and pharmaceuticals owing to its useful properties, e.g., power porosity and hydration swelling/moisture retention capabilities that are relevant to such applications. More recently, due to its high crystalline index and superior mechanical strengths, MCC was applied as a reinforcing component at 1–5% for PLA in a solvent casting process and was successfully subjected to HME for filament preparation and FDM 3D printing. Meanwhile, the MCC surface was modified with a titanate coupling agent to improve its compatibility with hydrophobic PLA.

Direct dissolution of cellulose can be achieved in several alkaline aqueous solvents under rather strict composition and temperature conditions, such as 7–10% NaOH/H2O or NaOH (7%)/urea (up to 13%)/H2O solutions at low temperature (<0 °C), as well as in a mixture of N,N-dimethylacetamide/lithium chloride (DMAC/LiCl), in N-methylmorpholine N-oxide (NMMO) and more recently, in ionic liquids. As recently demonstrated, cellulose dissolved in NMMO can be used as a feedstock ink and printed at 70 °C via DIW printing, and after cooling, the solidified cellulose/NMMO objects can be regenerated into cellulose scaffolds in water, showing a remarkable compressive Young’s modulus of 12.9 MPa and a tensile modulus of 160.6 MPa. Further chemical modifications of dissolved cellulose or the functionalization of cellulose fibers to alter the fiber–fiber interactions are strategic routes to improve the processability and potential applications of cellulose materials. Cellulose ethers and esters can be prepared via chemical reactions with dissolved cellulose. They are useful in various value-added applications, including as food additives, cosmetics, and pharmaceuticals. More importantly, the development of nanoscale cellulose (CNFs and CNCs) in nano-
personalized therapy. The release profile can be manipulated based on the effect of physiological conditions such as pH on the solubility, including whether the formulation has rapidly soluble, swellable/erodible, or insoluble yet slowly permeable properties. During the HME process, to obtain drug-loaded filament of cellulose ethers, a plasticizer such as triacetin, polyethylene glycol (PEG), or triethyl citrate (TEC) is needed to improve the thermoplasticity. Table 1 summarizes cellulose ethers used for controlled drug release based on the FDM technique.

CMC is the most widely used cellulose ether globally. In contrast to the other cellulose ethers discussed above, CMC can be ionic (the form typically used is CMC-Na), has a high viscosity and can act as a binder or thickening/gelation agent in formulating colloidal inks for DIW printing. Depending on the Mw, CMC can be used to adjust the flow and elastic properties of DIW inks: neat CMC with a Mw of 35 kDa acts as a dispersing/gelling agent, enhancing the stiffness of the gel network upon adding amounts up to 2 wt %. In contrast, longer CMC chains with a Mw of 250 kDa at 1 wt % induce a greater thickening effect in the DIW ink 4SS5 Bioglass for 3D printed scaffolds in tissue engineering application. Surface modification of CMC in hydrogel form would further favor its applicability. Aldehyde-modified CMC was mixed with

Table 1. Details of Different Cellulose Ethers Applied to FDM 3D Printing for Drug Delivery Device (DDD) Design

| Cellulose derivatives | Function of DDDs | Plasticizer | HME T (°C) | Screw speed (rpm) | FDM T (°C) | 3D design | Reference |
|-----------------------|-----------------|-------------|-------------|-------------------|-------------|-----------|-----------|
| EC                    | Barrier material suitable for printing capsules and coating layers for immediate or modified release | 10% TEC, 5% PEG | 160 | 100 | 100 | 200 | Disk | 36 |
| HPMC                  | 20–40% HPMC proportion could affect the release of nitrofurantoin | PLA as a carrier | 160–180 | 70–100 | 70–100 | 200 | Disk | 36 |
| HPC                   | Barrier material suitable for printing capsules and coating layers for immediate or modified release | None | 165 | 80 | 40 | 180 | Disk | 36 |
|                       | Capsule design and pulsatile release of drugs | 0–10 wt % PEG | 150–165 | 50–60 | – | 180 | Capsular device | 35 |
|                       | As a carrier polymer for theophylline release | Triacetin | 110 | – | – | 160 | Easy-flow tablet design | 59 |
|                       | As a carrier polymer for intragastric domperidone release | None | 145–150 | 20–25 | 10–20 | 210 | Hollow | 61 |

Figure 3. Gelation by mixing CMC and chemically modified gelatin solutions with a double-barrel syringe and steps in the fabrication of vascular structures using electrochemical cell transfer from a gold-coated rod to a gelatin-CMC hydrogel (a), schematic illustration of the strengthening mechanism at the alginate/MC hydrogel interface using a TSC solution (b), picture of a grid scaffold printed with 50 layers (height ∼12 mm) (c), star construct with 100 layers (height ∼24 mm) (d), and image of a hydrogel slab with knotting force (e). Note: (a) reproduced with copyright permission from the American Chemical Society, (b–e) reproduced with copyright permission from the American Chemical Society.
Table 2. Summary of Different Kinds of CNFs for 3D Printing with Respect to the Printing Technique, The Rheology Modification Method, and the Wide-Ranging Applications

| CNF type                        | Surface charge mmol/g | Load consistency | Rheology modifier/cross-linking | Application                                                                 | Printing technology and printer used                  | Cell line                          | ref. |
|---------------------------------|-----------------------|------------------|---------------------------------|------------------------------------------------------------------------------|------------------------------------------------------|------------------------------------|------|
| Carboxymethylated-periodate CNF | 3.9 wt %              | 3 wt %           | Ionic cross-linking by CaCl₂     | Inhibits bacterial growth and shows potential for wound dressing             | DIW, Envision TEC                                    |                                    | 73   |
| Mechanoenzymatically hydrolyzed CNF | 0.5–2 wt %           | 2.5% (w/v)       | Lignin sulfonate                 | Carbon precursors                                                            | DIW, Seraph Robotics                                 |                                    | 88   |
|                                  |                       |                  | 10–40% Alginate                 | Cartilage                                                                    | Electromagnetic jet technology, microvalve-based bioplotter from regenHU | Human nasoseptal chondrocytes | 45, 91, 94 |
|                                  |                       |                  |                                  |                                                                              |                                                      | Adipocytes                         | 107  |
|                                  |                       |                  | 1.9% (w/v) Alginate sulfate      | Cartilage                                                                    |                                                      | Human nasal chondrocytes           | 92   |
| TEMPO-oxidized CNF               | 0.54                  | 1 wt %           | Collagen rich bone mimetic and calcium phosphate coating | Attachment of hMSCs and promotion of differentiation toward osteogenesis; Supporting cell adhesion |                                                                 | hMSCs                              | 97   |
|                                  |                       |                  | EG-co-DMA                       | Gradient material                                                            |                                                      |                                    | 90   |
|                                  |                       |                  | 0.5 wt %                        | Ionic cross-linking by Cd²⁺                                                  |                                                      |                                    | 99   |
| Mechanical grinded CNF           | 0.5–2.0 wt %          | 0.5 wt %         | UV cross-linking of 5% GelMA     | Photoelectric ink for screen printing                                        |                                                      | NIH 3T3 fibroblasts               | 96   |
| Carboxymethylated CNF            | 0.2 wt %              |                  | Sulfactant, e.g., CTAB           | Electronic devices with CNTs                                                 |                                                      |                                    | 100  |

*Note: wt % denotes weight percentage, (w/v) denotes weight/volume ratio.*
hydrazide-modified gelatin, which then readily and rapidly forms a cross-linked hydrogel through the hydrazide/aldehyde coupling reaction during extrusion-based 3D printing. Manipulating the concentrations of the two hydrogel components can alter the stiffness of the formed hydrogel. The obtained gelatin-CMC hydrogel, as shown in Figure 3a, is a cyto-compatible matrix for vascular endothelial cells, providing a suitable microenvironment for angiogenesis.63

Methylcellulose (MC), as a viscosity-enhancing polymer, was blended with alginate to formulate a bioink,64 as shown in Figure 3b–e. The addition of MC to alginate mainly contributed to the formation of a semi-interpenetrating network-like structure. The strong hydrogen bonding among the abundant hydroxyl groups in MC and the carboxylic groups in the alginate, as well as the ionic cross-linking between alginate chains mediated by Ca2+, give the formulated bioink a high viscosity and excellent thixotropic properties. In addition, trisodium citrate (TSC) is applied to each printed layer at the interface of the alginate/MC ink to improve the interfacial bonding between the layers. Meanwhile, a low-viscosity TSC solution serving as a cell medium made the loading and depositing of cells in the highly viscous alginate/MC bioink easier.

