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Research Paper

Ordered mesoporous silica modified with lanthanum for ibuprofen loading and release behaviour

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ABSTRACT

The ordered mesoporous silicas SBA-15 and KIT-6, modified with lanthanum, have been for the first time applied in investigation of ibuprofen adsorption and release. The materials of hexagonal and regular structure were obtained by the hydrothermal method using a triblock copolymer Pluronic P123 as a template. The mesoporous silicas were impregnated with an aqueous solution of lanthanum(III) chloride in the amount necessary to obtain 1, 3 and 5 wt.% La loading. The physicochemical properties of the modified silicas were characterised by X-ray diffraction, transmission electron microscopy, UV–Vis spectrophotometry and low-temperature nitrogen sorption. The results showed that lanthanum strongly determined structural as well as textural properties of the silicas. The samples of modified silica were checked for the ability to adsorb and release of ibuprofen. The storage capacity of the modified silicas obtained increased with increasing their average pore diameter and percentage content of lanthanum. The amount of ibuprofen adsorbed onto KIT-6 silica modified with La was higher than that adsorbed onto SBA-15 materials. The high coverage of lanthanum on the surface of KIT-6 and SBA-15 solids was found to increase the amount of ibuprofen and the rate of its release.

1. Introduction

Ordered mesoporous silica materials discovered in 1990s have attracted great attention in different scientific fields. They have found applications in catalysis, separation, as sensors [1–3] and in adsorption processes [4,5]. Moreover, in recent years mesoporous silicas have been used for hosting and further delivery of various biomolecules [6–8] and drugs [9–12]. Thanks to their ordered structure, well-defined surface properties, high pore volume (0.6–1.0 cm^3/g) and surface area (600–1000 m^2/g) high drug loadings can be achieved [13]. It has been reported that both small and large drug molecules can be captured into the mesopores of ordered silica in the impregnation process and released by controlled diffusion [14]. One of the model drugs that has been applied in these studies is ibuprofen. It is a non-steroidal anti-inflammatory drug that has been widely used for the treatment of inflammation, pain or rheumatism [15]. However, ibuprofen has a short biological half-life (2 h) [16], therefore it is an appropriate candidate for sustained or controlled drug delivery. Several authors have investigated the ibuprofen storage and delivery properties of mesoporous silica materials [9,17–20]. It has been found that thanks to the suitable pore size and pore volume, mesoporous silica materials can be a support for the hosting and release of this drug. On the other hand, it has been also reported that the drug storage capacity of conventional mesoporous materials is relatively low, therefore mesoporous materials rich in Si–OH bonds could be modified with organosilanes of desirable functionalities [12,18,21,22]. A modification of this type can increase the interaction forces between the drug and the functional groups, therefore the drug release can be efficiently controlled. Apart from chemical functionalization of the mesopore wall, drug release can be fine-tuned by adjusting the pore diameter or by providing nanocaps for controlling the timing of the drug release [23]. We suggest that the modification of ordered mesoporous silica with lanthanum can influence the drug release rate. According to clinical studies, lanthanum has no toxic effects and its bioavailability is extremely low. The absolute bioavailability of lanthanum in human body is less than 0.002%, with the majority of an oral dose being excreted in the feces [24]. Furthermore, lanthanum oxide nanoparticles (LONP) have been used as a suitable candidate in biomedical applications. Samples coated with LONP have been developed as sensors of different molecules such as phosphate and glucose. Compounds containing lanthanum have been also used for magnetic field

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controlled targeted drug release [25]. Moreover, lanthanum is also applied in medicine to prevent high blood phosphate levels in dialysis patients. The accumulation of lanthanum in the body of dialysis patients is negligible, mainly because of its ultra-low gastrointestinal absorption and route of elimination [26]. Recently, the novel lanthanum compound has been developed as a promising anticancer drug [27]. Additionally, it has been reported in previous studies that lanthanum incorporated in ordered mesoporous silica increases their thermal stability [28–30]. Therefore, the main aim of this study was to analyse the effect of ordered mesoporous materials such as SBA-15 and KIT-6 modified with lanthanum on the loading and release of ibuprofen. The new materials with different amounts of lanthanum were synthesised and then characterised by various methods such as X-ray diffraction, transmission electron microscopy, laser diffraction, ultraviolet–visible spectrophotometry, N_2 sorption analysis. The structural effect of these materials on ibuprofen loading and release has been studied for the first time.

2. Material and methods

2.1. Sample preparation

2.1.1. SBA-15

Hexagonal mesoporous silica SBA-15 was prepared by the hydrothermal method described by Zhao et al. [4,31]. The synthesis was performed in polypropylene bottle. The synthesis procedure was as follows. A polypropylene bottle was loaded with 0.5 g of triblock copolymer Pluronic P123 (BASF) and 19 ml of 1.6 M HCl (Chempur). When the surfactant was dissolved, 1.1 g of tetraethyl orthosilicate (TEOS, Aldrich, 98%) was added dropwise. The final mixture of: 10 g P123: 0.10 mol TEOS: 0.60 mol HCl: 20 mol H_2O was stirred at 35 °C for 6 h and then it was placed in an oven for 24 h at 35 °C and subsequently for 6 h at 100 °C. The white solid product was filtered without washing and dried at 100 °C for 24 h in air oven. Finally, the product was calcined at 550 °C in air to remove the template.

