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Review

Cellulose-based hydrogels: Present status and application prospects

Chunyu Chang, Lina Zhang*

Department of Chemistry, Wuhan University, Wuhan 430072, China

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ABSTRACT

This review addresses recent progress in cellulose-based hydrogels design and fabrication. Firstly, hydrogels fabricated directly from native cellulose (including bacterial cellulose) via cellulose dissolution are introduced. Secondly, cellulose hydrogels based on its derivatives, including methyl cellulose (MC), hydroxypropyl cellulose (HPC), hydroxypropylmethyl cellulose (HPMC), and carboxymethyl cellulose (CMC), obtained by physical as well as chemical cross-linking strategies are considered. Thirdly, composite hydrogels prepared by using cellulose in conjunction with other polymers through blending, formation of polyelectrolyte complexes, and interpenetrating polymer networks (IPNs) technology are addressed. Finally, cellulose-inorganic hybrid hydrogels prepared by embedding inorganic nanoparticles in cellulose matrices are described and discussed. This review addresses the recent progress in cellulose based hydrogel designs and fabrication approaches, leading to the development of hydrogels from this class of carbohydrate polymers.

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* Corresponding author. Tel.: +86 27 87219274; fax: +86 27 68762005.
E-mail addresses: lnzhang@public.wh.hb.cn, linazhangwhu@gmail.com (L. Zhang).

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1. Introduction

Gels are defined as three-dimensional polymer networks swollen by large amounts of solvent. Hydrogels are, mainly, structures formed from biopolymers and/or polyelectrolytes, and contain large amounts of trapped water. Concerning definitions of hydrogel types, according to the source, hydrogels can be divided into those formed from natural polymers and those formed from synthetic polymers. On the basis of the cross-linking method, the hydrogels can be divided into chemical gels and physical gels. Physical gels are formed by molecular self-assembly through ionic or hydrogen bonds, while chemical gels are formed by covalent bonds (Silva, Richard, Bessodes, Scherman, & Merten, 2009). Hydrogels were first reported by Wichterle and Lím (1960). It is worth noting that the hydrogels have wide potential applications in the fields of food, biomaterials, agriculture, water purification, etc. Recently, scientists have devoted much energy to developing novel hydrogels for applications such as biodegradable materials for drug delivery (Bajpai, Shukla, Bhanu, & Kankane, 2008; Wu et al., 2008), tissue engineering (Khan, Tare, Richard, Oreffo, & Bradley, 2009; Lee & Mooney, 2001), sensors (Lee & Braun, 2003; Sorber et al., 2008), contact lenses (Katsoulos, Karageorgiadis, Vasileiou, Mousafeiropoulos, & Asimellis, 2009; Yasuda, 2006), purification (Ha et al., 2008) etc. Synthetic polymer-based hydrogels have been reported such those formed by cross-linking poly(ethylene glycol) (Nagahama, Ouchi, & Ohya, 2008), poly(vinyl alcohol) (Martens, Bryant, & Anseth, 2003), poly(amido-amine) (Ferruti, Bianchi, Ranucci, Chiellini, & Piras, 2005), poly(*N*-isopropylacrylamide) (Nayak, Lee, Chmielewski, & Lyon, 2004), polyacrylamide (Gao, Xu, Philbert, & Kopelman, 2007), and poly(acrylic acid) (Tomatsu, Hashidzume, & Harada, 2006) and their copolymers (Kim, Singh, & Lyon, 2006). Synthetic hydrogels like PEG-based hydrogels have advantages over natural hydrogels, such as the ability for photopolymerization, adjustable mechanical properties, and easy control of scaffold architecture and chemical compositions, but PEG hydrogels alone cannot provide an ideal environment to support cell adhesion and tissue formation due to their bio-inert nature (Zhu, 2010). A number of polysaccharides have similar properties to PEG in terms of biocompatibility and low protein and cell adhesion, and they can been biodegraded to nontoxic products that are easily assimilated by the body (Shoichet, 2010). Various hydrogels from natural polymers have been fabricated by using hyaluronate (Bhattacharyya, Guillot, Dabboue, Tranchant, & Salvetat, 2008), alginate (Chan, Whitney, & Neufeld, 2009), starch (Li, Xu, Pen, & Wang, 2008), gelatin (Gattás-Asfura et al., 2005), cellulose (Chang, Duan, Cai, & Zhang, 2010; Zhou, Chang, Zhang, & Zhang, 2007), chitosan, and their derivatives (Moura, Figueiredo, & Gil, 2007; Qu, Wirsén, & Albertsson, 2000; Vrana, Liu, McGuinness, & Cahill, 2008; Yamazaki et al., 2009), showing potential application in biomaterials field because of their safety, hydrophilicity, biocompatibility and biodegradability..

Cellulose, the most abundant renewable resource on earth, will become the main chemical resource in the future (Eichhorn, Young, & Davies, 2005; Schurz, 1999). Moreover, numerous new functional materials from cellulose are being developed over a broad range of applications, because of the increasing demand for environmentally friendly and biocompatible products (Klemm, Heublein, Fink, & Bohn, 2005). Cellulose having abundant hydroxyl groups can be used to prepare hydrogels easily with fascinating structures and properties. There is a need to study cellulose-based hydrogels in both fundamental research and industrial application. This review aims at highlighting the recent developments in cellulose-based hydrogels with emphasis on the fabrication, properties and possible applications. Recent literature has been cited to summarize the advances on cellulose-based hydrogel materials including pure cellulose, cellulose composite, and cellulose hybrid hydrogels. We hope that such selected information may assist us in rationally designing new, effective, and functional cellulose-based hydrogels.

2. Hydrogels prepared directly from native cellulose

Cellulose hydrogels can be prepared from a cellulose solution through physical cross-linking. Because cellulose has many hydroxyl groups which can form hydrogen bonding linked network easily. However, cellulose is very difficult to be dissolved in common solvents due to its highly extended hydrogen bonded structure (Edgar et al., 2001), so the major problem for preparing cellulose hydrogel is a lack of appropriate solvents. Recently, new solvents, such as *N*-methylmorpholine-*N*-oxide (NMMO), ionic liquids (ILs), and alkali/urea (or thiourea) aqueous systems have been developed to dissolve cellulose, providing great opportunities for the preparation of cellulose hydrogels. Bacterial cellulose (BC) is also a strong candidate for the fabrication of cellulose-based hydrogels, since certain bacterial species possesses the ability to create pure cellulose hydrogel.

2.1. LiCl/dimethylacetamide (DMAc) system

The development of LiCl/DMAc for cellulose as solvent has allowed the exploration of hydrogel production from native cellulose (Turbak, El-Kafrawy, Snyder, & Auerbach, 1981). Glasser et al. have prepared cellulose hydrogel in bead forms through dropwise addition of cellulose/LiCl/DMAc solution into non-solvent system such as azeotropic methanol or isopropanol (De Oliveira & Glasser, 1996a). Cellulose materials with a large molecular weight range (from DP_n 100 to DP_n 4000) can be dissolved in the LiCl/DMAc solution. Moreover, beads with the diameter ranged from 100 to 1500 μm have been prepared from cellulose solution.

A series of the solvent systems such as LiCl/DMAc for cellulose powder (CF11) (1:9), paraformaldehyde (PF)/dimethyl sulfoxide (DMSO) for cellulose pulp (1:15), and triethylammonium chloride (TEAC)/DMSO for the pulp (7: 13) have been used to fabricate directly cellulose hydrogels. However, the CF11 sample can not be dissolved in PF/DMSO and TEAC/DMSO, owing to its high crystallinity. The cellulose concentration in the LiCl/DMAc system has been determined to be 7 wt%. The physical properties of hydrogels, such as transparency, strength, and water content, mainly depend on the composition of the coagulation/regeneration bath. The maximum transparency of the hydrogels is 97% in the case of a non-aqueous organic solution. The presence of water has a very strong influence on the physical properties of cellulose solutions. Similar behavior has been observed in the tetrabutylammonium fluoride in dimethyl sulfoxide (TBAP/DMSO) system (Heinze, Dicke, Koschella, Klohr, & Koch, 2000). Östlund et al. have reported that transparent or opaque hydrogels can be obtained by tuning the cellulose concentration or water content in TBAP/DMSO system (Östlund, Lundberg, Nordstierna, Holmberg, & Nydén, 2009). Moreover, the transparent hydrogel from $NaOH/CS_2$ system has an extremely high tensile strength (13.7 MPa), while the maximum transparency (88%) is slightly lower than that of the hydrogels obtained from an organic cellulose solution (Saito, Sakurai, Sakakibara, & Saga, 2003).