Cellulose Nanomaterials. Bioinks with integrated cellulose nanomaterials have attracted a great deal of attention due to their renewable nature, outstanding mechanical properties, and biocompatibility. Wood-derived cellulose nanomaterials with different sizes can be produced in the form of CNFs or CNCs. Certain established processes, such chemical, enzymatic, and mechanical treatments, as well as the combination of these methods, can be applied to produce nanocelluloses from a variety of natural resources.4,67 The preparation of nanocelluloses, their material properties, and highlighted applications in various disciplines can be obtained from other comprehensive reviews on the relevant topics.3,4,17,68,69

Cellulose Esters. Cellulose acetate (CA), where the hydroxyl groups in cellulose are replaced by acetate groups, is one of the cellulose ester derivatives that results in the disruption of the inter- and intramolecular hydrogen bonds in cellulose. Unlike unaltered cellulose, CA can be dissolved in acetone and acetone-based solvent mixtures such as acetone/DMF. CA solution can be obtained when a large amount of CA with a consistency above 20 wt % is dissolved in organic solvent. Minseong Kim et al.65 utilized the viscoelastic properties of CA and developed 3D scaffolds using an electrohydrodynamic direct-jet process (spin printing). The scaffold is rapidly fabricated by quickly changing the solvent from acetone/DMF to ethanol.66 When using only acetone as the CA solvent, direct solvent evaporation can be conveniently applied.66 A higher CA consistency of 25−35 wt % was printed using a modified extrusion method, where a capillary nozzle connected to a fluid dispenser was used to deposit the CA solution. Post-treatment by immersing the printed object in a sodium hydroxide solution converted the CA to cellulose, which increased the Young’s modulus and tensile strength.

Cellulose Nanomaterials. Bioinks with integrated cellulose nanomaterials have attracted a great deal of attention due to their renewable nature, outstanding mechanical properties, and biocompatibility. Wood-derived cellulose nanomaterials with different sizes can be produced in the form of CNFs or CNCs. Certain established processes, such chemical, enzymatic, and mechanical treatments, as well as the combination of these methods, can be applied to produce nanocelluloses from a variety of natural resources.4,67 The preparation of nanocelluloses, their material properties, and highlighted applications in various disciplines can be obtained from other comprehensive reviews on the relevant topics.3,4,17,68,69

Briefly, CNFs consist of both amorphous and crystalline regions and is defined by cellulose fibrils with diameters of 5−
60 nm and lengths of approximately a micrometer. These flexible and long cellulosic nanofibrils give a gel-like consistency upon mechanical defibrillation. Chemical and enzymatic pretreatments facilitate the fibrillation of cellulose fibrils and reduce intensive energy consumption. For example, TEMPO/NaBr/NaClO pretreatment combined with mechanical defibrillation post-treatment is one of the typical procedures used to produce well-fibrillated CNF material from wood sources. A defined surface chemistry with abundant carboxylic groups and a small aldehyde content is obtained. The surface chemistry of CNF materials plays an important role, as the functional groups allow their use for biosensing and for the implementation of cross-linking chemistry in the hydrogel, which can further improve the mechanical properties of the material.

Unlike flexible CNFs, CNCs have a relatively high crystallinity (54–88%), possessing a diameter of 3–10 nm and a rod length of 50–500 nm (DP between 100 and 300), and intrinsically has a rod-like morphology, directionality with chiral nematic phases, and shear-thinning rheological properties. CNCs are primarily produced by acid hydrolysis. Reported studies on the preparation of CNCs have conventionally used strong mineral acids such as sulfuric acid, hydrochloric acid, phosphoric acid, and nitric acid for the hydrolysis reaction. To make these processes more sustainable and economical, organic acids such as formic acid, oxalic acid, and maleic acid have been employed to accomplish the hydrolysis as well, achieving a high yield of CNCs. These approaches are less corrosive and offer a competitive advantage because the acid used is easily recycled. Meanwhile, CNCs can also be produced by oxidation using ammonia persulfate, or TEMPO oxidants to impart further functionality by introducing carboxylic groups on the surface of CNCs.

Cellulose Nanofibrils (CNFs). CNFs in the form of hydrogels stand out as a platform biomaterial in bioink formulation for 3D printing owing to their low cytotoxicity and structural similarity to extracellular matrices (ECM). In Table 2, the authors have summarized different types of CNFs used in 3D printing strategies, highlighting the printing technique, rheology modification method, and the applications.

CNFs were first proposed for fabricating implants and scaffolds for tissue engineering applications using inkjet printing technique by Gatenholm et al. in 2011. The utilization of nanocellulose was accomplished by a bioplotting technique that ionically cross-linked oxidized nanocellulose with 0.05 M CaCl2. Rees et al. have also successfully printed carboxymethylated periodate-oxidized nanocellulose (C-periodate nanocellulose) on a TEMPO-mediated oxidized nanocellulose film, as shown in Figure 4a. C-periodate nanocellulose with a high consistency of 3.9 wt % shows a pronounced shear thinning and thixotropic behaviors, enabling the DIW process. However, TEMPO-mediated oxidized nanocellulose with a low consistency (0.9 wt %) tends to collapse after drying and leads to failure of the printing.

To improve the ink printability and the printed structure fidelity, CNF hydrogels can be formulated with an auxiliary material, which can be compatibly blended with CNFs to modify the ink rheological properties. Furthermore, the blended material with an increased loading consistency can improve the stability of the printed structure, especially after drying. As an ink modifier, water-soluble lignosulfonate (LS) has been applied to adjust the rheological properties of 2 wt % nanocellulose obtained via mechanoenzymatic hydrolysis, as shown in Figure 4d. The addition of 0–10% and 50% LS maintains the object geometry after printing. At high LS concentrations, the high viscosity of the suspending medium provides sufficient time to rebuild a continuous nanocellulose network and keep the cuboid geometry. With 50% LS, air drying leads to acceptably limited shrinkage due to the high load consistency. TEMPO-oxidized CNFs incorporated with alginate and glycerin have been developed as a 3D printable hydrogel. Replacing water with nonvolatile glycerin and increasing the solid content with a large ratio of alginate improve the printability of the formulated hydrogel.

Physical cross-linking is the most applicable and robust strategy for maintaining the 3D printed CNF geometry by introducing a cross-linkable network into the formulated CNF ink. Typically, cross-linking is realized by polymer chain entanglement or through physical interactions such as hydrogen bonds, ionic interactions, or thermal cross-linking. TEMPO-oxidized CNFs (0.44 mmol/g COOH groups) and a water-soluble copolymer, nonionic poly[(ethylene glycol methyl ether methacrylate)-co-N,N-dimethylacrylamide] (EG-co-DMA) were formulated into a nanocomposite hydrogel (Figure 4e). Combining the direct filament writing of the shear-thinning nanocomposite hydrogels and the subsequent “healing” of the filament during drying owing to the strong hydrogen bonding when the water was evaporated, a mechanically coherent bulk nanopaper was obtained. The homogeneous incorporation of highly hydrophilic EG-co-DMA into the cellulose nanofibrils, which acts as the energy-dissipating part of the nanopaper and mediates the frictional sliding of the CNFs during deformation owing to the fine adjustment of the Tg in EG-co-DMA, yielded a wide tenability window in terms of the mechanical properties of the nanocomposites. With manipulation of the compositional ratio of the nanocomposite hydrogel in adjacent filaments, a film prepared in this way featured mechanical gradients and gave an anisotropic response. These gradients are relevant to fundamental studies of the interactions of cells with CNF materials.

Ionically cross-linked alginate improved the shape fidelity when the ink was formulated by combining 2.5% (w/v) nanocellulose obtained via mechanoenzymatic hydrolysis with 10–40% of alginate, as demonstrated by Markstedt et al., owing to the good compatibility between alginate and CNFs. The integration of alginate into the bioink also improved the object resolution before cross-linking. This type of ink, with 20% blended alginate (Ink8020), showed the best performance in terms of rheological properties, compressive stiffness, and shape fidelity after ion cross-linking with Ca2+, as shown in Figure 4b. Ink8020 also supported human nasoseptal chondrocytes with a cell viability of 85.7 ± 1.9% after 7 days of culture. Recently, 60:40 CNF/alginate incorporating human-derived induced pluripotent stem cells has shown positive results for supporting cartilage production. In CNF/alginate prints, the pluripotency was initially maintained, and hyaline-like cartilaginous tissues with type II collagen were obtained after 5 weeks of culture. Meanwhile, no tumorigenic expression was observed in the CNF/alginate printed constructs. A thermal cross-linking strategy can be applied to CNF ink, in which a thermally sensitive biopolymer is employed as an auxiliary material in the ink formulation. For example, the gelation of collagen I to form a semifluid gel occurs upon changing the temperature from 4 to 37 °C, which has shown great potential in DIW with a thermally assisted syringe.

