# Self-Organized Nanogels from Pullulan-*g*-Poly(L-lactide) Synthesized by One-Pot Method: Physicochemical Characterization and *In Vitro* Doxorubicin Release

**Jung-Kyo Cho, Wooram Park, Kun Na**

*Department of Biotechnology, The Catholic University of Korea, Wonmi-gu, Bucheon 420743, Korea*

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**ABSTRACT:** Water-insoluble pullulan-*g*-poly(L-lactide) (PUPL) was successfully synthesized via a one-pot method in the presence of triethylamine in dimethyl sulfoxide, in an effort to design a novel anticancer agent carrier. Three samples (designated as PUPL 1, 2, and 3) were obtained, which differed in the moles of lactides grafted to the pullulan. The degrees of grafted lactide per 1 glucose unit in pullulan were 0.68, 0.60, and 0.45 for PUPL 1, 2, and 3, respectively. These copolymers were dissolved in several organic solvents, including dimethyl sulfoxide, acetone, and ethanol, but were insoluble in water. The self-organized nanogels were then prepared from the polymers via dialysis. To study the organizing behavior of the polymers, their critical association concentrations were measured. Their values were 5.0, 15.9, and 52.9 mg/L for PUPL 1, 2, and 3, respectively. The results showed that lactide in the polymers could function as a hydrophobic moiety for the formation of self-organized nanogels. To estimate the potential of PUPL 1 as an anticancer drug carrier, we used doxorubicin (DOX) as a model drug. The DOX loading efficiencies of PUPL 1 were more than 52%, which differed with differing initial DOX concentrations. High loading resulted in slower DOX release as the result of increases in hydrophobic interaction. In conclusion, PUPL nanogels may prove useful as anticancer drug carriers because of their low critical association concentrations and the controlled DOX release rate © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 113: 2209–2216, 2009

**Key words:** biodegradable; biomaterials; drug delivery systems; nanotechnology; self-organization

## INTRODUCTION

Self-organized nanogels produced from hydrophobically modified polysaccharides have been investigated extensively in the biomedical and pharmaceutical fields largely because of their biocompatibility and abundance, features that underlie their possible profound potential.[1–4] In particular, as the result of their unique properties (flexibility, swelling, and squeezing responding to change in environment condition), which enhance drug concentration in tumor sites, their potential in anticancer drug-delivery systems has been evaluated.[5–7] It has been well established that nanogels consist of a polycore and a hydrophilic shell, which provide a zero Gibb's energy, and are able to enclose a water-insoluble drug within the polycore and to protect against interactions with surrounding biological materials.[8,9] Considering these properties of nanogels, our group has reported on the properties of self-organizing nanogels consisting of pullulan conjugated to a hydrophobic moiety.[10] Hydrophobic interactions between the hydrophobic moieties exert noncovalent cross-linkages, thus rendering the gels an appropriate drug carrier for the treatment of tumors. However, these systems evidenced drug-loading contents that were lower than desired.

In this work, L-lactide was grafted to pullulan [i.e., pullulan-*g*-poly(L-lactide) (PUPL)] by the use of a one-pot method in an effort to augment drug-loading contents and to control the rate of degradation. Pullulan is a water-soluble neutral polysaccharide that has been used in biomedical applications[10,11] and as a film for foodstuffs that possess low gas barrier properties.[12] It is a linear polysaccharide harboring maltotriosyl repeating units united by α-(1→6)-linkages or chains of D-glucopyranosyl units that regularly alternate between one α-(1→6)-D and two α-(1→4)-D linkages.[13,14] Pullulan has some limitations in processing as a consequence of its melting temperature and, thus, we conducted acylation with acetic anhydride and L-lactide in an effort to improve its properties.[13,15–17]

*Correspondence to:* K. Na (kna6997@catholic.ac.kr).

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Of course, the synthesis of PUPL was already previously reported by two different groups. In 1998, pullulan was acylated via one-step ring-opening polymerization of lactide by the use of stannous octoate as a catalyst in dimethyl sulfoxide (DMSO). However, it required more than 1 week to synthesize when their method was used.[13] In the same journal, another group reported the graft polymerization of L-lactide on pullulan via the trimethylsilyl (TMS) protection method and studied their degradation properties.[15] However, three steps were required for the polymerization of this PUPL, and it was difficult to introduce the small number of poly(L-lactide) (PLLA) graft chains via this synthetic method. The same group synthesized PUPL via a coupling reaction between amino group end-capped PLLA and carboxymethyl pullulan. Although the number of PLLA graft chains and the chain length could be controlled, this method also required three steps.[16]

Here, to synthesize PLLA-grafted pullulan, triethylamine (TEA) we used as a catalyst because TEA reduced the activation energy of the ring-opening reaction.[18,19] When TEA is used as a catalyst, PLLA-grafted chitin/chitosan copolymers can be readily synthesized via ring-opening polymerization.[20,21] Thus, the synthesis of the lactide derivatives of other polysaccharides via this method is anticipated.

