Diversification of Nonionic Amphiphilic Poly(*N*-vinylacetamide) Hydrogels by a Double Network Approach

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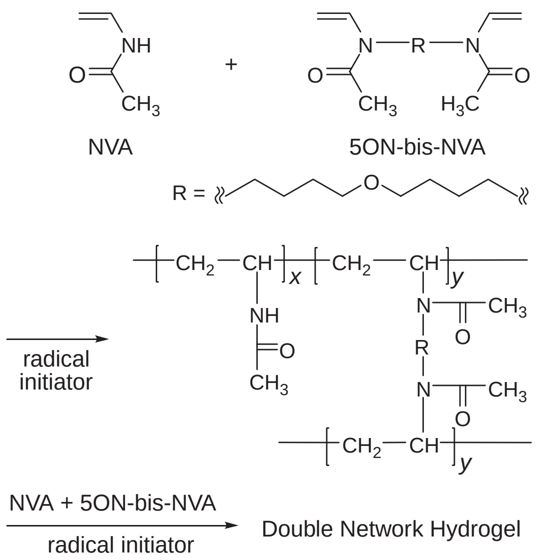
The amphiphilic aprotic vinyl monomer, *N*-vinylacetamide (NVA), was firstly employed to fabricate double network (DN) hydrogels in water at 37 °C. Although *N*,*N*-methylenebisacrylamide as a crosslinker did not form hydrogels, novel crosslinker which is based on the structure of NVA was effective in creating first and second network hydrogels. DN structures of nonionic NVA hydrogels will expand the pool of various functional hydrogels, as well as give rise to stronger NVA hydrogel preparations.

N-Vinylacetamide (NVA) is an *N*-vinylalkylamide derivative, which bears vinyl groups on nitrogen atoms and various alkyl side chains bound by amide linkages (Scheme 1).[1,2] NVA is an amphiphilic and aprotic monomer and distinguished from other widely used vinyl monomers, such as methacrylates and acrylamides. Superabsorbent hydrogels usually possess hydroxy or ionic groups in their structures, such as poly(vinyl alcohol) and poly(acrylic acid), thus their swelling ratios are influenced by ionic compounds within water. On the other hand, swelling ratios from nonionic NVA hydrogels are stable and do not change even in the presence of electolytes.[3] So, NVA hydrogels are considered suitable for biomedical applications, which require the absorption of blood, sweat, and other body fluids. Besides, its amphiphilic character is expected to give rise to high affinities towards various drugs and biomacromolecules. However, reports on NVA hydrogels are limited to a few dozen at the present time, although numerous studies on structures similar to polyacrylamide hydrogels have been made.



Scheme 1. Synthesis of NVA hydrogel.

One of the reasons for the poor variety of components on conventional NVA hydrogels might be ascribed to the simple radical polymerization. The reactivity of NVA on free radical polymerization is classified as a nonconjugated-type vinyl monomer, such as vinyl acetate, vinylpyrrolidone,[4] and different polymerizability results in the unavoidable block-like copolymer. Therefore, structural variety and various applications with amphiphilic poly(NVA) are difficult, when conventional methods are used for their preparation. Recently, double network (DN) hydrogels have received increasing interest from researchers, since DN structures provide dramatic improvements to mechanical strengths[5–7] and lead to the production of new intelligent materials, such as dual-stimuli-responsive degradation[8] and highly thermosensitive materials.[9]

In this letter, we firstly report the preparation of novel NVA hydrogels by a DN approach; NVA was simply polymerized in the first NVA hydrogel network. The DN approach will contribute to the wide expansion of functional NVA gels in the future. DN and single network (SN) hydrogel mechanical strengths were also investigated.

The novel crosslinker, *N*,*N*-5-oxanonamethylenebis-*N*-vinylacetamide (5ON-bis-NVA) was synthesized for this study, according to a previously reported method (Scheme 1).[10,11] A typical procedure for preparing NVA hydrogels is as follows: NVA (0.34 g, 4 mmol), 2,2′-azobis(2-methylpropionamidine) dihydrochloride (V-50; radical initiator) (11 mg, 0.04 mmol), and 5ON-bis-NVA (12 mg, 0.04 mmol) were dissolved in degassed water (2 mL) at 2 mol/L. The solution was injected between double glass plates that were separated by a silicon gasket (1.0- or 2.0-mm thickness) under a nitrogen atmosphere. After the first polymerization at 37 °C for 4 h, the obtained hydrogels were cut into squares (5 × 5 mm) for 1.0-mm hydrogels or disks (9-mm diameter) for 2.0-mm hydrogels, respectively. SN hydrogels were immersed in a second aqueous NVA solution (2 mol/L), containing 1 mol % 5ON-bis-NVA and 1 mol % V-50 at 4 °C for 1 day, until equilibrium was reached. A second network was then introduced by polymerization at 37 °C for 6 h between double glass plates that were separated by the same silicon gasket (1.0- or 2.0-mm thickness) under a nitrogen atmosphere. Each hydrogel was immersed into a large amount of distilled water for 1 week, changing water everyday to remove reaction residues. Table 1 shows hydrogel thicknesses, swelling ratios, and compression strengths under various conditions. The polymerization proceeded quantitatively for every first network preparation (Table 1, Run 1, 2, 5, and 6). Yields of DN hydrogels at sec-

Table 1. Preparation of NVA hydrogels[a]

