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Facile fabrication of colloidal particles based on the electrostatic aggregation of block copolymer micelles

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ABSTRACT

Block copolymer assembled colloidal particles were successfully prepared through electrostatic interactions between cationic polystyrene-*block*-poly(4-vinylpyridine) (PS-*b*-P4VP) and anionic polystyrene-*block*-poly(acrylic acid) (PS-*b*-PAA) in a one-pot process. The colloidal particles were prepared by simple mixing of complementary charged block copolymer micelle aqueous solution. This process presents the possibility of very simple and versatile method of mass production of BCM based colloidal particles. Both hairy and crew-cut types of block copolymer micelles (BCMs) showed different electrostatic assembly tendencies as confirmed by Field emission scanning electron microscopy (FE-SEM). These phenomena are mainly caused by the different degrees of electrostatic interdigitation and entanglement between the protonated and deprotonated corona block regions of the micelles.

1. Introduction

Over the past few years, colloidal particles containing encapsulated drugs have attracted considerable attention for their potential applications in biomedical fields as vehicles for drug-delivery, as imaging and diagnostic agents, for catalysis, and as enzyme-immobilizing hosts. Efforts to prepare colloidal particles for the encapsulation of hydrophobic materials have mainly focused on hollow-shell structures, micro-emulsion droplets, interface assemblies, and carbon materials [1–6]. Among various approaches for possible drug carriers, block copolymer micelles (BCMs) have been investigated because they have several advantages, including the capacity to solubilize hydrophobic molecules in aqueous solution in which they would otherwise be insoluble; the ability to shield hydrophobic functional molecules from environmental conditions; and BCM hydrophilic corona parts offer various opportunities for further applications such as targeting, sensing or diagnosis [7–12]. Recently, Irvine and coworkers reported the application of BCMs as carriers for hydrophilic drugs [13]. Furthermore, Zhang et al. and Hammond et al. have shown that BCMs could be used as drug carrier stacks inside a multilayer polymer film [14–16,19,20]. Furthermore, we recently reported that the charge densities of BCMs could be easily controlled by simply changing the solution pH [17,18].

Here, we report a facile, one batch process for the synthesis of versatile colloidal particles which were assembled utilizing electrostatic interactions between positively charged polystyrene-*block*-poly(4-vinylpyridine) (PS-*b*-P4VP) and negatively charged polystyrene-*block*-poly(acrylic acid) (PS-*b*-PAA). This versatile and simple approach for the construction of colloidal particles that incorporate the various advantages of BCMs enlarges the range of functional materials that can be used as encapsulating polymer containers.

2. Materials and methods

2.1. Materials

$PS_{(Mw=18.6K)}$-*b*-$P4VP_{(Mw=55.8K)}$($PS_{18.6K}$-*b*-$P4VP_{55.8K}$), $PS_{49.5K}$-*b*-$P4VP_{16.5K}$, $PS_{4.3K}$-*b*-$PAA_{19.5K}$, and PS_{16K}-*b*-PAA_{4K} block copolymers were purchased from Polymer Source.

2.2. Preparation of colloidal particles from BCMs

BCMs were prepared using methods described in our previous reports [17,18]. After forming PS-*b*-P4VP micelles at pH 2, the pH of the PS-*b*-P4VP micelle solution was adjusted to pH 4 using 0.1 M NaOH. In contrast, PS-*b*-PAA (50 mg) in 2 mL DMF/THF was dissolved in 48 mL water at pH 10 to prepare the anionic PS-*b*-PAA BCMs. The PS-*b*-PAA micelle solution was then adjusted to pH 5 using 0.1 M HCl. Subsequently, the pH-adjusted PS-*b*-P4VP micelle and PS-*b*-PAA micelle solutions (10 ml each) were mixed together

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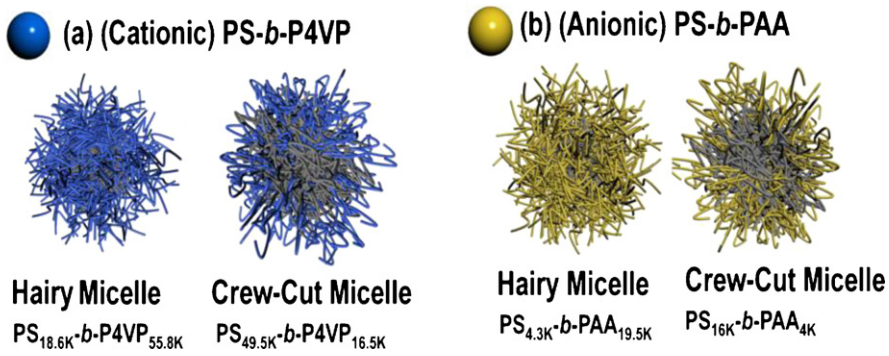


Fig. 1. Graphical images of different block ratio micelles with block molecular weights (Mw): (a) PS-*b*-P4VP and (b) PS-*b*-PAA.

