Cellulose-based hydrogels regulated by supramolecular chemistry

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Abstract
Supramolecular hydrogels based on cellulose attract increasing attention because of their novel structures and broad potential applications. In this review, hydrogels composed of cellulose are summarized according to category of supramolecular interactions in the networks including hydrogen bonds, electrostatic interactions, host-guest interactions, and others. Supramolecular cellulose-based hydrogels constructed by noncovalent bonding usually exhibit environmental friendliness, designing flexibility and diverse functions, and their properties are variable with incorporating different interactions in hydrogel networks. Moreover, with proper structures and networks, the supramolecular cellulose-based hydrogels are adaptable in diverse fields of research and practical applications, such as self-healing, shape memory, drug delivery, and some other renewable/sustainable materials. The future developments and challenges of the supramolecular hydrogels based on cellulose are discussed as well.

Keywords
cellulose, hydrogels, noncovalent bonds, self-healing, shape memory, supramolecular chemistry

1 | INTRODUCTION

Cellulose, as the most abundant natural renewable polymers on Earth, has been widely reported by researchers around the world.1 It is well-known that cellulose is widely distributed in nature and can be derived from a variety of sources including cotton, wood pulps, bacteria, algae, tunicates, and so on.2 Consisted of the repeated connection of D-glucose building blocks, cellulose is the polymer with high degree of crystallinity and multilayer aggregate structure based on its inherent supramolecular system.3 Moreover, the supramolecular interactions, mainly including hydrogen bonds, among nanoscale cellulose
microfibrils lead to the natural cellulose with high mechanical strength. Natural cellulose is composed of amorphous and crystalline regions, and the crystal, degree of crystallinity, and dimension of crystalline region in cellulose greatly depend on their sources and the processing conditions. Generally, cellulose can be processed with different methods to obtain nanocellulose, which has great potential in developing novel sustainable materials including sulfuric acid hydrolysis, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) oxidation, mechanical treatment, enzymolysis method, etc. Beside the advantages of natural polymers, such as renewability, biocompatibility, biodegradability, and low toxicity, cellulose has high Young’s modulus, high-specific surface area, and high chemical reactivity due to its structure in nanoscale. Therefore, cellulose has been widely used in the preparation of functional materials, including hydrogels, aerogels, films, etc., which have great application prospects in many fields such as biomedical, energy, cosmetic, and chemical industries.

As a typical type of soft materials, hydrogels are three-dimensional networks formed by hydrophilic or amphiphilic polymer via physical or chemical crosslinking, which consist of a large proportion of water. Similar to biological tissues, hydrogels with good biodegradability, bioimintability, and adaptability have been applied widely in biomimetic materials, drug delivery, tissue engineering, and so on. Typically, hydrogels can be classified according to their base material, size, crosslinking type, multifunctional response to external stimulus, etc. For example, hydrogels can be divided into biopolymer-based or synthetic polymer-based due to their natural or synthetic origin, and chemical or physical hydrogels are sorted by the main interactions (covalent and noncovalent bonding) in the crosslink network.

Synthetic hydrogels, with controllable compositions and architectures, as well as adjustable mechanical properties, have been developed over the last decades. However, lacking of suitable biological properties, synthetic hydrogels have limitation for the use in biomedical fields. Considering biodegradability, biocompatibility and nontoxicity, biopolymer-based especially cellulose-based hydrogels have acquired increasing attention. To obtain cellulose-based hydrogels, diverse design and ideas have been attempted, such as cellulose-only hydrogels where cellulose worked as based materials; cellulose nanocomposite hydrogels in which cellulose was applied as the nanofillers to enhance the mechanical performance of the materials remarkably. Different methods, including chemical reactions and physical interactions, are the key factors to improve the interfacial compatibility, mechanical property, and functionality of nanocomposite hydrogels.

In the crosslink network of hydrogels, besides the covalent bonding, the studies about noncovalent bonding have greatly developed due to the dynamic reversibility of physical interactions. Physical hydrogels based on noncovalent bonding, can also be generally called supramolecular hydrogels, obtained much attention with the development of supramolecular chemistry. The supramolecular interactions include hydrogen bonds, metal coordination, host-guest interaction, π–π stacking, hydrophobic interaction, and van der Waals interactions. The supramolecular interactions endow hydrogels with the dynamic network and are beneficial to fabricate multifunctional materials with excellent performance. Considering the great number of hydrogen bonds and some other noncovalent interactions in natural cellulose materials, cellulose-based supramolecular hydrogels, with environment-friendly nature and dynamic crosslinking, were used in a vast array of fields such as self-healing materials, drug delivery, waste treatment, tissue engineering, and some other applications.

In this review, we focus on the design, developments, and applications of cellulose-based supramolecular hydrogels in this decade. To be more specifically, we mainly summarize the development of the hydrogels containing cellulose based on hydrogen bonds, electrostatic interactions, and host-guest interactions (Figure 1). Moreover, several well-explored types of applications are taken for example including drug delivery, self-healing, and shape-memory materials. Both the properties and functions of these cellulose-based supramolecular hydrogels are addressed, and limitation and future development are discussed here.

## 2 | DESIGN OF SUPRAMOLECULAR HYDROGELS BASED ON CELLULOSE

Unlike covalent polymers, supramolecular polymers are formed by the self-assembly of reversible noncovalent bonds with low bond energy among monomers. Supramolecular polymers can reversibly generate and degrade due to the presence of noncovalent bonds. Comparing with covalent bond, which has a homolytic bond dissociation energy that ranges between 100 and 400 kJ/mol, noncovalent interactions are generally weak and vary from less than 5 kJ/mol for van der Waals forces to 250 kJ/mol for Coulomb interactions, as is shown in Table 1. It should be noted that there is something similar between supramolecular and covalent polymer systems, especially in their bonding strength. In our opinion, their similarity is mainly the interaction energies: the sum of several hydrogen bonds is as strong as a covalent bond. Furthermore, because of the superior reversibility and flexibility compared with covalent bonding, supramolecular hydrogels are considered to be a
kind of novel smart materials with characteristics such as self-healing and response to environmental stimuli. Here, cellulose-based hydrogels are summarized according to the types of primary supramolecular interactions in their networks. The design and construction of these hydrogels are also discussed and analyzed.

