Journal of Colloid and Interface Science 336 (2009) 235–243

Contents lists available at ScienceDirect

Journal of Colloid and Interface Science

www.elsevier.com/locate/jcis

A microfluidic approach to fabricate monodisperse hollow or porous poly(HEMA–MMA) microspheres using single emulsions as templates

Hao Zhang, Xiao-Jie Ju, Rui Xie, Chang-Jing Cheng, Ping-Wei Ren, Liang-Yin Chu *

School of Chemical Engineering, Sichuan University, Chengdu, Sichuan 610065, China

ARTICLE INFO

Article history:
Received 16 January 2009
Accepted 30 March 2009
Available online 5 April 2009

Keywords:
Microfluidic approach
Hollow microspheres
Porous microspheres
Poly(HEMA–MMA)
Monodisperse microspheres

ABSTRACT

We have successfully developed a novel and simple method to controllably prepare monodisperse poly(hydroxyethyl methacrylate–methyl methacrylate) (poly(HEMA–MMA)) microspheres with two distinct structures using single emulsions as templates. By employing a microfluidic emulsification approach to fabricate monomer-contained oil-in-water (O/W) emulsions as templates, and introducing proper initiators and different types of porogens, poly(HEMA–MMA) microspheres with hollow or porous structure are prepared in a controllable way. The shell thickness of hollow microspheres or the porosity of porous microspheres is controllably achieved by simply adjusting the porogen concentration. The prepared poly(HEMA–MMA) microspheres with controllable hollow or porous structures are favored for various potential applications. Furthermore, by using the simple preparation methodology proposed in this study, fabrication of monodisperse porous microspheres or hollow microcapsules with other materials can also be easily achieved.

1. Introduction

Poly(methyl methacrylate) (PMMA) particles have been reported to show slow biodegradability. The biodegradability can be improved through the copolymerization of MMA with 2-hydroxyethyl methacrylate (HEMA), which forms a more biodegradable polymer [1,2]. On the other hand, polymers based on HEMA attract great interest because of their biocompatibility. Therefore, poly(HEMA–MMA) copolymers have stimulated increasing interest and research attention in recent years due to their biocompatibility and water insolubility. Besides, the poly(HEMA–MMA) copolymers also have excellent chemical stability because of their three-dimensional polymeric networks [3]. All these favorable properties described above make poly(HEMA–MMA) microspheres extremely valuable for various applications in therapeutical and biotechnological fields [4–6], such as cell immobilization [4], drug delivery systems [7,8], packing materials in chromatography [9], and ophthalmology [10]. Hollow or porous structure and monodispersity are important and valuable for poly(HEMA–MMA) microspheres to improve their performance in their applications. For example, the hollow structure can increase the drug permeability from the microspheres in drug delivery [11,12], and the porous structure can significantly increase the specific surface area of poly(HEMA–MMA) microspheres for several potential applications such as the column packing materials in size exclusion chromatography [9]. Monodispersity is also very important for microspheres in various applications, especially in the field of drug delivery systems. Both the distribution of microspheres within the body and the interaction with biological cells are greatly affected by the particle size [13]. In addition, if monodisperse microspheres are available, the drug release kinetics can be manipulated, therefore making it easier to formulate more sophisticated drug release systems [14].

At present, poly(HEMA–MMA) hollow or porous microspheres are generally prepared by free radical suspension copolymerization by adding the porogen agent to form pores into the polymeric networks. However, it is difficult to control the monodispersity and adjust the morphology of the particles [15,16]. These limitations could be overcome by using other polymerization methods such as seeded emulsion polymerization [17], disperse polymerization [18], and the Shirasu porous glass (SPG) emulsification technique [19,20], which could prepare microspheres with perfect monodispersity and facile control of their morphology. However, the preparation processes and the following removal of porogen often involve complicated manipulations. In recent years, the appearance of microfluidic technology has simplified the preparation process of hollow or porous microspheres greatly. Researchers have applied microfluidic emulsification techniques to generate highly monodisperse emulsions and then combined with appropriate polymerization methods to synthesize microspheres using various materials [21–26]. For example, microspheres with various morphology and structures based on poly(*N*-isopropylacrylamide) [27–29], poly(tripropylene glycol diacrylate) [30], and some other

* Corresponding author. Fax: +86 28 8540 4976.
E-mail address: chuly@scu.edu.cn (L.-Y. Chu).

0021-9797/$ - see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.jcis.2009.03.070

multifunctional acrylates [31–36] have been successfully prepared by these technologies. However, there has been no report on fabricating monodisperse poly(HEMA–MMA) hollow or porous microspheres by a microfluidic approach up to now.

In the present work, we report a novel and simple method to controllably prepare monodisperse poly(HEMA–MMA) microspheres with two distinctly different structures (i.e., hollow and porous structures), in which a microfluidic device is introduced to fabricate monodisperse oil-in-water (O/W) emulsions as templates and UV-initiated free radical polymerization with different porogens is adopted to prepare the polymeric microspheres. The influences of types and concentrations of porogens on the morphology and pore structure of microspheres are characterized and investigated by optical microscopy and scanning electron microscopy (SEM). The prepared poly(HEMA–MMA) microspheres are featured with controllable hollow or porous structures.