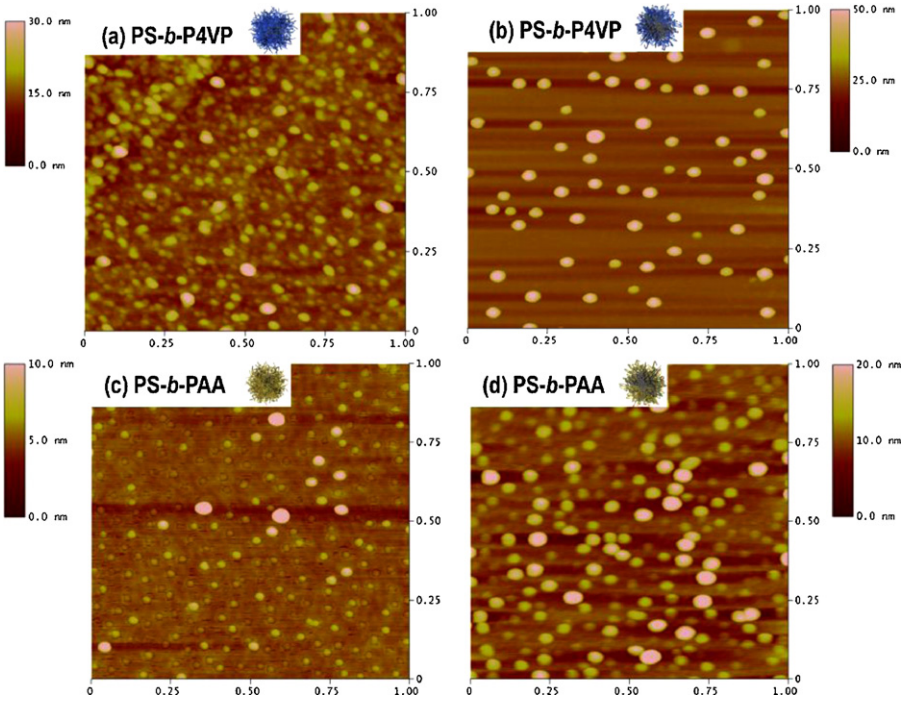


Fig. 2. AFM images of different block ratio micelles with block molecular weights (Mw): (a) hairy $PS_{18.6k}$ - *b* - $P4VP_{55.8k}$; (b) hairy $PS_{49.5k}$ - *b* - $P4VP_{16.5k}$; (c) crew-cut $PS_{4.3k}$ - *b* - $PAA_{16.5k}$; (d) crew-cut PS_{16k} - *b* - PAA_{4k} of the block copolymer micelles.

drop-wise with stirring to fabricate colloidal particles. The solution gradually became a light, misty suspension, an indication of micelle aggregation. After stirring for 24 h, the resulting particle solution was subjected to centrifugation (1500 rpm) to remove any residual micelles.

2.3. Characterization equipment

The ζ-potentials of BCMs were measured using an electrophoretic light scattering spectrophotometer (ELS-8000). The morphologies of the colloidal particles were examined using

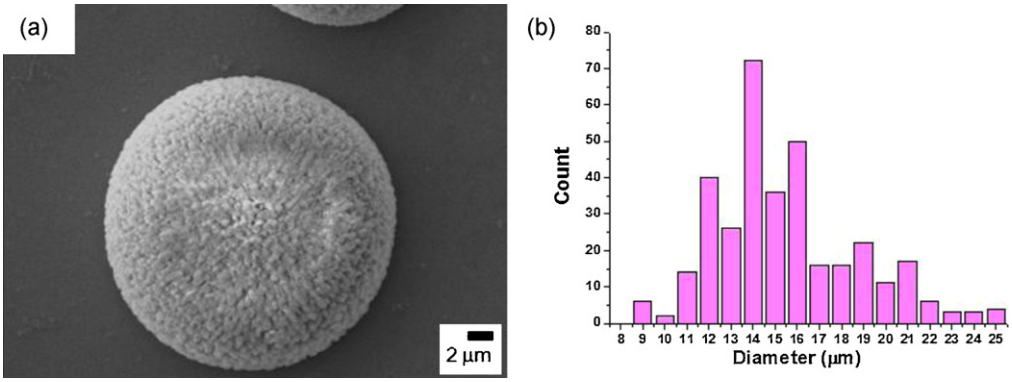


Fig. 3. (a) SEM images of colloidal particles derived from hairy block copolymer micelles (BCMs) and (b) size distributions.

