

Novel thermo-responsive polymers composed of sodium alginate and poly(*N*-isopropylacrylamide)

Oana-Nicoleta Ciocoiu ^{1*}, Georgios Staikos¹

¹Department of Chemical Engineering, University of Patras, GR – 26504, Patras, Greece

* E-mail address of presenting author: oanicoleta@chemeng.upatras.gr

ABSTRACT SUMMARY:

Thermoresponsive graft copolymers were synthesized. Thermally induced properties were introduced by grafting poly (*N*-isopropylacrylamide) chains onto a sodium alginate backbone. The products obtained exhibit a remarkable thermothickening behavior in aqueous solution if the degree of grafting, the concentration, and temperature are higher than some critical value correspondingly. This behavior is reversible and could find applications in oil rigs and drug delivery systems.

INTRODUCTION:

Thermothickening aqueous formulations, i.e. systems exhibiting viscosity increase by increasing temperature, contrary to the usual Arrhenius thermothinning behavior, have attracted a lot of interest during the last two decades. Most of these systems are based on graft copolymers, consisting in a hydrophilic backbone and side chains phase separating by heating.^{1-2,3,4,5}

Most synthetic polymers in solution precipitate by cooling, but some water soluble polymers phase separate upon heating, showing a lower critical solution temperature (LCST) behavior.^{6,7} Such thermosensitive polymers undergo reversible conformational or phase changes in response to negligible variations of temperature. There is a delicate free-energy balance between hydrophilic and hydrophobic interactions determining the solubility of the LCST polymers in water. Exactly this property is exploited for the synthesis of the above thermothickening graft copolymers. LCST polymers used for this purpose are poly (ethylene oxide)^{1,3}, ethyleneoxide - propylene oxide random copolymers², poly(*N*-isopropylacrylamide) (PNIPAM). The most studied synthetic thermoresponsive polymer is poly (*N*-isopropylacrylamide) (PNIPAM), undergoing a coil-globule transition in water at 32°C.^{7,8}

The hydrophilic backbone of the thermothickening graft copolymer consists in a water – soluble polymer of a relatively high molecular weight like poly (acrylic acid),^{1, 5, 9} partly hydrolyzed polyacrylamide², 2-acrylamido-2-methyl-propane sulfonic acid^{3,4}. In many cases polysaccharide backbones like carboxymethylcellulose,^{4, 10, 11} chitosan,¹² hyaluronan,¹³ dextran and sodium alginate (NaAl)¹¹ have been successfully used.

Whereas all these graft copolymers have different chemical compositions, their associating behavior follows the same general scheme. As temperature increases, a self-assembling of the side chains is induced, so that they function as responsive stickers which interconnect the hydrophilic counterpart (graft copolymer backbone), and a physical network can be formed, provided that the concentration is high enough to percolate through the whole volume. This

thermoresponsive behavior is of a great interest as it provides technological solutions when improved rheological properties above a given temperature are required, in a wide range of bioengineering¹⁴ and biomedical¹⁵ applications, with drug release¹² and tissue engineering¹⁶ being the most studied.

Alginic acid is a biopolymer extracted from different brown seaweeds, with many applications in food, pharmaceutical and medical industries,¹⁷ attracting a broad research interest, due to its biocompatibility and biodegradability. Moreover, as its repeating unit brings one carboxylic acid unit, it is accessible to chemical modifications which could enrich it with new properties and uses in new applications. Grafting of NaAl with PNIPAM chains in dimethylformamide was proposed by Kim et al.¹⁸ for the preparation of alginate-g-PNIPAM beads with Ca²⁺ in aqueous solution, bearing pores which are contracted and expanded as a function of temperature.

In this work we report on the synthesis of graft copolymers of NaAl with PNIPAM in aqueous solution, and study their solution behavior, envisaging to the development of thermothickening agents with potential applications in various fields.

EXPERIMENTAL METHODS:

5 % (w/v) solutions of NaAl and PNIPAM in water were mixed at different ratios. EDC and HoBt, dissolved in small quantities of water, were added. After 24 h the reaction mixture was fully neutralized with NaOH and the grafted copolymers were precipitated in a tenfold volume of acetone. Then, the products obtained were re-dissolved in water and freeze-dried.

The composition of the products obtained by grafting PNIPAM onto NaAl was assessed by elemental analysis, ¹H-NMR spectroscopy.

