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

Alireza Badiei[1*] • Ismayil Haririan[2] • Ali Jahangir[1] • Ghodsi Mohammadi Ziarani[3]

[1] School of Chemistry, College of Science, University of Tehran, Tehran, Iran
[2] Department of Pharmaceutics, Faculty of Pharmacy, University of Tehran, Tehran, Iran
[3] Department of Chemistry, Alzahra University, Tehran, Iran

Corresponding author: * **abadiei@khayam.ut.ac.ir**

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 N_2 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 SiO_2 unities. The pore size is changeable (pore diameter, d: 2 nm < d < 50 nm) and can be controlled and modified (Attard *et al*. 1995). The surface of pore walls of mesopores materials have a high concentration of silanol groups, absorption properties can be modified with functionalization of surface with different chemical species. Taking into account these features, the behavior of mesopores as drug delivery systems has been developed since 2001 (Regi *et al*. 2001) and is based on the ability of these materials to absorb pharmacological molecules.

A well-known example of mesoporous materials is the 2D-hexagonal SBA-15. SBA-15 pore size is around 2 nm that presents a large surface area, large pore size, and thick walls. The thickness of walls gives it improved thermal and mechanical stability compared to other mesoporous materials. Pore architecture of SBA-15 makes it a suitable delivery candidate for a variety of pharmaceutical molecules.

Ibuprofen is a well-documented and highly used anti-inflammatory drug (Han *et al*. 1999; Murata *et al*. 2000; Yiu *et al*. 2001; Fan *et al*. 2003) that contains one carboxylic acid group, which can form strong bonding with many functional groups. Also, it is a well-characterized drug, which can be monitored by use of UV–Vis spectroscopy, 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

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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 band 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 N_2 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-1, show a very similar type IV isotherm with the similar hysteresis loop at P/P_0 of 0.6 to 0.8; however, in saturated pressure, the adsorbed amount decreased after Ibuprofen adsorption and it may be obtained by the incorporation of the drug in pores. Note that the form of isotherms of these two samples SBA-15 and I-SBA-1 did not change significantly by incorporation of the drug. Furthermore, SBA-15 and I-SBA-1, unlike I-SBA-2, show a narrow and similar pore size distribution; however, the pore diameter decreased after drug adsorption and it may be attributed to the incorporation of drug molecules.

The diverse observed properties of I-SBA-2 may be attributed to the diverse occupation of pores with drug molecules. In N_2 adsorption/desorption isotherm of this sample, I-SBA-2, there is no hysteresis, and pore size distribution shows a very wide peak. As a result, these observations can indicate that drug molecules fill the pores of SBA-15 completely.

As seen in **Table 1**, the nitrogen sorption isotherm for the drug loaded samples, I-SBA-1 and I-SBA-2, showed a great decrease in V_P and S_{BET} compared with pure SBA-15, in such a manner that the surface area dropped to 311 m^2/g and 19 and pore volume decreased to 0.76 and 0.19 cm^3/g, respectively. This was due to the occupation of pores by Ibuprofen. This reduction in V_p was more in the I-SBA-2 sample. However, the average pore diameter (D_{BET}) of I-SBA-1 and I-SBA-2 increased equally. This reduction in V_p and equality in D_{BET} probably resulted from incorporation of Ibuprofen on the outer surface of SBA-15 in the I-SBA-2 sample.

