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Stimulus-responsive cellulose hydrogels in biomedical applications and challenges

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ABSTRACT

Stimuli-responsive cellulose hydrogels have garnered significant attention in the biomedical field owing to their extensive applications in tissue engineering and controlled drug delivery systems. Derived from cellulose and its derivatives, they are synthesized through physical or chemical cross-linking techniques, offering notable advantages such as cost-effectiveness and excellent biocompatibility. These hydrogels can respond to environmental stimuli, including pH variations, temperature fluctuations, and light exposure, enabling targeted drug release and promoting tissue regeneration. In tissue engineering, Stimuli-responsive cellulose hydrogels are used for the repair and regeneration of skin, bone, and other critical tissues. In drug delivery, they are optimized for oral, nasal, and ocular administration, as well as advanced cancer therapies. In addition, Stimuli-responsive cellulose hydrogels exhibit significant potential in disease diagnostics, particularly their conductive variants, which show promise in biosensing and diagnostic applications. However, despite their potential, challenges such as immune compatibility, long-term stability, and scalability in production remain barriers to clinical translation. Future research efforts should focus on multifunctional integration, advanced intelligent design, and enhanced stimulus responsiveness to fully unlock their potential in biomedical applications and facilitate their transition from laboratory research to practical use.

1. Introduction

In recent years, the depletion of non-renewable resources and the increasing emphasis on environmental sustainability have heightened interest in natural polymers [1]. Cellulose, the most abundant renewable natural resource, is widely distributed in nature. It constitutes the primary component of plant cell walls, accounting for approximately 40–50 % of their mass [2] (Fig. 1A). Beyond the plant kingdom, cellulose is also found in certain animals and microorganisms. The structure of cellulose is determined to be a straight chain polymer of β-D-glucose units connected by β-(1→4) glycoside bonds, with no branches in the structure [3] (Fig. 1B). The human body lacks β-glucosidase, rendering it incapable of breaking down cellulose for utilization [4]. When food containing cellulose enters the human body, it is first mechanically digested by the mouth and stomach, then ground and mixed into the small intestine. Although the small intestine cannot enzymolysis cellulose, it can promote intestinal peristalsis. In the process of cellulose degradation, the microbial community in the human gut is the real "main force". Some intestinal bacteria can produce cellulase, which gradually decomposes cellulose into oligosaccharides and glucose monomers for microbial metabolism and generates short-chain fatty acids such as acetic acid, propionic acid and butyric acid [5]. These products are not only used by microorganisms, but also partially absorbed by the human body to participate in energy metabolism, maintain intestinal environment stability, and reduce the risk of colorectal cancer. Notably, cellulose is particularly attractive for its excellent biocompatibility, abundant availability [6], low cost, high mechanical strength, good renewability, and biodegradability [7,8].

Hydrogels are three-dimensional (3D) network structures composed of hydrophilic polymer chains that are interconnected through chemical

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bonds [9,10], hydrogen bonds [11], van der Waals forces, and physical entanglements [12]. All materials required for their preparation contain some hydrophilic groups. Through meticulous design strategies, hydrogels can be structurally and functionally modified to tailor their physicochemical properties, including stiffness, pore size, viscoelasticity, microstructure, degradability, ligand presentation capabilities, and responsiveness to external stimuli. Furthermore, these attributes significantly influence cellular signaling and behavior [13,14]. Because hydrogel properties are comparable to the external environment of cells, hydrogels demonstrate exceptional biocompatibility along with favorable physical and mechanical characteristics, as well as long-term stability post-implantation [15]. Consequently, hydrogels serve as versatile platforms for a myriad of biomedical applications [16]. They have been used across various biomedical domains, including wound healing [14,17], tissue engineering [18], antitumor immunotherapy [19], disease modeling initiatives, cell delivery vectors, smart drug carriers, bioimaging techniques, biosensing applications, and conductive wearable or implantable biological devices [20].

The biocompatibility, degradability, non-toxicity and hydrophilicity of hydrogels extracted from natural polymers are significantly better than those of their composites [21]. Cellulose-based hydrogels play a crucial role in scientific research in various fields, including biomedicine, pharmaceuticals, food science and agriculture [22]. Due to its rich hydrophilic groups, cellulose has excellent water absorption and retention capabilities. In addition, its hydroxyl group, due to its strong reactivity, can be used as a site for chemical modification, thereby preparing various functional composite materials [23]. The preparation of cellulose hydrogels requires careful consideration of the types of cellulose, dissolution methods and hydrogel preparation techniques [24] (Fig. 1C). Traditional research on cellulose-based hydrogels is gradually unable to meet the growing demands for their functions and performances. Most traditional studies are limited to basic properties and simple applications, and fail to fully exert the potential value of cellulose-based hydrogels. Against this background, stimulus-responsive cellulose hydrogels emerged and became a research hotspot in this field. This type of hydrogel can respond sensitively and accurately to various

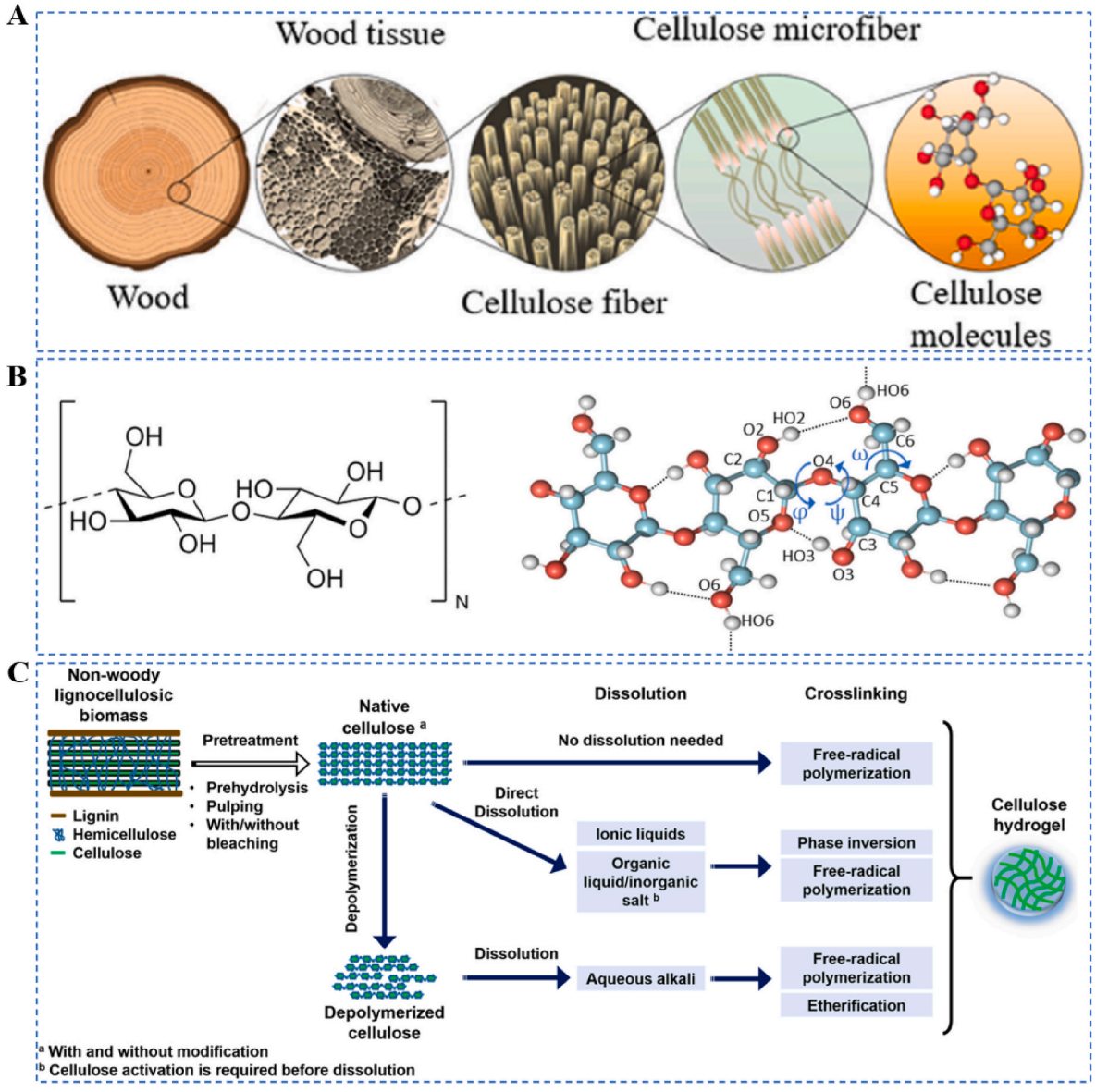

Fig. 1. Cellulose and cellulose hydrogels. (A) Sources of cellulose. This figure is reproduced with minor modifications from Ref. [2], Copyright © 2024 Chemosphere. published by Elsevier Ltd. **(B)** The structure of cellulose. This figure is reproduced with minor modifications from Ref. [3], Copyright © 2024 Carbohydrate Polymers. published by Elsevier Ltd. **(C)** Preparation principle of cellulose hydrogels. This figure is reproduced with minor modifications from Ref. [24], Copyright © 2021 Carbohydrate Polymers. published by Elsevier Ltd.

external stimuli, such as pH value [25], temperature [26], humidity, pressure, electric field, light [27], magnetic field [28], and chemical substances [29], etc. By carefully designing its physical/chemical cross-linking mode and stimulus response mechanism, researchers can effectively regulate the mechanical properties, response speed and functional diversity of hydrogels. For example, Ph-responsive cellulose hydrogels can precisely control drug release based on changes in environmental pH values, and this property is of great significance in fields such as tumor treatment. The microenvironment of tumor tissues is usually acidic. Ph-responsive hydrogels can specifically release drugs at the tumor site, improve the efficacy of drugs, and reduce damage to normal tissues at the same time [27,30,31]. Temperature-responsive hydrogels can be applied to smart switches and tissue engineering scaffolds, achieving specific functions based on temperature changes, providing new options for related medical devices and tissue repair [32].

This review systematically conducts the preparation and characterization of cellulose hydrogels, their derivatives, and nanocellulose hydrogels. By ingeniously combining physical and chemical cross-linking techniques, stimulus-responsive hydrogels with high strength, self-healing properties, and rapid response were successfully obtained. This type of hydrogel plays a key role in multiple fields. In tissue engineering, it can create a favorable growth environment for cells and promote tissue repair and regeneration. In terms of drug delivery, precise drug release can be achieved to enhance the therapeutic effect. When diagnosing diseases, by responding to specific stimuli, biomarkers can be detected more sensitively, facilitating early diagnosis. In the field of environmental monitoring, it can also be used to detect harmful substances. The article also highlights the significance of the green preparation process. By adopting this process, not only can the use of toxic reagents be avoided and the adverse impact on the environment be reduced, but also the biocompatibility and degradability of hydrogels can be enhanced, paving the way for their clinical application and commercialization. Furthermore, from the perspective of multidisciplinary integration and comprehensively considering factors such as regulations and costs, this article deeply explores the application prospects of cellulose hydrogels, providing strong support for subsequent research and industrial development, and is expected to promote greater breakthroughs in the fields of biomedicine and environmental engineering.

2. Cellulose hydrogels

2.1. Structure and properties of cellulose

Cellulose is an abundant, renewable polymer [33]. It is typically classified as either plant or bacterial cellulose, depending on its origin [34]. Cellulose consists of linear or helical macromolecular chains of D-glucose units linked by β(1→4)-glycosidic bonds between the C1 hemiacetal hydroxyl group and the C4 alcohol hydroxyl group [35]. Each chain has both reducing and nonreducing ends [36], and the D-glucose rings adopt a chair conformation [37]. Plant fibers are a significant source of cellulose and are widely available in the seeds, fruits, stems, and leaves of plants, including bamboo, kapok, flax, and ramie [38]. In contrast, bacterial cellulose is synthesized through the fermentation of certain microorganisms [39], including *Bacillus subtilis acetate*, *Agrobacterium tumefaciens*, *Pseudomonas aeruginosa*, *Rhizobium*, and *ascomycetes* [40]. Unlike plant cellulose, bacterial cellulose has a unique porous reticulated nanostructure [41]. In addition, it possesses a high water-retention capacity, polymerization degree, mechanical strength, and crystallinity [39].

Cellulose molecules contain numerous hydroxyl groups, which readily form intra- and intermolecular hydrogen bonds. These hydrogen bonds can cause cellulose molecules to aggregate [42–45] into crystalline fibrillar structures with parallel spiral assemblies that pack tightly together, thereby enhancing the linearity, rigidity, and structural integrity of cellulose [46]. This unique structure significantly affects the physical and chemical properties of cellulose, as well as its reactivity.

Most bioderived materials undergo physical, chemical, or biological modification or functionalization before use [47]. However, cellulose does not dissolve easily in common molecular solvents, including water, owing to its extensive inter- and intramolecular hydrogen bonds and tightly packed crystalline regions [48]. As a result, reactions under heterogeneous conditions are often limited to the cellulose fiber surface, which restricts the scope of cellulose modifications [49]. This poses a considerable obstacle to its conversion and use [50]. Nevertheless, the development of solvents capable of dissolving cellulose has enabled the preparation of functional cellulose materials in homogeneous systems using cellulose solutions as raw material, which can maximize the utilization rate of hydroxyl groups and ensure the uniformity of the reaction. Several cellulose dissolution systems have been developed, including *N*-methylmorpholine-*N*-oxide [51], ionic liquids [52], and alkali/urea systems [53].

2.2. Advantages of cellulose hydrogels

Hydrogels derived from cellulose exhibit notable benefits, including cost-effectiveness, abundant availability, robust mechanical properties, and favorable biocompatibility. As a naturally abundant polysaccharide, cellulose is both easily accessible and economical, making it highly suitable for large-scale utilization [54]. The mechanical robustness of these hydrogels can be further improved through chemical modifications, enhancing their suitability for applications requiring long-term implantation. Moreover, their excellent biocompatibility enables their use in diverse fields such as controlled drug delivery, tissue engineering, and wound care [55]. By incorporating specific modifications, these hydrogels can also be designed to exhibit pH-responsive behavior, facilitating targeted therapeutic delivery and the development of intelligent material systems.

In comparison to other advanced biomaterials like silk protein, chitosan, sodium alginate, and hyaluronic acid, cellulose hydrogels demonstrate distinct advantages in terms of affordability, resource availability, and mechanical performance. Although silk protein hydrogels are known for their exceptional biocompatibility and mechanical strength, their high production costs and limited availability restrict their widespread use [56]. Chitosan hydrogels, despite their antimicrobial and biodegradable characteristics, often exhibit only moderate mechanical strength [57]. Sodium alginate hydrogels, although cost-efficient and easy to process, typically lack the necessary mechanical robustness for certain demanding applications [58]. Hyaluronic acid hydrogels, despite their superior biocompatibility, are often hindered by high costs and limited mechanical durability [59]. In contrast, cellulose hydrogels offer a unique combination of low production costs, widespread availability, high mechanical integrity, and excellent biocompatibility, making them an ideal choice for large-scale and long-term biomedical applications [60]. Their multifunctional nature positions them as a highly competitive and versatile material in the realm of advanced biomaterials.

2.3. Classification of cellulose hydrogels

2.3.1. Natural cellulose hydrogel

Natural cellulose hydrogels, characterized by their three-dimensional network structures, can be synthesized through physical crosslinking methods (such as hydrogen bonding, freeze-thaw cycles, and ionic crosslinking) or chemical crosslinking approaches (such as covalent bonding and graft copolymerization). These materials exhibit high water content (>90%), excellent biocompatibility, degradability, and tunable mechanical properties, making them versatile polymeric materials. Their unique structural and functional attributes endow them with broad application potential in fields such as biomedicine, environmental engineering, and the food industry [61].

Wang et al. [62] proposed a design strategy based on supramolecular

engineering, which significantly improved the mechanical properties and ionic conductivity of cellulose hydrogels by introducing the strong coordination between bentonite (BT) and cellulose and the ion regulation ability of the nanoconfined cellulose-BT intercalation structure. An all-natural cellulose-Bt composite hydrogel has been successfully developed, which exhibits excellent mechanical properties (compressive strength up to 3.2 MPa, fracture strength up to 0.45 MJ m^{-3}) and ionic conductivity (89.9 and 25.8 mS cm^{-1} at 25 °C and −20 °C, respectively), as well as excellent freezing resistance. This study provides new ideas and theoretical support for the design of cellulose hydrogels and other functional materials.

2.3.2. Cellulose-derivative hydrogels

Cellulose derivatives prepared by chemical modification are mainly carried out by two methods: cellulose degradation and derivatization of the hydroxyl groups [63]. Common cellulose derivatives include sodium carboxyme thyl cellulose (CMC) [64,65], hydroxypropyl cellulose [66], hydroxyethyl cellulose [67], cellulose acetate [68], methylcellulose [69], and hydroxypropyl methylcellulose [70]. Hydrogels can be prepared directly from most cellulose derivatives because they are soluble in water or common organic solvents.

CMC is highly pH-sensitive, with a pKa of approximately 3–4, making it widely applicable for uses such as slow drug-release systems [71]. Many researchers have combined CMC with polyacids to develop pH-responsive composite polymers or hydrogels. Typical polyacids, such as polyacrylic acid and polymethacrylic acid, have a pKa of approximately 5–6. Hydroxypropyl cellulose hydrogels have been extensively studied owing to the high water solubility and temperature sensitivity of hydroxypropyl cellulose [72]. pH-sensitive polyacids are often used to prepare polyacid/hydroxypropyl cellulose composites through grafting or free-radical polymerization, thereby achieving both pH and temperature sensitivity. Karewicz et al. [73] synthesized alginate/hydroxypropyl cellulose hydrogel microspheres with temperature sensitivity, designed for the controlled release of the anticoagulant drug heparin. The hydrogel microspheres had a diameter of approximately 3 μm and featured a regular pore-like mesh structure on their surfaces. The release curve of heparin can be customized by the temperature and composition ratio of the preparation material used.

2.3.3. Nanocellulose hydrogels and their preparation

Nanocellulose is a kind of sustainable natural material prepared by modification of cellulose [74].Cellulose nanocrystals (CNC) [75] and Cellulose nanofibers (CNF) [46] are two important nanocellulose materials that are extracted from natural cellulose by acid hydrolysis and mechanical treatment (often combined with chemical pretreatment), respectively. The CNC is a short rod-shaped, approximately 3–10 nm in diameter and 100–300 nm in length, with high crystallinity (54–88 %) and high rigidity (approximately 7.5 GPa in strength), suitable for reinforcement composites, optical films and drug carriers. CNF is long fibrous, about 5–60 nm in diameter, up to several microns in length, low crystallinity (50–60 %), good flexibility, and can form a gel-like network structure, which is widely used in flexible films, packaging materials and biomedical fields. The main differences between the two are form, crystallinity and mechanical properties, and the choice depends on the specific application needs. CNC and CNF show great promise in areas such as coatings [76], biomedicine [77], energy storage [78], and separation technology [79]. CNFs possess excellent mechanical properties and tunable surface chemistry [80]. Current research on nanocellulose focuses on its outstanding physicochemical properties, new preparation techniques, and advanced surface modification methods [81,82]. However, owing to the complexity and low yield of nanocellulose production, it is mainly used as a reinforcement phase in composite materials.

2.3.3.1. CNC hydrogels. CNCs, including nanocrystalline cellulose and cellulose nano whiskers (CNWs), comprise rigid rod-like particles [83] with lengths of 100–200 nm and diameters of approximately 5–20 nm [84], making them considerably shorter than CNFs. Phan et al. [85] prepared thermos-responsive CNC hydrogels, which had effects on drug release and pharmacokinetics (Fig. 2A(i)) It has different forms at different temperatures and is injectable (Fig. 2A(ii)).

Research on single-component CNC hydrogels is limited, likely owing to the inability of CNCs to "entangle" sufficiently, as well as the high CNC concentrations (>10 wt%) required for gelation. Nevertheless, gelation can be achieved at lower CNC concentrations by changing the solution conditions, modifying the surface, or introducing adsorbent or non-adsorbent water-soluble polymers [86]. Chau et al. [87] showed that increasing the ionic strength of the suspension by adding salts inhibited electrostatic repulsion and increased molecular interactions, thereby reducing the sol-gel transition concentration to approximately 1.5 wt% CNC. Huang et al. [88] developed an injectable nanocomposite self-healing hydrogel prepared from CMC and aldehyde cellulose nanocrystals, which can keep wounds moist and absorb inflammatory exudates. This CMC/DACNC nanocomposite hydrogel exhibits high self-healing efficiency (approximately 5 min) and is injectable with commendable mechanical strength, making it suitable for use as a wound dressing for patients with deep burns.

2.3.3.2. CNF hydrogels. The high-energy mechanical homogenization of wood pulp produces CNFs with lengths greater than 1 μm and diameters of approximately 1 nm. CNFs are longer and more flexible than CNCs, with better entanglement tendencies, making them well-suited for hydrogel formation. Brusentsev et al. [89] used photocrosslinking to prepare CNF hydrogels, which showed good biocompatibility and laid a good foundation for tissue engineering (Fig. 2B). The delamination and primary fibrillation processes of CNFs are often coupled with enzymatic treatments, TEMPO oxidation, or other chemical modifications such as carboxyl methylation. Therefore, CNFs have diverse surface chemistries and charge densities [90].

Zheng et al. [91] used *in situ* radical polymerization to uniformly disperse CNF-graphene (GN) nanocomposites in PAA hydrogels, resulting in composite hydrogels with high ductility and conductivity. The conductivity of the composite hydrogel material was 2.5 S/m, whereas the compressive strength and tensile strength were 2.54 and 0.32 MPa, respectively. Notably, CNF can form a unique hierarchical structure that promotes the formation of a stable hydrogel network and increases the crosslinking density. However, the introduction of CNF can prevent the aggregation of graphene, while improving the mechanical properties of the composite hydrogel. Lu et al. [92] prepared CNF-CNT/PAAM composite hydrogel materials through one-pot free-radical polymerization, using CNF as the carrier. In this case, CNF not only provides a toughening effect as a nano-enhancer but also effectively aids in the uniform distribution of carbon nanotubes within the hydrogel matrix. The results indicate that the hydrogel exhibits high compressive and tensile strength, with a strain coefficient of approximately 11.8 when the strain ranges from 100 to 200 %. In addition, its pressure-sensing ability is effective within the pressure range of 0–140 kPa, and motion signals can be reliably detected after 100 load-to-unload cycles. Nanocellulose, with its strong hydrophilicity, can improve the compatibility of carbon materials with hydrogels. Moreover, nanocellulose can also serve as a dispersant for carbon materials and a strengthening agent for gel materials.

2.4. Preparation of cellulose hydrogel

Cellulose hydrogels can be prepared through physical or chemical crosslinking [93,94]. Crosslinking is a critical step in the preparation of hydrogels, as it restricts the mobility of the polymer chains [95–97], thereby converting the polymer from a bulk liquid into a gel. Hydrogels can be coupled with intracellular signals, trigger the operation of

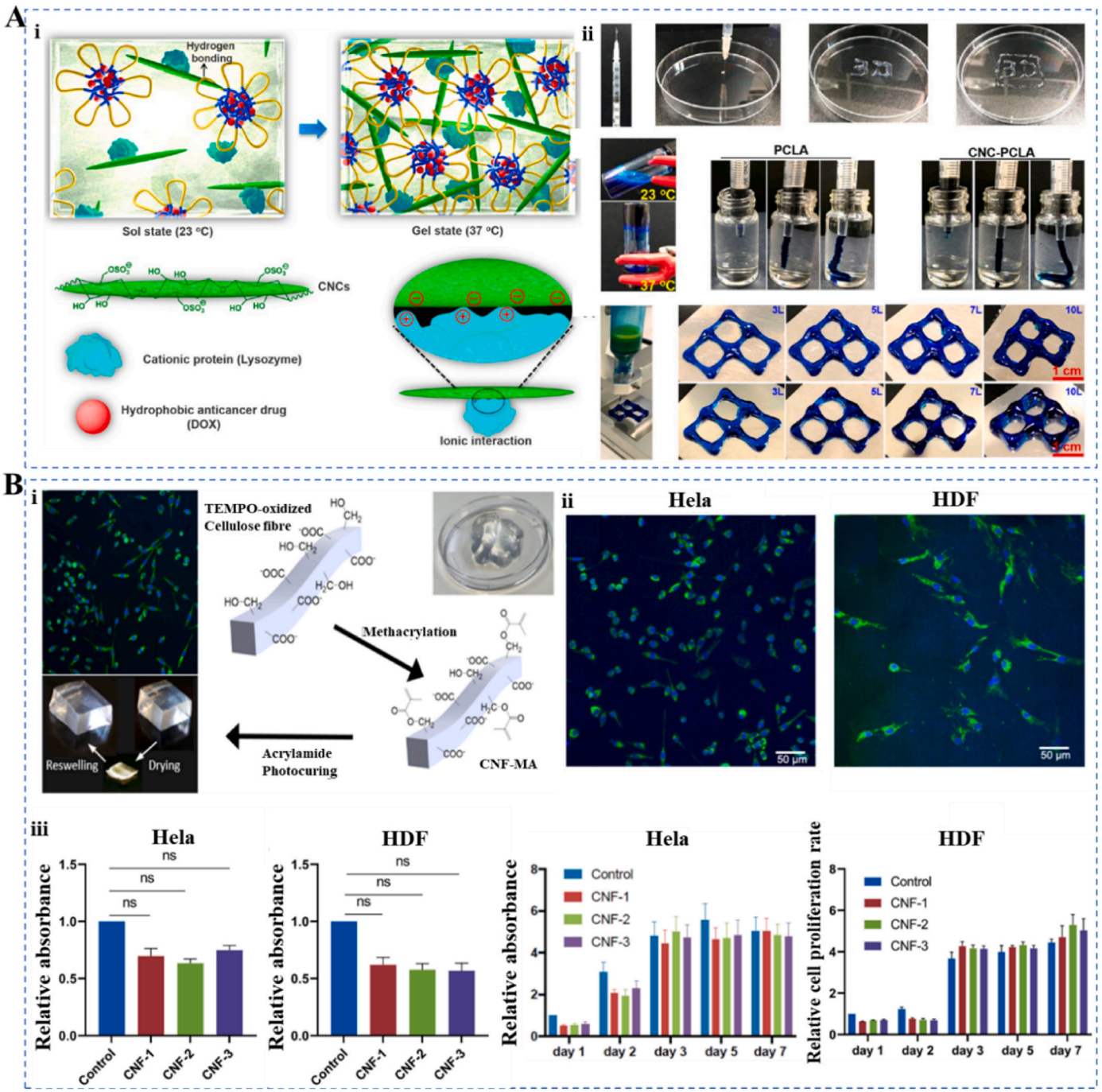

Fig. 2. Preparation of nanocellulose hydrogels. (A) Research on temperature-responsive hydrogels based on CNC cellulose. **(i)** Schematic diagram of loading DOX hydrogel; **(ii)** In vitro characterization of hydrogels. This figure is reproduced with minor modifications from Ref. [85], Copyright © 2022 ACS applied materials & interfaces. published by American Chemical Society. **(B)** Preparation of hydrogels based on CNF cellulose photocrosslinking and shape memory. **(i)** Preparation diagram; **(ii-iii)** Cell characterization. This figure is reproduced with minor modifications from Ref. [89], Copyright © 2023 Biomacromolecules. published by American Chemical Society.

intracellular mechanisms and drug release, and play a role in precise drug release [20,46] (Fig. 3A). Hydrogels prepared by different preparation methods have different properties (Table 1). And with the development of stimulus-responsive materials, cellulose hydrogels show great potential in this field. Li et al. [98] applied Interpenetrating Polymer Network (IPN) to develop carboxymethyl cellulose (CMC) hydrogels. Hydrogel units can withstand severe bending/compression deformation and operate normally at extreme temperatures (−30-70 °C) (Fig. 3B). Kang et al. [48] developed a hydrophilic cellulose based hydrogel sensitive to light and pH (Fig. 3C(i-ii)). The hydrogel was prepared based on Schiff base reaction and distributed uniformly under electron microscopy, providing a new idea for smart contact lenses (Fig. 3C(iii-iv)).

2.4.1. *Physical crosslinking*

Physically cross-linked hydrogels are formed by noncovalent interactions, such as hydrogen bonding, ionic bonding, electrostatic forces, van der Waals forces, and hydrophobic interactions. These hydrogels are nonpermanent and can revert to a solution upon heating; thus, they are also known as pseudogels or thermos reversible gels [99].