In this study, a series of water-insoluble PUPL copolymers possessing hydrophobic units of different lengths were synthesized via a one-pot synthetic method with the use of TEA as a catalyst. The synthesized polymers were characterized by $^1$H-NMR and Fourier transform infrared (FTIR) spectroscopy. Their synthetic mechanism was proposed from an organic chemical point of view. In addition, the physicochemical properties of self-organized nanogels prepared from the copolymer were studied, most notably critical association concentration (CAC), size, and size distribution. To confirm the potential of this compound as an anticancer agent carrier, we also conducted an *in vitro* release study of doxorubicin (DOX) in a physiological environment. The drug is commercially available in hydrochloride salt form and has proven useful in the treatment of solid tumors, including breast cancer, ovarian carcinoma, transitional cell bladder carcinoma, and thyroid carcinoma.[22] However, it also evidences cardiotoxicity in treated patients. Thus, the development of a new carrier system is needed for effective DOX delivery.

## EXPERIMENTAL

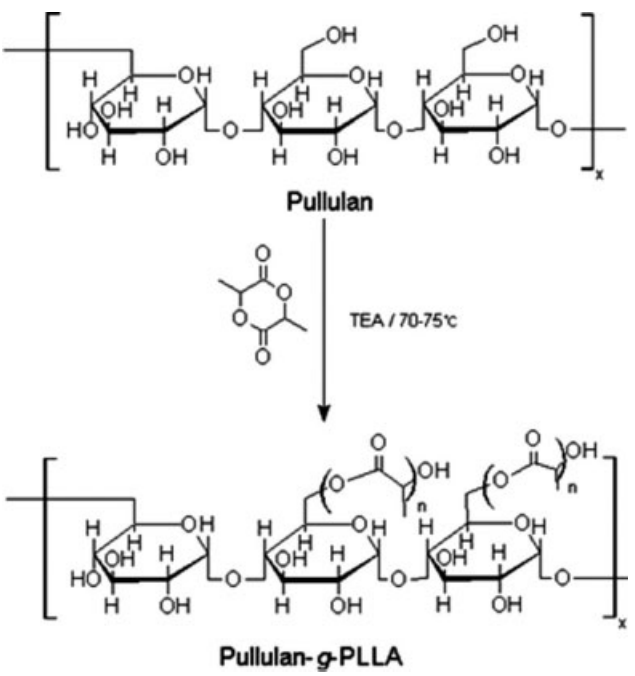
### Materials

Pullulan ($M_w$: $10^5$ g/mol) was purchased from Hayashibara (Okayama, Japan) and purified as follows: the pullulan (10 g) was dissolved in distilled water (100 mL) and precipitated into ethanol (1 L) followed by the redissolution of the precipitates in distilled water. The solution was dialyzed for 1 day by the use of a dialysis membrane (MWCO: 10,000) to remove the solvent and the small molecules in the raw materials. Via the dialysis process, the pullulan, which has a low molecular weight, was removed from the pullulan solution, thus resulting in a narrower molecular weight distribution and yielding a pullulan of slightly greater molecular weight.[13] The resultant solution was lyophilized for 3 days and stored in a dry desiccator. L-Lactide, TEA, and DMSO were acquired from Aldrich. L-Lactide was recrystallized from ethyl acetate before use. Triethylamine and DMSO were used without purification. All other chemicals and solvents were used as received. DOX was supplied by Sigma-Aldrich (St. Louis, MO) and used as received.

### Synthesis of pullulan-*g*-poly(L-lactide) copolymer

These syntheses were accomplished with stirring for 12 h in DMSO at 75°C with the use of TEA and pullulan as a catalyst and macroinitiator, respectively. The synthetic route is depicted in Scheme 1.

