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On the drug adsorption capacity of SBA-15 obtained from various detemplation protocols

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ABSTRACT

The effect of the mild detemplation method, based on Fenton chemistry (with and without previous solvent extraction), and calcination was evaluated by the drug uptake capacity of SBA-15 materials. A number of characterization techniques were applied for evaluation and comparison of the materials properties such as TGA, CNH, N_2 physisorption and ^{29}Si NMR. The mild Fenton detemplation method rendered a nearly pristine SBA-15 without structural shrinkage, low residual template, improved surface area, pore volume and silanol concentration. The drug (ibuprofen) adsorption experiments were carried out by solution immersion in powdery form. The mild detemplated samples experienced an enhanced uptake that could be explained by the enhanced density of silanols (mmol/g), originated from the absence of calcination in the Fenton approaches.

1. Introduction

Organized mesoporous materials (OMMs) have found a wide range of applications such as separation, optical, adsorption and heterogeneous catalysts [1–5]. OMMs are especially known for their regular pore network and high pore volumes with the possibility of combining micro- and mesopores. These materials are synthesized by hydrothermal treatment in the presence of a structure-directing agent, also called template, around which the inorganic framework is formed [6]. The template is usually an organic compound, which determines the pore topology by filling the pore space and maintaining a close geometrical correspondence with the inorganic framework.

The use of mesoporous materials as drug delivery carriers was first introduced by Vallet-Regi et al. [7]. Their potential application as drug carriers is due to their biological stability and their well-defined structure, porosity and chemical homogeneity. This represents an advantage compared to many other host materials normally used for drug delivery applications.

In several studies [8,9], it has been demonstrated that the inclusion of poorly water-soluble drugs into the pores of a mesoporous silica improves the drug's solubility rate. When a drug is adsorbed into the pores of the silica material, it is present in the molecular/amorphous state and this form provides faster dissolution rates than the crystalline phase, especially when the solubility is limited by the crystal energy [10].

A number of aspects related to the host-guest chemistry influence the maximum drug uptake and release [11–14]. These aspects comprise the nature of the drug (the drug must have certain organic functional groups which allow the formation of hydrogen bonds with the silanol groups of the hosting material), surface's nature (concentration of silanol groups and surface functionalization), effect of the solvent as well as the silica pore size distribution and pore volume.

SBA-15 is an attractive mesoporous material since it possesses a high pore volume, wide pores and a relatively low-cost template is employed in the synthesis [15–17]. The major problem with SBA-15 as drug carrier is the relatively weak intermolecular hydrogen bonds with the drug; thus the drug uptake is relatively limited despite its large pore volume. Typically 15 wt% of ibuprofen has been reported, that is relatively low as compared to MCM-41 with uptakes up to 30 wt%. Surface functionalization can enhance the drug uptake; Song et al. [18] found that ibuprofen uptake can be enhanced significantly after post-synthesis amination, with uptakes of 20–37 wt%. This is due to the stronger host–guest interaction of ($-NH_3^+ \ldots -OOC-$) than a hydrogen bond between the silanol group of the silica and the carboxyl group of the ibuprofen. Native and modified SBA-15 have been also successfully applied to the adsorption of heparin, a highly sulphated linear polysaccharide, that mediates a range of

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biological and physiological activities such as anticoagulation, vascular regeneration, antiviral activity and release of lipoprotein lipase and hepatic lipase [19,20].

The surface properties of the SBA-15 silica can be adjusted by the detemplation method as well. By detemplation we mean the step where the organic agent has to be removed from the cavities of the solid in order to develop the porosity after synthesis. The conventional detemplation method is calcination at high temperature in air atmosphere. The high temperatures usually applied, around 550 °C, combined with the steam formed during template removal provoke a partial collapse of the structure with the formation of siloxane bonds at the expense of losing silanols. This means that removing the template at lower temperatures, or chemically without heat, is highly desirable in order to obtain larger pore volumes and a higher density of surface silanols.

In this communication, we have investigated the effect of various detemplation methods on the final ibuprofen uptake. In particular we have employed a method using $OH^{\bullet}$ radicals that are generated from H_2O_2 and catalyzed by discrete amounts of Fe cations (Fenton chemistry), that was reported to remove the template of zeolite beta [21,22] and MCM-41 [23]. It was found that this method enhances the drug uptake of SBA-15 by 50% with respect to the calcined material; the effect is ascribed to the increase of surface area and concentration of silanols.

2. Experimental

Synthesis: The SBA-15 mesophase was synthesized according to the procedure followed by Zhao et al. [15,16]. The gel composition was: 4.0 g of P-123; 120.0 g of 2.0 M HCl; 30.0 g of H_2O; 8.5 g of TEOS. The resulting slurry was aged at 105 °C for 24 h and dried at 110 °C overnight.