2.2. NMMO system

The use of NMMO provides a simple physical technology to the still dominating viscose-technology for producing regenerated cellulose fibers, films, food casings, membranes, sponges, beads and others without hazardous byproducts (Fink, Weigel, Purz, & Ganster, 2001). Cellulose of high molecular weight can be dissolved in $NMMO/H_2O$ at high temperature to form transparent solution. Cellulose crystal structure is destroyed to become amorphous when NMMO molecules become mobile at 100 °C, and cellulose starts

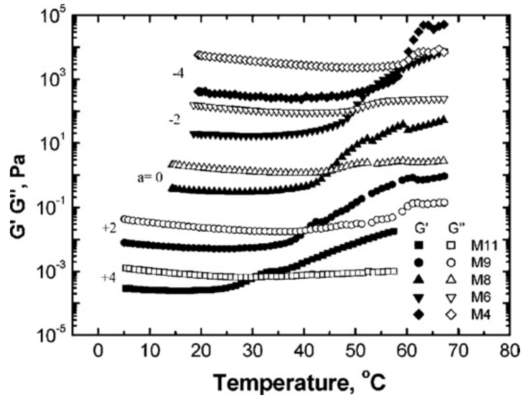

Fig. 1. Temperature dependence of the storage modulus G' and loss modulus G'' for 5 wt% cellulose solution with different molecular weights. The data are shifted along the vertical axis by 10^a to avoid overlapping (Cai & Zhang, 2006).

to replace water molecules that are bonded to NMMO when the mixture is heated to 150 °C. Regenerated cellulose products can be obtained by adding excess water into the cellulose/NMMO/water solution (Zhao et al., 2007). However, there have been few reports on transparent hydrogels prepared directly from the cellulose solution in NMMO system.

2.3. ILs system

Cellulose can be dissolved in some hydrophilic ionic liquids, such as 1-butyl-3-methylimidazolium chloride (BMIMCl) and 1-allyl-3-methylimidazolium chloride (AMIMCl) (Swatloski, Spear, Holbrey, & Roger, 2002; Zhang, Wu, Zhang, & He, 2005). The regenerated cellulose products have been obtained by subsequent addition of water, ethanol, or acetone, show the same degree of polymerization as the initial cellulose, indicating no degradation. By changing the regeneration instrument and process, regenerated cellulose materials can be adopted in various forms, such as film, beads, and gels (Zhu et al., 2006). Cellulose hydrogels have been prepared by regenerating the cellulose solution from its ionic liquid (1-allyl-3-methylimidazolium chloride, AMIMCl) (Li, Lin, Xiao, Wan, & Cui, 2009a) using deionized water as coagulant. Kadokawa et al. have reported that flexible gels can be obtained by dissolving cellulose in 1-butyl-3-methylimidazolium chloride and keeping it at room temperature for 7 days (Kadokawa, Murakami, & Kaneko, 2008).

2.4. Alkali/urea or thiourea aqueous systems

We have developed a novel solvent for cellulose, namely, 7 wt% NaOH/12 wt% urea mixture in water precooled to −12 °C, in which cellulose ($M_w < 1.2 \times 10^5$) could be dissolved rapidly. The cellulose dissolution at low temperature arises as a fast dynamic self-assembly process among solvent small molecules (NaOH, urea and water) and the cellulose macromolecules (Cai et al., 2008). Interestingly, cellulose hydrogels can be formed via destructing the stability of cellulose solution by increasing the temperature to 50 °C or reducing it to −20 °C. The gelation behavior of cellulose solution has been investigated by using rheological experiments to probe the influence of cellulose molecular weight, concentration, and temperature, on the gelation point. The gelation temperature of cellulose solution ($M_\eta = 11.4 \times 10^4$) decreases from 60.3 to 30.5 °C for concentrations 3 wt% to 5 wt%. Further, 5 wt% cellulose solution decreases from 59.4 to 30.5 °C when the molecular weight is increased from 4.5×10^4 to 11.4×10^4 as shown in Fig. 1 (Cai & Zhang, 2006).

Another new solvent for cellulose is 9.5 wt% NaOH/4.5 wt% thiourea aqueous solutions pre-cooled to −5 °C, which can dissolve cellulose to prepare transparent cellulose solutions (Lue, Zhang, & Ruan, 2007). The cellulose inclusion complex (ICs) associated with cellulose, NaOH, thiourea, and water clusters can be easily created at low temperature, leading to the good stability of cellulose in aqueous solution. Cellulose hydrogels have been created via physical cross-linking of the macromolecular chains in the cellulose solution at elevated temperature. By using a pre-gelation process, cellulose hydrogel membranes have been created in NaOH/thiourea aqueous solvent system. At a relative low pre-gelation temperature, the elongation and toughness of the hydrogel membranes are found to be 192% and 1.97 MPa, respectively, which are much larger than that prepared by the general solution casting method (Liang, Zhang, Li, & Xu, 2007). However, in the range from 10 to 30 °C, the sol–gel transition of cellulose in the NaOH/thiourea system is partially reversible, the gels formed at 30 °C for a long period of time can be transformed to the liquid state again after stirring at −5 °C because of the reconstruction of the hydrogen-bonding networks between cellulose and solvent takes place, leading to good dispersion of cellulose. Interestingly, the physical gel formed at temperatures above 60 °C is irreversible due to the alteration of the solvent components caused by reaction between NaOH and thiourea at high temperature, leading to the difficulty in the reconstruction of initial complex (Lue & Zhang, 2008). The sol-gel transition of cellulose solution in 6 wt% NaOH/5 wt% thiourea system with cellulose concentration from 6 to 4 wt% occurs in the temperature range from 20 to 40 °C. Thus, either at a higher temperature or a longer time, the gelation of cellulose solution can occur. These hydrogels are composed of relatively small network units with an average diameter of 47 nm (Weng, Zhang, Ruan, Shi, & Xu, 2004). Fig. 2 shows the AFM images of the cellulose gels spread on the substrate after being dispersed in pure water. The visualized gels exhibit a structure of nanoparticles in size, and the average dimension of the cross-section for those nanoparticles is 47 nm. This indicates that the intramolecular hydrogen bonds of cellulose, which sustains the chain stiffness, have been destroyed in NaOH/thiourea system, leading to the formation of flexible chains (or random coil). This finding is in good agreement with the spherical IC of cellulose in NaOH/thiourea system (Lue et al., 2007). However, weak gels are only obtained by using the preparation method from pure cellulose solution via heating or storage for long time.

2.5. BC hydrogels

Bacterial cellulose (BC) synthesized by nanopathogenic microbial strains such as *Acetobacter xylinum* is an ultra-fine network structure. BC has high mechanical properties including tensile strength and modulus, high water-holding capacity, high crystallinity, and high biocompatibility. On the basis of the high purity, and unusual physicochemical properties, BC-based hydrogels offer a wide range of applications in the biomaterials fields such as tissue engineering scaffold (Kakugo, Gong, & Osada, 2007), meniscus implant (Bodin, Concaro, Brittberg, & Gatenholm, 2007), and dental implants (Klemm, Schumann, Udhardt, & Marsch, 2001).

Gelin et al. have performed a detailed analysis of the water interaction properties in as-biosynthesised BC gels using dielectric spectroscopy. The results indicate that only about 10% of the 99 wt% water present in BC gels behaved like free bulk water and the majority of the water molecules in the gels are more or less tightly bound to the cellulose (Gelin et al., 2007). Synthesized tubular BC gel with proper fibril orientation created by culturing BC in oxygen-permeable silicone tubes with inner diameter <8 mm. The fibrils are oriented along the longitudinal axis of the silicone tube, independent of gravity, oxygen availability, and the morphology of the inner surface of the silicone tube, but dependent

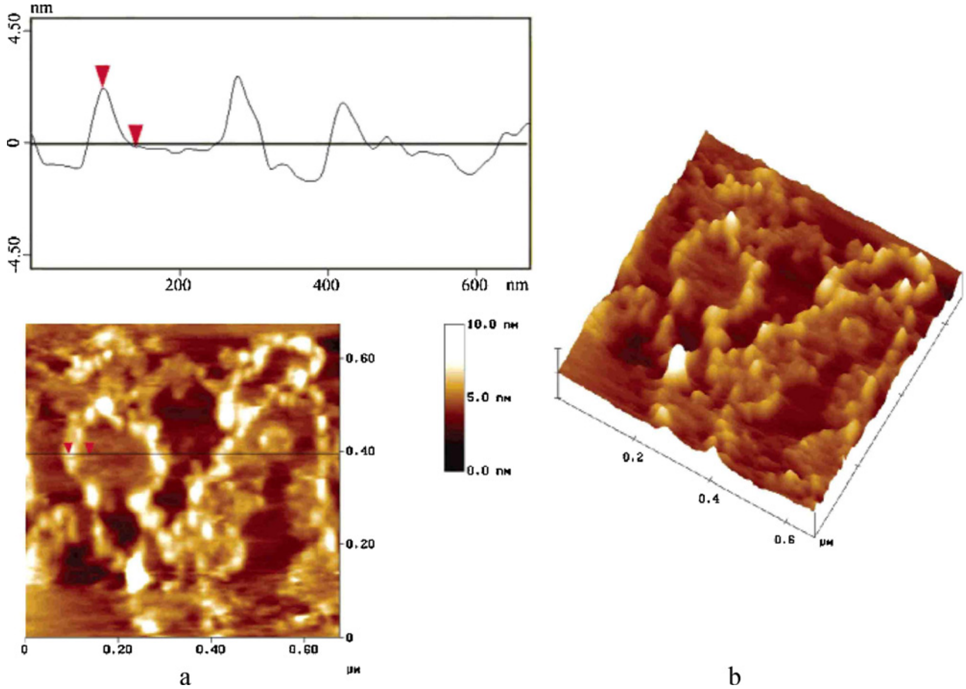

Fig. 2. AFM image of the gel from the 5 wt% cellulose solution spread on the substrate after being dispersed in pure water: (a) top-view image of the height scan and height profile analysis; (b) three-dimensional topography image (Weng et al., 2004).

on the curvature of the silicone tube (Putra, Kakugo, Furukawa, Gong, & Osada, 2008). In recent years, BC has been used for designing various composite hydrogels which include xylogucan, pectin, gelatin and other synthesized polymers with improved functional properties.