2.1 Hydrogen bonds

The hydrogen bond (H-bond) is one of the most well-known and universal physical interactions in supramolecular chemistry. Due to the directionality and versatility of H-bond, it plays an important role in many essential biological processes such as DNA replication, molecular recognition, and protein folding.10 H-bonds are formed when an electron-deficient hydrogen atom interacts with the electronegative atom that possesses available nonbonding electron lone pairs. Compared to some other noncovalent bonds, H-bonds with high strength, high orientation, and dynamic reversibility are widely used in the design of supramolecular hydrogels.11 Indeed, the strength of H-bonds mainly depends on the solvent, the number and sequence of the H-bond donors and acceptors. The association constants \( (K_a) \) of H-bonding pairs ranges from \(<100 \text{ M}^{-1}\) to \(>10^6 \text{ M}^{-1}\).12 Thus, the H-bonding can vary from highly dynamic to quasicovalent, which offers the H-binding-based materials high tunability and designing flexibility.

| Type of interaction or bonding | Strength (kJ/mol) |
|-------------------------------|-------------------|
| Coulomb                       | 250               |
| Hydrogen bond                 | 10-65             |
| Ion-dipole                    | 50-200            |
| Cation-π                      | 5-80              |
| π-π                           | 0-50              |
| Van der Waals forces          | <5                |
| Metal-ligand                  | 0-400             |
| Hydrophobic effects           | Difficult to assess|
Taking the advantages of H-bonds, researchers around the world have designed and fabricated various kinds of materials.\textsuperscript{11,13,14} As for the hydrogels based on cellulose, many novel ideas have been attempted recently. Cellulose, with a number of hydroxyl on its surface, has inherent supramolecular system, mainly including H-bonds. Inspired by natural mussel chemistry, Wu et al.\textsuperscript{15} developed a facile approach to prepare stable intelligent hydrogels based on microcrystalline cellulose (MCC) and konjac glucomannan (KGM). The FTIR spectra showed strong intermolecular H-bonds between MCC and KGM. These hydrogels exhibited strong mechanical strength and rapid self-healing properties. Besides, these hydrogels had a more distinct pH sensitivity and a much lower initial burst release behavior than KGM hydrogels, which may be promising carriers for controlled drug delivery. As is shown in Figure 2A, Biyani and colleagues\textsuperscript{16} reported the preparation of supramolecular nanocomposites by functionalizing cellulose nanocrystals (CNCs) with 2-ureido-4-pyrimidone (UPy). The obtained materials showed improved mechanical properties and efficient optical healing through H-bonds.

Due to the widespread presence of H-bonds in most cellulose-based materials, creative studies were performed by combing other interactions with H-bonds. Qing and Wu et al.\textsuperscript{17} introduced cellulose nanofibrils (CNF) into poly(acrylic acid) (PAA) matrix, which significantly improved the properties of the obtained hydrogel electrolytes. And the ionic conductivity was improved together with the mechanical performance because of physical entanglements and H-bonds among PAA and cellulose in the network. As is shown in Figure 2B, Gong et al.\textsuperscript{18} fabricated anisotropic hydrogels with perfectly aligned multiscale hierarchical fibrous structures by breaking and reforming H-bonds. By drying the diluted physical hydrogel in air, sufficiently high tensile strength is built along the length direction. And the polymer chains are aligned, and multiscale fibrous structures are spontaneously formed in the bulk material. In this work, as the relatively rigid polymers, cellulose are susceptible to mechanical signal, and their H-bonds helped the formation of anisotropic structures. Besides these single noncovalent interactions, Mao and colleagues\textsuperscript{19} designed hydrogel networks which contained chain entanglements, crystallization, covalent bonds, and H-bonds (Figure 2C). In these double-network cellulose/silk fibroin hydrogels, a green gas (CO\textsubscript{2}) worked as media to induce physical crosslinking. Introducing CO\textsubscript{2} into hydrogels, the pH reduction induced the ordered aggregation of cellulose chains and generated H-bonds between these chains, leading to the formation of hydrogels. And the hydrogels displayed significantly improved mechanical strength. Above examples indicate that the prominent effect of H-bonds on constructing cellulose-based hydrogels, including improving their properties and widening the applications, and fabrication of stimuli-responsive materials or composites with biomimetic structure.

Compared with some other supramolecular interactions, the formation of H-bonds is more flexible. It is reported that a large number of H-bonds can significantly improve the mechanical properties of hydrogels. Moreover, due to their responsiveness to pH, H-bonds had more advantages in the design and construction of environmentally responsive materials.

### 2.2 Electrostatic interactions

Electrostatic interactions, electrostatic attraction indeed, exist among molecules with opposite charges. By designing and synthesizing the charged monomers or polymer chains, electrostatic interactions are facilely introduced into the supramolecular hydrogels. Together with its biodegradability and nontoxicity, the special chemical features of cellulose, especially the hydroxyl groups with high reactivity on its surface, have gained cellulose great interests in being modified into charged polymers such as carboxymethyl cellulose (CMC) and quaternized cellulose. As a result, there are many studies about cellulosic hydrogels based on electrostatic interactions and their applications.

Langer and colleagues\textsuperscript{20} fabricated the self-assembled hydrogels based on electrostatic forces between negatively charged biopolymers (hyaluronic acid and CMC) and positively charged cetyltrimethylammonium bromide. These hydrogels exhibited broad tunability of mechanical properties, shear-thinning, and self-healing properties. As is shown in Figure 3A, MacLachlan and colleagues\textsuperscript{21} described an impressive CO\textsubscript{2}-switchable hydrogel by adding imidazole to a suspension of CNCs. Sparging CO\textsubscript{2} into this suspension, charged hydrogen carbonate and imidazolium salts were formed, which led to an increase in ionic strength and better screening of the negatively charged CNC particles. Hydrogels were subsequently formed due to agglomeration of the CNCs. By sparging N\textsubscript{2} into the dispersion, the reaction was reversed and the ionic strength decreased, the CNC particles redisperse and form a stable suspension. Using this approach, the gelation of CNC hydrogels could be switched by simply sparging CO\textsubscript{2} or N\textsubscript{2} gas, without the need for any extensive chemical functionalization, or the addition of acids or bases as a trigger. These CO\textsubscript{2}-responsive materials have been widely used for CO\textsubscript{2} capture and CO\textsubscript{2} sensing. As illustrated in Figure 3B, Huang and colleagues\textsuperscript{22} developed a biocompatible hydrogel with a double-membrane structure from cationic CNC and anionic alginate. The architecture of this hydrogel involves an external membrane...
FIGURE 2 Fabrication of cellulose-based hydrogels through hydrogen bonds and different interactions. (A) Cellulose nanocrystals functionalized with hydrogen-bonding ureidopyrimidone (UPy) for nanocomposites. Reproduced with permission from Ref. [16]. Copyright 2013, American Chemical Society. (B) Anisotropic hydrogels fabricated by breaking and reforming hydrogen bonds. Reproduced with permission from Ref. [18]. Copyright 2018, Wiley-VCH. (C) Double-network cellulose/silk fibroin hydrogels crosslinked through hydrogen bonds, covalent crosslinks, and crystallization. Reproduced with permission from Ref. [19]. Copyright 2020, American Chemical Society.
FIGURE 3 Fabrication of cellulose-based hydrogels through electrostatic interactions. (A) Cellulose nanocrystal hydrogels switched by CO₂ or N₂ gas via electrostatic forces. Reproduced with permission from Ref. [21]. Copyright 2018, American Chemical Society. (B) Cationic cellulose nanocrystals (CNCs) synthesized by the physical adsorption strategies for consolidating hydrogels through electrostatic interactions with anionic alginate. Reproduced with permission from Ref. [23]. Copyright 2016, American Chemical Society. (C) Tannic acid coated CNCs (TA@CNCs) reinforcing gel network by hydrogen bonds and electrostatic interactions. Reproduced with permission from Ref. [24]. Copyright 2019, The Royal Society of Chemistry.
composed of neat alginate, and an internal composite hydrogel consolidates by electrostatic interactions between cationic CNC and anionic alginate. Without chemical modification, it is efficient to construct supramolecular hydrogels with electrostatic interactions. Yang and colleagues constructed a novel dynamic self-adhesive and self-healable conductive hydrogel by combining hydrogen bonds and electrostatic interactions (Figure 3C). Tannic acid coated CNCs (TA@CNCs) acted as dynamic reinforcing bridges in the dual crosslinking network. Chang and colleagues successfully introduced quaternized tunicate CNCs (Q-TCNCs) into the crosslink network of hydrogel. The obtained hydrogels were reinforced with electrostatic interactions between the positive charges of Q-TCNCs and negative charges of PAA chains. The mechanical properties, including strength, ductility, elasticity, and toughness of hydrogels, were improved significantly. Moreover, the nanocomposite hydrogels exhibited controllable swelling ratio and pH-sensitive swelling behaviors after incorporation of Q-TCNCs. Yang and Wang used the quaternary ammonium group modified β-cyclodextrin (CD+) as the electropositive binding site, and used CMC as the electronegative binding site to form the double network structure. Through electrostatic and host-guest interactions, the cellulose drug-loaded hydrogel beads have potential application in pharmaceutical. Recently, Liu et al. prepared pH-sensitive nanogels based on CMC and bovine serum albumin with a simple and green electrostatic interaction approach, which offered an effective strategy for combining chemoradioisotope therapy of cancer.

