Hydrophobic Functionalization of Mesoporous SBA-15 with Polyisoprene as a New Drug Delivery System

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A novel delivery carrier system has been successfully conducted based on the ordered mesoporous silica SBA-15 with hydrophobic polyisoprene polymerized in the pores network. It is interesting to find that the result system still holds a relatively large pore size (6.5 nm) and pore volume (0.72 $cm^3\,g^{-1}$), which will benefit for the storage of drugs with relatively large molecules.

Over the past decade, there has been rapid growth in the fabrication of drug delivery systems because of their promise application in health care products.[1] Both organic and inorganic matrices had been investigated in various delivery process.[2,3] Self-ordered mesoporous silica materials with highly ordered pore structure and narrow pore size distribution, large surface area, and pore volume enable it to be an ideal host to construct new drug delivery systems.[4] Maria et al. had modified the surface of the pore wall of SBA-15 with octyltrimethoxysilane and octadecyltrimethoxysilane to obtain a delivery system.[5] Sousa and his co-workers had demonstrated a hybrid biological-inorganic material prepared by filling a mesoporous silica structure with collagen.[6] Until now, to the best of our knowledge, a little research had been directed to fabricate hydrophobic polymer inside SBA-15 channels as carrier system for the delivery of the oil soluble drugs.

In this paper, we report a nanocomposite delivery based on mesoporous silica SBA-15 with hydrophobic polyisoprene coating in the pore channels. How to introduce polyisoprene (PI) formed inside the mesopores is the key point, because of the easy effumability of the monomer isoprene. Here, we develop a facile method to conduct free-radical polymerization of isoprene inside SBA-15 in toluene solution and prepared successfully the delivery system of SBA–PI. It is interesting to find that the result system still hold a relatively large pore size of about 6.5 nm and high pore volume of 0.72 $cm^3\,g^{-1}$, which will benefit it for drug storage with relatively large molecules. For the lipophilic effect of PI, there are about 31 wt % (IBU/silica) drug ibuprofen was capsulated in the SBA–PI channels.

The mesoporous material SBA-15 was prepared according the report by Zhao, through sol–gel process under acid condition.[7] The delivery system was prepared as below: First, 0.2 g of SBA-15, 1.0 g of isoprene, and 0.02 g of free radical initiator azoisobutyronitrile was added into 2 mL of toluene at ambient temperature, and then PI nanocasting SBA-15 (SBA–PI) can be obtained via in situ free-radical polymerization by increase the temperature to 80 °C under nitrogen. The loading of drug ibuprofen (Aldrich) inside the samples SBA–PI were carried out as follow process: 0.3 g of the samples was added to 20 mL of ibuprofen–hexane solution (35 mg mL^{-1}) and soaked under stirring at 40 °C for 48 h, the powder thus obtained was designated as SBA–PI–IBU.

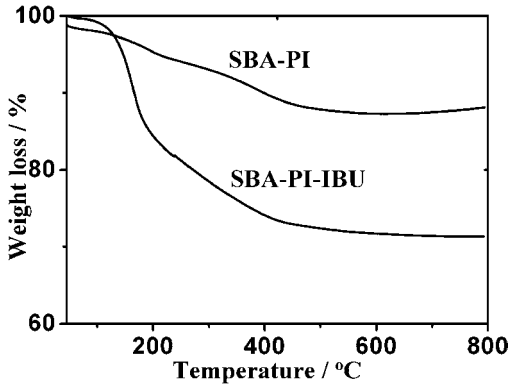

Figure 1. TGA curves of the samples SBA–PI and SBA–PI–IBU.

FT-IR is known to provide surface information of materials for identification of chemical groups. The delivery system SBA–PI was obtained after polymerization of PI in the channels of SBA-15, as evidenced by IR bands at 1357, 1454, and 1645 cm^{-1} for the $-CH_3$, $-CH_2-$, and C=C groups, characteristic of the presence of PI in SBA–PI (not shown). Further characteristics of thermogravimetric analysis (TGA) of the sample SBA–PI indicates a weight loss of 11 wt % when SBA–PI were heated up to 800 °C in nitrogen (Figure 1).

