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Microwave-assisted graft copolymerization of ε-caprolactone onto chitosan via the phthaloyl protection method

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Abstract

The graft polymerization of ε-caprolactone onto chitosan was carried out smoothly under microwave irradiation, via a protection-graft-deprotection procedure with phthaloylchitosan as precursor and stannous octoate as catalyst. The chemical structure of the obtained chitosan-g-polycaprolactone was characterized by FT-IR and NMR spectroscopy. By microwave irradiation, the chitosan-g-polycaprolactone with high grafting percentage above 100% was achieved in rather short time. And the graft copolymerization was greatly improved at the higher power outputs of 450 and 600 W in the studying range. After deprotection, the phthaloyl group was removed and the amino group was regenerated. Thus, the chitosan-g-polycaprolactone copolymer was an amphoteric hybrid with both a large amount of free amino groups and hydrophobic polycaprolactone side chains.

Keywords: Chitosan; Caprolactone; Graft copolymers; Ring-opening polymerization; Microwave

1. Introduction

Chitosan is the fully or partly N-deacetylated derivative of chitin, a well-known abundant natural polymer having the similar structure with cellulose. Much attention has been paid on modification and utilization of chitosan, due to its good biodegradability, biocompatibility and bioactivity (Kumar, 2000; Kurita, 2001; Roberts, 1992). Graft copolymers based on chitosan are attractive to expand the applications as functional hybrid materials, for example, chitosan-g-polystyrene, chitosan-g-poly(ethylene glycol), chitosan-g-poly (vinyl acetate) and so on (Don, King, & Chiu, 2002; Jenkins & Hudson, 2001; Shantha & Harding, 2002). However, these polymers have limited biodegradability because of the presence of their nondegradable branches.

Polycaprolactone is one of the biodegradable industrial polyesters with excellent mechanical strength, biocompatibility and nontoxicity. It has been frequently explored as implantable carriers for drug delivery systems and as surgical repair materials (Amass, Amass, & Tighe, 1998; Pitt, 1999; Vainonpaa, Rokkanen, & Tormala, 1989). It is promising to combine chitosan with polycaprolactone to produce a completely degradable biosynthetic polymer hybrid applicable for a variety of purpose. Generally, polycaprolactone is prepared from catalyzed ring-opening polymerization of ε-caprolactone (Kowalski, Duda, & Penczek, 2000; Storey & Sherman, 2002; Storey & Taylor, 1998). Choi, Kim, and Park (1999) synthesized starch-g-polycaprolactone copolymers by the grafting reaction between hydroxyl groups of starch and ε-caprolactone monomers in the presence of water as a swelling agent and catalyzed by stannous octoate. Later, Detchprohm, Aoi, and Okada (2001) reported synthesis of chitin-g-oligo(ε-caprolactone) with the similar method, in which the oligo(ε-caprolactone) side chains were grown from chitin or chitosan at the amino groups. However, when we consider the unique structure of chitosan, it is important to maintain the aminosaccharide unit for various specific functions, including biological activities and cationic polymer properties (Muzzarelli & Peter, 1997). In the present study, we intended to apply the graft copolymerization of ε-caprolactone onto chitosan via phthaloyl-protected chitosan (PHCS) as intermediate, which phthaloyl group could be deprotected easily to regenerate the free amino groups (Kurita, Ikeda, Yoshida, Shimojoh, & Harata, 2002;

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Nishimura, Kohgo, & Kurita, 1991; Yoksan, Akashi, Biramontri, & Chirachaanchai, 2001).

On the other hand, for ring-opening polymerization of ε-caprolactone, it commonly took 20 h or more to get the reaction completed by conventional heating in the previously mentioned cases. Some reports (Fang, Simone, Vaccaro, Huang, & Scola, 2002; Liao et al., 2002) revealed that the ring-opening polymerization of ε-caprolactone proceeded smoothly and efficiently under microwave irradiation. The convenience of ring-opening polymerization of caprolactone by microwave radiation offers the possibility of an extension of the method to graft chitosan with caprolactone. Moreover, a number of derivatives of chitosan or starch have been achieved by the microwave-assisted modification (Koroskynyi & McCarthy, 2002; Lewandowicz et al., 2000; Liu, Li, Li, & Fang, 2004; Satgé et al., 2002). So this work is concerned with the microwave-assisted graft copolymerization of ε-caprolactone onto chitosan via phthaloylchitosan intermediate.

