Incorporation of Ibuprofen into SBA-15; Drug Loading and Release Properties

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ABSTRACT

The development of mesoporous materials like SBA-15 offers new possibilities for incorporating biological agents into silica structures and controlling the release kinetics from the matrix due to its well-arranged pore architecture. These materials show significant mesoporosity associated with their hexagonally organized channels, narrow pore size distribution, and large surface area. Ibuprofen was selected as a model molecule since it is a well-documented and highly used anti-inflammatory drug. Furthermore, its molecular size (about 1.0 nm) is suitable for incorporation into the mesopores of the SBA-15 material (pore size is 4.6-10 nm). Mesoporous silica SBA-15 was prepared to evaluate its application as a carrier for Ibuprofen drug delivery. The loaded SBA-15 was characterized by thermo gravimeter analysis, X-ray diffraction, scanning electron microscopy, and N2 adsorption/desorption isotherm. The incorporation procedure resulted in a significant improvement of the amount of Ibuprofen loaded into SBA-15, and in vitro drug release was investigated.

Keywords: drug release, mesopores, model drug, UV-Vis
Abbreviations: SBA-15, Santa Barbara arrays-15; SEM, scanning electron microscopy; TGA, thermo gravimeter analysis; XRD, X-ray diffraction

INTRODUCTION

The discovery of silica-based mesoporous materials, in 1992, has attracted vast interest permitting extension of the potential applications of the host–guest system (Beck et al. 1992; Kresge et al. 1992). These applications include a wide range of subjects, from catalysis to controlled drug delivery. In fact, mesoporous materials comprise a new generation of materials that built up from SiO2 unities. The pore architecture of SBA-15 makes it a suitable desilication system, by the absorbance band at 264 nm. We chose Ibuprofen as the model drug because of its suitable molecule size (about 1.0 nm), which warrants its incorporation into SBA-15 channels.

The aims of this work were to compare different methods for incorporation of Ibuprofen into SBA-15 and then investigate Ibuprofen release from the surface of the mesopore.

MATERIALS AND METHODS

Materials

Tetraethyl orthosilicate (TEOS, 98%), hydrogen chloride (HCl, 37%) and acetone 99% were purchased from Merck (Darmstadt, Germany) with a purity greater than 99.9%. Surfactant pluronic P123 (EO20-PO70-EO20) and Ibuprofen were obtained from Sigma-Aldrich Co. (St. Louis, USA). All other chemicals and solvents were of analytical grade.

Synthesis of SBA-15

Mesoporous SBA-15 was synthesized by a standard method (Zhao et al. 1998). 4 g of an amphiphilic triblock copolymer, P123 (as a template) was dispersed in 30 g of water and stirred for 4 h and then 120 g of 2 M HCl solution was added and stirred for 2 h. Then 8.54 g of TEOS was added to the homogeneous solution under stirring at 100 rpm during 20 min. The resulting gel was aged at 40°C for 24 h and finally heated to 100°C for 48 h. After synthesis, the solid was filtered, washed with distilled water and dried at room temperature and followed by calcination at 600°C to decompose the template.

Drug loading on SBA-15

The model drug Ibuprofen was used to evaluate the performance of SBA-15 as a hosting system. Two procedures were used to charge the material with Ibuprofen. In method 1 the drug was dissolved in hexane (33 mg/mL) and the synthesized SBA-15 was added (33 mg/mL of hexane), stirred for 24 h while preventing the
evaporation of hexane (I-SBA-1). The amount of absorbed Ibuprofen was determined by thermogravimetry, resulting in 30% in weight with respect to the starting material.

In method 2 the synthesized SBA-15 was soaked in a solution of Ibuprofen in hexane (33 mg/mL) and stirred until the solvent evaporated entirely. 100% of the drug was absorbed in and out of SBA-15 channels surface (I-SBA-2).

On the basis of the suggested method for dissolution studies on Ibuprofen tablets in The United States Pharmacopeia, the Ibuprofen release profile was achieved by soaking SBA-15 disks in 700 mL of potassium monobasic phosphate buffer (pH 7.2). This buffer was used as a simulated body fluid (SBF). The temperature was fixed at 37°C and the solutions were continually stirred at 100 rpm during test. A UV-1700 Shimadzu UV spectrophotometer was used to monitor the amount of drug released as a function of time. The amount of drug was found from the intensity of the absorption bands at 226 nm.

