Synthesis of Thermo/pH-Sensitive Stimuli-Responsive Triblock-Copolymer by RAFT Polymerization for Drug Controlled Release

Chih-Yu Kuo, Ting-Yu Liu*, Wen-Yen Chiu*
Polymeric Nanomaterials Laboratory, Institute of Polymer Science and Engineering,
National Taiwan University, 1 Roosevelt Road, 4th Sec., Taipei 10617, Taiwan
E-mail: f99549022@ntu.edu.tw (C.Y. Kuo), tyliu@ntu.edu.tw (T.Y. Liu),
ycchiu@ntu.edu.tw (W.Y. Chiu)

Abstract

Over the past decade, living/controlled polymerization especially reversible addition-fragmentation transfer (RAFT) polymerization has been received great attention because it can not only obtain well-defined structure of copolymer with low polydispersity but have less restriction of monomers and reaction conditions. To biotechnology applications, the synthesis of functional copolymers in aqueous system under moderate conditions without protection processes is the most important target in developing the living polymerization. One of the well-known advantages in RAFT polymerization was yielding the water-soluble polymers with expected structures, by choosing the appropriate chain transfer agents (CTA)[1,2].

In this study, we have successfully prepared dual functional stimuli-responsive (thermo/pH-sensitive) triblock-polymers via RAFT polymerization of N-isopropylacrylamide (NIPAAm) and acrylic acid (AA) by using trithiocarbonate, S,S-bis(a,a'-dimethyl-a"-acetic acid)trithiocarbonate (CMP) as a chain transfer agent, in order to perform hydrophilic and hydrophobic dual functional polymers[3] [Figure 1]. The affinity between polymers and solvents with various temperature and pH-values would make the difference self-assembly morphology of micells, which is useful in drug controlled release. The chain length of hydrophilic or hydrophobic fragment also could be modulated by tuning the feeding ratio of monomers [Figure 2], so that we could precisely dominate the affinity between polymers and solvents to fabricate a variety of micells. The drug controlled release behaviors of the dual functional stimuli-responsive polymer (PAA-PNIPAAm-PAA) micelles could be obtained by using mutual temperature and pH control [Figure 3]. Furthermore, the drug could be controlled release by high frequency magnetic field (conducting heating effect) via the magnetic nanoparticles loaded in the micells of PAA-PNIPAAm-PAA, which is now in progress in our group.

Reference

1. Schilli, C. M.; Zhang, M. F.; Rizzardo, E.; Thang, S. H.; Chong, Y. K.; Edwards, K.; Karlsson, G.; Muller, A. H. E., *Macromolecules*, **37**, 7861(2004).
2. C. Yang and Y.-L. Cheng, *Journal of Applied Polymer Science*, **102**, 191-1201(2006).
3. P-E Millarda, L Barner, J Reinhardt, M R. Buchmeiser, C Barner-Kowollik, A H.E. Müller, *Polymer*, **51**, 4319-4328(2010)

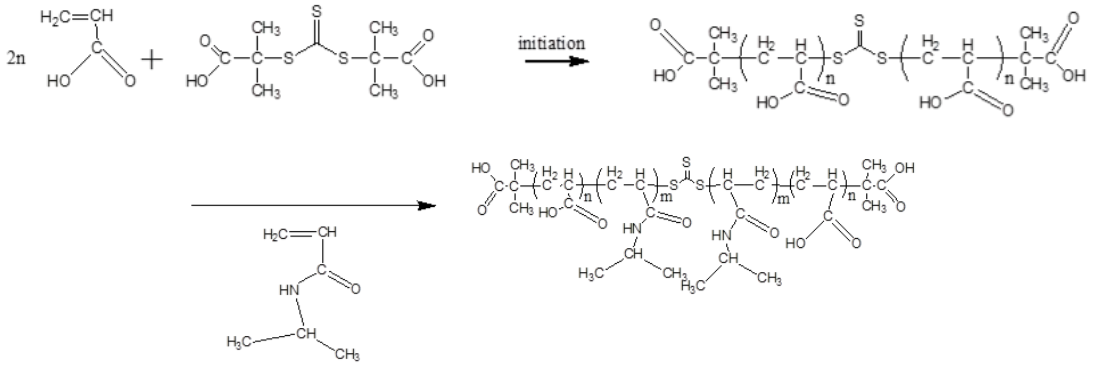

Figure 1 Synthesis triblock copolymer (PAA-PNIPAAm-PAA) by using trithiocarbonate, S,S-bis(a,a'-dimethyl-a"-acetic acid)trithiocarbonate (CMP) as a chain transfer agent

