Carbohydrate Polymers 83 (2011) 1499–1506

Contents lists available at ScienceDirect

Carbohydrate Polymers

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

Preparation and properties of new micellar drug carriers based on hydrophobically modified amylopectin

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ARTICLE INFO

Article history:
Received 18 June 2010
Received in revised form
23 September 2010
Accepted 30 September 2010
Available online 7 October 2010

Keywords:
Amylopectin
Hydrophobic modification
Self-aggregates
Amphiphilic polysaccharide
Drug carrier

ABSTRACT

Hydrophilic amylopectin was modified by grafting hydrophobic poly (lactic acid) chains. The ^{13}C NMR and X-ray diffraction (XRD) analyses confirmed the modification reaction. For the resultant amphiphilic derivatives with various grafting yields, their self-association behavior and micellar aggregates were investigated by fluorometry, transmission electron microscopy and dynamic light scattering. The critical aggregation concentration (cac) was found to be in the range from 0.038 to 0.190 mg/L and the mean diameter (MD) was observed to be in the range from 20.7 to 77.2 nm in aqueous solutions at 25 °C. With the increase of the grafting yield, the cac value decreased while the MD value increased. For the resultant micellar aggregates, their drug loading and in vitro drug release characteristics were studied using indomethacin as the model drug. It was found that such micellar aggregates could be used as potential nanocarriers for drug delivery.

1. Introduction

As one of the most abundant polysaccharides in nature, starch is a mixture of amylose, a linear polymer of α-D-glucopyranosyl units linked to 1,4-α-D-glucosidic linkages, and amylopectin, a branched polymer of α-D-glucopyranosyl units containing 1,4-α-D-glucosidic linear linkages and 1,6-α-D-glucosidic linkages at the branch points (Fanta & Doane, 1986; Phillips, 1980). The main biosources for the commercial production of starch are potatoes, wheat, corn and rice. Most starches used in industry usually contain between 20% and 30% amylose with the remainder being amylopectin (70–80%) and minor components (less than 1%) such as lipids and protein (Whistler, BeMiller, & Paschall, 1984). Up to now, various starch and their derivatives have been used to prepare biodegradable materials with potential applications in a large number of areas such as medicine, pharmacy, agriculture, biology, environmental remediation and protection (Athawale & Lele, 2000; Lee & Mooney, 2001; Park, Shalaby, & Park, 1993; Zhang & Chen, 2002). In particular, starch-based drug delivery systems are of interest for biomedical use due to their good hydrophilicity, biocompatibility and biodegradability (Elvira, Mano, San Román, & Reis, 2002; Geresh et al., 2004; Henrist, Van Bortel, Lefebvre, & Remon, 2001; Silva, Gurruchaga, & Goñi, 2009; Sinha & Kumria, 2001).

Since 1950, considerable effort has gone into hydrophobically modified derivatives of hydrophilic polysaccharides (Akiyama et al., 2007; Ferruti, Tanzi, & Vaccaroni, 1979; Gros & Feuge, 1962; Kawakami, Ihara, Nishioka, Kitsuki, & Suzuki, 2006; Kosan, Meister, Liebert, & Heinze, 2006; Li & Zhang, 2008; Liu & Zhang, 2007a, 2007b; Wolff, Olds, & Hilbert, 1951; Zhang, 2001; Zhang, Zhang, & Li, 2000). The resultant polysaccharide amphiphiles have found extensive applications in colloid science, environmental technology, biotechnology and biomedical engineering. Particularly, they have become the focus of broad research for their ability to form the self-aggregates in aqueous solutions in order to develop effective drug delivery vehicles (Daoud-Mahammed & Gref, 2007; Jeong et al., 2006; Jung, Jeong, & Kim, 2003; Lu, Zhang, Liu, & Chen, 2008; Yang, Kuang, Li, et al., 2008; Yang, Kuang, Wang, & Zhang, 2008; Yang, Zhang, Wen, Liang, & Zhang, 2007). The as-obtained micellar nanocarriers can protect the drug against in vivo degradation, control the drug release, and have a good colloidal stability (Akiyoshi et al., 1998; Lemarchand, Gref, & Couvreur, 2004). In addition, such carrier materials may achieve an active targeting towards tumors or inflammatory tissues due to their specific interaction with cells or mucosal surfaces (Illum, Farraj, & Davis, 1994; Na et al., 2003).

In this work, we modify hydrophilic amylopectin by grafting hydrophobic poly(lactic acid) (PLA) for the fabrication of polymeric micelles for drug delivery. It is known that amylopectin is

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doi:10.1016/j.carbpol.2010.09.061

Table 1
The synthetic conditions and structure parameters of modified amylopectin samples.