The previously purified pullulan was dissolved in DMSO with stirring at room temperature under dry $N_2$. To this pullulan solution, the calculated quantity of L-lactide was added, to a concentration of 10% (w/v). When the mixture was clearly soluble, it was stirred in a preheated oil bath adjusted to 70–75°C.




**Scheme 1** Chemical structures of pullulan-*g*-poly(L-lactide).

TEA was introduced into this solution, when the ratio of TEA to DMSO was 1.67 (v/v) %. All these processes were conducted for 2 h under $N_2$.

After 12 h of reaction, the reactant solution was filtrated through a 0.5-μm syringe filter. The filtrate was then dialyzed against distilled water by the use of a dialysis membrane (MWCO: 10,000), with the distilled water being exchanged every 2 h in the first 12 h for 2 days. The resultant product was then lyophilized for 3 days and stored at −20°C until use.

### Characterization of PUPL copolymer

The $^1$H-nuclear magnetic resonance ($^1$H-NMR) spectra were recorded on a UNITYplus-300 (Varian, 300 MHz) using DMSO-$d_6$ and TMS as a solvent and an internal reference, respectively. The ratio of integration of peaks at 1.4 ppm (the lactide methyl protons, 6H) and 5.2 ppm (3H) was used to determine the degree of substitution (DS) for the polymers.[13]

The FTIR spectra were recorded on a Perkin-Elmer FTIR system (Spectrum GX; Perkin-Elmer, Waltham, MA) at an ambient temperature with the use of KBr pellets. By observing the new peaks and comparing them with those of the raw pullulan on the spectroscopy, the formed chemical bonds were verified.

Dynamic laser scattering measurements were conducted in distilled water at 25°C on a Zetasizer (Malvern, Worcestershire, UK). Their size, size distribution, and polydispersity indices were measured at a concentration of 1 g/L.

### Preparation of nanoparticles from PUPL copolymer

Self-assembled nanoparticles were prepared via the dialysis method, resulting in a narrow size distribution. In brief, the calculated amount of PUPL (25 mg) was dissolved in DMSO (10 mL) at a concentration of 2.5 mg/mL. The solutions were filtered through a 0.5-μm syringe filter and dialyzed against distilled water by the use of a dialysis membrane (MWCO: 1000) for 2 days, with the distilled water being exchanged every 2 h during the first 24 h. The resultant nanoparticle mixture was stored at 4°C until characterization.

### Measurements of fluorescence spectroscopy (pyrene)

For the measurement of fluorescence spectroscopy, the stock solutions of pyrene ($5.0 \times 10^{-5} M$) were prepared in acetone. To coat the bottom of the vials with pyrene, 24 μL of pyrene solution was added to vials, and the solvent was evaporated overnight at room temperature under $N_2$. The prepared nanoparticles (their concentrations were 1.0–$10^{-4}$ g/L) in distilled water were added to the vials, which were shaken every hour at 65°C for a total period of 3 h. Then, the equilibrium state of the pyrene and nanoparticles was achieved by allowing the mixture to cool overnight at room temperature. The fluorescence spectroscopy measurement conditions adopted herein were as follows: spectrum type (Excitation), emission wavelength (390 nm), and slit width (EX/EM 1.5 nm). The final pyrene concentration in the vials was $6.0 \times 10^{-7} M$.[23,24]

### Drug loading and *in vitro* release test

The drug release test was conducted only on the PUPL 1 polymer, because of its hydrophobicity, which is the highest relative to other series. In brief, the calculated quantities of PUPL 1 polymer (40 mg) and predesalted DOX (2, 5, and 10 mg) were dissolved in 10 mL of DMSO, respectively, i.e., 4, 10, and 20% drug loading samples. The solution was then stirred at room temperature and dialyzed against phosphate buffer solution (pH 9.5) with the use of a dialysis membrane with a MWCO of 1000 for 1 day. After filtration through a 0.45-μm syringe filter, the filtrates were stored in a refrigerator until the release test. To determine the drug loading efficiency of the PUPL 1 nanoparticles, the filtrate was lyophilized and dissolved in DMSO, followed by 2 h of vigorous stirring, followed by 3 min of sonication (VCX 750, Sonics & Materials, Newtown, CT). The resultant solution was then centrifuged for 30 min at 20,000 × *g* (Combi-514R, Hanil Science Industry, Incheon, Korea) and the supernatant was analyzed at 490 nm using UV-spectroscopy (UV-2450, Shimadzu, Kyoto, Japan). The *in vitro* release test was conducted as follows: 1 mL of DOX-loaded nanoparticle solution was pipetted into a dialysis membrane and introduced into 10 mL of phosphate-buffered saline (PBS), followed by stirring at 50 rpm and 37°C. At the predetermined times, the medium was removed and exchanged with fresh PBS. The quantity of DOX in PBS was detected via UV spectroscopy and determined using a standard curve at 365 nm. Due to the light sensitivity of doxorubicin, all above tests were conducted in darkness.