Considering advantages of electrostatic interactions, some multifunctional hydrogels can be fabricated to promote the application of integrated electronic skin with high sensory properties and comfortable user experience. Electrostatic interactions can not only play vital roles in the crosslink networks, but also provide some ideas for constructing novel electronic materials and expanding the application fields of cellulose-based hydrogels.

### 2.3 Host-guest interactions

Host-guest interaction is another important noncovalent bonding in designing physical hydrogels, due to the combination of multiple dynamic interactions between two corresponding compounds including hydrophobic interactions, hydrogen bonding, π-π stacking, etc. Compared with some other physical interactions, host monomers have higher complexation strength and more specific recognition with guest monomers. The host-guest interactions exist widely due to the diversity of host-guest pairs. And well-explored host compounds, including crown ethers, CDs, and cucurbiturils, which are easy to modify polymer chains and use to construct a variety of supramolecular polymers with well-defined macromolecular architectures. Taking advantages of their special hydrophilic and hydrophobic structure, host-guest supramolecular polymers have broad application prospects in different fields.

Recently, supramolecular polymers formed via host-guest interactions has developed rapidly. As is shown in Table 2, there are many typical types of host-guest unites have been reported, but only little parts of them was used in cellulose-based hydrogels due to the difficulties in fabrication process. Some properties and functions of typical host and guest molecules are presented in Table 2, aiming to make the most of host-guest interactions and cellulose-based hydrogels, and widen their applications in biomedical and smart materials fields. Based on the dynamic host-guest interaction of α-CD, Yuan et al. developed a host-controlled approach to achieve supramolecular self-assembly. Adjusted by the host-guest pairs, the copolymer fabrication shows smart self-rearrange and deformable behavior. Moreover, Yuan et al. also constructed a UV-visible light controlled supramolecular system based on the host-guest interaction between ethyl cellulose and α- or β-CD. Harada and colleagues synthesized supramolecular hydrogels with properties such as self-healing and photoresponse. Hydrogels with great performance constructed through host-guest interactions based on cucurbiturils and pillararenes have been studied as well. For the cellulose hydrogels based on host-guest interactions, as is shown in Figure 4A, Sherman et al. assembled supramolecular hydrogels from highly branched cucurbit[8]uril-threaded polyrotaxanes (HBP-CB[8]) and naphthyl-functionalized hydroxyethyl cellulose (HECNp), which exploiting the CB[8] host-guest complexation. Due to the extensive choice of aromatic molecules that are known to bind with CB[8] to form binary complexes, hydrogels based on HBP-CB[8] can be endowed with a broader scope of adaptive functionalities such as pH, redox, and light responsiveness. As shown in Figure 4B, Wang and colleagues prepared pH-responsive hydrogels with an amphiphilic crosslinking agent. The crosslinking agent could be encapsulated by poly β-CD (β-CDP) through host-guest interaction, and attracted by carboxyl groups on CMC through electrostatic interaction. Then, a three-dimensional gel network structure was formed based on these host-guest interactions. The pH environment could affect the existing state of crosslinking agent and CMC, which further affect gel formation. The linear β-CDP with the remaining hydrophobic cavity can be equipped with hydrophobic drug molecules to
TABLE 2 Some typical types of host-guest interactions and their characteristics

| Host-guest interactions | Functions | Applications | Host/guest pair examples | Association constants [M⁻¹] | Ref. |
|------------------------|-----------|--------------|--------------------------|-----------------------------|------|
| Crown ether-based host monomers | Selective complexation with metal ions and excellent dynamic properties | Heavy metal adsorption-separation materials, chemically modified electrodes and magnetic materials | Dibenzo-24-crown-8 (DB24C8)/pyridinium-modified cyclic tertiary ammonium salts | 9.5 × 10⁴ [34,35] | |
| Cyclodextrin-based host monomers | Accessibility on large scale, biocompatibility and biodegradability | Chiral separation materials, catalysts, biosensors and potential biomedical materials such as drug carriers | βCD/adamantane (Ad), βCD/ferrocene (Fc) | 1.5 × 10⁴, 1.7 × 10⁴ [36,37] | |
| Calixarene-based host monomers | High reactivity and simplicity of modification | Electrochemical sensors, ion detection, etc. | calix[5]arene/C₆₀, sulfonato-calix[4]arene/methyl viologen | 10⁻⁴, 4.27 × 10⁵ [38-40] | |
| Cucurbituril-based host monomers | High specificity and selectivity | Drug delivery and controlled release, crosslinkers for functional multilayer films or gels | CB[8]/1-benzyl-3-vinylimidazolium bromide (1:2) | Kₐ₁ = 4.21 × 10⁷, Kₐ₂ = 4.25 × 10⁵ [41,42] | |
| Pillararene-based host monomers | Particular guest recognition features with the rigid and symmetrical pillar-like structure | Certain special fields including substrate adsorption and artificial light-harvesting systems | P5A/1,6-hexamethylenedipyridine derivative | 10⁴ [43-45] | |