3. Hydrogels from cellulose derivatives

Water soluble cellulose derivatives are mostly biocompatible which can be used as thickener, binding agents, emulsifiers, film formers, suspension aids, surfactants, lubricants and stabilizers, especially as additives in food, pharmaceutical, and cosmetic industries. Selective cellulose derivatives, including methyl cellulose (MC), hydroxypropyl cellulose (HPC), hydroxypropylmethyl cellulose (HPMC), and carboxymethyl cellulose (CMC) have been used to fabricate cellulose-based hydrogels through physical cross-linking and chemical cross-linking. In the case of physical cross-linked gels, there is no covalent bonding formation or breakage and the cross-linked network is formed through ionic bonding, hydrogen bonding, or an associative polymer-polymer interaction (Weng et al., 2004). In general, chemical cross-linked hydrogels are prepared through cross-linking two or more kinds of polymer chains with a functionalized cross-linker (Deng, He, Wu, & Yang, 2008) or under UV light (Guo & Chu, 2005).

3.1. Physical cross-linking

In the family of thermo-reversible hydrogels, hydrophobically modified cellulose is one of the largest members. When hydroxyl groups are substituted partly by methyl groups or hydroxylpropyl groups, some hydrogen bonds are prevented and the resultant derivatives become water soluble. MC aqueous solutions posses the unusual property of forming reversible physical gels, due to hydrophobic interactions when heated above a particular temperature (Li, Thangamathesvaran, Yue, Hu, & Lam, 2001). HPMC has a higher gelation temperature than MC, which forms firmer gels with equivalent substitution and molecular weight. There is evidence that the gelation of cellulose derivatives results from the exclusion of water from heavily methoxylated regions of polymer (Sammon, Bajwa, Timmins, & Melia, 2006).

Sekiguchi et al. have studied the hydrophobic interactions and hydrogen bonds contributed to thermally reversible gelation of methylcellulose aqueous solution by using near infrared spectroscopy (IR), differential scanning calorimetry (DSC), and small angle X-ray scattering (SAXS). The results showed that the gelation behavior of a series of regioselectively substituted 2,3-di-*O*-methylcellulose (2,3MC-*n*: $n = 1–3$) is differed from that for randomly substituted O-methylcellulose (R-MC). This indicates that the gelation of 2,3MC-*n* and R-MC solutions may be caused by cooperation of the hydrophobic interaction among methyl groups with the intermolecular hydrogen bonds among hydroxyl groups at C6 position, depending on the distribution of methyl groups (Sekiguchi, Sawatari, & Konodo, 2003). By using heating-cooling cycles, MC in cold de-ionised water shows a higher gelation rate at higher concentrations. The gelation rate during the second heating-cooling cycle is higher than that in the first cycle (Joshi, Liang, & Lam, 2008). MC hydrogels are employed to coat the surface of a polystyrene dish and uses to cultivate human embryonic stem (hES) cell clumps for the formation of embryoid bodies (EBs) in liquid suspension culture (Yang et al., 2007). The hES cells within the EBs are shown to express molecular markers specific for representative cells from the three embryonic germ layers, indicating the MC-coated dish can be used to produce a large scale of hES cell derivatives through the formation of EBs.

The HPC microgels with thermally responsive properties have been synthesized through chemically cross-linking HPC polymer chains in water-surfactant (dodecyltrimethylammonium bromide) dispersion (Lu, Hu, & Gao, 2000). The size distribution of microgels becomes broader with increasing of HPC concentration. Moreover, the particle size increases quickly with an increase of temperature to above the lower critical solution temperature (LCST). Furthermore, the formation and volume phase transition of the HPC microgels occur in salt solution (Xia, Tang, Lu, & Hu, 2003). The results from dynamic laser light scattering (Fig. 3a) reveal that the higher NaCl concentration leads to the smaller average hydrodynamic radii $<R_h>$ of the microgels, suggesting that more compact

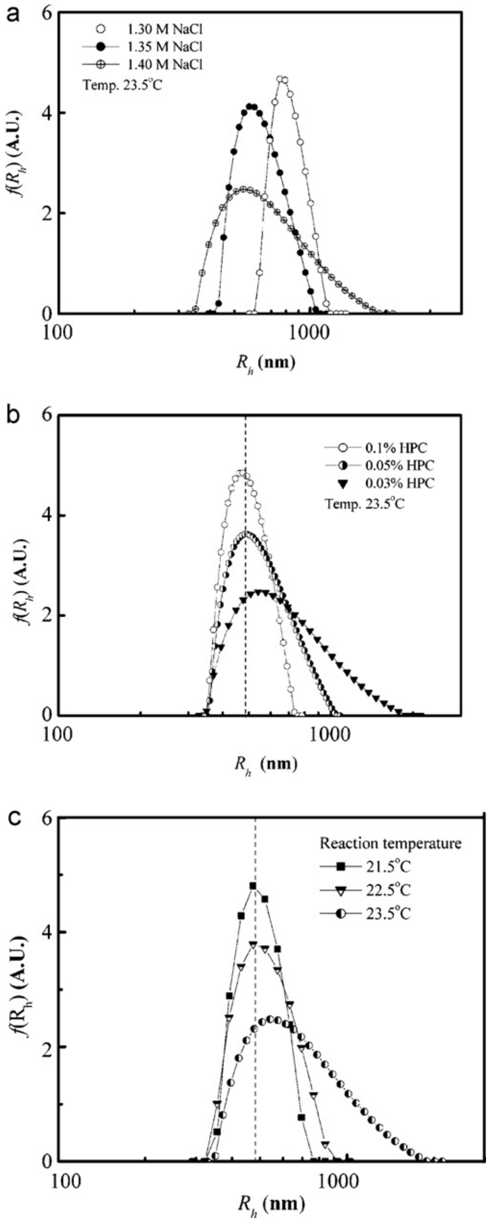

Fig. 3. Hydrodynamic radius distributions ($f(R_h)$) of HPC microgel particles ($C = 5.0 \times 10^{-5}$ g/mL) in deionized water at 23.5 °C. (a) The HPC microgels are prepared in various NaCl concentrations, while the HPC polymer chains concentration and reaction temperature are kept at 0.03 wt% and 23.5 °C, respectively. (b) The HPC microgels are made at 23.5 °C in various HPC polymer concentrations, while NaCl concentration is kept at 1.4 M. (c) The HPC microgels are made at different temperatures, while HPC polymer concentration and NaCl concentrations are kept at 0.03% and 1.4 M (Xia et al., 2003).

microgels can form in higher salt concentration. The $<R_h>$ values of the microgels hardly change with an increase in the HPC concentration (Fig. 3b), whereas the radius distribution become narrower with an increase of HPC concentration or decrease in temperature (Fig. 3c). Kato and Gehrke have fabricated HPC hydrogels by freeze-drying, and found that they have a microporous structure and fast response properties. After the freezing treatment, an effective diffusion coefficient for shrinkage can be determined by fitting Fick's law to the data (5.2×10^{-4} cm^2/s), which is an increase of two orders of magnitude over that of non-porous gel (6.0×10^{-6} cm^2/s) (Kato & Gehrke, 2004).

In biomedical applications, cellulose derivatives have been used for preparation of biomaterial matrices. Hydroxypropylmethyl cellulose (HPMC) is a methylcellulose modified with a small amount of propylene glycol ether groups attached to the anhydroglucose of the cellulose. Weiss' group (in France) has developed a series of biomaterials based on HPMC. The first generation of injectable calcium phosphate ceramics suspensions is composed of a mixture of HPMC solution and biphasic calcium phosphate granules. (Weiss, Gauthier, Bouler, Grimandi, & Daculsi, 1999) The aggregation and gelation behavior of HPMC (19–24% methoxyl and 7–12% hydroxypropyl, $M_w = 4.3 \times 10^5$) aqueous solutions are concluded as follows: (i) polymer reptation increases due to thermal motion, leading to a weaker network; (ii) above 55 °C, the polymer chains become more hydrophobic and polymer clusters start to form; (iii) the number of physical cross-links between polymer clusters and the respective lifetimes increases and a three-dimensional network is formed (Silva et al., 2008). These materials exhibit good biocompatibility, and have convenient rheological properties for injection. However, the viscous suspension shows a tendency to flow after implantation *in vivo*. Therefore, the second generation of products which can suppress the long-term flow through easily controllable cross-linking of silated HPMC (Si-HPMC) has been developed (Vinatier et al., 2009). Si-HPMC is non-toxic and biocompatible, so that it can be widely used in biomedical areas, such as scaffold for cell culture, cartilage model and implanted in bone defects (Bourges, Weiss, Daculsi, & Legeay, 2002). Si-HMPC based hydrogels are developed as a scaffold for 3D culture of osteogenic cells, which would be suitable for both *in vitro* culture and *in vivo* injection. The results from mineralization assay and gene expression analysis of osteblastic markers and cytokines indicate that all of the cells cultured in 3D into this hydrogel exhibit a more mature differentiation status from cells cultured as a monolayer on plastic. This Si-HPMC hydrogel is well suited to support osteoblastic, survival, proliferation, and differentiation when it is used as a new scaffold, and represents a potential basis for an innovative bone repair material (Trojani et al., 2005).