## RESULTS AND DISCUSSION

### Synthesis and characterization of PUPL copolymer

The copolymers harboring pullulan and L-lactide were prepared with the use of pullulan and TEA as a macroinitiator and catalyst, respectively. The synthetic block copolymers were characterized by $^1$H-NMR and FTIR spectroscopy, and successful synthesis was verified via comparison of Refs. 13 and 15.

The $^1$H-NMR spectra of pullulan and PUPL 1 are provided in Figure 1. Typically, the methyne and

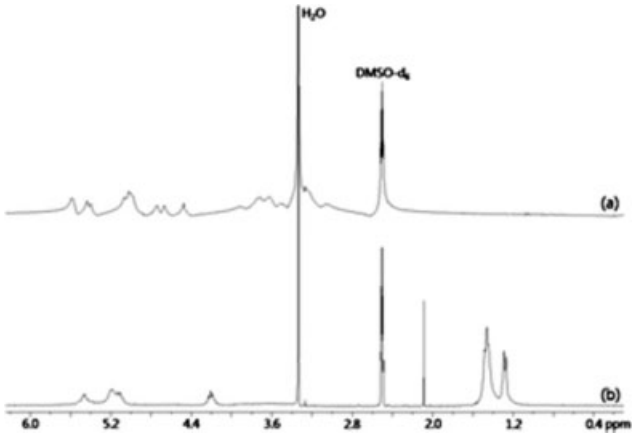



**Figure 1** $^1$H-NMR spectra of (a) pullulan and (b) PUPL 1.

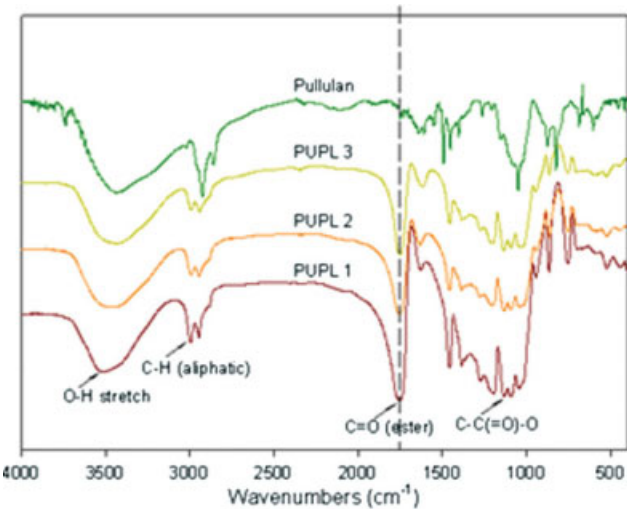



**Figure 2** FTIR spectra of PUPL 1-3 and pullulan on a KBr plate. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

methylene proton signals of the pullulan were observed at $\delta = 3.5–5.5$ ppm, as was shown in Figure 1(a).[15] Upon the grafting of PLLA into pullulan, new peaks relevant to PLLA appeared at $\delta = 1.5$ and 5.1 ppm, as shown in Figure 1(b). By comparing the intensities of the peaks from $\delta = 5.1$ to 5.6 ppm, the degree of substitution can be estimated and is shown in Table I. Here, the degree of substitution refers to the average number of —OH groups on the anhydroglucose ring that had been reacted with L-lactide.[13] The greater the amount of lactide was in the feeds, the greater the degree of substitution, as was expected. By altering the feed ratio, we could control the degree of substitution (0.45–0.68), resulting in various types of copolymers. The characteristic peaks observed at $\delta = 1.66$ and 5.09 of monomer (L-lactide) were not observed in Figure 1(b), thus indicating that the unreacted monomer in the product did not remain.

