Soft Matter

PAPER

Using polymeric additives to enhance molecular gelation: impact of poly(acrylic acid) on pyridine-based gelators†

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The effect of polymeric additives on molecular gelation was explored using poly(acrylic acid) and pyridine-based gelators. A significant reduction in the critical gel concentration (cgc) and an increase in gel strength were observed when the polymer was present during gel formation. Detailed studies revealed that the polymer is adsorbing onto the growing fibers, reducing the growth rates, and leading to thinner fibers. These and other morphological changes lead to improved gel properties by increasing the number of fiber–fiber entanglements. Several other polymers were briefly examined and these studies revealed that polymer structure is important. The polymer containing a complementary functional group relative to the gelator (*e.g.*, H-bond donor/acceptor) provided the lowest cgc.

Introduction

Over the past two decades, several hundred molecules have been discovered to reversibly form gels in a variety of solvents and conditions.[1] These soft materials are being widely investigated for applications in medicine,[2] sensing,[3] remediation,[4] and materials science.[5] Despite the diversity of structures represented within this class of materials, it is well known that gelation is extremely sensitive to structure, and even minor structural modifications can disrupt gelation ability. For example, we reported that although **1** gels a variety of organic solvent/water mixtures,[3b] subsequent derivatives were either gelators with higher critical gel concentrations (cgc) or non-gelators.[6] This poorly understood relationship between structure and gelation ability makes it difficult to improve or modify existing gelators for specific applications. It is within this context that alternative methods for improving gel properties became appealing. Because gelation is similar to crystallization, we (and others) anticipated that polymeric additives, which are commonly utilized to alter crystallization processes of pharmaceutical compounds[7,8] and inorganic materials,[9] might be useful for improving molecular gelation.

Hanabusa and co-workers were the first to use polymeric additives in molecular gelation.[10] They demonstrated that adding polyethylene glycol and poly(*N*-vinylpyrrolidone) increased the gel strength of an L-valine-based gelator, while polystyrene (albeit in a different solvent) had no effect. No hypothesis was put forward to explain the role of polymer. More recently, polymers with functional groups that complement the gelator structure were targeted, based on the premise that there is a specific gelator-polymer interaction. For example, Shinkai and co-workers added complementary and non-complementary polynucleotides to nucleotide-containing gelators.[11] They hypothesized that the polymer acted as a template to force the gelators into a one-dimensional architecture, thereby facilitating aggregation (and gelation) at lower concentrations. Similarly, Wang and co-workers reported that a cationic polyelectrolyte modifies the gelation properties of an anionic dendrimer.[12] Again, a specific gelator-polymer interaction was suggested to account for these improved properties. In both of these examples, the authors speculate that the polymer is playing an integral role in the gelator self-assembly and is co-localized within the fiber.[13]

An alternative view put forth by Liu and co-workers is that the polymers modify the nucleation and growth processes involved in gelation.[14] Specifically, they proposed that the polymers adsorb onto the fibers and create defect sites at the fiber tip, which leads to branching. This hypothesis is related to one of the mechanisms in small molecule crystal formation, which involves selective polymer adsorption onto one face of a crystal, decreasing its growth rate relative to the other faces.[15] Wan and co-workers invoked a similar mechanism to rationalize the effect of poly(2-hydroxyethyl methacrylate) on a sugar-based gelator, adding that the polymer adsorption might also increase the surface tension.[16] Surface effects were also proposed by Reinhoudt and co-workers, who observed gel formation using boronic-acid functionalized polymers with sugar-based gelators.[17]

Overall, these studies have shown that polymeric additives can increase gel strength and stability, as well as lower the cgc, which are important in molecular gel applications. As a result, polymer-modified gelations have the potential to become broadly useful.

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Nevertheless, the mechanism of the polymer-based enhancement is often unknown, making it challenging to identify suitable polymers for different gelators and applications. Thus, an improved understanding of the role(s) of polymeric additives is needed to generalize this method.

We report herein the discovery of a new polymer-enhanced molecular gelation and studies aimed at elucidating the mechanism. Specifically, poly(acrylic acid) (PAA) was found to significantly increase the gel strength as well as decrease the cgc of **1** in 1/1 DMSO/H_2O (v/v). The effect of PAA on the gel microstructure and the rate of nucleation and growth were investigated. Overall, the results are consistent with a mechanism involving PAA adsorption during fiber growth. The net result is thinner fibers, which are either longer or greater in number (or both), that reduce cgc and increase strength by creating more fiber-fiber entanglements. An examination of other polymers revealed that these effects are specific to poly(acrylic acid). Together, these results highlight that, similar to crystallization, the impact of polymers on gelation is both multifaceted and structure-dependent.
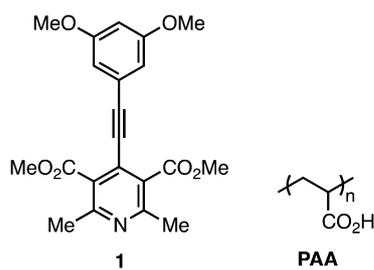
Results and discussion