3.2. *Chemical cross-linking*

3.2.1. *Cross-linking reagents*

The stable structure and effective swelling of cellulose-based hydrogels often require a chemically cross-linked network. Some di-functional molecules are employed as the cross-linker for cellulose or its derivatives to covalently bind different polymer molecules in a three dimensional hydrophilic network. Sannino et al. have exploited superabsorbent hydrogels based on cellulose through cross-linking CMC and HEC with divinylsulfone (DVS). Fig. 4 shows the schematic images of hydrogel networks (Marcì, Mele, Palmardo, Pulito, & Sannino, 2006). These polyelectrolyte hydrogels display high sensitivity in sorption capacity to variations of the ionic strength and pH of the external solution (Sannino, Madaghiele, Lionetto, Schettino, & Maffezzoli, 2006). These superabsorbent hydrogels are also developed to treat edemas for body water elimination (Sannino et al., 2003a). If HPC hydrogels are synthesized at certain temperatures in the single-phase regime, they remain nonporous, whereas when cross-linked in the biphasic regime become microporous (Kabra, Gehrke, & Spontak, 1998). Hirsch and Spontak have discussed the dynamic mechanical properties and swelling capacities of these hydrogels as a function of cross-linking temperature (Hirsch & Spontak, 2002). The nonporous HPC hydrogels prepared at temperatures below the cloud point of aqueous HPC are not very temperature-dependent, and the modulus of microporous HPC hydrogels can be improved through the use of longer cross-linking times. Thermally sensitive hydrogels have been synthesized by crosslinking hydropropyl cellulose (HPC) with poly(ethylene glycol) diglycidyl ether. The hydrogels swell at low temperature (20 °C) and contract at relative high temperature (60 °C) (Marsano, Bianchi, & Sciutto, 2003). HPC hydrogels, prepared by cross-linked HPC with epichlorohydrin (ECH) and

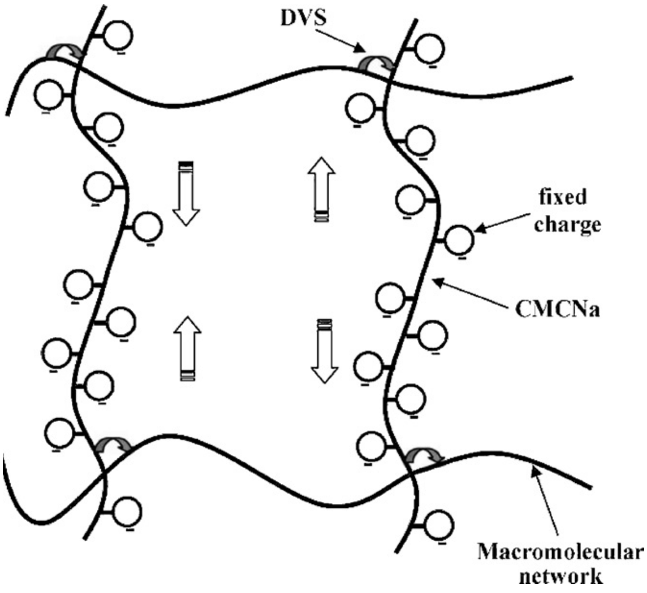

Fig. 4. CMCNa/HEC macromolecular network, with the charged chains acting as contraction or expansion devices. Large arrows indicate the contraction or expansion of the polyelectrolyte chains (Marcì et al., 2006).

ammonia, show an excellent ability to absorb anionic dye. The maximum adsorption capacity at room temperature has been found to be 2478 (g/kg) at pH 3.96 (Yan, Shuai, Gong, Gu, & Yu, 2009).

The swelling properties of hydrogels can be modulated by changing the distance between cross-links, by changing of the molecular weight of poly(ethylene glycol) diglycidyl ether, or inserting poly(ethylene glycol) as the spacers of macromolecule chains when DVS is used as cross-linker (Sannino, Maffezzoli, & Nicolais, 2003b). For the applications in food, drugs and biomaterials, the hydrogels including cross-linkers should be non-toxic. However, both DVS and ECH are well known toxic agents, and they should be effectively removed before the hydrogels are obtained. Therefore, scientists devote their energies to developing new biocompatible cross-linkers for producing cellulose based hydrogels.

The water soluble carbodiimide is used as a cross-linker to fabricate cellulose based hydogels for improving the potential biocompatibility of the hydrogel, since carbodiimide molecules are not incorporated into the cross-linking bonds. However, they can be converted into urea derivatives, which can be easily washed out from the polymeric network with a low degree of cytotoxicity. The swelling ratio of hydrogels is influenced by the chemical composition of CMC and HEC, and the desiccation process. Dry hydrogel pills are envisaged to be administered orally, which then swell at the strong acid pH of the stomach, thereby giving a sense of fullness, and to be finally expelled by in the feces (Sannino et al., 2006). Demitri et al. have reported the preparation of HEC/CMC hydrogels with citric acid as a cross-linker which can overcome toxicity and costs, compared with former reagents. The esterification mechanism based on an anhydride intermediate formation is proposed to explain the reaction of cellulose with citric acid. The swelling ratio of hydrogels depends on the reaction time and citric acid concentration. The swelling ratio of hydrogel with a citric acid concentration of 3.75% can reach 900 (Demitri et al., 2008).

3.2.2. Radical cross-linking

Irradiation is a useful method for obtaining chemical hydrogels, including irradiation of solid polymer, monomer (in bulk or in solution) or polymer aqueous solution (Rosiak & Ulanski, 1999). The advantage of radical cross-linking is that cross-linkers, which limited the applications of hydrogels in the food, drug, and pharmaceutical industries due to their toxicity, are not required in the fabrication process, leading to high purity of the hydrogel product. The concentrated aqueous solutions of cellulose derivatives, such as CMC, HPC, and MC, can be cross-linked under ionizing radiation to prepare cellulose based hydrogels (Fei, Wach, Mitomo, Yoshii, & Kume, 2000). Bin et al. have found that carboxymethyl cellulose with high degree of substitution (DS) and high concentration can be effectively cross-linked to form CMC hydrogels through irradiation (Bin, Wach, Mitomo, Yoshii, & Kume, 2000). The effects of the aging time, concentration, and dose rate on the cross-linking of CMC in aqueous solutions under ionizing radiation are also examined. Gels formed faster at initial stage of irradiation at a lower dose rate of γ rays. Similar observations are made for pure radiation induced cross-linking of CMC low doses (Liu, Peng, Li, & Wu, 2005). Electron-beam (EB) technique has revealed that the process is concentration dependent. Moderately and highly concentrated CMC solution irradiated under an EB and γ rays (in the absence of air) can form gel fractions up to 90–95% as a result of the ionizing radiation. The presence of air during the irradiation diminishes the maximum gel fracture, and the ratio of cross-linking is the lowest for highly concentrated solutions irradiated by an EB (Wach, Mitomo, Yoshii, & Kume, 2001). The DS of the CMC used in the above work is about 2.2, and CMC with a relative lower DS (0.64) has been also successfully used to prepare hydrogels (Liu, Zhai, Li, & Wu, 2002). EB irradiation exhibits higher gel fraction (up to 90%) than γ irradiation (65%) for the preparing of HPC hydrogels have also been obtained (Wach, Mitomo, Yoshii, & Kume, 2002).

Two competing processes, degradation and cross-linking, take place at high-energy irradiation of cellulose derivatives with either electron beam or gamma rays (Wach et al., 2001). The examined polymers undergo degradation when exposed to ionizing radiation at ambient temperature in solid state and aqueous solutions of low concentration (less than 10 wt%), while the best results of cross-linking have been obtained at high concentration (25–40 wt%, depending on the polymer) (Petrov, Petrova, Tchorbanov, & Tsvetanov, 2007). Fei et al. have studied degradation and cross-linking of different types of cellulose derivatives using high-energy radiation, and found that chemical hydrogels can be made under mild conditions that do not degrade polysaccharides (Fei et al., 2000). Hydrogels are also prepared by cross-linking cellulose derivatives with functional monomers through EB irradiation. For example, Ibrahim et al. have designed a superabsorbent hydrogel via radiation cross-linking of CMC and acrylamide (AAm) monomers with an EB accelerator. The optimum concentration of CMC/AAm is 90/10, and the resulting hydrogels possess good water retention capacity (Ibrahim, El Salmawi, & Zahran, 2007). Recently, CMC/AM hydrogels prepared by gamma irradiation have been evaluated for the possible use in drug delivery systems, and the percentage release of drug (methylene blue indicator) from the hydrogels increases to reach 80% after 3 h at pH 2 compared to 100% at pH 8. (El-Din, Alla, & El-Naggar, 2010) A novel cellulose based hydrogel through inserting acrylic onto cellulose backbone has been heterogeneously synthesized under radical copolymerizing in the presence of *N,N*-dimethylacrylamide (Trombino et al., 2009). This biomaterial can be applied in pharmaceutical field both as prodrug of *trans-ferulic* acid and as carrier for photo and thermodegradable drugs to improve their stability.