Sample no.	Amylopectin/LA (feed ratio, g/g)	Sn $(Oct)_2$ (wt%)	Temperature (°C)	Time (h)	GY (%)	DS	DP
Amy-g-PLA1	3.0/50.0	0.01	100.0	5.0	17.8	0.82	1.33
Amy-g-PLA2	3.0/50.0	0.01	100.0	7.0	24.4	1.02	1.42
Amy-g-PLA3	3.0/50.0	0.01	100.0	9.0	32.0	1.28	1.64
Amy-g-PLA4	3.0/50.0	0.01	100.0	12.0	32.8	1.35	1.81

rich in waxy maize starch and potato starch (Ellis et al., 1998). Its structure is similar to glycogen, the branched glucose storage polymer in humans. Therefore, it has a low immunogenicity and is especially suitable for the preparation of drug carriers (Brecher, Owen, & Bandarenko, 1997). PLA is a biodegradable polymer with low toxicity, excellent biocompatibility and bioabsorbability in vivo (Liu & Zhang, 2007a, 2007b). It has been widely used in biomedical applications such as sustained drug delivery systems, implants for orthopedic devices and absorbable fibers (Wu et al., 2005). The combination of amylopectin with PLA will result in a totally biodegradable polysaccharide derivative with an amphiphilic character. Moreover, such a polymeric amphiphile is expected to self-assemble into nanosize core–shell type micelles at aqueous environment for the incorporation and controlled release of hydrophobic drugs. Although amylopectin has been used to prepare hydrophilic matrices, films or hydrogels for pharmaceutical applications (Guo, Heinamaki, & Yliruusi, 2002; Nabais et al., 2007; Tabata, Matsui, & Ikada, 1998), no study is dealt with the micellar drug carrier based on hydrophobically modified amylopectin.

2. Materials and methods

2.1. Materials

Amylopectin (from waxy corn) was purchased from Tokyo Chemical Industry Co., Ltd. (Japan). The weight average molecular weight was determined to be 9.33×10^{-6} g/mol by static light scattering. Lactic acid (90% aqueous solution) was purchased from Guanghua Chemical Company in Guangdong (China). Tin octoate [stannous 2-ethylhexanoate; $Sn(Oct)_2$] was purchased from Alfa Aesar and used as received. Pyrene and indomethacin were purchased from Fluka. Pyrene was purified by recrystallizing twice from ethanol and drying under vacuum. Dimethyl sulfoxide (DMSO) was dried over molecular sieves and then vacuum-distilled. All other chemicals were of analytical grade and used as received.

2.2. Modification reaction of amylopection and its confirmation

A required amounts of amylopectin and aqueous lactic acid (LA) were added to a 250 mL three-necked flask equipped with a mechanical stirrer and vacuum pump system. After the stirring at 75 °C for 30 min, the temperature of the reaction system was thermostated to be 100 °C by a temperature controlling system. When the amylopectin was dissolved fully in the lactic acid, a required amount of $Sn(Oct)_2$ was added to the flask. The modification reaction was conducted at 100 °C under vacuum (<1 mm Hg) for a predetermined time. At the completion of reaction, the system was cooled to room temperature. The resultant product was washed twice with acetone under vigorous stirring. Then the product was further purified by Soxhlet extraction to remove completely the unreacted LA monomer as well as PLA homopolymer that may be formed during the reaction. The extraction was performed for 24 h with acetone as the extracting solvent. The final product was dried at 60 °C under vacuum. Table 1 gives the synthetic conditions for the modified amylopectin samples used in this study. Based on gravimetric measurement, the grafting yield (GY) was determined according to the following equation:

$$GY = \frac{(w_2 - w_1) \times 100}{w_1} \quad (1)$$

where w_1 and w_2 are the weights of the amylopectin before and after the grafting reaction, respectively.

For the confirmation of the modification reaction and the structure characterization, IR spectra were recorded on Fourier-transform infrared (FTIR) spectrometer (Nicolet 670, USA). Amylopectin and its graft copolymer were mixed with KBr and pressed to a plate for measurement. NMR spectra were obtained on a Bruker AV400 spectrometer (Bruker, Germany) at 400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR, respectively. Amylopectin or its graft copolymer was dissolved in DMSO-d_6, where the concentration was about 5 mg/mL.

2.3. Formation and characterization of micellar self-aggregates

The micellar self-aggregates of the modified amylopectin were prepared by a dialysis method. A required amount of the modified amylopectin sample was dissolved in DMSO. The resultant solution was dialyzed using a dialysis membrane bag with a molecular weight cut-off (MWCO) of 8000 g/mol against deionized water. The deionized water was exchanged every 2 h for the first 6 h and every 6 h for additional 18 h. After that, the dialyzed solution was analyzed or freeze-dried.

For the characterization of the micellar aggregates, fluorescence spectra were recorded on a spectrofluorophotometer (RF-5301PC, Shimadzu, Japan). The excitation wavelength was 330 nm and the fluorescence emission spectra were recorded in the range from 350 to 500 nm. The morphological examination of the aggregates was performed using a JEM-2010HR high-resolution transmission electron microscope. A drop of sample solution (2 mg/mL) containing 0.2 wt% phosphotungstic acid (PTA) was deposited onto a 200 mesh copper grid coated with carbon. Excess of solution was removed with a Kimwipes delicate wipe. The size and size distribution of the micellar aggregates were investigated by dynamic light scattering (DLS) using a BI-200SM Goniometer particle size analyzer (Brookhaven, USA). Each analysis lasted for 300 s and was performed at 25 °C with angle detection of 90°.

