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Self-Healing Supramolecular Polymers *via* Host-Guest Interactions

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Abstract: Self-healing or self-repairing materials are 'smart materials' that repair damage caused by mechanical force and are a key development of 21st century materials chemistry and engineering. In this review we describe a few excellent examples of self-healing supramolecular polymers based on host-guest interactions and discuss their advantages and versatility.

Keywords: Host-guest interaction, self-healing, supramolecular polymer.

1. INTRODUCTION

Chemists aim to make supramolecular polymers with beautiful topological structures. However, to use them as smart materials is a recent goal. Supramolecular polymers refer to polymers constructed not by conventional covalent polymerization of monomers, but rather by at least partially non-convalent interactions. The fact that noncovalent interactions are reversible and sensitive to the local chemical environment indicates that supramolecular polymers based on these weak interactions can be easily and reversibly broken and recovered as compared to conventional polymers, this unique reversibility makes supramolecular polymers easily processed, fabricated, and recycled. They are self-healing and stimuli responsive with shape-memory or tunable properties [1-10]. By taking advantage of the noncovalent interactions to make networks, supramolecular polymers can heal themselves spontaneously when damaged. These noncovalent interactions include hydrogen bonding, π-π stacking interactions, ionic bonds, metal-ligand coordination, etc. Each of these non-covalent interactions has distinct bond strength and advantages.

Although many efforts have been made towards supramolecular polymer/gel networks through host-guest interactions, these materials have been studied mostly for their responsiveness. It has been reported that supramolecular polymers based on host-guest interactions respond to pH, photo-irradiation, anions/cations, temperature, as well as solvent. Very recently, host-guest interactions have been used to construct self-healing supramolecular polymers and gels. In this paper, we review research advances in the construction of self-healing supramolecular polymers based on host-guest interactions. For an overview of other noncovalent interactions, please see other reviews [11-14].

2. HOST-GUEST CHEMISTRY

In supramolecular chemistry, host-guest chemistry investigates complexes that form between a host and a guest through noncovalent interactions. Besides those mentioned above, noncovalent interactions in host-guest complexes include the van der Waals force, charge-transfer interaction, ion-dipole interaction, hydrophobic interaction, etc. Supramolecular chemists originally concentrated on recognition studies of metal or ammonium ions. Over the past three decades, chemists synthesized and exploited a wide variety of macrocyclic hosts such as crown ethers (cryptands), cyclodextrins, calix[*n*]arenes, cucurbit[*n*]urils, cyclophanes, and pillararenes [15-17]. With their diverse structures and solubilities in organic or aqueous solution, each of those hosts has unique molecular recognition properties towards different guests (Fig. **1**).

2.1. Cyclodextrins

Cyclodextrins (CDs) are well-known water-soluble cyclic-oligosaccharide host molecules made from starch by enzymatic conversion. The CDs can form inclusion complexes with a variety of guests (especially neutral guests) through hydrophobic interactions due to their relatively hydrophobic interiors and hydrophilic exteriors. They have been widely used in catalytic chemistry, drug delivery system, food industries, as well as in analytical fields [18]. Their molecular recognition is particularly valuable for the synthesis of supramolecular polymers [19, 20].

The Harada group reported the first example based on host-guest interactions in the fabrication of a self-healing supramolecular polymer. They showed that redox-responsive self-healing materials could be made through host-guest interactions [21]. In this article the authors reported that by mixing pAA (poly(acrylic acid)) containing β-CD as host units with pAA containing ferrocene (Fc) as guest units, a transparent supramolecular hydrogel formed immediately (Fig. **2**).

They found that redox stimuli (both chemical and electrochemical redox reactions) efficiently induce a sol-gel phase transitions in the supramolecular hydrogel. The β-CD strongly bound to the Fc group due to hydrophobic interactions between host and guest, but had low affinity toward the Fc^+ group. Moreover, when the hydrogel was cut and the surfaces re-joined, the crack disappeared after standing for 24 h. Competition experiments (adding a competitive guest to occupy the cavity of β-CD so that β-CD could not bind the Fc group) indicated that the self-healing property of the hydrogel is due to the encapsulation of the Fc moieties into the β-CD on the damaged surfaces (Fig. **3**). Interestingly, if the cut surfaces were treated with an oxidant, healing did not occur due to the weak binding between β-CD and the Fc^+ group. The surfaces re-joined if treated with a reductant and allowed to stand for 1 day.