Impact of PAA on cgc

Polyacrylic acid was identified amongst a series of polymers as a promising additive for **1** because it led to an impressive 90% reduction in cgc with 0.2 wt% added (see Table 1 and ESI†). A control experiment using an equal mass of monomer (*i.e.*, acrylic acid) only showed a 20% reduction in cgc. A second control, which probed the effect of solution pH by adding HCl, gave a similar 20% reduction in cgc, indicating that the solution pH plays a minor, but contributing role.[18] The effect of polymer molecular weight and concentration on cgc were also examined. The gelation was sensitive to polymer molecular weight (M_w), with the highest M_w PAA giving the lowest cgc. In contrast, the

gelation was fairly insensitive to changes in the PAA concentration. Further studies were initiated to explore the impact of PAA ($M_w = 450$ kDa) on gel properties and the mechanism of enhancement.

Impact of PAA on gel strength

Molecular gels are typically much weaker than polymer-based chemical gels because the crosslinking mechanism is different (*i.e.*, physical *versus* chemical). This feature has limited molecular gel-based applications. It is within this context that Hanabusa[10] and others[11,12,14,16,17] have probed the effect of polymer additives on the molecular gel strength (*i.e.*, elastic modulus, breaking stress).[19] In most cases, an increase in the elastic modulus (G′), which reflects the resistance to deformation when a stress is applied, has been observed. We also found an increase in the elastic modulus of gelator **1** when PAA is added (Fig. 1A).[20] An additional measurement of gel strength is the breaking stress (σ_b), which represents the force necessary to completely disrupt the mechanical integrity of the gel network. Gels prepared in the presence of PAA exhibited a significantly larger breaking stress, represented by the intersection between the G′ and G″ curves, than those without PAA (Fig. 1B).[21] The observed increase in gel strength and breaking stress could be due to a change in the gel microstructure, such as an increase in the number of fiber-fiber entanglements (due to branching, more fibers, or longer fibers), or an increase in the strength of the interactions between the fibers. To evaluate the latter, a control experiment was performed wherein a PAA solution was added to an unstable gel (ESI†). The gel remained unstable, indicating that the polymer is not modifying the fiber-fiber interactions under these conditions. Therefore, we initiated microscopy studies to evaluate the influence of PAA on the gel morphology.

Impact of PAA on gel microstructure

Characterization of gel morphology is typically performed using several microscopic techniques with varying degrees of spatial resolution. Beginning with the lowest spatial resolution, optical microscopy was used to determine the overall gel microstructure. Optical microscope images acquired on gels of **1** indicated that the gel microstructure consisted of a dense network of high aspect-ratio fibers regardless of whether polymer was added (Fig. 2A and B). Scanning electron microscopy (SEM) images
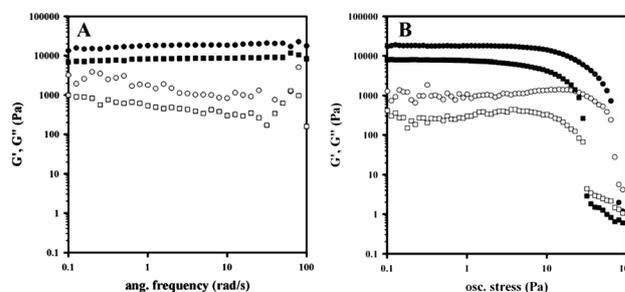
Table 1 Dependence of cgc on [PAA] and molecular weight (M_w)[a]

Sample	wt (%)	M_w (kDa)	cgc (mM)
1	–	–	10 ± 1
1 + PAA	0.2	450	2.5 ± 0.3
1 + acrylic acid	0.2	–	8 ± 2
1 + HCl (pH = 4)	–	–	8.0 ± 0.7
1 + PAA	0.2	2	6.7 ± 0.7
1 + PAA	0.2	750	1.0 ± 0.2
1 + PAA	0.02	450	6.6 ± 0.7
1 + PAA	2	450	3.5 ± 0.6

[a] All measurements were performed in triplicate in 1/1 DMSO/H_2O (v/v).