expand the application of these hydrogels in drug delivery. Moreover, Wang and colleagues also constructed a cellulose-based self-assembled hydrogel through the host-guest interaction between hydrophobic lauryl side chains grafting on hydroxyethyl cellulose (HEC-C₁₂) and β-CD. The loading and in vitro release of Eugenol (EG) were investigated, which confirmed these hydrogels could have a potential application as efficient bacteriostasis materials for biomedicine. Lin and Dufresne used grafted β-CD as targeting sites, and introduced pluronic polymers on the surface of CNCs by inclusion interaction between β-CD and hydrophobic segment of the polymer. The in situ obtained hydrogels were also used as drug carrier for in vitro release of doxorubicin and exhibited prolonged drug release with special release kinetics. Combining with the good biocompatibility of hydrogels, some hydrophobic drug molecules can be used more efficient with the help of host compounds in host-guest chemistry. As a result, cellulose-based hydrogels constructed by host-guest interactions would have great potential applications in biomedicine, especially in the field of drug controlled release.

2.4 Other noncovalent interactions

There are some other kinds of noncovalent interactions that have been reported to regulate the supramolecular cellulose-based hydrogels including hydrophobic interactions, crystallization, the metal coordination bonds, and multiple intermolecular interactions and so on. For example, Serizawa and colleagues designed cellulose oligomer hydrogels composed of well-grown crystalline nanoribbon networks (Figure 5A). This method can be applied in the one-pot preparation of double network hydrogels, which exhibit superior mechanical properties. As illustrated in Figure 5B, Chang and colleagues reported a facile strategy to prepare highly ordered nanocomposite hydrogels with ultrahigh strength. Loosely crosslinked network was first constructed by the host-guest interactions between adamantane moiety contained polymers and β-CD modified tunicate CNCs (TCNCs). Subsequently, dual physically crosslinked hydrogels were obtained by introducing Fe³⁺ ions into the prestretched supramolecular hydrogels for the formation of coordination bonds and freezing oriented TCNCs. Taking advantages of both host-guest and electrostatic interactions, the oriented TCNCs were locked in polymeric networks. The resultant hydrogels with highly ordered architectures exhibited outstanding mechanical performances, and could be used as potential biomimetic materials for biomedical applications.

As shown in Figure 5C, Zhang and colleagues realized the anisotropic structure of the cellulose hydrogels by the breakage and rearrangement of inner H-bonds...
of cellulose. Ozcan and colleagues chose CNF, chitosan (CS), and copper ion (Cu$^{2+}$) to fabricate cellulose-based materials, where CS is incorporated as a soft phase in CNF film to induce additional H-bonds networks, Cu$^{2+}$ is for the ionic interaction, and also serves as “crosslink points.” This approach provides a method to design and fabricate practical and cost-effective cellulose-based materials for various potential applications. From these studies, it is shown that the supramolecular interactions in the network of cellulose-based hydrogels have great advantages, such as flexibility, green and biocompatibility, and they are ready for widespread use in the future.

### 3 | PROPERTIES AND APPLICATIONS

#### 3.1 | Self-healing

Due to unavoidable degradation and unexpected damage from constant stress and strain, the traditional hydrogels often have a limited lifespan. In order to overcome these issues, self-healing hydrogels currently attract great interest. Self-healing, self-repair, and self-recovery synonymously refer to the ability of materials to self-mend damage and restore their associated functionalities and structures. Generally, the self-healing process is based on the concept of constructing dynamic
chemistry, as is shown in Figure 6. The key feature of self-healing mechanisms is the dynamic reversibility of covalent bonds or noncovalent interactions in polymer networks. According to the discussion above, supramolecular interactions are no doubts the ideal approach to construct hydrogels with excellent self-healing abilities without incorporating healing agents. Combining the dynamic reversibility of supramolecular interactions and biocompatibility of sustainable cellulose, supramolecular cellulose-based hydrogels could have wide applications in health care electronic devices and biomedical materials.
In the past decades, cellulose-based hydrogels with self-healing property through different supramolecular interactions have attracted more and more attention. As is shown in Figure 7A, Ha and colleagues\(^70\) fabricated thin and foldable self-healing gel electronics on a poly(vinyl alcohol)/CNCs (PVA/CNCs) composite film. The self-healing property of the materials can be activated by spraying water on the film surface, via dynamic formation of hydrogen bonding. Sui and colleagues\(^71\) prepared an injectable polysaccharide hydrogel based on cellulose acetate, hydroxypropyl CS, and amino-modified CNCs (CNC-NH\(_2\)) under physiological conditions, where CNC-NH\(_2\) acted as both physical and chemical crosslinker. The hydrogen bonds among amino and hydroxyl groups, and dynamic enamine bonds in the crosslinked network endowed the polysaccharide hydrogel with self-healing ability and pH-responsive property. Wan and colleagues\(^72\) designed functional network hydrogels based on dynamic CNCs-Fe\(^{3+}\) coordination bonds (Figure 7B). These hydrogels demonstrated autonomously self-healing capability within only 5 min without the need of any stimuli or healing agents. This is ascribing to the reorganization of CNCs and Fe\(^{3+}\) via ionic coordination. Moreover, Rowan and colleagues\(^73\) reported a polymer blend reinforced with CNCs could be healed upon exposure to elevated temperature via π-π interactions. Foster and colleagues\(^16\) reported the supramolecular nanocomposites based on modified CNCs which were light healable because of hydrogen bonds. Ikkala and colleagues\(^24\) prepared hydrogels by combining hard nanocrystalline cellulose domains with soft supramolecularly crosslinked polymeric domains. Through dynamic host-guest interactions between the CB[8] and guest monomers, PVA polymers containing CNCs could realize rapid self-healing even upon aging for several months.

As is reported, self-healing hydrogels with supramolecular interactions have been studied a lot. However, self-healing hydrogels seldom possess both robust mechanical properties and rapid self-healing properties at the same time. Besides, a large portion of reported hydrogels can realize self-healing only with external stimuli such as temperature, pH, redox, electrical field, magnetic field, and light. Hence, the development of hydrogels with good mechanical property and autonomous self-healing is still necessary. Notably, although the single bond energy of covalent bonds is higher than some supramolecular interactions, self-healing hydrogels formed by physical crosslinking could have suitable mechanical properties via advisable design, and it is believed that cellulose can work as a kind of natural nanofiller to enhance the self-healing hydrogels as well.

