Colloids and Surfaces B: Biointerfaces 123 (2014) 75–81

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com/locate/colsurfb

Transformable core–corona nanoparticles: Simultaneous change of core morphology and corona wettability in response to temperature

Takuya Matsuyama, Ayaka Kimura, Taka-Aki Asoh[1], Takuma Suzuki, Akihiko Kikuchi*

Department of Materials Science and Technology, Tokyo University of Science, 6-3-1 Niijuku, Katsushika-ku, Tokyo 125-8585, Japan

ARTICLE INFO

Article history:
Received 18 July 2014
Received in revised form 22 August 2014
Accepted 24 August 2014
Available online 30 August 2014

Keywords:
Poly(*N*-isopropyl acrylamide)
Atom transfer radical polymerization
Macromonomer method
Nanoparticle
Transformable

ABSTRACT

We prepared transformable thermoresponsive nanoparticles with variable core softness, controlled by the nanoparticle core's glass transition temperature (T_g). The nanoparticles were prepared by the dispersion copolymerization of butyl methacrylate (BMA) and/or methyl methacrylate (MMA) with a poly(*N*-isopropylacrylamide) (PNIPAAm) macromonomer in a polar solvent. The shape of the nanoparticle core changed with temperature. We then prepared poly(vinyl alcohol) (PVA) films with dispersed thermoresponsive nanoparticles, to elongate the nanoparticles through a uniaxial stretching of the films at 60 °C. In this manner, the nanoparticle shape changed from spherical to rod-like morphologies, depending on the degree of film extension. Additionally, the rod-shaped nanoparticles only changed back to spheres with temperature modulation. The nanoparticle core's T_g value affected the rate of its physical transformation from rods to spheres at 37 °C, with a slower rate observed for increased T_g. As the nanorod shape change was relatively minor at 37 °C, we could control the shape of these transformable nanoparticles under various physiological conditions, a highly desirable feature for drug delivery applications.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

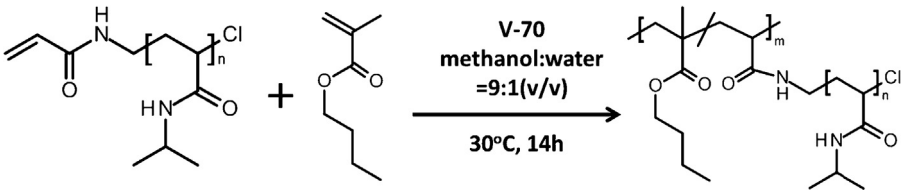
Nanoparticles have been widely employed in both the technology, and biomedical fields owing to their favorable size and extremely large surface area. In particular, nanoparticles are able to deliver encapsulated agents to cells; therefore, they can be used as an effective therapy in imaging and/or drug delivery applications. Control of the nanoparticle cellular uptake is required for an efficient diagnosis and/or therapeutic use. The design of the particle backbone and its surface plays a key role for its interaction with cells; thus, core–corona nanoparticles, designed to have a functional separation between the core and corona, have attracted considerable attention [1].

Controlling interactions between biomolecules and material surfaces of is a key issue in the field of biomaterials science. For example, cells and proteins can interact with different surface properties, including functional groups [2], surface charges [3], wettability [4], and stiffness [5]. When stimulus-responsive polymers are grafted on a material's surface, its properties can be altered by an external stimulus, such as temperature [4,6], pH [7], redox potential [8], light [9], and specific chemicals concentrations. Therefore, the interaction between biomolecules and materials can be controlled by external stimuli. In particular, the adhesion of cells to a surface can be altered through the surface's properties. Okano et al. reported on adhered cells that were grown to full confluency, in thermoresponsive poly (*N*-isopropylacrylamide) (PNIPAAm)-grafted cell culture dishes; after recovery, they switched their surface properties from hydrophobic to hydrophilic upon decreasing the temperature below 32 °C [4]. We previously prepared thermoresponsive core–corona type nanoparticles with a well-defined PNIPAAm corona layer [10]. These nanoparticles have a high dispersity in aqueous media and aggregate above PNIPAAm's lower critical solution temperature (LCST), approximately 32 °C.

On the other hand, cells can recognize a material's topology as well as its surface features [11]. For example, phagocytosis was affected by the size, shape, and number of particles, because the number of internalized particles was limited by the macrophage's phagocytic capacity [12,13]. Mitragotri et al. reported that the nanoparticle–cell interaction in phagocytosis was affected by the nanoparticle's shape [14]. In addition, a particle's shape affects T cell activation, as it is enhanced with larger contact surfaces [15]. Thus, the nanoparticle design appears important for the regulation

* Corresponding author. Tel.: +81 3 5876 1415; fax: +81 3 5876 1639.
E-mail address: kikuchia@rs.noda.tus.ac.jp (A. Kikuchi).
[1] Current address: Advanced Research Institute for Natural Science and Technology, Osaka City University, 3-3-138 Sugimoto, Sumiyoshi-ku, Osaka-shi 558-8585, Japan.

http://dx.doi.org/10.1016/j.colsurfb.2014.08.031
0927-7765/© 2014 Elsevier B.V. All rights reserved.



Scheme 1. Synthesis of the thermoresponsive core–corona-type transformable nanoparticles by dispersion polymerization.

of inter-cellular migration and cell activation. However, few studies have focused on the factors controlling particle morphology.