The FTIR spectroscopy of pullulan and the series of PUPL are provided in Figure 2. The O—H stretch at 3400 $cm^{-1}$ was shifted to a greater wave number as the degree of esterification increased, along with the appearance of the peaks near 1750 $cm^{-1}$, which was indicative of carbonyl absorption of an ester group. As the degree of substitution increased, the peak intensity indicative of the ester group became stronger. Generally, it was reported that the carbonyl absorption of the pure PLLA was observed at 1759 $cm^{-1}$.[13] The peaks indicative of pure PLLA did not appear, implying that the PLLA homopolymer was absent from our products. By comparing the spectra of pullulan and PUPL, we verified the successful synthesis of the copolymers.

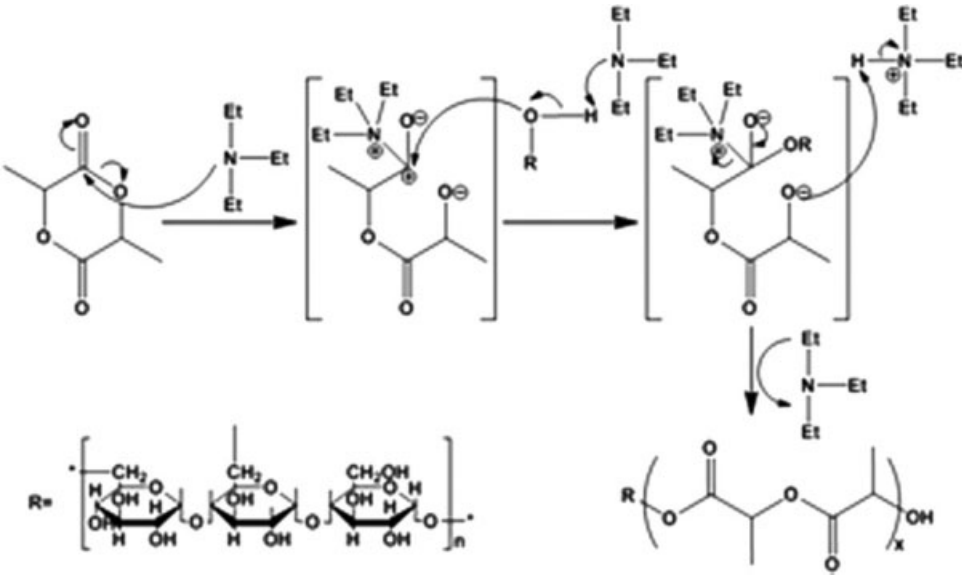
**TABLE I**
**Characterization of Pullulan-*g*-Poly(L-lactide) Copolymer**

| Sample | Feed ratio[a] | DS[b] | Appearance | Yield (%) | CAC (mg/L)[c] |
|---|---|---|---|---|---|
| PUPL 1 | 20 : 1 | 0.68 | White powder | 40 | 5.0 |
| PUPL 2 | 10 : 1 | 0.60 | Sticky mass | 53 | 15.9 |
| PUPL 3 | 5 : 1 | 0.45 | Sticky mass | 80 | 52.9 |

[a] Feed ratio means the molar ratio of L-lactide to repeating units of pullulan in the reactants.
[b] DS indicates the degree of substitution of lactide per 1 anhydroglucose unit of pullulan on the basis of the $^1$H-NMR results.
[c] CAC was determined by the fluorescence spectroscopy.

The synthesized polymers evidenced different appearances according to the feed ratio of L-lactide as compared with native pullulan, which appeared as a white flaky substance. PUPL 1 appeared as white powder that could be easily treated, whereas PUPL 2 and 3, which contained a relatively small quantity of PLLA, appeared as a sticky substance. This finding implies that the incorporation of hydrophilic pullulan units and the branched structure into the copolymers confers a "softness" to them by lowering their crystallinity.[15,25] Thus, according to the application, their physical forms are expected to be controlled by the of L-lactide feed ratio. Their solubility in several solvents was different from that of native pullulan, which was soluble in water and DMSO, whereas the increasing DS of lactide rendered the copolymer insoluble in water. The obtained polymers proved soluble in several organic solvents, including acetone, ethanol, and others. However, they were found to be insoluble in organic solvents containing chlorides, such as chloroform.

