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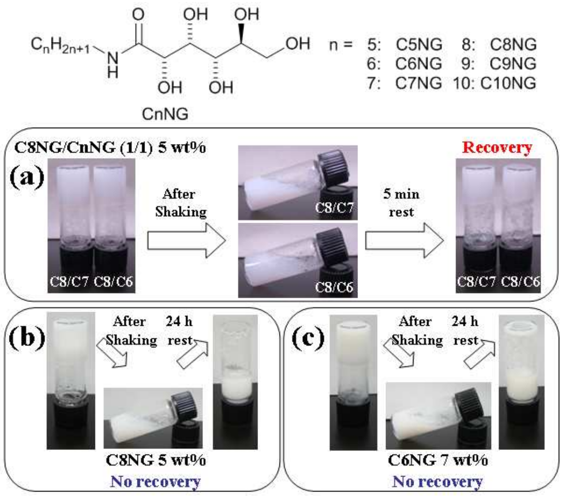
Graphical Abstract:



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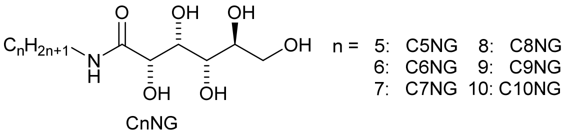
We determined the onset of thixotropy in hydrogels when two homologues of low-molecular-weight hydrogelators, *N*-alkyl-D-glucamides, were mixed. Intriguingly, the hydrogels generated from the individual components did not show such behaviour. The mixing induced onset of thixotropy might be attributed to the improved network quality.



Scheme 1. Chemical structures of *N*-alkyl-D-glucamides.

Hydrogels, which are hydrophilic polymeric materials, facilitate activity of cells[1a] and have applications in pharmaceuticals,[1b] biomedicals,[1d,e] and tissue engineering.[1e,f] Creation of novel hydrogels that are different from ordinary hydrogels, which are primarily composed of polymers, is a developing field in material chemistry. Low-molecular-weight gelators (LMWGs)[2,3] are novel hydrogels, which show unique properties comparable to polymer-based hydrogels, such as multi-stimuli responsiveness,[4] and have potential applications in medicinal and optoelectronic fields.[5,6] For creating such types of LMWGs extensive investigation is required for the suitable molecular motifs containing various functionalities. Moreover, methods to easily and effectively add functionalities to hydrogels made from known LMWGs need to be explored.

Here, we report the functionalization of hydrogels by mixing two LMWGs, *N*-alkyl-D-glucamides, with alkyl chains of different lengths. We observed that mixing of the two components enhances the gelation effect and mechanical properties of the two-component systems, especially the thixotropic property, which is known as shear thinning,[7] and other unique properties related to molecular network in the hydrogel.[8] Previously, we reported the enhancement in thixotropic properties of organogels by mixing LMWGs (alkylhydrazides, alkylamides or alkylureas having different alkyl chains).[9] We now extend this two-component mixing method for the creation of a new hydrogel based on *N*-alkyl-D-glucamide, which is a LWMG that has been studied extensively by Fuhrhop et al. and other researchers.[10-14] Note that hydrogelation properties and the microstructure of crystal fibres formed by mixing the two *N*-alkyl-D-glucamides (*N*-octyl and *N*-dodecyl) have also been investigated;[10c] however, mixing induced onset of thixotropy is the focus of this report. Several systems that involve mixing-induced enhancement of gel properties or formation of gels have been extensively investigated.[15,16] Our strategy involves simply mixing homologues of LMWGs; these LMWG homologues contain the same polar hydrogen bonding moiety with hydrophobic alkyl chains of different lengths.

The synthesis of N-alkyl-D-glucamides, CnNG (n = 5–10) with alkyl chains of different lengths was performed following established procedures (Scheme 1).9 Initially, we evaluated the hydrogelation ability of each compound. Table 1 lists the critical gelation concentration (CGC) for each CnNG, i.e. one-component hydrogels. As described previously in literature,9 C8NG formed an opaque hydrogel , but started to crystallize within several days. Furthermore, C10NG, C9NG and C7NG formed opaque hydrogels, but crystallized within several hours, whereas C5NG remained as an aqueous solution after the gelation test. A weak hydrogelation was observed with C6NG (7 wt%), but no crystallization was observed over a 3 month period. Next, we evaluated hydrogelation with binary mixtures of CnNGs (Table 1). In

Table 1 Critical gel concentration (CGC) for hydrogels from CnNGs (see ESI,† Fig. S1 and Fig. S2 for photos after gelation test).