This is the first excellent example where host-guest interactions create simple, reversible, and stimuli-responsive self-healing materials! This self-healing hydrogel is potentially useful in drug-delivery especially because the CDs are environmentally benign.

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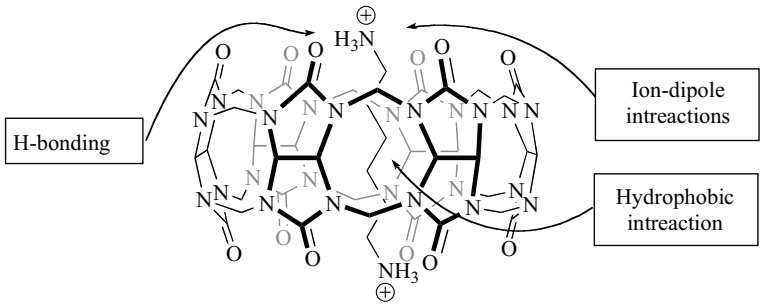

Fig. (1). A host-guest complex (protonated diaminohexane bound within cucurbit[6]uril) showing typical host-guest interactions.

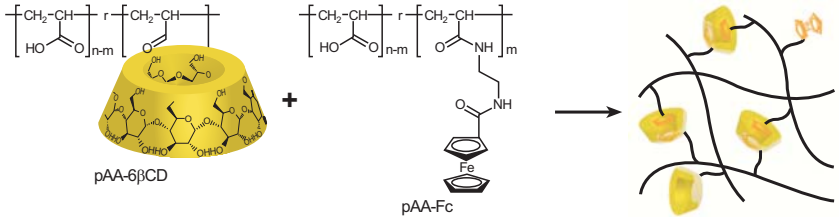

Fig. (2). Formation of hydrogel from CD-polymer and Fc-guest polymer. Reproduced with permission from reference [21]. Copyright 2011 Nature.

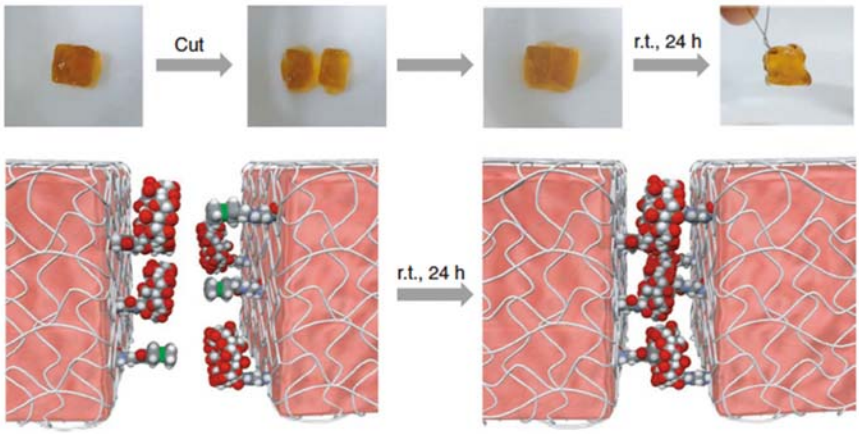

Fig. (3). Photographs & schematic of the self-healing procedure. Reprinted with permission from reference [21]. Copyright 2011 Nature.