In this study, we also attempted to determine the mechanism underlying the synthesis of PUPL copolymers, as is shown in Scheme 2. The reaction began with the activation of the carbonyl group of lactone by TEA. The esterification reaction involves the nucleophilic attack of the hydroxyl group on the



**Scheme 2** Proposed mechanism of the acylation of pullulan using TEA as a catalyst.

carbonyl group of lactone. The hydroxyl groups of pullulan functioned as an initiator of the polymerization. However, the hydroxyl group of pullulan is insufficiently nucleophilic to attack the carbonyl group of lactones. Thus, this limited nucleophilicity requires alkaline conditions for the production of the more reactive alkoxide anion in pullulan. This condition can be achieved via the addition of TEA to the reaction mixture. This can be explained as follows: TEA scavenges $H^+$ from the hydroxyl group in pullulan, thus rendering it more nucleophilic.[19] In addition, TEA attacks the carbonyl group in lactone, rendering it a carbocation, which can be readily attacked by nucleophiles.[18,20] The role of TEA in the reaction is to lower the activation energy for the formation of the carbocation. This translates to a shortening of the reaction time. Thus, the grafting reaction of L-lactide to the hydroxyl group of pullulan occurs via the cleavage of the acyl-oxygen bond of L-lactide, making an ester linkage to the copolymer backbone.[13] This synthesis occurred in a single-step fashion, and required a shorter reaction time relative to the previously reported synthetic method.

### Hydrodynamic diameter and its size distribution of nanoparticles in aqueous medium

The nanogels were prepared via the dialysis method, which prevented the uncontrolled rapid precipitation of the polymer during the process of self-assembly. The hydrodynamic diameters of the nanogels and its distribution in an aqueous environment were estimated using dynamic light scattering technology at 25°C (1.0 g/L). Their size and distribution are provided in Figure 3. Their sizes were dependent on the content of lactide grafted to pullulan. The size of the nanogels decreased as the ratio of PLLA (hydrophobic group) increased. This can be explained in that higher lactide contents provide a better chance for hydrophobic interaction between the lactide portions of the PUPL copolymers in the interior structure, thus resulting in a squeezing of particle size. Ouchi et al. reported the polymeric self-aggregates from PUPL via a three-step graft polymerization of L-lactide to pullulan by the TMS protection method. The same group synthesized PUPL via a coupling reaction between the amino group end-capped PLLA and the carboxymethyl pullulan. The aggregates had relatively smaller particle sizes in a range of 39–100 nm.[26] They involved a more rigid amide linkage than the ester bond in their block copolymers, such that the increased hydrophobicity may result in a reduction in the sizes of their aggregates. This phenomenon is contrary to our previous report regarding

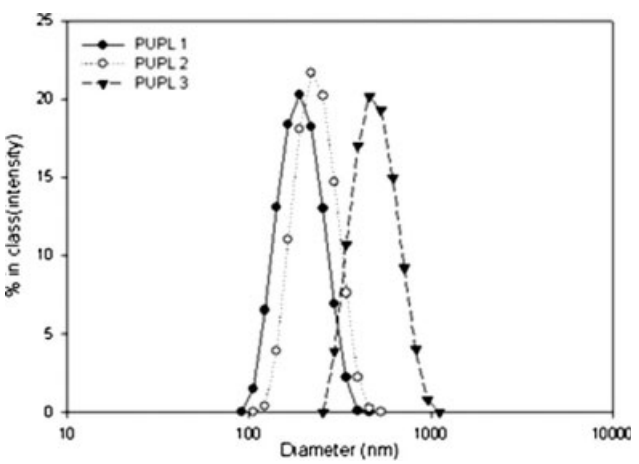



**Figure 3** Particle size distributions of PUPL nanogels determined by dynamic laser scattering at 25°C.

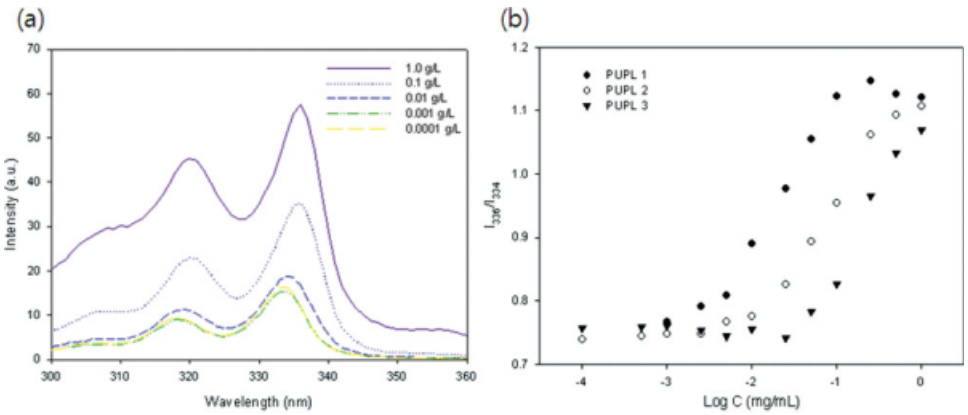



**Figure 4** Excitation spectra of pyrene ($6.0 \times 10^{-7}M$) in distilled water in the presence of PUPL 1 as a function of concentration (emission wavelength was 390 nm) (a) and the plot of intensity ratio $I_{336}/I_{334}$ from excitation spectra vs. Log C of PUPL nanogels (b).

