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Micro and Macro Characterization of PEO-PPO-PEO Triblocks Hydrogels

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Summary: Amphiphilic poly(ethylene oxide) - poly(propylene oxide) triblock copolymers are very appealing materials for biomedical application since they can be easily injected as liquid at room temperature while they produce a gel when in the body. On the other hand, these materials no longer hold the gel state when in presence of solvent (as physiological solutions) due to the dilution of the system. To overcome these limitations Cohn and coworkers[1] have synthesized a novel thermoresponsive systems by extending the chain of the commercially available PEO-PPO copolymer named F127. The aim of this study was to evaluate the effect of the chemical modification on the macroscopic, rheological, and microscopic, transport, properties of these new materials.

Keywords: microrheology; PEO-PPO block copolymers; transport properties

Introduction

The amphiphilic poly(ethylene oxide) - poly(propylene oxide) triblock copolymers, commercially known as Pluronics® or Poloxamer® or Synperonic®, represent a particularly appealing class of materials since they undergoreverse thermal gelation (RTG). They consist, indeed, of hydrophilic part, that maintains the system's solubility in water, and of a hydrophobic part, that provides the associative behaviour in water. By increasing the temperature these systems self-organize in ordered structure undergoing to a sol-gel transition.[1,2] The self-assembling process occurs through a micellization characterized by two key parameters: the critical micellization concentration (CMC) and critical micellization temperature (CMT).[3] These parameters are depending on PEO-PPO-PEO chemical-physical parameters such as block composition (PEO/PPO ratio) and molecular weight (PEO and PPO block length). The chemical structure of Pluronic triblock copolymers is showed in Figure 1 and, in particular, for Pluronic F127 $m = 99$ and $n = 67$, respectively.

PEO-PPO-PEO triblocks hydrogels no longer hold the gel state when in presence of solvent (as physiological solutions) due to the dilution of the system.[4] To overcome these limitations Cohn et al. realized chain-extended F127 by the bulk polymerization of poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock ($\overline{M}_w = 12{,}600$, 70 wt-% PEO) with hexamethylene diisocyanate (HDI) at several degree of polymerization.[1]

The aim of this study was to evaluate the effect of the chemical modification on the macroscopic, rheological, and microscopic, transport, properties of these new materials.

Materials and Methods

The PEO-PPO-PEO triblock copolymer (F127) was obtained from SIGMA and used as received. The new materials was synthesized by bulk polymerizing F127 with hexamethylene diisocyanate (modified

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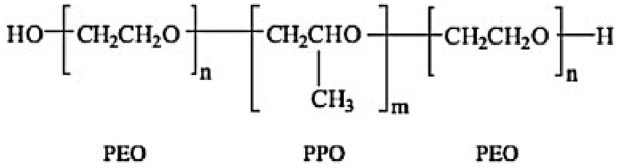

$$HO-\left[CH_2CH_2O\right]_n-\left[CH_2\underset{CH_3}{\underset{|}{C}}HO\right]_m-\left[CH_2CH_2O\right]_n-H$$

Figure 1.
Chemical structure of Pluronic triblock copolymers.

F127).[1] The aqueous solutions concentration of unmodified and modified F127 was 20% (w/v). Rheological properties were evaluated by a rotational rheometer (Bohlin Gemini). Both dynamic–mechanical and viscometric analyses were performed. Transport properties were investigated by using FRAP (Fluorescence Recovery After Photobleaching). This technique is based on the measurement of the fluorescence in a particular sample region. A small portion of the sample is exposed to a laser radiation able to extinguish fluorescence. In this area the fluorescence gradually reappears thanks to the particles transport phenomenon. By analyzing the recovery fluorescence rate it is possible to evaluate the diffusion coefficient of fluorescent particles. The fluorescent probes for FRAP tests were rigid beads of 26 nm diameter (Duke Scientific). The rheological and transport properties were investigated in the range of temperature 5–50 °C.

Results and Discussion

The macroscopic analysis (zero shear viscosity reported in Figure 2 and mechanical spectra here not reported) shows a slightly increase of mechanical properties of the modified F127 in comparison with the commercial one ($\eta_{\text{unmodified}} = 0.98$ Mpas and $\eta_{\text{modified}\cdot} = 5.3$ MPas, at 50 °C).