Run	First network /mol L^{-1}	Second network /mol L^{-1}	Thickness Gasket /mm	Thickness Gel[b] /mm	Swelling ratio[c]	Compression[d] strength /MPa	Compression[d] strain /mm
1	2.0	—	1.0	1.7	14.4	0.51	1.2
2	2.0	—	2.0	3.0	12.6	0.33	2.2
3	2.0	2.0	1.0	2.2	9.9	1.6	1.3
4	2.0	2.0	2.0	3.7	9.7	2.3	2.9
5	4.0	—	1.0	1.5	9.7	1.3	1.1
6	4.0	—	2.0	3.1	9.4	1.4	2.6

[a] [NVA]:[V-50]:[5ON-bis-NVA] = 100:1:1, polymerized in water at 37 °C for 4 h for the first network and for 6 h for the second network. [b] Swollen hydrogels at room temperature. [c] The swelling ratio was defined as $(W_s - W_d)/W_d$. [d] Determined by a compressive tester (EZ Test, Shimadzu, Co.).

ond networks were calculated via weight increases of dried gels, compared to those of SN gels (86 and 78% yields for Run 3 and 4 in Table 1, respectively).

The thickness of hydrogels could be influenced by the compression procedure, and it is not simply in proportion to the swelling ratio. Thus, the degree of swelling of the hydrogel was calculated by the use of the following equation: $(W_s - W_d)/W_d$, where W_s is the weight of the swollen hydrogel at room temperature and W_d is that of the dried gel. For example, the SN hydrogel prepared with a 1-mm gasket swelled to 1.7-mm thicknesses (Table 1, Run 1). Then, the SN hydrogel was compressed to 1.0 mm to prepare the DN hydrogel (Table 1, Run 3), swollen to 2.2-mm thickness. As a result, similar swelling ratios were obtained for the DN hydrogel and the SN hydrogel with the twice condensed concentration of a one pot preparation (Table 1, Run 3 and 5; Figures 1b and 1c). The same tendency was observed in the case of the 2-mm gasket (Table 1, Run 2, 4, and 6), suggesting that the double network exists within the hydrogel relatively homogeneously. It is noteworthy that when *N*,*N*-methylenebisacrylamide was used as a crosslinker instead of 5ON-bis-NVA it did not form secondary networks in the DN hydrogel preparation, probably because different radical reactivities with NVA were unfavorable, especially in the creation of hydrogels at 37 °C.[12] All hydrogels were quite transparent, indicating that NVA polymerized homogeneously (Figure 1).

In order to compare the mechanical strength of hydrogels, the maximal compression strength was determined by fractures using a compressive tester (EZ Test, Shimadzu, Co.) with a speed of 1 mm/min as shown in Figure 2 ($n = 3$). The average values are also listed in Table 1. Furthermore, the compression strength ratio DN/SN is a reasonable value around 7 (Table 1, Run 2 and 4).[5] The possibility of crack initiation before the fracture stress could be exclude, because of no significant difference between 1- and 2-mm hydrogels. Although no significant difference was observed for DN hydrogels and SN hydrogels with twice condensed concentration, the average value from DN hydrogels was slightly higher than that from SN hygrogel, and it provides basic information of mechanical strength on nonionic DN hygrogel (Figures 2b and 2c).

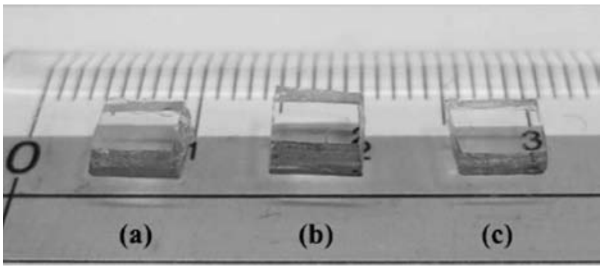


Figure 1. Photos of NVA hydrogels of the SN with 2 mol/L (a), DN with twice 2 mol/L (b), and SN with 4 mol/L (c).

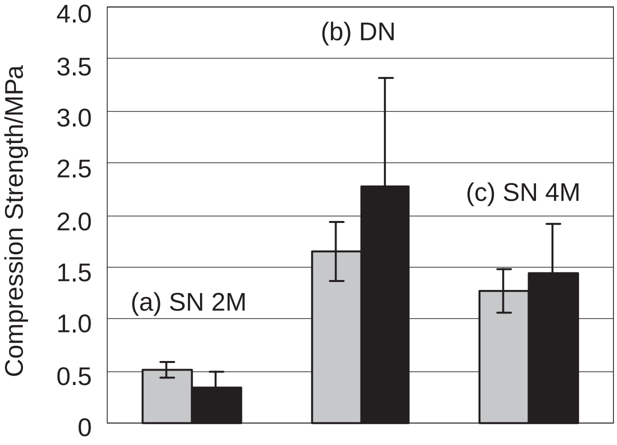


Figure 2. NVA hydrogel compression strengths of SN with 2 mol/L (a), DN with twice 2 mol/L (b), and SN with 4 mol/L (c). The light bars on the left and the dark bars on right indicate hydrogels prepared with 1- and 2-mm gaskets, respectively.

In conclusion, amphiphilic aprotic NVA hydrogels were applied in DN structures, using a novel crosslinker at 37 °C in aqueous solvents. Further investigations with a variety of functionalities from DN gels composed of *N*-vinylalkylamide are currently underway.

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11 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/.
12 The NVA (0.34 g, 4 mmol), *N*,*N*-methylenebisacrylamide (6.2 mg, 0.04 mmol), and V-50 (11 mg, 0.04 mmol) were dissolved in degassed water, then warmed up to 37 °C for 4 h to yield only fluidic mixture.