pullulan-derived nanogels,[27–29] in which it was reported that the more hydrophobic moiety induced greater hydrophobic interaction between the polymers for the purpose of minimizing the interfacial energy.[30] This explanation does not apply in this case. Rather, the formed nanogels swelled as a function of the ratio of the hydrophilic portion. Due to the relatively small degree of polymerization and L-lactide substitution in the block copolymers (PUPL 3), the rigid chain of PLLA occupied a smaller portion, which made the our approach to the synthesis of the polymer chains (PUPL 3) easier than that of other polymers (PUPL 1). Thus, the size of the PUPL 3 particles was largest in the prepared nanogels.

The observed narrow size distribution of the nanogels implies that the systems may evidence uniformity in terms of drug loading, drug release, bioavailability, and efficacy.[31]

### Critical aggregation concentration of the copolymers in aqueous medium

The synthetic polymers were composed of two different parts. The primary chain is hydrophilic pullulan, whereas the branched chain is hydrophobic poly(L-lactide). Thus, these materials evidence an amphiphilic property and will self-organize in water. To observe the organizing behavior of the copolymers in aqueous media, we used pyrene as a fluorescence probe. Pyrene has been used as an effective fluorescence probe because of its several favorable properties, ie, the long lifetime of pyrene monomers and the efficient formation of excimers.[23] At a low concentration of PUPL 1 nanoparticles, the changes in the total fluorescence intensity and shift of the (0, 0) band at 334 nm in aqueous medium are negligible. That is, pyrene in a more polar environment has a very small absorption at 336 nm. However, as the concentrations of the polymer solution increased, the total fluorescence intensity and the shift of the (0, 0) band could be clearly observed. This finding shows that the pyrene is transferred from the aqueous polar environment to the less polar micellar domain.[24] The fluorescence intensity is constant below a certain concentration, but above this concentration it increases in accordance with a function of log c. At this concentration, referred to as the CAC, the micelle is formed and the pyrene is partitioned between the aqueous and self-assembled micelle domain.[24] The (0, 0) band at 334 nm shifted to 336 nm upon the addition of PUPL 1 [Fig. 4(a)]. The CAC was determined from the crossover point at a low concentration, as is shown in Figure 4(b). As the degree of PLLA substitution increased, the CAC was reduced. This indicates that the number of stable micelles increases with decreases in the CAC.[31] This stability may be explained by the increased hydrophobic interaction and rigidity of PLLA chains in the copolymers as a function of the hydrophobic segment (PLLA).

### *In vitro* drug release test

In an effort to assess the potential of PUPL for DOX delivery carrier, various concentrations of DOX (2, 5, and 10 mg) were loaded into 40 mg of PUPL 1, respectively, and their particle sizes, loading contents, and efficiencies were evaluated. The mean diameter of drug-loaded PUPL 1 at pH 7.4 increased slightly. This result may indicate that the addition of

**TABLE II**
**Characterization of DOX-Loaded PUPL1 Nanoparticles**

| Sample | PUPL1/DOX weight ratio (mg/mg) | Size (nm) ± SD | Drug contents (%, w/w) | Loading efficiency (%, w/w) |
|---|---|---|---|---|
| PUPL 1-1 | 20 | 202.00 ± 4.58 | 2.74 | 67.7 |
| PUPL 1-2 | 8 | 288.67 ± 1.15 | 6.60 | 63.6 |
| PUPL 1-3 | 4 | 341.00 ± 23.9 | 11.5 | 51.8 |