4. Cellulose-polymer composite hydrogels

4.1. Blending composites

4.1.1. Blending with natural polymers

Blending of different polymers is an extremely attractive inexpensive and advantageous method to obtain new structural

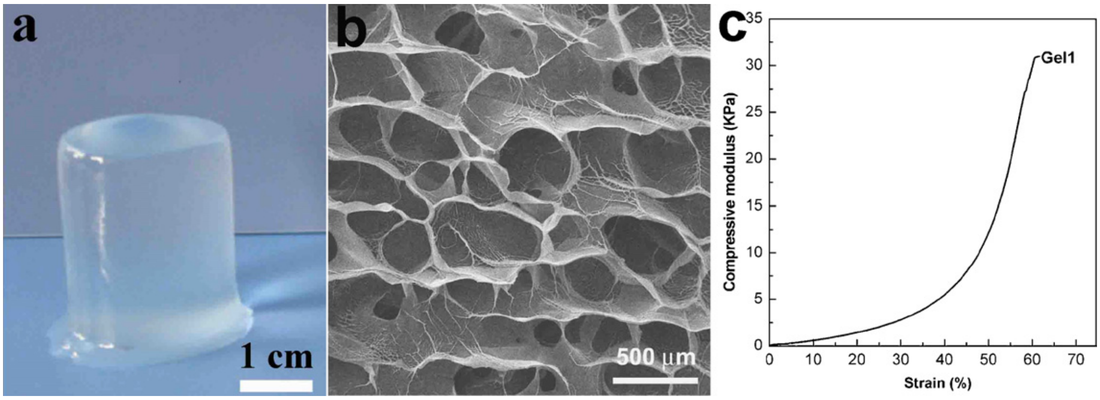

Fig. 5. Photograph (a), SEM image (b), and compressive stress–strain curve (c) of cellulose/SA hydrogel (Chang et al., 2009a).

materials (Bajpai et al., 2008). Cellulose (or its derivatives) blended with natural biodegradable polymers, such as chitin, chitosan (Dang & Dang, 1996), starch (Faroongsarng & Sukonrat, 2008; Hebeish, Higazy, El-Shafei, & Sharef, 2010), alginates (Isklan, 2005; Liang et al., 2004), and hyaluronic acid (Sannino et al., 2004), have created novel materials to fit the special applications, such as blending with chitosan for heavy metal removal, with starch for foods, and with alginates for tissue engineering.

Blending of cellulose and chitin in the same solvent system is an effective way to produce phase-separated composite hydrogels. Chitin/cellulose beads have been prepared by coagulating a mixture of 4 wt% cellulose solution and 2 wt% chitin solution in 6 wt% NaOH/5 wt% thiourea aqueous system. The q_e adsorption value of heavy metal ions on the beads is in the order of $Pb^{2+} > Cd^{2+} > Cu^{2+}$ in the low ion concentration solution, indicating a selective adsorption (Zhou, Zhang, Zhou, & Guo, 2004). The adsorption ability of lead on the blend beads is higher than that of pure chitin flakes, owing to the relatively large surface area and high hydrophilicity of the blend beads. The hydrophilic skeleton and microporous-network structure of cellulose improve the adsorption ability of lead on chitin (Zhou, Zhang, & Guo, 2005).

Cellulose-chitosan hydrogel beads are prepared by blending cellulose powder to chitosan solution. Subsequently, the hydrogel beads were cross-linked by ethylene glycol diglycidyl ether. The results indicate that the addition of cellulose to chitosan made the hydrogel beads materially denser and the cross-linking reaction can improve the chemical stability of beads in the solutions with pH values down to 1. These beads have high adsorption capacity for Cu adsorption (Li & Bai, 2005). Chitosan has been also blended with highly concentrated carboxymethylated cellulose solution to form physical hydrogels, which are cross-linked by irradiation (Zhao & Mitomo, 2008). A compression molding technique is used for cellulose/chitosan/NMMO system for preparing blend films (Shih, Shieh, & Twu, 2009). The surface of the films containing 3 wt% chitosan is smooth, but the films containing 5 wt% chitosan become coarse due to phase separation. These blend films have shown non-diffusible antibacterial properties, according to the results of antibacterial assessment. Chitin/cellulose and cellulose/starch composite gel prepared from ionic liquids have also been reported. These hydrogels have been obtained by keeping the homogeneous mixture for several days (Kadokawa, Murakami, Takegawa, & Kaneko, 2010; Takegawa, Murakami, Kaneko, & Kadokawa, 2010). An injectable hydrogel has been prepared via ionic and hydrophobic interactions between chitosan and methylcellulose chains in the presence of various salts under mild conditions without organic solvent, high temperature or harsh pH. Chitosan/methylcellulose/Na_3PO_4 hydrogels exhibit good cell viability and proliferation, indicating potential use as a three-dimensional synthetic for tissue engineering (Tang et al., 2010).

Baumann et al. have developed a series of physical hydrogel blends composed of methyl cellulose and hyaluronan, which meet the design criteria of injectability, safe swelling, high residual particle load, significantly slower *in vitro* degradation, and satisfactory diffusivity of molecules up to 150 kg/mol. They can be used as polymeric carriers for independent delivery for one or more drugs, from 1 to 28 days, for application in spinal cord injury repair strategies (Baumann et al., 2009). Hydroxyethyl cellulose-sodium alginate blend polymeric beads have been fabricated, and beads have been assessed for controlled release of diclofenac sodium and ibuprofen drugs. The results reveal various factors such as composition of the blend, cross-linking agent, and drug concentration influence the release behavior (Rao et al., 2006). Sodium alginate has been used as pore size expander for the blending with cellulose to create cellulose-sodium alginate hydrogels. These hydrogels have macroporous structure, excellent mechanical strength, and high equilibrium swelling ratio in water, as shown in Fig. 5. The introduction of sodium alginate into cellulose hydrogels increases significantly the pore size and swelling ratio of hydrogel samples, while cellulose contributes to enhance the mechanical properties of the hydrogels (Chang, Duan, & Zhang, 2009a). Temperature and pH sensitive photoluminescence of methyl cellulose-riboflavin hydrogels have been prepared by blending methyl cellulose with riboflavin (Saha, Manna, & Nandi, 2009). The photoluminescence of these hydrogels is 93 times higher in the gel state compared to the sol state at $pH \leq 7$.

4.1.2. Blending with polyvinyl alcohol

Polyvinyl alcohol (PVA) is a good candidate for the preparation of hydrogels which can be cross-linked by using several methods, including chemical agents, electron beam, γ-irradiation, or physically thermal cycling. For biomedical applications, physical cross-linking has the advantage of avoiding residual amounts of toxic chemical cross-linker, and higher mechanical strength than PVA gels cross-linked by either chemical or irradiation techniques (Ivanov, Popa, Ivanov, & Popa, 2007). We have studied the effect of cross-linking methods on structure and properties of cellulose/PVA hydrogels (Chang, Lue, & Zhang, 2008). In our findings, chemical hydrogels, prepared by cross-linking cellulose and PVA with ECH, have a high swelling ratio, but low mechanical strength as a result of the weak hydrogen bonding between cellulose and PVA. However, physical hydrogels prepared via solution blending of cellulose and PVA and repeating freezing/thawing cycles exhibit a dense structure between cellulose and PVA, leading to high mechanical strength. In addition, BC fibers of an average diameter of 50 nm have been used in combination with PVA, which can be transformed into a hydrogel through freezing/thawing cycles to form biocompatible nanocomposites. The nanocomposites possess a broad range of mechanical properties, and can be made with mechanical properties similar to that of cardiovascular tissue, such as aorta and heart valve leaflets (Millon & Wan, 2006). CMC/PVA copolymer hydrogels have been prepared by using electron beam irradiation technique, which can be used as dye removal materials. The results indicate that the hydrogel composition is an effective parameter in determining the dyes sorption character, and the adsorption capacities varies as direct pink 3B > acid green B > ismative violet 2R (Taleb, Abd El-Mohdy, & Abd El-Rehim, 2009).

4.2. *Polyelectrolyte complexes*

Polyelectrolytes are water-soluble, but complexes formed by strong electrostatic interactions between oppositely charged polyelectrolyte in water are insoluble. Thus, the polymeric complexes materials can be prepared as films, fibers, and hydrogels. Carboxymethyl cellulose (CMC) is negatively charged polyelectrolyte. Therefore, complex hydrogels can be constructed by introducing other positively charged polyelectrolyte in the presence of CMC. An amphoteric hydrogel membrane has been prepared by blending of chitosan and CMC solution, and then cross-linking with glutaraldehyde. The hydrogel is a smart one, and can bend toward either anode or cathode, depending on the pH of the solution, and its electromechanical behavior is influenced by other factors such as ionic strength and electric field strength (Shang, Shao, & Chen, 2008). In Britton-Robinson buffer solution with ionic strength of 0.2 M (pH 6), the maximum equilibrium bending angle of the hydrogel is determined to be 90°. Homogeneous polyelectrolyte complex membranes based on CMC and chitosan have been fabricated by dissolving the polyelectrolyte complex in aqueous NaOH and casting on polysulfone ultra-filtration membrane after filtration. Permeation flux (J) of membrane depends on temperature and the water content in aqueous ethanol. The complex membranes show highly improved permeation flux without sacrificing selectively, e.g., $J = 1.14\,\mathrm{kg/m^2h}$, α (separation factor) = 1062 in dehydrating 10 wt% water-ethanol at 70 °C (Zhao et al., 2009).

