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Biodegradable Nanoporous Microspheres by RAFT Polymerization and UV Irradiation

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ABSTRACT

Nanoporous microspheres based on chitosan, polycaprolactone (PCL), polylactide (PLA) and photodegradable poly(methyl vinyl ketone) (PMVK) were synthesized and characterized. In this study, two types of porous microspheres were fabricated from graft copolymers of PMVK onto chitosan and biodegradable triblock copolymers from PCL, PLA, and PMVK. The synthesized block copolymers were characterized by FT-IR, 1H NMR spectroscopies. Gel permeation chromatography (GPC) was used to evaluate molecular weight and molecular weight distribution and monitor photodegradabilities of block copolymers. The morphology of microparticles before and after UV irradiation confirmed by SEM and TEM images showed that spherical microspheres before UV irradiation were changed to disk-shaped microparticles, owing to collapsing of PMVK moieties by UV irradiation.

1. INTRODUCTION

Chitin, a polysaccharide composed of β-(1→4)-2-acetamido-2-deoxy-D-glucose units, is the most abundant natural polymer. Chitosan (CS) is the derivative of chitin employed for N-deacetylation, which is not complete. CS has primary amine groups that have special properties and it makes CS helpful in medicine applications. It's physicochemical and biological properties such as adhesive, nontoxic, biocompatible, and biodegradable. These properties led to the recommendation as advanced materials especially in pharmaceutical and medical fields.

Microspheres composed of chitosan have many advantages including the control the release of active agents, ease of crosslinking due to free amine groups, and the increase of residual time at the site of absorption because of its mucoadhesive properties. (Aminabhavi 2004)

Poly vinyl ketones, photodegradable polymers decomposed by Norrish Type I, II reactions, have been used as packing materials and agricultural films, as well as

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special applications for imaging, microfabrication and sensing. (Sugita 1997, Burstyn 2004)

In this study, graft copolymerization of poly (methyl vinyl ketone) onto chitosan was conducted by free radical polymerization using potassium persulfate (KPS) or ceric ammonium nitrate (CAN) as an initiator and characterized by FT-IR and ^{1}H-NMR spectroscopies. (Chung, 2017) Nanoporous microspheres were fabricated by water-in-oil (W/O) emulsion method with glutaraldehyde (GA), followed by UV irradiation to obtain nanopores. In the synthesis of biodegradable triblock copolymers, ring opening polymerization of lactide was first conducted followed by RAFT polymerization of methyl vinyl ketone (MVK), and then used to fabricate microsphere by emulsion method. In order to polymerize by RAFT method, macro-CTA (chain transfer agent) was synthesized by reacting carboxylic acid-terminated CTA, S-1-dodecyl-S'-(α,α'-dimethyl-α''-acetic acid) trithiocarbonate (DDMAT) with hydroxyl terminated PLA-PCL-PLA triblock copolymer, and then used for the synthesis of block copolymer with methyl vinyl ketone (MVK).

2. Fabrication of microspheres

To a solution of purified chitosan (0.5 g) in 2% acetic acid, ceric ammonium nitrate (CAN) as an initiator in 1N nitric acid was added under nitrogen atmosphere for 30 min at 60°C. Purified MVK (27.3 mmol) prepurged with nitrogen gas was then added to the above mixture. The graft copolymerization was carried out for overnight at 60°C under nitrogen atmosphere. The resultant solution was precipitated in 10 wt % sodium hydroxide solution, extracted in acetone using soxhlet extraction apparatus, and finally dried under vacuum.Graft copolymers were dissolved in 4% acetic acid solution for overnight with a mechanical stirring at 1500 rpm, and liquid paraffin oil containing Tween 80 (1.5 v/v %) was added to above solution using syringe pump with dropping rate of 0.1ml/min. After crosslinked by glutaraldehyde, microspheres were separated by centrifugation at 4000 rpm for 10 min. The porous microspheres with rough surfaces were then prepared by ultraviolet irradiation, using UV cross linker under light at 312 nm for 3 h.

3. Characterizations

As shown in Figure 1, after photodegradation of PMVK contents in graft copolymers by UV irradiation, several characteristic peaks were observed at 2.25 ~ 2.8 and 5.96 ~ 6.23 ppm which were corresponding to methyl group bonded to new enol group and vinyl group, meaning that PMVK was photodegraded by Norrish II reaction mechanism at lower temperature.

The microspheres from chitosan and its graft copolymer were fabricated using emulsion crosslinking technique, and evaluated by SEM micrographs to compare the sizes and morphologies before and after UV irradiation. Figure 2(a) shows the SEM images of graft copolymer microspheres before UV irradiation whose size were approximately 5 μm having relatively smooth surfaces. However, as shown in Figure 2(b), those after UV irradiation for 3 h have shown rough surfaces, meaning that PMVK grafted onto chitosan was degraded by UV irradiation.