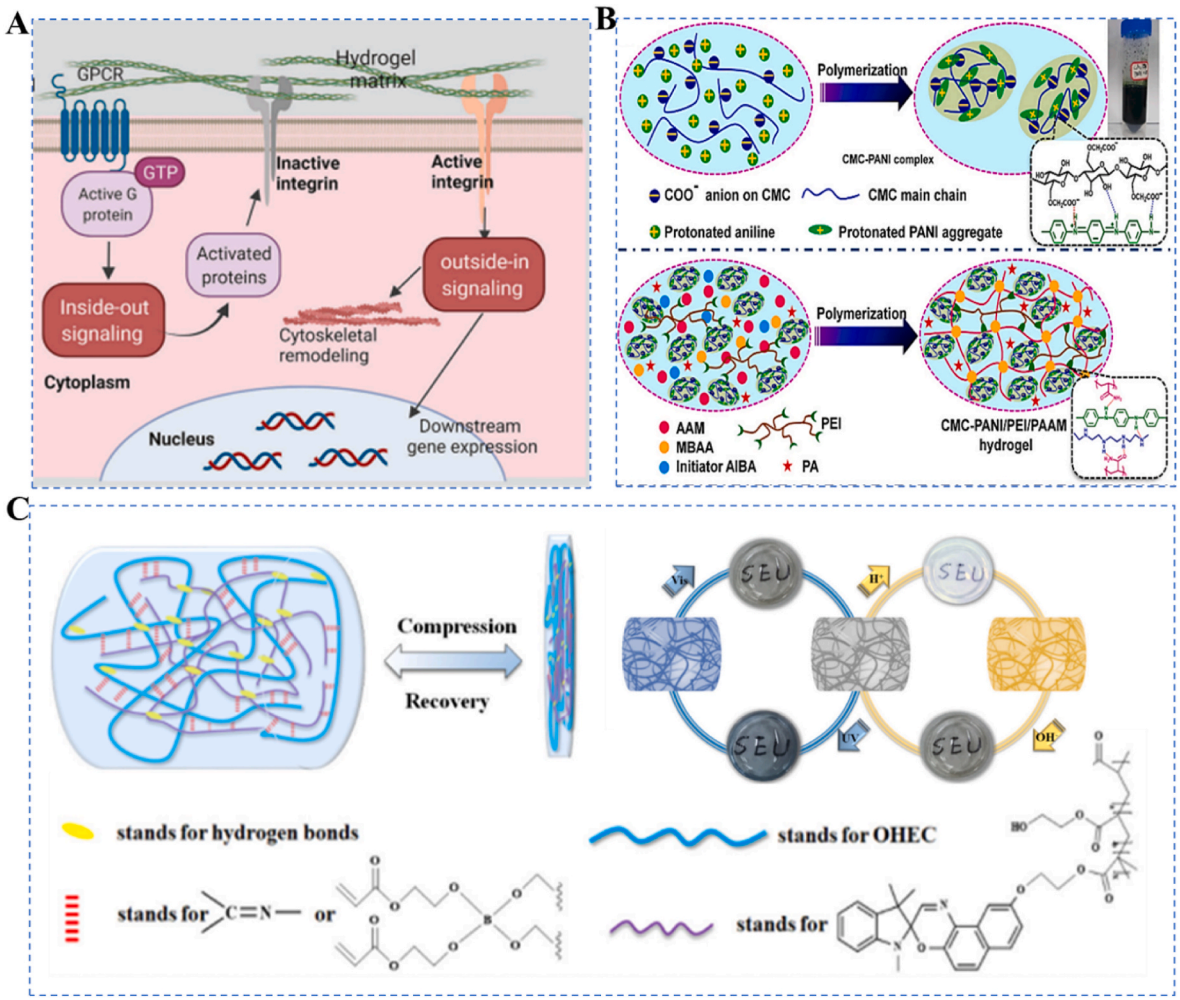

Fig. 3. Structure and formation principle of hydrogels. (A) Signal coupling triggered by the hydrogel in the cell. adapted and reprinted with permission. This diagram is reproduced with minor modifications from Ref. [20], Copyright © 2022 Journal of colloid and interface science. published by Elsevier. **(B)** Development of carboxymethyl cellulose (CMC) hydrogels. carboxymethyl cellulose (CMC); polyaniline (PANI); polyethyleneimine/polyacrylamide (PEI/PAAM). This diagram is reproduced with minor modifications from Ref. [98], Copyright © 2022 Carbohydrate Polymers. published by Elsevier Ltd. **(C)** Preparation mechanism of oxyhydroxyethyl cellulose based hydrogel used in smart contact lenses. This diagram is reproduced with minor modifications from Ref. [48], Copyright © 2022 International journal of biological macromolecules. published by Elsevier.

Cellulose hydrogels are often physically cross-linked because the abundant hydroxyl groups of cellulose facilitate the formation of hydrogen-bonding networks. However, they generally have weaker mechanical properties than chemically cross-linked hydrogels [95].

2.4.1.1. Hydrogen bonding. Hydrogen bonding is essential for the formation and stabilization of biological systems and hydrogels. This bonding occurs through many weak single hydrogen bonds that assemble components into complex structures called multiple hydrogen bonds [99]. The dynamic nature of hydrogen bonds allows them to break and reorganize during material deformation, dissipating energy and giving materials their unique strength, toughness and elasticity. For example, cellulose contains strong inter- and intramolecular hydrogen bonds, which makes it insoluble in water and organic solvents in general. Zhou et al. [100] prepared pH-responsive gels based on carboxypropyl cellulose and carboxymethyl chitosan through hydrogen bonding and Schiff base reaction. The hydrogel is homogeneous in structure and loaded with phenylalanine. When pH value is 6.8, the drug release rate increases significantly (Fig. 4A(i-iii)) Within the molecule, hydroxyl groups and sterically regulated chain conformations form a strong hydrogen bonding network that enables the preparation of cellulose hydrogels. Orasugh et al. [101] incorporated CNCs into poloxam 407 (PM)-based hydrogels, where the formation of strong hydrogen bonds resulted in high intensity and sustained drug release. Overall, the ability of hydrogen bonding to form complex structures, dissipate energy and enhance materials makes it a valuable tool for developing advanced hydrogels for drug delivery and tissue engineering applications.

2.4.1.2. Ionic bonding. Ionic crosslinking is characterized by its simple reaction conditions and the ability to perform crosslinking at room temperature [102]. Hujaya et al. [103] developed cellulose hydrogels prepared by CNF through ionic complexation, and DOX released abruptly when pH increased to 7.4, and had a slow release state when pH decreased to 4 (Fig. 4B). Chen et al. [104] used a straightforward impregnation technique to produce high-strength, self-healing cellulose hydrogels. The composite of sodium carboxymethyl cellulose (CMC) and polyacrylic acid-Fe^{3+} (PAA-Fe^{3+}) was used to fabricate a multifunctional hydrogel. The results indicate that with a water content of 37.7 %, the elastic modulus of the synthesized hydrogel material is 0.41 MPa, whereas its breaking strength reaches 4.42 MPa. Furthermore, this composite hydrogel exhibits an enhanced self-healing rate and greater elongation at break, achieving a remarkable self-healing rate of up to 85 %.

Table 1
Properties of cellulose hydrogels prepared by different methods.

Preparation method	Experimental condition	Swelling ratio	Hardness (kPa)	Elasticity (%)	Modulusofelasticity (kPa)	Compression Modulus(kPa)	Fracture strain(%)	Rupture stress(kPa)	Strain sensitivity	Viscosity (Pa.s)	Fatigue resistance (number of cycles)
Physical crosslinking [123–125]	Room temperature, pH7.4	15–20	10–20	80–90	10–50	20–60	200–300	50–100	0.5–1.0	0.1–0.5	100–200
Chemical crosslinking [126–128]	Room temperature, pH7.4	10–15	50–100	70–80	50–200	100–300	150–250	100–200	1.0–2.0	0.5–1.0	500–1000
IPNs [129–131]	Room temperature, pH7.4	8–12	100–200	60–70	100–300	200–400	100–200	200–300	2.0–3.0	1.0–2.0	1000–2000

2.4.1.3. Hydrophobic association. Hydrophobic association hydrogels typically refer to the formation of hydrogels through hydrophobic interactions among molecules, characterized by both hydrophilic and hydrophobic components. This phenomenon occurs as the hydrophilic chains fold in an aqueous environment, exposing the hydrophobic structures that become surrounded by polar groups. Upon reaching a critical gel concentration, these components aggregate into micelles, resulting in gel formation [105]. Hydrophobic association hydrogels are generally synthesized via two primary methods: one involves amphiphilic polymers containing both hydrophilic and hydrophobic moieties, where the latter serves as crosslinking points within the network structure. When these amphiphilic polymers are introduced into water, their hydrophobic segments coalesce, facilitating hydrogel formation through macromolecular chains or intermolecular associations [106]. In addition, a stable 3D network can be established using a predominant amount of a hydrophilic monomer copolymerized with minor quantities of monomers possessing hydrophobic groups and incorporating surfactants. Hydrophobic interactions are crucial in the recombination and folding of biomacromolecules, as well as in micelle assembly. Furthermore, these interactions can be harnessed to develop shear-thinning hydrogels. Liu et al. [107] prepared cellulose hydrogels through static π-π stacking, electric power, hydrophobic interaction hydrogen bonding, and weak entanglement, which has high tensile and adhesion, and has been widely used in electronic skin and healthcare (Fig. 4C).

2.4.1.4. Host–guest/hydrophobic interactions. Host–guest interactions are noncovalent interactions between two or more molecules with complementary structures in the form of molecular recognition. Cyclodextrin is a supramolecular hydrogel widely used to induce host–guest interactions [108]. Typically, cyclodextrin molecules bind to host molecules, whereas guest molecules interact with cyclodextrin through hydrophobic interactions to form supramolecular hydrogels. In the presence of water, a diverse array of small guest molecules can be encapsulated within the cavities of large ring molecules through host–guest interactions, resulting in the formation of a host–guest complex. The binding and dissociation of this complex are influenced by environmental factors such as temperature, REDOX conditions, light exposure, and pH levels. The strength of the binding interaction is quantified by the binding constant, which is typically associated with characteristics of the guest molecule, including molecular volume, structural configuration, and hydrophobicity. Jiang et al. [19] prepared self-healing, Ph-responsive injectable cellulose hydrogels using host-guest interaction. Using DOX as a model drug, hydrogels enhance the antitumor efficacy of DOX and reduce the side effects of DOX (Fig. 4D).

2.4.1.5. Other physical crosslinking strategies. The freeze-thaw method involves subjecting hydrogel to low temperatures for freezing, followed by thawing at ambient temperature and repeating this freeze-thaw cycle to create a novel type of hydrogel. This process does not require the addition of crosslinking agents or organic solvents, resulting in a gel with excellent biocompatibility and mechanical strength that surpasses those of hydrogels produced through chemical crosslinking. In the freeze-thaw process, freezing temperature, freezing duration, and cycle times have significant effects on the properties of hydrogels. Freeze-thawing improves the properties of polymer gels without compromising their biocompatibility or biodegradability. For instance, polyvinyl alcohol (PVA)/cellulose nanocrystal (CNC) hydrogels formed by freeze-thawing exhibit enhanced compression properties. The number of freeze-thaw cycles significantly affects the properties and microstructures of hydrogels, such as their porosity [96]. Fraser et al. synthesized polyvinyl alcohol hydrogels incorporating varying concentrations of sodium alginate (SA) and CNCs via the freeze-thaw technique, subsequently combining them with polypyrrole (PPy)/-cellulose to yield multifunctional conductive hydrogels [41]. These

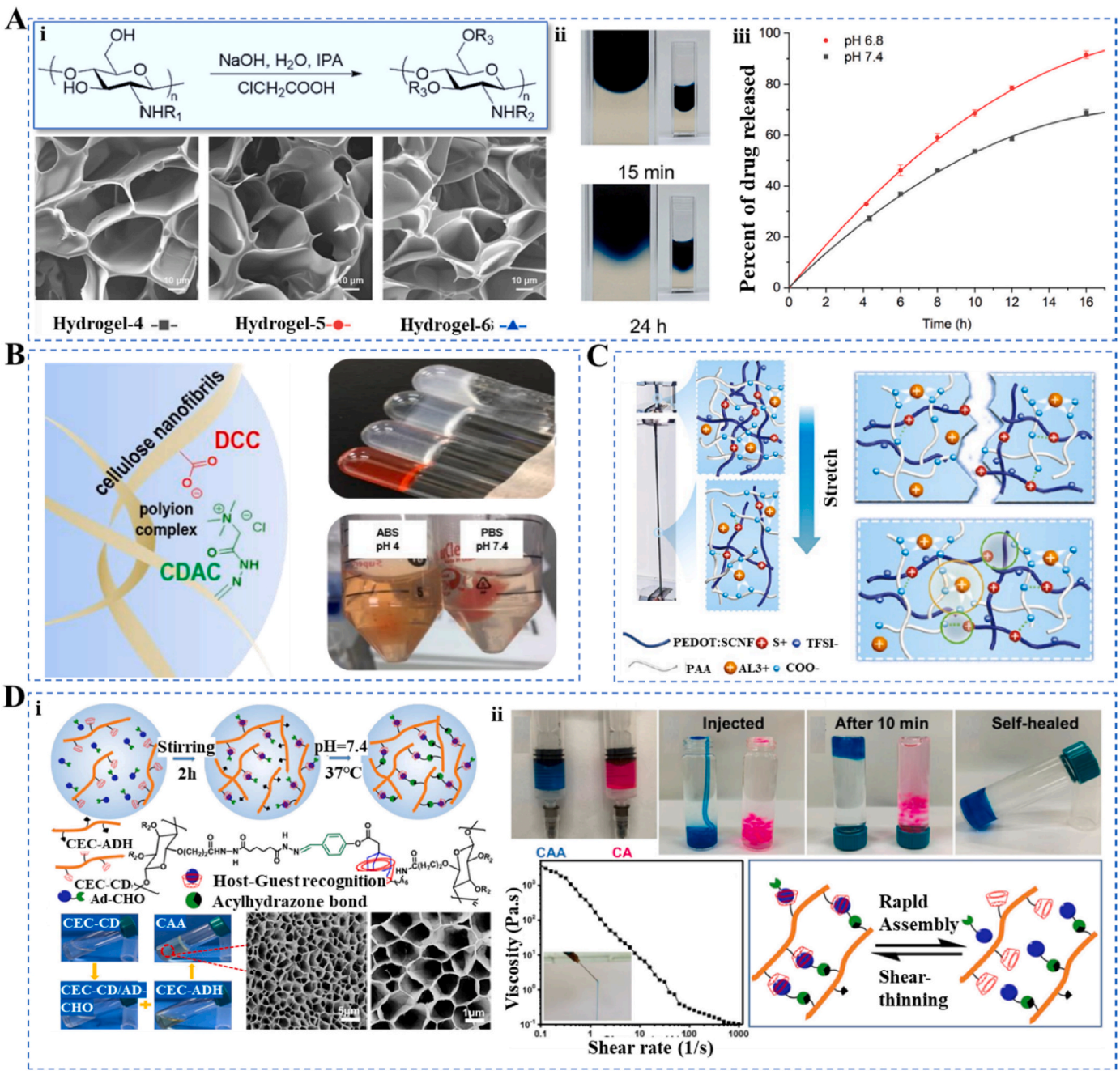

Fig. 4. Study on the preparation of cellulose hydrogels using physical crosslinking. (A) Diagram of preparation of cellulose hydrogels using hydrogen bond crosslinking [100]. **(i)** Method and transmission electron microscopy of carboxymethyl chitosan (CMCS) hydrogel crosslinking; **(ii)** The boundaries of hydrogels are blurred due to the recombination of imine bonds between Ox-HPC and CMCS; **(iii)** The proportion of drug released by hydrogels with different pH is also different. The Figure is reproduced with minor adaptations from Ref. Copyright © 2023 Carbohydrate polymers. published by Elsevier Ltd. **(B)** A multi-ionic complex hydrogel prepared by two oppositely charged derivatives Nanocellulose (CNF), pH 4 fully releases adriamycin. This figure is reproduced with minor modifications from Ref. [103], Copyright © 2018 Acta biomaterialia. published by Elsevier B.V. **(C)** Mechanism of the self-healing process of preparing cellulose-based hydrogels using hydrophobic interactions. The Figure is reproduced with minor adaptations from Ref. [107], Copyright © 2023 ACS Nano. published by American Chemical Society. **(D)** Preparation of cellulose hydrogels by Host–guest/hydrophobic interactions **(i)** Dynamic self-healing CAA schematic diagram and SEM images of CEC-CD, CEC-CD/AD-CHO and CEC-ADH; **(ii)** (a) Injectability of hydrogels and the Schematic illustration of dynamic cross-link formation utilizing guest-host interactions. The Figure is reproduced with minor adaptations from Ref. [19], Copyright © 2022 Acta Biomaterialia. published by Elsevier BV.

materials exhibit outstanding characteristics, including high toughness, compressive resistance, strain sensitivity, and elevated elastic modulus.

Photo-crosslinking is triggered by high-energy irradiation, such as ultraviolet (UV)–visible light, enabling rapid *in situ* hydrogel formation. Ruthenium-based photochemical crosslinking used blue light instead of UV irradiation to create covalent crosslinks in hydrogel networks [96]. Photo-crosslinking produces hydrogels with good tissue adhesion and antimicrobial properties [109].

Radiation-induced crosslinking is an environmentally friendly technique for hydrogel preparation, as it does not require any catalysts or chemicals [110]. It is also fast and efficient, synthesizing homogeneous hydrogels in one step. This method can be controlled by adjusting the type and dose of radiation. For example, γ-ray irradiation has been successfully used to prepare methyl hydroxyethyl

cellulose/polyethylene glycol hydrogels.

2.4.2. Chemical crosslinking

The chemical crosslinking method involves guiding certain molecular substances with bifunctional groups to chemically bond various polymers through covalent interactions, thereby constructing 3D network hydrogels [64]. Hydrogels synthesized via the chemical crosslinking approach typically exhibit enhanced structural integrity and superior swelling properties [49]. Current research methodologies predominantly focus on the homo-polymerization or copolymerization of free radicals [111]. Wang et al. [112] used liquid metal (LM) microdroplets for free-radical polymerization in conjunction with MXene, sulfonated bacterial nanocellulose (BNC), and polyacrylic acid (PAA) to fabricate cellulose hydrogels exhibiting excellent electrical conductivity. The gel's folding behavior is attributed to its unique gelatinization mechanism coupled with the presence of MXene nanosheets, which enhance detection sensitivity. In addition, this material demonstrates commendable interfacial adhesion capabilities that

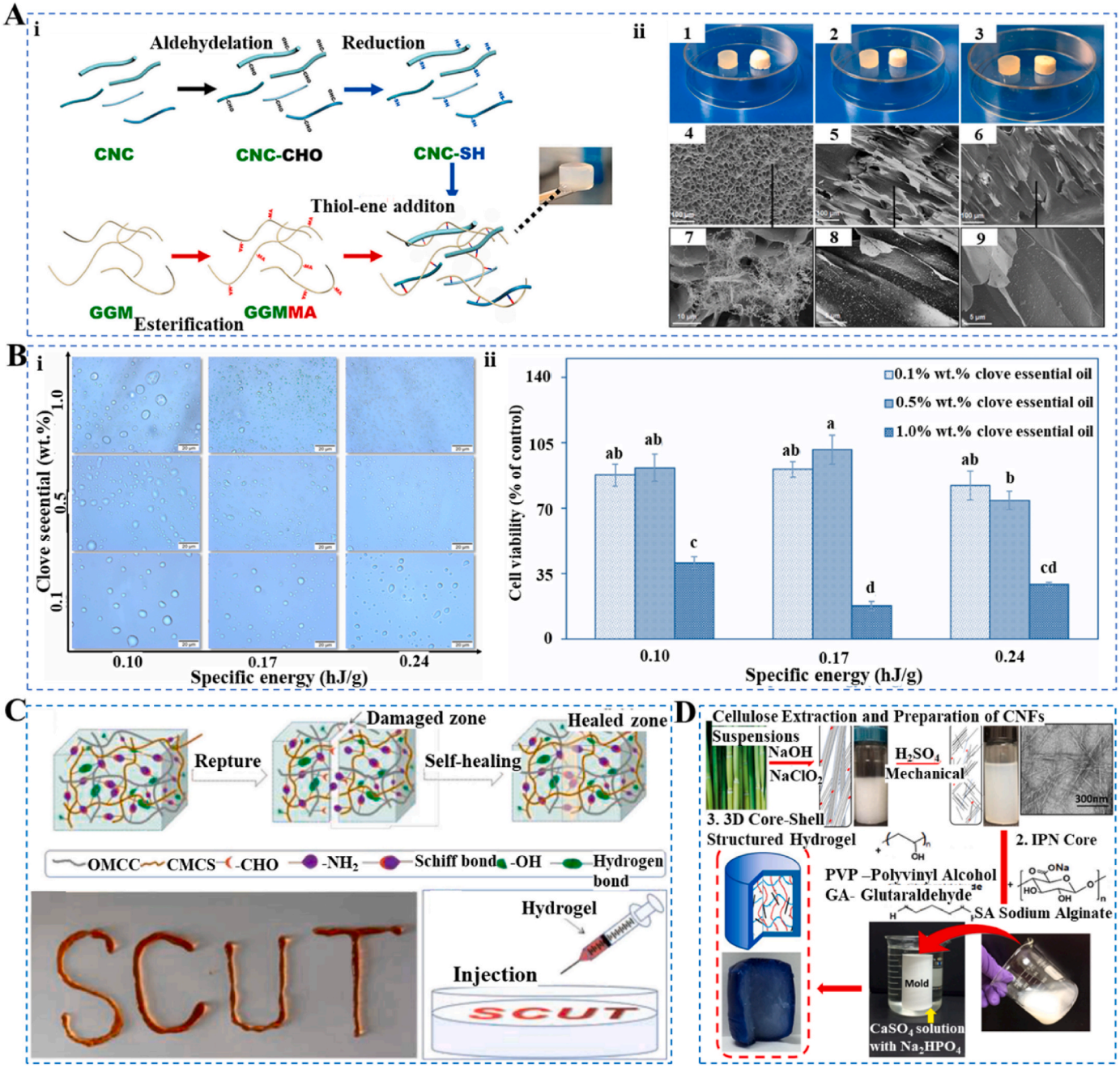

Fig. 5. Chemical crosslinking mechanism of cellulose based hydrogels. **(A)** Schematic diagram of preparation of CNC-based hydrogels by free radical polymerization [113]. **(i)** Cross-linking of CNC hydrogels; **(ii)** Electron microscope characterization. This diagram is reproduced with minor modifications from reference, Copyright © 2022 Carbohydrate polymers. published by Elsevier Ltd. **(B)** Preparation of CNF hydrogel filled with clove essential oil emulsion. **(i)** Electron microscope images of different anterior ultrasound; **(ii)** Cell viability after 24 h of hydrogel incubation. This diagram is reproduced with minor modifications from Ref. [116], Copyright © 2019 Ultrasonics Sonochemistry. published by Elsevier B.V. **(C)** Schematic diagram of Schiff base reaction to prepare cellulose hydrogels. This diagram is reproduced with minor modifications from Ref. [117], Copyright © 2022 International journal of biological macromolecules. published by Elsevier. **(D)** Schematic diagram of preparation of cellulose hydrogels by IPNs. This diagram is reproduced with minor modifications from Ref. [122], Copyright © 2016 Carbohydrate polymers. published by Elsevier Ltd.

facilitate effective bonding between disparate materials. Moreover, it possesses self-healing properties; upon the application of external force, it can rapidly revert to its original state, thus improving material utilization efficiency.

2.4.2.1. Free-radical polymerization. Free-radical polymerization is a method for generating polymer chains by adding an initiator, which creates a polymer reaction center that subsequently reacts with monomers to form new reaction centers [113] (Fig. 5A). Photopolymerization, a subtype of free-radical polymerization, is initiated by irradiation with electron beams, rays, or microwaves. This process can be conducted at room temperature without the need for initiators or other chemical reagents, thereby improving the safety of the resultant hydrogel.

2.4.2.2. Emulsion polymerization. The emulsion polymerization technique facilitates the synthesis of nanohydrogels through polymerization within the core of oil-in-water (O/W) droplets, using surfactants as stabilizing agents. Nanocellulose is recognized as an optimal emulsifying agent owing to its favorable wettability, low toxicity, excellent biocompatibility, and sustainability [114,115]. Huerta et al. [116] used high-intensity ultrasound to generate emulsion-filled cellulose nanofiber (CNF) hydrogels, with clove essential oil (0.1 %, 0.5 %, and 1.0 % by weight) serving as the dispersing phase. The resulting hydrogels exhibit commendable cytocompatibility and hold promise as alternative scaffolds for tissue engineering applications (Fig. 5B).

2.4.2.3. Schiff base reaction. Schiff bases are a class of organic compounds containing imine or azomethine groups that typically form through the condensation of an amine and a reactive carbonyl group. Yin et al. [117] used Schiff base reaction to construct self-healing hydrogels, which have excellent swelling and mechanical properties (Fig. 5C). Owing to their pharmacological and physiological activities, Schiff bases have become a prominent area of research. Kang et al. [48] developed a composite hydrogel primarily composed of oxidized hydroxyethyl cellulose and allyl copolymers, in which the oxidized hydroxyethyl cellulose molecular chains served as biomolecular templates for the formation of Schiff bases, boronic acid radicals and hydrogen bonds, resulting in unique mechanical properties. These hydrogels demonstrated good pH responsiveness and non-cytotoxicity in vitro.

2.4.3. IPNs

Another approach to preparing cellulose hydrogels involves creating an IPN. IPN technology represents a distinctive polymer blend or polymer alloy network achieved through the interpenetration and entanglement of two or more polymers via physical or chemical interactions [118]. The IPN architecture facilitates a stable amalgamation of polymers exhibiting markedly different properties and functions, thereby enabling functional complementarity among the components. Characterized by features such as cellular structure, biphasic continuity, and interfacial penetration, IPNs exhibit unique synergistic effects in terms of functionality and performance. The following sections discuss these crosslinking mechanisms with some examples of relevant applications. IPNs represent a specialized class of composite polymer materials, typically formed by the interconnection of two or more cross-linked networks through topological entanglement or various physical interactions, including ionic bonds, hydrogen bonds, van der Waals forces, and hydrophobic interactions [119]. Compared with physical or chemical cross-linked hydrogels, hydrogels prepared by the IPN method have superior mechanical strength and flexibility, which makes them have a great development space. These interactions effectively prevent the gel from undergoing physical separation without disrupting the chemical bonds within it. The mutual cross-osmosis and mechanical entanglement among multiple polymers promote forced miscibility and synergistic effects that enhance salt tolerance. Unlike traditional single-network hydrogels, IPN hydrogels amalgamate the benefits of both physical and chemical hydrogels, significantly improving their mechanical strength and salt resistance, while broadening their applicability [120]. Toledo et al. [121] synthesized full IPN hydrogels composed of CMC and cross-linked polyacrylic acid (cPAA) by blending CMC solution with cPAA at varying mass ratios followed by crosslinking CMC chains using citric acid. This straightforward approach circumvents the necessity for toxic crosslinkers; consequently, CMC:cPAA hydrogels demonstrate enhanced mechanical properties (141±3 kPa) and swelling characteristics (58±2 g g^{-1}) compared to PAA. Yue et al. [122] fabricated core-shell structured hydrogels via an interpenetrating polymer network (IPN) approach by combining polyvinyl alcohol (PVA) and sodium alginate (SA), crosslinked with Ca^{2+}. The incorporation of cellulose nanofibrils (CNF) facilitates the formation of hydrogen bonds within the PVA-SA matrix, thereby enhancing the density, viscoelasticity, and mechanical strength of the hydrogels (Fig. 5D).

2.5. Characterization of cellulose hydrogels

Key physicochemical properties of hydrogels include mechanical strength, swelling behavior, biocompatibility, elasticity, and release kinetics. The hydrogels used in drug-delivery systems must have excellent mechanical strength (depending on the degree of crosslinking) to maintain physical integrity until the drug is released and to regulate the release rate and duration [38].

2.5.1. Biocompatibility

Biocompatibility, which includes histocompatibility and blood compatibility, is a fundamental requirement for biological materials. Cellulose hydrogels exhibit exceptional biocompatibility, non-toxicity, and biodegradability, making them particularly well-suited for biomedical applications [64]. Hydrogels with excellent biocompatibility can avoid rejection by organisms and play a positive role in promoting cell growth, adhesion, and differentiation.

2.5.2. Adhesion

Owing to various biological fluids, such as blood, interstitial fluid, and excretory fluid, the physiological environment on the surface of the tissue is humid. Therefore, biomedical hydrogels must be appropriately designed to achieve sustained adhesion to wet surfaces and to promote tissue repair and regeneration. Their strong adhesion enables them to bind closely to tissues or organs and play a role in repair and protection [132].

2.5.3. Antibacterial property

Owing to their high similarity to the natural extracellular matrix and the ease of customization through the combination of spatial properties, hydrogels have been widely used as surface modifiers for various implantable devices, such as orthopedic implants [133], micro-capacitors, and biosensors. Antibacterial activity is desirable for all implantable materials, as it reduces the risk of implant-associated infections. The hydrogel coating can mitigate the foreign body reaction of the implantable sensor and serve as a barrier between the sensor and the biological environment.

2.5.4. Mechanical properties

Hydrogels with excellent mechanical properties can be used as artificial cartilage and skeletal muscle tissue because they can reorganize their structure and restore the original function after a fracture, thereby extending their service life [133]. The mechanical properties of hydrogels depend on their composition and structure, allowing for design and optimization according to specific needs.

2.5.5. Moisture absorption

In terms of swelling, because the polymer chain can absorb a large

Table 2
Properties of cellulose hydrogels in response to different stimuli.