2.4. Drug loading by micellar self-aggregates

The loading of hydrophobic indomethacin drug in the inner cores of the resultant micelles was carried out by a solvent-evaporation method reported in our previous work (Yang, Kuang, Wang, et al., 2008). The micelle sample (200 mg) was firstly dispersed in a 70 mL phosphate buffer solution (pH 7.4), and then a solution containing a known amount of indomethacin in 5 mL of ethanol was added slowly into the micelle dispersion under constant stirring. After that, stirring was continued at 50 °C for 24 h in open air for the encapsulation of indomethacin into the micellar aggregates and the evaporation of the ethanol. Due to a small amount of ethanol, the micelles could be stable in the system. At last, the system was centrifuged at 4000 rpm for 10 min in order to remove the unloaded indomethacin, and then the supernatant containing indomethacin-loaded micelles was obtained. The pre-

cipitate containing unloaded indomethacin was dissolved in 50% ethanol solution, and its amount was analyzed by UV–vis spectrophotometry (UV-3150, Shimadzu, Japan) at 318 nm. The loading capacity (LC) and the loading efficiency (LE) were determined according to the following equation:

$$\mathrm{LC} = \frac{(m_1 - m_2) \times 100}{m_3} \quad (2)$$

$$\mathrm{LE} = \frac{(m_1 - m_2) \times 100}{m_1} \quad (3)$$

where m_1 is the total weight of indomethacin used, m_2 is the weight of unloaded indomethacin, and m_3 is the weight of the micelle sample.

2.5. In vitro release of drug-loaded micellar aggregates

The in vitro drug release study was carried out at 37 °C under magnetic stirring. The lyophilized micellar aggregates loaded with indomethacin were firstly suspended in a phosphate buffer solution (pH 7.4), and then introduced into a dialysis membrane bag with a MWCO of 35,000, which was placed into 100 mL of phosphate buffer solution (pH 7.4). At predetermined time intervals, 2 mL aliquots of the aqueous solution were withdrawn and replaced by fresh release medium. The drug content released was determined by measuring the UV absorbance (UV-3150, Shimadzu, Japan) at the wavenumber of 318 nm. The cumulative releases were determined by comparing the amount of the released drug and the total drug loading.

3. Results and discussion

3.1. Synthesis and characterization of hydrophobically modified amylopectin

The hydrophobic modification of amylopectin by grafting poly(lactic acid) (PLA) chains was carried out at 100 °C under vacuum (<1 mm Hg) by in situ reaction of amylopectin with aqueous lactic acid (LA) in the absence of any organic solvents. Stannous 2-ethylhexanoate was used as the reaction catalyst. When the temperature ranged from 75 to 100 °C, amylopectin can be dissolved well in aqueous LA solution, resulting in a homogeneous reaction system to promote the modification of amylopectin. This synthesis strategy is similar to the method reported by Gong, Wang, and Tu (2006). They prepared the graft copolymers of cornstarch with poly(lactic acid) (PLA) by in situ polymerization of cornstarch with lactic acid, and found that the graft copolymerization proceeded mainly through initiating the ring-opening polymerization (ROP) of lactide from the hydroxyl groups of cornstarch catalyzed by $Sn(Oct)_2$. In addition, Dubois, Krishnan, and Narayan (1999) prepared aliphatic polyester-grafted starch by in situ ROP of caprolactone in the presence of starch-like polysaccharides, wherein the in situ ROP is conducted in the bulk. In this study, a series of modified amylopectin samples with different grafting yields of PLA, namely Amy-g-PLA1, Amy-g-PLA2, Amy-g-PLA3 and Amy-g-PLA4, were prepared by the change of reaction time, as shown in Table 1. Within the reaction time range investigated, increasing reaction time up to 9.0 h is accompanied by an obvious increase of the grafting yield (GY), but beyond that a further increase of reaction time does not cause a significant change of GY.

Fig. 1 shows the IR spectra of amylopectin and its PLA-modified derivative (Amy-g-PLA1). Compared with the IR spectrum of pure amylopectin, the PLA-modified derivative has a new strong characteristic absorption peak around 2977 cm^{-1}, which can be attributed to the carbonyl group of the grafted PLA. The methyl asymmetric deformation of the PLA appears at about 1453 cm^{-1}. The 1150

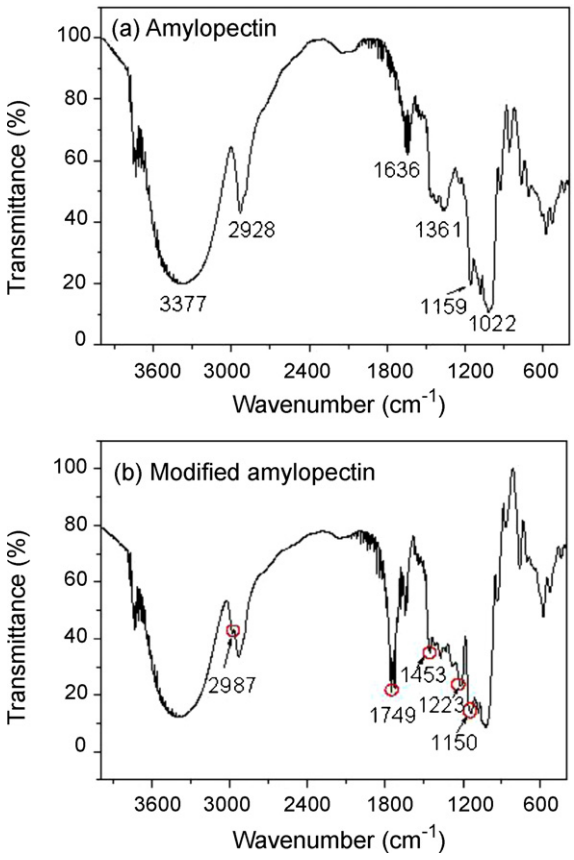

Fig. 1. The FTIR spectra of amylopectin and its PLA-modified derivative (Amy-g-PLA1).

and 1223 cm^{-1} doublets observed in the derivative are assigned to the symmetric C–O–C stretching modes of the ester group. There is another new peak at 2987 cm^{-1}, which can be assigned to the stretching of $CH(-CH(CH_3))$ of the PLA. Moreover, the relative intensity of hydroxyl groups within amylopectin at about 3377 cm^{-1} became weak after the modification. These results suggest that the PLA was grafted to the backbone of amylopectin.