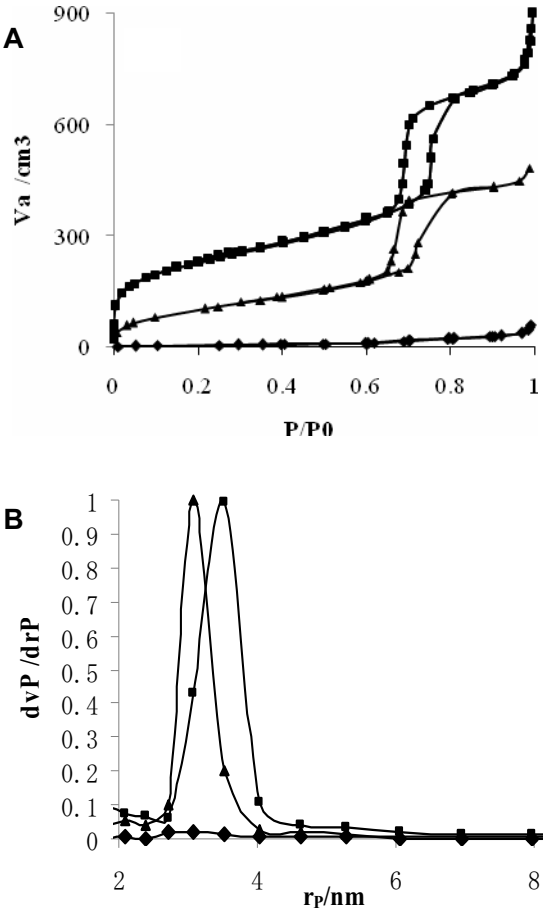

Fig. 1 (**A**) N_2 adsorption/desorption isotherms and (**B**) pore size distribution of SBA-15 (■), I-SBA-1 (▲) and I-SBA-2 (♦).

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

Sample	S_{BET} (m^2/g)	V_p (cm^3/g)	D (nm)
SBA-15	788	1.17	7.1
I-SBA-1	311	0.76	6.2
I-SBA-2	19	0.19	6.2

Drug release

Fig. 2 shows the percentage of drug release as a function of time (hour) for the loaded samples with Ibuprofen according to methods 1 (left) and 2 (right). The period of time that passed for release of 50 and 75% of Ibuprofen from I-SBA-1 and I-SBA-2 are presented in **Table 2**.

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-

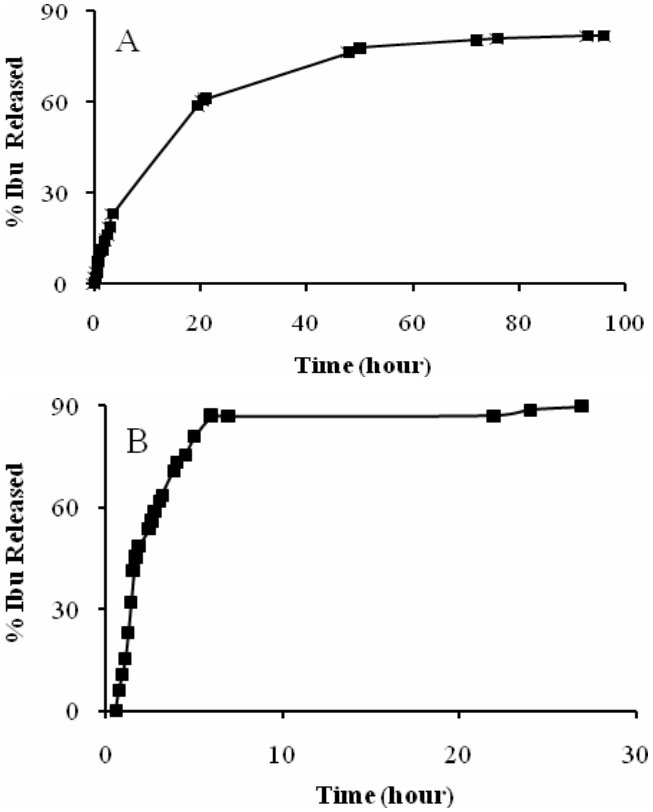

Fig. 2 Ibuprofen % release from I-SBA-1 (**A**) and I-SBA-2 (**B**).

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

Sample	50% release	75% release
I-SBA-1	20 hour	45 hour
I-SBA-2	2 hour	4.5 hour

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.

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