Several instrumental techniques were used for sample characterization. Thermogravimetry analysis (TGA) was carried out using a Perkin-Elmer Pyris Diamond TG analyzer.

Small angle XRD patterns were recorded on a Philips X'Pert multipurpose diffractometer. The diffractograms were recorded over the range 0.5–10.0° (2θ) with a step size of 0.02° and an accumulation time of 5 s.

Surface area and porosity were determined from nitrogen adsorption–desorption isotherms obtained on a BELSORP mini II analyzer.

Particle morphology was analyzed by scanning electron microscopy (SEM) using a Leo 1455VP.

RESULTS AND DISCUSSION

Synthesized SBA-15 samples before and after drug loading were characterized by XRD. Synthesized SBA-15 showed the characteristic reflection peaks at 0.8, 1.6 and 1.7 indicating the formation of hexagonal structure. The drug loaded samples, I-SBA-1 and I-SBA-2, exhibit a similar pattern to that observed for pure SBA-15. However loading SBA-15 with Ibuprofen decreased the intensities of the peaks.

The surface morphology of SBA-15 particles is shown in Fig. 1. SBA-15 material is observed to contain length hair-like material arranged in a bundle of diameter of ~2 µm and length of 30–50 µm. Drug-loaded samples (I-SBA-1, I-SBA-2) showed a similar morphology. There was no significant change due to drug loading.

Fig. 1 shows N2 adsorption/desorption isotherms and pore size distribution of synthesized samples, SBA-15, I-SBA-1 and I-SBA-2 and their structural parameters are presented in Table 1.

SBA-15 and I-SBA-1, unlike I-SBA-2, show a very similar type IV isotherm with the similar hysteresis loop at P/P0 of 0.6 to 0.8; however, in saturated pressure, the ad- 

<table>
<thead>
<tr>
<th>Sample</th>
<th>S BET (m²/g)</th>
<th>V p (cm³/g)</th>
<th>D (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBA-15</td>
<td>788</td>
<td>1.17</td>
<td>7.1</td>
</tr>
<tr>
<td>I-SBA-1</td>
<td>311</td>
<td>0.76</td>
<td>6.2</td>
</tr>
<tr>
<td>I-SBA-2</td>
<td>19</td>
<td>0.19</td>
<td>6.2</td>
</tr>
</tbody>
</table>

Table 1 Structure parameters of SBA-15 and drug loaded samples.

The dissolution rate of Ibuprofen released from the surface of I-SBA-2 was significantly faster than from I-SBA-1 because in I-SBA-2 drug molecules are probably connected to the outer surface mostly; then it can release Ibuprofen easily compared with the attachment of method 1.

CONCLUSIONS

The release behavior of drug-loaded SBA-15 according to two different methods was studied and compared. 30 and 100% of the drug, Ibuprofen, was loaded in method 1 and 2, respectively. In method 1, Ibuprofen was incorporated into SBA-15 pores so that 90% of the loaded drug was released in 96 hrs. In method 2 drugs were connected to the outer surface of SBA-15, so that the application of this method for drug loading occasioned an increase of release rate in I-

Fig. 1 (A) N 2 adsorption/desorption isotherms and (B) pore size distribution of SBA-15 (●), I-SBA-1 (▲) and I-SBA-2 (●).
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SBA-2 so that 90% of the loaded drug was released in 27 hrs. The application of method 2 can increase the release rate of drugs from the surface of mesoporous materials.

ACKNOWLEDGEMENT

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REFERENCES


**Table 2** Comparison of drug release rate from surface of I-SBA-1 and I-SBA-2.

<table>
<thead>
<tr>
<th>Sample</th>
<th>50% release</th>
<th>75% release</th>
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<tbody>
<tr>
<td>I-SBA-1</td>
<td>20 hour</td>
<td>45 hour</td>
</tr>
<tr>
<td>I-SBA-2</td>
<td>2 hour</td>
<td>4.5 hour</td>
</tr>
</tbody>
</table>

**Fig. 2** Ibuprofen % release from I-SBA-1 (A) and I-SBA-2 (B).