From the macroscopic rheological measurements it was observed that the chemical modification does not alter the transition threshold. Indeed, both from the macro-

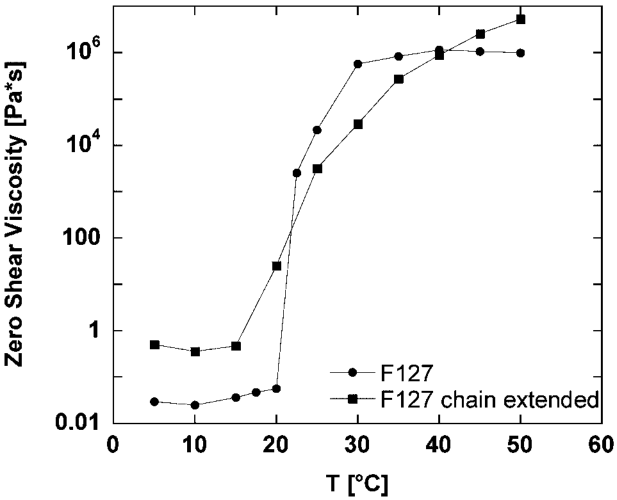

Figure 2.
Zero shear viscosity as function of temperature for commercial and chain extended Pluronic F127.

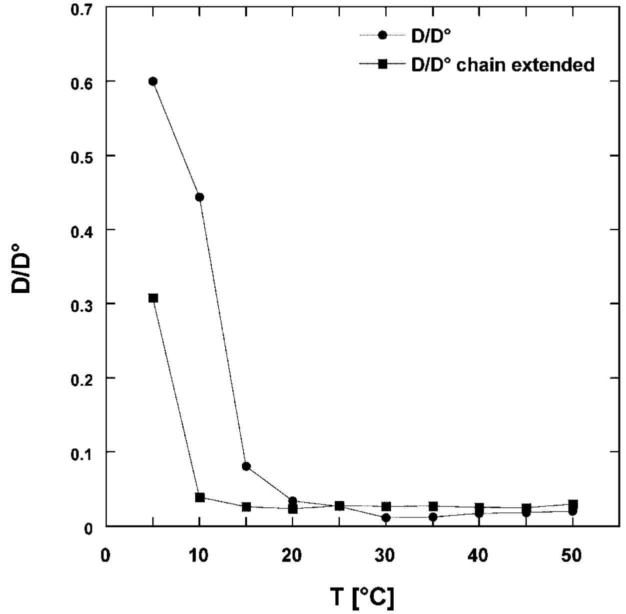

Figure 3.
Normalized diffusion coefficient as function of temperature for or commercial and chain extended Pluronic F127. The values of diffusion in F127 had been normalized respect the data in water in order to decouple the effect of beads diffusion in the solvent of solution.

scopic dynamic–mechanical and viscometric results the sol-gel transition occurred in the range 20–25 °C, whereas different kinetics of gelation were observed (Figure 2): zero shear rate viscosity data show a more gradual temperature transition of chain extended F127.

On the other hand, from the microscopic results a different transition threshold was found. As observed in Figure 3, in which the normalized diffusion coefficient as function of temperature is reported, for unmodified F127 the diffusion coefficient decreased abruptly in the range 5–15 °C and for the modified F127 the transition occurs in the range 5–10 °C.

The microscopic analysis detected the transition from solution to micellar gel several degrees earlier. This discrepancy indicates that local structural changes, which do not affect the macroscopic properties, occur at an early stage of micellization. By increasing the temperature of the PEO-PPO-PEO system, indeed, the unimers start to aggregate to minimize the surface energy and when the temperature reaches the sol-gel transition temperature, then, these aggregates form micelles to minimize the exposed surface of hydrophobic blocks to the water. The different temperature values may be explained by taking into account that the diffusivity properties are influenced by the formation and the presence of unimers, while they do not influence the rheological response.

Conclusions

The sol gel transition for F127 and chain-extended F127 was detected using micro and macro characterizaion. Different transition threshold in temperature was estimated due to the different way to “feel” the system (investigation of macro-system and micro-system) by the two different approaches. As demonstred by viscoelastic and transport properties, the chain-extended material presents a different and more progressive sol-gel transition respect the unmodifed F127. The chain-extended F127 shows higher mechanical properties than the unmodifed one while its transport properties remain unchanged in the gel state.

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