Preparation method	Experimental condition	Swelling ratio	Hardness (kPa)	Elasticity (%)	Modulusofelasticity (kPa)	Compression Modulus(kPa)	Fracture strain(%)	Rupture stress(kPa)	Strain sensitivity	Viscosity (Pa.s)	Fatigue resistance (number of cycles)
pH-responsive hydrogels [143–145]	Room temperature,pH5.0	18–22	30–80	80–90	30–100	60–150	200–300	80–150	1.0–2.0	0.3–0.8	300–600
	Room temperature,pH7.4	12–15	50–150	70–80	50–150	100–250	150–250	100–200	1.5–2.5	0.8–1.5	500–1000
Temperature-responsive hydrogels [146–148]	25 °C,pH7.4	20–25	20–50	85–95	20–80	40–100	250–350	60–120	0.8–1.5	0.2–0.8	200–400
	37 °C,pH7.4	10–15	80–150	70–80	80–150	150–300	150–250	150–250	1.5–2.5	0.8–1.5	500–1000
Humidity responsive hydrogel [149–151]	Relative humidity 30 %	10–15	20–60	75–85	20–60	40–100	150–250	50–100	0.8–1.5	0.2–0.8	200–400
	Relative humidity 90 %	20–25	10–40	85–95	10–40	30–60	250–350	30–80	0.5–1.0	0.1–0.5	100–200
Pressure responsive hydrogel [152–154]	0.1 MPa,Room temperature	12–18	50–150	70–80	50–150	100–250	150–250	100–200	1.0–2.0	0.5–1.0	500–1000
	1 MPa,Room temperature	8–12	100–300	60–70	100–300	200–400	100–200	200–300	2.0–3.0	1.0–2.0	1000–2000
Electro - responsive hydrogel [155–157]	Room temperature, applied electric field (1 V/cm)	10–15	80–200	70–80	80–200	150–300	150–250	150–250	1.5–2.5	0.8–1.5	500–1000
	Room temperature, applied electric field(5 V/cm)	8–12	150–350	60–70	150–350	250–450	100–200	250–350	2.5–3.5	1.5–2.5	1500–3000
Photo-responsive hydrogel [60,158,159]	Room temperature,UV light	5–10	100–250	60–70	100–250	200–400	100–200	200–300	2.0–3.0	1.0–2.0	1000–2000
Magnetic- responsive hydrogel [160–162]	Room temperature, external magnetic field	10–15	50–150	70–80	50–150	100–250	150–250	100–200	1.5–2.5	0.8–1.5	500–1000
Chemically responsive Hydrogels [21,163,164]	Room temperature,NaCl-containing solution	15–20	40–120	75–85	40–120	80–200	200–300	80–150	1.0–2.0	0.3–0.8	300–600
	Room temperature,Ca^{2+} containing solution	8–12	100–300	60–70	100–300	200–400	100–200	200–300	2.0–3.0	1.0–2.0	1000–2000
Multi-responsive hydrogel [60,165,166]	37 °C,pH 5.0	8–12	150–300	60–70	150–300	300–500	100–200	250–350	2.5–3.5	1.5–2.5	1500–3000
	25 °C,pH 7.4,Relative humidity 60 %	15–20	50–150	80–90	50–150	100–250	200–300	100–200	1.5–2.5	0.8–1.5	500–1000

amount of water through the hydrophilic groups (-OH, -COOH, -$CONH_2$, and -SO_3H), it simulates biological tissue during swelling. In the field of tissue engineering, proper swelling of hydrogels promotes the diffusion of nutrients and other molecules, further aiding cell migration through hydrogels [134]. In the field of wound dressing, it promotes the rapid absorption of wound exudate and plays the role of sealing and hemostasis [135]. Hydrogel swelling has three main stages: water diffusion, polymer chain loosening, and swelling [136]. The water content of cellulosic hydrogel is as high as 99.9 wt%, which can achieve significant swelling.

2.5.6. *Drug slow-release performance*

The microporous structure of hydrogels is well-suited for drug delivery, and the slow release of drugs can be achieved using various mechanisms based on diffusion, swelling, chemical reactions, or other environmental stimuli. Among these, the diffusion mechanism of drug release is widely accepted. In the field of biomedicine, the long-term use of drugs and their instantaneous release can cause severe toxicity to the body. Cellulosic hydrogels, emerging as a novel class of sustained-release drug carriers, possess a porous 3D architecture characterized by tunable cross-linking density and pore size, an open pore structure, and a high specific surface area. These features facilitate the loading and release of drug molecules through the modulation of external environmental conditions. Consequently, they are gaining increasing prominence in the domain of controlled drug release [137].

3. Stimuli-responsive cellulose hydrogels

The properties of stimulus-responsive cellulose hydrogels are closely related to their structural design. In particular, the correlation between the physical/chemical cross-linking mode and the stimulus-response mechanism directly determines their mechanical properties, response speed and functional diversity. Physical crosslinking gives hydrogels dynamic and reversible properties, which is suitable for fast response scenarios, but has low mechanical strength. Chemical crosslinking improves mechanical properties through a stable covalent bond network, but may limit dynamic response. Through collaborative physical/chemical crosslinking, hydrogels with high strength and multiple stimulus responses can be designed to extend their application range. And the hydrogels with different stimulus response have different properties (Table 2). Stimulation-responsive cellulose hydrogels respond sensitively to a variety of external stimuli, including pH, temperature, humidity, pressure, electric field, light, magnetic field, and chemicals [138,139]. These stimuli can significantly affect the phase state, volume, shape, molecular polarity, reaction rate and recognition ability of hydrogels. For example, Ph-responsive hydrogels can be used in targeted drug delivery systems, whereas temperature-responsive hydrogels are suitable for smart switches and tissue-engineered stents [138,140]. These ingenious designs offer broad prospects for applications such as chemical sensors, memory components, artificial muscles, controlled release drug delivery systems, immobilized enzymes, and tissue engineering. By further optimizing its stimulation response performance, cellulose stimulus-responsive hydrogels are expected to achieve breakthrough applications in more high-tech fields [141,142].

3.1. *pH-responsive cellulose hydrogels*

pH-responsive cellulose hydrogels alter their shape and volume in response to changes in environmental pH, making them highly valuable for applications such as drug delivery and tissue engineering [100,145]. These hydrogels typically contain anionic (such as COO^- or OPO_3^{2-}) or cationic groups (such as NH_3^+, NRH_2^+, or NR_3^+) within their main or side chain structures. These groups accept or release protons depending on the environmental pH, which alters the concentration of internal and external ions. Consequently, the hydrogen bonds between the macromolecular chain segments dissociate or associate, affecting the volume

of solubilization and thereby increasing or decreasing the ability of the hydrogel to bind water. Thus, the network structure and volume of the hydrogel change in response to pH [167].

pH-responsive cellulose hydrogels have extensive application prospects in bio- and chemical sensors, bioimaging, cancer diagnostics, and drug-release systems, such as for *in vitro*-activated anticancer drugs [168]. Wang et al. [169] developed a pH-responsive biobased cellulose hydrogel from CNFs, SA, urea, iron 1,3,5-benzene tricarboxylic acid, and calcium chloride. This hydrogel exhibited a high water uptake of 101 g/g at pH 11 (Fig. 6A(i-ii)) Wang et al. [170] prepared an antimicrobial INP hydrogel from polyacrylic-acid-grafted quaternized cellulose and PVA. The hydrogel demonstrated excellent mechanical properties and self-healing behavior. In addition, it was resistant to microbial degradation, thereby prolonging its service life in natural environments.

3.2. Thermo-responsive cellulose hydrogels

Thermo-responsive cellulose hydrogels adjust their swelling rate and

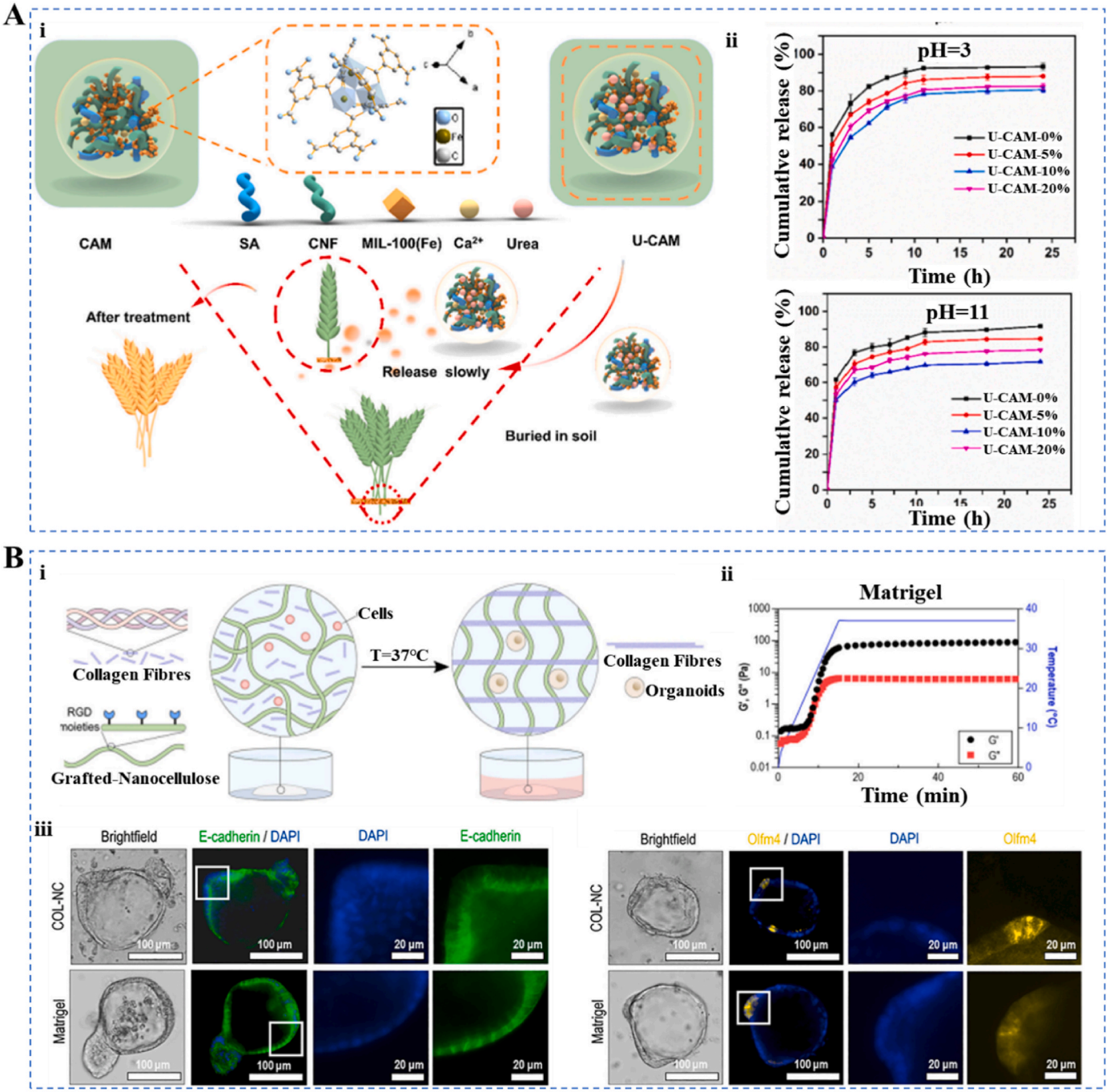

Fig. 6. Study on PH and temperature responsive cellulose based hydrogels. (A) A Ph-sensitive hydrogel was prepared with cellulosic hydrogel and MIL-100 (Fe) for stable release of urea: **(i)** Hydrogel preparation diagram; **(ii)** Release curves of urea in pH3 and 11 hydrogels. This diagram is reproduced with minor modifications from Ref. [169], Copyright © 2021 International journal of biological macromolecules. published by Elsevier. **(B)** Application of temperature-responsive collagen-nanocellulose hydrogels to intestinal organoids: **(i)** Schematic diagram of hydrogel formation; **(ii)** Rheological characterization of hydrogels. **(iii)** Expression of E-cadherin and Olfm4 in cells treated with water gel. This diagram is reproduced with minor modifications from Ref. [179], Copyright © 2021 Materials science & engineering C, Materials for biological applications. published by Elsevier B.V.

volume in response to external temperature changes [171,172]. Their molecular structures typically contain a balance of hydrophilic and hydrophobic groups, whose hydrophilicity and hydrogen bonding are affected by temperature [173]. There are three main types of thermo-responsive cellulose hydrogels: low-temperature-soluble, high-temperature-soluble, and regenerative hydrogels [174]. Low-temperature-soluble hydrogels have a lower critical solution temperature (LCST) [175]; they exist as low-viscosity fluids below the LCST and swell to form a gel above it. In contrast, high-temperature-soluble cellulose hydrogels have an upper critical solution temperature

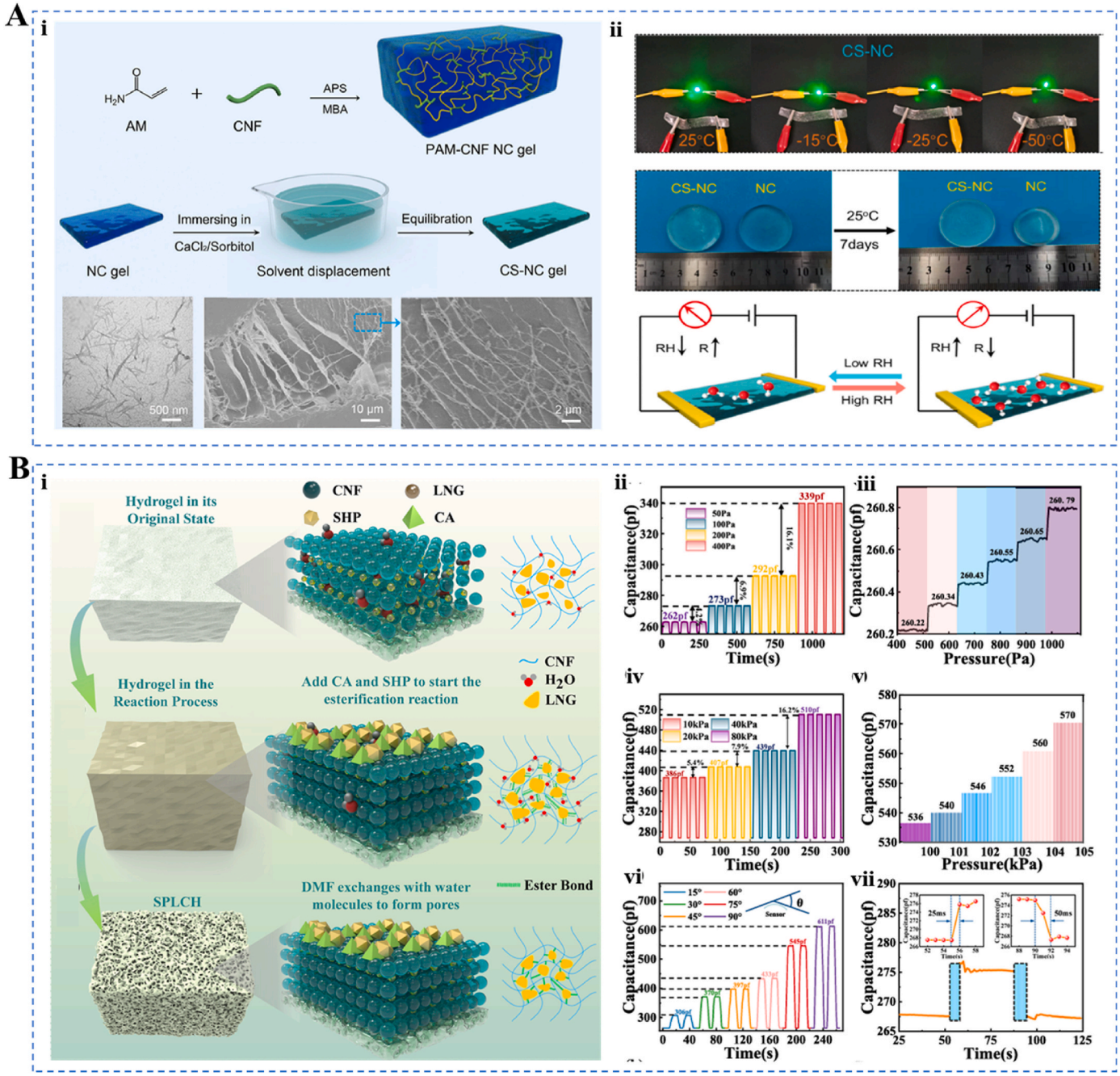

Fig. 7. Application of Humidity- and Pressure-Responsive Cellulose Hydrogels. (A) Research and Application of Humidity-Based Pressure-Conductive CNF Hydrogels: **(i)** Schematic Construction of CNF Hydrogel and Scanning Electron Microscopy Characterization; **(ii)** Mechanism Diagram of LED Lamp Brightness in Hydrogel at Various Temperatures and Humidity Levels. This figure is reproduced with minor modifications from Ref. [151], Copyright © 2022 ACS applied materials & interfaces. published by American Chemical Society. **(B)** Preparation of Flexible Capacitive Pressure Sensors, which is based on the cellulose hydrogel system.**(i)** The lignin-cellulose hydrogel (SPLCH) is synthesized using the solvent exchange technique.**(ii)** When conducting tests in the low-pressure region, starting from a fixed pressure, the pressure value is gradually increased in a multiplicative manner during consecutive loading and unloading cycles.**(iii)** In the low-pressure region, different pressure values are continuously applied to obtain more comprehensive data for analyzing its performance.**(iv)** For tests in the high-pressure region, with fixed test conditions maintained, the pressure is continuously increased in a multiplicative manner during consecutive loading and unloading cycles, and the pressure is applied continuously. **(v)** In the high-pressure region, different pressure values are applied continuously to further study the performance of the sensor under high-pressure and variable-pressure conditions. **(vi)** The bending test is carried out to evaluate its flexibility and structural stability. **(vii)** The response-recovery time test is performed to assess the response speed and recovery ability of the sensor. This figure is reproduced with minor modifications from Ref. [183], Copyright © 2025 International journal of biological macromolecules. published by Elsevier.

(UCST); these hydrogels are solid below the UCST and low-viscosity fluids above it [176].

Low-temperature-soluble cellulose hydrogels have achieved breakthroughs in the biomedical and chemical industries [177]. Their applications include tissue engineering, cell culture, drug release, fluorescence imaging, chromatography, industrial water treatment, catalytic synthesis, and smart textiles. Chen et al. [178] prepared a multifunctional CMC/polyacrylamide hydrogel that could respond to temperature and detect body movements and physiological conditions. Some studies have shown that collagen nanocellulose can be used as intestinal heat-sensitive hydrogel, which provides a new research strategy for organoids [179] (Fig. 6B(i-ii)).

3.3. Humidity-responsive cellulose hydrogels

Cellulose and its derivatives readily absorb moisture owing to interactions between their hydrophilic hydroxyl groups [180] and environmental water. This water-absorption behavior, along with structural changes induced by variations in hygroscopic gradients [181], facilitates humidity-responsiveness. In low-humidity environments, humidity sensors require homogeneous single materials to achieve effective moisture absorption [150]. Conversely, when environmental humidity fluctuates, hydrogels with asymmetric compositions or structures generate differential hygroscopic volume expansions, thereby facilitating moisture-driven responses [150].

Humidity-responsive cellulose hydrogels are extremely sensitive to changes in ambient humidity. In terms of flexible humidity sensor, it can monitor the environmental humidity in real time and accurately, and is widely used in weather monitoring, smart home and other fields. In the research and development of artificial muscle, the hydrogel can simulate muscle movement, providing a new material choice for the development of biomedical and robotics technology; In biomedical applications, such as wound dressings, it can automatically adjust the moisture content according to the moisture condition of the wound, helping to promote wound healing, showing unique application advantages. Yu et al. [151] developed a highly ionically conductive organic hydrogel enhanced by CNFs, which demonstrated excellent anti-freezing and anti-dehydration properties (Fig. 7A(i)) In this system, multiple hydrogen bonds formed between water molecules and binary polar solvents, as well as between polymer chains. This enabled the creation of a retractable humidity sensor. The results will help advance the field of stretchable and high-performance humidity-sensing technologies (Fig. 7A(ii)).

3.4. Pressure-responsive cellulose hydrogels

Pressure-responsive cellulose hydrogels adjust their volumes in response to applied pressure [153,182]. Chen et al. [153] developed a conductive hydrogel and proposed the concept of rough surface to detect cerebral hemorrhage, heartbeat, respiration and pulse in patients. This ability to enhance flexible pressure sensors offers novel perspectives and potential.

Wang et al. [183] developed a capacitive pressure sensor with a solvent-exchanged porous lignin-cellulose hydrogel (SPLCH) as the dielectric layer. The detection range and sensitivity of the sensor were adjusted by regulating the ratio of alkaline lignin (AL) to sodium lignosulfonate (SL). The compression modulus of SPLCH ranged from 310 to 320 kPa. The capacitive pressure sensor prepared in this way exhibited a sensitivity of 5.18 kPa^{-1} and 2.87 kPa^{-1}, a wide detection range (0–185.22 kPa), a short response and recovery time (25–50 ms), a low detection limit (1.875 Pa), and good loading stability (20,000 cycles). Ultimately, it was applied to detect scenarios such as respiration, swallowing, human motion signals, speech recognition, pedometers, and Morse code information transmission (Fig. 7B(i-iv)). Typically, these hydrogels swell under elevated water pressures and contract under reduced water pressures. In addition, studies have shown that the phase transition temperature of these materials is influenced by pressure changes [184]. Effectively, this means they respond to temperature. Consequently, pressure-responsive hydrogels can be used in drug-delivery systems similar to thermo-responsive hydrogels [152].

Research on the controlled-release behavior of pressure-responsive hydrogels is limited [185]. However, they may parallel the extracellular matrix surrounding biological tissues such as bone, muscle, and blood vessels, which exist in dynamic pressure environments. In these settings, the extracellular matrix functions as a reservoir for various growth factors [182]. Mechanical stimulation via pressure releases these growth factors into surrounding cells, thereby modulating various physiological processes.

Dang et al. [186] developed a self-healing and biocompatible pressure-responsive cellulose hydrogel using a one-pot method involving the free-radical polymerization of CMC, acrylamide, and acrylic acid. The resultant hydrogel exhibited pronounced and rapid responses to pressure, in addition to excellent mechanical properties and deformation resistance. Thus, it holds significant potential for use in physiological monitoring.

3.5. Electro-responsive cellulose hydrogels

Electro-responsive hydrogels typically consist of polyelectrolytes that shrink or swell in response to an electric field [187]. This behavior arises from the ion concentration gradient between the inside and outside of the hydrogel when subjected to an electric field, leading to variations in osmotic pressure and, consequently, changes in volume. Most electro-responsive cellulose hydrogels contain chemically bonded ionizing groups, which are crucial to their electro-responsive behavior [188].

Electro-responsive cellulose hydrogels contract or expand under the action of an electric field. Based on this characteristic, in the development of artificial skin, it can simulate the electrical and mechanical properties of skin, and realize the tactile sensing and self-healing functions [189]. In the field of soft robots and bionic prosthetics, as a core material, it can enable robots and prosthetics to respond quickly and accurately to external electrical signals, significantly improving their flexibility and functionality. Cellulose can yield electro-responsive hydrogels through chemical or physical crosslinking, copolymerization, or blending [190]. Yue et al. [191] used an efficient and straightforward free-radical polymerization method to synthesize self-healing hydrogels from modified CNCs, reduced graphene oxide, and acrylate monomers (Fig. 8A(i)) After cutting the hydrogel and allowing it to self-heal at 25 °C, its original mechanical properties and electrical conductivity were restored within 12 s. Even after five cutting and self-healing cycles, the cutting growth rate only decreased from 95.0 % to 94.3 %. This electrically conductive hydrogel with room temperature self-healing leverages the advantages of supramolecular chemistry and polymer nanoscience, making it suitable for applications in artificial skin, soft robotics, bionic prosthetics, and energy storage devices (Fig. 8A(ii)).

3.6. Photo-responsive cellulose hydrogels

Photo-responsive cellulose hydrogels undergo rapid chemical or physical transformations in response to light, including UV, visible, and infrared (IR) wavelengths [192,193]. Typically, this response is reversible; that is, when the light source is removed, the hydrogel reverts to its initial state. Although research on photosensitive hydrogels is still in the preliminary stage compared to that on other stimuli-responsive hydrogels, they have significant application potential owing to their safety, cleanliness, and ease of use based on the controllability of light sources.

Photo-responsive cellulose hydrogels undergo rapid chemical or physical changes under light conditions, and this change is usually reversible. In the field of electronic skin and smart devices, it can sense and respond to external stimuli in real time, effectively improving the intelligence level of devices; In the field of drug release, accurate drug

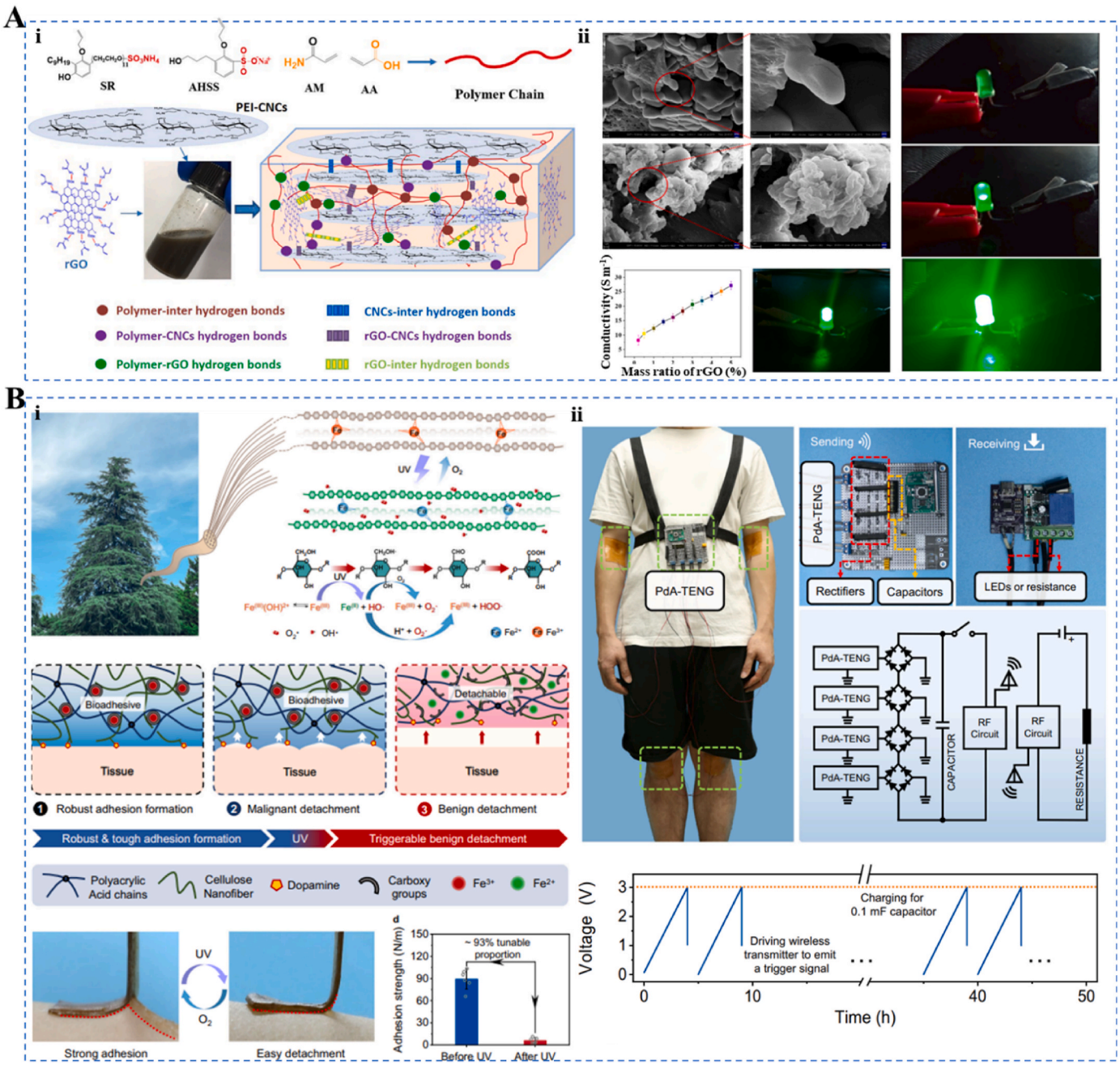

Fig. 8. Construction of electro-responsive and photo-driven nanocellulose hydrogels. (A) Preparation and characterization of conductive cellulose nano-hydrogels: **(i)** Hydrogels were prepared by free radical polymerization of six main forms of hydrogen; **(ii)** Comparison of scanning electron microscopy, electrical conductivity and brightness during hydrogel self-healing. This figure is reproduced with minor modifications from Ref. [191], Copyright © 2021 European Polymer Journal. published by Elsevier Ltd. **(B)** Preparation and characterization of light-driven and conductive nano-cellulosic hydrogels: **(i)** Construction of light-driven nano-cellulosic/Fe^{3+} based dynamic hydrogels; **(ii)** Motion detection system construction diagram. This figure is reproduced with minor modifications from Ref. [194], Copyright © 2024 Nature communications. published by Springer Nature.

release can be achieved through precise control of illumination, and the accuracy of drug treatment can be improved. In terms of self-healing materials, the use of its photo-response characteristics can realize the self-healing of materials, extend the service life of materials, and show great application potential in many fields. Zhang et al. [194] prepared a multi-flow form of cellulose nano-supramolecular hydrogel (Fig. 8B(i)). The coordination between Fe ions and polymer chains produces an adhesive detachable friction nanogenerator that can acquire real-time, self-powered monitoring and wireless whole-body motion signals, opening up possibilities for diverse potential applications in electronic skin and smart devices (Fig. 8B(ii)). Kim et al. [195] developed a composite multifunctional hydrogel that grafted CMC, azobenzene, and β-cyclodextrin dimer to form a host–guest complex, which is photo-reactive to light at 365 nm and 450 nm, enabling the hydrogel to have self-healing and controlled drug-release properties.

3.7. *Magnetic-responsive cellulose hydrogels*

Magnetic field response Cellulose hydrogels are magnetically responsive by adding magnetic particles. In the drug delivery system, with the help of the external magnetic field, it can realize the targeted transportation and precise release of drugs, which greatly improves the

therapeutic effect of drugs. In the field of biomedicine, it can be applied to cell separation, magnetic hyperthermia and other aspects, providing innovative methods and means for disease treatment and biological research, and has important clinical application and scientific research value.

Magnetic particles are incorporated into the hydrogel matrix to give the cellulose hydrogel a magnetic response, which exhibits expansion under the action of an external magnetic field, and these particles produce local temperature increases within the hydrogel, resulting in volume changes [196]. Three methods are commonly used to fabricate magnetically responsive hydrogels: coating a hydrogel matrix with magnetic particles; encapsulating magnetic particles within a hydrogel matrix; interspersing layers of hydrogel with magnetic particles.