To confirm further this modification reaction and elucidate the microstructure of the derivative, ^1H NMR and ^{13}C NMR analyses were carried out. Fig. 2a shows the ^1H NMR spectra of amylopectin and its PLA-modified derivative (Amy-g-PLA1). It was found that the ^1H NMR spectrum of the derivative showed not only the characteristic proton peaks of amylopectin at 3.5–5.5 ppm (Peng & Perlin, 1987) but also new proton signals at 4.16 and 5.10 ppm, which were assigned to the methenyl protons of the PLA at the terminal groups and the repeat units, respectively (Chung, Waldron, & Zentner, 1996). Meanwhile, other new proton signals at 1.27 and 1.43 ppm were also observed for the modified amylopectin, which could be attributed to the methyl protons of the PLA at the terminal groups and the backbones. Fig. 2b gives the ^{13}C NMR spectra of amylopectin and its PLA-modified derivative (Amy-g-PLA1). From the spectrum of amylopectin, it was observed that the main peaks appeared at 101.5, 79.8, 74.2, 72–73 and 61.5 ppm, which could be attributed to the ^{13}C-chemical shifts of C1, C4, C3, C2, C5 and C6 carbons at the glucopyranan unit of amylopectin, respectively, according to previous ^{13}C NMR analyses for amylopectin (Dais & Perlin, 1982a, 1982b; Peng & Perlin, 1987). In contrast, the spectrum of the derivative shows not only the main characteristic peaks of amylopectin moiety but also additional peaks at three spectrum regions of 16.4–20.1, 65.6–67.9 and 169.4–174.2 ppm, which could be attributed to the ^{13}C-chemical shifts of the methyl carbons,

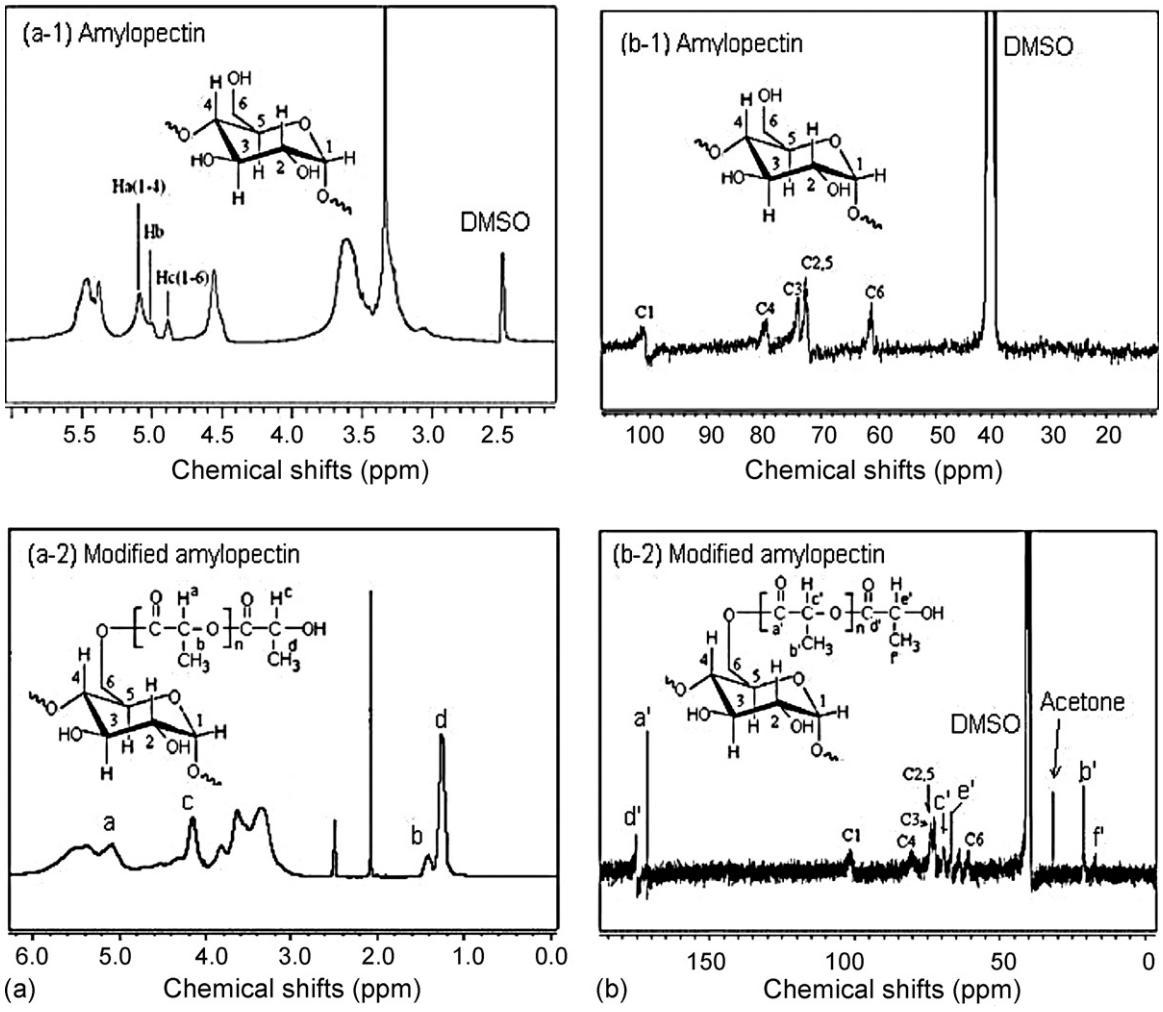

Fig. 2. The ^{1}H NMR (a) and ^{13}C NMR (b) spectra of amylopectin and its PLA-modified derivative (Amy-g-PLA1) in DMSO-d_6.