To measure the viscosity of semi-dilute solutions we have used an automated microviscometer AMVn (Anton Paar GmbH – Graz/Austria-Europe). The automated microviscometer AMVn is based on the “rolling ball” principle. The sample to be measured is introduced in a glass capillary in which a steel ball rolls. The viscous properties of the test fluid can be determined by measuring the rolling time of the steel ball. A change in the inclination angle of the capillary varies the shear stress. This makes the AMVn also well suited for applications on the non-Newtonian fluids. A built-in Pt100 thermometer ensures exact temperature measurement and temperature control.

RESULTS AND DISCUSSION:

Figure 1 shows the variation of the dynamic viscosity, η_{dyn} , as a function of the concentration, *c*, for four graft copolymers of different molecular weight PNIPAM side chains, with three different compositions

in PNIPAM, in water, at 40°C, i.e. a temperature well above the LCST of PNIPAM (32,5°C), so that a thermothickening behavior should be exhibited, if the polymer concentration is higher than a critical value, if the molecular weight of the PNIPAM side chain is high enough and if the degree of grafting is sufficient.

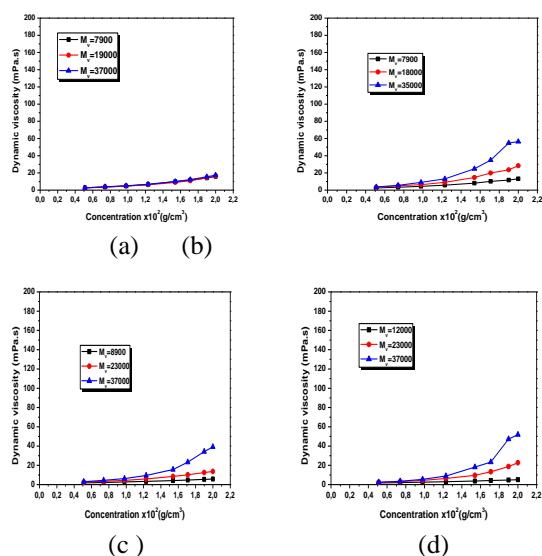


Fig. 1: Variation of the dynamic viscosity vs. concentration of the graft copolymers G30 (a), G40 (b), G50 (c) and G67 (d) in solution, in water, at 40°C, with different molecular weight of the PNIPAM side chains

We observe that η_{dyn} increases by increasing c for all the graft copolymers. Nevertheless, when the degree of grafting is low, 30%, Figure 1 (a), the increase in the viscosity of the three graft copolymers versus concentration is similar to what would be expected for usual semidilute polymer solutions. At this point, the conclusion is that a degree of grafting of the order of 30% in PNIPAM is lower than the critical value, so that a thermothickening behavior to be observed. Figure 1 (b) show that the concentration increases after 1.2×10^2 for all graft copolymer phenomenal which can be related with a thermothickening phenomenon. In Figure 1 (c), where the viscosity results obtained with the G50 graft copolymers are shown, we observe that as the concentration increases over about 1.00×10^2 g/cm³ the dynamic viscosity of the graft copolymer with PNIPAM side chains of higher molecular weight, $\overline{M}_v = 3.7 \times 10^4$, increases abruptly, more than two orders of magnitude, showing a behavior that should be related with a thermothickening phenomenon. Similar behavior, but not in the same extent is shown by the graft copolymer of lower molecular weight PNIPAM side chains, $\overline{M}_v = 2.3 \times 10^4$, while the copolymer with $\overline{M}_v = 8.9 \times 10^3$ does not show a viscosity increase indicating any thermothickening behavior. According to these results the degree of grafting 50% seems to be above the critical value, but only if the molecular weight of the PNIPAM side chains is also high enough, i.e. higher than about 8×10^3 . This estimation is further

corroborated by the results obtained with G67, Figure 1 (d).

CONCLUSIONS:

Thermally responsive graft copolymers with a hydrophilic and biodegradable backbone of sodium alginate (NaAl), and side chains of poly (N-isopropylacrylamide), (PNIPAM), which is a polymer exhibiting a lower critical solution temperature (LCST) phase behavior in aqueous solution, were synthesized.

According to viscosimetric results obtained in pure aqueous solution if the molecular weight of the PNIPAM side chains is high enough, and the concentration of the solution higher than a critical value, a very abrupt increase of the solution viscosity is observed by increasing temperature (thermothickening behavior).

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