2. Experimental

2.1. Materials

Chitosan (degree of deacetylation = 100%, determined by the *C*/*N* value of elemental analysis) was purchased from Yuhuan Ocean Biochemical Co. Ltd (Zhejiang, China). ε-Caprolactone (SOLVAY, England) was used without further purification. Stannous octoate was distilled under a vacuum and dissolved with freshly dried toluene. Phthalic anhydride, hydrazine monohydrate and dimethylformamide (DMF) were supplied by the First Reagent Factory of Shanghai (China).

2.2. Methods

2.2.1. Phthaloylchitosan

Chitosan was heated with excess phthalic anhydride in dried DMF to give PHCS according to the previously reported procedure (Kurita et al., 2002; Nishimura et al., 1991). It was obtained as a yellow powdery material and the degree of substitution (DS) of phthaloyl groups was calculated to be about 1.05 from the *C*/*N* value of elemental analysis. IR (KBr, cm^{-1}): ν3460 (OH), 1777 and 1712 (C=O anhydride), and 721 (aromatic ring).

2.2.2. Microwave-assisted graft copolymerization

The microwave-assisted graft copolymerization was carried out in a 2.45-GHz microwave oven (SANYO, EV350S). The typical procedure was described as follows: PHCS (1 g) was placed in a dried glass reactor, and a certain amount of mixture of ε-caprolactone monomer and stannous octoate (1 mol% to ε-caprolactone) was poured into the reactor. The reactor was sealed under high-purity (99.999%) N_2 gas and preswelling of PHCS with monomer was conducted overnight. Then the reactor was irradiation at pointed microwave power for a predetermined period of time. The obtained product (PHCS-g-polycaprolactone) was extracted with acetone in a Soxhlet apparatus for 24 h to remove the homopolymers. IR (KBr, cm^{-1}): ν3460 (OH), 3000–2800 (C–H), 1777 and 1716 (C=O anhydride and C=O ester), and 721 (aromatic ring).

2.2.3. Deprotection of the graft product

The phthaloyl-protected graft copolymer (1 g) was stirred in 20 ml of water and heated to 100 °C under nitrogen. Hydrazine monohydrate was added and the reaction was continued for 2 h to deprotect the phthaloyl group. The yellow solution was allowed to cool to room temperature in precipitate. Then the precipitate was collected, washed thoroughly with water and ethanol and dried to obtain the final product, chitosan-g-polycaprolactone. IR (KBr, cm^{-1}): ν3440 (OH and NH), 3000–2800 (C–H), 1725 (C=O ester), 1644 (N–H amide), and 1270–1150 (C–O ester).

2.2.4. Characterization

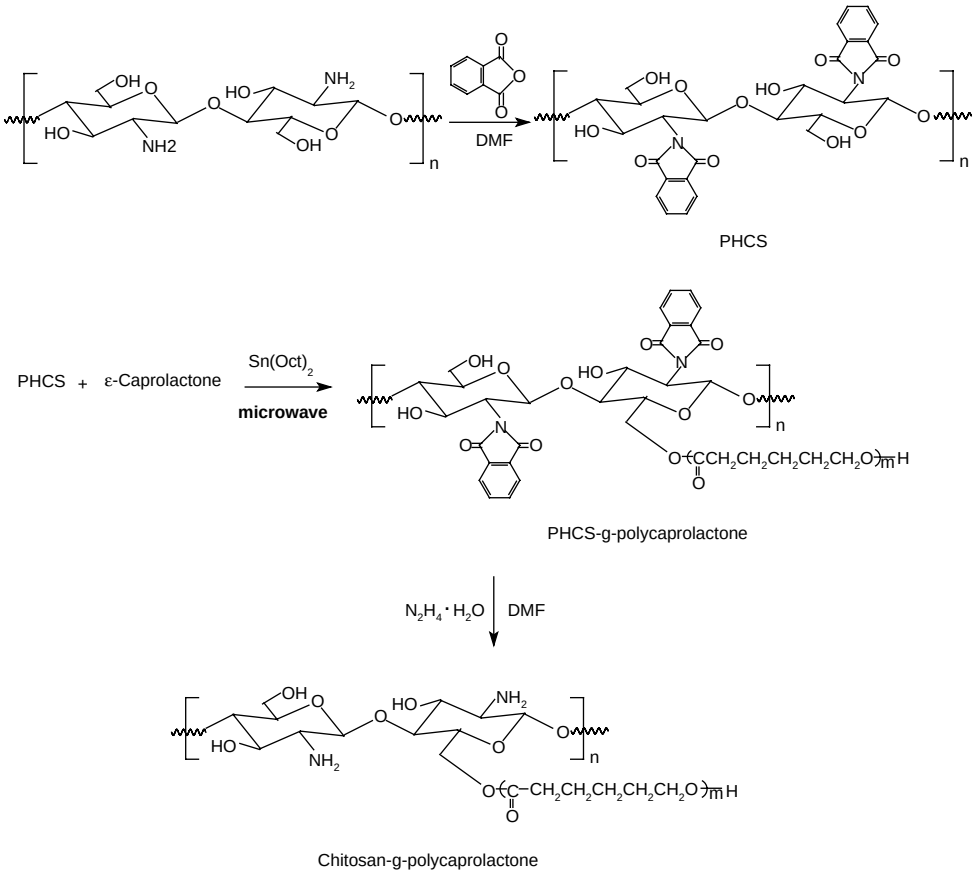
All infrared spectra were obtained from samples in KBr pellets using a Bruker EQUINOX 55 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were taken by a Bruker AV 400 spectrometer operating at 400.13 and 100.6 MHz, respectively, in D_2O/CF_3COOD 95:5 v/v. Elemental analyses were performed with an Elementar Vario EL-III elemental analyzer.