XRD patterns of the samples SBA-15, SBA–PI, and SBA–PI–IBU were compared in Figure 2. For the sample SBA-15 and SBA–PI, a well-resolved peak together with two small peaks

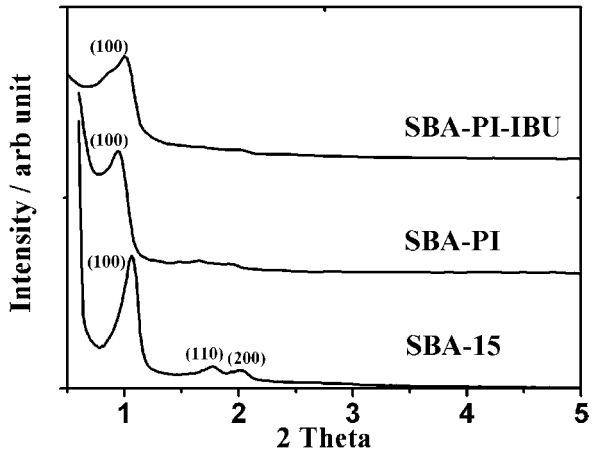

Figure 2. Low-angle powder XRD patterns for the samples SBA-15, SBA–PI, and SBA–PI–IBU.

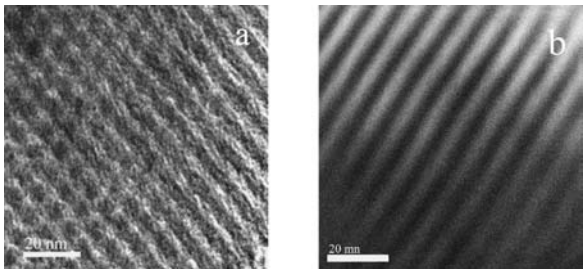

Figure 3. TEM images of the sample SBA–PI–IBU: perpendicular to and along the direction of the hexagonal pore arrangement.

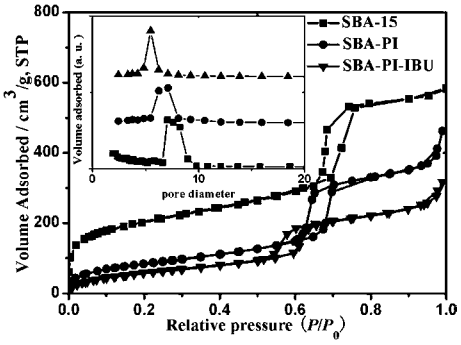

Figure 4. Nitrogen adsorption/desorption isotherms of the samples SBA-15, SBA–PI, and SBA–PI–IBU; (inset) pore size distributions of the samples.

can be indexed as the diffraction planes (100), (110), and (200) due to the hexagonal array the SBA-15 mesoporous networks, indicating that well-ordered mesoporous structures have not been disturbed after polymerization of PI inside SBA-15 channels. The only reflection of (100) of sample SBA–PI–IBU was retained, which indicates that IBU storage did not result in the damage of the ordered hexagonal structure. The slight shift of the diffraction peaks to lower angle and the decrease of intensity was owing to introducing polymers and loading IBU drugs inside the pores as described by others.[8] The ordered porous structure is maintained for SBA–PI–IBU shown in Figure 3, illustrating that the uniform polymerization was achieved throughout the porous network.