Polyvinylamine (PVAm) is commercially available, including a range of copolymers with poly(*N*-vinylformamide) (PNVF). They can be used as cationic polymers to prepare complexes with CMC. PVAm/CMC and PVAm-*co*-PNVF/CMC complex films are macroscopic, homogeneous, and transparent. The influence of various factors such as functions of polymer ratio, polymer composition, and relative humidity on the dry mechanical properties of the complexes have been discussed (Feng, Pelton, & Leduc, 2006). Hydrogen bonding is the main intermolecular interaction in the dried complex films, whereas in the hydrogel, ionic cross-linking dominates. The swelling behavior of PVAm/CMC complex hydrogel has been determined by the balance between ionic cross-links which decrease swelling and Donnan effects. Fig. 6 shows the swelling behavior of hydrogel membranes with various compositions under different pH. Two main observations from this figure are: (i) at constant composition, the minimum swelling occurs at pH 4–7 depending on composition; (ii) at neutral pH the minimum swelling corresponds to the CMC/PVAm film with an intermediate dry mass ratio of 3:1. It is further noted that the complex films can be dissolved at pH < 2 and pH > 12, namely the hydrogel membranes are stable in the neutral medium. Excess polyions in the hydrogels increase swelling: excess ammonium groups result in highest swelling at low pH. Similarly, excess carboxyl groups cause maximum swelling at high pH. The minimum swelling corresponds to the CMC/PVAm membrane with an intermediate dry mass ratio of 3:1 at neutral pH (Feng & Pelton, 2007).

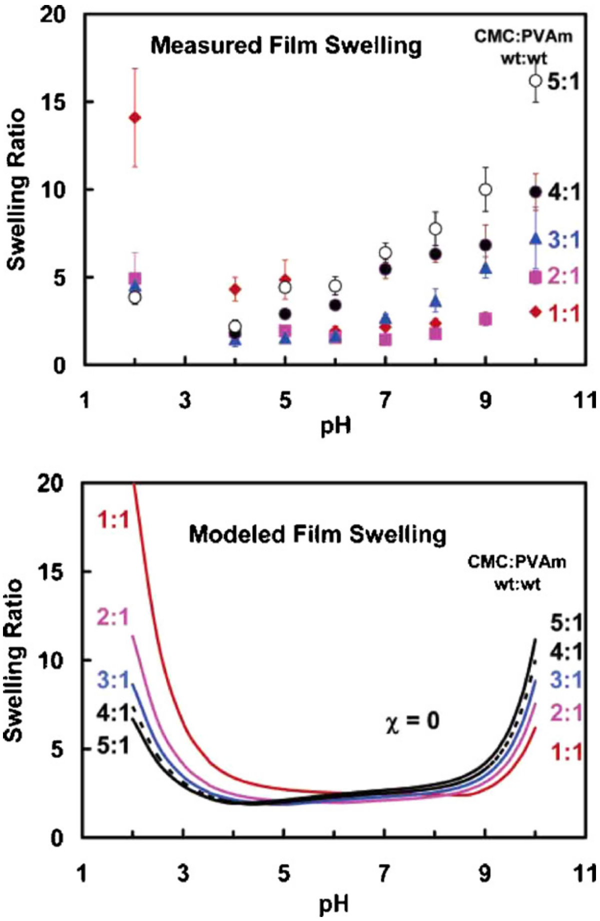

Fig. 6. Influence of pH on the swelling of CMC/PVAm complex membranes. The labels give the CMC/PVAm mass ratio. The pH is controlled by buffers with an ionic strength of 0.1 M. The points are experimental data, and curves are simulation results. The error bars represent standard deviations based on three measurements (Feng & Pelton, 2007).

4.3. *Interpenetrating polymer networks (IPNs)*

Interpenetrating polymer networks (IPNs) are defined as a combination of two or more polymers in network from that are synthesized in juxtaposition (Sperling, 1994). In the context of cellulose based hydrogels, IPNs can be divided into two types: sequential IPN and semi-IPN. For sequential IPN, cellulose is used as the first network and the second network is formed by polymerizing in the presence of the cellulose network. When cellulose or its derivative is linear or branched in a cross-linked network, it is called as semi-IPN hydrogel. High mechanical strength double-network (DN) hydrogel with bacterial cellulose and gelatin has been prepared by Gong et al. (Nakayama et al., 2004). This hydrogel is prepared by immersing BC gel in aqueous gelatin solution and cross-linking with *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (EDC), which belonged to sequential IPN hydrogel. Fig. 7 shows typical compressive (a) and elongational (b) stress–strain curves of BC-gelatin DN hydrogel, gelatin, and BC gels. The compressive fracture strength of the DN hydrogel in the direction perpendicular to the stratified structure is very high (3.7 MPa), which is about 31 times higher than that of gelatin gel (0.12 MPa). Further, the tensile strength of the DN hydrogel along the direction of stratified layer is nearly 3 MPa, which is 112 times larger than that of gelatin gels. This double network hydrogel exhibits not only a mechanical strength as high as several megapascals but also a low frictional coefficient of the order of 10^{-3}.

By employing cellulose hydrogel as the first network and *in situ* polymerizing/cross-linking *N*-isopropylacrylamide, we have successfully prepared IPN hydrogels based on cellulose and poly(*N*-isopropylacrylamide). The first network is created by chem-

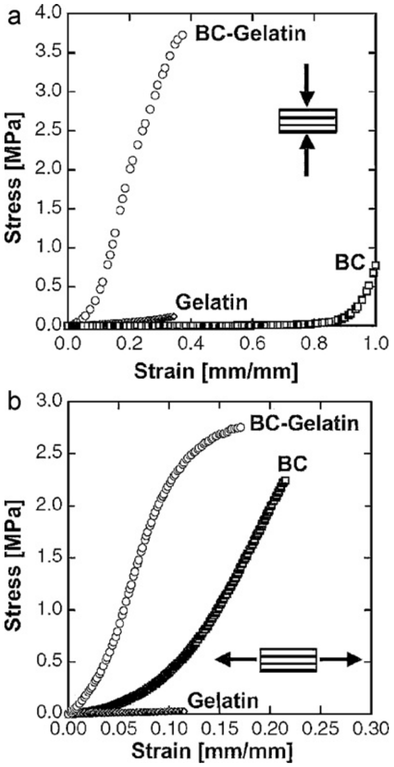

Fig. 7. (a) Compressive and (b) elongational stress–strain curves of BC-gelatin double network, gelatin and BC gels (Nakayama et al., 2004).

ically cross-linking cellulose with epichlorohydrin (ECH), and the second network is prepared by polymerizing/cross-linking *N*-isopropylacrylamide with *N,N′*-methylenebisacryamide (BIS) as cross-linker and ammonium persulfate (APS) as initiator. These hydrogels exhibit high mechanical strength and adjustable thermosensitivity, which depend strongly on the weight ratio between of the two polymer networks ($W_{\text{First network}}/W_{\text{Second network}}$) (Chang, Han, & Zhang, 2009c). Buyanov et al. have prepared bacterial cellulose-polyacrylamide (BC-PAAm) hydrogels by the synthesis of PAAm networks inside the BC matrices. These hydrogels exhibit superior mechanical properties, including compression strength of up to 10 MPa and are able to withstand long-term cyclic stresses (up to 2000–6000 cycles) without substantial reduction of mechanical properties (Buyanov, Gofman, Revel'skava, Khripunov, & Tkachenko, 2010). The dependence of the properties of hydrogels on the BC matrix preparation conditions, gel synthesis conditions and the BC content in the hydrogels has also been studied.

Semi-interpenetrating networks technology has been employed to prepare poly(*N,N*-dimethylacrylamide)/cellulose hydrogels in LiCl/DMAc (Williamson, Armentrout, Porter, & McCormick, 1998). The composite hydrogels are optically transparent, and exhibit a one-stage thermal degradation profile. The hydrogels containing 25% cellulose have 6-fold higher storage modulus and lower equilibrium water content than the *N,N*-dimethylacrylamide control system. High-strength cellulose/poly(ethylene glycol) gels have been prepared by swelling cellulose gel membranes in a low molecular weight polyethylene glycol (PEG). The cellulose gel membranes have been fabricated by a pre-gelation method through employing cellulose solutions in aqueous NaOH/thiourea at low temperature (Liang et al., 2007). These materials exhibit high mechanical performance, and their tensile strength increased sharply from 3.5 to 7.9 MPa with an increase in the molecular weight of PEG from 200 to 800 g/mol (Liang, Wu, Tian, Zhang, & Xu, 2008).