Fig. 1 Plots of the elastic (G′, filled symbols) and storage (G″, open symbols) moduli as a function of (A) frequency and (B) stress for gel samples of **1** (18 mM) without PAA (■, □) and with 0.2 wt% PAA (●, ○) in 1/1 DMSO/H_2O (v/v).
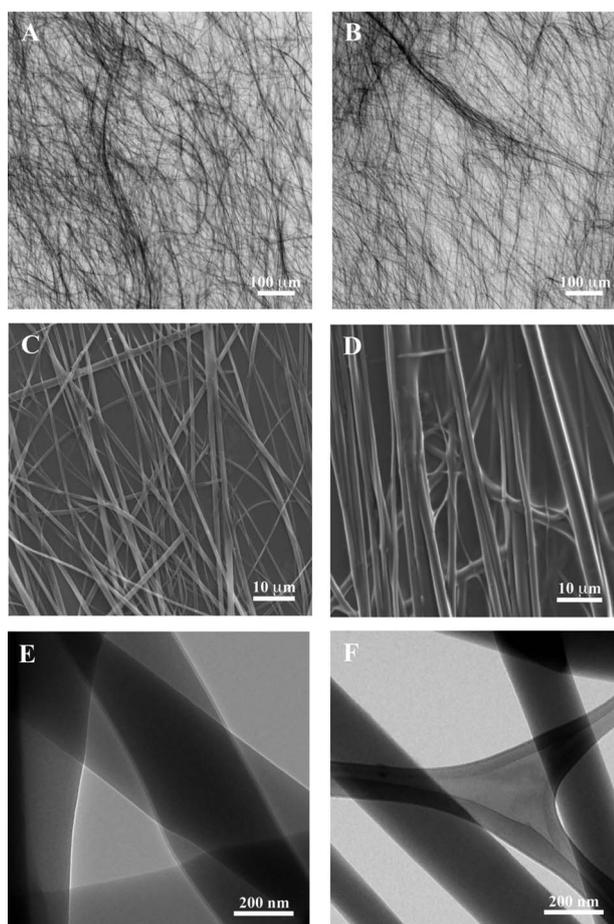
Fig. 2 Representative microscope images for gels of **1** (2.6 mM) in 1/1 DMSO/H$_2$O (v/v) (A, C, E) without PAA and (B, D, F) with 0.2 wt% PAA.

Fig. 3 TEM fiber diameter distributions of **1** without PAA (grey) and with 0.2 wt% PAA (black) in 1/1 DMSO/H$_2$O (v/v).

revealed "bundling" of fibers, which may be an artefact of the drying process (Fig. 2C and D). As a result, transmission electron microscopy (TEM) was used to determine whether there is a fundamental difference between gel fiber diameters with and without PAA. The TEM images have sufficient contrast and resolution to measure the individual fiber diameters, regardless of whether they are aggregated into larger bundles (Fig. 2E and F). The average fiber diameters were smaller when PAA was present during gel formation (Fig. 3), suggesting that the polymer was impacting the nucleation and/or growth processes. Although the fiber diameters were different, powder X-ray diffraction (PXRD) analysis revealed that the molecular packing remains unchanged (Fig. 4A). Overall, these microstructure studies revealed that the enhanced gel strength in the presence of PAA was likely due to changes in the fiber dimensions. Further studies were needed to determine whether the fiber length and/or number have also been altered in the presence of PAA.

Impact of PAA on nucleation and growth

Gelation is similar to crystallization in that there is a nucleation event followed by growth.[22] Most nucleation processes are believed to be heterogeneous, wherein external surfaces (*e.g.*, dust) induce nucle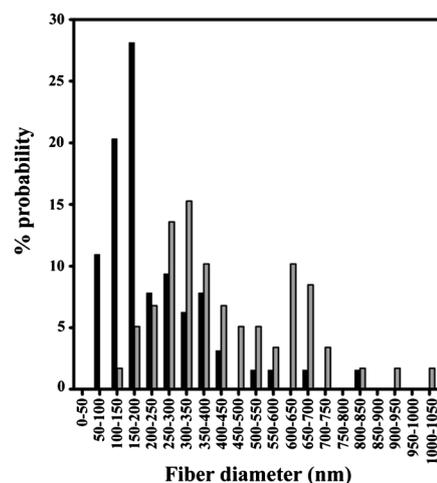ation. Additives can alter nucleation rates by creating additional nucleation sites, changing the gelator super-saturation, and adsorbing onto the nuclei. An increase in nucleation would increase the number of fibers in the gel, which could explain the enhanced gel strength with added PAA.