Shown in Figure 4 is N_2 adsorption/desorption isotherms of the samples SBA-15, SBA–PI, and SBA–PI–IBU. Both samples yielded type IV isotherms with a H1 hysteresis loop, which are typical for mesoporous materials with two-dimensional structures.[7] Pore volume, pore size, and Brunauer–Emmett–Teller (BET) surface area data are summarized in Table 1. Compared with SBA-15, the surface area of the sample SBA–PI was observed reduce from 643 to 312 $m^2 g^{-1}$, attributing to the formation of PI nanocasting inside the mesopores. The pore volume of SBA–PI decreased from 0.81 to 0.72 $cm^3 g^{-1}$ further confirmed the conclusion. It is worth to mention that the delivery system hold an average pore sizes of 6.5 nm and 0.72 $cm^3 g^{-1}$ pore volume even though 11 wt % PI formed inside the pores, which may be superior for loading drugs with large molecular weights. The wall thickness of SBA–PI can be calculated as 3.8 nm, which is 1-nm thicker than that of the sample SBA-15, which reveals that a 1-nm coating layers of PI had been formed inside mesopores of SBA-15.

Table 1. Textural parameters of various samples

Sample	SBET/$m^2 g^{-1}$	Pore size/nm	V_p/$cm^3 g^{-1}$
SBA-15	643	6.8	0.81
SBA–PI	312	6.5	0.72
SBA–PI–IBU	227	5.4	0.49

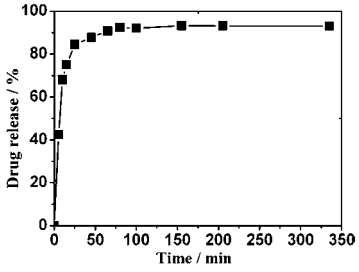

Figure 5. The IBU-release curve of SBA–PI mesoporous system in phosphate buffer (pH = 7.4).

Control of drug release through the porous network was demonstrated by measuring uptake and release of ibuprofen (IBU, an analgesia and anti-inflammatory drug) in Phosphate buffer (pH = 7.4) at 37 °C as measured by UV–vis. The amount of drug adsorbed was monitored by UV spectroscopy and TGA which shows that about 31 wt % (IBU/silica) drug ibuprofen was anchored in the SBA–PI channels. The cumulative percentage release of IBU from SBA–PI was depicted in Figure 5. It was observed that IBU-loaded SBA–PI had a burst release and an initial release of about 68% during the first 10 min. The total cumulative percentage release amount is up to 93% in 80 min.

In summary, a novel delivery carrier system has been successfully conducted based on the ordered mesoporous silica SBA-15 with hydrophobic polyisoprene coating inside the pores. It is interesting to find that the result system still hold a relatively large pore size (6.5 nm) and pore volume (0.72 $cm^3 g^{-1}$), which will benefit for drug storage with relatively large molecules, such as therapeutic protein, and gene regulating medicines. The aim of our work is to explore a new drug carrier systems based on highly ordered meoporous silica for potential applications in many aspects of bio/life sciences.

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References

1 S.-W. Song, K. Hidajat, S. Kawi, *Langmuir* **2005**, *21*, 9568.
2 N. Nasongkla, X. Shuai, H. Ai, *Angew. Chem., Int. Ed.* **2004**, *43*, 6323.
3 Q. Yang, S. Wang, P. Fan, L. Wang, Y. Di, K. Lin, F. Xiao, *Chem. Mater.* **2005**, *17*, 5999.
4 D. Zhao, Q. Huo, J. Feng, B. F. Chmelka, G. D. Stucky, *J. Am. Chem. Soc.* **1998**, *120*, 6024.
5 C. D. Juan, M. B. S. Edesia, I.-B. Isabel, L. D. Antonio, P.-P. Joaquin, V.-R. Maria, *J. Mater. Chem.* **2006**, *16*, 462.
6 L. B. Fagundes, T. G. F. Sousa, A. Sousa, V. V. Silva, E. M. B. Sousa, *J. Non-Cryst. Solids* **2006**, *352*, 3496.
7 D. Zhao, J. Feng, Q. Huo, N. Melosh, G. H. Frdrickson, B. F. Chmelka, G. D. Stuck, *Science* **1998**, *279*, 548.
8 J. Sauer, F. Marlow, F. Schüth, *Phys. Chem. Chem. Phys.* **2001**, *3*, 5579.

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