In this study, we attempted to design transformable nanoparticles having different thermoresponsive properties between the particle core and corona. We prepared nanoparticles having a poly(butyl methacrylate) (PBMA) core and PNIPAAm corona through the macromonomer method, in which both the core morphology and corona wettability could be changed simultaneously through temperature modulation. Thus, the obtained PBMA-*g*-PNIPAAm nanoparticles changed shape at physiological temperatures, due to the PBMA core's T_g being approximately 20 °C [16]. In addition, the nanoparticle core stiffness was altered by the copolymerization of methyl methacrylate (MMA) and butyl methacrylate (BMA). The nanoparticle's shape changes were investigated by elongating them from spheres to rods followed by retuning their morphology through temperature modulation. Therefore, both the nanoparticle shape and surface wettability were controlled by altering the temperature. These nanoparticles can be used for phagocytosis by target cells for effective therapeutic or bioimaging applications.

2. Materials and methods

2.1. Materials

N,*N*-dimethylformamide (DMF), tetrahydrofuran (THF), ethanol, hydrazine monohydrate, triethylamine (TEA), CuCl, *N*-isopropylacrylamide (NIPAAm), acryloyl chloride, butyl methacrylate (BMA), methyl methacrylate (MMA), poly(vinyl alcohol) (PVA, degree of polymerization: 1500–1800), and 2,2′-azobis(4-methoxy-2,4-dimethylvaleronitrile) (V-70) were all purchased from Wako Pure Chemical Industries Ltd. (Osaka, Japan). The NIPAAm was purified by recrystallization from hexane and dried at room temperature in vacuo. The BMA was purified by distillation at reduced pressure under a nitrogen atmosphere, and the fraction boiled at 42 °C/9 mmHg was collected for use. The MMA was purified similar to BMA with the fraction boiled at 27 °C/34 mmHg was collected for use. *N*-(chloromethyl)phthalimide (CMP) was purchased from Aldrich (MO, USA). The NMR solvents; D_2O, $CDCl_3$, and DMSO-d6 were purchased from Acros Organics (NJ, USA).

2.2. Methods

2.2.1. Preparation of thermoresponsive transformable nanospheres

We have already reported on the synthesis of PNIPAAm macromonomers with controlled chain lengths [10]. In this work, a PNIPAAm macromonomer with M_n = 10,400 and $M_w/M_n \leq 1.15$ was used. The PNIPAAm macromonomer (0.02 mmol) and BMA (2.0 mmol) were placed into a round-bottomed flask with a three-way stopcock together with the azo-initiator (V-70, 1 mol% with respect to the BMA monomer) in 2.0–20 mL of a mixed methanol/water (9/1, v/v) solution. N_2 gas was bubbled through the solution for 5 min to remove oxygen, and then sealed flask was placed in a 30 °C water bath and maintained for 14 h. This synthetic procedure is illustrated in Scheme 1. The obtained nanoparticles were purified by dialysis in methanol and pure water using a regenerated cellulose tube (Spectra/Por, MWCO: 50000) to remove unreacted monomers and macromonomers. The resulting thermoresponsive core–corona type nanospheres were analyzed by gel permeation chromatography (GPC), with Tosoh columns TSKgel G3000HHR and TSKgel G5000HHR connected serially, at 45 °C using DMF and 10 mM LiCl as an eluent, as part of a JASCO system consisting of a PU-2080 Plus intelligent HPLC pump, a UV-2075 Plus intelligent UV/VIS detector, an RI-2031 Plus intelligent RI detector, and a CO-2060 Plus column oven (JASCO, Tokyo, Japan), and characterized with differential scanning calorimetry at a 10 °C/min heating rate, from −20 °C to 180 °C (DSC: X-DSC7000, Seiko Instruments Inc., Japan); scanning electron microscopy at a 15 kV acceleration voltage (SEM, JSM-6060, JEOL Ltd., Tokyo, Japan); and dynamic light scattering (DLS, Zetasizer 3000HSA, Malvern Instruments, Worcestershire, UK).

2.2.2. Adjustment of nanoparticle core T_g

We adjusted the thermoresponsive nanoparticle core's T_g by using PBMA and its derivatives. The T_g of PBMA was approximately 20 °C [16]. As PMMA has a higher T_g (105 °C) [17], adding MMA to the monomer solution used for nanoparticle preparation may lead to changes in the nanoparticle core's T_g value. Thus, the following BMA:MMA molar ratios were studied: 100:0, 90:10, 80:20, and 70:30. The other polymerization conditions were kept constant to obtain thermoresponsive nanoparticles with different core T_g values. The T_g values of the nanoparticle core were identified as inflection points in the DSC exothermic curves shown in Supplementary materials Fig. S1.

2.2.3. Preparation of nanorods

The nanoparticles shape was then changed from a sphere to a rod [18]. First, 8 mL of an ~2 wt% dispersed nanoparticle aqueous solution was added to 12 mL of a 10 wt% PVA aqueous solution and mixed thoroughly by gentle stirring. Then this solution was cast into a flat Petri dish (approximately 196 cm^2 for 20 mL) and dried at room temperature for 3 days while preventing contamination from air-borne dust. The PVA films (thickness: 50 μm) containing the core–corona type nanoparticles were thus obtained. These films were then cut in 10 mm × 50 mm strip specimens, stretched uniaxially between two clamps, up to four- or six-times their length, in a custom-made deformation apparatus at 60 °C. The stretched nanoparticles were recovered after dissolving the PVA films in water at 4 °C, followed by centrifugal separation at 4 °C. The deformed nanoparticles were examined by SEM. All data reported herein are expressed as the mean of 30 samples, including standard deviation (SD).

2.2.4. Temperature-dependent nanorod morphology changes

The obtained nanorods dispersed in water were incubated in a water bath set at a selected temperature (20–50 °C). The nanorods (or nanoparticles) were recovered at predetermined time points, and their morphology was observed by SEM. Their aspect ratio (AR) was calculated as the ratio of the major to minor axis. The samples were immediately frozen by immersing the sample tube into

Download English Version:

https://daneshyari.com/en/article/599470

Download Persian Version:

https://daneshyari.com/article/599470

Daneshyari.com