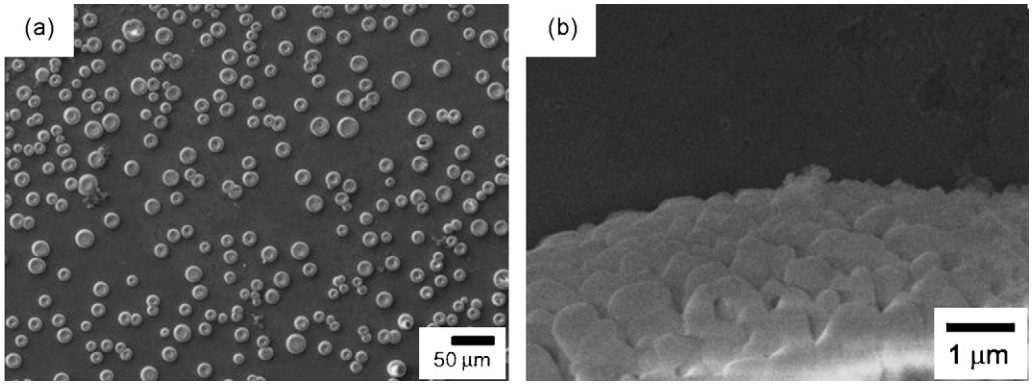


Fig. 4. SEM images of colloidal particles derived from hairy block copolymer micelles (BCMs) at relatively (a) low (200 times) and (b) high (15,000 times) magnifications.

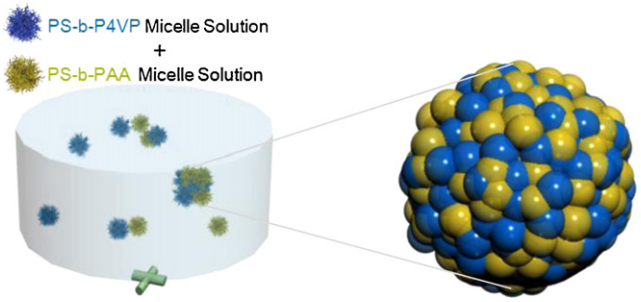
a field-emission SEM (JEOL JSM-7401F). The different BCMs ($PS_{18.6K}$-*b*-$P4VP_{55.8K}$, $PS_{49.5K}$-*b*-$P4VP_{16.5K}$, $PS_{4.3K}$-*b*-$PAA_{19.5K}$, and PS_{16K}-*b*-PAA_{4K}) adsorbed onto silicon substrates were measured with an atomic force microscope in tapping mode (Nanoscope IIIa, Digital Instruments).

3. Results and discussion

The block copolymer micelles used in this research can be divided into two types depending on the composition ratio of the block copolymers and can be further classified into hairy and crew-cut micelles. Fig. 1a and b shows the graphical images of the PS-*b*-P4VP and PS-*b*-PAA micelles, respectively.

Hairy micelles are made from block copolymers in which the corona blocks are much longer than the core blocks, whereas crew-cut micelles are characterized by a relatively larger core and a shorter corona. Due to the difference in their hydrophobic core spaces, hairy and crew-cut micelles are able to encapsulate relatively smaller or larger amounts of hydrophobic functional materials. For this reason, both micelle types were used as drug carrier elements for the preparation of colloidal particles. This is also supported by the prepared hairy and crew-cut BCMs which were investigated using AFM in tapping mode, as shown in Fig. 2. The morphology of each crew-cut micelles is clear and sphere compared with hairy micelles.

Upon mixing, the complementary charged PS-*b*-P4VP micelle (pH 4) and PS-*b*-PAA micelle (pH 5) solutions rapidly assemble to form colloidal particles, based on the electrostatic interactions, as schematically shown in Scheme 1. The ζ-potentials of the micelles of $PS_{18.6K}$-*b*-$P4VP_{55.8K}$ and $PS_{49.5K}$-*b*-$P4VP_{16.5K}$ at pH 4 were $+25 \pm 2.9$ mV and $+22 \pm 4.7$ mV and those of $PS_{4.3K}$-*b*-$PAA_{19.5K}$ and PS_{16K}-*b*-PAA_{4K} at pH 5 were -30 ± 6.3 and -29 ± 4.1 mV, respectively.