Lin et al. [197] developed a magnetically responsive hydrogel drug-delivery system featuring an stimulus-responsive release mechanism. In this system, β-cyclodextrin was cross-linked with a cellulose hydrogel via epichlorohydrin to establish a network structure, which acted as a loading "container" for the drug. Fe_3O_4 nanoparticles were uniformly incorporated into the cellulose backbone, thereby enhancing the magnetic response of the hydrogel.

3.8. Chemically responsive cellulose hydrogels

Nanocellulose hydrogels, with their unique porous structures, hydrophilicity, biocompatibility, biodegradability, and high specific surface areas, are well-suited for sensitive analyte detection when combined with other substances. Applications include healthcare [198], diagnostics [199], environmental monitoring [200], and food quality control [201]. Hai et al. [202] developed a nanocellulose hydrogel featuring a reversible ClO^-/SCN^- switch for the cultivation and release of multicellular cancer spheroids. The coordination crosslinking structure between Eu^{3+} and 2,6-pyridine dicarboxylic acid in the nanocellulose matrix was disrupted in the presence of ClO^- owing to coordination between ClO^- and Eu^{3+}, leading to fluorescence quenching. Upon the introduction of SCN^-, the filamentous hydrogel exhibiting red fluorescence was regenerated, allowing for full reversibility of the gel network by modulating the ClO^- and SCN^- concentrations [203]. Leveraging these response characteristics facilitated real-time monitoring of tumor growth within the nanocellulose hydrogel, while enabling the controlled release of the tumor cells as needed. This approach holds significant potential for advancing cancer biology research, metastasis studies, and invasion models [204].

3.9. Multi-stimuli-responsive cellulose hydrogels

In addition to stimulus-responsive hydrogels that respond to a single stimulus, researchers have developed cellulose hydrogels that respond to two or more stimuli, including combinations such as acids and UV light, magnetic fields and reducing conditions, pH levels and glucose concentrations, pH variations and redox reactions, and even combinations of acids, UV light, and pH changes. This versatility allows multi-responsive hydrogels to meet the diverse requirements of specific applications and environments. Multi-responsive cellulose hydrogels are typically prepared by copolymerization or polymer modification to create asymmetric materials or structures [205].

Multi-stimulus responsive cellulose hydrogels can respond to many different types of stimuli simultaneously. In the field of wearable electronic devices, it can adapt to complex environmental changes and realize multi-functional sensing; In terms of sustainable manufacturing, it can be used to prepare environmentally friendly multi-functional anti-counterfeiting materials to promote green development; In the drug delivery system, it can meet the demand of drug release under complex environment and improve the therapeutic effect. In tissue engineering, it provides more refined and precise environmental regulation for tissue repair and regeneration, showing significant application potential in many frontier fields. Dang et al. [186] used a one-pot method to prepare a thermo-pressure-responsive conductive hydrogel, a hydrogel with self-healing and viscosity (Fig. 9A(i)) It exhibits different states at different temperatures, and has self-healing ability and excellent mechanical ability at 80 °C (Fig. 9A(ii-iii)). It can promote the development of wearable electronic devices and sustainable manufacturing of environmental protection multi-functional anti-counterfeiting materials (Fig. 9A(iv)).

Bagheri et al. [206] prepared a multi-responsive hydrogel using CMC and polyaniline as raw materials. This biodegradable and antibacterial hydrogel reacted quickly to changes in voltage and environmental pH. Furthermore, it effectively removed toxins from wastewater and decomposed microorganisms in the soil, achieving a degradation rate of up to 91.7 %. Dang et al. constructed a temperature- and pressure-responsive cellulose hydrogel for use in anti-counterfeiting materials and flexible electronic sensors [186]. Yuan et al. constructed a temperature and CO_2 stimulus-responsive cellulose-based hydrogel as a drug delivery system for DOX [207]. Wang et al. [208] prepared CNC-based pressure, temperature and electro-responsive hydrogels through a one-pot method, which provides multiple development possibilities for the sensing function of wearable electronic devices (Fig. 9B (i)). The change of resistance of gel in water at different temperature. Hydrogels are highly stretchable, pressure-responsive and electrically conductive under pressure (Fig. 9B(ii-iii)). This work proposes a strategy for manufacturing conductive hydrogels with excellent properties, enabling their multifunctional sensing applications in wearable electronic devices (Fig. 9B(iv)).

4. Utilization of cellulose stimulus-responsive hydrogels

4.1. Applications for tissue engineering

When human tissue is injured, its ability to regenerate is minimal. Tissue engineering has become one of the most promising medical solutions, especially for the healing of chronic wounds. In recent years, nanocellulose hydrogels have been widely used in the field of tissue engineering owing to their unique 3D porous structure, excellent mechanical properties, and good biocompatibility [209]. Lan et al. [210] constructed a meniscal hydrogel (TCNF/ALG) by combining human meniscal fibrochondrocytes, TEMPO-oxidized CNF, and alginate precursors to construct the hydrogel, which had a comparable compression modulus with the collagen-based construct. When used as scaffolds, hydrogels can be used for biological applications such as arthroscopy, vascular stents, and skin grafts. Hydrogels simulate extracellular matrix to provide an environment for cell growth, proliferation, and differentiation for 3D printing [211]. 3D bioprinting is a process that uses biocompatible "inks" to create 3D entities of specific shapes from digital models [212], and a variety of natural biopolymer hydrogels (gelatin, cellulose, chitosan, and SA) have been widely adopted as tissue engineering scaffold materials. Nanocellulose materials have great potential for 3D bioprinting owing to their printability, shear-thinning behavior, and excellent biocompatibility. Abouzeid et al. [213] prepared 3D printed scaffolds using Ca^{2+} cross-linked CNF/SA hydrogel. The results demonstrated that compared with 100 % SA and 100 % CNF, the hydrogels prepared at the optimal ratio of 50 % CNF, 50 % SA, and 3 % calcium chloride exhibited better mechanical properties under 50 % compression strain. In addition, scaffolds of different shapes were printed based on the optimal hydrogel ratio, revealing the significant potential of CNFs/SA 3D printed scaffolds for bone tissue engineering applications.

4.1.1. Skin tissue engineering

The skin acts as a protective barrier against environmental threats such as mechanical damage, radiation, chemicals, bacteria, and viruses [214]. When the skin is damaged, changes in cellular functionality and the pH of the microenvironment occur. Wound dressings are a simple yet effective approach for managing skin injuries [206]. Notably, the advent

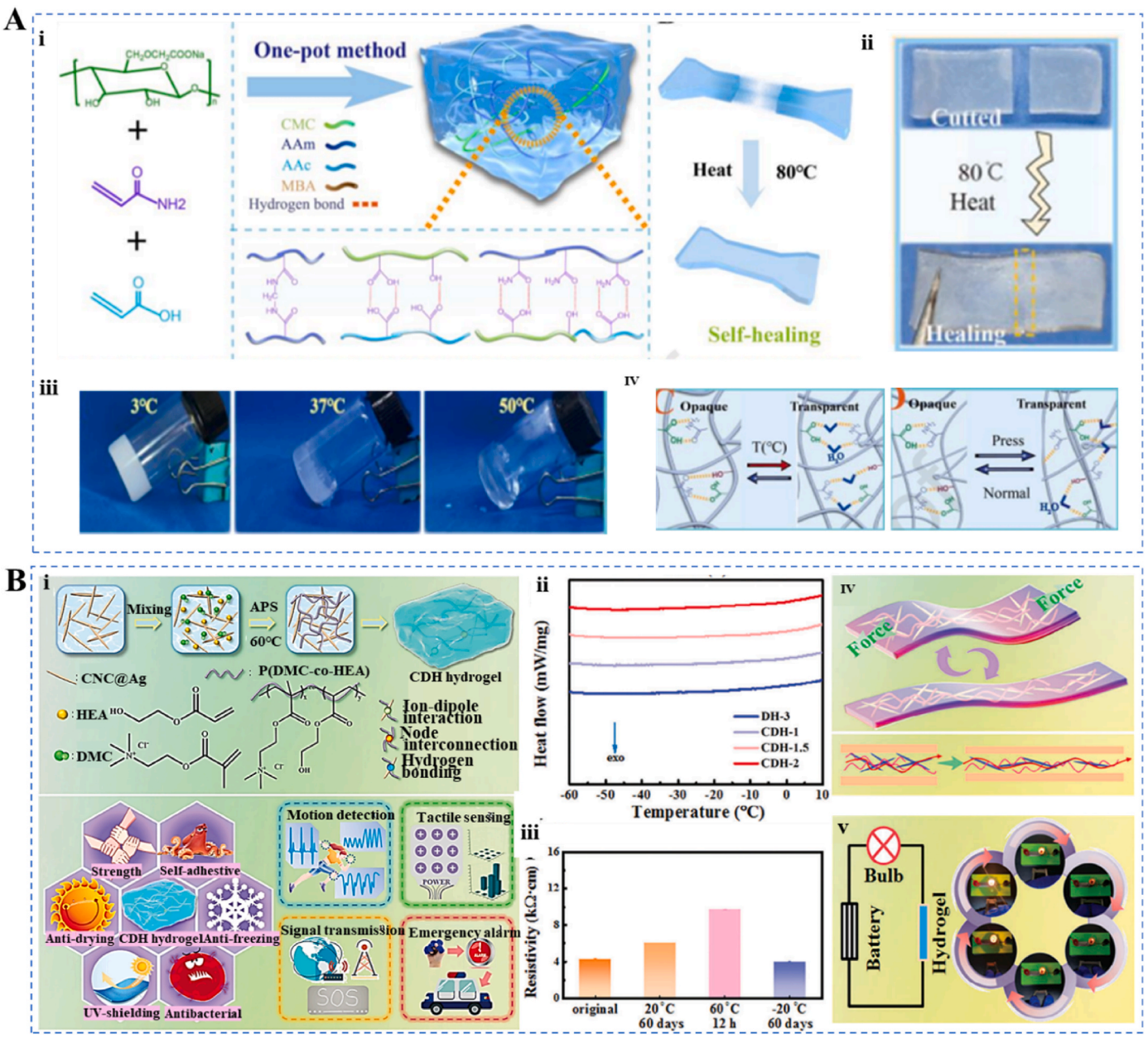

Fig. 9. Study on multiple stimulus-responsive cellulose-based hydrogels. (A) Preparation of temperature - and pressure-responsive hydrogels using CMC, acrylamide and acrylic acid: **(i)** Schematic diagram of hydrogel preparation; **(ii)** Healing process of hydrogels; **(iii)** Changes of hydrogels at different temperatures; **(iv)** The mechanism of hydrogel temperature response and pressure response. This figure is reproduced with minor modifications from Ref. [186], Copyright © 2024 Biosensors & bioelectronics. published by Elsevier. **(B)** Preparation of temperature- and CO_2-responsive ethyl cellulose skeleton hydrogels: **(i)** Diagram of hydrogel synthesis; **(ii)** TEM images at different temperatures and CO_2 durations; **(iii)** The DMAEMA at different concentrations is temperature-dependent. This figure is reproduced with minor modifications from Ref. [208], Copyright © 2016 Carbohydrate polymers. published by Elsevier Ltd.

of stimulus-responsive materials has greatly enhanced skin healing, regeneration, and monitoring. These dressings can swell to absorb discharge, while maintaining moisture and pH levels over time. Controlling the thickness and density of the hydrogel is essential for meeting the requirements for wound healing [215]. Given the high incidence of infections, these dressings should also have antibacterial properties to minimize bacterial colonization. Nanocellulose hydrogels are frequently combined with other materials and technologies to create highly efficient stents and bioactive wound dressings [216]. These hydrogels are loaded with antibacterial components (such as Ag, ZnO, chitosan, and tannic acid) [88,217,218] or antibiotics [219] to achieve sterilization.

Innovative stimulus-responsive hydrogels are increasingly used in wound dressings with real-time monitoring capabilities. A reusable and wearable paper-based smart has been developed that can simultaneously assess pH and uric acid levels at the wound site, while transmitting real-time data to medical personnel via radio technology [220]. In addition, woven cellulose lyocell fabrics coated with a thin layer of copper through electroless copper plating have been developed for skin temperature monitoring [221]. Biomimetic actuators have significant potential for the treatment of soft-tissue injuries.

Liu et al. [222] combined polydopamine containing tetracycline hydrochloride with carboxylated CNFs to form hydrogels via Ca^{2+} crosslinking. Under low-pH conditions or near-infrared (NIR) radiation, the hydrogels released tetracycline hydrochloride on demand, promoting skin regeneration. In another study, Huang et al. [88] prepared injectable hydrogels using dynamic Schiff base cross-linked

water-soluble CMC and dialdehyde nanocellulose crystals, which were effective in promoting wound healing. In another study, white light and NIR dual response CNF cellulose hydrogels were constructed for skin wound treatment [223]. Shi et al. [223] developed a white light and NIR dual response CNF hydrogel, which has the effect of hemostasis, antibacterial and promoting wound healing (Fig. 10A). Hydrogels exhibit different states at different temperatures (Fig. 10B). NIR and white light irradiation significantly promoted wound healing in mice, and had broad prospects in hemostasis and wound healing (Fig. 10C).

Many studies have found that bacterial nanocellulose significantly enhances wound healing. Chinga-Carrasco and Syverud [224] reported the antibacterial effects of hydrogels containing CMC fibers. In addition, pH-responsive cellulose hydrogels exhibit controlled drug release during wound treatment, further promoting the healing process.

However, despite these promising outcomes, comprehensive information on how cellulose hydrogels interact within the human body remains limited. This raises concerns, particularly given the increasing emergence of bacterial resistance to antibiotics. Therefore, continuous validation of the antibacterial agents in cellulose hydrogels is required before they can receive medical certification.

4.1.2. *Bone tissue engineering*

Small bone defects can induce self-regeneration and repair within the body; however, defects that exceed a critical size cannot cause

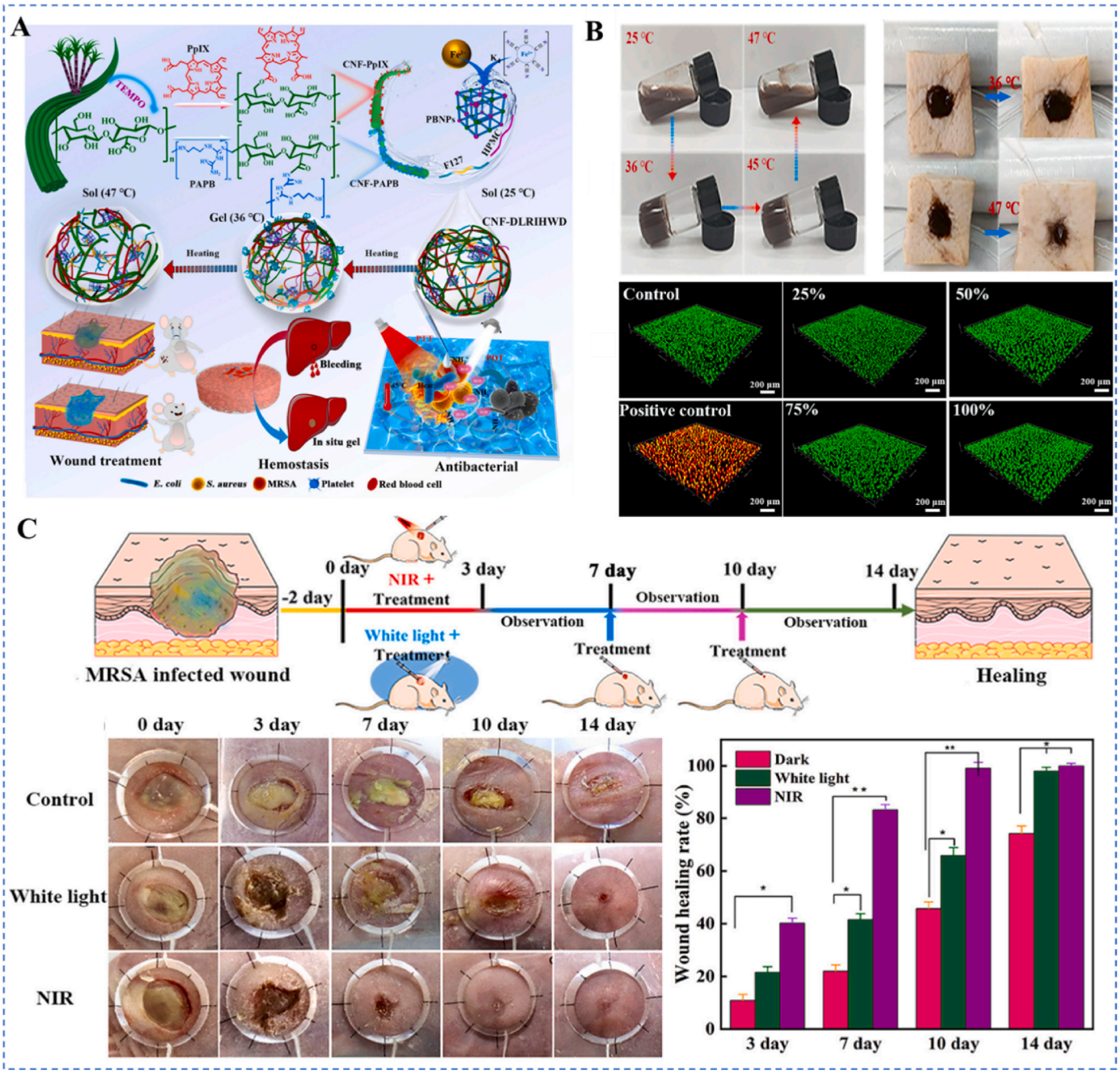

Fig. 10. Construction of nanocellulose hydrogel with white light and NIR response based on CNF. (A) Schematic illustration of the construction mechanism for hydrogel-based systems; **(B)** Evaluation of hydrogel properties at varying temperatures and biocompatibility assessment in L929 cells; **(C)** An animal wound model was established and treated with the hydrogel, demonstrating significant wound healing under NIR treatment. This figure is reproduced with minor modifications from Ref. [223], Copyright © 2022 Carbohydrate polymers. published by Elsevier Ltd.

spontaneous regeneration [225]. Consequently, artificial interventions are often required to facilitate bone healing and repair [226]. Bone fractures can naturally heal through a sophisticated process involving immune system activation, cellular migration, differentiation, and apoptosis. stimulus-responsive cellulose materials, including stimulus-responsive cellulose hydrogels, have extensive applicability for the repair and regeneration of bone tissue with no adverse effects [227].

Cellulose exhibits excellent mechanical, physical, and chemical properties, including high stability under acidic conditions, favorable chiral characteristics, substantial tensile strength, commendable elastic modulus, low density or lightweight nature, remarkable biodegradability, abundant hydroxyl functional groups on its surface for potential chemical modification, and enhanced wettability [41]. Li et al. [228] demonstrated that titanium dioxide nanotubes encapsulated with simvastatin within a thermo-sensitive chitosan-glycerin-hydroxypropyl methylcellulose hydrogel represent a promising orthopedic implant material exhibiting significant antibacterial activity in vivo. Furthermore, this hydrogel remains in a sol state at normal body temperature (37 °C), facilitating the controlled release of simvastatin and promoting the differentiation of MC3T3-E1 osteoblastic cells.

CNFs have also been integrated into polyurethane matrices within thermoplastic elastomers to create nanocomposites with shape-memory properties and rapid reactivity. These materials are suitable for drug-delivery systems, implants, and shape-memory scaffolds. Furthermore, they can serve as scaffolds for the reconstruction and repair of bone defects [229]. The introduction of four-dimensional printing has accelerated the precise fabrication of structures that mimic target tissues, facilitating cell migration and proliferation, while promoting tissue remodeling and vascularization.

4.1.3. Cardiac tissue

Cardiac tissue engineering is dedicated to solving the problem of myocardial damage repair. Stimulus-responsive cellulose hydrogels have become a research hotspot due to their unique advantages. It can simulate the microenvironment of the heart, provide support for cells, promote the regeneration of cardiac tissue, and has broad prospects in the treatment of heart diseases.

Tohidi et al. [230] prepared the collagin-hyaluronic acid composite hydrogel, by adding bacterial cellulose and gold nanoparticles, has the properties of electrical conductivity, injectability and self-healing. Experiments show that its elastic modulus is significantly increased, the electrical conductivity reaches approximately 0.09S/m, and it can promote the beating of human stem cells, providing a multifunctional material platform for cardiac tissue engineering. Wang et al. [231] prepared the micropatterned hydrogel is composed of highly ordered cellulose nanocrystals and methacrylate gelatin. Experiments show that this hydrogel can induce the alignment of cardiomyocytes, monitor the cell state in real time through color changes, and obvious wavelength changes can be observed under drug treatment and electrical stimulation, providing a visualization means for cardiomyocyte research. Yeh et al. [232] prepared human amniotic fluid stem cell fragment using a thermally responsive methylcellulose hydrogel system. In animal experiments, the cardiac function of immunosuppressed rats transplanted with this segment was significantly improved, proving its important value in cardiac repair.

Stimulus-responsive cellulose hydrogels have shown great potential in cardiac tissue engineering, but still face challenges. If the mechanical properties of the CL-HA composite hydrogel need to be optimized to better match the myocardium, more in vivo and in vitro experiments are required to evaluate its functions. The preparation process and detection sensitivity of micro-pattern hydrogels need to be further improved. The clinical application of hAFSCs fragment fragments still needs to solve problems such as immune rejection. In the future, with the deepening of research, stimulus-responsive cellulose hydrogels are expected to bring more effective treatment options to cardiac tissue engineering.

4.1.4. Neural tissue

Stimulation-responsive cellulose hydrogels have demonstrated multiple advantages in neural tissue engineering. Through mechanisms such as guiding neuron growth, promoting cell survival and differentiation, responding to stimuli to promote nerve regeneration, and inhibiting scar formation, they provide effective solutions for neural tissue repair. In the future, with the in-depth research on hydrogels, it is expected to further optimize their performance and promote the clinical application of neural tissue engineering. Zhang et al. [233] prepared S/OHEC/r-GO/asiaticoside liposome hydrogel. After adding rGO and applying electrical stimulation, it could promote the differentiation of PC12 cells. Moreover, asiaticoside released by the hydrogel could inhibit the growth of fibroblasts and the secretion of collagen, and reduce scar formation. These studies show that stimulus-responsive cellulose hydrogels in neural tissue engineering can guide the growth of neurons, promote cell survival and differentiation, respond to stimuli to promote nerve regeneration and inhibit scarring, and have great application potential.

4.1.5. Alternative approaches in tissue engineering

A new avenue of research explores the use of stimuli-responsive cellulose hydrogels in various tissue regeneration applications, including muscle, nerve, cartilage, and cardiac tissue repair. Revascularization is vital in the treatment of cardiovascular diseases. Tubular bacterial cellulose is a promising biomaterial for small-caliber vascular transplantation owing to its nanofiber network structure, water retention ability, and plasticity [234]. However, two primary requirements must be met before clinical implantation for blood vessel transplantation: first, the hydrogel tubes must promote healthy host cell proliferation to enable nutrient exchange, and second, they must remain unobstructed to prevent thrombus formation.

In a recent study, Kong et al. [235] developed a highly anisotropic, robust, and conductive wood CNF/polyacrylamide hydrogel inspired by the multistage architecture and hierarchical organization of muscle tissue. This biomimetic hydrogel combines the exceptional tensile strength of natural wood with the flexibility and high water content of hydrogels, achieving excellent mechanical strength, flexibility, and ionic conductivity. Such multifunctional nanocellulose hydrogels are poised to guide the future development of tissue engineering materials.

The scaffold-based culture system facilitates the migration and attachment of cells within the pores of the scaffold, with cellular growth and division subsequently filling these spaces, resulting in 3D cultured cell structures [179]. This approach represents a predominant method for 3D cell culture today, particularly in tissue engineering and related disciplines. By emulating the extracellular matrix, natural hydrogel scaffolds offer a spatial microenvironment conducive to cell proliferation, differentiation, migration, and interaction, establishing them as promising materials for scaffolding applications [236].

Notably, cell viability, metabolic activity, and key cellular marker expression levels were maintained throughout this process. The stiffness of the collagen/nanocellulose hydrogels played a critical role in organoid formation and development. CNC hydrogels offer an economical, thermo-responsive, and sustainable matrix for organoid growth.

Li et al. [237] reported a reactive oxygen species-responsive PVA/-cellulose hydrogel system that could deliver basic fibroblast growth factors directly to the myocardial infarction target site. This cellulose stimulus-responsive hydrogel system shows promise for myocardial regeneration owing to its enhanced angiogenic potential and ability to restore cardiac function.

4.2. Applications in drug delivery

Cellulose hydrogels are extensively used in drug-delivery systems because of their unique ability to expand, influencing their shape, stability, and volume [238]. The 3D cross-linked networks of cellulose hydrogels allow them to incorporate various stimuli-responsive groups and structures, along with abundant water [239]. These properties

endow cellulose hydrogels with environmental responsiveness, ionic conductivity, stretchability, softness, and biocompatibility, which are crucial for drug delivery and release systems. Various stimulus-responsive cellulose hydrogels have been used as stimuli-responsive carriers for anti-inflammatory, antibacterial, and anticancer drugs.

4.2.1. For oral administration

Given the significant variation in pH levels within the human digestive tract, oral formulations are the predominant dosage forms used in hydrogel pharmaceutical preparations. Hydrogels can affect changes in gastrointestinal pH owing to their intentional swelling capacity, thus promoting slow or controlled drug release. In the acidic environment of the stomach, hydrogels remain in their original state without swelling, effectively encapsulating and protecting the drugs contained within them. Upon reaching the neutral conditions of the intestine, an increase in pH triggers hydrogel swelling and subsequent drug release, allowing for absorption within the intestinal lining and achieving therapeutic effects. Therefore, for pharmaceuticals that exhibit instability under acidic gastric conditions, pH-sensitive hydrogels can be strategically used as delivery vehicles. For instance, Nakamura et al. [240] developed a modified polyethylene glycol graft copolymer of methacrylic acid (PEG-g-PMAA) hydrogel specifically designed for oral insulin administration. Animal studies have demonstrated that following oral delivery via this gel formulation, insulin is absorbed through the small intestine, resulting in hypoglycemic outcomes. Furthermore, hydrogels can also serve as carriers for orally administered hydrophobic drugs; for example, Caldorera-Moore et al. [241] synthesized P(AA-co-MMA) hydrogels loaded with fluorescein, where incorporating a hydrophobic monomer (MMA) enhanced fluorescein's loading capacity.

The application of stimulus-responsive hydrogels to improve the bioavailability of oral administration has become a research hotspot. A heat-sensitive hydrogel was prepared by using methylcellulose nanoemulsion, which can achieve rapid oral drug release [242]. Chen et al. [242] developed a thermos-responsive nanoemulsion gel based on methylcellulose for the preparation of oral dosage forms. When the temperature is high, the nano emulsion condenses, and becomes a flowing emulsion with the decrease of temperature, and the distribution is uniform. (Fig. 11A(i-ii)) Different oral dosage forms can be prepared using multifunctional thermal processing methods, and drugs with low

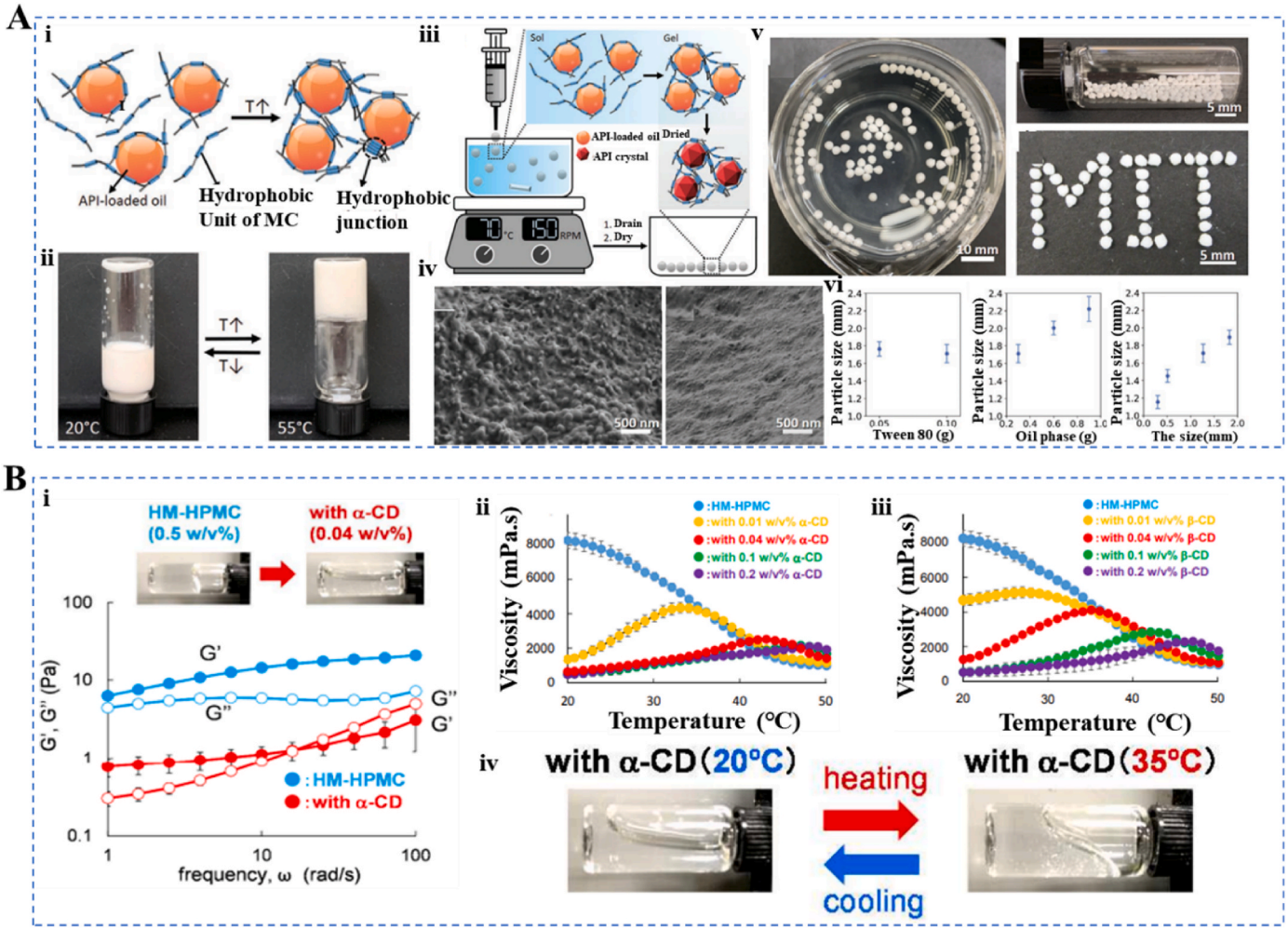

Fig. 11. Investigation of stimulus-responsive Hydrogels for Oral and Ocular Applications. (A) Examination of Thermo responsive Methylcellulose Hydrogels for Oral Drug Delivery. **(i)** Schematic illustration of hydrogel formation mechanism; **(ii)** State transitions of the hydrogel at 20 °C and 55 °C; **(iii)** Diagram of particle preparation via thermal gelation method; **(iv)** Scanning electron microscopy (SEM) images of particles; **(v)** Optical micrographs of particles; **(vi)** Correlation between particle characteristics and process parameters. This figure is reproduced with minor modifications from Ref. [242], Copyright © 2021 Advanced materials (Deerfield Beach, Fla). published by Wiley-Blackwell. **(B)** Study and Application of Thermo responsive Hydroxypropyl Methylcellulose Hydrogels for Ophthalmic Medications. **(i)** Rheological profiles of hydrogels with and without cyclodextrin addition; **(ii-iii)** Viscosity variations of hydrogels with different compositions at varying temperatures; **(iv)** Changes in hydrogel state in water at 20 °C and 35 °C. This figure is reproduced with minor modifications from Ref. [247], Copyright © 2017 Molecular pharmaceutics. published by American Chemical Society.

solubility can be released quickly through rapidly degradable methylcellulose. (Fig. 11A(iii-vi))

4.2.2. For nasal administration

Oral drug delivery can result in suboptimal bioavailability. In such cases, nasal administration is a more appealing alternative to invasive parenteral routes [243]. Nasal administration has several advantages because of the extensive surface area of the nasal cavity, the rich vascular network in the nasal submucosa, and the high permeability and blood flow through the nasal epithelium, all of which contribute to rapid drug absorption. In addition, because the absorbed drugs enter the bloodstream directly, they bypass first-pass metabolism in the liver. Smart polymers can modulate the drug-release profiles of nasally administered drugs, enhance drug penetration, and protect drugs from mucosal enzymes.