### 3.2 | Shape memory

Among these smart and adaptive materials, shape memory hydrogels (SMHs) have been of widespread interest in recent years, which have the ability to “memorize” a temporary shape and recover its initial permanent shape via external stimuli such as temperature, pH and light, etc.\(^75\) Compared with covalent bonds, supramolecular interactions are reversible and can respond to various
stimuli, which can be used as the dynamic crosslinkage to construct stimulus-responsive materials. According to the studies, there are dual- and triple-shape hydrogels with different designs of network shown in Figure 8, and one of the key feature of shape memory effect is the additional crosslinks to reversibly fix the network in a nonentropic conformation. Similar to self-healing, supramolecular interactions have potential here due to their reversibility and flexibility.

With host-guest interactions and hydrogen bonds, Willner and colleagues made an elegant work and constructed light-responsive SMHs based on CMC chains, which were modified with β-CD units, photoisomerizable azobenzene and self-complementary nucleic acid as tethers. As is shown in Figure 9A, by alternating the photoisomerization of the azobenzene units between the trans and cis states, the hydrogel was cycled between low-stiffness and high-stiffness states. Through host-guest interactions, these cellulose-based hydrogels realized the shape memory, self-healing, and controlled drug release functions upon light (UV/Vis) trigger. Chen and colleagues presented a novel and facile method to produce a multivalent cations-triggered shape memory sodium CMC/polyacrylamide hydrogel with tunable
mechanical properties based on electrostatic interactions. The interactions between sodium CMC and transition metal ions can be applied as “temporary crosslinks” to stabilize the temporary shape and render the hydrogel with shape memory properties. As illustrated in Figure 9B, Zhang and colleagues designed multitriggered DNA/bipyridinium dithienylethene (DTE) hybrid hydrogels based on CMC. Due to the reversible electron acceptor performances between the open- and closed-state DTE photoisomers, electrostatic interactions among the hydrogel networks could be regulated by light (UV/Vis). CMC chains modified with electron-donating dopamine sites and with the self-complementary nucleic acid or half G-quadruplex were used as the functional polymer scaffolds for the formation of the stimuli-responsive hydrogels. Specifically, for the shape-memory matrices, the shaped stiff hydrogels were crosslinked by the donor-acceptor interactions and the self-complementary H-bonds. The light- or redox-induced separation of the donor-acceptor interactions yielded the shapeless hydrogels of low stiffness, where the self-complementary DNA or the K\(^+\)-stabilized G-quadruplexes provided the memory code for the regeneration of the shaped stiff hydrogels. These stimuli-responsive supramolecular interactions endowed the hydrogels with abilities of shape memory and self-healing. Moreover, on the basis of dynamic phenylboronic acid-catechol interactions, Chen and colleagues developed a novel multifunctional supramolecular hydrogel with self-healing, shape memory, and adhesive properties.

From the search result, it is obvious that supramolecular interactions, such as hydrogen bonds, electrostatic interactions, hydrophobic interactions, and so on, do play a key role in the design of SMHs. Because of the hydroxyl groups with high reactivity on the surface of cellulose, it is facile to compound with other functional polymers in SMHs. To improve the mechanical property and biocompatibility of the supramolecular hydrogels, cellulose and its derivative could be utilized to serve as fillers in a noncovalently crosslinked SMHs, which could have great potential in practical applications.

### 3.3 Drug delivery

With the flexible polymer networks, hydrogels are considered to be of great potential in wound dressing and drug delivery because of their porous structure and high water content similar to biological tissues. In addition, the drug release system formed by hydrogels can further realize the drug controlled release and targeted release due to its responsiveness to environmental stimuli such as temperature, pH, chemicals, electric and magnetic fields. The loaded drugs in the hydrogels could be released through the change of swelling and shrinkage property. As is reported, researchers have engineered different hydrogels at the molecular level with the drug delivery under diverse mechanism (Figure 10). The incorporation of cellulose derivatives can also benefit for regulating the pore size of hydrogels, which can be applied as “on-off” release devices. Combining with the advantages of biomaterials and hydrogels, cellulose-based hydrogels have broad application prospects in the field of drug release in vivo.
For example, Liu et al. reported a pH/near-infrared-responsive (NIR) hydrogel for on-demand drug delivery and wound healing (Figure 11A). This hydrogel was designed by introducing polydopamine into CNFs oxidized by TEMPO, and it was crosslinked with calcium ion through ion-crosslinking. Li and colleagues prepared an injectable hydrogel through electrostatic interactions between positively charged nanoparticles and polyelectrolytes, sodium CMC. Nanosized cationic micelles were designed by self-assembly of methoxyl poly(ethylene glycol)-block-poly(ε-caprolactone) (PEG-b-PCL) and poly(ε-caprolactone)-block-poly(hexamethylene guanidine) hydrochloride-block-poly(ε-caprolactone) (PCL-b-PHMG-b-PCL), and the PCL core of the micelles could efficiently encapsulate a hydrophobic drug. Curcumin-loaded hydrogels prepared by this method were used as wound dressing materials which can promote wound healing and reduce bacterial infection via releasing curcumin. In Figure 11B, Lee and colleagues developed thermosensitive hydrogel barrier by combining mitomycin C (MMC) with modified tempo oxidized nanocellulose (cTOCN) via hydrogen bonds followed by integration with methyl cellulose (MC). The MMC was successfully combined with cTOCN and ensured controlled release of MMC from hydrogels throughout 14 days. Besides the controlled delivery of MMC, due to perfect loading, noncytotoxicity, good injectability, degradation, and mechanical stability, this study also realized fast thermoreversible phenomenon (30 s) of optimized hydrogels. Maulvi et al. dispersed timolol maleate encapsulated
ethyl cellulose nanoparticles in acrylate hydrogel and implanted the same in hydrogel contact lenses, to provide controlled drug delivery at therapeutic rates without compromising critical lens properties. Similarly, Auzely-Velty and colleagues designed a hybrid hydrogel by entrapping lipid nanoparticles within carboxymethylcellulose to achieve localized and sustained release of lipophilic drugs.

According to previous report, polysaccharide nanocrystals in drug delivery system exhibited prominent sustained release profiles. The unique aspect ratio and the high specific surface area of cellulose provide a good option for drug carrier and delivery applications. Take a full use of the biological characteristics of cellulose and the reversibility of supramolecular chemistry, cellulose-based supramolecular hydrogels are expected to broader applications in drug delivery.

4 | CONCLUSIONS AND PERSPECTIVES

As the most plentiful sustainable biomass resources, cellulose has obtained much attention because of the impressive structure and inherent supramolecular system. In this review, we focus on the current excellent research about cellulose-based supramolecular hydrogels. Ranging from the design to properties of supramolecular hydrogels based on cellulose, we mainly summarize the development of hydrogels containing cellulose based on hydrogen bonds, electrostatic interactions, and host-guest interactions. Moreover, some well-explored applications, including drug delivery, self-healing, and shape-memory materials, are discussed. Based on the research mentioned above, it can be concluded that the development of cellulose-based supramolecular hydrogels will be even more promising in the future. As one of the most prominent types of polymers employed in biomedical fields, cellulose-based hydrogels have great applications potential for biomimetic materials including wound dressing, cell culture, tissue engineering, cosmetics and soft robotics.