2. Materials and methods

2.1. Materials

Methyl methacrylate (99.5%, Tianjin Bodi Chemical, China) and 2-hydroxyethyl methacrylate (99%, Tianjin Chemical Reagents, China) were analytical grade reagents and used as comonomers without further purification. Ethylene glycol dimethacrylate (EGDMA, Alfa Aesar) was used as crosslinker. Ammonium persulfate (APS, Shanghai Chemical Reagents, China) was used as water-soluble initiator and 2,2-dimethoxy-2-phenylacetophenone (BDK, Haining Paulyuan Dyestuffs, China) was used as oil-soluble initiator. Poly(vinyl alcohol) (PVA, M_w = 80,000 Da, 87–89% hydrolyzed, Chengdu Kelong Chemicals, China) was used as stabilizer, glycerol (Chengdu Kelong Chemicals) and polyglycerol polyricinoleate (PGPR 90, Danisco, Denmark) were used as thickener agent and surfactant, respectively. All of these chemicals were reagent grade and used without further purification. 1-Octanol (Chengdu Kelong Chemicals) was used as porogen to prepare hollow microspheres and poly(vinyl pyrrolidone) K30 (PVP K30, M_w = 30,000 Da, Shanghai Yuanju Biotech, China) was used as porogen to prepare porous microspheres. Deionized water (18.2 MΩ, 25 °C, Millipore, Milli-Q) was used throughout the experiments.

2.2. Fabrication of microfluidic flow-focusing device and O/W emulsions

The microfluidic flow-focusing device was fabricated by assembling borosilicate glass capillary tubes on glass slides [37,38]. The inner dimension of the square capillary tube (Vitrocom) was 1.0 mm. The cylindrical capillary had an inner diameter of 580 μm and an outer diameter of 1.0 mm. A micropuller (Narishige, Japan) was used to taper the end of the cylindrical capillary, and the orifice dimension of the tapered end was adjusted by a microforge (Narishige, Japan). The orifice diameter of the tapered end of the cylindrical capillary was 100 μm. The cylindrical capillary with a tapered end was inserted into the square capillary tube coaxially ensured by matching the outer diameter of the cylindrical tube to the inner dimension of the square one. A transparent epoxy resin was used to seal the tubes where required. The formation of O/W emulsions using flow-focusing within a microcapillary device is illustrated in Fig. 1. Two immiscible liquids were separately supplied to the microfluidic device through polyethylene tubing attached to syringes driven by syringe pumps (LSP01-1A, Baoding Longer Precision Pumps).

2.3. Preparation of poly(HEMA–MMA) hollow microspheres

Poly(HEMA–MMA) microspheres with hollow internal structures were prepared via the interface-initiated polymerization using 1-octanol as porogen, as illustrated in Fig. 1A (A1 → A3). The preparation recipe is given in Table 1. HEMA and MMA comonomers were mixed and served as the inner oil phase, which contained EGDMA, PGPR, and 1-octanol (oil phase 1). The aqueous solution containing PVA, glycerol, and APS was used as the outer continuous phase fluid (water phase 1). The oil and aqueous solutions were separately pumped into the microfluidic flow-focusing devices for preparing monodisperse O/W emulsions. The flow rates of the oil solution (Q_i) and aqueous solution (Q_o) were selected as Q_i = 200 μl/h and Q_o = 3000 μl/h, respectively. The prepared O/W emulsions were collected in a self-made cylindrical quartz vessel (6 cm in diameter and 9 cm in height) equipped with inlet and outlet for nitrogen gas, and then the system was bubbled with nitrogen gas to remove oxygen dissolved in the continuous phase. A 250-W UV lamp with an illuminance spectrum of 250–450 nm

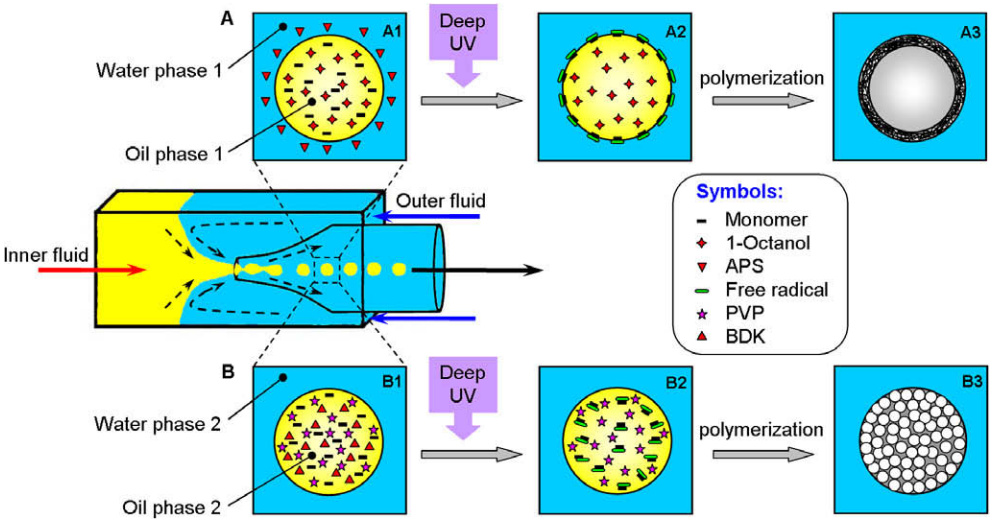

Fig. 1. Schematic illustration of the capillary microfluidic device and polymerization process for preparing monodisperse poly(HEMA–MMA) hollow (A: A1 → A3) and porous (B: B1 → B3) microspheres initiated at the interface of and inside the single emulsion droplet, respectively. "Water phase 1" is deionized water containing PVA, glycerol, and APS; and "Oil phase 1" is the mixed solution of HEMA and MMA containing EGDMA, PGPR, and 1-octanol. "Water phase 2" is deionized water containing PVA and glycerol; and "Oil phase 2" is the mixed solution of HEMA and MMA containing EGDMA, PGPR, PVP, and BDK.