3. Results and discussion

3.1. Ring-opening graft polymerization of ε-caprolactone onto phthaloyl-protected chitosan by microwave irradiation

Preparation of graft copolymer was prepared according to the procedure shown in Scheme 1. To establish a method of preparing chitosan-g-polycaprolactone copolymer with the free amino groups, three-step reactions involving phthaloylation of chitosan, microwave-assisted graft copolymerization with ε-caprolactone and deprotection to regenerate amino groups were carried out carefully. The convenience of ring-opening polymerization of caprolactone by microwave radiation offers the possibility of an extension of the method to graft it onto PHCS (Fang et al., 2002; Liao et al., 2002), whose hydroxyl groups would be excellent candidates for initiating sites. Simultaneously, shortened reaction time was expected as well as comparative grafting percentage.

Fully deacetylated chitosan was first phthaloylated to protect the amino group. The introduction of bulk phthaloyl groups caused not only the destruction of crystalline structure of chitosan, but also the increasing hydrophobility. This will enhance the affinity between hydrophobic ε-caprolactone monomer and hydroxyl group of chitosan, and consequently promote the later graft copolymerization. Even now, it was a heterogeneous reaction in the beginning.



Scheme 1.

Microwave heating, which is totally different from conventional heating, was utilized here to favor the reaction more rapidly and efficiently. In order to make good use of the reactants in this rapid heterogeneous graft copolymerization, the soakage of PHCS with liquid ε-caprolactone monomer was achieved overnight in advance. The results of polymerization trials with varying the amounts of ε-caprolactone in feed were summarized in Table 1. Both the yield and the grafting percentage of polycaprolactone increased with the ε-caprolactone amount in the feed. And the graft copolymers having rather high grafting percentage of 120 and 232% were obtained (trials 4 and 5, respectively) when they were irradiated by microwave at 450 W for 15 min. Obviously, the graft copolymerization of ε-caprolactone onto PHCS was greatly accelerated and enhanced under microwave irradiation.

3.2. Characterization of chitosan-g-polycaprolactone

The products in different steps were all determined by FT-IR spectroscopy, as shown in Fig. 1. The results also suggested the whole protection-graft-deprotection procedure. After PHCS was treated with ε-caprolactone monomer under microwave irradiation, the PHCS-g-polycaprolactone showed stronger absorbance at 2800–3000 cm^{-1} for νC–H (of CH_2) in FT-IR spectrum, which implied significantly the successful graft copolymerization of ε-caprolactone onto PHCS. But it was not easy to discern the characteristic peaks of ester groups belonging to polycaprolactone branches, interfered with the strong absorption of carbonyl anhydride of phthalimido group. Then the raw grafting product was dealt with the deprotected reaction by incubation with hydrazine. The evidence that the characteristic absorption of phthalimido group at 1777, 1712 (carbonyl anhydride) and at 721 cm^{-1} (phenyl ring) disappeared confirmed the removal of the phthaloyl group. The IR spectra of the chitosan-g-polycaprolactone

Table 1
Synthesis of chitosan-g-polycaprolactone under microwave irradiation

Trial[a]	ε-Caprolactone (g)	Chitosan-g-polycaprolactone	
		Yield (g)	Grafting percentage[b] (wt%)
1	0.6	0.6	10.0
2	1.0	0.7	25.8
3	1.6	0.9	41.8
4	2.0	1.0	120
5	3.0	1.1	232

[a] Feed amount of PHCS, 1 g. Microwave irradiation, 450 W for 15 min.
[b] Grafting percentage of polycaprolactone = [(weight of introduced polycaprolactone branches)/(weight of chitosan main chain)] × 100, determined by ^{1}H NMR.