Measuring the number of nuclei was not feasible, however, because of the high density of fibers formed under the gelation conditions, and the competing formation of single crystals at lower concentrations. Instead, gelator supersaturation was determined by measuring the variable-temperature equilibrium solubility. No significant change in solubility was observed in the presence or absence of PAA, indicating that supersaturation was unaffected by the polymer (ESI†). Similarly, the induction time, which was estimated by the first visual observation of fibers, was the same regardless of whether PAA was added (~4 min, ESI†).

Initial rates of fiber growth were measured using time-resolved hot-stage optical microscopy. Increasing concentrations of PAA led to decreasing growth rates (Fig. 4B).[20,23] One explanation is that the polymer is adsorbing onto the fibers, which hinders growth by physically blocking gelator access to the growing fiber. We further speculated that the PAA adsorbs onto the sides (long axis) of the fibers because the TEM studies indicated that thinner fibers are formed under these conditions. Based on previously reported polarized Raman spectroscopic studies and single-
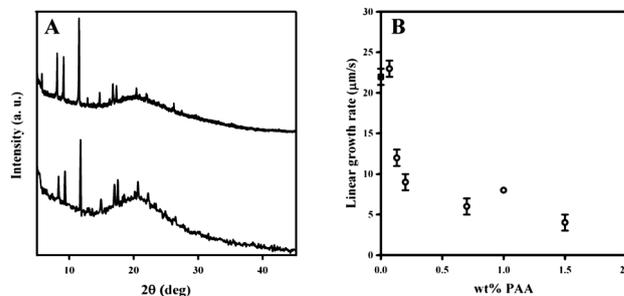

Fig. 4 (A) PXRD patterns for gels of **1** (26 mM) with 1.0 wt% PAA (top) and without PAA (bottom) in 2.3/1 DMSO/H$_2$O (v/v). (B) Plot of the linear growth rate *versus* [PAA] for **1** (5.2 mM) in 1/1 DMSO/H$_2$O (v/v). Note that ■ represents [PAA] = 0 wt%.

crystal X-ray diffraction analysis,[3b] the gelator molecules are oriented perpendicular to the fiber's long axis. Thus, one explanation for the polymer adsorption is an interaction between the basic nitrogen of pyridine **1** and the acidic carboxylic acid of PAA.[24] This hypothesis is supported by the fact that the sodium salt of poly(acrylic acid) (PAA-Na), which cannot participate in these H-bonding interactions, only leads to a 34% reduction in cgc under the same conditions (ESI†). One consequence of the slower growth when the polymer is present is that the solution will remain supersaturated for a longer period of time. Under these conditions primary nucleation, wherein new fibers grow from other fibers, can become important. This process would increase the number of fibers and could explain the enhanced gel strength. Unfortunately, due to the high density of fibers, and their long length, we were unable to determine whether the number and/or length were changed when PAA was added.

To summarize, these nucleation and growth studies suggest that the enhanced gel strength with PAA is due to polymer adsorption, which reduces fiber growth rates, and leads to subsequent changes in the gel morphology.

Impact of polymer structure

To determine the impact of polymer structure, several other polymers were examined (ESI†). For example, a 0.2 wt% of polystyrene sulfonate sodium salt (PSS-Na, M_w = 500 kDa) provided a cgc that was similar to PAA-Na (*i.e.*, 37% and 34%, respectively). In contrast, polystyrene sulfonic acid (PSS) had no impact on the cgc, which was surprising because even non-polymeric acids (*e.g.*, HCl and acrylic acid) provided a cgc reduction. Combined, these results highlight the importance of polymer structure and suggest that complementary functional groups between the gelator and polymer (*e.g.*, pyridine and carboxylic acid) are optimal for enhancing gelation.

Conclusions

Using polymeric additives to improve the strength and versatility of molecular gels is an exciting, yet underutilized technique. Only a handful of examples have been reported and as a result, little is known about the mechanism. We demonstrated herein that one mechanism for polymer enhancement involves polymer adsorption, leading to a change in gel fiber dimensions and linear growth rate. This mechanism is similar to one involved in small molecule crystallizations with additives.[15] The nature and existence of complementary interactions between the gelator and polymer appear to be an important factor. Overall, these studies suggest that consideration of the gelator functional groups, as well as their orientation within the gel fibers, may be useful in identifying suitable polymers. Our future studies will focus on determining the generality of polymer-enhanced gelations.

Experimental

General procedure for gel formation

A 4 mL vial was charged with a known weight of **1** and a known volume of 1/1 DMSO/H_2O (v/v) solution (or a known volume of a polymer solution of fixed concentration in 1/1 DMSO/H_2O (v/v).) The vial was sealed with a Teflon-lined cap and the

mixture was heated until it formed a homogeneous solution. The solution was cooled to rt under ambient conditions. Vial inversion was used to determine whether a stable gel had formed.

Acknowledgements

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