Sample	CGC (wt%)	Sample* ratio(w/w)	CGC (wt%)	Sample* ratio(w/w)	CGC (wt%)
C10NG	5.0	C10/C9 1/1	5.0 (PG)	C9/C7 1/1	3.0
C9NG	3.0	C10/C8 1/1	3.0	C9/C6 1/1	3.0
C8NG	3.0	C10/C7 1/1	3.0	C8/C7 1/1	2.0
C7NG	3.0 (K)	C10/C6 1/1	3.0	C8/C6 1/1	2.0
C6NG	7.0	C9/C8 1/1	3.0	C7/C6 1/1	5.0
C5NG	S(10.0)				

*‘Cn’ etc. denotes CnNG. wt% refers to the total weight of all of the components. **Key**: K: solidified with crystalline appearance. S: solution at the concentration. PG: partial gel at the concentration.

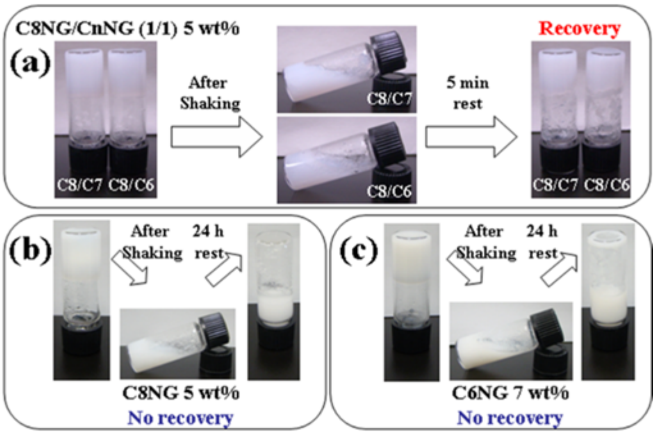


Fig. 1 Images of hydrogels before, during and after gelation and thixotropic tests. (a) C8NG/CnNG 1/1 (w/w) 5 wt%, (b) C8NG 5 wt%, and (c) C6NG 7 wt% hydrogels.

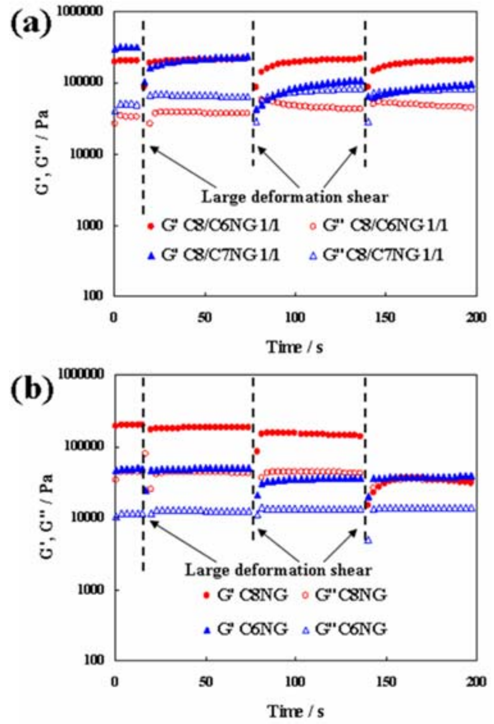


Fig. 2 Periodic step-shear test results for hydrogels. (a) C8NG/CnNG 1/1 (w/w) 5 wt%, (b) C8NG 5 wt% and C6NG 7 wt% hydrogels.

these results, all hydrogels, i.e. two-component hydrogels, were either opaque or turbid, and the hydrogenation ability of different CnNG mixtures showed gelation ability that is either similar to or better than individual components. The poor hydrogelation ability of C7NG/C6NG (5 wt%) was probably due to the high CGC of C6NG and the tendency of C7NG to appropriate CnNGs enhanced the hydrogelation abilities of the mixture and inhibited the tendency of the hydrogelators to crystallize.

The obtained hydrogels were evaluated for their thixotropic properties. One-component hydrogels did not exhibit thixotropic behaviour; however, the hydrogels obtained from two-component mixtures C8NG/C6NG (1/1, w/w) and C8NG/C7NG (1/1, w/w) were clearly thixotropic (Fig. 1). Whereas previous reports show that the two-component hydrogel formed with C8NG /sodium dodecyl sulfate as better hydrogel,[10b,12] it was only weakly thixotropic (see ESI,† Fig. S3). Therefore, these results, showed that C8NG/C6NG and C8NG/C7NG were good examples of mixing-induced thixotropy in hydrogels.

