Size controlled of core-corona type nanospheres using thermoresponsive macromonomers with various chain lengths

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ABSTRACT SUMMARY
We prepared thermoresponsive polymeric nanospheres, those consisted of hydrophobic cores and hydrophilic corona layers on their surfaces. Corona layers are composed of poly(N-isopropylacrylamide) (PNIPAAm) chains with a narrow polydispersity index which prepared by atom transfer radical polymerization (ATRP). Nanospheres were prepared by dispersion copolymerization of styrene with PNIPAAm macromonomer in polar solvent. Obtained nanospheres are monodisperse in diameters and showed diameter changes: being decreased with increasing temperature as well as the amount and chain length of macromonomer.

INTRODUCTION
Polymeric micro-and/or nano-spheres have been utilized in biomedical fields especially in diagnostics because of their extremely large surface area. Therefore, both surface design and diameter control of polymeric sphere are required.1) Polymeric nanospheres are usually prepared by emulsion or dispersion polymerization. However, in these preparation methods, surface design of polymeric nanosphere is often difficult for suppressing undesirable biomolecule interaction. Recently, design of nanosphere was attracted its shape and surface design3) for biomaterials. We focused on macromonomer method, which is utilized to synthesize core-corona type polymeric nanospheres, based on free radical copolymerization of hydrophobic monomers and hydrophilic macromonomers in polar organic solvents.4) For preparation of well-defined nanosphere, PNIPAAm with controlled chain lengths as functional corona layers were grafted on nanosphere surface. In this study, PNIPAAm macromonomers with controlled chain length was prepared through ATRP and then macromonomer was copolymerized with styrene to form core-corona type nanospheres. Effect of chain length and amount of PNIPAAm macromonomer effect on nanosphere diameter and/or characteristics are investigated. In addition, interaction with blood cells will present.

EXPERIMENTAL METHODS
Monodisperse PNIPAAm was prepared by ATRP using N-(chloromethyl)phthalimide as an ATRP initiator. Molecular weight of prepared PNIPAAm was measured by 1H-NMR and gel permeation chromatography (GPC) with N,N-dimethylformamide (DMF) as an eluent. Phthalimide end group of PNIPAAm was transformed to primary amino group using hydrazine followed by reacting with acryloyl chloride to form PNIPAAm macromonomers. Transformation of terminal group of PNIPAAm at each step was confirmed by 1H-NMR. To prepare nanospheres, PNIPAAm macromonomer and styrene were copolymerized in selective solvent. Dynamic light scattering (DLS) and scanning electron microscope (SEM) were used to determine the diameters of the prepared nanospheres.

RESULTS AND DISCUSSION
The weight-average molecular weight (Mw) and molecular size distribution was measured by GPC. Number-average molecular weight (Mn) agree well with the values estimated from the number of ATRP initiation site measured by 1H-NMR spectroscopy, result in obtained PNIPAAm with controlled chain length. Terminal group of PNIPAAm was transformed to vinyl group as PNIPAAm macromonomer. Nanospheres were prepared by free radical copolymerization of PNIPAAm macromonomer...
and styrene. Figure 1 shows SEM image of prepared nanospheres, by using $M_n$ 6000 of PNIPAAm macromonomer with feed styrene:PNIPAAm ratio 100:1 (mol/mol). As a result, spherical shapes and narrow size distribution was observed. In addition, nanosphere have corona layer with PNIPAAm brushes. PNIPAAm exhibits a thermo-reversible phase transition in aqueous solution at lower critical solution temperature (LCST). Nanospheres were colloidally stable at 20°C, but precipitated at 37°C in DPBS due to the dehydration of grafted PNIPAAm chains and aggregation between spheres.

Figure 1. SEM image of prepared thermoresponsive core-corona type nanospheres using PNIPAAm macromonomer ($M_n$: 6000), Styrene:PNIPAAm=100:1 (molar ratio).

We regulated nanospheres diameter by PNIPAAm macromonomer chain length. Diameter of nanosphere was decreased with molecular weight of PNIPAAm increased (Figure 2). A mean diameter was controllable from 200 to 800 nm by macromonomer chain length as shown in Figure 2. Then, nanospheres were prepared with feed styrene:PNIPAAm ratio from 100:0.5 (mol/mol) to 100:3 (mol/mol). Diameter of nanospheres decreased with the increased amount and/or chain lengths of PNIPAAm macromonomer. Therefore, PNIPAAm macromonomer have important role as a dispersant during polymerization of styrene. Thus, we regulated diameter of nanosphere using PNIPAAm macromonomer with controlled chain length. In addition, red blood cell was not hemolyzed by prepared nanospheres, those may be biocompatible.

Figure 2. Effect of PNIPAAm macromonomer chain length on nanospheres size, in feed ratio styrene:PNIPAAm = 100:1 (molar ratio) error bar is size particle distribution.

**CONCLUSION**

In conclusions, we successfully prepared well-defined core-corona type nanosphere with regulated diameter which changed dispersion stability in response to temperature. In particular, nanosphere size was regulated by PNIPAAm macromonomer chain length and/or amount. In fact, diameter of nanosphere was controlled from 200 nm to 800 nm by macromonomer chain length. These thermoresponsive nanospheres may be utilized to the diagnosis.

**REFERENCES**


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