Semi-IPN hydrogels based on linear hydroxypropyl cellulose (HPC) and cross-linked poly[(*N-tert*-butylacrylamide)-*co*-acrylamide] (poly(NTBA-*co*-AAm)) have been obtained. In this case TBA is the temperature sensitive monomer, AAm can improve the mechanical strength of PTBA hydrogels, and HPC has both hydrophilic properties and good biocompatibility. Therefore, semi-IPN hydrogels have good mechanical strength, temperature sensitivity, and enhanced biocompatibility. Moreover, these semi-IPN hydrogels are temperature-sensitive and their volume phase transitions exist between 18 and 22 °C, irrespective of the amounts of HPC and BIS. However, below 18 °C, the swelling ratios of hydrogels are affected by the content of HPC and BIS, and the lower the BIS and the higher HPC contents in semi-IPN hydrogels, the faster the response rate as the temperature change (Caykara, Sengiil, & Birlik, 2006). Highly hydrophilic and pH sensitive semi-IPN hydrogels have been also prepared through constructing poly(acrylic acid) network with BIS as cross-linker and potassium persulphate (KPS) as initiator in the presence of carboxymethyl cellulose (CMC). The semi-IPN hydrogels can be used as vehicles for controlled delivery of ciprofloxacine (Cfx). The release of Cfx is dependent on pH, ion strength, and temperature (Bajpai & Mishra, 2008).

5. Cellulose-inorganic hybrid hydrogels

In recent years, polymeric-inorganic hybrid materials have attracted increasing attention due to potential applications in electric, optical, magnetic, and biological etc. fields (Nie, Pang, Wang, Lu, & Zhu, 2005). Introduction of inorganic into cellulose hydrogel networks is an effective way to develop materials with high functionality. For instance, biphasic calcium phosphate mixed with Si-HMPC is used as an injectable and self-crosslinkable bone substitute and also developed for filling bone defects. Bone has grown centripetally and progressed towards the center of the defects after the injectable materials are implanted into critically sized bone defects and remain in place for 8 weeks. The yield strength for the hybrid hydrogel-filled defects is 16.4 ± 7.2 MPa, significantly higher than for the host trabecular bone tissue (2.7 ± 0.4 MPa). These results show that biphasic calcium phosphate particles support the bone healing process by osteoconduction while the Si-HMPC hydrogel secrete intergranular space for bone ingrowth (Fellah et al., 2006).

Hutchens et al. have used bacterial cellulose (BC) as a template for the ordered formation of calcium-deficient hydroxyapatite (CdHAP). Their results indicate that CdHAP spherical clusters (1 μm) composed of nanosized crystallites have formed within the BC network, and it is highly likely that the CdHAP has an octacalcium precursor similar to natural bone apatite. The formation of this composite is similar to the physiological biomineralization of bone producing apatite crystals of comparable shape and size (Hutchens, Benson, Evans, O'Neill, & Rawn, 2006). The bioactivity of the CdHAP and the biocompatibility of the BC hydrogel substantiate these cellulose- CdHAP hydrogels as a potential orthopedic biomaterial. BC-CdHAP nanocomposites have been produced by introducing the mineral phase into the bacteria culture media during the formation of cellulose fibrils (Grande, Torres, Gomez, & Banó, 2009). By using CMC, the average diameter of cellulose fibers is almost 50% lower than the average diameter of unmodified BC fibers.

Novel heparin/cellulose/charcoal composites have been prepared at room temperature to enhance the biocompatibility and blood compatibility of activated charcoal (Park et al., 2008). The coating of activated charcoal reduces the surface pore size of the samples and protein adsorption while maintaining the bulk material's ability to adsorb small drug molecules. Therefore, it may be useful for direct hemoperfusion to remove free-diluted and protein-bound toxins of small size. IL is also applied to synthesize cellulose/single-walled carbon nanotubes (SWCNTs) complex (Li, Meng, Zhang, Fu, & Lu, 2009b). The fluorescence microscopy images of Hela cells on the composite, SWCNTs, and a glass slide after culturing for 24 h are shown in Fig. 8. Healthy cells exhibit green nuclei, uniform chromatin, and intact cell membrane, while cells in necrosis or in a late stage of apoptosis have red nuclei with damaged cell membranes. The cells culture on composite scaffold and a glass slide are healthy with green nuclei (Fig. 8a and c), but some cells culture on purified SWCNTs are in late stage of apoptosis (Fig. 8b). These results indicate that the hybrid material can promote the growth of Hela cells, showing good biocompatibility, compared to pure SWCNT scaffolds.

Macroporous cellulose-tungsten carbide composite beads have been fabricated for expanded bed application. Gelatinized cassava starch can be used as porogenic agent and tungsten carbide as high-density material. When the cassava starch is digested by amylase and the additional starch component is removed from the cellulose bead, the macropore structure appears in the hydrogel beads. There are two sets of pores: the normal diffusion pore (micropore) with characteristics of all hydrogel materials, and the much larger through pore (macropore) enabling part of flow to pass through each individual particle. These beads exhibit higher flow velocities of 500–900 cm/h (the expansion factor is 2–3) than streamline series and streamline Direct (Xia, Lin, & Yao, 2007). Further, their functional groups (diethylaminoethyl) are anchored on the beads as anion-exchangers for expanded bed adsorption, leading to the high adsorption capacity for bovine serum albumin (Xia, Lin, & Yao, 2008).

Cellulose-based hydrogels prepared by adding quantum dots (QDs) are an excellent model for understanding the influence of the interaction of QDs and macromolecular networks, because of the fluorescent properties of the QDs. Multifunctional hybrid microgels have been designed by using thermal sensitive HPC microgels and cysteamine-capped CdTe nanocrystals through the classical bioconjugation method. (Dou, Yang, Tao, Li, & Sun, 2010) The results indicated that QDs were covalently bonded to the polymer chains and dispersed throughout the microgels. Recently, we have employed cellulose hydrogel matrix and inorganic nanoparticles to fabricate cellulose-inorganic hybrid hydrogels (Chang, Peng, Zhang, & Pang, 2009b). Strong fluorescence hydrogels have been obtained from cellulose and quantum dots (QDs) in NaOH/urea aqueous system via a mild chemical cross-linking process. The CdSe/ZnS nanoparticles are embedded firmly in the cellulose matrices, as a result of the strong interactions between the CdSe/ZnS nanoparticles and cellulose. The cellulose-QDs hydrogels under UV lamp exhibit nearly pure color from green to red, depending on the sizes of QDs, as shown in Fig. 9. Moreover, the hybrid hydrogels possess good transparency and compressive strength. This is a new pathway for the development of safe and biocompatible biopolymer-QDs hydrogels. Cellulose-Fe_3O_4 microspheres have been prepared by sol-gel transition method. By using porous cellulose microphere as the matrix, Fe_3O_4 nanoparticles are "*in situ*" synthesized in the pores of cellulose microphere. The magnetic cellulose beads can efficiently adsorb the organic dyes from wastewater, and the used sorbents can be recovered completely. Their adsorption kinetics can be are fitted well by a pseudo-second-order equation. The shape of Fe_3O_4 nanoparticles is spherical and their average diameter is about 20 nm. These hybrid materials exhibit sensitive magnetic-inducted delivery and super paramagnetic properties (Luo, Liu, Zhou, & Zhang, 2009). Hybrid beads containing Fe_2O_3 and activated carbon can be fabricated via an optimal dropping technology for adsorption of organic dyes. Two organic dyes (methyl orange and methylene blue) are used as model dyes. The beads show high absorption capacity for both dyes. The absorption kinetics is fast with 180 min to reach equilibrium time, and the kinetic data are fitted well by a pseudo-second-order model. The magnetic properties of the beads allow their separation from the effluent by applying a magnetic field, leading to the development of a clean and safe process for water pollution remedy (Luo & Zhang, 2009). Electroconductive hydrogels (ECHs) are

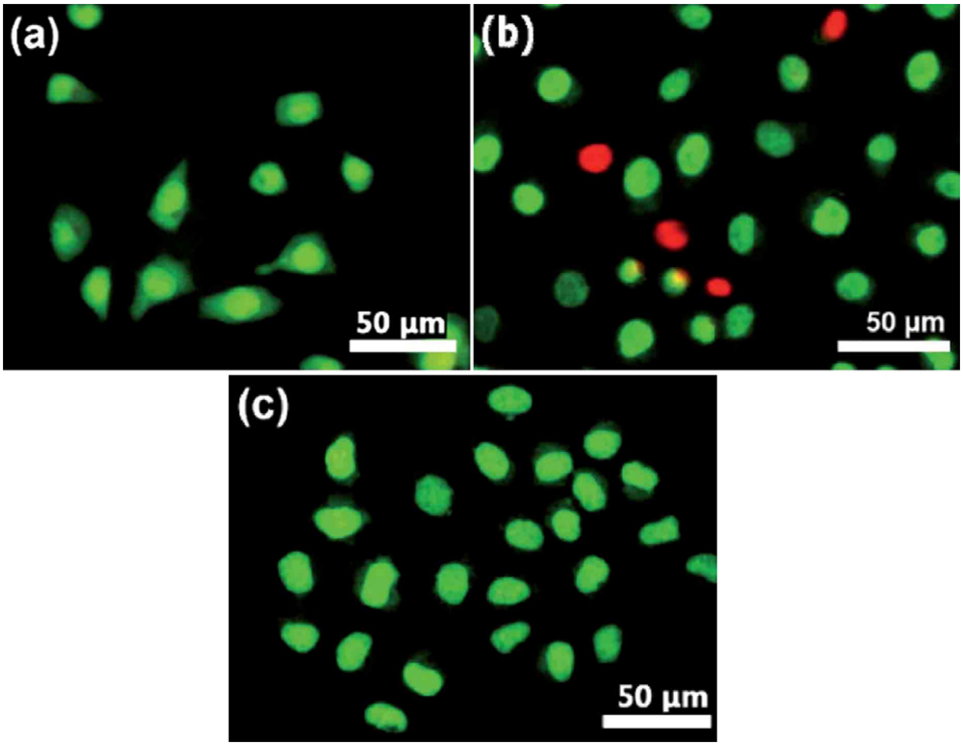

Fig. 8. Fluorescence microscopy images of Hela cells cultured for 24 h on (a) the composite, (b) the SWCNTs and (c) a glass slide. The cells are stained by acridine orange and ethidium bromide (Li et al., 2009b).