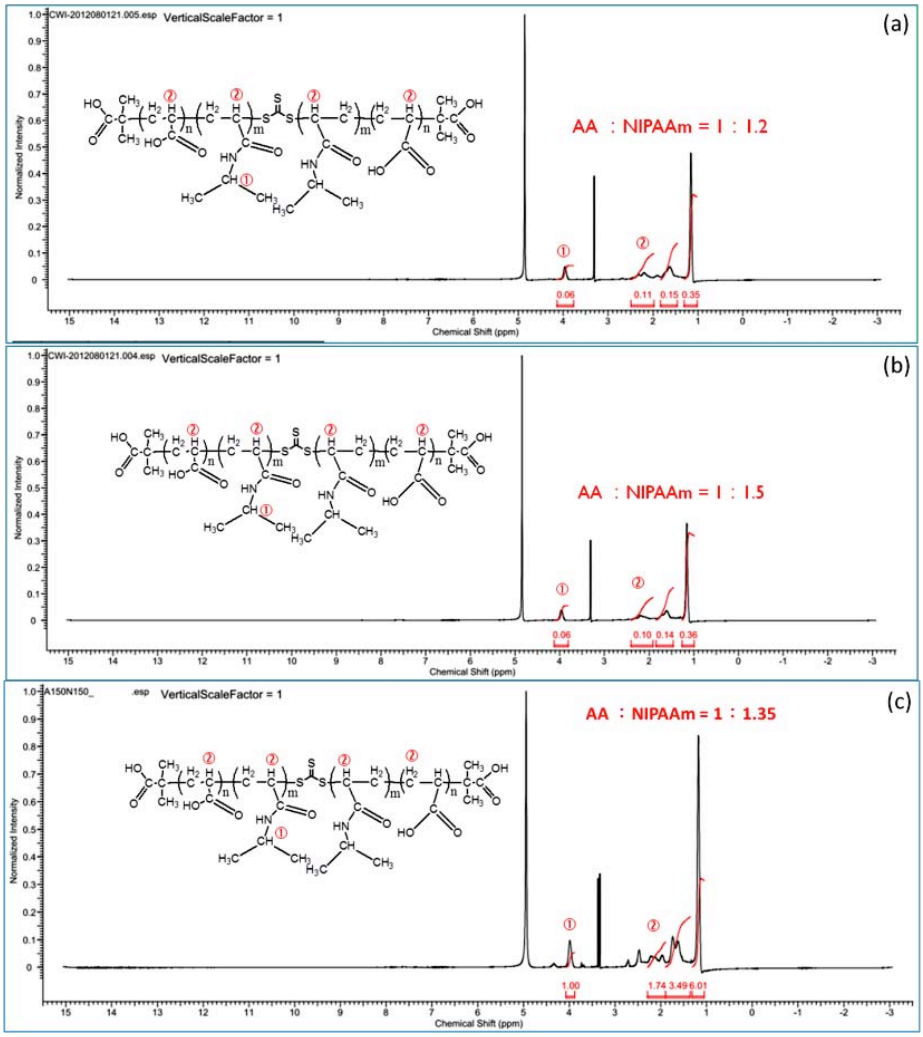

Figure 2 Synthesis of different chain length of hydrophilic/hydrophobic fragment in triblock copolymer (PAA-PNIPAAm-PAA) by tuning the feeding ratio of monomers.

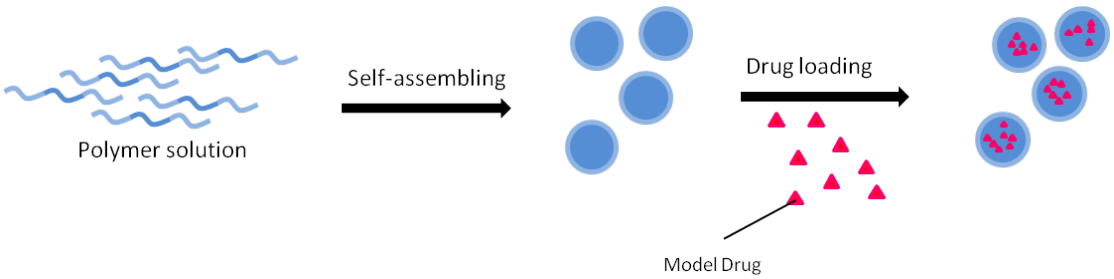

Figure 3 Schematic illustration of the synthesis and structure of the self-assembled triblock copolymer nanocarriers for controlled drug release.