methene groups and carbonyl groups in PLA moiety (Donabedian & McCarthy, 1998; Hiltunen, Harkonen, Seppala, & Vaananen, 1996), respectively. All these NMR analyses verify further the grafting modification of amylopectin.

Based on the peak assignments of amylopectin ring carbons as well as the carbonyl carbons in LA moiety, two structural parameters, DS and DP, could be estimated. DS, defined as the average number of hydroxyl groups in amylopectin substituted by lactyl units per glucopyranan residue of amylopectin, can be obtained by the following equation (Gong et al., 2006):

$$\mathrm{DS} = \frac{I(c,t)}{I(st)/6} \tag{4}$$

where $I(c,t)$ is the NMR signal integral of the terminal LA methyl carbon, and $I(st)$ is that of the six starch ring carbons. DP, defined as the average length of PLA grafts on amylopectin backbone, can be calculated by the following equation (Gong et al., 2006):

$$\mathrm{DP} = \frac{I(c,t) + I(c,i)}{I(c,t)} \tag{5}$$

where $I(c,t)$ and $I(c,i)$ are the NMR signal integrals of the terminal LA methyl carbon and the internal LA methyl carbon, respectively. As a result, the DS and DP values were estimated, respectively, to be 0.82 and 1.33 for Amy-g-PLA1, 1.02 and 1.42 for Amy-g-PLA2, 1.28 and 1.64 for Amy-g-PLA3, as well as 1.35 and 1.81 for Amy-g-PLA4, as listed in Table 1. It was found that the DS and DP of the derivative increased with the increase of the grafting yield. It seems that the structural parameters (GY and DS) of the modified amylopectin can be easily modulated by changing the reaction time.

3.2. Micellar aggregate characteristics of hydrophobically modified amylopectin in aqueous solution

The self-aggregation behavior of the modified amylopectin in aqueous medium was investigated by fluorometry in the presence of pyrene as a fluorescent probe. It is known that the variation in the ratio (I_1/I_3) of intensity of first (372 nm) to the third (383 nm) vibronic peaks is quite sensitive to the polarity of microenvironment where pyrene is located (Winnik & Regismond, 1996). Fig. 3 gives the change of I_1/I_3 with the concentration for various derivative samples. At lower concentrations, the I_1/I_3 values remain nearly unchanged. With a further increase of the concentration, the intensity ratio starts to decrease, implying the formation of the micellar self-aggregates with hydrophobic domains. In this case, the critical aggregation concentration (cac) could be determined by the crossover point of two straight lines, as indicated in Fig. 3. In contrast, the self-aggregation behavior and cmc value were not detected by fluorometry for aqueous solution of the unmodified amylopectin. As a result, the cac value was found to be 0.190 mg/L for Amy-g-PLA1, 0.064 mg/L for Amy-g-PLA2, 0.049 mg/L for Amy-g-PLA3 and 0.038 mg/L for Amy-g-PLA4, respectively. It is obvious that the cac value of the modified amylopectin decreases with its GY or DS value (Table 1), which was similar to that reported by Lee,