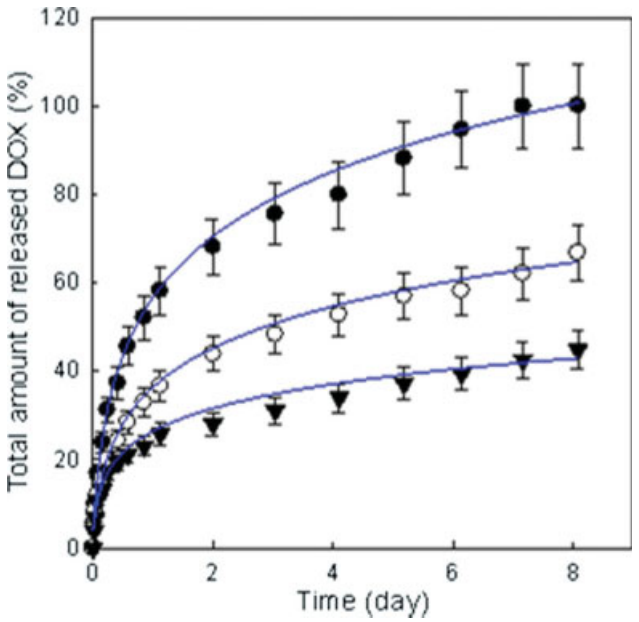



**Figure 5** Release profile of doxorubicin from DOX-loaded PUPL 1 nanogels as a function of drug loading content. PUPL 1-1 (●), PUPL 1-2 (○), PUPL 1-3 (▼).

the hydrophobic drug reduced the degree of hydrophilic repulsion between the PUPL 1 particles, and increased the hydrophobic interactions between lactide groups and/or hydrophobic drugs. The hydrophobic interactions resulted in the growth of the particles. This hypothesis was supported by the results of the drug-loading content tests. The drug-loading contents of PUPL 1 increased as the polymer/drug feeding ratio increased, resulting in an increase in particle size (Table II).

The nanogels evidenced superior drug-containment properties. In our previous report, the DOX loading efficiency of nanogels from pullulan derivatives was less than 20%.[8,9] However, in the case of the PUPL 1 nanogels, the loading efficiency was shown to be in excess of 50%, and the maximum loading content is 11.5%. In an attempt to assess the DOX release kinetics, DOX-loaded PUPL 1 nanogels were dispersed in a dialysis tube containing PBS buffer (pH 7.4). The total quantities of DOX released from PUPL1-1 (20 wt % ratio of PUPL1/DOX), PUPL1-2 (8 wt % ratio of PUPL1/DOX) and PUPL1-3 (4 wt % ratio of PUPL1 to DOX) over 2 days were 69, 42, and 29%, respectively (Fig. 5). DOX release from the nanogels demonstrated first-order like kinetics; an increased drug-loading content resulted in slower DOX release. Regression equation for each group was $y = 2.163e^{+1} \ln X$ ($R^2 = 0.9970$), $y = 1.394e^{+1} \ln X$ ($R^2 = 0.9960$), and $y = 0.7537e^{+1} \ln X^1 \ln X$ ($R^2 = 0.9807$), for PUPL1-1,-2, and -3, respectively. The slower release of PUPL 1-2 and 1-3 resulted in an enhanced hydrophobic interaction between DOX and the hydrophobic moieties. This result is similar to the reports of other researchers.[11,32,33] Hydrophobic drugs in the nanospheres were partially crystallized at a higher drug loading content. However, at lower drug loading, the hydrophobic drug existed as a molecular dispersion in the nanoparticles.[33] The crystallized drug is expected to be dissolved and to diffuse more slowly into the outer aqueous phase relative to the molecular dispersion. Thus, the rate of release of the hydrophobic drug from the higher-drug-loaded nanoparticles was slower than that from the lower-drug-loaded nanoparticles.[33] Therefore, we can control the drug-release kinetics by varying the drug-loading contents using this system. In particular, since the hydrolysis of PLLA grafted to pullulan may result in the disintegration of the nanogel, the potential of the nanogel on long-term drug delivery should be investigated.

## CONCLUSIONS

Water-insoluble PUPL was successfully synthesized in this study, via a one-pot method using TEA as a catalyst, in an effort to develop new anticancer drug vehicles. The nanogels were prepared from the copolymers by a simple dialysis method. Their size and CAC could be varied as a function of hydrophobic moiety (PLLA) in the feed. The release study on a hydrophobic drug, DOX, evidenced a relatively sustained release profile over 8 days. These materials are expected to prove useful in the hydrophobic drug carrier in a controlled fashion, by adjusting the balance between hydrophobicity and hydrophilicity.

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