Scheme 1. A illustration of the preparation of block copolymer micelle (BCM) aggregated colloidal particles.

Initially, the hairy BCM BCM-based colloidal particles were investigated using SEM. As shown in Fig. 3a, colloidal particles prepared from hairy BCMs are spherical and are tightly aggregated due to their electrostatic interdigitation or to the entanglement between the long corona chains of the PS-*b*-P4VP and PS-*b*-PAA micelles. In addition, the average size of these colloidal particles, measured from low magnification images, was 16.8 ± 6.4 μm with relatively broad size distribution (Fig. 3b).

Low and high magnification images of hairy BCM based colloidal particles were presented in Fig. 4. The samples were prepared by spin coating of BCM mixed solution, which presents the possibility of very simple and versatile process of mass production of BCM based colloidal particles.

On the other hand, the crew-cut BCM-based colloidal particles were prepared as shown in Fig. 5a. The average diameter of these colloidal particles was 5.7 ± 3.7 μm as shown in Fig. 5b. The crew-cut-based colloidal particles also had donut-like structures with vacant interior regions due to poorer aggregation of the micelle

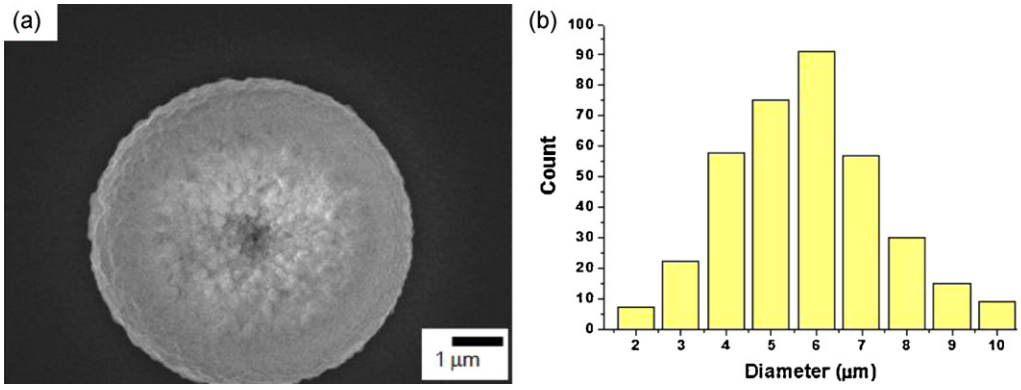


Fig. 5. (a) SEM images of colloidal particles derived from crew-cut block copolymer micelles (BCMs) and (b) size distributions.

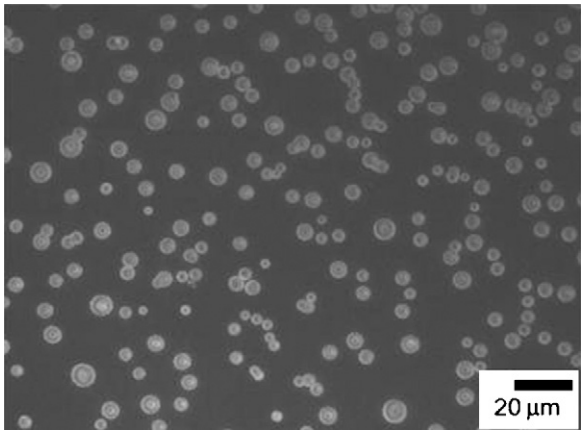


Fig. 6. SEM images of colloidal particles derived from crew-cut block copolymer micelles (BCMs) at relatively low magnifications (500 times).

assembly in the central region of the particles. This phenomenon strongly suggests that the degree of intermicellar entanglement between the hydrophilic corona block chains of the crew-cut PS-*b*-P4VP and PS-*b*-PAA micelles is relatively lower than that of the hairy micelles. On the other hand, the relatively limited possibility of intermicellar aggregation results in a narrower size distribution for the colloidal particles prepared from crew-cut BCMs.

Furthermore the crew-cut BCM based colloidal particles had a more uniform and regular size distribution than did the hairy BCM-based colloidal particles supported with Fig. 6.

4. Conclusion

In summary, we have succeeded in fabricating block copolymer micelle colloidal particles using micelle aggregation based on electrostatic interactions without any post-treatment. A certain block ratio of hydrophobic to hydrophilic regions plays an important role in the formation of relatively larger or smaller sized colloidal particles. To our knowledge, no previous studies have reported the preparation of micelle-only colloidal particles in a one-pot assembly. These fabricated colloidal particles are expected to be very useful for biomedical applications as hydrophobic drug delivery systems.

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