As a result of the tremendous interest in natural cellulose-based bioinks, a product is being commercialized under the
trademark CELLINK by CELLINK AB (Sweden). CELLINK bioink is formulated with 2% (w/w) plant-derived CNFs and 0.5% (w/w) sodium alginate. The formation of 3D bioprinted human nasal chondrocyte-laden auricular constructs with open inner structures and high shape fidelity using CELLINK is demonstrated in Figure 4c. The printed 3D construct mimics the biological environment while offering an improved nutrient supply to embedded cells and supporting the redifferentiation of human chondrocytes in vitro. 

Apart from the physical cross-linking discussed above, the printed CNF geometry can also be enhanced by chemical cross-linking within CNF or with the network of the auxiliary material. The abundant hydroxyl groups in cellulose and the aldehyde and carboxylate groups introduced on the surface of CNF by TEMPO oxidation provide feasible routes for various chemical cross-linking strategies, which can be directly applied to print CNF or indirectly to the auxiliary material. In a cell-laden bioink formulated by blending CNFs with hyaluronic acid (HA), the cross-linking of HA was performed using a small amount of H$_2$O$_2$. Ink with 70% CNF and 30% HA showed the highest compressive stiffness, and promising results in adipose tissue engineering were confirmed: after 3D bioprinting, the adipocytes accumulated more lipids, and the gene expression level of adipogenic markers increased. HA with tyramine groups as a base component incorporated with CNF represents an elegant approach to develop tissue-specific bioinks. Similarly, xylan modified with tyramine groups was integrated with CNFs in the formulated bioink. The cross-linking proceeded within seconds in the presence of both horseradish peroxidase and H$_2$O$_2$. Most importantly, the strong affinity between xylan and CNF is beneficial for the ink compatibility.

Photoinduced curing is an easily applicable and convenient post-treatment that improves the stability of the printed structure by incorporating a photoinitiator and a photo-cross-linkable auxiliary material. Irradiation can be applied in situ and after printing. For example, methacrylated gelatin (GelMA) is a naturally derived photo-cross-linkable reagent from collagen with favorable properties for improving biological interactions. A low-concentration GelMA (5% (w/v)) precursor solution improved the printability of mechanically grinded CNF with a
gradient concentration up to 2% (w/v) and enhanced the mechanical properties and shape fidelity of the printed constructs, as shown in Figure 5i. NIH 3T3 fibroblasts were included in the inks for bioprinting, which showed low cytotoxicity and high cell viability. Our own ongoing study has shown that even lower concentrations of GelMA (0.2% to 1% (w/v)) can modify the surface of TEMPO-oxidized CNFs, preserving the printed structure and tailoring the mechanical properties of the printed scaffold after UV cross-linking.

Printing a supporting sacrificial polymer is an indirect way to obtain good hydrogel shape fidelity and impart porosity to gels. Recently, 1 wt % TEMPO-oxidized anionic CNFs and nanochitin (ChNF) were successfully shaped into a gyroidal hydrogel structure by a reverse templating sacrificial approach, as shown in Figure 5ii. The sacrificial templates were prepared by a lithographic 3D printing technique based on a mixture of methacrylates and acrylamides, which are easily solubilized in NaOH. The remaining CNF scaffolds, which were sequentially deposited with a collagen-mimetic coating and a calcium phosphate coating, facilitated the attachment of human mesenchymal stem cells (hMSCs) and encouraged their differentiation toward osteogenesis. TEMPO-oxidized CNFs supported the cell adhesion since the negatively charged carboxyl groups (0.54 mmol/g) electrostatically attract the positively charged collagen I, which is one of the most important proteins governing cell adhesion, at physiological pHs. The authors also stated that the scaffold shape could be recovered after rehydration, even though air drying led to collapse of the macropores.

In addition, CNF can be applied as the carrier for the 3D printing of electronics. Photoelectronic ink was fabricated with TEMPO-CNF and CdS quantum dots by controlling the carboxylic charge density and the molar ratio of Cd2+. The homogeneous ink composite showed stability with excellent fluidity and rheology. In another study, a conductive ink consisting of highly charged carboxymethylated CNFs and carbon nanotubes (CNTs) with potential applications in printing electronics was demonstrated, as shown in Figure 7.
revealed that thermal annealing of the surface tension between the two would improve their morphological, thermal, and mechanical properties. Furthermore, CNCs have demonstrated the printability of a mild acid-hydrolysis treatments of cellulosic materials and have also been utilized to formulate inks for 3D printing. CNCs are characterized by superior mechanical strength and inherent stiffness, allowing them to be incorporated into 3D printed polymers to provide the necessary toughness. The application of CNC gels to DIW printing was first shown by Gilberto Siqueira et al. As illustrated in Figure 7A, they overcame the low consistency ink loading of CNFs by using the maximum 20 wt % of freeze-dried and redispersed CNFs. Furthermore, CNCs surface-modified with methacrylic anhydride to introduce a vinyl functionality were UV cured with a solution containing a 2-hydroxyethyl methacrylate (HEMA) monomer, polyether urethane acrylate (PUA), and a photoinitiator. The modification allowed a high solid loading of CNCs in the ink. The composite showed higher transparency than unmodified composites. Importantly, the CNC-reinforced monomer inks yielded a high degree of CNC alignment along the printing direction. Recently, an ink formulated with CNC-filled poly(ethylene glycol) diacrylate (PEGDA) demonstrated good printability, fidelity, and mechanical integrity for a complex design obtained via SLA printing, as shown in Figure 7B.

Three-dimensional CNC aerogels with well-controlled overall structures and dual porous structures were fabricated using the DIW method followed by freeze-drying and had a high CNC consistency (from 11.8 to 30 wt %) based on an initial CNC suspension and redispersed freeze-dried CNCs. A post-cross-linking method using the addition of a wet-strength additive, polyamide-epichlorohydrin (Kymene), was applied to enhance the mechanical properties of CNC aerogels in both dry and wet forms. The porous aerogel exhibits great potential for complex and customized applications in the context of tissue engineering. Jia et al. have demonstrated the printability of a mild acid-hydrolyzed CNC, pre-disk-milled-oxalic-acid-hydrolyzed CNC (DM-OA-CNC), which showed potential as a tissue engineering scaffold due to its high thermal stability, excellent biocompatibility, and porous structure.

Lignin-coated CNC (L-CNC), which has recently been used as a reinforcing component in both resin and filaments, can be printed via SLA or FDM. L-CNC is obtained by the SO₂-water (SEW) fraction method with sticky lignin precipitated with CNC. The presence of the hydrophobic lignin makes CNC less polar, which decreases the surface tension between the L-CNC and a nonpolar matrix, such as ABS or methacrylate (MA) resin. In the twin-screw blending of L-CNC/ABS, a high loading up to 10 wt % L-CNC was achieved in the composite, which was used to produce the feedstock filament for FDM printing. Meanwhile, dispersion of only 0.5 wt % of L-CNC in the MA resin via sonication greatly enhanced the tensile strength and modulus of the printed object after UV-curing post-treatment.

Liu et al. studied the formation of stabilized liquid tubules by injecting aqueous CNC-based nanoparticles into amine end-functionalized polystyrene in toluene. The liquid tubules (Figure 7C) were controlled using self-assembly and jammed at the water/toluene interface by fine-tuning the pH, the concentrations of CNC and the polymer ligand, and the flow rate. Translating liquid to continuous tubules could boost the 3D printing of low-viscosity liquids (especially CNC suspensions), overcoming the typical issue of low load consistency.