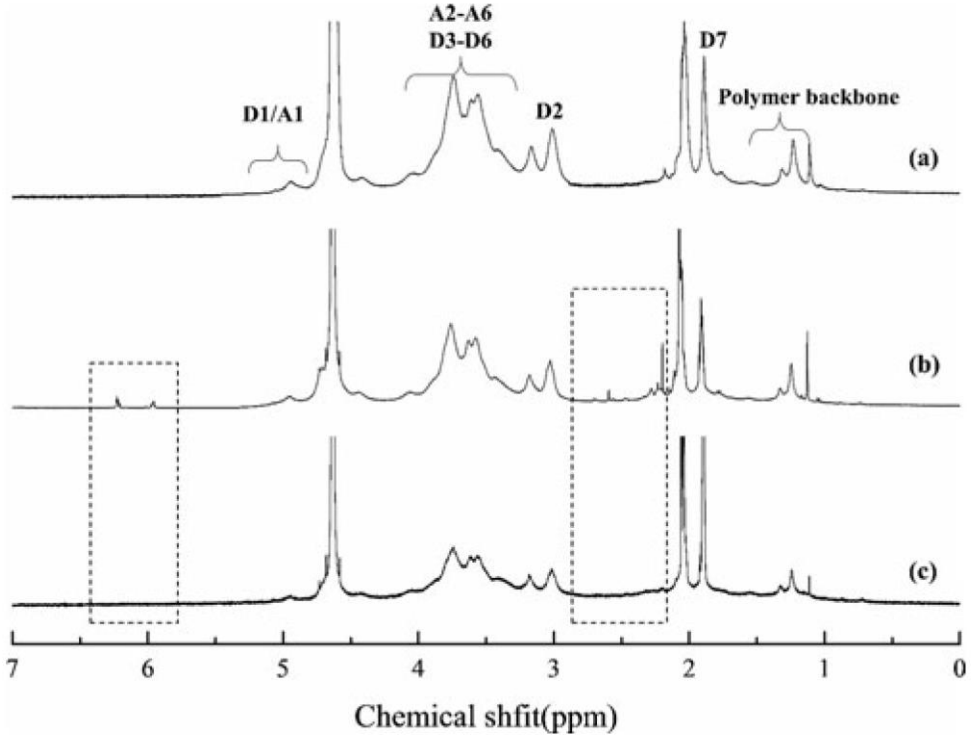
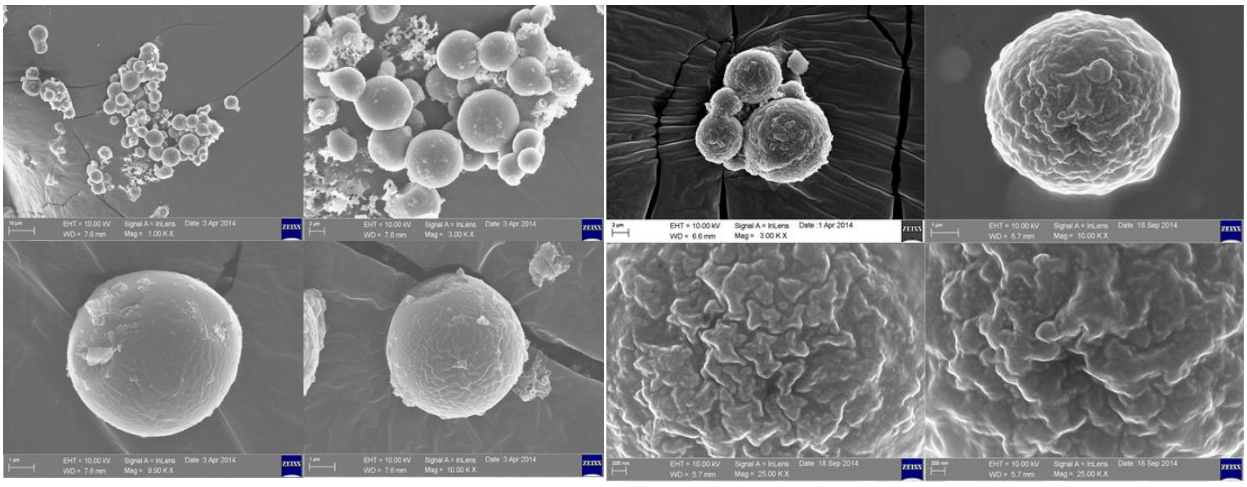


Figure 1. [1]HNMR spectra of (a) CS-g-PMVK, (b) CS-g-PMVK after UV irradiation for 1 h, and (c) Those after removed photodegraded by products.



(a) (b)

Figure 2. SEM images of CS-g-PMVK microspheres (a) before and (b) after UV irradiation. (Chung 2017)

4. Conclusion

Chitosan-graft-poly (methyl vinyl ketone) (CS-g-PMVK) as a matrix for controlled drug delivery system was successfully synthesized, characterized, and used to fabricate the microspheres by water-in-oil emulsion crosslinking method. Grafting yield percentage was confirmed to be 38.10% by thermal analysis, which means PMVK was grafted 38.10% per weight of chitosan. After UV irradiation, the microspheres had rough surfaces with the diameter of 5 μm.

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