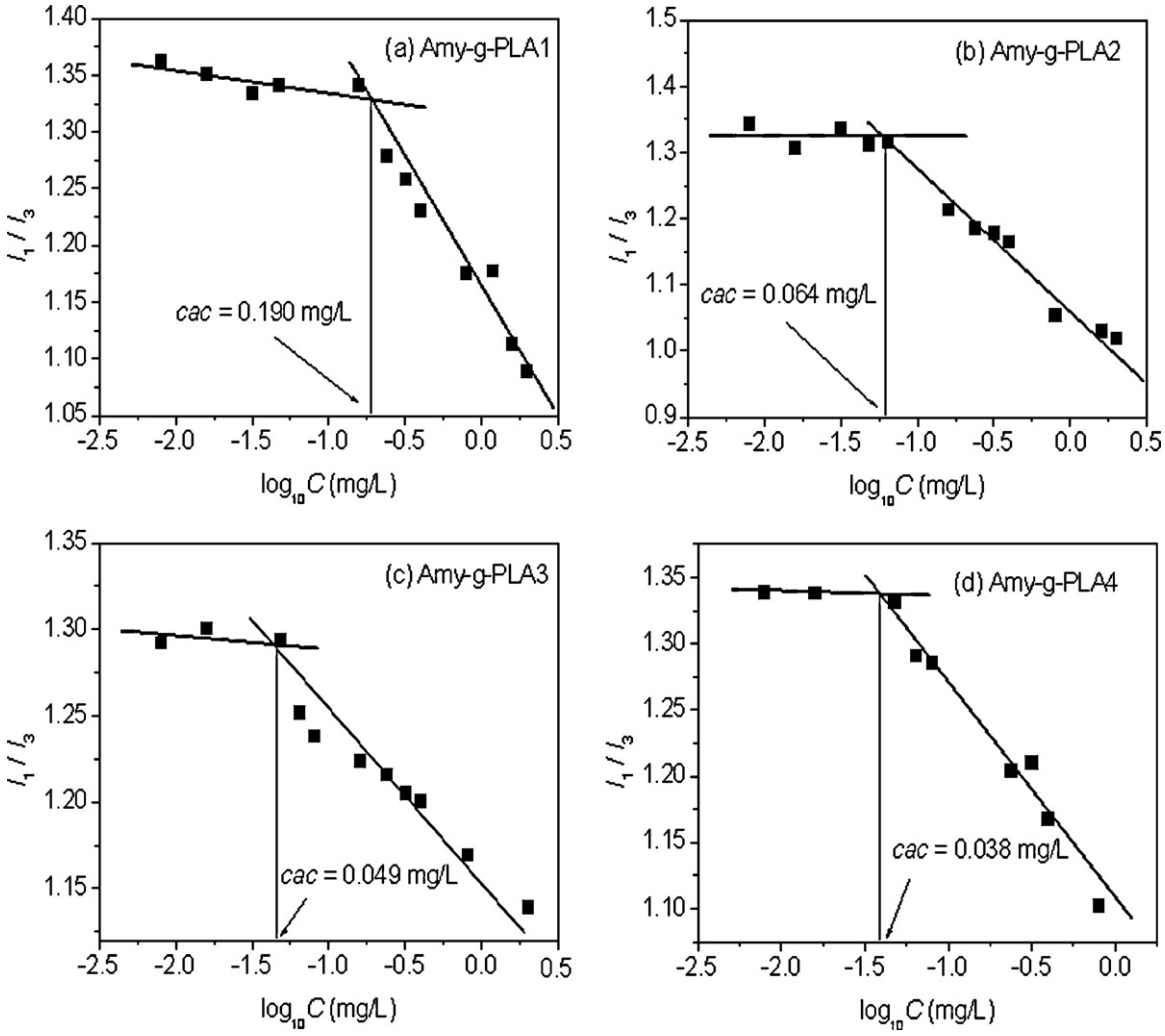

Fig. 3. The change of the intensity ratio (I_1/I_3) versus the concentration (C) for various modified amylopectin samples.

Huang, and Lee (2006) when they studied the aggregation behavior of amphiphilic poly(L-lactide)-graft-chondroitin sulfate copolymer in aqueous solution. In comparison with low molecular weight surfactants (Zhang, 2001), the modified amylopectin has a lower cac value. This implies that such self-aggregates are easier to be formed and have a good colloidal stability when compared with low molecular weight surfactants.

To confirm the formation of the micellar aggregates, the transmission electron microscopy (TEM) observation was carried out for aqueous Amy-g-PLA4 solution with the concentration higher than the cac. From the TEM image shown in Fig. 4, the micellar aggregates with an average size of about 35 nm were observed. Moreover, they have a roughly spherical morphology. In contrast, the micellar aggregates were not observed by TEM for aqueous solution of the unmodified amylopectin. This reveals further that the hydrophobically modified amylopectin with an amphiphilic character could self-assemble into the micellar aggregates by hydrophobic PLA segment self-association and hydrophilic amylopectin segment contacting with water phase, as illustrated in the inset of Fig. 4. For the micellar aggregates formed from various modified amylopectin samples, their mean diameters and their size distributions in aqueous media were measured by dynamic light scattering (DLS) analyses, as indicated in Fig. 5. In a 2.0% concentration of aqueous sample solution, the mean diameter (MD) of the micellar aggregates was measured to be 20.7 nm for Amy-g-PLA1, 25.6 nm for Amy-g-PLA2, 31.3 nm for Amy-g-PLA3, and 77.2 nm for Amy-g-PLA4, respectively. From these results, it was found that the MD value of the modified amylopectin increased with the increase of its GY or DS value (Table 1). This may be attributed to the enhanced surface tension resulting from the increased hydrophobicity–hydrophilicity balance when the hydrophobic PLA segment content in the modified derivative of amylopectin increases (Gao, Wang, Fan, & Ma, 2005). In addition,

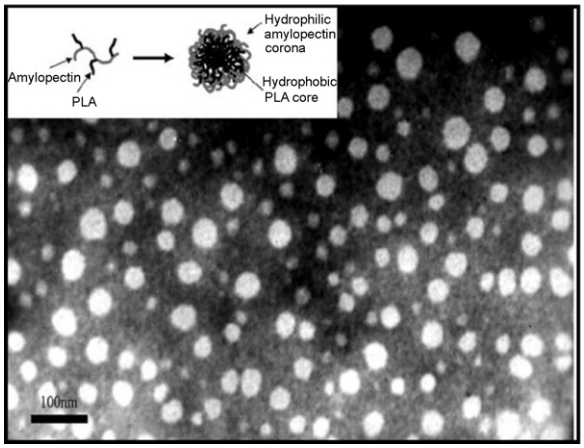

Fig. 4. TEM photograph of the self-aggregates formed from Amy-g-PLA4 in aqueous solution. The inset figure shows a schematic structure of the self-aggregates.