### HEMICELLULOSES: PROPERTIES AND ASPECTS FOR 3D PRINTING

Hemicelluloses are soluble, branched, and amorphous heteropolysaccharides, the majority of which are xylans in hardwoods and glucomannans in softwood. In another alternative method of cross-linking glycans, hemicelluloses firmly link together with cellulose fibers in plant cell walls through a complex bonding network. After being fractionated from woody biomasses, the high physical affinity between hemicelluloses and the cellulose surface is retained. This gives hemicelluloses an applicable niche as anchor polymers to engineer the surface of cellulose fibers. Structurally, hemicellulose contains either pentose or hexose with many free hydroxyl groups, which are easily functionalized by, for example, esterification, etherification, or reductive amination. In our past studies, tuning the surface properties of CNFs (wettability and surface rigidity) using hardwood hemicellulose from spruce, galactoglucomannan (GGM), and its derivatives (GGM-graft-fatty acid, GGM-block-fatty acid, and GGM-block-PDMS) was investigated. By employing different cross-linking strategies, hemicellulose-based hydrogels can also be prepared by methacrylate derivatization and thiol functionalization. This has inspired the utilization of hemicellulose derivatives as promoting agents in the 3D printing of nanocelluloses, which offer a cross-linking network by binding with the cellulose matrix in the wooden bioink. As demonstrated by Markstedt et al., tyramine-modified xylan acts as both a fiber surface modifier and a biodegradable cross-linker in the formulation of nanocellulose bioinks.

Moreover, hemicelluloses are now more accessible due to cost-effective and sustainable extraction methods such as hot water extraction. A more recent patented technology that integrates a vacuum into the process design has claimed that water-soluble and polymeric hemicelluloses can be extracted at almost 100% yield from commercial wood chips at a lower temperature (<150 °C) than what is used in conventional hot-water extractions. Our recent study focused on using bulk pure GGM from spruce as a renewable alternative biopolymer to replace the synthetic biodegradable polymer PLA in FDM printing. By using a solvent blending method, a homogeneous...
composite can be obtained from two biopolymers with different polarities. During HME and FDM processes, GGM showed steady thermal stability without severe degradation. It is worth noting that the mechanical properties of the HME filament remained similar to those of a PLA filament when 20% of the PLA was replaced.

**LIGNIN: PROPERTIES AND ASPECTS FOR 3D PRINTING**

There are still very few studies on 3D printing using lignin as the major ink component compared to other biopolymers. A recent review by Graichen et al. noted that scalable lignin-based products obtained by applying 3D printing approaches would be promising. 3D printing approaches, including the choice of printing technologies and the formulation of lignin-based inks, remain to be developed.

Lignin, one of the wood biorefinery side products and waste-stream products, has an annual production of 140 million tons and shows great economical potential for biobased products, including as a 3D printing feedstock, demonstrating that money can be made from lignin. Recently, a few studies have introduced lignin into printing inks as a performance enhancer. For example, lignin-coated CNC was recently applied to both FDM and SLA 3D printing in combination with ABS and methacrylate resin, respectively. In both cases, the addition of lignin-coated CNC increased the mechanical properties, such as the mechanical strength and thermal stability of the printed matrix. The lignin plays an important role in making the blends compatible and particularly in improving the thermal stability. Thus, Kraft lignin incorporated with ABS, for example, shows the potential use of lignin/ABS composite in FDM 3D printing. The cost of using ABS decreased when lignin partially replaced ABS with the assistance of a decreased amount of PEO (plasticizer). Moreover, the investigation of the adhesive function of lignin as a new type of resin is another direction for the SLA printing technique.

The complex structure of lignin products varies greatly depending on the origin, extraction process, and any post-treatment. The carboxylic, aldehyde, and sulfonate group contents also differ and determine the properties of the lignin products. To improve the processability and broaden the applicability of lignin, modification approaches are desired to increase its chemical reactivity. In fact, lignin possesses a certain amount of thermoplastic behavior and thus has been blended with different synthetic polymers, as discussed above. To achieve satisfactory miscibility and improved properties, such as the mechanical strength of lignin-based composites, modifications are often needed. As an example, a lignin-based thermoplastic was prepared by altering the molecular weight and then coupling with polybutadiene. The enhanced thermoplastic properties of lignin-based products will ensure better performance of lignin-based filaments in FDM-based printing. 3D printing enables vast applications of lignin-based materials as biobased plastics. Above all, to realize biomedical and pharmaceutical applications, both the plastics and the printed scaffolds need to be biocompatible and nontoxic.

More recently, lignin in different forms has been intensively studied for biomedical applications and as a drug delivery carrier, particularly due to its antioxidant activity. In a study of engineering PLA-lignin nanofibers, the antioxidant activity increased with an increase in the lignin content. However, high doses of lignin inhibited cell proliferation. Thus, good biocompatibility is achieved at a balanced lignin concentration. Blends with thermoplastics are suitable inks for FDM printing. For DIW, water-based hydrogels of hyaluronan, alginate, gelatin, and, more recently, cellulose nanomaterials have been developed as ink formulations. However, a balance between the hydrophilicity and the hydrophobicity of the matrix surface is critical for cell adhesion. Thus, lignin, with its hydrophobic character, could be incorporated into hydrogels to tune the hydrophilicity of the resulting matrix. Another emerging area of application is the development of lignin-based nanoparticles as nanocarriers for drug delivery. Stable lignin-based nanosystems may offer promising nanodelivery solutions for medical applications when hydrogel inks are developed for printing.

**PRESENT AND FUTURE PERSPECTIVES**

The application of wood-derived biopolymers to 3D printing techniques for biomedical applications is an emerging field that offers unexploited potential to seek more advanced functional materials from the most abundant and sustainable resources on earth, as well as to respond to the global trends toward personalized medicine and therapy. Cellulose and its versatile derivatives have been widely studied in the fabrication of customized DDDs capable of controlled drug release by using 3D and FDM printing combined with an HME step. More importantly, due to the biocompatibility, superior mechanical properties, promotion of cellular interactions and tissue development, mimicking of the extracellular matrix, and in vitro biodegradability of nanocellulose, it is currently extensively employed as part of a new generation of nanomaterials for versatile global biomedical applications. Both nanocelluloses and their nanocomposites are used to fabricate tissue engineering scaffolds and cartilage implants via 3D bioprinting techniques. In particular, CNF with its intrinsic gel-formability satisfies the application criteria for bioplotting, inkjet printing, and extrusion-based printing. Hemicelluloses hold great promise as promoting agents, acting as both fiber surface modifiers and cross-linkable auxiliary materials in the formulation of CNF-based bioinks for 3D printing. Lignin is the next most studied woody polymer and possesses versatile properties suitable for several 3D printing techniques. Due to the thermoplastic nature of lignin, lignin has been incorporated into thermoplastic polymers such as ABS for FDM printing.

Nevertheless, the utilization of wood-derived biopolymers as nontoxic and biocompatible biomaterials in biomedical applications is limited by FDA requirements regarding endotoxin levels. Cellulose and its derivatives such as HPC (21CFR172.870), CMC (packaging), Na-CMC, methyl ethyl cellulose (21CFR172.872), and FiberLean MFC (a composite of microfibrillated cellulose and minerals) have received clearance from the FDA as Generally Recognized As Safe (GRAS) food substances or for use in food packages. Moreover, the use of MCC as a pharmaceutical excipient and as a food additive dates back to the 1940s.

The in vivo degradation of nanocellulose is another critical issue limiting its development in biomedical applications. The unavailability of enzymes to break the β-(1,4)-glycosidic linkages and the extraordinarily high degree of crystallinity in nanocelluloses make their degradation quite slow in the human body, leading to nonbiodegradability. To address this issue, many attempts have been made to enhance the degradability of cellulose products in vivo, such as periodate oxidation to

DOI: 10.1021/acssuschemeng.7b03924
ACS Sustainable Chem. Eng. 2018, 6, 5661–5680
introduce 2,3-dialdehyde groups in the nanocellulose chain, enzymatic degradation using the synergistic effect of nano-complexed exoglucanase and free endoglucanase, and irradiation with γ-radiation to enhance the degradation rate. On the other hand, nonbiodegradable cellulose could be used as a durable supportive material in applications such as cartilage meniscus implants, bone tissue implants, and cardiovascular implants. Combined with advanced 3D printing techniques, patient-specific or customized implants can be accessibly manufactured, easing the complexities of tissue regeneration and drug delivery.