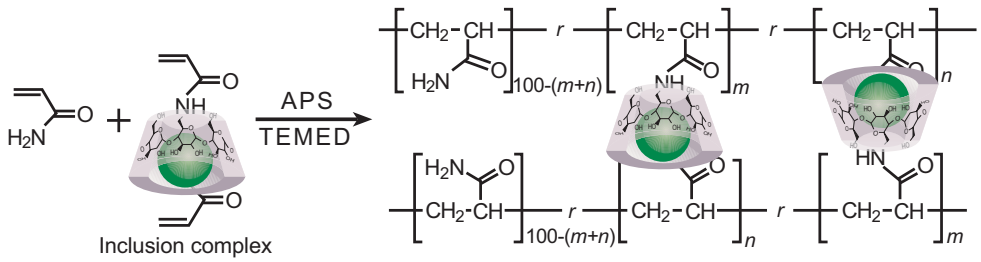

Fig. (4). Preparation of supramolecular hydrogels of the αCD-*n*Bu gel (*m*, *n*) and the βCD-Ad gel (*m*, *n*). Reproduced with permission from reference [22]. Copyright 2013 Wiley.

Instead of putting the host and guest separately onto the two polymer chains described above, Harada recently reported a cross-linked polymer with β-CD and adamantane moieties on the same polymer chain (Fig. **4**). The hydrogel formed in water exhibited a self-healing property and amazing shape recovery upon releasing the stress suggested the possibility of shape memory due to reversible host-guest interactions between the polymer branches [22].

By using a poly(glycidyl methacrylate) (PGMA) having Fc units and a bis-β-CD derivative, the Liu group made self-healing supramolecular polymers with electrically driven mobile properties [23]. The Yuan group also reported utilization of Fc- and β-CD-terminated bis-monomers to form water-soluble AA-BB-type supramolecular polymers based on host-guest interactions of the Fc and CD. The electrochemical-responsive Fc-CD association/dissociation makes these nanofibers uniquely self-degradable and healable *via* redox control [24]. Chen and co-workers have shown recently the first fabrication of host-guest (CD and N-vinylimidazole) supramolecular self-healing gels through a rapid non-contact procedure known as "magnetically induced frontal polymerization" (MIFP). The gels are able to spontaneously heal them-

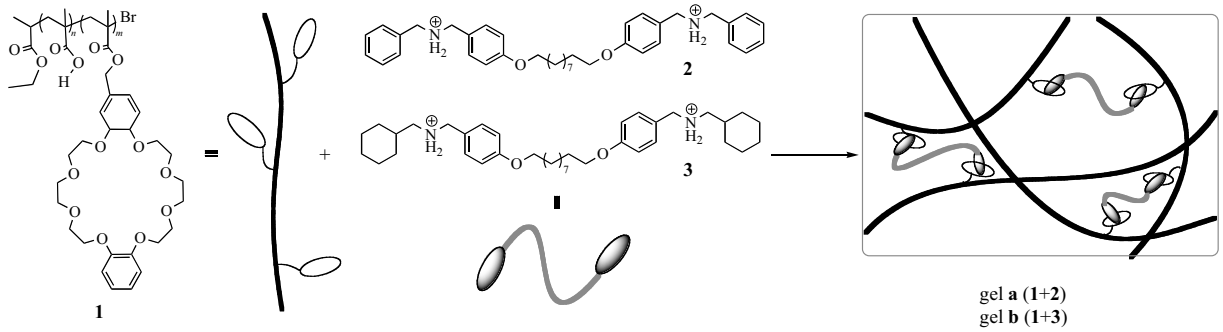

Fig. (5). Schematic of supramolecular gels prepared by crown ether units. Reproduced with permission from reference [28]. Copyright 2012 Wiley.

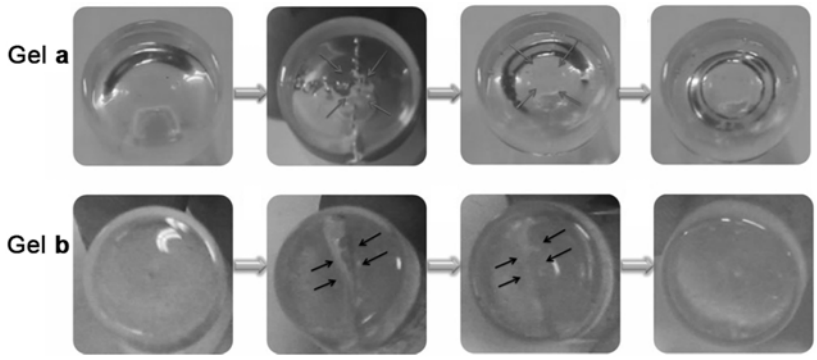

Fig. (6). Photographs of the self-healing process for gel **a** and gel **b** after damage. Reprinted with permission from reference [28]. Copyright 2012 Wiley.