Cellulose-hydrogels for intranasal drug delivery have been synthesized from various cellulose derivatives, including CMC, hydroxypropyl methylcellulose, methylcellulose, and ethyl cellulose [244]. These cellulose derivatives promote sustained drug release owing to their high viscosity when swollen in the nasal cavity. Furthermore, their excellent adhesion properties enhance intranasal absorption. Cellulose hydrogels have been extensively used for nasal mucosa absorption, increasing the potency and bioavailability of many hydrophobic drugs [186].

Among cellulose derivatives, CMC is a favored formulation for the nasal delivery of apomorphine, which regulates motor responses in Parkinson's disease. It demonstrates sustained nasal release, significantly outperforming starch-based formulations [49]. After intranasal administration, insulin-loaded cellulose thermogels markedly improved insulin retention and absorption, reducing blood glucose levels to approximately 40–50 % of baseline concentrations.

4.2.3. For ocular administration

Ocular delivery is mainly used to treat local eye diseases [245]. However, the drops are quickly cleared from the eye owing to tear discharge and blinking. In addition, the eye has low corneal permeability as an inherent protective mechanism. This results in a short drug retention time and limited absorption, which often reduces therapeutic effectiveness, so extending the contact time of the drug with the cornea can significantly improve the treatment of eye diseases. To this end, the researchers investigated the use of viscosifiers (such as cellulose derivatives), bonding polymers (such as polysaccharides), and *in situ* gel systems in delivering ocular drugs at optimal concentrations.

Preparation of pH-responsive hydrogels with SA and methylcellulose for continuous delivery of ophthalmic drugs. The hydrogel was converted from solution to gel at a pH of 4.7–7.4 to achieve sustained delivery of sparfloxacin, which delivered well in corneal penetration tests performed in goat eyes [246]. Another study prepared a heat-responsive hydrogel with α-cyclodextrin and hydroxypropyl methylcellulose, which showed a reversible sol-gel transition, resulting in rapid gelation of the ocular surface [247] and sustained absorption of diclofenac sodium in the eye. Iohara et al. [247] developed a thermos-responsive hydrogel based on hydrophobic modification. Hydrogels formed by different proportions of cyclodextrin and hydroxypropyl methyl cellulose have different stress forces (Fig. 11B(i-iii)) and exhibit reversible transformation at 20–30 °C. The fluid flow of diclofenac was strong at room temperature and low at physiological temperature, which significantly improved the eye absorption of diclofenac (Fig. 11B(iv)).

4.2.4. For digestive system administration

4.2.4.1. Stomach-specific administration. Insulin is traditionally administered via subcutaneous injections; however, repeated injections over time can reduce patient adherence. To address this issue and enhance patient comfort, pH-responsive hydrogels comprising acrylic-grafted CMCs and polyacrylic acid were developed for oral insulin delivery [206]. The distinct swelling behavior of these hydrogels was pH-dependent, which in turn affected their enzymatic degradation. Specifically, enzymatic degradation was inhibited in artificial gastric fluid containing pepsin (pH 1.2), whereas it was accelerated in artificial intestinal fluid supplemented with pancreatic enzymes (pH 6.8). Furthermore, insulin release increased under conditions that mimicked the small intestine. After 2 h of artificial gastric fluid, less than 10 % of the encapsulated insulin was released.

A dual-response drug-delivery system was prepared from methylcellulose and alginate [248]. The hydrogel exhibited both pH and thermo-responsiveness. Drugs were easily incorporated into the mixed polymer solution at ambient temperature, and the system transitioned to a gel upon exposure to elevated temperatures within the body. This system relied on the thermal gelation properties of methylcellulose and the sensitivity of alginate to low-pH environments. Consequently, bovine serum albumin had a lower release rate in acidic simulated gastric fluid than in neutral simulated intestinal fluid.

4.2.4.2. Colon-specific administration. Intestinal immune homeostasis and microbiome composition are pivotal in the pathogenesis and progression of inflammatory bowel disease (IBD). Treating IBD is challenging because of the significant side effects and limited therapeutic efficacy of first-line medications. Given the high concentration of polysaccharide enzymes in the colon, hydrogels targeting this region are often designed using polysaccharides or polyesters. Drug release from these hydrogels is typically triggered by pH changes or enzymatic degradation [249].

To achieve targeted drug release, Asadi et al. [250] used Eudragit® FS100 and polylactic acid to design and fabricate a 3D-printed tablet shell filled with 100 μL of an *N*-acetylglucosamine-loaded methylcellulose hydrogel. The researchers investigated how the polymer mixing ratio and methylcellulose concentration affected the physical, thermal, and material properties of the different tablet components, with a focus on their influence on the in vitro drug-release kinetics. Hydrogels with Eudragit® FS100/polylactic acid (80/20), filled with n-acetylglucosamine and methylcellulose, exhibited the best results in terms of printability, machinability, and drug-release kinetics, while maintaining cytocompatibility. The development of these tablets represents a significant milestone toward personalized medicine, enabling tailored delivery of various drug doses and combinations directly to sites of inflammation (Fig. 12A(i-ii))

4.2.5. For transdermal administration

Cutaneous and transdermal drug delivery has become an effective alternative to traditional drug-delivery routes. Dermal delivery targets deeper skin layers, with the drug penetrating the outermost layer of the skin (the stratum corneum), whereas transdermal delivery facilitates drug transport to the dermis before entering the systemic circulation. These methods offer several advantages, including sustained release at a consistent rate, rapid cessation by simply removing the device, suitability for self-administration, and avoidance of first-pass hepatic metabolism and gastrointestinal incompatibilities [251].

Kwon et al. [252] prepared a pH-sensitive hydroxyethyl cellulose/-hyaluronic acid hydrogel to support the active compound isoquinoline and validated its potential for treating skin lesions associated with pH imbalance. Hyaluronic acid is highly compatible with skin tissues and contains pH-responsive functional groups, whereas hydroxyethyl cellulose serves as a scaffold for constructing hydrogels with varying mass ratios of hyaluronic acid. The hydrogels were synthesized through chemical crosslinking and characterized using scanning electron microscopy. The swelling behavior and polymer ratios were examined at pH 1–13. The hydrogel with a 1:3 mass ratio of hydroxyethyl cellulose to hyaluronic acid exhibited optimal rheological properties and bonding characteristics and was subsequently used to investigate the relationship between pH and drug-release efficiency. The isoliquiritin release

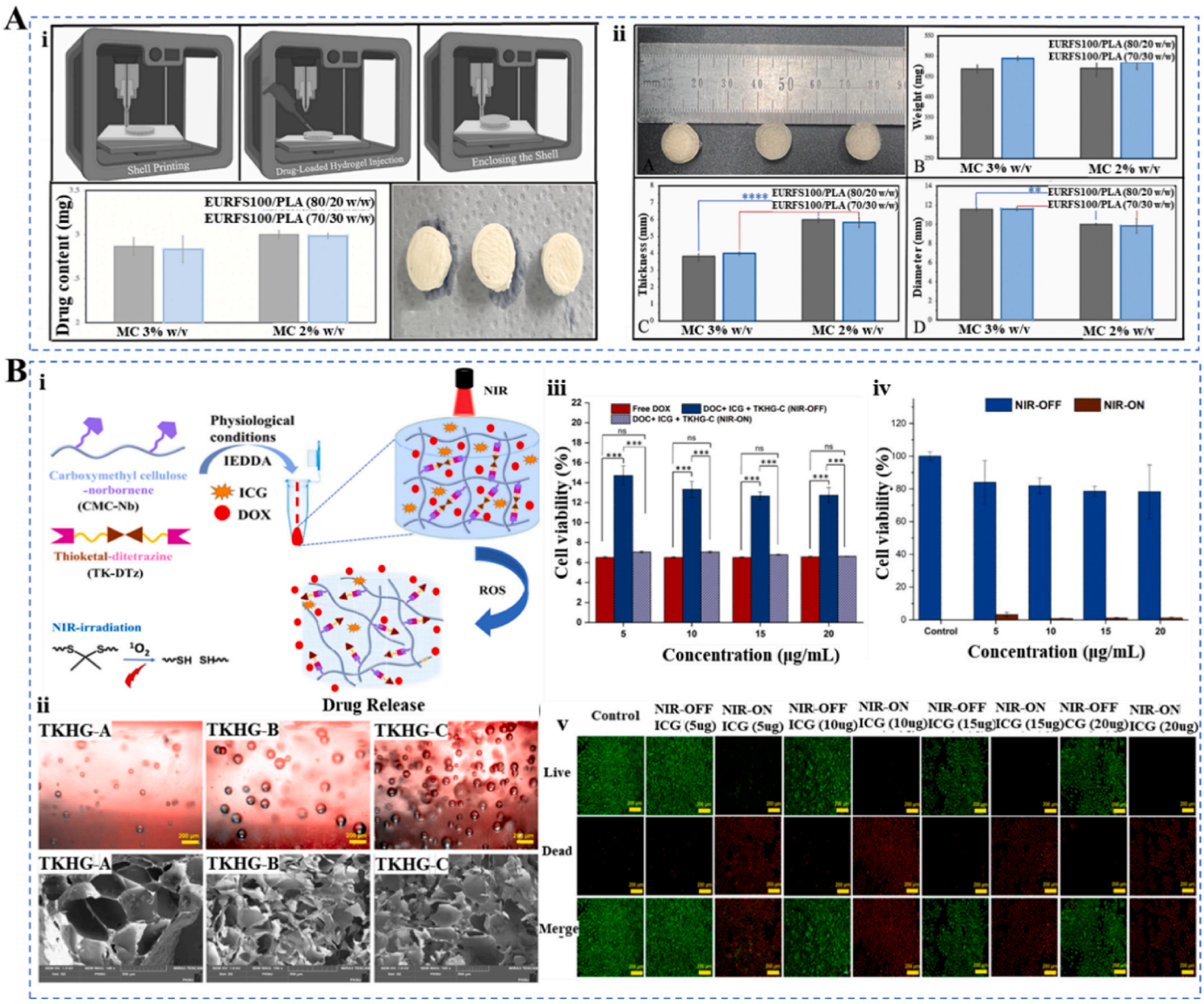

Fig. 12. Application of Cellulose stimulus-responsive Hydrogels in Drug Delivery. (A) 3D-Printed pH and NIR-Responsive Carboxymethyl Cellulose Hydrogels for Enhanced Oral Drug Delivery. **(i)** The process of 3D printing preparation of tablets was shown. The drug loading of N-acetylglucosamine (GlcNAc) in different samples remained stable without significant difference. In addition, after the in vitro release test, the structural integrity of the 3D printed tablets was maintained without significant deformation; **(ii)** The mechanical properties and physical stability of tablets under different conditions were investigated. This figure is reproduced with minor modifications from Ref. [250], Copyright © 2023 International journal of pharmaceutics. published by Elsevier. **(B)** ROS-Responsive Hydrogels Based on Carboxymethyl Cellulose with NIR Sensitivity. **(i)** Preparation Schematic; **(ii)** Scanning Electron Microscopy and Optical Microscopy Imaging; **(iii)** Anti-Cancer Efficacy; **(iv)** Cell Viability Under NIR Light Irradiation; **(v)** Photothermal Effect Verified by Live Cell Staining. This figure is reproduced with minor modifications from Ref. [258], Copyright © 2024 International journal of pharmaceutics. published by Elsevier.

efficiency exceeded 70% at pH7. This pH responsiveness also provided antibacterial activity against *Propionibacterium acnes* proliferation at pH7. In addition, the hydrogel demonstrated excellent skin permeability, primarily via hair follicles.

4.2.6. *Delivery systems for cancer treatment*

Chemotherapy uses various compounds to destroy cancer cells and is the primary treatment for cancer [253]. Although generally effective, chemotherapy is often associated with significant systemic toxicity, as the diminished bioavailability of antitumor agents and their short release half-life [254] necessitate high doses and frequent administration to achieve therapeutic effects without inducing severe side effects [255].

Modifying the surface charge of cellulose has been explored for targeted anticancer drug-delivery systems [256]. Cellulose colloids and nanoparticles with opposing charges can be combined to create cellulose filaments and membranes that are electrically conductive and capable of transporting drugs and antibiotics. A characteristic feature of cancer is the acidification of the extracellular environment (low pH) alongside the alkalization of the intracellular cytoplasm (high pH), resulting in a pH gradient wherein cancer cells exhibit a higher pH (pH $>$ 7.2) compared to normal cells (pH 7.2–7.4). Carboxyl cellulose, noted for its enhanced hydrophilicity and adjustable dimensional properties, shows promise for mimicking protein transport, thereby facilitating the entry of substances into cell membranes. In addition, cellulose is biocompatible with a tailorable structure and properties, making it suitable for sustained-release and targeted drug-delivery systems.

CMC-based hydrogel nanocomposites, in which the CMC nanoparticles are interconnected via graphene quantum dots (GQDs), have been explored for cancer treatment [257]. GQDs exhibit significantly

lower cytotoxicity than other inorganic quantum dots and do not release toxic metal ions upon degradation. The resulting nanocomposite hydrogels demonstrated enhanced swelling capacities, improved degradation kinetics, and reduced toxicity toward blood cancer cells (K562). Moreover, they exhibited pH-responsive drug release. The incorporation and controlled release of DOX was examined as a model chemotherapeutic agent. The integration of GQDs into the CMC membrane imparted pH sensitivity to the system, thereby extending the DOX release duration. Cytotoxicity assays with K562 cells indicated that the DOX/CMC/GQD nanocomposite hydrogel could be a long-acting and highly effective anticancer therapeutic agent.

Ali et al. [258] developed a novel NIR-responsive hydrogel using a labile thioaldehyde crosslinker of reactive oxygen species (Fig. 12B(i)). The crosslinker featured a terminal tetrazine group and underwent a Diels–Alder click reaction with norbornene-modified CMCs. The reaction was biologically orthogonal and exhibited inverse electron demand characteristics. Hydrogels formed rapidly under physiological conditions, generating nitrogen gas as a byproduct, which resulted in porous structures within the hydrogel network (Fig. 12B(ii)). Indocyanine green and DOX were encapsulated within this porous hydrogel matrix. Following NIR irradiation, the hydrogel demonstrated spatiotemporal release of the encapsulated DOX (>96 %) owing to reactive oxygen species-mediated cleavage of the thioketone bonds formed by interactions with indocyanine green; conversely, minimal release (<25 %) occurred in the absence of NIR light. *In vitro* cytotoxicity assays showed that the hydrogel exhibited high cytocompatibility with no toxic effects on HEK-293 cells (Fig. 12B(iii-iv)). Hydrogels containing both DOX and indocyanine green significantly enhanced chemotherapy efficacy and effectively inhibited HeLa cancer cell proliferation upon exposure to NIR light (Fig. 12B(v)).

4.3. Applications in disease diagnostics

Compared to traditional paper-based tests, hydrogel-based diagnostic methods remain largely unexplored despite offering several advantages [259]. Modulating the pH and ionic strength can substantially enhance enzyme activity and extend the reactivity duration of hydrogels. To optimize interactions among the analyzed molecules or elements, fiber networks within hydrogels may be functionalized with proteins and other biomolecules [149].

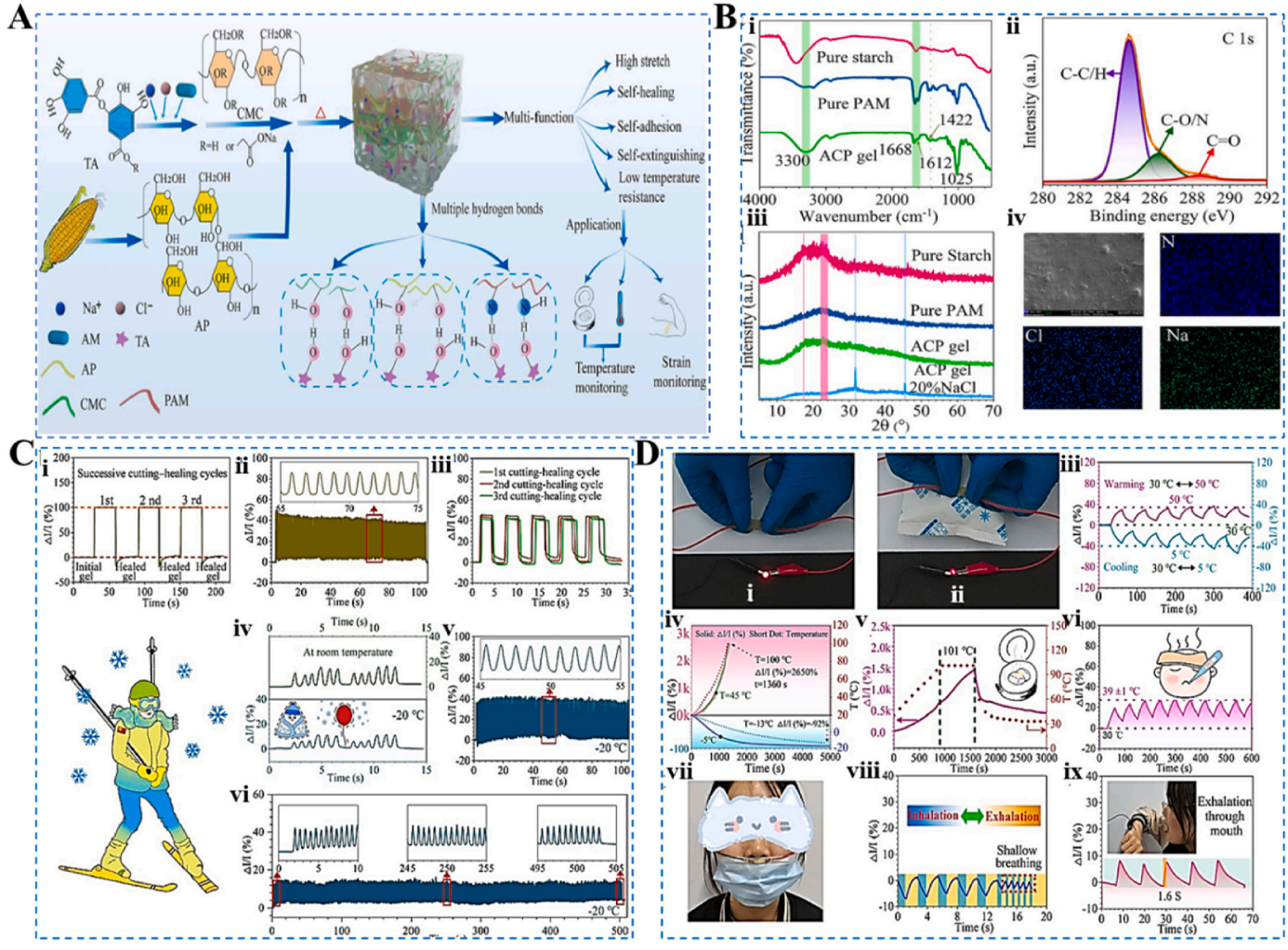

Fig. 13. Application of cellulose hydrogels in disease diagnosis. (A) Schematic illustration of the preparation process for hydrogels based on carboxymethyl cellulose, amylopectin, and polyacrylamide [261]. **(B)** In vitro characterization of hydrogels: **(i)** Fourier Transform Infrared Spectroscopy (FTIR); **(ii)** X-ray Photoelectron Spectroscopy (XPS); **(iii)** X-ray Diffraction (XRD); **(iv)** Scanning Electron Microscopy (SEM) [261]. **(C)** Relative current changes in hydrogels at varying temperatures: **(i)** Current changes during cutting-healing cycles; **(ii)** Current changes during bending-healing cycles at 90°; **(iii)** Continuous healing-induced current changes over three cycles; **(iv- vi)** Hydrogel attachment to balloon surfaces at room temperature and −20 °C [261]. **(D)** In vivo and in vitro relative current changes in hydrogels at different temperatures: **(i)** LED brightness at room temperature; **(ii)** LED brightness under ice pack conditions; **(iii- iv)** Relative current changes at temperature ranges of 5–30 °C, 30–50 °C, and 20–100 °C; **(v-ix)** simulating scenarios such as cooking, heating, breathing, and exhaling. This figure is reproduced with minor modifications from Ref. [261], Copyright © 2023 Carbohydrate polymers. published by Elsevier Ltd.

Conductive hydrogels have garnered significant interest in disease diagnostics [260]. Bian et al. [149] incorporated carboxyl CNFs to achieve a uniform distribution of opaque conductive poly(3, 4-ethylenedioxythiophene): polystyrene sulfonate (PEDOT:PSS) within cross-linked polyacrylamide matrices. This resulted in stretchable and transparent conductive IPN hydrogels designed for high-performance multi-sensor systems. Conductive hydrogels have excellent water response behavior over a wide humidity range (0–85 % relative humidity) owing to the formation of hydrogen bonds between water molecules and hydrophilic groups. These hydrogels also exhibited outstanding strain-sensing capabilities, with high sensitivity, rapid response times, and reliable stability and reproducibility across a broad range of elongations (0–83.7 %). Notably, the conductive hydrogels could detect and differentiate between complex human activities from physiological signals. The incorporation of carboxyl CNFs and PEDOT:PSS effectively improved humidity sensitivity, and the resultant hydrogels demonstrated considerable potential for noncontact sensing applications related to human respiration and finger movements.

Zhao et al. [261] developed a hydrogel with an INP structure composed of amylopectin, CMC, and polyacrylamide using a “cooking” method (Fig. 13A). The hydrogel, prepared by adding tannic acid, exhibits good elongation at break (90 %), low-temperature resistance, self-quenching ability, self-repair, and good adhesion (Fig. 13B). Hydrogel-based sensor devices effectively monitor human movement and subtle changes in expression, enabling real-time monitoring under challenging conditions. The sensors maintain accuracy even after repeated cutting and healing cycles, exposure to low temperatures, and prolonged use (up to one month). Furthermore, the gel can detect temperature variations across a broad operational range, with a sensitivity of up to 33 %·°C^{-1}, making it highly promising for temperature-monitoring applications (Fig. 13C). Notably, the hydrogel sensor shows potential for use in food processing, disease diagnosis, and medical treatment by rapidly assessing cooking processes and respiratory rates. This work introduces new possibilities for the design and fabrication of sugar-based gels with multifunctional properties and applications in electronic devices (Fig. 13D).

4.4. Status and challenges of in vivo research and clinical translation

Cellulose based stimulus-responsive hydrogels face many key challenges in the process of advancing in vivo research and clinical conversion. Although cellulosic materials themselves have good histocompatibility, they may induce the body’s immune response after chemical modification or compounding with other components, which poses a potential risk to the safety of their clinical applications. Secondly, the long-term stability and degradation kinetics of the material need to be systematically studied to ensure that its durable properties in vivo do not lead to adverse reactions, whereas the biocompatibility of its degradation products also needs to be fully evaluated. In terms of industrialization, the existing laboratory preparation process is difficult to meet the needs of large-scale production, especially in ensuring the consistency of material properties and reducing production costs, there are significant bottlenecks. In addition, as a novel biomaterial, cellulosic hydrogels must pass a rigorous regulatory approval process, including a thorough evaluation of their biosafety, functional effectiveness, and quality control systems to meet the relevant standards for medical devices and drug delivery systems. The solution of these challenges requires multidisciplinary collaborative innovation, combining the advantages of materials science, biomedical and engineering technology, through systematic preclinical research and rigorous clinical trials, and ultimately achieving the leap from basic research to clinical application.

5. Challenges and conclusion

Cellulose-based stimulus-responsive hydrogels, characterized by their abundant hydroxyl groups, facile chemical modification properties, and the tunability and dynamic reversibility of physically cross-linked networks, have demonstrated broad application prospects in fields such as biomedicine and environmental engineering. However, practical applications currently face numerous challenges. The stimulus response mechanisms are relatively simplistic: Existing mechanisms are predominantly basic, particularly in terms of responsiveness to biological signals, which requires further exploration. Most research focuses on responses to common physical and chemical stimuli, while studies on the recognition and response to complex biological signals remain limited, thereby restricting precise regulation within organisms. Insufficient response speed and sensitivity: Current hydrogels exhibit relatively low response speeds and sensitivities, making it challenging to meet the demands for real-time monitoring and precise control. In scenarios such as disease diagnosis and drug release, the inability to rapidly and accurately respond to environmental changes has affected therapeutic efficacy and diagnostic accuracy. Research-to-production disconnect: Although heat-sensitive cellulose hydrogels have entered industrial production, most research remains at the laboratory scale. During the transition from laboratory to large-scale production, issues such as prolonged response times and insufficient precision hinder product quality consistency. Additionally, high production costs impede widespread application. The efficiency of functional modifications needs improvement: Functional modification efficiency must be enhanced, necessitating the development of more efficient surface modification technologies to expand functional and environmental response capabilities. Existing methods are often complex and inefficient, limiting hydrogel applications across various fields.

To address these challenges, future research could focus on the following directions. Developing multi-stimulus responsive and intelligent applications: Efforts should be directed toward developing cellulose hydrogels capable of responding to multiple stimuli (e.g., temperature-pH dual-response systems) and integrating artificial intelligence technology for intelligent applications, such as constructing smart drug delivery systems and environmental monitoring sensors to meet requirements in complex environments. Optimizing performance and expanding response ranges: By refining gel network structures and incorporating conductive materials, the response speed and sensitivity of hydrogels can be improved. Simultaneously, novel functional modification methods should be explored to broaden environmental response capabilities and enable functionality under a wider range of conditions. Promoting practical applications and industrialization: Addressing issues of prolonged response times and low precision will facilitate applications in bionic materials and soft robotics. Green and sustainable preparation processes should be developed to reduce costs, promoting large-scale applications and bridging the gap between laboratory research and actual production. Exploring biomedical potential: Further investigation into the potential of cellulose hydrogels in biomedical fields such as tissue engineering, drug delivery, wound repair, and disease diagnosis is warranted. New biomedical materials should be developed to provide effective solutions to clinical challenges.

Cellulose hydrogels possess significant commercial potential; however, successful commercialization requires passing stringent regulatory approvals and meeting the requirements of institutions such as the FDA and EMA. This involves comprehensive biocompatibility testing, material characterization, preclinical and clinical trials, and adherence to GMP-compliant manufacturing processes to establish a robust foundation for commercialization. Future research should prioritize regulatory compliance, manufacturing process optimization, and marketing strategy formulation to accelerate clinical and commercial applications.

In summary, while significant progress has been made in cellulose-based stimulus-responsive hydrogel research, many challenges persist. Through multifunctional integration, intelligent design, enhancement of response performance, and promotion of practical applications, breakthroughs in biomedicine and environmental engineering are anticipated. This article reviews the preparation and characterization of

cellulose and its derivative hydrogels, classifies intelligent stimulus-responsive cellulose hydrogels, and evaluates their applications in tissue engineering, drug delivery, wound dressings, and disease diagnosis, providing a basis for subsequent research on cellulose-based stimulus-responsive hydrogels.