Another challenge lies on the fact that the production of nanocellulose is not yet cost-effective and completely environmentally friendly. The high price of medical-grade nanocellulose products hinders their comprehensive study and further application. On the market, GrowDex from UPM (Finland) is one commercial CNF hydrogel product used as a cell culture medium. Cellink is the only company that has commercialized nanocellulose-based bioinks for the 3D bioprinting of human organs and tissue. In particular, research initiatives and efforts are needed to develop 3D printable woody bioinks aimed at minimizing the cost while still satisfying the needs of versatile applications.

There is a vast available amount of lignin. However, due to its complex structure, its high value applications in such areas as the biomedical field are just beginning to be explored. Its antioxidant activity and hydrophobic character may open opportunities for medical applications and drug delivery. However, its concentration-dependent effect on cell viability should be considered, and further evaluation should be carried out to understand its biocompatibility and cytotoxicity.

Finally, wood-derived biopolymers are so-called bioinert materials: they offer excellent biocompatibility without promoting biological activities. Therefore, the application of wood-derived biopolymers in the tissue engineering field is expected to create bioactive woody bioinks through applicable functionalization. For instance, grafting peptides onto cellulose or xyloglucan promotes cell adhesion and proliferation. Another study has shown that epichlorohydrin-cross-linked HEC/soy protein composite films had an anticoagulation effect on platelets, which decreased the risk of thrombotic complications and promoted hemopoiesis for wound dressing. In summary, wood-derived biopolymers are amenable to chemical functionalization, and adaptation of their chemistry could result in significant changes in the material properties, such as their processability, degradation, stiffness, and physiologically relevant bioactivities.

With ongoing studies to fully understand how a tissue or scaffold constructed by 3D printing with woody bioinks behaves in vivo and in the human body, we will hopefully begin to see a transition from laboratory investigations of the 3D printing of wood-derived bioinks for constructing prototype biomedical devices to more clinical trials and finally to commercial products for therapy in the next decade. Overall, 3D printing is a promising and exciting tool for broadening the utilization of wood-derived biopolymers in tissue engineering and regenerative medicine, but a considerable amount of effort is still needed in the area of woody bioink development before it reaches its full potential.

As concluding remarks, the authors strongly postulate the following:

1. Multicomponent systems, e.g., nanocomposites, are a promising trend in formulating woody bioinks, such as formulating nanocellulose hydrogels for better printability and shape fidelity.
2. Surface modification of wood-derived biopolymers to improve their compatibility with resin materials would definitely attract more attention as a component material for 3D printing.
3. Lignin and hemicelluloses, which are abundant, easily modified, and biodegradable, will definitely attract more attention as a component material for 3D printing.

Author Contributions
W. Xu mainly outlined and drafted the paper; X. Wang, N. Sandler, S. Willför, and C. Xu revised and gave valuable comments on the paper. All the authors have given approval to the final version of the paper.

Notes
The authors declare no competing financial interest.

Biographies

Mr. Wenyang Xu completed an M.S. degree in Chemical Engineering with the Faculty of Science and Engineering of Åbo Akademi University, Finland, in 2015. Currently, he is a Ph.D. candidate under the supervision of Dr. Chunlin Xu and Professor Stefan Willför in the Laboratory of Wood and Paper Chemistry at Åbo Akademi University. His research topic is the utilization of wood-derived biopolymers via 3D printing techniques for biomedical applications.
Dr. Xiaoju Wang received her Ph.D. degree from the Laboratory of Inorganic Chemistry at Åbo Akademi University, Finland, in 2012. Currently, she is a senior postdoctoral researcher in the group of Professor Stefan Willfors group in the Laboratory of Wood and Paper Chemistry at Åbo Akademi University, Finland. Her recent research has focused on sol–gel-derived bioactive glasses and their composite materials with wood-derived biopolymers as well as with synthetic biodegradable polymers for various tissue engineering applications. She has published 13 scientific papers in international peer-reviewed journals.

Dr. Niklas Sandler is a Professor of Pharmaceutical Technology and Vice Rector at Åbo Akademi University, Finland. He graduated from the University of Helsinki in 2003. He has been a postdoctoral fellow at the University of Otago, New Zealand, a senior researcher at AstraZeneca Pharmaceutical and Analytical R&D, UK, and a Professor of Industrial Pharmacy at the University of Helsinki. In 2009, he was appointed as Professor in Pharmacy at Åbo Akademi University, where he heads the research on pharmaceutical technology. He has pioneered research around printable drug delivery systems. He works together with colleagues and the coauthors of this review in the Drug Development and Diagnostic strategic profiling area of AAU.

Dr. Stefan Willfors has been a Professor of Renewable Materials Chemistry in the Faculty of Science and Engineering, Laboratory of Wood and Paper Chemistry at Åbo Akademi University, Finland, since 2009. Prof. Willfors also has the title of Docent in Biomaterials Chemistry at the University of Helsinki, Finland. He is the Chairman of the Board for the Johan Gadolin Process Chemistry Centre, a Centre of Excellence funded by ÅAU during 2015-2018. He obtained a Master of Science in Chemical Engineering in 1996 and a Doctorate of Chemical Engineering in Forest Products Chemistry in 2002 at ÅAU. Prof. Willfors’s main research focus is concentrated on promoting the sustainable and multipurpose use of wood for fiber products and for high-value biomaterials and biochemicals. Recently, emphasis has been placed on developing biocomposites and novel materials for health-related applications through the utilization of 3D bioprinting. Furthermore, Prof. Willfors works closely with the traditional pulp and paper industry. He was Dean for Chemical Engineering at ÅAU from 2010–2014 and is currently a board member or representative in, e.g., Industrial Biotechnology Cluster Finland, Clinc Innovation Ltd. (an innovation cluster in the bioeconomy, energy, and cleantech) and the National Bioeconomy Panel appointed by the Ministry of Employment and the Economy. He is also a member of the editorial board of the international peer-reviewed journals Holzforschung, Nordic Pulp and Paper Research Journal, Cellulose Chemistry and Technology, and the Journal of Wood Chemistry and Technology. He is an author of 180 peer-reviewed scientific articles and book chapters and has 3 original patents and patent applications and >150 conference presentations and reports. His publications have an H-index of 38 and 5019 citations (Google Scholar) as of November 2017.

Dr. Chunlin Xu (Researcher ID: H-5224-2012) is an Adjunct Professor at Åbo Akademi University (AAU), Finland. He received his Ph.D. in chemical engineering from AAU, Finland, in 2008. His Ph.D. research focused on forest products chemistry. In 2009-2011, he worked as a postdoctoral research fellow with Prof. Harry Brumer at the School of Biotechnology and Wallenberg Wood Science Center, KTH, the Royal Institute of Technology, Stockholm, Sweden, and developed carbohydrate bioengineering approaches for the functionalization of various biomasses. In late 2011, he rejoined ÅAU to start his own research group in biorenewable materials with a focus on the development of biobased functional materials towards various high-end applications. His research activities have been mainly focused on the characterization of plant cell wall components, biomass processing and fractionation, carbohydrate chemistry and polysaccharide modification and the development of biobased functional materials using various advanced manufacturing techniques, such as 3D printing. He has published 60+ scientific papers in international peer-reviewed journals.

ACKNOWLEDGMENTS

This work is part of the activities within the Johan Gadolin Process Chemistry Centre, the Centre of Excellence established by Åbo Akademi University during 2015–2018. C. Xu (project number: 298325) and X. Wang (project number: 268455) thank the financial support on their research work from Academy of Finland.

REFERENCES

(1) Klemm, D.; Heublein, B.; Fink, H. P.; Bohn, A. Cellulose: fascinating biopolymer and sustainable raw material. Angew. Chem., Int. Ed. 2005, 44 (22), 3358.
M. The catalytic valorization of lignin for the production of renewable materials.

ACS Sustainable Chemistry & Engineering

Current Opinion in Biomedical Engineering

printing of nano-cellulosic biomaterials for medical applications.

Watari, F. 3D-printed biopolymers for tissue engineering application.

and the chemical sciences.

for the 3D structuring of artificial cellular environments.

M.; Hampl, J.; Williamson, A. Mimicking the biological world: Methods

2014

Nat. Biotechnol.

Marques, S.; Bogel-Lukasik, R. Hemicelluloses for fuel ethanol: a review.

Bioresour. Technol.

G.; Himmel, M. E.; Hu, L. Wood-derived materials for green chemistry, self-assembly, and applications.

US20150167234A1, 2013.