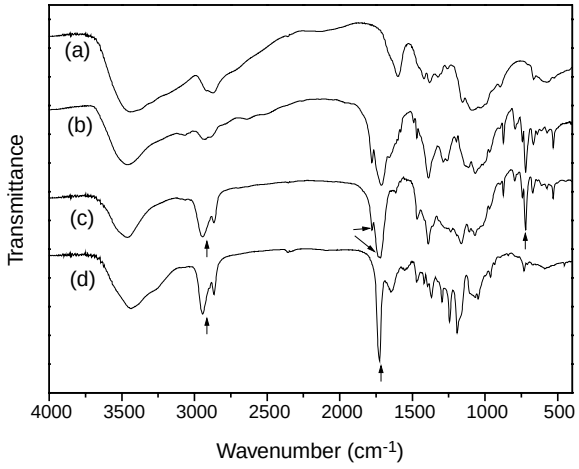


Fig. 1. IR spectra of chitosan (a), PHCS (b), PHCS-g-polycaprolactone before deprotection (c) and the final chitosan-g-polycaprolactone copolymer (d).

copolymer showed strong bands characteristic of ester group, particularly at 1725 and 1270–1150 cm^{-1}, and of methylene group, at 2800–3000 cm^{-1}, due to polycaprolactone side chain, and the characteristic amide N–H bending band of chitosan at 1640 cm^{-1}. On the other hand, the final chitosan-g-polycaprolactone could be solubilized in aqueous acid, which declared the regeneration of free amino groups. These facts exactly demonstrated the chemical structure of the graft copolymer of chitosan with free amino groups and polycaprolactone side chains.

To further confirm the chemical structure of chitosan-g-polycaprolactone, ^{1}H and ^{13}C NMR were also investigated. Fig. 2 showed a typical example of ^{1}H NMR of the final chitosan-g-polycaprolactone copolymer. Signals due to

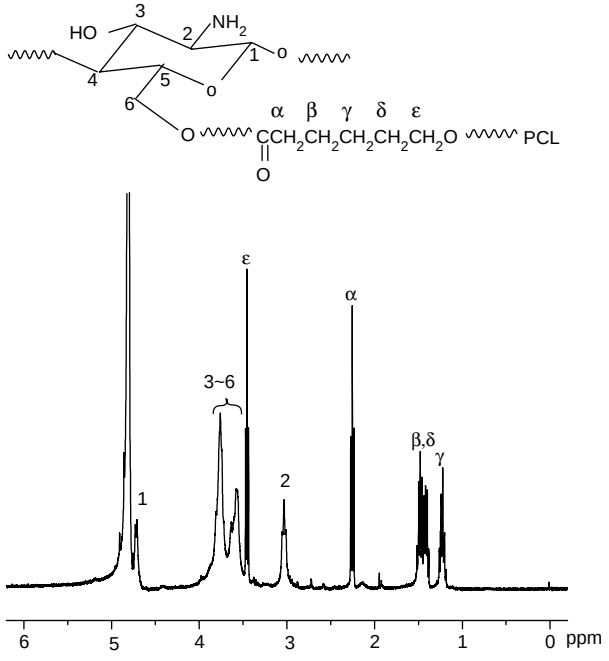


Fig. 2. ^{1}H NMR spectrum of chitosan-g-polycaprolactone.

Table 2
^{13}C NMR chemical shifts of chitosan-g-polycaprolactone

Type of carbon	Chemical shifts (ppm)
C-1	97.6
C-2	55.8
C-3	70.1
C-4	76.6
C-5	74.8
C-6	60.0
C-α	33.7
C-β	24.5
C-γ	24.0
C-δ	30.9
C-ε	61.6
C=O	179.0

the α-, β-, γ-, δ-, and ε-methylene protons to the carbonyl group of the grafted polycaprolactone were observed at 2.2, 1.4(β + δ), 1.2 and 3.4 ppm, respectively, while the proton signals of chitosan backbone were observed at 3.0 ppm for H_2, at 3.4–4.0 ppm for H_3–H_6 (overlapped with ε-methylene protons) and at 4.7 ppm for H_1 (overlapped with active proton of D_2O). On the basis of above results, the grafting percentage of polycaprolactone could be calculated by the signal intensities of six protons of β-, γ- and δ- due to polycaprolactone side chain and the single signal intensity of H_2 due to pyranose of chitosan backbone. The results of the peak assignment of ^{13}C NMR spectrum were summarized in Table 2. It also confirmed the success of the introduction of polycaprolactone branches onto chitosan.