2.1.2. KIT-6

Cubic mesoporous silica KIT-6 was synthesised as follows: 4.0 g of Pluronic P123 (BASF), 144 g of distilled water and 7.9 g of hydrochloric acid (Chempur, 37%) were placed in a polypropylene bottle [4]. The mixture was stirred for 3 h at 35 °C. After complete dissolution of triblock copolymer, 4.0 g of 1-butanol was added immediately. After 1 h stirring, 8.6 g of TEOS were added to the homogeneous clear solution. The mixture was kept under vigorous and continuous stirring at 35 °C for 24 h. Subsequently, the reaction mixture was aged at 100 °C for 24 h under static conditions. The product was filtered without washing and dried at 100 °C for 24 h in air oven. Finally, the sample was calcined at 550 °C in air to remove the template.

2.1.3. Modification of mesoporous silica with lanthanum(III) chloride

Incipient wetness technique was used to impregnate mesoporous silicas SBA-15 and KIT-6 with an aqueous solution of lanthanum(III) chloride ($LaCl_3$, Aldrich) in the amount necessary to obtain 1, 3 or 5 wt.% La loading. The materials were successively dried at 105 °C for 5 h and calcined for 3 h at 400 °C (2 °C/min).

2.2. Sample characterisation

2.2.1. Powder X-ray diffraction (XRD)

All the samples obtained were characterised by powder X-ray diffraction using a D8 Advance Diffractometer made by Bruker with the copper $K_{\alpha 1}$ radiation ($\lambda = 1.5406$ Å). The XRD patterns were recorded at room temperature with a step size 0.02° in the low-angle range and 0.05° in the high-angle range.

2.2.2. Transmission electron microscopy (TEM)

For TEM measurements, powdered samples were deposited on a grid with a perforated carbon film and transferred to a JEOL 2000 electron microscope operating at 80 kV.

2.2.3. Ultraviolet–visible spectrophotometry (UV–Vis)

UV–Vis spectra were recorded using a Varian-Cary 300 Scan UV–Vis spectrophotometer. The ordered mesoporous silicas were placed into a cell equipped with a quartz window. The Kubelka–Munk function (F(R)) was used to convert reflectance measurements into equivalent absorption spectra using the reflectance of SPECTRALON as reference.

2.2.4. Nitrogen sorption

The pore structure of the samples obtained was characterised on the basis of low-temperature nitrogen adsorption–desorption isotherms measured on a sorptometer Quantachrome Autosorb iQ. Prior to adsorption measurements, the samples were degassed in vacuum at 300 °C for 2 h. Surface area and pore size distribution were calculated by BET (the relative pressure p/p_0 range taken into account in the BET calculations was 0.006–0.2) and BJH methods, respectively. Total pore volume and average pore diameter were determined as well.

2.2.5. Particle size distribution

Particle size distribution of the obtained materials was measured by Mastersizer 2000 (Malvern, UK) equipped with a Hydro dispersion unit. A helium–neon laser generating light of $\lambda = 632.8$ nm and a blue semiconductor light source generating light of $\lambda = 466$ nm, used in the particle size analyser, ensured a wide range of measurements 0.02 ÷ 2000 μm. The obtained materials were dispersed in the surfactant before measurements. The refractive index was measured by a refractometer Refracto 30PX/GS (Mettler Toledo) to be 1.46 and was used to calculate the particle size distribution. Then the samples were dispersed in distilled water and introduced into the camera optical unit. The results were obtained in the form of percentages of $d(0.1)$, $d(0.5)$ and $d(0.9)$ which are defined as:

- $d(0.1)$ (μm) – 10% of the particle distribution is below this value,
- $d(0.5)$ (μm) – median of particle distribution (50% of the distribution above this value and 50% below),
- $d(0.9)$ (μm) – 90% of the particle distribution is below this value.

The results were also presented by using Sauter mean diameter (SMD), $D_{(3,2)}$ which gives information about an average of particle size and by volume mean diameter, $D_{(4,3)}$.

2.3. Ibuprofen loading

Mesoporous silica materials modified with lanthanum – 1, 3 or 5 wt.% (0.25 g) were added into 50 ml of IBU (ibuprofen, BASF, USP, Ph. E. grade) solution in hexane (35 mg ml^{-1}), followed by stirring at room temperature for 72 h in a closed batch to prevent the evaporation of hexane. The loaded materials were then filtered and dried for 24 h at 100 °C. The amount of ibuprofen adsorbed was calculated by subtracting the amount found in the supernatant liquid after adsorption from the amount of ibuprofen present before addition of the adsorbent, measured by UV absorption at the λ_{max} of ibuprofen 272 nm.

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