J. R. Soc., Interface (25) Sultan, S.; Siqueira, G.; Zimmermann, T.; Mathew, A. P. 3D printing of biomaterials.

Bandyopadhyay, A.; Bose, S.; Das, S. 3D printing of biomaterials.

MRS Bull. 2015, 40 (2), 108.

(28) Mandycky, C.; Wang, Z.; Kim, K.; Kim, D.-H. 3D bioprinting for engineering complex tissues. Biotechnol. Adv. 2016, 34 (4), 422.

(29) Ozbolat, I. T.; Hospodiuk, M. Current advances and future perspectives in extrusion-based bioprinting. Biomaterials 2016, 76, 321.

(30) Yu, D.-G.; Branford-White, C.; Ma, Z.-H.; Zhu, L.-M.; Li, X.-Y.; Yang, X.-L. Novel drug delivery devices for providing linear release profiles fabricated by 3DP. Int. J. Pharm. 2009, 370 (1), 160.

(31) Njuguna, J.; Nassiopoulos, E. Cellulose-based bio-and nanocomposites: a review. Int. J. Polym. Sci. 2011, 1.

(5) Kalia, S.; Dufresne, A.; Cherian, B. M.; Kaith, B.; Avérous, L.; Ngjupala, J.; Nasiopoulos, E. Cellulose-based bio-and nanocomposites: a review. Int. J. Polym. Sci. 2011, 1.

(6) Gibson, L. J. The hierarchical structure and mechanics of plant materials. J. R. Soc., Interface 2012, 9 (76), 2749.

(7) Von Schoultz, S. Method for extracting biomaterial. Patent US20150167234A1, 2013.

(8) Klemm, D.; Kramer, F.; Moritz, S.; Lindström, T.; Ankerfors, M.; Gray, D.; Dorris, A. Nanocelluloses: A new family of nature-based materials. Angew. Chem., Int. Ed. 2011, 50 (24), 5438.

(9) Azadi, P.; Inderwildi, O. R.; Farnood, R.; King, D. A. Liquid fuels, hydrogen and chemicals from lignin: A critical review. Renewable and Sustainable Energy Rev. 2013, 21, 506.

(10) Thakur, V. K.; Thakur, M. K.; Raghavan, P.; Kessler, M. R. Progress in green polymer composites from lignin for multifunctional applications: a review. ACS Sustainable Chem. Eng. 2014, 2 (5), 1072.

(11) Heitner, C.; Dimmel, D.; Schmidt, J. Lignin and lignitans: advances in chemistry; CRC Press, 2016.

(12) Jouanin, L.; Lapierre, C. Lignins: biosynthesis, biodegradation and biotechnology. Academic Press, 2012, Vol. 61.

(13) Scheller, H. V.; Ulsvikov, P. Annu. Rev. Plant Biol. 2010, 61, 263.

(14) Mäki-Arvela, P. i.; Salmi, T.; Holomb, B.; Willför, S.; Murzin, D. Y. Synthesis of sugars by hydrolysis of hemicelluloses-a review. Chem. Rev. 2011, 111 (9), 5638.

(15) Liu, J.; Willför, S.; Xu, C. A review of bioactive plant polysaccharides: Biological activities, functionalization, and biomedical applications. Bioact. Carbohydr. Diet. Fibre 2015, 5 (1), 31.

(16) Boerjan, W.; Albers, J.; Baucher, M. Lignin biosynthesis. Annu. Rev. Plant Biol. 2003, 54 (1), 519.

(17) Habibi, Y.; Lucas, L. A.; Rojas, O. J. Cellulose nanocrystals: chemistry, self-assembly, and applications. Chem. Rev. 2010, 110 (6), 3479.

(18) Zaluzek, J.; Bruijnincx, P. C.; Jongerius, A. L.; Weckhuysen, B. M. The catalytic valorization of lignin for the production of renewable chemicals. Chem. Rev. 2010, 110 (6), 3552.

(19) Girio, F. M.; Fonseca, C.; Carvalheiro, F.; Dauarte, L. C.; Marques, S.; Bogel-Lukasik, R. Hemicelluloses for fuel ethanol: a review. Bioresour. Technol. 2010, 101 (13), 4775.

(20) Murphy, S. V.; Atala, A. 3D bioprinting of tissues and organs. Nat. Biotechnol. 2014, 32 (8), 773.

(21) Schober, A.; Fernekorn, U.; Singh, S.; Schlingloff, G.; Gebinoga, M.; Hampl, J.; Williamson, A. Mimicking the biological world: Methods for the 3D structuring of artificial cellular environments. Engineering in Life Sciences 2013, 13 (4), 352.

(22) Gross, B. C.; Ekel, J. L.; Lockwood, S. Y.; Chen, C.; Spence, D. M. Evaluation of 3D printing and its potential impact on biotechnology and the chemical sciences. Anal. Chem. 2014, 86 (7), 3240.

(23) Li, X.; Cui, R.; Sun, L.; Afantis, K. E.; Fan, Y.; Feng, Q.; Cui, F.; Watari, F. 3D-printed biopolymer for tissue engineering application. Int. J. Polym. Sci. 2014, 2014, 1.

(24) Van Wijk, A.; van Wijk, I. 3D Printing with Biomaterials: Towards a Sustainable and Circular Economy; IOS Press, 2015.

(25) Sultan, S.; Siqueira, G.; Zimmermann, T.; Mathew, A. P. 3D printing of nano-cellulosic biomaterials for medical applications. Current Opinion in Biomedical Engineering 2017, 2, 29.

(26) Ferris, C. J.; Gilmore, K. G.; Wallace, G. G. Biofabrication: an overview of the approaches used for printing of living cells. Appl. Microbiol. Biotechnol. 2013, 97 (10), 4243.

(27) Bandyopadhyay, A.; Bose, S.; Das, S. 3D printing of biomaterials. MRS Bull. 2015, 40 (2), 108.
(49) Kolakovic, R.; Vitata, T.; Ihalainen, P.; Genina, N.; Peltonen, J.; Sandler, N. Printing technologies in fabrication of drug delivery systems. Expert Opin. Drug Delivery 2013, 10 (12), 1711.

(50) Sandler, N.; Preis, M. Printed drug-delivery systems for improved patient treatment. Trends Pharmacol. Sci. 2016, 37 (12), 1070.

(51) Chua, C. K.; Yeong, W. Y. Bioprinting Principles and Applications; World Scientific, 2015.

(52) Pfister, A.; Landers, R.; Laib, A.; Hübler, U.; Schmelzeisen, R.; Millhaupt, R. Biofunctional rapid prototyping for tissue-engineering applications: 3D bioplotting versus 3D printing. J. Polym. Sci., Part A: Polym. Chem. 2004, 42 (3), 624.

(53) Murphy, C. A.; Collins, M. N. Microcrystalline cellulose reinforced polyactic acid biocomposite filaments for 3D printing. Polym. Compos. 2016, DOI: 10.1002/pc.24069.

(54) Sen, S.; Martin, J. D.; Argyropoulos, D. S. Review of cellulose non-derivating solvent interactions with emphasis on activity in inorganic molten salt hydrates. ACS Sustain. Chem. Eng. 2013, 1 (8), 858.

(55) Isik, M.; Sardon, H.; Mecerreyes, D. Ionic liquids and cellulose: dissolution, chemical modification and preparation of new cellulolic materials. Int. J. Mol. Sci. 2014, 15 (7), 11922.

(56) Budtova, T.; Navard, P. Cellulose in NaOH—water based solvents: a review. Cellulose 2016, 23 (1), 5.

(57) Heinze, T.; Kosschella, A. Solvents applied in the field of cellulose chemistry: a mini review. Polim. Cinc. Tecnol. 2005, 15 (2), 84.

(58) Li, L.; Zhu, Y.; Yang, J. 3D bioprinting of cellulose with controlled porous structures from NMMO. Mater. Lett. 2018, 210, 136.

(59) Pietrzak, K.; Isreb, A.; Allnann, M. A flexible-dose dispenser for immediate and extended release 3D printed tablets. Eur. J. Pharm. Biopharm. 2015, 96, 380.

(60) Boetker, J.; Water, J. J.; Aho, J.; Arnfast, L.; Bohr, A.; Rantanen, J. Modifying release characteristics from 3D printed drug-eluting products. Eur. J. Pharm. Sci. 2016, 90, 47.