selves when broken and have great mechanical strength. After being doped with Fe_3O_4, the self-healing of the gels was greatly accelerated under a magnetic field due to the combination of host-guest interactions and the magneto-caloric effect. This method gives "new insight into the rapid fabrication of novel bio-inspired materials" [25].

2.2. Crown Ether

As the first generation of hosts in supramolecular chemistry, the crown ether captures cationic guests through cation-dipole interactions with large stabilization energy [26]. After many years of study, the complexation of crown ether and its derivatives with guests are quite detailed. They have been used to construct supramolecular polymers with novel properties [27].

The first example was reported by the Huang group in 2012 [28]. They prepared two polymeric gels by mixing a poly (methyl methacrylate) (PMMA) polymer possessing dibenzo[24]crown-8 (DB24C8) units with two different bis-ammonium salts in organic co-solvents (Fig. **5**).

One of the gels (gel **a**) can undergo reversible gel-sol transitions by changing the pH because the host-guest interactions between the crown ether and the ammonium group are sensitive to pH. This property makes the gels degradable materials controlled by pH. Both gels also showed self-healing properties but gel **b** self-repaired faster than the other after damage due to multiple noncovalent interactions including electrostatics, hydrogen-bonding, and host-guest interactions (Fig. **6**).

Later, Huang and co-workers prepared another supramolecular polymer gel by orthogonal self-assembly of a homoditopic host, a bisammonium salt and a metallic cross-linker. The gel exhibits quadruple-stimuli induced reversible gel-sol transitions and possesses self-healing capabilities. Moreover, the healed gel retains its shape well even after multiple mechanical movements. Because of these interesting properties, the gel could be used as a soft material [29]. Chen and co-workers made a similarly stimuli-responsive and self-healing supramolecular polymer gel using a bis(crown ether) derivative and a copolymer possessing dibenzylamonium units [30, 31]. Through click chemistry, the Ikeda group made two glycidyl triazole polymers that separately contained crown ether units and secondary ammonium groups. The organo-gel was made by mixing these two polymers in $CHCl_3$ or $C_2H_2Cl_4$ (Fig. **7**). As expected, the gel was stimuli responsive to multiple stimuli including temperature, pH or competitive guests. It was self-healing [32].

2.3. Cucurbiturils

Cucurbit[*n*]urils (CB[*n*]s) are a macrocyclic molecule made from glycoluril. Due to their exceptional recognition properties in aqueous solution, these pumpkin-shaped hosts have become key building block for various self-organizing and stimulus-controlled assemblies including supramolecular catalysts, advanced materials and drug carriers [33-36].

CB[8] has a relative larger cavity, which allows it to hold bigger guests or even two different kinds of guests. For example, CB[8] can form a 1:1 inclusion complex with methyl viologen (MV). The addition of naphthalene (Np) creates a very stable 1:1:1 ternary complex (MV and Np are encapsulated in CB[8]) [37]. Based on this, the Scherman group reported the first example of a supramolecular polymeric hydrogel *via* CB host-guest interactions in 2010 [38]. Zhang *et al.* also made a serial of novel CB[8]-based supramolecular polymers [39]. In the follow-up studies, Scherman and co-workers reported that the self-assembled supramolecular hydrogels contained up to 99.75% water [40].