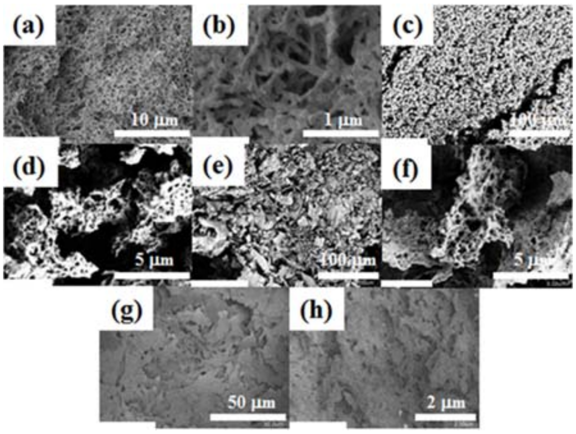


Fig. 3 SEM images of CnNG xerogels. (a and b) C8NG (3 wt%); (c and d) C6NG (7 wt%); (e and f) C8NG/C6NG 1/1 (2 wt%); and (g and h) C8NG/C7NG 1/1 (2 wt%). The values in parentheses are the concentration of the hydrogels prior to generation of the xerogels.

Rheological tests identified that gelation occurred with both one- and two-component mixtures, and the results obtained were similar to that observed for polymer-based gel (see ESI,† Fig. S4 and Fig. S5).[17] In the frequency sweep, the existence of a gel was shown by a profile with a pseudo plateau and a storage modulus (*G*′) > loss modulus (*G*″). With increasing stress, the relationship between the *G*′ and *G*″ for each hydrogel was switched from *G*′ > *G*″ (gel state) to G′ < *G*″ (sol state).

To evaluate the thixotropic behaviours, the rheometry of each hydrogel was investigated by step-shear measurement (Fig. 2). The C8NG/C6NG hydrogels repeatedly showed recovery of *G*′ and *G*″ (with *G*′ > *G*″) after a large shear, whereas the hydrogel with C8NG/C7NG showed recovery only after the first deformation shear and subsequently attained a sol-like state (similar values were obtained for *G*′ and *G*″). The moduli were also recovered for hydrogels made with C8NG and C6NG (C8NG showed a two-fold recovery). However, these measurements using small amounts of gels possibly do not reflect the large-scale properties of the gel, e.g. self-support of the gel itself as observed in Fig. 1c. Fig. 2 shows the mixing induced changes in mechanical properties of CnNG(s) hydrogels qualitatively.

The thermal properties of one- and two-component CnNG hydrogels were characterized by differential scanning calorimetry (DSC). The analysis of DSC curves (see ESI,† Table S1 and Fig S6) indicated that sol-to-gel and gel-to-sol transition for these hydrogels involved similar ΔH's. However, the peak temperatures for the transitions in two-component hydrogels were higher than that observed for one-component gels. This suggested that hydrogelation with two-component mixtures led to the formation of a denser and finer structural network than that in one-component hydrogels.

The investigation into the microstructures of hydrogels were conducted by scanning electron microscopy (SEM) analysis of the xerogels obtained from the one- and two-component hydrogels (Fig. 3). These results suggested that the two-component CnNG hydrogels had the same submicrometer order fibrous and network character as that of the one-component hydrogel. Fuhrhop et al. have provided SEM evidence for the formation of fibres of a single component in a CnNGs-based multi-gelator gels through a process of self-sorting[10c]; however, no evidence for self-sorting could be discerned in the data from our experiments.

X-ray diffraction (XRD) analysis of the crystal fibres of the hydrogels (see ESI,† Fig. S7) showed that similar single peaks were observed for two- and one-component hydrogels; moreover, the XRD peak positions for the hydrogels were comparable to that obtained for one-component CnNG xerogels. The position of these peaks nearly corresponded to contour molecular length and alkyl chain length of CnNG (see ESI,† Fig. S8) and suggested that these hydrogelators formed lamellar or bilayer-like structures, as shown previously.[10a-c] There is no direct evidence for self-sorting in these experiments as observed in Fuhrhop's mixed CnNG hydrogelators; however, such an occurrence could be masked if the peaks representing the different self-sorting structures in multi-gelator gel overlapped.

Considering self-sorting of CnNG as reported previously,[10c] the mixing-induced regulation of rheological properties of two-component hydrogels (i.e. prevention of crystallization, reduced CGC and onset of thixotropic behaviour) can be attributed to the possibility that the CnNGs in the two-components hydrogel reinforced each other. In this speculation, one fibre and/or network is extended by an addition of other fibre and/or network, which then enables effective crosslinking of fibres and/or network and results in inhibition of crystallization, reduction of CGC and the onset of thixotropy in two-component hydrogels.

In conclusion, we demonstrated that simply mixing two *N*-alkyl-D-glucamide hydrogelators induces thixotropic behaviour in the two-component hydrogel, while the one-component hydrogel did not exhibit such a behaviour. Through this study, we extended the 'mixing' strategy used for preparing organogels to the creation of new hydrogels with LMWGs composed of a polar head group and an alkyl substitution. We are now extending this mixing strategy further to other molecular hydrogelators.

Notes and references

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