(61) Chai, X.; Chai, H.; Wang, X.; Yang, J.; Li, J.; Zhao, Y.; Cai, W.; Tao, T.; Xiang, J. Fused Deposition Modeling (FDM) 3D Printed Tablets for Intragastric Floating Delivery of Domperidone. Sci. Rep. 2017, 7 (1), DOI: 10.1038/s41598-017-0397-x.

(62) Eqtesadi, S.; Motealleh, A.; Miranda, P.; Lemos, A.; Rebelo, A.; Ferreira, J. M. A simple recipe for direct writing of 45S5 Bioglass® 3D scaffolds. Mater. Lett. 2013, 93, 68.

(63) Kageyama, T.; Osaki, T.; Enomoto, J.; Myasnikova, D.; Nittami, T.; Hozumi, T.; Ito, T.; Fukuda, J. In situ cross-linkable gelatin-CMC hydrogels designed for rapid engineering of perfusable vasculatures. ACS Biomater. Sci. Eng. 2016, 2 (6), 1059.

(64) Li, H.; Tan, Y. J.; Leong, K. F.; Li, L. 3D bioprinting of highly thixotropic alginate/methylcellulose hydrogel with strong interface bonding. ACS Appl. Mater. Interfaces 2017, 9 (23), 20086.

(65) Kim, M.; Kim, G. 3D multi-layered fibrous cellulose structure using an electrohydrodynamic process for tissue engineering. J. Colloid Interface Sci. 2015, 457, 180.

(66) Pattinson, S. W.; Hart, A. J. Additive manufacturing of cellulosic molecules for tissue engineering. Patent 2015, 6, 1048.

(67) Camarero Espinosa, S.; Kuhnt, T.; Foster, E. J.; Weder, C. Isolation of thermally stable cellulose nanocrystals by phosphoryl acid hydrolysis. Biomacromolecules 2013, 14 (4), 1223.

(68) Yu, H.; Qin, Z.; Liang, B.; Liu, N.; Zhou, Z.; Chen, L. Facile extraction of thermally stable cellulose nanocrystals with a high yield of 93% through hydrochloric acid hydrolysis under hydrothermal conditions. J. Mater. Chem. A 2013, 1 (12), 3938.

(69) Cao, Y.; Jiang, Y.; Song, Y.; Cao, S.; Miao, M.; Feng, X.; Fang, J.; Shi, L. Combined bleaching and hydrolysis for isolation of cellulose nanofibrils from waste sawdust. Carbohydr. Polym. 2015, 131, 152.

(70) Chen, L.; Wang, Q.; Hirth, K.; Baer, C.; Agarwal, U. P.; Zhu, J. Tailoring the yield and characteristics of wood cellulose nanocrystals (CNC) using concentrated acid hydrolysis. Cellulose 2015, 22 (3), 1753.

(71) Li, B.; Xu, W.; Kronlund, D.; Mätttänen, A.; Liu, J.; Smätt, J.-H.; Peltonen, J.; Willförr, S.; Mu, X.; Xu, C. Cellulose nanocrystals prepared via formic acid hydrolysis followed by TEMPO-mediated oxidation. Carbohydr. Polym. 2015, 133, 605.

(72) Xu, W.; Grénman, H.; Liu, J.; Kronlund, D.; Li, B.; Backman, P.; Peltonen, J.; Willförr, S.; Sundberg, A.; Xu, C. Mild Oxalic-Acid-Catalyzed Hydrolysis as a Novel Approach to Prepare Cellulose Nanocrystals. ChemNanoMat 2017, 3 (2), 109.

(73) Leung, A. C.; Hrapovic, S.; Lam, E.; Liu, Y.; Male, K. B.; Mahmoud, K. A.; Luong, J. H. Characteristics and Properties of Carboxylated Cellulose Nanocrystals Prepared from a Novel One-Step Procedure. Small 2011, 7 (3), 302.

(74) Montanari, S.; Roumani, M.; Heux, L.; Vignon, M. R. Topochemistry of carboxylated cellulose nanocrystals resulting from TEMPO-mediated oxidation. Macromolecules 2005, 38 (5), 1665.

(75) Hirota, M.; Tamura, N.; Saito, T.; Isogai, A. Water dispersion of cellulose II nanocrystals prepared by TEMPO-mediated oxidation of mercerized cellulose at pH 4.8. Cellulose 2010, 17 (2), 279.

(76) Gatenholm, P.; Backdahl, H.; Tzarvaras, T. J.; Davalos, R. V.; Sano, M. B. Three-dimensional bioprinting of biosynthetic cellulose (BC) implants and scaffolds for tissue engineering. Patent US8691974B2, 2014.

(77) Shao, Y.; Chaussy, D.; Grosseau, P.; Beneventi, D. Use of microfibrillated cellulose/lignosulfonate blends as carbon precursors: impact of hydrogel rheology on 3D printing. Ind. Eng. Chem. Res. 2015, 54 (43), 10575.

(78) Leppinniemi, J.; Lahtinen, P.; Paajanen, A.; Mahlberg, R.; Metsä-Kortelainen, S.; Pinomaa, T.; Pajari, H.; Vikholm-Lundin, I.; Pursula, P.; Hytönen, V. P. 3D-Printable Bioactivated Nanocellulose—Alginite Hydrogels. ACS Appl. Mater. Interfaces 2017, 9 (26), 21599.

(79) Wang, B.; Benitez, A. J.; Lossada, F.; Merindol, R.; Walther, A. Bioinspired mechanical gradients in cellulose nanofibril/polymer nanopapers. Angew. Chem. 2016, 128 (20), 6070.

(80) Nguyen, D.; Hägg, D. A.; Forsman, A.; Ekholm, J.; Nimkfraredana, P.; Brantsing, C.; Kalogeropolous, T.; Zausn, S.; Concaro, S.; Britberg, M.; et al. Cartilage Tissue Engineering by the 3D
Bioprinting of iPSC Cells in a Nanocellulose/Alginate Bioink. Sci. Rep. 2017, 7 (1), DOI: 10.1038/s41598-017-00690-y.

(92) Henriksson, I.; Gatenholm, P.; Hägg, D. Increased lipid accumulation and adipogenic gene expression of adipocytes in 3D bioprinted nanocellulose scaffolds. Biofabrication 2017, 9 (1), 015022.

(93) Avila, H. M.; Schwarz, S.; Rollot, N.; Gatenholm, P. 3D bioprinting of human chondrocyte-laden nanocellulose hydrogels for patient-specific auricular cartilage regeneration. Bioprinting 2016, 1, 22.

(94) Müller, T.; Amoroso, M.; Hägg, D.; Brantsing, C.; Rollot, N.; Apelgren, P.; Lindahl, A.; Kööly, L.; Gatenholm, P. In Vivo Chondrogenesis in 3D Bioprinted Human Cell-laden Hydrogel Constructs. Plast. Reconst. Surg. Global Open 2017, 5 (2), e1227, DOI: 10.1097/GOX.0000000000001227.

(95) Markstedt, K.; Escalante, A.; Toriz, G.; Gatenholm, P. Biomimetic inks based on cellulose nanofibers and crosslinkable xylenes for 3D printing. ACS Appl. Mater. Interfaces 2017, 9 (46), 40878.

(96) Shin, S.; Park, S.; Park, M.; Jeong, E.; Na, K.; Yoon, H. J.; Hyun, J. Cellulose Nanofibers for the Enhancement of Printability of Low Viscosity Gelatin Derivatives. Bioresources 2017, 12 (2), 2941–2954.

(97) Torres-Rendon, J. G.; Femmer, T.; De Laporte, L.; Tiggès, T.; Rahimi, K.; Gremse, F.; Zafaris, S.; Lederle, W.; Ifuku, S.; Wessling, M. J. A. Bioactive 3D printed scaffold formed by sacrificial templating of nanocellulose and nanochitin hydrogels as instructive platforms for biomimetic tissue engineering. Adv. Mater. 2015, 27 (19), 2989.

(98) Uquillas, J. A.; Akkus, O. Modeling the electromobility of type-I collagen molecules in the electrochemical fabrication of dense and aligned tissue constructs. Ann. Biomed. Eng. 2012, 40 (8), 1641.

(99) Tang, A.; Liu, Y.; Wang, Q.; Chen, R.; Liu, W.; Fang, Z.; Wang, L. A new photoelectric ink based on nanocellulose/CDs quantum dots for screen-printing. Carbohydr. Polym. 2016, 148, 29.