CRediT authorship contribution statement

Huaqian Xue: Writing – original draft. **Cong Zhu:** Writing – review & editing. **Yifan Wang:** Investigation, Data curation. **Qiancheng Gu:** Software. **Yunyuan Shao:** Visualization, Data curation. **Anqi Jin:** Validation. **Xiaofen Zhang:** Supervision. **Lanjie Lei:** Project administration, Funding acquisition. **Yongliang Li:** Project administration, Funding acquisition.

Ethics approval and consent to participate

There are no human and animal subjects in this review and informed consent is not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The authors do not have permission to share data.

References

[1] Y. Hou, Q.F. Guan, J. Xia, Z.C. Ling, Z. He, Z.M. Han, H.B. Yang, P. Gu, Y. Zhu, S. H. Yu, H. Wu, Strengthening and toughening hierarchical nanocellulose via humidity-mediated interface, ACS Nano 15 (1) (2021) 1310–1320, https://doi.org/10.1021/acsnano.0c08574.

[2] S. Mohammed, J. Aburabie, R. Hashaikeh, A review on the potential of cellulose nanomaterials for the development of thin film composite polyamide membranes for water treatment, Chemosphere 363 (2024) 142927, https://doi.org/10.1016/j.chemosphere.2024.142927.

[3] A. Khodayari, U. Hirn, S. Spirk, Y. Ogawa, D. Seveno, W. Thielemans, Advancing plant cell wall modelling: atomistic insights into cellulose, disordered cellulose, and hemicelluloses - a review, Carbohydr. Polym. 343 (2024) 122415, https://doi.org/10.1016/j.carbpol.2024.122415.

[4] P. Zhang, Z. Chen, L. Zhou, J. Gao, H. Zheng, H. Lin, G. Zhu, X. Qin, W. Cao, Carboxymethyl cellulose and carboxymethyl chitosan-based composite nanogel as a stable delivery vehicle for oyster peptides: characterization, absorption and transport mechanism, Food Chem. 442 (2024) 138464, https://doi.org/10.1016/j.foodchem.2024.138464.

[5] M.A. Soltan, R.S. Shewita, O.A. Matroud, L.A. Alkeridis, S. Sayed, M. Shukry, S. A. El-Shobokshy, Lignocellulose and probiotic supplementation in broiler chicken diet: effect on growth performance, digestive health, litter quality, and genes expression, Poult. Sci. 103 (6) (2024) 103735, https://doi.org/10.1016/j.psj.2024.103735.

[6] T. Li, C. Chen, A.H. Brozena, J.Y. Zhu, L. Xu, C. Driemeier, J. Dai, O.J. Rojas, A. Isogai, L. Wågberg, L. Hu, Developing fibrillated cellulose as a sustainable technological material, Nature 590 (7844) (2021) 47–56, https://doi.org/10.1038/s41586-020-03167-7.

[7] E.J. Foster, R.J. Moon, U.P. Agarwal, M.J. Bortner, J. Bras, S. Camarero-Espinosa, K.J. Chan, M.J.D. Clift, E.D. Cranston, S.J. Eichhorn, D.M. Fox, W.Y. Hamad, L. Heux, B. Jean, M. Korey, W. Nieh, K.J. Ong, M.S. Reid, S. Renneckar, R. Roberts, J.A. Shatkin, J. Simonsen, K. Stinson-Bagby, N. Wanasekara, J. Youngblood, Current characterization methods for cellulose nanomaterials, Chem. Soc. Rev. 47 (8) (2018) 2609–2679, https://doi.org/10.1039/c6cs00895j.

[8] A.K. Mohanty, S. Vivekanandhan, J.M. Pin, M. Misra, Composites from renewable and sustainable resources: challenges and innovations, Science 362 (6414) (2018) 536–542, https://doi.org/10.1126/science.aat9072.

[9] X. Zhao, X. Chen, H. Yuk, S. Lin, X. Liu, G. Parada, Soft materials by design: unconventional polymer networks give extreme properties, Chem. Rev. 121 (8) (2021) 4309–4372, https://doi.org/10.1021/acs.chemrev.0c01088.

[10] N. Mahmoudi, Y. Wang, N. Moriarty, N.Y. Ahmed, N. Dehorter, L. Lisowski, A. R. Harvey, C.L. Parish, R.J. Williams, D.R. Nisbet, Neuronal replenishment via hydrogel-rationed delivery of reprogramming factors, ACS Nano 18 (4) (2024) 3597–3613, https://doi.org/10.1021/acsnano.3c11337.

[11] Y. Chen, X. Wang, S. Tao, Q. Wang, P.Q. Ma, Z.B. Li, Y.L. Wu, D.W. Li, Research advances in smart responsive-hydrogel dressings with potential clinical diabetic wound healing properties, Mil Med Res 10 (1) (2023) 37, https://doi.org/10.1186/s40779-023-00473-9.

[12] Y. Fang, S. Huang, X. Gong, J.A. King, Y. Wang, J. Zhang, X. Yang, Q. Wang, Y. Zhang, G. Zhai, L. Ye, Salt sensitive purely zwitterionic physical hydrogel for prevention of postoperative tissue adhesion, Acta Biomater. 158 (2023) 239–251, https://doi.org/10.1016/j.actbio.2022.12.045.

[13] X. Li, K. Cui, T. Kurokawa, Y.N. Ye, T.L. Sun, C. Yu, C. Creton, J.P. Gong, Effect of mesoscale phase contrast on fatigue-delaying behavior of self-healing hydrogels, Sci. Adv. 7 (16) (2021), https://doi.org/10.1126/sciadv.abe8210.

[14] S. Nasra, M. Patel, H. Shukla, M. Bhatt, A. Kumar, Functional hydrogel-based wound dressings: a review on biocompatibility and therapeutic efficacy, Life Sci. 334 (2023) 122232, https://doi.org/10.1016/j.lfs.2023.122232.

[15] L. Chang, H. Du, F. Xu, C. Xu, H. Liu, Hydrogel-enabled mechanically active wound dressings, Trends Biotechnol. 42 (1) (2024) 31–42, https://doi.org/10.1016/j.tibtech.2023.06.004.

[16] S.H. Aswathy, U. NarendraKumar, I. Manjubala, The influence of molecular weight of cellulose on the properties of carboxylic acid crosslinked cellulose hydrogels for biomedical and environmental applications, Int. J. Biol. Macromol. 239 (2023) 124282, https://doi.org/10.1016/j.ijbiomac.2023.124282.

[17] L. Li, X. Cheng, Q. Huang, Y. Cheng, J. Xiao, J. Hu, Sprayable antibacterial hydrogels by simply mixing of aminoglycoside antibiotics and cellulose nanocrystals for the treatment of infected wounds, Adv. Healthc. Mater. 11 (20) (2022) e2201286, https://doi.org/10.1002/adhm.202201286.

[18] K. Ganguly, S.D. Dutta, A. Randhawa, D.K. Patel, T.V. Patil, K.T. Lim, Transcriptomic changes toward osteogenic differentiation of mesenchymal stem cells on 3D-printed GelMA/CNC hydrogel under pulsatile pressure environment, Adv. Healthc. Mater. (2023) e2202163, https://doi.org/10.1002/adhm.202202163.

[19] X. Jiang, F. Zeng, X. Yang, C. Jian, L. Zhang, A. Yu, A. Lu, Injectable self-healing cellulose hydrogel based on host-guest interactions and acylhydrazone bonds for sustained cancer therapy, Acta Biomater. 141 (2022) 102–113, https://doi.org/10.1016/j.actbio.2021.12.036.

[20] H. Cao, L. Duan, Y. Zhang, J. Cao, K. Zhang, Current hydrogel advances in physicochemical and biological response-driven biomedical application diversity, Signal Transduct. Target. Ther. 6 (1) (2021) 426, https://doi.org/10.1038/s41392-021-00830-x.

[21] H. Liu, Y. Hu, Y. Liu, R. Hu, X. Wu, B. Li, A review of recent advances in biomedical applications of smart cellulose-based hydrogels, Int. J. Biol. Macromol. 253 (Pt 6) (2023) 127149, https://doi.org/10.1016/j.ijbiomac.2023.127149.

[22] V. Rahmanian, T. Pirzada, S. Wang, S.A. Khan, Cellulose-based hybrid aerogels: strategies toward design and functionality, Adv. Mater. 33 (51) (2021) e2102892, https://doi.org/10.1002/adma.202102892.

[23] B. Thomas, M.C. Raj, A.K. B, R.M. H, J. Joy, A. Moores, G.L. Drisko, C. Sanchez, Nanocellulose, a versatile green platform: from biosources to materials and their applications, Chem. Rev. 118 (24) (2018) 11575–11625, https://doi.org/10.1021/acs.chemrev.7b00627.

[24] L.C. Wong, C.P. Leh, C.F. Goh, Designing cellulose hydrogels from non-woody biomass, Carbohydr. Polym. 264 (2021) 118036, https://doi.org/10.1016/j.carbpol.2021.118036.

[25] S. Jung, J. Kim, J. Bang, M. Jung, S. Park, H. Yun, H.W. Kwak, pH-sensitive cellulose/chitin nanofibrillar hydrogel for dye pollutant removal, Carbohydr. Polym. 317 (2023) 121090, https://doi.org/10.1016/j.carbpol.2023.121090.

[26] H. Shang, X. Yang, H. Liu, Temperature-responsive hydrogel prepared from carboxymethyl cellulose-stabilized N-vinylcaprolactam with potential for fertilizer delivery, Carbohydr. Polym. 313 (2023) 120875, https://doi.org/10.1016/j.carbpol.2023.120875.

[27] S.Y. Park, J.H. Kang, H.S. Kim, J.Y. Hwang, U.S. Shin, Electrical and thermal stimulus-responsive nanocarbon-based 3D hydrogel sponge for switchable drug delivery, Nanoscale 14 (6) (2022) 2367–2382, https://doi.org/10.1039/d1nr06074k.

[28] T. Su, X. Zhang, Z. Wang, Y. Guo, X. Wei, B. Xu, H. Xia, W. Yang, H. Xu, Cellulose nanocrystal-based polymer hydrogel embedded with iron oxide nanorods for efficient arsenic removal, Carbohydr. Polym. 331 (2024) 121855, https://doi.org/10.1016/j.carbpol.2024.121855.

[29] A. Pardo, M. Gomez-Florit, M.D. Davidson, M. Öztürk-Öncel, R.M.A. Domingues, J.A. Burdick, M.E. Gomes, Hierarchical design of tissue-mimetic fibrillar hydrogel scaffolds, Adv. Healthc. Mater. 13 (16) (2024) e2303167, https://doi.org/10.1002/adhm.202303167.

[30] R. Solanki, D. Bhatia, Stimulus-responsive hydrogels for targeted cancer therapy, Gels 10 (7) (2024), https://doi.org/10.3390/gels10070440.

[31] F. Ullah, M.B. Othman, F. Javed, Z. Ahmad, H. Md Akil, Classification, processing and application of hydrogels: a review,Materials science & engineering, C, Materials for biological applications 57 (2015) 414–433, https://doi.org/10.1016/j.msec.2015.07.053.

[32] M. Peydayesh, E. Boschi, M. Bagnani, D. Tay, F. Donat, H. Almohammadi, M. Li, M. Usuelli, T. Shiroka, R. Mezzenga, Hybrid amyloid-chitin nanofibrils for

magnetic and catalytic aerogels, ACS Nano 18 (8) (2024) 6690–6701, https://doi.org/10.1021/acsnano.4c00883.
[33] R. Koshani, M. Tavakolian, T.G.M. van de Ven, Cellulose-based dispersants and flocculants, J. Mater. Chem. B 8 (46) (2020) 10502–10526, https://doi.org/10.1039/d0tb02021d.
[34] M. Oprea, S.I. Voicu, Recent advances in composites based on cellulose derivatives for biomedical applications, Carbohydr. Polym. 247 (2020) 116683, https://doi.org/10.1016/j.carbpol.2020.116683.
[35] U.D. Hemraz, E. Lam, R. Sunasee, Recent advances in cellulose nanocrystals-based antimicrobial agents, Carbohydr. Polym. 315 (2023) 120987, https://doi.org/10.1016/j.carbpol.2023.120987.
[36] D. Sawada, Y. Nishiyama, R. Shah, V.T. Forsyth, E. Mossou, H.M. O'Neill, M. Wada, P. Langan, Untangling the threads of cellulose mercerization, Nat. Commun. 13 (1) (2022) 6189, https://doi.org/10.1038/s41467-022-33812-w.
[37] P.A. Spies, T. Keplinger, N. Horbelt, F. Reppe, E. Scoppola, M. Eder, P. Fratzl, I. Burgert, M. Rüggeberg, Cellulose lattice strains and stress transfer in native and delignified wood, Carbohydr. Polym. 296 (2022) 119922, https://doi.org/10.1016/j.carbpol.2022.119922.
[38] S.D. Dutta, D.K. Patel, K.-T. Lim, Functional cellulose-based hydrogels as extracellular matrices for tissue engineering, J. Biol. Eng. 13 (1) (2019), https://doi.org/10.1186/s13036-019-0177-0.
[39] M.F. Moradali, B.H.A. Rehm, Bacterial biopolymers: from pathogenesis to advanced materials, Nat. Rev. Microbiol. 18 (4) (2020) 195–210, https://doi.org/10.1038/s41579-019-0313-3.
[40] S.D. Dutta, D.K. Patel, K.T. Lim, Functional cellulose-based hydrogels as extracellular matrices for tissue engineering, J. Biol. Eng. 13 (2019) 55, https://doi.org/10.1186/s13036-019-0177-0.
[41] Z. Sun, Y. Kuang, M. Ahmad, Y. Huang, S. Yin, F. Seidi, S. Wang, Enhanced osmotic energy conversion through bacterial cellulose based double-network hydrogel with 3D interconnected nanochannels, Carbohydr. Polym. 305 (2023) 120556, https://doi.org/10.1016/j.carbpol.2023.120556.
[42] D. Zhao, Y. Zhu, W. Cheng, W. Chen, Y. Wu, H. Yu, Cellulose-based flexible functional materials for emerging intelligent electronics, Adv. Mater. 33 (28) (2021) e2000619, https://doi.org/10.1002/adma.202000619.
[43] C. Zhao, X. Gong, X. Lin, C. Zhang, Y. Wang, Regenerated cellulose/polyvinyl alcohol composite films with high transparency and ultrahigh haze for multifunctional light management, Carbohydr. Polym. 321 (2023) 121303, https://doi.org/10.1016/j.carbpol.2023.121303.
[44] C. Wang, Y. Liao, H.Y. Yu, Y. Dong, J. Yao, Homogeneous wet-spinning construction of skin-core structured PANI/cellulose conductive fibers for gas sensing and e-textile applications, Carbohydr. Polym. 319 (2023) 121175, https://doi.org/10.1016/j.carbpol.2023.121175.
[45] A.A. Shamsuri, K. Abdan, T. Kaneko, A concise review on the physicochemical properties of biopolymer blends prepared in ionic liquids, Molecules 26 (1) (2021), https://doi.org/10.3390/molecules26010216.
[46] Q. Yuan, L.Z. Huang, P.L. Wang, T. Mai, M.G. Ma, Cellulose nanofiber/molybdenum disulfide aerogels for ultrahigh photothermal effect, J. Colloid Interface Sci. 624 (2022) 70–78, https://doi.org/10.1016/j.jcis.2022.05.102.
[47] Comment on J. Kang, A.M. Kang, Physicochemical stimuli as tuning parameters to modulate the structure and stability of nanostructured lipid carriers and release kinetics of encapsulated antileprosy drugs, by R. Kanwar, M. Gradzielski, S. Prevost, G. Kaur, M. S. Appavou and S. K. Mehta, J. Mater. Chem. B 7 (2019) 6539, https://doi.org/10.1039/d0tb01160f. J Mater Chem B. 8 (44) (2020) 10205-10208.
[48] M. Kang, O. Oderinde, X. Han, G. Fu, Z. Zhang, Development of oxidized hydroxyethyl cellulose-based hydrogel enabling unique mechanical, transparent and photochromic properties for contact lenses, Int. J. Biol. Macromol. 183 (2021) 1162–1173, https://doi.org/10.1016/j.ijbiomac.2021.05.029.
[49] D.E. Ciolacu, R. Nicu, F. Ciolacu, Cellulose-based hydrogels as sustained drug-delivery systems, Materials 13 (22) (2020), https://doi.org/10.3390/ma13225270.
[50] R.E. Jones, D.S. Foster, M.T. Longaker, Management of chronic wounds-2018, JAMA 320 (14) (2018) 1481–1482, https://doi.org/10.1001/jama.2018.12426.
[51] M. Žiganova, R. Merijs-Meri, J. Zicāns, A. Ābele, I. Bochkov, T. Ivanova, Accelerated weathering testing (AWT) and bacterial biodegradation effects on poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV)/Rapeseed microfiber biocomposites properties, Polymers 16 (5) (2024), https://doi.org/10.3390/polym16050622.
[52] R.P. Swatloski, S.K. Spear, J.D. Holbrey, R.D. Rogers, Dissolution of cellulose [correction of cellose] with ionic liquids, J. Am. Chem. Soc. 124 (18) (2002) 4974–4975, https://doi.org/10.1021/ja025790m.
[53] J. Cai, L. Zhang, Rapid dissolution of cellulose in LiOH/urea and NaOH/urea aqueous solutions, Macromol. Biosci. 5 (6) (2005) 539–548, https://doi.org/10.1002/mabi.200400222.
[54] Y. Long, M. Dimde, J.M. Adler, R.M. Vidal, T.L. Povolotsky, P. Nickl, K. Achazi, J. Trimpert, B.B. Kaufer, R. Haag, C. Nie, Sulfated cellulose nanofiber hydrogel with mucus-like activities for virus inhibition, ACS Appl. Mater. Interfaces 16 (49) (2024) 67504–67513, https://doi.org/10.1021/acsami.4c17998.
[55] Y. Liu, Y. Wu, X. Zhou, Y. Mo, Y. Zheng, G. Yuan, M. Yang, All-Cellulose-based flexible Zinc-Ion battery enabled by waste pomelo peel, J. Colloid Interface Sci. 678 (Pt B) (2025) 497–505, https://doi.org/10.1016/j.jcis.2024.09.036.
[56] T. Arndt, U. Chatterjee, O. Shilkova, J. Francis, J. Lundkvist, D. Johansson, B. Schmuck, G. Greco, E. NordbergÅ, Y. Li, L.U. Wahlberg, M. Langton, J. Johansson, C. Götherström, A. Rising, Tuneable recombinant spider silk protein hydrogels for drug release and 3D cell culture, Adv. Funct. Mater. 34 (35) (2024) 2303622, https://doi.org/10.1002/adfm.202303622.
[57] J. Xu, L. Chang, Y. Xiong, Q. Peng, Chitosan-based hydrogels as antibacterial/antioxidant/anti-inflammation multifunctional dressings for chronic wound healing, Adv. Healthc. Mater. 13 (30) (2024) e2401490, https://doi.org/10.1002/adhm.202401490.
[58] X. Yang, C. Huang, H. Wang, K. Yang, M. Huang, W. Zhang, Q. Yu, H. Wang, L. Zhang, Y. Zhao, D. Zhu, Multifunctional nanoparticle-loaded injectable alginate hydrogels with deep tumor penetration for enhanced chemo-immunotherapy of cancer, ACS Nano 18 (28) (2024) 18604–18621, https://doi.org/10.1021/acsnano.4c04766.
[59] J.A. Burdick, G.D. Prestwich, Hyaluronic acid hydrogels for biomedical applications, Adv. Mater. 23 (12) (2011) H41–H56, https://doi.org/10.1002/adma.201003963.
[60] B. Li, M. Xu, B. An, W. Sun, R. Teng, S. Luo, C. Ma, Z. Chen, J. Li, W. Li, S. Liu, Mechanical and thermal responsive chiral photonic cellulose hydrogels for dynamic anti-counterfeiting and optical skin, Mater. Horiz. (2025), https://doi.org/10.1039/d4mh01646g.
[61] J. Gao, X. Li, L. Xu, M. Yan, H. Bi, Q. Wang, Transparent multifunctional cellulose-based conductive hydrogel for wearable strain sensors and arrays, Carbohydr. Polym. 329 (2024) 121784, https://doi.org/10.1016/j.carbpol.2024.121784.
[62] S. Wang, L. Yu, S. Wang, L. Zhang, L. Chen, X. Xu, Z. Song, H. Liu, C. Chen, Strong, tough, ionic conductive, and freezing-tolerant all-natural hydrogel enabled by cellulose-bentonite coordination interactions, Nat. Commun. 13 (1) (2022) 3408, https://doi.org/10.1038/s41467-022-30224-8.
[63] M. Tavakolian, S.M. Jafari, T.G.M. van de Ven, A review on surface-functionalized cellulosic nanostructures as biocompatible antibacterial materials, Nano-Micro Lett. 12 (1) (2020), https://doi.org/10.1007/s40820-020-0408-4.
[64] H. Nasution, H. Harahap, N.F. Dalimunthe, M.H.S. Ginting, M. Jaafar, O.O. H. Tan, H.K. Aruan, A.L. Herfananda, Hydrogel and effects of crosslinking agent on cellulose-based hydrogels: a review, Gels 8 (9) (2022), https://doi.org/10.3390/gels8090568.
[65] Z. Li, M. Zhang, Progress in the preparation of stimulus-responsive cellulose hydrogels and their application in slow-release fertilizers, Polymers 15 (17) (2023), https://doi.org/10.3390/polym15173643.
[66] L. Yan, Q. Shuai, X. Gong, Q. Gu, H. Yu, Synthesis of microporous cationic hydrogel of hydroxypropyl cellulose (HPC) and its application on anionic dye removal, Clean: Soil, Air, Water 37 (4–5) (2009) 392–398, https://doi.org/10.1002/clen.200900006.
[67] A. Salama, S. Etri, S.A.A. Mohamed, M. El-Sakhawy, Carboxymethyl cellulose prepared from mesquite tree: new source for promising nanocomposite materials, Carbohydr. Polym. 189 (2018) 138–144, https://doi.org/10.1016/j.carbpol.2018.02.016.
[68] V.E. Ahmadi, M.H. Khaksaran, A.M. Apak, A. Apak, M. Parlak, U. Tastan, I. I. Kaya, A.K. Sadaghiani, A. Koşar, Graphene-coated sintered porous copper surfaces for boiling heat transfer enhancement, Carbon Trends 8 (2022), https://doi.org/10.1016/j.cartre.2022.100171.
[69] S.M.F. Kabir, P.P. Sikdar, B. Haque, M.A.R. Bhuiyan, A. Ali, M.N. Islam, Cellulose-based hydrogel materials: chemistry, properties and their prospective applications, Prog. Biomater. 7 (3) (2018) 153–174, https://doi.org/10.1007/s40204-018-0095-0.
[70] M. Rasoulzadeh, H. Namazi, Carboxymethyl cellulose/graphene oxide bio-nanocomposite hydrogel beads as anticancer drug carrier agent, Carbohydr. Polym. 168 (2017) 320–326, https://doi.org/10.1016/j.carbpol.2017.03.014.
[71] L. Cui, J. Li, S. Guan, K. Zhang, K. Zhang, J. Li, Injectable multifunctional CMC/HA-DA hydrogel for repairing skin injury, Mater. Today Bio 14 (2022) 100257, https://doi.org/10.1016/j.mtbio.2022.100257.
[72] B. Tang, J. Shan, T. Yuan, Y. Xiao, J. Liang, Y. Fan, X. Zhang, Hydroxypropylcellulose enhanced high viscosity endoscopic mucosal dissection intraoperative chitosan thermosensitive hydrogel, Carbohydr. Polym. 209 (2019) 198–206, https://doi.org/10.1016/j.carbpol.2018.12.103.
[73] A. Karewicz, K. Zasada, D. Bielska, T.E. Douglas, J.A. Jansen, S.C. Leeuwenburgh, M. Nowakowska, Alginate-hydroxypropylcellulose hydrogel microbeads for alkaline phosphatase encapsulation, J. Microencapsul. 31 (1) (2014) 68–76, https://doi.org/10.3109/02652048.2013.805841.
[74] S. Liu, S.A. Qamar, M. Qamar, K. Basharat, M. Bilal, Engineered nanocellulose-based hydrogels for smart drug delivery applications, Int. J. Biol. Macromol. 181 (2021) 275–290, https://doi.org/10.1016/j.ijbiomac.2021.03.147.
[75] X. He, Q. Lu, Design and fabrication strategies of cellulose nanocrystal-based hydrogel and its highlighted application using 3D printing: a review, Carbohydr. Polym. 301 (Pt B) (2023) 120351, https://doi.org/10.1016/j.carbpol.2022.120351.
[76] D. Li, D. Dai, G. Xiong, S. Lan, C. Zhang, Composite nanocoatings of biomedical magnesium alloy implants: advantages, mechanisms, and design strategies, Adv Sci (Weinh) 10 (18) (2023) e2300658, https://doi.org/10.1002/advs.202300658.
[77] K. Löbmann, A.J. Svagan, Cellulose nanofibers as excipient for the delivery of poorly soluble drugs, Int. J. Pharm. 533 (1) (2017) 285–297, https://doi.org/10.1016/j.ijpharm.2017.09.064.
[78] G.L. Berto, B.D. Mattos, J. Velasco, B. Zhao, F. Segato, O.J. Rojas, V. Arantes, Endoglucanase effects on energy consumption in the mechanical fibrillation of cellulose fibers into nanocelluloses, Int. J. Biol. Macromol. 243 (2023) 125002, https://doi.org/10.1016/j.ijbiomac.2023.125002.
[79] K. Heise, E. Kontturi, Y. Allahverdiyeva, T. Tammelin, M.B. Linder, Nonappa, O. Ikkala, Nanocellulose: recent fundamental advances and emerging biological and biomimicking applications, Adv. Mater. 33 (3) (2021) e2004349, https://doi.org/10.1002/adma.202004349.