As far as we believe, cellulose-based supramolecular hydrogels play a far greater role in future research and applications beyond the current uses, while there are much room for improvement. First, the preparation of multifunctional cellulose hydrogels is mostly complicated at the present. The high production cost and technical requirements hinder its practical application, so simpler and more efficient methods are necessary for further popularization even commercialization. In addition to its apparent function, biomimetic cellulose-based hydrogels are supposed to have more similar structures and properties to tissues and organisms at the molecular level such as the hydrogels with well-organized structures. And for the better use in biomedicine, cellulose-based supramolecular hydrogels need to be more concerned with the multiple stimuli-responsive behaviors and degradation mechanisms under physiological conditions. Complexed with bioactive molecule, macromolecule, nanoparticles, or fluorescent molecular with aggregation-induced emission character, cellulose-based hydrogels can have further improvement in biomedical fields such as bioprobes for diagnosis and therapy, bioimaging, etc. Though many cellulose-based supramolecular hydrogels have been constructed for biomedical applications in recent years, most of them are only realized in labs and just proof of concept. A few can be commercialized or applied for clinical study. The industrial production of cellulose-based hydrogels still faces many challenges. The stability and fatigue resistance of supramolecular hydrogels are the key problems that should not be ignored. In terms of applications, with the development of artificial intelligence, supramolecular cellulose-based hydrogels will have great potential to be applied in 3D printing, electronic skins, intelligent soft robots, and so on in the future.
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**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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**REFERENCES**

1. Bethke K, Palantöken S, Andrei V, et al. Functionalized cellulose for water purification, antimicrobial applications, and sensors. Adv Funct Mater. 2018;28:1800409.

2. Trache D, Hussin MH, Haafiz MKM, Thakur VK. Recent progress in cellulose nanocrystals: sources and production. Nanoscale. 2017;9:1763–1786.

3. Gao H-L, Zhao R, Cui C, et al. Bioinspired hierarchical helical nanocomposite macrofibers based on bacterial cellulose nanofibers. Natl Sci Rev. 2020;7:73–83.

4. De France KJ, Hoare T, Cranston ED. Review of hydrogels and aerogels containing nanocellulose. Chem Mater. 2017;29:4609–4631.

5. Tu H, Zhu M, Duan B, Zhang L. Recent progress in high-strength and robust regenerated cellulose materials. Adv Mater. 2020:2000682.

6. Vázquez-González M, Willner I. Stimuli-responsive biomolecule-based hydrogels and their applications. Angew Chem, Int Ed. 2020;59:15342–15377.
7. Li C, Iscen A, Sai H, et al. Supramolecular-covalent hybrid polymers for light-activated mechanical actuation. Nat Mater. 2020;19:900–909.

8. Liu K, Kang Y, Wang Z, Zhang X. 25th Anniversary article: reversible and adaptive functional supramolecular materials: “Noncovalent Interaction” matters. Adv Mater. 2013;25:5530–5548.

9. Hoeben FJM, Jonkheijm P, Meijer EW, Schrenning A. About supramolecular assemblies of pi-conjugated systems. Chem Rev. 2005;105:1491–1546.

10. van Kuringen HPC, Schrenning A. Hydrogen bonding in supramolecular nanoporous materials. In Li ZT, ed. Lecture notes in chemistry, hydrogen bonded supramolecular materials. Springer, Berlin, Heidelberg: 2015:43–67.

11. Ji X, Shi B, Wang Hu, et al. Supramolecular construction of multifluorescent gels: interfacial assembly of discrete fluorescent gels through multiple hydrogen bonding. Adv Mater. 2015;27:8062–8066.

12. Brunsveld L, Folmer BJB, Meijer EW, Sijbesma RP. Supramolecular polymers. Chem Rev. 2001;101:4071–4097.

13. Mai W, Yu Q, Han C, Kang F, Li B. Self-healing materials for energy-storage devices. Adv Funct Mater. 2020;30:1909912.

14. Yan Q, Zhou M, Fu H. Study on mussel-inspired tough TA/PANI@CNCs nanocomposite hydrogels with superior self-healing and self-adhesive properties for strain sensors. Composites, Part B. 2020;201:108356.

15. Wang L, Du Y, Yuan Y, et al. Mussel-inspired fabrication of konjac glucomannan/microcrystalline cellulose intelligent hydrogel with pH-responsive sustained release behavior. Int J Biol Macromol. 2018;113:285–293.

16. Biyani MV, Foster EJ, Weder C. Light-healable supramolecular nanocomposites based on modified cellulose nanocrystals. ACS Macro Lett. 2013(2):236–240.

17. Li L, Liu L, Qing Y, et al. Stretchable alkaline poly(acrylic acid) electrolyte with high ionic conductivity enhanced by cellulose nanofibrils. Electrochim Acta. 2018;270:302–309.

18. Mredha MdTI, Guo YZ, Nonoyama T, Nakajima T, Kurokawa T, Gong JP. A facile method to fabricate anisotropic hydrogels with perfectly aligned hierarchical fibrous structures. Adv Mater. 2018;30:1704937.

19. Wang Z, Hu W, Du Y, et al. Green gas-mediated cross-linking generates biomolecular hydrogels with enhanced strength and excellent hemostasis for wound healing. ACS Appl Mater Interfaces. 2020;12:13622–13633.

20. Appel EA, Tibbitt MW, Greer JM, et al. Exploiting electrostatic interactions in polymer-nanoparticle hydrogels. ACS Macro Lett. 2015;4:848–852.

21. Oechslle A-L, Lewis L, Hamad WY, Hatzikiriakos SG, MacLachlan MJ. CO₂-switchable cellulose nanocrystal hydrogels. Chem Mater. 2018;30:376–385.

22. Wang R, Zhang M, Guan Y, Chen M, Zhang Y. A CO₂-responsive hydrogel film for optical sensing of dissolved CO₂. Soft Matter. 2019;15:6107–6115.

23. Lin N, Géze A, Wouessidjewe D, Huang J, Dufresne A. Biocompatible double-membrane hydrogels from cationic cellulose nanocrystals and anionic alginate as complexing drugs co-delivery. ACS Appl Mater Interfaces. 2016;8:6880–6889.

24. Shao C, Meng L, Cui C, Yang J. An integrated self-healable and robust conductive hydrogel for dynamically self-adhesive and highly conformable electronic skin. J Mater Chem C. 2019;7:15208–15218.

25. Zhang T, Cheng Q, Ye D, Chang C. Tunicate cellulose nanocrystals reinforced nanocomposite hydrogels comprised by hybrid cross-linked networks. Carbohydr Polym. 2017;169:139–148.

26. Yang L, Wang T. Preparation of cellulose drug-loaded hydrogel beads through electrostatic and host-guest interactions. J Appl Polym Sci. 2018;135:46593.