(100) Håkansson, K. M.; Henriksson, I. C.; de la Peña Vázquez, C.; Kuzmenko, V.; Markstedt, K.; Enoksson, P.; Gatenholm, P. Solidification of 3D Printed Nanofibril Hydrogels into Functional 3D Cellulose Structures. Advanced Materials Technologies 2016, 1 (7), 1600096.

(101) Adams, J. J.; Duoss, E. B.; Malkowski, T. F.; Motala, M. J.; Ahn, B. Y.; Nuzzo, R. G.; Bernhard, J. T.; Lewis, J. A. Conformal Printing of Electrically Conductive Antennas on Three-Dimensional Surfaces. Adv. Mater. 2011, 23 (11), 1335.

(102) Tardy, B. L.; Yokota, S.; Ago, M.; Xiang, W.; Kondo, T.; Bordes, R.; Rojas, O. J. Nanocellulose-Surfactant Interactions. Curr. Opin. Colloid Interface Sci. 2017, 29, 57.

(103) Dong, J.; Li, M.; Zhou, L.; Lee, S.; Mei, C.; Xu, X.; Wu, Q. The influence of grafted cellulose nanofibers and postextrusion annealing treatment on selected properties of poly (lactic acid) filaments for 3D printing. J. Polym. Sci. Part B: Polym. Phys. 2017, 55 (11), 847.

(104) Žepić, V.; Poljanšek, I.; Oven, P.; Cop, M. COST-FP1105: Properties of PLA films reinforced with unmodified and acetylated freeze dried nanofibrillated cellulose. Holzforschung 2016, 70 (12), DOI: 10.1515/hf-2016-0096.

(105) Pei, A.; Zhou, Q.; Berglund, L. A. Functionalized cellulose nanocrystals as biobased nucleation agents in poly (l-lactide) (PLLA) – Crystallization and mechanical property effects. Compos. Sci. Technol. 2010, 70 (5), 815.

(106) Misoum, K.; Belgacem, M. N.; Bras, J. Nanofibrillated cellulose surface modification: a review. Materials 2013, 6 (5), 1745.

(107) Müller, M.; Östörk, E.; Arlov, O.; Gatenholm, P.; Zenobi-Wong, M. Algininate–nanocellulose bioinks for cartilage bioprinting applications. Ann. Biomed. Eng. 2017, 45 (1), 210.

(108) Siqueira, G.; Kokkinis, D.; Libanori, R.; Hausmann, M. K.; Gladman, A. S.; Neels, A.; Tingaut, P.; Zimmermann, T.; Lewis, J. A.; Studart, A. R. Cellulose Nanocrystal Inks for 3D Printing of Textured Cellular Architectures. Adv. Funct. Mater. 2017, 27 (12), 1604619.

(109) Palaganas, N. B.; Mangadloa, J. D.; de Leon, A. C. C.; Palaganas, J. O.; Pangilinan, K. D.; Lee, Y. J.; Advincula, R. C. 3D Printing of Photocurable Cellulose Nanocrystal Composite for Fabrication of Complex Architectures via Stereolithography. ACS Appl. Mater. Interfaces 2017, 9 (39), 34314.
(19) Maleki, L.; Edlund, U.; Albertsson, A.-C. Biocatal. Bioprocess.
2015, 16 (2), 667.
(20) Pahimelinas, N.; Kilpeläinen, P.; Master, E.; Ilvesniemi, H.; Seppälä, J. Novel thiol-amine-and amino acid functional xylan derivatives synthesized by thiol–ene reaction. Carbohydr. Polym.
2015, 131, 392.
(21) Willför, S.; Rehn, P.; Sundberg, A.; Sundberg, K.; Holmblom, B. Recovery of water-soluble acetylgalactoglucomannans from mechanical pulp of spruce. Tappi J. 2003, 86 (11), 27–32.
(22) Xu, W.; Pranovich, A.; Uppstu, P.; Wang, X.; kronlund, D.; Hemming, J.; Ohlom, H.; Moritz, N.; Preis, M.; Sandander, N.; Willför, S.; Xu, C. Novel biorenewable composite of wood polysaccharide and polylactic acid for three dimensional printing. Carbohydr. Polym. 2018, 187, 51.
(23) Graitichen, F. H.; Grigsby, W. J.; Hill, S. J.; Raymond, L. G.; Sanglard, M.; Smith, D. A.; Thorlby, G. J.; Torr, K. M.; Wames, J. M. Yes, we can make money out of lignin and other bio-based resources. Ind. Crops Prod. 2017, 106, 74.
(24) Akato, K.; Tran, C. D.; Chen, J.; Naskar, A. K. Poly (ethylene oxide)-assisted macromolecular self-Assembly of lignin in ABS matrix for sustainable composite applications. ACS Sustainable Chem. Eng. 2015, 3 (12), 3070.
(25) Upton, B. M.; Kasko, A. M. Strategies for the conversion of lignin to high-value polymeric materials: Review and perspective. Chem. Rev. 2016, 114 (4), 2275.
(26) Ragauskas, A. J.; Beckham, G. T.; Biddy, M. J.; Chandra, R.; Chen, F.; Davis, M. F.; Davison, B. H.; Dixon, R. A.; Glinna, P.; Keller, M.; et al. lignin valorization: improving lignin processing in the biorefinery. Science 2014, 344 (6185), 1246843.
(27) Labrousset, S.; Avrouré, L. Chemical modification of lignins: Towards biobased polymers. Prog. Polym. Sci. 2014, 39 (7), 1266.
(28) Kdala, J. F.; Kubo, S. Lignin-based polymer blends: analysis of intermolecular interactions in lignin–synthetic polymer blends. Composites, Part A 2004, 35 (3), 395.
(29) Bouajila, J.; Dole, P.; Joly, C.; Limare, A. Some laws of a lignin plasticization. J. Appl. Polym. Sci. 2006, 102 (2), 1445.
(30) Shi, B.; Shleip, M. Thermoplastic films containing lignin and their optical polarization properties. J. Polym. Eng. 2016, 36 (5), DOI: 10.1515/polyeng-2015-0052.
(31) Saito, T.; Brown, R. H.; Hunt, M. A.; Pickel, D. L.; Pickel, J. M.; Messman, J. M.; Baker, F. S.; Keller, M.; Naskar, A. K. Turning renewable resources into value-added products: development of lignin-based thermoplastic. Green Chem. 2012, 14 (12), 3295.
(32) Kai, D.; Ren, W.; Tian, L.; Chee, P. L.; Liu, Y.; Ramakrishna, S.; Loh, X. J. Engineering Poly (lactide)–Lignin Nanofibers with Antioxidant Activity for Biomedical Application. ACS Sustainable Chem. Eng. 2016, 4 (10), 5268.
(33) Hunt, N. C.; Grover, L. M. Cell encapsulation using biopolymer gels for regenerative medicine. Biotechnol. Lett. 2010, 32 (6), 733.
(34) Chia, H. N.; Wu, B. M. Recent advances in 3D printing of biomaterials. J. Biol. Eng. 2015, 9 (1), DOI: 10.1186/s13036-015-0001-4.
(35) Smetana, K. Cell biology of hydrogels. Biomaterials 1993, 14 (14), 1046.
(36) Yamamla, N.; Kisin, E. R.; Menas, A. L.; Farca, M. T.; Khalilullin, T. O.; Vogel, U. B.; Shurin, G. V.; Schweller-Berry, D.; Fournier, P. M.; Star, A.; et al. In vitro toxicity evaluation of lignin-(un)coated cellulose based nanomaterials on human AS49 and THP-1 cells. Biocatal. Biotransform. Biomacromolecules 2016, 17 (11), 3464.
(37) Quraishi, S.; Martins, M.; Barros, A. A.; Gurikov, P.; Raman, S.; Smirnova, I.; Duarte, A. R. C.; Reis, R. L. Novel non-cytotoxic alginate–lignin hybrid aerogels as scaffolds for tissue engineering. J. Supercrit. Fluids 2015, 105, 1–8.
(38) Figueredo, P.; Lintinen, K.; Kiriæsis, A.; Hynynen, V.; Liu, Z.; Bauleth-Ramos, T.; Rahikkala, A.; Coreia, A.; Kohout, T.; Sarmento, B.; et al. In vitro evaluation of biodegradable lignin-based nanoparticles for drug delivery and enhanced antiproliferation effect in cancer cells. Biomaterials 2017, 121, 97.