[80] F. Riehle, D. Hoenders, J. Guo, A. Eckert, S. Ifuku, A. Walther, Sustainable chitin nanofibrils provide outstanding flame-retardant nanopapers, Biomacromolecules 20 (2) (2019) 1098–1108, https://doi.org/10.1021/acs.biomac.8b01766.
[81] N. Fatema, R.M. Ceballos, C. Fan, Modifications of cellulose-based biomaterials for biomedical applications, Front. Bioeng. Biotechnol. 10 (2022) 993711, https://doi.org/10.3389/fbioe.2022.993711.
[82] L.S. Pachuau, A mini review on plant-based nanocellulose: production, sources, modifications and its potential in drug delivery applications, Mini Rev. Med. Chem. 15 (7) (2015) 543–552, https://doi.org/10.2174/1389557515666150415150327.
[83] Y. Xu, A. Atrens, J.R. Stokes, A review of nanocrystalline cellulose suspensions: rheology, liquid crystal ordering and colloidal phase behaviour, Adv. Colloid Interface Sci. 275 (2020) 102076, https://doi.org/10.1016/j.cis.2019.102076.
[84] X. Song, L. Zhou, B. Ding, X. Cui, Y. Duan, J. Zhang, Simultaneous improvement of thermal stability and redispersibility of cellulose nanocrystals by using ionic liquids, Carbohydr. Polym. 186 (2018) 252–259, https://doi.org/10.1016/j.carbpol.2018.01.055.
[85] V.H.G. Phan, M. Murugesan, H. Huong, T.T. Le, T.H. Phan, P. Manivasagan, R. Mathiyalagan, E.S. Jang, D.C. Yang, Y. Li, T. Thambi, Cellulose nanocrystals-incorporated thermosensitive hydrogel for controlled release, 3D printing, and breast cancer treatment applications, ACS Appl. Mater. Interfaces 14 (38) (2022) 42812–42826, https://doi.org/10.1021/acsami.2c05864.
[86] S.R.S. Veloso, A.G. Azevedo, P.F. Teixeira, C.B.P. Fernandes, Cellulose nanocrystal (CNC) gels: a review, Gels 9 (7) (2023), https://doi.org/10.3390/gels9070574.
[87] M. Chau, S.E. Sriskandha, D. Pichugin, H. Thérien-Aubin, D. Nykypanchuk, G. Chauve, M. Méthot, J. Bouchard, O. Gang, E. Kumacheva, Ion-mediated gelation of aqueous suspensions of cellulose nanocrystals, Biomacromolecules 16 (8) (2015) 2455–2462, https://doi.org/10.1021/acs.biomac.5b00701.
[88] W. Huang, Y. Wang, Z. Huang, X. Wang, L. Chen, Y. Zhang, L. Zhang, On-demand dissolvable self-healing hydrogel based on carboxymethyl chitosan and cellulose nanocrystal for deep partial thickness burn wound healing, ACS Appl. Mater. Interfaces 10 (48) (2018) 41076–41088, https://doi.org/10.1021/acsami.8b14526.
[89] Y. Brusentsev, P. Yang, A.W.T. King, F. Cheng, M.F. Cortes Ruiz, J.E. Eriksson, I. Kilpeläinen, S. Willför, C. Xu, L. Wågberg, X. Wang, Photocross-linkable and shape-memory biomaterial hydrogel based on methacrylated cellulose nanofibres, Biomacromolecules 24 (8) (2023) 3835–3845, https://doi.org/10.1021/acs.biomac.3c00476.
[90] H. Lu, V. Guccini, H. Kim, G. Salazar-Alvarez, G. Lindbergh, A. Cornell, Effects of different manufacturing processes on TEMPO-oxidized carboxylated cellulose nanofiber performance as binder for flexible lithium-ion batteries, ACS Appl. Mater. Interfaces 9 (43) (2017) 37712–37720, https://doi.org/10.1021/acsami.7b10307.
[91] C. Zheng, K. Lu, Y. Lu, S. Zhu, Y. Yue, X. Xu, C. Mei, H. Xiao, Q. Wu, J. Han, A stretchable, self-healing conductive hydrogels based on nanocellulose supported graphene towards wearable monitoring of human motion, Carbohydr. Polym. 250 (2020) 116905, https://doi.org/10.1016/j.carbpol.2020.116905.
[92] Y. Lu, Y. Yue, Q. Ding, C. Mei, X. Xu, Q. Wu, H. Xiao, J. Han, Self-recovery, fatigue-resistant, and multifunctional sensor assembled by a nanocellulose/carbon nanotube nanocomplex-mediated hydrogel, ACS Appl. Mater. Interfaces 13 (42) (2021) 50281–50297, https://doi.org/10.1021/acsami.1c16828.
[93] M. Isik, H. Sardon, D. Mecerreyes, Ionic liquids and cellulose: dissolution, chemical modification and preparation of new cellulosic materials, Int. J. Mol. Sci. 15 (7) (2014) 11922–11940, https://doi.org/10.3390/ijms150711922.
[94] S. Alven, B.A. Aderibigbe, Chitosan and cellulose-based hydrogels for wound management, Int. J. Mol. Sci. 21 (24) (2020), https://doi.org/10.3390/ijms21249656.
[95] R. Curvello, V.S. Raghuwanshi, G. Garnier, Engineering nanocellulose hydrogels for biomedical applications, Adv. Colloid Interface Sci. 267 (2019) 47–61, https://doi.org/10.1016/j.cis.2019.03.002.
[96] S.H. Zainal, N.H. Mohd, N. Suhaili, F.H. Anuar, A.M. Lazim, R. Othaman, Preparation of cellulose-based hydrogel: a review, J. Mater. Res. Technol. 10 (2021) 935–952, https://doi.org/10.1016/j.jmrt.2020.12.012.
[97] T. Huber, S. Feast, S. Dimartino, W. Cen, C. Fee, Analysis of the effect of processing conditions on physical properties of thermally set cellulose hydrogels, Materials 12 (7) (2019), https://doi.org/10.3390/ma12071066.
[98] Y. Li, Q. Gong, L. Han, X. Liu, Y. Yang, C. Chen, C. Qian, Q. Han, Carboxymethyl cellulose assisted polyaniline in conductive hydrogels for high-performance self-powered strain sensors, Carbohydr. Polym. 298 (2022) 120060, https://doi.org/10.1016/j.carbpol.2022.120060.
[99] J. Zhou, X. Wang, Y. Li, H. Li, K. Lu, Preparation of cellulose nanocrystal-dressed fluorinated polyacrylate latex particles via RAFT-mediated Pickering emulsion polymerization and application on fabric finishing, Cellulose 27 (11) (2020) 6617–6628, https://doi.org/10.1007/s10570-020-03227-1.
[100] Y. Zhou, Z. Zhai, Y. Yao, J.C. Stant, S.L. Landrum, M.J. Bortner, C.E. Frazier, K. J. Edgar, Oxidized hydroxypropyl cellulose/carboxymethyl chitosan hydrogels permit pH-responsive, targeted drug release, Carbohydr. Polym. 300 (2023) 120213, https://doi.org/10.1016/j.carbpol.2022.120213.
[101] J.T. Orasugh, G. Sarkar, N.R. Saha, B. Das, A. Bhattacharyya, S. Das, R. Mishra, I. Roy, A. Chattoapadhyay, S.K. Ghosh, D. Chattopadhyay, Effect of cellulose nanocrystals on the performance of drug loaded in situ gelling thermo-responsive ophthalmic formulations, Int. J. Biol. Macromol. 124 (2019) 235–245, https://doi.org/10.1016/j.ijbiomac.2018.11.217.
[102] J. Shen, L. Lu, R. He, Q. Ye, C. Yuan, L. Guo, M. Zhao, B. Cui, Starch/ionic liquid/hydrophobic association hydrogel with high stretchability, fatigue resistance, self-recovery and conductivity for sensitive wireless wearable sensors, Carbohydr. Polym. 346 (2024) 122608, https://doi.org/10.1016/j.carbpol.2024.122608.
[103] S.D. Hujaya, G.S. Lorite, S.J. Vainio, H. Liimatainen, Polyion complex hydrogels from chemically modified cellulose nanofibrils: structure-function relationship and potential for controlled and pH-responsive release of doxorubicin, Acta Biomater. 75 (2018) 346–357, https://doi.org/10.1016/j.actbio.2018.06.013.
[104] W. Chen, Y. Bu, D. Li, C. Liu, G. Chen, X. Wan, N. Li, High-strength, tough, and self-healing hydrogel based on carboxymethyl cellulose, Cellulose 27 (2) (2019) 853–865, https://doi.org/10.1007/s10570-019-02797-z.
[105] J. Skopinska-Wisniewska, S. De la Flor, J. Kozlowska, From supramolecular hydrogels to multifunctional carriers for biologically active substances, Int. J. Mol. Sci. 22 (14) (2021), https://doi.org/10.3390/ijms22147402.
[106] S. Li, Y. Gao, H. Jiang, L. Duan, G. Gao, Tough, sticky and remoldable hydrophobic association hydrogel regulated by polysaccharide and sodium dodecyl sulfate as emulsifiers, Carbohydr. Polym. 201 (2018) 591–598, https://doi.org/10.1016/j.carbpol.2018.08.100.
[107] C. Liu, Y. Wang, S. Shi, Y. Zheng, Z. Ye, J. Liao, Q. Sun, B. Dang, X. Shen, Myelin sheath-inspired hydrogel electrode for artificial skin and physiological monitoring, ACS Nano 18 (40) (2024) 27420–27432, https://doi.org/10.1021/acsnano.4c07677.
[108] Y.H. Zhang, C.S. Liu, Y. Tian, J. Wang, S. Xin, X. Sheng, An eco-friendly photo-responsive hyaluronic acid-based supramolecular polysaccharide hybrid hydrogels for plant growth regulation and heavy metal ions adsorption, Int. J. Biol. Macromol. 242 (Pt 4) (2023) 125194, https://doi.org/10.1016/j.ijbiomac.2023.125194.
[109] C. Qi, J. Liu, Y. Jin, L. Xu, G. Wang, Z. Wang, L. Wang, Photo-crosslinkable, injectable sericin hydrogel as 3D biomimetic extracellular matrix for minimally invasive repairing cartilage, Biomaterials 163 (2018) 89–104, https://doi.org/10.1016/j.biomaterials.2018.02.016.
[110] W. Shen, P. Pei, C. Zhang, J. Li, X. Han, T. Liu, X. Shi, Z. Su, G. Han, L. Hu, K. Yang, A polymeric hydrogel to eliminate programmed death-ligand 1 for enhanced tumor radio-immunotherapy, ACS Nano 17 (23) (2023) 23998–24011, https://doi.org/10.1021/acsnano.3c08875.
[111] M.N. Alam, M.S. Islam, L.P. Christopher, Sustainable production of cellulose-based hydrogels with superb absorbing potential in physiological saline, ACS Omega 4 (5) (2019) 9419–9426, https://doi.org/10.1021/acsomega.9b00651.
[112] M. Wang, O.J. Rojas, L. Ning, Y. Li, X. Niu, X. Shi, H. Qi, Liquid metal and Mxene enable self-healing soft electronics based on double networks of bacterial cellulose hydrogels, Carbohydr. Polym. 301 (Pt A) (2023) 120330, https://doi.org/10.1016/j.carbpol.2022.120330.
[113] Q. Wang, W. Xu, R. Koppolu, B. van Bochove, J. Seppälä, L. Hupa, S. Willför, C. Xu, X. Wang, Injectable thiol-ene hydrogel of galactoglucomannan and cellulose nanocrystals in delivery of therapeutic inorganic ions with embedded bioactive glass nanoparticles, Carbohydr. Polym. 276 (2022) 118780, https://doi.org/10.1016/j.carbpol.2021.118780.
[114] H. Dupont, V. Héroguez, V. Schmitt, Elaboration of capsules from Pickering double emulsion polymerization stabilized solely by cellulose nanocrystals, Carbohydr. Polym. 279 (2022) 118997, https://doi.org/10.1016/j.carbpol.2021.118997.
[115] X. Yu, J. Ji, Q.Y. Wu, L. Gu, Direct-coating of cellulose hydrogel on PVDF membranes with superhydrophilic and antifouling properties for high-efficiency oil/water emulsion separation, Int. J. Biol. Macromol. 256 (Pt 2) (2024) 128579, https://doi.org/10.1016/j.ijbiomac.2023.128579.
[116] R.R. Huerta, E.K. Silva, T. El-Bialy, M.D.A. Saldaña, Clove essential oil emulsion-filled cellulose nanofiber hydrogel produced by high-intensity ultrasound technology for tissue engineering applications, Ultrason. Sonochem. 64 (2020) 104845, https://doi.org/10.1016/j.ultsonch.2019.104845.
[117] H. Yin, P. Song, X. Chen, Q. Huang, H. Huang, A self-healing hydrogel based on oxidized microcrystalline cellulose and carboxymethyl chitosan as wound dressing material, Int. J. Biol. Macromol. 221 (2022) 1606–1617, https://doi.org/10.1016/j.ijbiomac.2022.09.060.
[118] J. Cavalcante, D.G. Oldal, M.V. Peskov, A.K. Beke, R. Hardian, U. Schwingenschlögl, G. Szekely, Biobased interpenetrating polymer network membranes for sustainable molecular sieving, ACS Nano 18 (10) (2024) 7433–7443, https://doi.org/10.1021/acsnano.3c10827.
[119] J. Wu, W. Xue, Z. Yun, Q. Liu, X. Sun, Biomedical applications of stimuli-responsive "smart" interpenetrating polymer network hydrogels, Mater. Today Bio 25 (2024) 100998, https://doi.org/10.1016/j.mtbio.2024.100998.
[120] A.P. Dhand, J.H. Galarraga, J.A. Burdick, Enhancing biopolymer hydrogel functionality through interpenetrating networks, Trends Biotechnol. 39 (5) (2021) 519–538, https://doi.org/10.1016/j.tibtech.2020.08.007.
[121] P.V.O. Toledo, D.P.C. Limeira, N.C. Siqueira, D.F.S. Petri, Carboxymethyl cellulose/poly(acrylic acid) interpenetrating polymer network hydrogels as multifunctional adsorbents, Cellulose 26 (1) (2019) 597–615, https://doi.org/10.1007/s10570-018-02232-9.
[122] Y. Yue, J. Han, G. Han, A.D. French, Y. Qi, Q. Wu, Cellulose nanofibers reinforced sodium alginate-polyvinyl alcohol hydrogels: core-shell structure formation and property characterization, Carbohydr. Polym. 147 (2016) 155–164, https://doi.org/10.1016/j.carbpol.2016.04.005.
[123] P. Wei, X. Yu, Y. Fang, L. Wang, H. Zhang, C. Zhu, J. Cai, Strong and tough cellulose hydrogels via solution annealing and dual cross-linking, Small 19 (28) (2023) e2301204, https://doi.org/10.1002/smll.202301204.
[124] J. Yang, C.R. Han, F. Xu, R.C. Sun, Simple approach to reinforce hydrogels with cellulose nanocrystals, Nanoscale 6 (11) (2014) 5934–5943, https://doi.org/10.1039/c4nr01214c.

[125] A. Ghilan, L.E. Nita, D. Pamfil, N. Simionescu, N. Tudorachi, D. Rusu, A.G. Rusu, M. Bercea, I. Rosca, D.E. Ciolacu, A.P. Chiriac, One-step preparation of carboxymethyl cellulose-phytic acid hydrogels with potential for biomedical applications, Gels 8 (10) (2022), https://doi.org/10.3390/gels8100647.
[126] S. Radoor, J. Karayil, A. Jayakumar, D.R. Kandel, J.T. Kim, S. Siengchin, J. Lee, Recent advances in cellulose- and alginate-based hydrogels for water and wastewater treatment: a review, Carbohydr. Polym. 323 (2024) 121339, https://doi.org/10.1016/j.carbpol.2023.121339.
[127] J. Wu, X. Wu, F. Yang, X. Liu, F. Meng, Q. Ma, Y. Che, Multiply cross-linked poly (vinyl alcohol)/cellulose nanofiber composite ionic conductive hydrogels for strain sensors, Int. J. Biol. Macromol. 225 (2023) 1119–1128, https://doi.org/10.1016/j.ijbiomac.2022.11.173.
[128] N. Peng, Y. Wang, Q. Ye, L. Liang, Y. An, Q. Li, C. Chang, Biocompatible cellulose-based superabsorbent hydrogels with antimicrobial activity, Carbohydr. Polym. 137 (2016) 59–64, https://doi.org/10.1016/j.carbpol.2015.10.057.
[129] J. Liu, Q. Li, Y. Su, Q. Yue, B. Gao, Characterization and swelling-deswelling properties of wheat straw cellulose based semi-IPNs hydrogel, Carbohydr. Polym. 107 (2014) 232–240, https://doi.org/10.1016/j.carbpol.2014.02.073.
[130] A.W.M. El-Naggar, M.M. Senna, T.A. Mostafa, R.H. Helal, Radiation synthesis and drug delivery properties of interpenetrating networks (IPNs) based on poly(vinyl alcohol)/methylcellulose blend hydrogels, Int. J. Biol. Macromol. 102 (2017) 1045–1051, https://doi.org/10.1016/j.ijbiomac.2017.04.084.
[131] N. Naseri, B. Deepa, A.P. Mathew, K. Oksman, L. Girandon, Nanocellulose-based interpenetrating polymer network (IPN) hydrogels for cartilage applications, Biomacromolecules 17 (11) (2016) 3714–3723, https://doi.org/10.1021/acs.biomac.6b01243.
[132] C. Ouyang, H. Yu, L. Wang, Z. Ni, X. Liu, D. Shen, J. Yang, K. Shi, H. Wang, Tough adhesion enhancing strategies for injectable hydrogel adhesives in biomedical applications, Adv. Colloid Interface Sci. 319 (2023) 102982, https://doi.org/10.1016/j.cis.2023.102982.
[133] H.G. Oliveira Barud, S. Barud Hda, M. Cavicchioli, T.S. do Amaral, O.B. de Oliveira Junior, D.M. Santos, A.L. Petersen, F. Celes, V.M. Borges, C.I. de Oliveira, P.F. de Oliveira, R.A. Furtado, D.C. Tavares, S.J. Ribeiro, Preparation and characterization of a bacterial cellulose/silk fibroin sponge scaffold for tissue regeneration, Carbohydr. Polym. 128 (2015) 41–51, https://doi.org/10.1016/j.carbpol.2015.04.007.
[134] S.H. Aswathy, U. NarendraKumar, I. Manjubala, Physicochemical properties of cellulose-based hydrogel for biomedical applications, Polymers 14 (21) (2022), https://doi.org/10.3390/polym14214669.
[135] E. Guamba, N.S. Vispo, D.C. Whitehead, A.K. Singh, R. Santos-Oliveira, D. Niebieskikwiat, C. Zamora-Ledezma, F. Alexis, Cellulose-based hydrogels towards an antibacterial wound dressing, Biomater. Sci. (2022), https://doi.org/10.1039/d2bm01369j.
[136] L. Jaiswal, S. Shankar, J.W. Rhim, Carrageenan-based functional hydrogel film reinforced with sulfur nanoparticles and grapefruit seed extract for wound healing application, Carbohydr. Polym. 224 (2019) 115191, https://doi.org/10.1016/j.carbpol.2019.115191.
[137] Y. Yang, W. Nan, R. Zhang, S. Shen, M. Wu, S. Zhong, Y. Zhang, X. Cui, Fabrication of carboxymethyl cellulose-based thermo-sensitive hydrogels and inhibition of corneal neovascularization, Int. J. Biol. Macromol. 261 (Pt 2) (2024) 129933, https://doi.org/10.1016/j.ijbiomac.2024.129933.
[138] M. Bilal, H.M.N. Iqbal, S.F. Adil, M.R. Shaik, A. Abdelgawad, M.R. Hatshan, M. Khan, Surface-coated magnetic nanostructured materials for robust bio-catalysis and biomedical applications-A review, J. Adv. Res. 38 (2022) 157–177, https://doi.org/10.1016/j.jare.2021.09.013.
[139] M.P.H. Pedige, T.A. Asoh, Y.I. Hsu, H. Uyama, Stimuli-responsive composite hydrogels with three-dimensional stability prepared using oxidized cellulose nanofibers and chitosan, Carbohydr. Polym. 278 (2022) 118907, https://doi.org/10.1016/j.carbpol.2021.118907.
[140] N. Shahid, A. Erum, S. Hanif, N.S. Malik, U.R. Tulain, M.A. Syed, Nanocomposite hydrogels-A promising approach towards enhanced bioavailability and controlled drug delivery, Curr. Pharm. Des. 30 (1) (2024) 48–62, https://doi.org/10.2174/0113816128283466231219071151.
[141] R. Nasseri, N. Bouzari, J. Huang, H. Golzar, S. Jankhani, X.S. Tang, T. H. Mekonnen, A. Aghakhani, H. Shahsavan, Programmable nanocomposites of cellulose nanocrystals and zwitterionic hydrogels for soft robotics, Nat. Commun. 14 (1) (2023) 6108, https://doi.org/10.1038/s41467-023-41874-7.
[142] Y. Yang, L. Sha, H. Zhao, Z. Guo, M. Wu, P. Lu, Recent advances in cellulose microgels: preparations and functionalized applications, Adv. Colloid Interface Sci. 311 (2023) 102815, https://doi.org/10.1016/j.cis.2022.102815.
[143] N. Chen, H. Wang, C. Ling, W. Vermerris, B. Wang, Z. Tong, Cellulose-based injectable hydrogel composite for pH-responsive and controllable drug delivery, Carbohydr. Polym. 225 (2019) 115207, https://doi.org/10.1016/j.carbpol.2019.115207.
[144] M. Tsirigotis-Maniecka, L. Szyk-Warszyńska, Ł. Lamch, J. Wężgowiec, P. Warszyński, K.A. Wilk, Benefits of pH-responsive polyelectrolyte coatings for carboxymethyl cellulose-based microparticles in the controlled release of esculin, Mater Sci Eng C Mater Biol Appl 118 (2021) 111397, https://doi.org/10.1016/j.msec.2020.111397.
[145] G. Yang, Z. Zhang, K. Liu, X. Ji, P. Fatehi, J. Chen, A cellulose nanofibril-reinforced hydrogel with robust mechanical, self-healing, pH-responsive and antibacterial characteristics for wound dressing applications, J. Nanobiotechnol. 20 (1) (2022) 312, https://doi.org/10.1186/s12951-022-01523-5.
[146] H.E. Emam, T.I. Shaheen, Design of a dual pH and temperature responsive hydrogel based on esterified cellulose nanocrystals for potential drug release, Carbohydr. Polym. 278 (2022) 118925, https://doi.org/10.1016/j.carbpol.2021.118925.
[147] X. Wang, Y. Yang, H. Huang, K. Zhang, Temperature-responsive, manipulable cavitary hydrogel containers by macroscopic spatial surface-interior separation, ACS Appl. Mater. Interfaces 13 (1) (2021) 1573–1580, https://doi.org/10.1021/acsami.0c19448.
[148] W. Liu, B. Zhang, W.W. Lu, X. Li, D. Zhu, K. De Yao, Q. Wang, C. Zhao, C. Wang, A rapid temperature-responsive sol-gel reversible poly(N-isopropylacrylamide)-g-methylcellulose copolymer hydrogel, Biomaterials 25 (15) (2004) 3005–3012, https://doi.org/10.1016/j.biomaterials.2003.09.077.
[149] Z. Bian, Y. Li, H. Sun, M. Shi, Y. Zheng, H. Liu, C. Liu, C. Shen, Transparent, intrinsically stretchable cellulose nanofiber-mediated conductive hydrogel for strain and humidity sensing, Carbohydr. Polym. 301 (Pt A) (2023) 120300, https://doi.org/10.1016/j.carbpol.2022.120300.
[150] W. Zeng, C. Jiang, D. Wu, Heterogeneity regulation of bilayer polysaccharide hydrogels for integrating pH- and humidity-responsive actuators and sensors, ACS Appl. Mater. Interfaces 15 (12) (2023) 16097–16108, https://doi.org/10.1021/acsami.3c01244.
[151] J. Yu, Y. Feng, D. Sun, W. Ren, C. Shao, R. Sun, Highly conductive and mechanically robust cellulose nanocomposite hydrogels with antifreezing and antidehydration performances for flexible humidity sensors, ACS Appl. Mater. Interfaces 14 (8) (2022) 10886–10897, https://doi.org/10.1021/acsami.2c00513.
[152] B. Li, Y. Chen, W. Wu, X. Cao, Z. Luo, Copolymer-grafted cellulose nanocrystal induced nanocomposite hydrogels with enhanced strength, high elasticity and adhesiveness for flexible strain and pressure sensors, Carbohydr. Polym. 317 (2023) 121092, https://doi.org/10.1016/j.carbpol.2023.121092.
[153] M. Chen, H. Wan, Y. Hu, F. Zhao, X. An, A. Lu, Rationally designed cellulose hydrogel for an ultrasensitive pressure sensor, Mater. Horiz. 10 (10) (2023) 4510–4520, https://doi.org/10.1039/d3mh01051a.
[154] Y. Li, P. Ren, Z. Sun, R. Xue, D. Ding, W. Tian, F. Ren, Y. Jin, Z. Chen, G. Zhu, High-strength, anti-fatigue, cellulose nanofiber reinforced polyvinyl alcohol based ionic conductive hydrogels for flexible strain/pressure sensors and triboelectric nanogenerators, J. Colloid Interface Sci. 669 (2024) 248–257, https://doi.org/10.1016/j.jcis.2024.05.011.
[155] Z. Zhang, Z. Chen, Y. Wang, Y. Zhao, Bioinspired conductive cellulose liquid-crystal hydrogels as multifunctional electrical skins, Proc. Natl. Acad. Sci. U. S. A. 117 (31) (2020) 18310–18316, https://doi.org/10.1073/pnas.2007032117.
[156] B. Wan, N. Liu, Z. Zhang, X. Fang, Y. Ding, H. Xiang, Y. He, M. Liu, X. Lin, J. Tang, Y. Li, B. Tang, G. Zhou, Water-dispersible and stable polydopamine coated cellulose nanocrystal-MXene composites for high transparent, adhesive and conductive hydrogels, Carbohydr. Polym. 314 (2023) 120929, https://doi.org/10.1016/j.carbpol.2023.120929.
[157] C. Qian, T. Higashigaki, T.A. Asoh, H. Uyama, Anisotropic conductive hydrogels with high water content, ACS Appl. Mater. Interfaces 12 (24) (2020) 27518–27525, https://doi.org/10.1021/acsami.0c06853.
[158] R. Raho, N.Y. Nguyen, N. Zhang, W. Jiang, A. Sannino, H. Liu, M. Pollini, F. Paladini, Photo-assisted green synthesis of silver doped silk fibroin/carboxymethyl cellulose nanocomposite hydrogels for biomedical applications, Mater Sci Eng C Mater Biol Appl 107 (2020) 110219, https://doi.org/10.1016/j.msec.2019.110219.
[159] Y. Fan, Z. Yue, E. Lucarelli, G.G. Wallace, Hybrid printing using cellulose nanocrystals reinforced GelMA/HAMA hydrogels for improved structural integration, Adv. Healthc. Mater. 9 (24) (2020) e2001410, https://doi.org/10.1002/adhm.202001410.
[160] S.L. Arias, A. Shetty, J. Devorkin, J.P. Allain, Magnetic targeting of smooth muscle cells in vitro using a magnetic bacterial cellulose to improve cell retention in tissue-engineering vascular grafts, Acta Biomater. 77 (2018) 172–181, https://doi.org/10.1016/j.actbio.2018.07.013.
[161] J.G. Roth, L.G. Brunel, M.S. Huang, Y. Liu, B. Cai, S. Sinha, F. Yang, S.P. Paşca, S. Shin, S.C. Heilshorn, Spatially controlled construction of assembloids using bioprinting, Nat. Commun. 14 (1) (2023) 4346, https://doi.org/10.1038/s41467-023-40006-5.
[162] F. Halouane, Y. Oz, D. Meziane, A. Barras, J. Juraszek, S.K. Singh, S. Kurungot, P. K. Shaw, R. Sanyal, R. Boukherroub, A. Sanyal, S. Szunerits, Magnetic reduced graphene oxide loaded hydrogels: highly versatile and efficient adsorbents for dyes and selective Cr(VI) ions removal, J. Colloid Interface Sci. 507 (2017) 360–369, https://doi.org/10.1016/j.jcis.2017.07.075.
[163] Z. Rao, Y. Dong, J. Liu, X. Zheng, Y. Pei, K. Tang, Genipin-crosslinked gelatin-based composite hydrogels reinforced with amino-functionalized microfibrillated cellulose, Int. J. Biol. Macromol. 222 (Pt B) (2022) 3155–3167, https://doi.org/10.1016/j.ijbiomac.2022.10.088.
[164] R.M. Abdelaziz, A. El-Maghraby, W.A. Sadik, A.M. El-Demerdash, E.A. Fadl, Biodegradable cellulose nanocrystals hydrogels for removal of acid red 8 dye from aqueous solutions, Sci. Rep. 12 (1) (2022) 6424, https://doi.org/10.1038/s41598-022-10087-1.
[165] S.D. Al-Qahtani, G.M. Al-Senani, M. Alrasheedi, A. Mohammed, Multi-stimuli responsive viologen-imprinted polyvinyl alcohol and tricarboxy cellulose nanocomposite hydrogels, Sensors (Basel) 24 (21) (2024), https://doi.org/10.3390/s24216860.
[166] X. Liu, Y. Zhang, Y. Liu, S. Hua, F. Meng, Q. Ma, L. Kong, S. Pan, Y. Che, Injectable, self-healable and antibacterial multi-responsive tunicate cellulose nanocrystals strengthened supramolecular hydrogels for wound dressings, Int. J. Biol. Macromol. 240 (2023) 124365, https://doi.org/10.1016/j.ijbiomac.2023.124365.