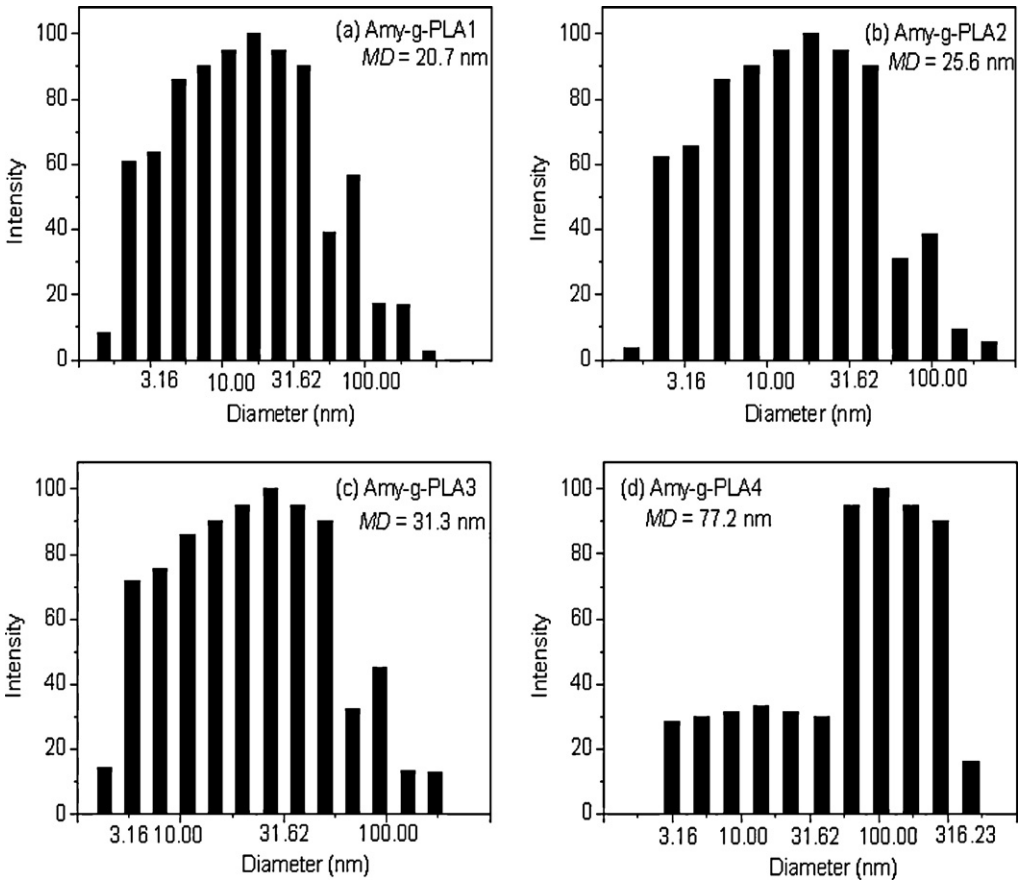

Fig. 5. The size distributions of the micellar aggregates in aqueous solutions of the modified amylopectin samples.

the micellar aggregates formed from Amy-g-PLA4 with higher DS and GY has a wider size distribution when compared with those formed by other samples. This may be attributed to the fact that Amy-g-PLA4 has more grafted PLA chains with different lengths, which resulted in the formation of the micellar aggregates with different diameters. Similar phenomenon was also observed by Feng and Dong (2006) when they investigated the self-assembled properties of biodegradable poly(L-lactide)-grafted chitosan in aqueous medium.

3.3. Drug loading and in vitro release by micellar aggregates based on hydrophobically modified amylopectin

For the resultant micellar aggregates based on the modified amylopectin, their drug loading characteristics were investigated using water insoluble indomethacin as the model drug. Fig. 6 gives the loading capacity (LC) and the loading efficiency (LE) for three micellar aggregates, namely as Aggregate I based on Amy-g-PLA1, Aggregate II based on Amy-g-PLA2 and Aggregate III based on Amy-g-PLA4. Among them, Aggregate III has the highest LC and LE values while Aggregate I has the lowest LC and LE values. The stronger loading ability of Aggregate III could be attributed to the formation of more and bigger micellar aggregates with hydrophobic core due to the use of Amy-g-PLA4 with higher DS and GY values.

Further study was dealt with the in vitro release of the entrapped indomethacin from the micellar aggregates. As shown in Fig. 7a, these drug-loaded aggregates exhibited a controlled drug release behavior without any burst release. For example, the cumulative release during a period of 8 h was observed to be 46.0% for Aggregate I, 37.0% for Aggregate II and 20.0% for Aggregate III, respectively. In contrast, the release amount of the loaded indomethacin from Aggregate III is slower. This resulted from strong hydrophobic interaction between water-insoluble indomethacin and Aggregate III. To understand the release mechanism of the indomethacin from the micellar aggregates, the data from the curves of Fig. 7a were fitted to the Korsmeyer–Peppas equation (Costa & Sousa, 2001):

$$\frac{Q_t}{Q_0} = K_k\, t^n \tag{6}$$

where Q_t is the amount of drug released in time t, Q_0 is the initial amount of drug in the solution, K_k is the release constant, and n is

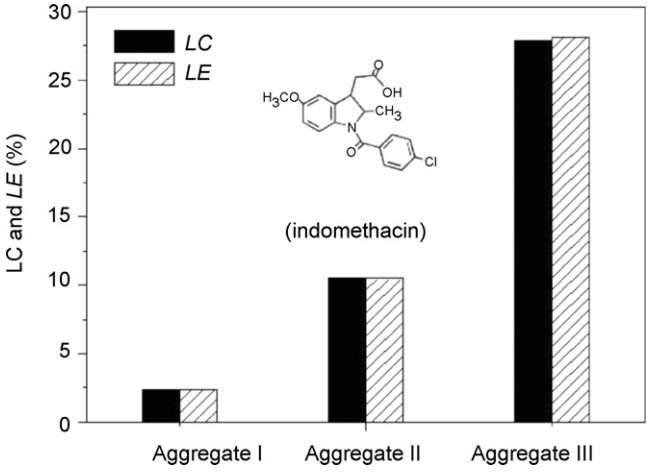

Fig. 6. The loading capacity (LC) and the loading efficiency (LE) of various micellar aggregates for indomethacin drug (pH 7.4, 25 °C).