3.3. Effect of microwave conditions on chitosan-g-caprolactone copolymer

To estimate the effect of microwave conditions on the graft copolymerization of ε-caprolactone onto PHCS, these experiments were carried out in two series with the feed ratio of ε-caprolactone monomer to PHCS of 1:1 (series I and 2:1 (series II)), respectively. Fig. 3 showed the grafting

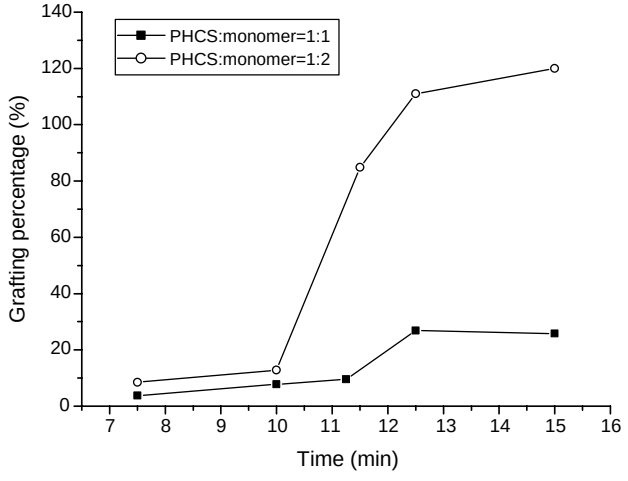


Fig. 3. Effect of microwave energy on grafting percentage of chitosan-g-polycaprolactone (450 W).

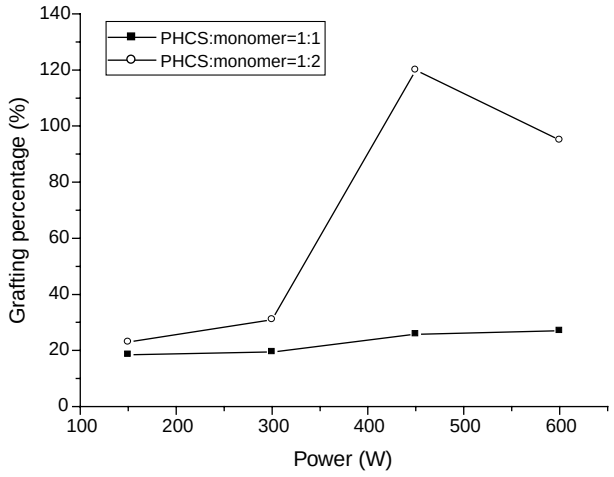


Fig. 4. Effect of irradiation power on grafting percentage of chitosan-g-polycaprolactone.

percentage of chitosan-g-polycaprolactone versus time plots with constant power output (450 W). It was found that the longer the microwave irradiation time, the higher the grafting percentage was. It reached nearly 27% in series I and above 100% in series II under microwave irradiation after about 12.5 min at 450 W. But when the irradiation time continued up to 15 min, obvious increase of the grafting percentage was observed no more.

Considering the constant microwave energy equal to 450 W for 15 min on the reactants, four different levels of microwave output power were examined and the results were displayed in Fig. 4. The grafting percentage of chitosan-g-polycaprolactone was measured as 19, 20, 26, 27% in series I; and 23, 38, 120, 95% in series II for 150, 300, 450, and 600 W, respectively. Dependence was found between the grafting percentage and power level especially in series II. When the power output was above 450 W, the graft copolymerization of polycaprolactone onto chitosan was greatly improved. Nevertheless, the microwave irradiation is a nonisothermal procedure though it is rapid. When the power of 450 and 600 W was applied, discoloration of the production was observed as a result of overheating.

4. Conclusions

The graft copolymerization of ε-caprolactone onto chitosan was successfully conducted by microwave irradiation, using phthaloylchitosan as intermediate. High grafting percentage of polycaprolactone was achieved in rather short time under microwave irradiation, compared to the conventional heating method. When the power output was above 450 W, the microwave graft polymerization of ε-caprolactone onto chitosan was greatly accelerated and improved. What's more, the phthaloyl group was introduced not only to protect the amino group but also to improve the hydrophobic nature of chitosan. The obtained chitosan-g-polycaprolactone, with large amount of free amino groups and hydrophobic polycaprolactone side chains, was anticipated as a degradable amphoteric material having wide potential applications in biomedical materials. Further work on its thermal properties, biodegradation behaviour and so on is in progress.

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