27. Liu K, Zheng D, Zhao J, et al. pH-Sensitive nanogels based on the electrostatic self-assembly of radionuclide I-131 labeled albumin and carboxymethyl cellulose for synergistic combined chemo-radioisotope therapy of cancer. J Mater Chem B. 2018;6:4738–4746.

28. Qi M, Pan H, Shen H, et al. Nanogel multienzyme mimics synthesized by biocatalytic ATRP and metal coordination for bioresponsive fluorescence imaging. Angew Chem Int Ed. 2020;59:11748–11753.

29. Chen D, Zhao X, Wei X, et al. Ultrastretchable, tough, antifreezing, and conductive cellulose hydrogel for wearable strain sensor. ACS Appl Mater Interfaces. 2020;12:53247–53256.

30. Wei Z, Yang JH, Zhou J, et al. Self-healing gels based on constitutional dynamic chemistry and their potential applications. Chem Soc Rev. 2014;43:8114–8131.

31. Yang H, Yuan B, Zhang X, Scherman OA. Supramolecular chemistry at interfaces: host-guest interactions for fabricating multifunctional biointerfaces. Acc Chem Res. 2014;47:2106–2115.

32. Zheng B, Wang F, Dong S, Huang F. Supramolecular polymers constructed by crown ether-based molecular recognition. Chem Soc Rev. 2012;41:1621–1636.

33. Gong Q, Li Y, Liu X, Xia Z, Yang Y. A facile preparation of polyaniline/cellulose hydrogels for all-in-one flexible supercapacitor with remarkable enhanced performance. Carbohydr Polym. 2020;245:116611.

34. Soto MA, Tiburcio J. Self-assembly of a supramolecular network with pseudo-rotaxane cross-linking nodes and its transformation into a mechanically locked structure by rotaxane formation. Chem Commun. 2016;52:14149–14152.

35. Xia D, Wang P, Ji X, Khashab NM, Sessler JL, Huang F. Functional supramolecular polymeric networks: the marriage of covalent polymers and macrocycle-based host-guest interactions. Chem Rev. 2020;120:6070–6123.

36. Harada A, Kobayashi R, Takashima Y, Hashidzume A, Yamaguchi H. Macroscopic self-assembly through molecular recognition. Nat Chem. 2011;3:34–37.

37. Harada A, Takashima Y, Nakahata M. Supramolecular polymeric materials via cyclodextrin-guest interactions. Acc Chem Res. 2014;47:2128–2140.

38. Rebek Jr J. Host-guest chemistry of calixarene capsules. Chem Commun. 2000:637–643.

39. Guo D-S, Chen S, Qian H, Zhang H-Q, Liu Y. Electrochemical stimulus-responsive supramolecular polymer based on sulfonatocalixarene and viologen dimers. Chem Commun. 2010;46:2620–2622.

40. Guo D-S, Liu Y. Calixarene-based supramolecular polymerization in solution. Chem Soc Rev. 2012;41:5907–5921.
41. Liu J, Tan CSY, Yu Z, Lan Y, Abell C, Scherman OA. Biomimetic supramolecular polymer networks exhibiting both toughness and self-recovery. *Adv Mater*. 2017;29:1604951.

42. Qin B, Yin Z, Tang X, et al. Supramolecular polymer chemistry: from structural control to functional assembly. *Prog Polym Sci*. 2020;100:101167.

43. Shao L, Pan Y, Hua B, et al. Constructing adaptive photosensitizers via supramolecular modification based on pillararene host-guest interactions. *Angew Chem Int Ed*. 2020;59:11779–11783.

44. Ji X, Ahmed M, Long L, Khashab NM, Huang F, Sessler JL. Adhesive supramolecular polymeric materials constructed from macromolecule-based host-guest interactions. *Chem Soc Rev*. 2019;48:2682–2697.

45. Zhang H, Liu Z, Zhao Y. Pillararene-based self-assembled amphiphiles. *Chem Soc Rev*. 2018;47:5491–5528.

46. Yan Q, Yuan J, Kang Y, Yin Y. Dynamic supramacromolecular self-assembly: deformable polymer fabricated nanostructures through a host-controlled approach. *Polym Chem*. 2010;1:423–425.

47. Jian C-M, Liu B-W, Chen X, Zhou S-T, Fang T, Yuan J-Y. Construction of photoresponsive supramolecular micelles based on ethyl cellulose graft copolymer. *Chin J Polym Sci*. 2014;32:690–702.

48. Kakuta T, Takashima Y, Nakahata M, Otsubo M, Yamaguchi H, Harada A. Preorganized hydrogel: self-healing properties of supramolecular hydrogels formed by polymerization of host-guest-monomers that contain cyclodextrins and hydrophobic guest groups. *Adv Mater*. 2013;25:2849–2853.

49. Tamesue T, Takashima Y, Yamaguchi H, Shinkai S, Harada A. Photoswitchable supramolecular hydrogels formed by cyclodextrins and azobenzene polymers. *Angew Chem Int Ed*. 2010;49:7461–7464.

50. Zhang J, Liu J, Yu Z, Chen S, Scherman OA, Abell C. Patterned arrays of supramolecular microcapsules. *Adv Funct Mater*. 2018;28:1800550.

51. Li ZY, Zhang Y, Zhang C-W, et al. Cross-linked supramolecular polymer gels constructed from discrete multi-pillar 5 aren metalloacycles and their multiple stimuli-responsive behavior. *J Am Chem Soc*. 2014;136:8577–8589.

52. Tan CSY, Liu J, Groombridge AS, Barrow SJ, Dreiss CA, Scherman OA. Controlling spatiotemporal mechanics of supramolecular hydrogel networks with highly branched cucurbit 8 uril polyrotaxanes. *Adv Funct Mater*. 2018;28:1702994.

53. Fan X, Wang T, Miao W. The preparation of pH-sensitive hydrogel based on host-guest and electrostatic interactions and its drug release studies in vitro. *J Polym Res*. 2018;25:215.

54. Sun N, Wang T, Yan X. Self-assembled supermolecular hydrogel based on hydroxyethyl cellulose: formation, in vitro release and bacteriostasis application. *Carbohydr Polym*. 2017;172:49–59.

55. Lin N, Dufresne A. Supramolecular hydrogels from in situ host-guest inclusion between chemically modified cellulose nanocrystals and cyclodextrin. *Biomacromolecules*. 2013;14:871–880.

56. Khabibullin A, Alizadehgiashi M, Khuu N, Prince E, Tebbe M, Kumacheva E. Injectable shear-thinning fluorescent hydrogel formed by cellulose nanocrystals and graphene quantum dots. *Langmuir*. 2017;33:12344–12350.

57. Hata Y, Kojima T, Koizumi T, et al. Enzymatic synthesis of cellulose oligomer hydrogels composed of crystalline nanoribbon networks under macromolecular crowding conditions. *ACS Macro Lett*. 2017;6:165–170.