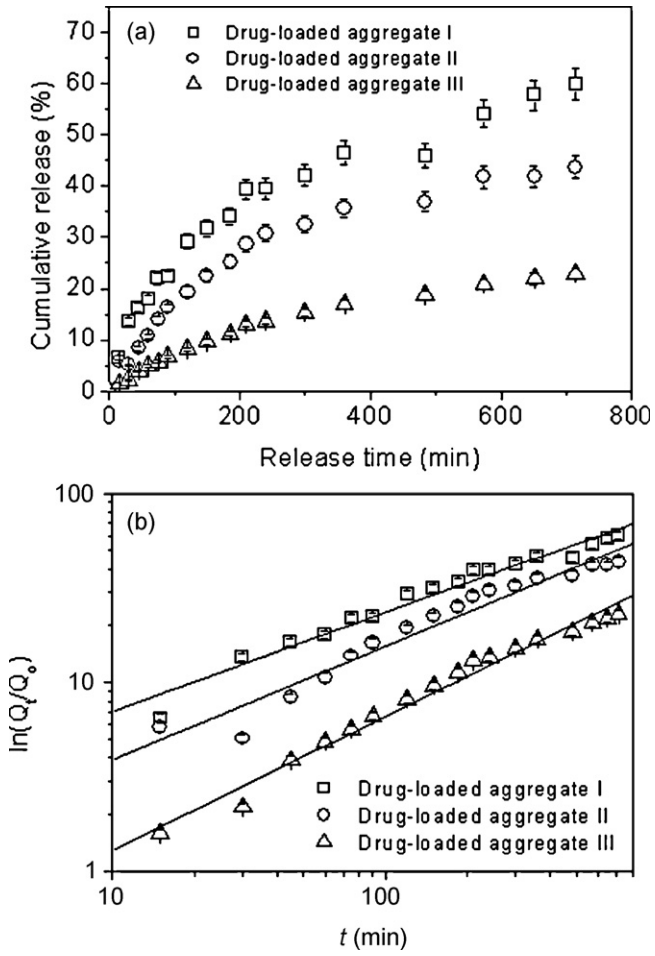

Fig. 7. (a) In vitro drug release profiles for various drug-loaded micellar aggregates (pH 7.4, 25 °C); (b) the double-logarithmic plots of the cumulative drug release (Q_t/Q_0) as a function of time (t) for the drug-loaded micellar aggregates.

the release exponent. Fig. 7b gives the double-logarithmic plots of the cumulative drug release (Q_t/Q_0) as a function of time (t) for these drug-loaded micelles. The linear relationship with the determination coefficient (R) of more than 0.980 for each system suggested that the in vitro release release behavior could be described by Korsmeyer–Peppas equation. For the drug-loaded aggregate I, the K_k and n values were found to be 1.69 ± 0.08 and 0.71 ± 0.03, respectively. For the drug-loaded aggregate II, the K_k and n values were found to be 0.99 ± 0.05 and 0.60 ± 0.03, respectively. For the drug-loaded aggregate III, the K_k and n values were found to be 0.72 ± 0.04 and 0.52 ± 0.02, respectively. Among them, the drug-loaded aggregate III has the smallest K_k and n values. All the n values are between 0.5 and 1.0, indicating that the drug release mechanism belongs to anomalous transport (Costa & Sousa, 2001). It is known (Klein, Miller, Anderson, & DeCosse, 1987) that indomethacin is a nonsteroidal anti-inflammatory drug that reduces fever, pain and inflammation and has been widely used alone or in combination chemotherapy regimens. To reduce its side effects and target it to specific sites, some carrier materials such as polymeric microspheres (Aggarwal, Kaur, Tiwary, & Gupta, 2001), polymeric nanoparticles (Zhang et al., 2006), and submicron emulsions (Friedman, Schwarz, & Weisspapir, 1995) have been developed. However, these drug-delivery systems suffer usually from a lower loading capacity and an obvious burst effect. Therefore, the micellar aggregates developed in this study may be used as a potential drug carrier.

4. Conclusions

The hydrophobic modification of hydrophilic amylopectin was carried out by grafting biodegradable PLA chains. By the change of reaction time, the grafting extent of PLA on the amylopectin backbone could be easily modulated. When the increase of PLA grafting extent, the critical aggregation concentration of the modified amylopectin in aqueous solution decreased, and the mean diameter of corresponding micellar aggregates increased. The TEM images revealed that the self-aggregates were spherical. When these micellar nano-aggregates were used as the drug carrier, it was found that they had a good loading capacity and in vitro release properties for hydrophobic indomethacin drug.

Acknowledgements

This work is supported by the NSF of China (21074152, 20874116 and J0730420) and the NSF of Guangdong Province in China (8151027501000004 and 9151027501000105) as well as the Doctoral Research Program of Education Ministry in China (20090171110023).

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