Another type of hydrogel is formed by adding CB[8] to a mixture of the naphthyl-functionalized cellulose (HEC-Np) and an MV unit functionalized with poly(vinyl alcohol) (PVA-MV) in water. In this system, CB[8] is a linking agent to combine two different

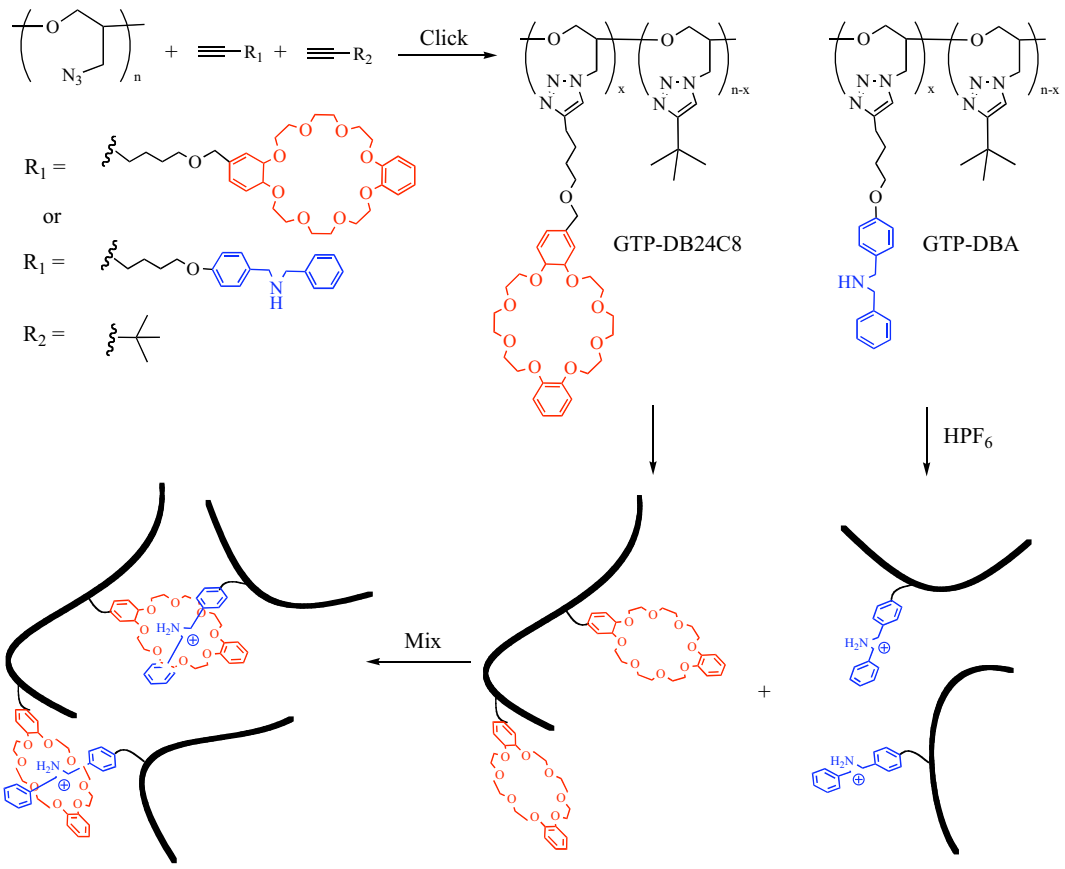

Fig. (7). Synthesis of GTPs containing a crown ether or a secondary ammonium units for the preparation of supramolecular gels. Reprinted with permission from reference [32]. Copyright 2013 American Chemical Society.