[167] Y. Sheng, J. Gao, Z.Z. Yin, J. Kang, Y. Kong, Dual-drug delivery system based on the hydrogels of alginate and sodium carboxymethyl cellulose for colorectal cancer treatment, Carbohydr. Polym. 269 (2021) 118325, https://doi.org/10.1016/j.carbpol.2021.118325.
[168] B. Zhang, C. Hu, M. Wang, H. Wei, S. Li, H. Yu, Y. Wu, G. Wang, T. Guo, H. Chen, Facile fabrication of a thermal/pH responsive IPN hydrogel drug carrier based on cellulose and chitosan through simultaneous dual-click strategy, J. Colloid Interface Sci. 678 (Pt A) (2025) 827–841, https://doi.org/10.1016/j.jcis.2024.08.208.
[169] Y. Wang, H. Shaghaleh, Y.A. Hamoud, S. Zhang, P. Li, X. Xu, H. Liu, Synthesis of a pH-responsive nano-cellulose/sodium alginate/MOFs hydrogel and its application in the regulation of water and N-fertilizer, Int. J. Biol. Macromol. 187 (2021) 262–271, https://doi.org/10.1016/j.ijbiomac.2021.07.154.
[170] Y. Wang, Z. Wang, K. Wu, J. Wu, G. Meng, Z. Liu, X. Guo, Synthesis of cellulose-based double-network hydrogels demonstrating high strength, self-healing, and antibacterial properties, Carbohydr. Polym. 168 (2017) 112–120, https://doi.org/10.1016/j.carbpol.2017.03.070.
[171] İ. Tarhanlı, E. Senses, Cellulose nanocrystal and Pluronic L121-based thermo-responsive composite hydrogels, Carbohydr. Polym. 321 (2023) 121281, https://doi.org/10.1016/j.carbpol.2023.121281.
[172] L. Moradi, L. Witek, V. Vivekanand Nayak, A. Cabrera Pereira, E. Kim, J. Good, C. J. Liu, Injectable hydrogel for sustained delivery of progranulin derivative Atsttrin in treating diabetic fracture healing, Biomaterials 301 (2023) 122289, https://doi.org/10.1016/j.biomaterials.2023.122289.
[173] Q. Sun, S. Tao, G. Bovone, G. Han, D. Deshmukh, M.W. Tibbitt, Q. Ren, P. Bertsch, G. Siqueira, P. Fischer, Versatile mechanically tunable hydrogels for therapeutic delivery applications, Adv. Healthc. Mater. 13 (18) (2024) e2304287, https://doi.org/10.1002/adhm.202304287.
[174] Y. Zhou, Y. He, S. Zhao, S. Qi, L. Wang, Y. Niu, Q. Xu, C. Xu, J. Wang, Multi-gradient energy-saving smart windows with thermo-response and multimodal thermal energy storage, Mater. Horiz. (2024), https://doi.org/10.1039/d4mh01259c.
[175] J. Zhang, L. Zeng, Z. Qiao, J. Wang, X. Jiang, Y.S. Zhang, H. Yang, Functionalizing double-network hydrogels for applications in remote actuation and in low-temperature strain sensing, ACS Appl. Mater. Interfaces 12 (27) (2020) 30247–30258, https://doi.org/10.1021/acsami.0c10430.
[176] K.F. Chen, Y. Zhang, J. Lin, J.Y. Chen, C. Lin, M. Gao, Y. Chen, S. Liu, L. Wang, Z. K. Cui, Y.G. Jia, Upper critical solution temperature polyvalent scaffolds aggregate and exterminate bacteria, Small 18 (11) (2022) e2107374, https://doi.org/10.1002/smll.202107374.
[177] Z. You, Y. Dong, X. Li, P. Yang, M. Luo, Z. Zhu, L. Wu, X. Zhou, M. Chen, One-pot synthesis of multi-functional cellulose-based ionic conductive organohydrogel with low-temperature strain sensitivity, Carbohydr. Polym. 251 (2021) 117019, https://doi.org/10.1016/j.carbpol.2020.117019.
[178] Z. Chen, J. Liu, Y. Chen, X. Zheng, H. Liu, H. Li, Multiple-stimuli-responsive and cellulose conductive ionic hydrogel for smart wearable devices and thermal actuators, ACS Appl. Mater. Interfaces 13 (1) (2021) 1353–1366, https://doi.org/10.1021/acsami.0c16719.
[179] R. Curvello, D. Alves, H.E. Abud, G. Garnier, A thermo-responsive collagen-nanocellulose hydrogel for the growth of intestinal organoids, Mater Sci Eng C Mater Biol Appl 124 (2021) 112051, https://doi.org/10.1016/j.msec.2021.112051.
[180] Z. Han, H. Zhu, J.H. Cheng, Constructing a novel humidity sensor using acrylic acid/bagasse cellulose porous hydrogel combining graphene oxide and citral for antibacterial and intelligent fruit preservation, Carbohydr. Polym. 326 (2024) 121639, https://doi.org/10.1016/j.carbpol.2023.121639.
[181] L. Cui, W. Wang, J. Zheng, C. Hu, Z. Zhu, B. Liu, Wide-humidity, anti-freezing and stretchable multifunctional conductive carboxymethyl cellulose-based hydrogels for flexible wearable strain sensors and arrays, Carbohydr. Polym. 342 (2024) 122406, https://doi.org/10.1016/j.carbpol.2024.122406.
[182] K. Ganguly, S.D. Dutta, A. Randhawa, D.K. Patel, T.V. Patil, K.T. Lim, Transcriptomic changes toward osteogenic differentiation of mesenchymal stem cells on 3D-printed GelMA/CNC hydrogel under pulsatile pressure environment, Adv. Healthc. Mater. 12 (11) (2023) e2202163, https://doi.org/10.1002/adhm.202202163.
[183] J. Wang, J. Shu, H. Liu, D. Ren, J. Song, T. Zhang, Z. Li, Y. Huang, Y. Huang, Flexible capacitive pressure sensor with high sensitivity and wide detection range applying solvent-exchanged porous lignin-cellulose hydrogel as the dielectric layer, Int. J. Biol. Macromol. 303 (2025) 140702, https://doi.org/10.1016/j.ijbiomac.2025.140702.
[184] H. Wang, Z. Li, M. Zuo, X. Zeng, X. Tang, Y. Sun, L. Lin, Stretchable, freezing-tolerant conductive hydrogel for wearable electronics reinforced by cellulose nanocrystals toward multiple hydrogen bonding, Carbohydr. Polym. 280 (2022) 119018, https://doi.org/10.1016/j.carbpol.2021.119018.
[185] P. Rahmani, A. Shojaei, T. Sakorikar, M. Wang, Y. Mendoza-Apodaca, M. D. Dickey, Liquid metal nanoparticles physically hybridized with cellulose nanocrystals initiate and toughen hydrogels with piezoionic properties, ACS Nano 18 (11) (2024) 8038–8050, https://doi.org/10.1021/acsnano.3c11063.
[186] X. Dang, Y. Fu, X. Wang, A temperature and pressure dual-responsive, stretchable, healable, adhesive, and biocompatible carboxymethyl cellulose-based conductive hydrogels for flexible wearable strain sensor, Biosens. Bioelectron. 246 (2024) 115893, https://doi.org/10.1016/j.bios.2023.115893.
[187] E.K. Gebeyehu, X. Sui, B.F. Adamu, K.A. Beyene, M.G. Tadesse, Cellulosic-based conductive hydrogels for electro-active tissues: a review summary, Gels 8 (3) (2022), https://doi.org/10.3390/gels8030140.
[188] H. Zhang, X. Gan, Z. Song, J. Zhou, Amphoteric cellulose-based double-network hydrogel electrolyte toward ultra-stable Zn anode, Angew Chem. Int. Ed. Engl. 62 (13) (2023) e202217833, https://doi.org/10.1002/anie.202217833.
[189] S. Huang, S. Shuyi, H. Gan, W. Linjun, C. Lin, X. Danyuan, H. Zhou, X. Lin, Y. Qin, Facile fabrication and characterization of highly stretchable lignin-based hydroxyethyl cellulose self-healing hydrogel, Carbohydr. Polym. 223 (2019) 115080, https://doi.org/10.1016/j.carbpol.2019.115080.
[190] X. Li, Q. Luo, M. Shen, S. Yao, S. Ren, F. Jiang, Z. Zhou, T. Lei, L. Dai, A novel electrocatalyst from TOCN/CGG hydrogel-supported Fe-rich sludge and its performance in treating azo dyes-contaminated water, Carbohydr. Polym. 346 (2024) 122669, https://doi.org/10.1016/j.carbpol.2024.122669.
[191] L. Yue, X. Zhang, Y. Wang, W. Li, Y. Tang, Y. Bai, Cellulose nanocomposite modified conductive self-healing hydrogel with enhanced mechanical property, Eur. Polym. J. 146 (2021), https://doi.org/10.1016/j.eurpolymj.2020.110258.
[192] Y. Li, H. Cao, W. Liu, P. Liu, Effective degradation of tetracycline via recyclable cellulose nanofibrils/polyvinyl alcohol/Fe(3)O(4) hybrid hydrogel as a photo-Fenton catalyst, Chemosphere 307 (Pt 1) (2022) 135665, https://doi.org/10.1016/j.chemosphere.2022.135665.
[193] C. Sang, S. Wang, X. Jin, X. Cheng, H. Xiao, Y. Yue, J. Han, Nanocellulose-mediated conductive hydrogels with NIR photoresponse and fatigue resistance for multifunctional wearable sensors, Carbohydr. Polym. 333 (2024) 121947, https://doi.org/10.1016/j.carbpol.2024.121947.
[194] L. Zhang, L. Chen, S. Wang, S. Wang, D. Wang, L. Yu, X. Xu, H. Liu, C. Chen, Cellulose nanofiber-mediated manifold dynamic synergy enabling adhesive and photo-detachable hydrogel for self-powered E-skin, Nat. Commun. 15 (1) (2024) 3859, https://doi.org/10.1038/s41467-024-47986-y.
[195] Y. Kim, D. Jeong, V.V. Shinde, Y. Hu, C. Kim, S. Jung, Azobenzene-grafted carboxymethyl cellulose hydrogels with photo-switchable, reduction-responsive and self-healing properties for a controlled drug release system, Int. J. Biol. Macromol. 163 (2020) 824–832, https://doi.org/10.1016/j.ijbiomac.2020.07.071.
[196] P. Aravind, V. Subramanyan, S. Ferro, R. Gopalakrishnan, Eco-friendly and facile integrated biological-cum-photo assisted electrooxidation process for degradation of textile wastewater, Water Res. 93 (2016) 230–241, https://doi.org/10.1016/j.watres.2016.02.041.
[197] F. Lin, J. Zheng, W. Guo, Z. Zhu, Z. Wang, B. Dong, C. Lin, B. Huang, B. Lu, Smart cellulose-derived magnetic hydrogel with rapid swelling and deswelling properties for remotely controlled drug release, Cellulose 26 (11) (2019) 6861–6877, https://doi.org/10.1007/s10570-019-02572-0.
[198] J. Kim, A.S. Campbell, B.E. de Ávila, J. Wang, Wearable biosensors for healthcare monitoring, Nat. Biotechnol. 37 (4) (2019) 389–406, https://doi.org/10.1038/s41587-019-0045-y.
[199] M.L. Sin, K.E. Mach, P.K. Wong, J.C. Liao, Advances and challenges in biosensor-based diagnosis of infectious diseases, Expert Rev. Mol. Diagn 14 (2) (2014) 225–244, https://doi.org/10.1586/14737159.2014.888313.
[200] X. Chen, F. Wang, J.Y. Hyun, T. Wei, J. Qiang, X. Ren, I. Shin, J. Yoon, Recent progress in the development of fluorescent, luminescent and colorimetric probes for detection of reactive oxygen and nitrogen species, Chem. Soc. Rev. 45 (10) (2016) 2976–3016, https://doi.org/10.1039/c6cs00192k.
[201] J. Chen, Y. Huang, P. Kannan, L. Zhang, Z. Lin, J. Zhang, T. Chen, L. Guo, Flexible and adhesive surface enhance Raman scattering active tape for rapid detection of pesticide residues in fruits and vegetables, Anal Chem. 88 (4) (2016) 2149–2155, https://doi.org/10.1021/acs.analchem.5b03735.
[202] J. Hai, X. Zeng, Y. Zhu, B. Wang, Anions reversibly responsive luminescent nanocellulose hydrogels for cancer spheroids culture and release, Biomaterials 194 (2019) 161–170, https://doi.org/10.1016/j.biomaterials.2018.12.016.
[203] J. Hai, T. Li, J. Su, W. Liu, Y. Ju, B. Wang, Y. Hou, Reversible response of luminescent terbium(III)-Nanocellulose hydrogels to anions for latent fingerprint detection and encryption, Angew Chem. Int. Ed. Engl. 57 (23) (2018) 6786–6790, https://doi.org/10.1002/anie.201800119.
[204] A. Grada, M. Otero-Vinas, F. Prieto-Castrillo, Z. Obagi, V. Falanga, Research techniques made simple: analysis of collective cell migration using the wound healing assay, J. Invest. Dermatol. 137 (2) (2017) e11–e16, https://doi.org/10.1016/j.jid.2016.11.020.
[205] M.M. Al-Rajabi, Y.H. Teow, Synthesis of thermoresponsive composite hydrogel from Pluronic F127 reinforced by oil palm empty fruit bunches-extracted cellulose for silver sulfadiazine drug delivery, Sustain. Chem. Pharm. 31 (2023), https://doi.org/10.1016/j.scp.2022.100939.
[206] N. Bagheri, M. Mansour Lakouraj, V. Hasantabar, M. Mohseni, Biodegradable macro-porous CMC-polyaniline hydrogel: synthesis, characterization and study of microbial elimination and sorption capacity of dyes from waste water, J. Hazard Mater. 403 (2021) 123631, https://doi.org/10.1016/j.jhazmat.2020.123631.
[207] W. Yuan, H. Zou, J. Shen, Amphiphilic graft copolymers with ethyl cellulose backbone: synthesis, self-assembly and tunable temperature-CO2 response, Carbohydr. Polym. 136 (2016) 216–223, https://doi.org/10.1016/j.carbpol.2015.09.052.
[208] Y. Wang, A. Yao, H. Zhong, Y. Mo, H. Zhang, J. Shang, J. Lan, W. Fan, X. Chen, S. Lin, Silver nanoparticle-decorated cellulose nanocrystal reinforced ionic polymer hydrogel with high conductivity and environmental tolerance for multifunctional sensing and emergency alarm system, Small (2024) e2405826, https://doi.org/10.1002/smll.202405826.
[209] M. Sreedharan, R. Vijayamma, E. Liyaskina, V.V. Revin, M.W. Ullah, Z. Shi, G. Yang, Y. Grohens, N. Kalarikkal, K. Ali Khan, S. Thomas, Nanocellulose-based hybrid scaffolds for skin and bone tissue engineering: a 10-year overview, Biomacromolecules 25 (4) (2024) 2136–2155, https://doi.org/10.1021/acs.biomac.3c00975.

[210] X. Lan, Z. Ma, A.R.A. Szojka, M. Kunze, A. Mulet-Sierra, M.J. Vyhlidal, Y. Boluk, A.B. Adesida, TEMPO-oxidized cellulose nanofiber-alginate hydrogel as a bioink for human meniscus tissue engineering, Front. Bioeng. Biotechnol. 9 (2021) 766399, https://doi.org/10.3389/fbioe.2021.766399.
[211] R.J. Mondschein, A. Kanitkar, C.B. Williams, S.S. Verbridge, T.E. Long, Polymer structure-property requirements for stereolithographic 3D printing of soft tissue engineering scaffolds, Biomaterials 140 (2017) 170–188, https://doi.org/10.1016/j.biomaterials.2017.06.005.
[212] J. Yang, X. An, L. Liu, S. Tang, H. Cao, Q. Xu, H. Liu, Cellulose, hemicellulose, lignin, and their derivatives as multi-components of bio-based feedstocks for 3D printing, Carbohydr. Polym. 250 (2020) 116881, https://doi.org/10.1016/j.carbpol.2020.116881.
[213] R.E. Abouzeid, R. Khiari, D. Beneventi, A. Dufresne, Biomimetic mineralization of three-dimensional printed alginate/TEMPO-oxidized cellulose nanofibril scaffolds for bone tissue engineering, Biomacromolecules 19 (11) (2018) 4442–4452, https://doi.org/10.1021/acs.biomac.8b01325.
[214] L. Gravitz, Skin, Nature 563 (7732) (2018) S83, https://doi.org/10.1038/d41586-018-07428-4.
[215] R. Derwin, D. Patton, P. Avsar, H. Strapp, Z. Moore, The impact of topical agents and dressing on pH and temperature on wound healing: a systematic, narrative review, Int. Wound J. 19 (6) (2022) 1397–1408, https://doi.org/10.1111/iwj.13733.
[216] M. Suneetha, S.Y. Won, S.M. Zo, S.S. Han, Fungal carboxymethyl chitosan-impregnated bacterial cellulose hydrogel as wound-dressing agent, Gels 9 (3) (2023), https://doi.org/10.3390/gels9030184.
[217] C. Mao, Y. Xiang, X. Liu, Z. Cui, X. Yang, K.W.K. Yeung, H. Pan, X. Wang, P. K. Chu, S. Wu, Photo-inspired antibacterial activity and wound healing acceleration by hydrogel embedded with Ag/Ag@AgCl/ZnO nanostructures, ACS Nano 11 (9) (2017) 9010–9021, https://doi.org/10.1021/acsnano.7b03513.
[218] N. Li, X. Yang, W. Liu, G. Xi, M. Wang, B. Liang, Z. Ma, Y. Feng, H. Chen, C. Shi, Tannic acid cross-linked polysaccharide-based multifunctional hemostatic microparticles for the regulation of rapid wound healing, Macromol. Biosci. 18 (11) (2018) e1800209, https://doi.org/10.1002/mabi.201800209.
[219] M.F. Yazdanbakhsh, A. Rashidi, M.K. Rahimi, R. Khajavi, H. Shafaroodi, The effect of impregnated alpha-cellulose nanofibers with ciprofloxacin hydrochloride on Staphylococcus aureus in vitro and healing process of wound in rat, Regenerative Engineering and Translational Medicine 4 (4) (2018) 247–256, https://doi.org/10.1007/s40883-018-0066-y.
[220] Q. Zhu, Y. Jin, W. Wang, G. Sun, D. Wang, Bioinspired smart moisture actuators based on nanoscale cellulose materials and porous, hydrophilic EVOH nanofibrous membranes, ACS Appl. Mater. Interfaces 11 (1) (2019) 1440–1448, https://doi.org/10.1021/acsami.8b17538.
[221] A.E. Felber, M.H. Dufresne, J.C. Leroux, pH-sensitive vesicles, polymeric micelles, and nanospheres prepared with polycarboxylates, Adv. Drug Deliv. Rev. 64 (11) (2012) 979–992, https://doi.org/10.1016/j.addr.2011.09.006.
[222] Y. Liu, Y. Sui, C. Liu, C. Liu, M. Wu, B. Li, Y. Li, A physically crosslinked polydopamine/nanocellulose hydrogel as potential versatile vehicles for drug delivery and wound healing, Carbohydr. Polym. 188 (2018) 27–36, https://doi.org/10.1016/j.carbpol.2018.01.093.
[223] X. Shi, Z. Chen, Y. He, Q. Lu, R. Chen, C. Zhao, D. Dong, Y. Sun, H. He, Dual light-responsive cellulose nanofibril-based in situ hydrogel for drug-resistant bacteria infected wound healing, Carbohydr. Polym. 297 (2022) 120042, https://doi.org/10.1016/j.carbpol.2022.120042.
[224] G. Chinga-Carrasco, K. Syverud, Pretreatment-dependent surface chemistry of wood nanocellulose for pH-sensitive hydrogels, J. Biomater. Appl. 29 (3) (2014) 423–432, https://doi.org/10.1177/0885328214531511.
[225] A. Ho-Shui-Ling, J. Bolander, L.E. Rustom, A.W. Johnson, F.P. Luyten, C. Picart, Bone regeneration strategies: engineered scaffolds, bioactive molecules and stem cells current stage and future perspectives, Biomaterials 180 (2018) 143–162, https://doi.org/10.1016/j.biomaterials.2018.07.017.
[226] M. Walker, Skeleton keys in the phage world, Commun. Biol. 5 (1) (2022) 1195, https://doi.org/10.1038/s42003-022-04155-5.
[227] W. Talaat, S. Aryal Ac, S. Al Kawas, A.B.R. Samsudin, N.G. Kandile, D.R. K. Harding, M.M. Ghoneim, W. Zeiada, J. Jagal, A. Aboelnaga, M. Haider, Nanoscale thermosensitive hydrogel scaffolds promote the chondrogenic differentiation of dental pulp stem and progenitor cells: a minimally invasive approach for cartilage regeneration, Int J Nanomedicine 15 (2020) 7775–7789, https://doi.org/10.2147/ijn.S274418.
[228] B. Li, L. Zhang, D. Wang, F. Peng, X. Zhao, C. Liang, H. Li, H. Wang, Thermosensitive -hydrogel-coated titania nanotubes with controlled drug release and immunoregulatory characteristics for orthopedic applications, Mater Sci Eng C Mater Biol Appl 122 (2021) 111878, https://doi.org/10.1016/j.msec.2021.111878.
[229] Y. Wang, Z. Cheng, Z. Liu, H. Kang, Y. Liu, Cellulose nanofibers/polyurethane shape memory composites with fast water-responsivity, J. Mater. Chem. 6 (11) (2018) 1668–1677, https://doi.org/10.1039/c7tb03069j.
[230] H. Tohidi, N. Maleki, A. Simchi, Conductive, injectable, and self-healing collagen-hyaluronic acid hydrogels loaded with bacterial cellulose and gold nanoparticles for heart tissue engineering, Int. J. Biol. Macromol. 280 (Pt 2) (2024) 135749, https://doi.org/10.1016/j.ijbiomac.2024.135749.
[231] J. Wang, Q. Liu, J. Gong, Z. Wan, J. Zhou, C. Chang, D. Zhang, Micropatterned hydrogels with highly ordered cellulose nanocrystals for visually monitoring cardiomyocytes, Small 18 (45) (2022) e2202235, https://doi.org/10.1002/smll.202202235.
[232] Y.C. Yeh, W.Y. Lee, C.L. Yu, S.M. Hwang, M.F. Chung, L.W. Hsu, Y. Chang, W. W. Lin, M.S. Tsai, H.J. Wei, H.W. Sung, Cardiac repair with injectable cell sheet fragments of human amniotic fluid stem cells in an immune-suppressed rat model, Biomaterials 31 (25) (2010) 6444–6453, https://doi.org/10.1016/j.biomaterials.2010.04.069.
[233] F. Zheng, R. Li, Q. He, K. Koral, J. Tao, L. Fan, R. Xiang, J. Ma, N. Wang, Y. Yin, Z. Huang, P. Xu, H. Xu, The electrostimulation and scar inhibition effect of chitosan/oxidized hydroxyethyl cellulose/reduced graphene oxide/asiaticoside liposome based hydrogel on peripheral nerve regeneration in vitro, Mater Sci Eng C Mater Biol Appl 109 (2020) 110560, https://doi.org/10.1016/j.msec.2019.110560.
[234] Z. Siddiqui, B. Sarkar, K.K. Kim, N. Kadincesme, R. Paul, A. Kumar, Y. Kobayashi, A. Roy, M. Choudhury, J. Yang, E. Shimizu, V.A. Kumar, Angiogenic hydrogels for dental pulp revascularization, Acta Biomater. 126 (2021) 109–118, https://doi.org/10.1016/j.actbio.2021.03.001.
[235] W. Kong, C. Wang, C. Jia, Y. Kuang, G. Pastel, C. Chen, G. Chen, S. He, H. Huang, J. Zhang, S. Wang, L. Hu, Muscle-inspired highly anisotropic, strong, ion-conductive hydrogels, Adv. Mater. 30 (39) (2018) e1801934, https://doi.org/10.1002/adma.201801934.
[236] J. Lou, D.J. Mooney, Chemical strategies to engineer hydrogels for cell culture, Nat. Rev. Chem 6 (10) (2022) 726–744, https://doi.org/10.1038/s41570-022-00420-7.
[237] Z. Li, D. Zhu, Q. Hui, J. Bi, B. Yu, Z. Huang, S. Hu, Z. Wang, T. Caranasos, J. Rossi, X. Li, K. Cheng, X. Wang, Injection of ROS-responsive hydrogel loaded with basic fibroblast growth factor into the pericardial cavity for heart repair, Adv. Funct. Mater. 31 (15) (2021), https://doi.org/10.1002/adfm.202004377.
[238] A. Verma, B. Sharma, S. Kalia, W.F. Alsanie, S. Thakur, V.K. Thakur, Carboxymethyl cellulose based sustainable hydrogel for colon-specific delivery of gentamicin, Int. J. Biol. Macromol. 228 (2023) 773–782, https://doi.org/10.1016/j.ijbiomac.2022.12.249.
[239] S. Zong, H. Wen, H. Lv, T. Li, R. Tang, L. Liu, J. Jiang, S. Wang, J. Duan, Intelligent hydrogel with both redox and thermo-response based on cellulose nanofiber for controlled drug delivery, Carbohydr. Polym. 278 (2022) 118943, https://doi.org/10.1016/j.carbpol.2021.118943.
[240] K. Nakamura, R.J. Murray, J.I. Joseph, N.A. Peppas, M. Morishita, A.M. Lowman, Oral insulin delivery using P(MAA-g-EG) hydrogels: effects of network morphology on insulin delivery characteristics, J. Control. Release 95 (3) (2004) 589–599, https://doi.org/10.1016/j.jconrel.2003.12.022.
[241] M. Caldorera-Moore, K. Maass, R. Hegab, G. Fletcher, N. Peppas, Hybrid responsive hydrogel carriers for oral delivery of low molecular weight therapeutic agents, J. Drug Deliv. Sci. Technol. 30 (Pt B) (2015) 352–359, https://doi.org/10.1016/j.jddst.2015.07.023.
[242] L.H. Chen, P.S. Doyle, Design and use of a thermogelling methylcellulose nanoemulsion to formulate nanocrystalline oral dosage forms, Adv. Mater. 33 (29) (2021) e2008618, https://doi.org/10.1002/adma.202008618.
[243] Y. Li, X. Wu, Q. Zhu, Z. Chen, Y. Lu, J. Qi, W. Wu, Improving the hypoglycemic effect of insulin via the nasal administration of deep eutectic solvents, Int. J. Pharm. 569 (2019) 118584, https://doi.org/10.1016/j.ijpharm.2019.118584.
[244] S. Castellani, R. Mallamaci, E. De Giglio, A. Caponio, L. Guerra, G. Fracchiolla, G. Trapani, K. Kristan, R.A. Cardone, G. Passantino, N. Zizzo, G. Franzino, D. Larobina, A. Trapani, M. Conese, Slightly viscous dispersions of mucoadhesive polymers as vehicles for nasal administration of dopamine and grape seed extract-loaded solid lipid nanoparticles, Int. J. Pharm. 659 (2024) 124255, https://doi.org/10.1016/j.ijpharm.2024.124255.
[245] S. Gade, K. Glover, D. Mishra, S. Sharma, O. Guy, R.F. Donnelly, L.K. Vora, R.R. S. Thakur, Hollow microneedles for ocular drug delivery, J. Control. Release 371 (2024) 43–66, https://doi.org/10.1016/j.jconrel.2024.05.013.
[246] N. Khan, M. Aqil, S.S. Imam, A. Ali, Development and evaluation of a novel in situ gel of sparfloxacin for sustained ocular drug delivery: in vitro and ex vivo characterization, Pharm Dev Technol 20 (6) (2015) 662–669, https://doi.org/10.3109/10837450.2014.910807.
[247] D. Iohara, M. Okubo, M. Anraku, S. Uramatsu, T. Shimamoto, K. Uekama, F. Hirayama, Hydrophobically modified polymer/α-cyclodextrin thermoresponsive hydrogels for use in ocular drug delivery, Mol. Pharm. 14 (8) (2017) 2740–2748, https://doi.org/10.1021/acs.molpharmaceut.7b00291.
[248] V. Piazzini, E. Landucci, M. Urru, A. Chiarugi, D.E. Pellegrini-Giampietro, A. R. Bilia, M.C. Bergonzi, Enhanced dissolution, permeation and oral bioavailability of aripiprazole mixed micelles: in vitro and in vivo evaluation, Int. J. Pharm. 583 (2020) 119361, https://doi.org/10.1016/j.ijpharm.2020.119361.
[249] H. Liu, Z. Cai, F. Wang, L. Hong, L. Deng, J. Zhong, Z. Wang, W. Cui, Colon-targeted adhesive hydrogel microsphere for regulation of gut immunity and flora, Adv Sci (Weinh) 8 (18) (2021) e2101619, https://doi.org/10.1002/advs.202101619.
[250] M. Asadi, Z. Salehi, M. Akrami, M. Hosseinpour, S. Jockenhövel, S. Ghazanfari, 3D printed pH-responsive tablets containing N-acetylglucosamine-loaded methylcellulose hydrogel for colon drug delivery applications, Int. J. Pharm. 645 (2023) 123366, https://doi.org/10.1016/j.ijpharm.2023.123366.
[251] J.S. Park, J.H. Seo, M.Y. Jeong, I.G. Yang, J.S. Kim, J.H. Kim, M.J. Ho, S.G. Jin, M. K. Choi, Y.S. Choi, M.J. Kang, Carboxymethyl cellulose-based rotigotine nanocrystals-loaded hydrogel for increased transdermal delivery with alleviated skin irritation, Carbohydr. Polym. 338 (2024) 122197, https://doi.org/10.1016/j.carbpol.2024.122197.
[252] S.S. Kwon, B.J. Kong, S.N. Park, Physicochemical properties of pH-sensitive hydrogels based on hydroxyethyl cellulose-hyaluronic acid and for applications as transdermal delivery systems for skin lesions, Eur. J. Pharm. Biopharm. 92 (2015) 146–154, https://doi.org/10.1016/j.ejpb.2015.02.025.
[253] A. Fischer, P. Zhang, Y. Ouyang, Y.S. Sohn, O. Karmi, R. Nechushtai, E. Pikarsky, I. Willner, DNA-tetrahedra Corona-modified hydrogel microcapsules: "smart"

ATP- or microRNA-responsive drug carriers, Small 18 (52) (2022) e2204108, https://doi.org/10.1002/smll.202204108.
[254] B. Li, H. Shao, L. Gao, H. Li, H. Sheng, L. Zhu, Nano-drug co-delivery system of natural active ingredients and chemotherapy drugs for cancer treatment: a review, Drug Deliv. 29 (1) (2022) 2130–2161, https://doi.org/10.1080/10717544.2022.2094498.
[255] H. Ma, G. Yu, J. Cheng, L. Song, Z. Zhou, Y. Zhao, Q. Zhao, L. Liu, X. Wei, M. Yang, Design of an injectable magnetic hydrogel based on the tumor microenvironment for multimodal synergistic cancer therapy, Biomacromolecules 24 (2) (2023) 868–885, https://doi.org/10.1021/acs.biomac.2c01300.
[256] M. Rakib Hasan Khan, R. Shankar Hazra, G. Nair, J. Mohammad, L. Jiang, K. Reindl, M. Khalid Jawed, S. Ganai, M. Quadir, Cellulose nanofibers as Scaffold-forming materials for thin film drug delivery systems, Int. J. Pharm. 627 (2022) 122189, https://doi.org/10.1016/j.ijpharm.2022.122189.
[257] R. Rakhshaei, H. Namazi, H. Hamishehkar, M. Rahimi, Graphene quantum dot cross-linked carboxymethyl cellulose nanocomposite hydrogel for pH-sensitive oral anticancer drug delivery with potential bioimaging properties, Int. J. Biol. Macromol. 150 (2020) 1121–1129, https://doi.org/10.1016/j.ijbiomac.2019.10.118.
[258] I. Ali, A. Rizwan, T.T. Vu, S.H. Jo, C.W. Oh, Y.H. Kim, S.H. Park, K.T. Lim, NIR-responsive carboxymethyl-cellulose hydrogels containing thioketal-linkages for on-demand drug delivery system, Int. J. Biol. Macromol. 260 (Pt 2) (2024) 129549, https://doi.org/10.1016/j.ijbiomac.2024.129549.
[259] S. Hamd-Ghadareh, A. Salimi, S. Parsa, S.J. Mowla, Development of three-dimensional semi-solid hydrogel matrices for ratiometric fluorescence sensing of Amyloid β peptide and imaging in SH-SY5 cells: improvement of point of care diagnosis of Alzheimer's disease biomarker, Biosens. Bioelectron. 199 (2022) 113895, https://doi.org/10.1016/j.bios.2021.113895.
[260] X. Rong, Q. Ding, L. Chen, S. Yang, J. Lou, Z. Liu, X. Li, Y. Jiang, X. Wang, W. Han, Hyper strength, high sensitivity integrated wearable signal sensor based on non-covalent interaction of an ionic liquid and bacterial cellulose for human behavior monitoring, Mater. Horiz. 11 (10) (2024) 2420–2427, https://doi.org/10.1039/d3mh01696j.
[261] J. Zhao, X. Zhao, L. Leng, J. Xu, X. Yang, W. Cui, J. Zheng, R. Hu, High-stretchable, self-healing, self-adhesive, self-extinguishing, low-temperature tolerant starch-based gel and its application in stimuli-responsiveness, Carbohydr. Polym. 307 (2023) 120600, https://doi.org/10.1016/j.carbpol.2023.120600.