Detemplation protocols: Calcination was carried out at 550 °C for 5 h in air. The heating rate to reach this temperature was 1 °C/min. The resulting material was termed CA. Solvent extraction was carried out on the mesophase in absolute ethanol (Aldrich, ≥99.5%) under reflux (78 °C) for 24 h using a ratio of 75 ml/g. The resulting material was dried in a vacuum oven at 110 °C (SE). The Fenton detemplation protocol consisted of the following steps. In a typical experiment, 1.0 g of as-synthesized precursor, or SE material, was mixed with 25 ml of water and 25 mg of iron nitrate, $Fe(NO_3)_3{\bullet}9H_2O$ (≥98%, Riedel-de Haën). This mixture was placed in an oil bath at 70 °C. Then 50 ml of hydrogen peroxide (commercial grade 30 wt%, Merck) were added; part of the H_2O_2 (10 ml) is added at the start of the experiment, which gives an initial concentration of 8.6 wt% H_2O_2. The remaining is added at a rate of 48 ml/h. The reaction took about 7 h. After that, the sample was separated by filtration and dried at 110 °C (denoted by F). A similar protocol was applied to a solvent extracted mesophase (denoted by SE-F).

Drug uptake experiments: Ibuprofen ((RS)-2-(4-(2-methylpropyl)phenyl)propanoic acid, Sigma Aldrich, ≥98% GC) was dissolved in hexane (33 mg ibuprofen/ml hexane) and the host material was suspended in a ratio of 33 mg SBA-15/mL hexane. The mixture was sealed and stirred for 24 h at room temperature. The ibuprofen-loaded material was then filtered using a glass filter of porosity 3 and dried at 60 °C under vacuum. The amount of adsorbed drug was determined by TGA and UV–vis as discussed below.

Characterization methods: The template content was quantified by CHN analyses; more details can be found elsewhere [24]. N_2 adsorption at −196.2 °C was performed using an ASAP 2420 gas adsorption analyzer; see [25] for more details.

The amount of drug loaded into the materials was determined by two different methods: i) Thermogravimetry analysis (TGA) and ii) UV-spectrophotometry. The first method was based on the weight loss of the loaded samples by thermogravimetric analysis (TGA) between 200 and 700 °C in a run using air. The TGA runs were carried out on a Mettler-Toledo analyzer (TGA/SDTA851e) using a flow of synthetic air of 100 mL/min NTP. The temperature was increased from 30 to 700 °C at 10 °C/min. The patterns were corrected using a blank curve, which uses an empty crucible and a similar temperature program. In the UV-spectrophotometry method, the hexane–ibuprofen solution was analyzed in a Multi-Spec-1501 (Shimadzu) before and after the loading process; 1 mL of extracted hexane solution was diluted to 50 mL in hexane and measured at 262 nm. The amount of loaded ibuprofen was determined by deducting the concentration of this sample from the initial one (33 mg/mL).

^{29}Si Solid State NMR spectra were measured on a Varian VXR-400S spectrometer using a frequency of 79.44 MHz with the following conditions: spinner of 7-mm zirconium, spinning speed 5 KHz, acquisition time 0.2 s, acquisition delay 20 s, radiofrequency length 3.2 μs, and spectral window 30,007 Hz. These spectra were referenced to tetramethylsilane (TMS) and the number of scans was 3200. The total Si–OH concentration was calculated based on the method reported by Igarashi et al. [26]. Small angle X-ray scattering (SAXS) measurements were performed at room temperature using a Bruker NanoStar instrument [25].

3. Results and discussion

SAXS analysis of the SBA-15 mesophase reveals a hexagonally packed cylindrical morphology characterized by a distance between the cylinders of 12.4 nm (Fig. 1, Table 1). Thermogravimetric analysis shows that the precursor requires temperatures of 450–550 °C to burn-off the surfactant with a weight loss of 47 wt% (Fig. S-1); this corresponds to a carbon content of 29.7 wt% (Table 1). Calcination of the precursor gives rise to a structural shrinkage of 10% as can be seen in the reduction of a_0 from 12.4 to 11.1 nm (Table 1). This effect can be visualized in the SAXS pattern with a shift towards higher angles (Fig. 1). The precursor was subjected to ethanol extraction to reduce the amount of template, which was found to be 5.7 wt% based on carbon (Table 1) after the extraction. Calcination of the solvent extracted material produced a similar shrinkage as the directly calcined material; this is consistent with a previous study on solvent extraction of SBA-15 mesophases [27].

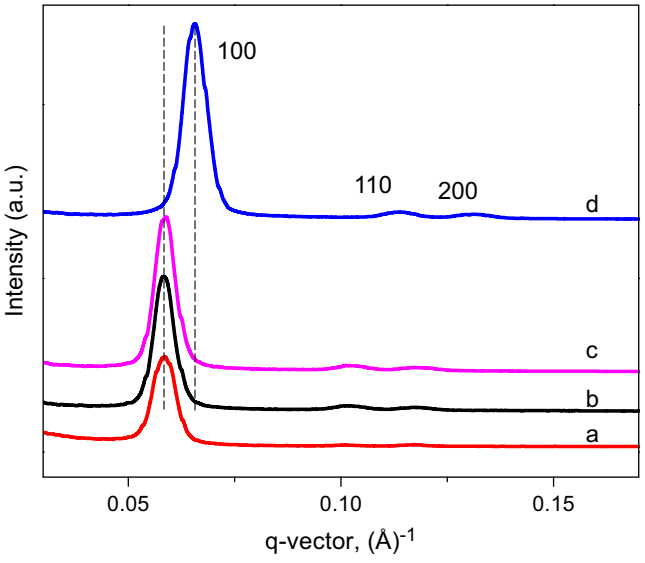

Fig. 1. SAXS patterns for a) precursor; b) F; c) SE-F and d) CA.

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