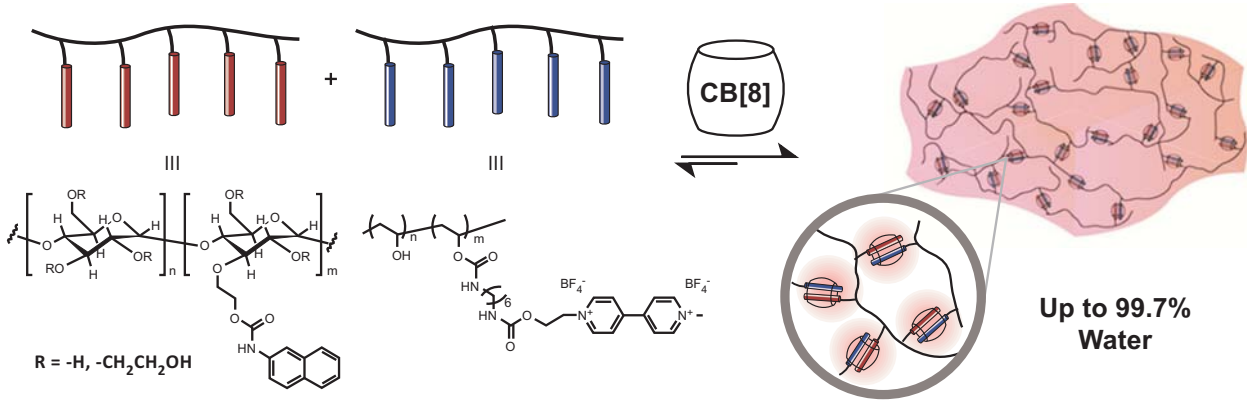

Fig. (8). Schematic of a supramolecular hydrogel. Reprinted with permission from reference [40]. Copyright 2012 American Chemical Society.

polymers and form a copolymer (Fig. **8**). The hydrogel had highly tunable mechanical properties and was responsive to temperature, competing secondary guests, and redox conditions.

To study the self-healing properties of the hydrogel after breakdown at high shear rates, step-rate experiments were performed. The exceptionally fast (seconds) and total recovery (~ 100%) of viscosity after deformation of the hydrogel is highly related to the strong host-guest interactions and the extremely rapid association kinetics ($k_a \approx 10^8$ M^{-1} s^{-1}). The shear-thinning and fast recovery properties make these materials potential candidates for use as 'shear-thinning' materials in various biomedical and industrial applications (Fig. **9**).

In addition to these examples, the Kim group has reported hydrogels from polymer containing CB[6] and alkylamonium guest units derived from 1,6-diaminohexane (DAH) and spermine (SPM) [41]. Our group is attempting to make mechanically stronger self-healing polymers by mixing polymer containing CB[7] with an Fc derivative. This has the highest binding constant of CB[7] with the Fc-guest interaction at ~10^{15} M^{-1} [42, 43].

2.4. Other Hosts

Other hosts include calix[n]arenes [44, 45] and pillararenes [46, 47]. Both of them are easily functionalized and have shown their excellent recognition properties towards different guests. They are

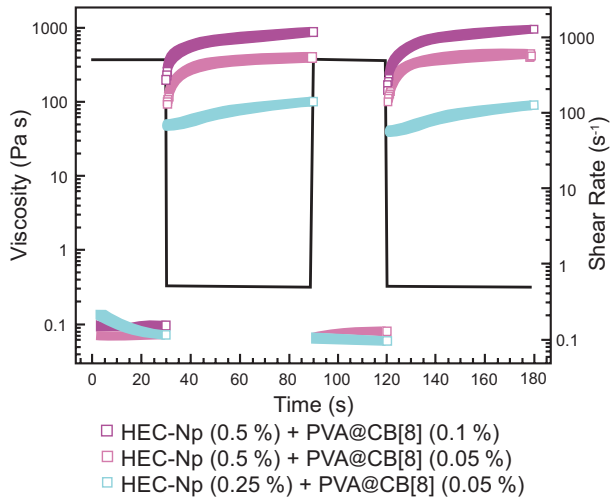

Fig. (9). Step-rate time-sweep measurements. Reproduced with permission from reference [40]. Copyright 2012 American Chemical Society.

also good candidates for making supramolecular polymers, but have not yet been used in the construction of self-healing materials.

5. CONCLUSION

Self-healing supramolecular materials made through host-guest interactions have exceptional properties including autonomously self-healing, self-degradability, shape-memorization, etc. They are useful in many applications including drug-delivery systems and bio-inspired materials. Commonly, supramolecular self-healing materials rely on the reversible and dynamic nature of supramolecular interactions. This raises another question into the mechanical properties of the material. But with the further investigation into the recognition properties of various hosts and the development of polymer chemistry, an increasing number of interesting self-healing materials will be prepared in the future based on host-guest interactions to compensate for this deficiency.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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