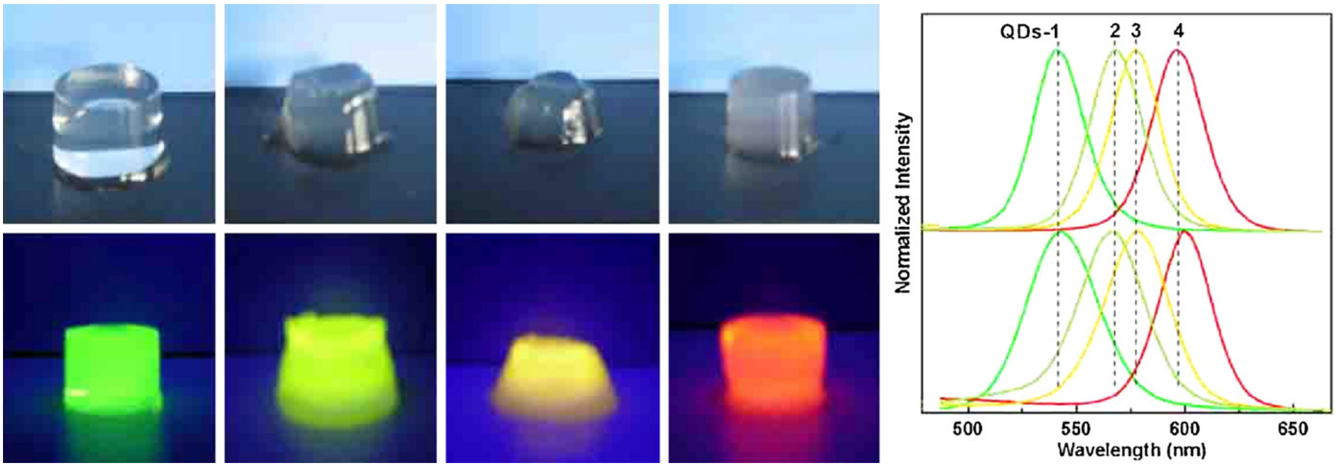

Fig. 9. The appearances of the cellulose-QDs hydrogels under visible light (left, top) and a 302 nm UV lamp (left, bottom), and PL spectra of CdSe/ZnS (core/shell) QDs in buffer solution (right, top) with emission peaked at 541 nm, 568.5 nm, 577 nm, 596 nm, and in the cellulose-QDs hydrogels (right, bottom) with emission peaked at 549.5 nm, 566.5 nm, 577 nm, 599 nm with a laser line at 400 nm used for excitation. The average diameters of the QDs nanocrystals are 2.8 nm (green), 3.0 nm (yellowish-green), 3.2 nm (yellow) and 3.6 nm (red) (Chang, Han, & Zhang, 2009c).

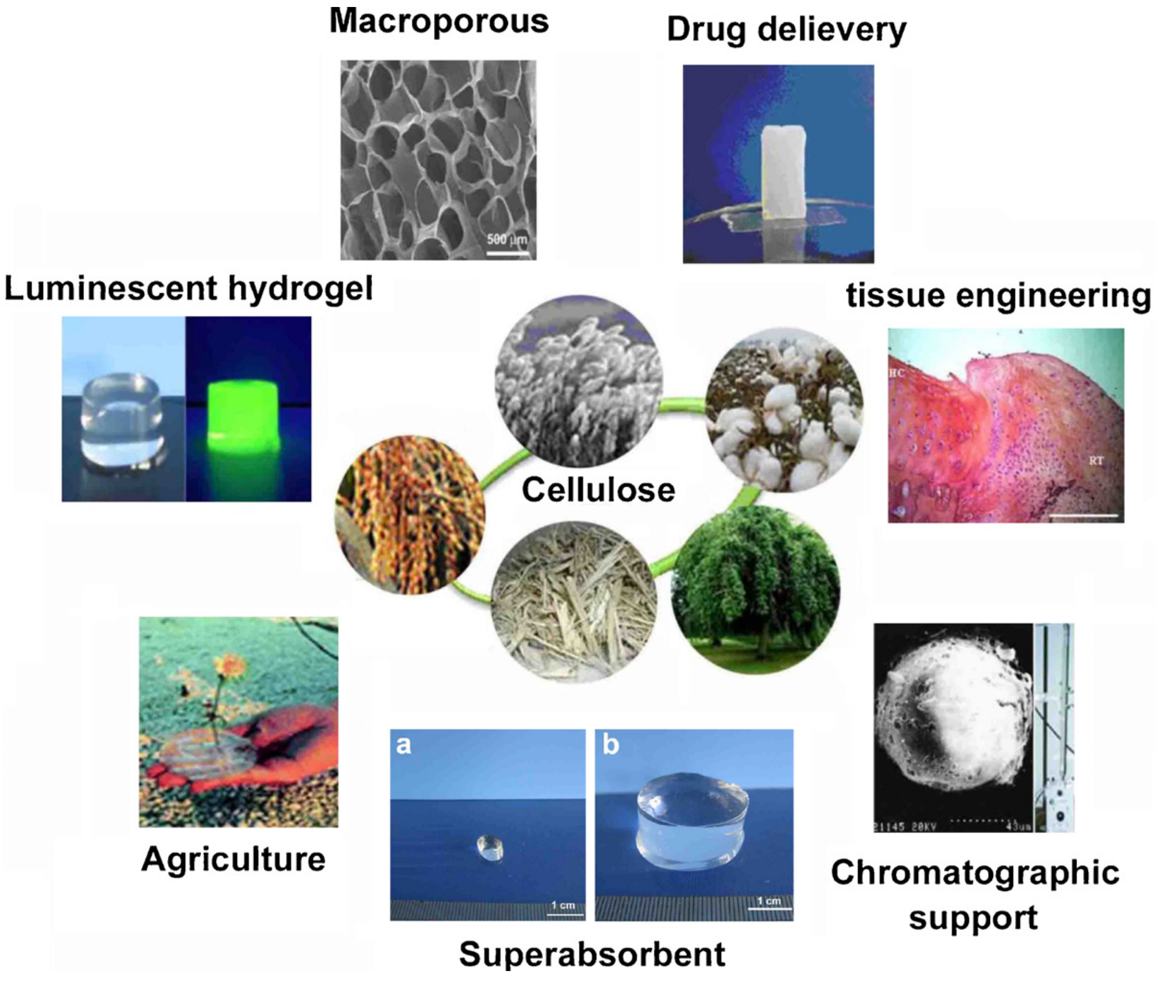

Fig. 10. Prospects for applications and developments of cellulose-based hydrogels (Chang et al., 2009a; Chang et al., 2009b; Chang et al., 2010; Liang et al., 2007; Marcì et al., 2006; Vinatier et al., 2009; Xiong et al., 2005).

a composite of biomaterials that bring together the redox switching and electrical properties of inherently conductive electroactive polymers (CEPs) with the facile small molecule transport, high hydration levels and biocompatibility of cross-linked hydrogels (Guiseppi-Elie, 2010).

6. Conclusion and further outlook

Cellulose hydrogels have been reported, along with identifying novel cellulose solvents such as LiCl/DMAc, NMMO, IL, and NaOH/urea (or thiourea) aqueous solution. With the development of cellulose derivatives, mainly cellulose ether, some stimuli-responsive hydrogels have been developed from MC, HPC, HPMC, and CMC, by both chemical and physical methods, leading to temperature sensitive hydrogels and pH sensitive hydrogels. Composite hydrogels from cellulose and other polymers have been prepared by blending, complex formation, and IPN technology, to combine the different properties of cellulose and other polymers. Various composite hydrogels can be designed in wide size from macroscopic materials such as membranes, fibers, and beads to microscopic materials such as microgels, and nanogels. Furthermore, cellulose hydrogel (including BC) can be used as matrices to incorporate inorganic nanoparticles for preparing cellulose-inorganic hybrid hydrogels. With the development of nanotechnology, this strategy is suitable for fabricating novel cellulose-based hydrogels with multifunctional properties.

Cellulose-based hydrogels have many favorable properties such as hydrophilicity, biodegradability, biocompatibility, transparency, low cost, and non-toxicity. Therefore, cellulose-based hydrogels have wide applications in tissue engineering (Vinatier et al., 2009), controllable delivery system (Chang et al., 2010), blood purification (Ye, Watanabe, Iwasaki, & Ishihara, 2003), sensor (Sannino, Pappada, Giotta, & Maffezzoli, 2007), agriculture (Ibrahim et al., 2007), as well as water purification (Zhou et al., 2005) and chromatographic supports (Xiong et al. 2005Xiong, Zhang, & Wang, 2005). Fig. 10 shows prospects for the various applications of cellulose-based hydrogels. Moreover, cellulose is environmental friendly and low-cost hydrogels, which will form a viable substitute for petroleum-based materials in near future.

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