58. Yan X, Xu D, Chi X, et al. A multiresponsive, shape-persistent, and elastic supramolecular polymer network gel constructed by orthogonal self-assembly. *Adv Mater*. 2012;24:362–369.

59. Zhang T, Zuo T, Hu D, Chang C. Dual physically cross-Linked nanocomposite hydrogels reinforced by tunable cellulose nanocrystals with high toughness and good self-recoverability. *ACS Appl Mater Interfaces*. 2017;9:24230–24237.

60. Tsujiya H, Sinawang G, Asoh T-A, et al. Supramolecular bio-composite hydrogels formed by cellulose and host-guest polymers assisted by calcium ion complexes. *Biomacromolecules*. 2020;21:3936–3944.

61. Hu D, Cui Y, Mo K, et al. Ultrahigh strength nanocomposite hydrogels designed by locking oriented tunicate cellulose nanocrystals in polymeric networks. *Composites Part B*. 2019;170:108118.

62. Ye D, Yang P, Lei X, et al. Robust anisotropic cellulose hydrogels fabricated via strong self-aggregation forces for cardiomyocytes unidirectional growth. *Chem Mater*. 2018;30:5175–5183.

63. Li K, Skolrood LN, Aytug T, Tekinalp H, Ozcan S. Strong and tough cellulose nanofibril composite films: mechanism of synergistic effect of hydrogen bonds and ionic interactions. *ACS Sustainable Chem Eng*. 2019;7:14341–14346.

64. Taylor DL, In Het Panhuis M. Self-healing hydrogels. *Adv Mater*. 2016;28:9060–9093.

65. Li Y, Xu Y, Tao L, Wei Y. Preparation and bio-medical applications of dynamic chemistry based self-healing hydrogels. *Acta Polymerica Sinica*. 2020;51:30–38.

66. Heidarian P, Kouzani AZ, Kaynak A, et al. Dynamic plant-derived polysaccharide-based hydrogels. *Carbohydr Polym*. 2020;231:115743.

67. Lehn J-M. From supramolecular chemistry towards constitutional dynamic chemistry and adaptive chemistry. *Chem Soc Rev*. 2007;36:151–160.

68. Wang MX, Chen YM, Gao Y, et al. Rapid self-recoverable hydrogels with high toughness and excellent conductivity. *ACS Appl Mater Interfaces*. 2018;10:26610–26617.

69. Wei Z, Yang JH, Liu ZQ, et al. Novel biocompatible polysaccharide-based self-healing hydrogel. *Adv Funct Mater*. 2015;25:1352–1359.

70. Kim JW, Park H, Lee G, et al. Paper-like, thin, foldable, and self-healable electronics based on PVA/CNC nanocomposite film. *Adv Funct Mater*. 2019;29:1905968.

71. Liu H, Li C, Wang B, et al. Self-healing and injectable polysaccharide hydrogels with tunable mechanical properties. *Cellulose*. 2018;25:559–571.

72. Liu Y-J, Cao W-T, Ma M-G, Wan P. Ultrasensitive wearable soft strain sensors of conductive, self-healing, and elastic hydrogels with synergistic “soft and hard” hybrid networks. *ACS Appl Mater Interfaces*. 2017;9:25559–25570.

73. Fox J, Wie JJ, Greenland BW, et al. High-strength, healable, supramolecular polymer nanocomposites. *J Am Chem Soc*. 2012;134:5362–5368.

74. Mckee JR, Appel EA, Seitsonen J, Kontturi E, Scherman OA, Ikkala O. Healable, stable and stiff hydrogels: combining conflicting properties using dynamic and selective...
three-component recognition with reinforcing cellulose nanorods. *Adv Funct Mater.* 2014;24:2706–2713.
75. Chan BQYu, Low ZWK, Heng SJW, Chan SY, Owh C, Loh XJ. Recent advances in shape memory soft materials for biomedical applications. *ACS Appl Mater Interfaces.* 2016;8:10070–10087.
76. Löwenberg C, Balk M, Wischke C, Behl M, Lendlein A. Shape-memory hydrogels: evolution of structural principles to enable shape switching of hydrophilic polymer networks. *Acc Chem Res.* 2017;50:723–732.
77. Wang C, Fadeev M, Zhang J, et al. Shape-memory and self-healing functions of DNA-based carboxymethyl cellulose hydrogels driven by chemical or light triggers. *Chem Sci.* 2018;9:7145–7152.
78. Li N, Chen G, Chen W, et al. Multivalent cation-triggered rapid shape memory sodium carboxymethyl cellulose/polyacrylamide hydrogels with tunable mechanical strength. *Carbohydr Polym.* 2017;178:159–165.
79. Li Z, Davidson-Ronenfeld G, Vázquez-González M, et al. Multi-triggered supramolecular DNA/bipyridinium di thiénylthiène hydrogels driven by light, redox, and chemical stimuli for shape-memory and self-healing applications. *J Am Chem Soc.* 2018;140:17691–17701.
80. Li Z, Lu W, Ngai T, et al. Mussel-inspired multifunctional supramolecular hydrogels with self-healing, shape memory and adhesive properties. *Polym Chem.* 2016;7:5343–5346.
81. Li S, Wang L, Zheng W, Yang G, Jiang X. Rapid fabrication of self-healing, conductive, and injectable gel as dressings for healing wounds in stretchable parts of the body. *Adv Funct Mater.* 2020;30:2002370.
82. Kabir SMF, Sikdar PP, Haque B, Bhuiyan MAR, Ali A, Islam MN. Cellulose-based hydrogel materials: chemistry, properties and their prospective applications. *Prog Biomater.* 2018;7:153–174.
83. Forero-Doria O, Polo E, Marican A, et al. Supramolecular hydrogels based on cellulose for sustained release of therapeutic substances with antimicrobial and wound healing properties. *Carbohydr Polym.* 2020;242:116383.
84. Peppas NA, Hilt JZ, Khademhosseini A, Langer R. Hydrogels in biology and medicine: from molecular principles to bio nanotechnology. *Adv Mater.* 2006;18:1345–1360.
85. Liu Y, Sui Y, Liu C, et al. A physically crosslinked poly dopamine/nanocellulose hydrogel as potential versatile vehicles for drug delivery and wound healing. *Carbohydr Polym.* 2018;188:27–36.
86. Zhu Y, Luo Q, Zhang H, et al. A shear-thinning electrostatic hydrogel with antibacterial activity by nanoengineering of polyelectrolytes. *Biomater Sci.* 2020;8:1394–1404.
87. Sultana T, Van Hai H, Park M, Lee S-Y, Lee B-T. Controlled release of Mitomycin C from modified cellulose based thermogel prevents post-operative de novo peritoneal adhesion. *Carbohydr Polym.* 2020;229:115552.