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RESEARCH ARTICLE

A Study of Controlled Release of Aspirin by Mesoporous SBA-15

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Abstract: Mesoporous SBA-15 materials with high surface area were synthesized using hydrothermal method. These materials have large surface area, therefore good adsorber, besides the large pores offer sites for drug loading. The synthesized mesoporous materials were loaded with aspirin. Then controlled release of aspirin by the materials was studied in phosphate buffer system using UV- Visible spectrophotometer to monitor the concentration. The prepared samples were characterized by XRD, Nitrogen adsorption-desorption studies, TEM, IR and TGA. The benign nature of the SBA-15 materials makes it an ideal carrier for aspirin and facilitates the controlled release of the drug.

Keywords: Drug delivery, Mesoporous, SBA-15, Aspirin

Introduction

According to the classification made by IUPAC, porous solids can be arranged in three main categories, depending on their pore size (diameter, d), in micro- ($d < 2$ nm), meso- ($2 \text{ nm} < d < 50$ nm), and macroporous materials ($d > 50$ nm)[1]. Mesoporous SBA-15 materials has received much attention in various fields of applications such as catalysis[2-5], adsorption[6-11] and as drug delivery support[12]. There has been a lot of attention also in designing novel drug delivery models using porous solids including SBA-15[13]. Amine functionalized SBA-15 and MCM-41 materials have been studied for controlled release of drugs[14]. Aspirin or acetyl salicylic acid is most widely used drug in the world for various diseases[15]. Pure SBA-15 has also been used for controlled release of other drugs[16]. There has been a suggestion that aspirin can be used for hypertension in low doses. Controlled release of aspirin can be helpful for treating hypertension. Sustained release methods of aspirin have been studied in past[17] and in recent times with carriers like ethyl cellulose[18]. Modified layered double hydroxides[19] have also been studied. In this paper, we report the sustained release behavior of aspirin from unmodified SBA-15 silica carriers.

Experimental

Poly(ethylene glycol) block poly(propylene glycol) block poly(ethylene glycol), P123,

($EO_{20}PO_{70}EO_{20}$, MW=5800 g/mol) and acetyl salicylic acid (aspirin) were purchased from Aldrich. Tetraethylorthosilicate (TEOS) was bought from Merck and used as the silica source. The materials were used without further purification or any modification.

Preparation of SBA-15

The SBA-15 materials were prepared by hydrothermal method described by Stucky *et al.*,[20] with some minor modification. In a typical synthetic procedure, 4 g of the surfactant Pluronic P123 were dissolved in 140 mL of 2 N hydrochloric acid by continuous stirring using a mechanical stirrer in a Teflon beaker. The temperature of the mixture was then kept a 40 °C and 8.6 g of Tetraethylorthosilicate (TEOS) was added dropwise to the mixture while stirring was continued. The mixture was stirred for 12 hours and then aged at 100 °C for another 48 hours in a Teflon lined autoclave. Then the product was filtered, washed with distilled water and ethanol. The products were then dried at 80 °C in an air oven for 12 hours. In the final step, the organic template was removed from the silica materials by calcination at 550 °C for 5 hours before attaining the calcination temperature at a heating rate of 3 °C per minute. The final product was a pure white powder.

Loading of Aspirin into SBA-15 and release in phosphate buffer system

Acetyl salicylic acid (aspirin) is soluble in alcohol and we prepared ethanolic solutions of aspirin for our study. A 25 mg/L solution in absolute ethanol was prepared for the drug loading procedures where 0.5 g of the calcined SBA-15 materials were suspended in 50 mL of drug solution and stirred using a magnetic stirrer for 24 hours at 40 °C. Then the resulting materials were filtered, dried first in air and then at 50 °C for 12 hours. These are SBA-15 materials loaded with the drug and were designated as aspirin@SBA-15. The loading amount of the drug was determined using thermogravimetric analysis (TGA). The absorption maxima (λ_{max}) of the aspirin solution used was found to be 288 nm (λ_{max}=288 nm) and the release behavior was studied at that wavelength in phosphate buffer (pH 7.4). A sample of 50 mg aspirin@SBA-15 was added into 50 mL phosphate buffer solution and stirred at a low rpm (~80-110). A 5 mL aliquot of the sample was removed using a filter syringe at different time intervals and subjected to UV-Visible spectrophotometric analysis at 288 nm. Equal volume of buffer was added to compensate for the volume loss.

Characterization of materials

Small angle XRD spectra were recorded on a Rigaku x-ray diffractometer for 2θ values from 0.5-10° using Cu-Kα source (λ = 1.54 Å). The nitrogen adsorption-desorption isotherms were measured using Micromeritics Tristar 3000 instrument. Before adsorption, the samples were degassed at 300 °C for 3 h. The method of Barrett, Joyner and Halenda (BJH)[21] was used for the mesopore size distributions from the experimental isotherms. High resolution Transmission Electron Micrographs (TEM) were captured with JEOL JEM 2100 TEM instrument operated at 200 kV. Ethanolic suspension of the samples were prepared on dry carbon coated Cu-grid. The FT-IR (KBr) spectra of pure SBA-15 and drug loaded SBA-15 were recorded on Shimadzu IR Affinity-1 IR spectrometer. The thermogravimetric analysis was done with a Mettler Toledo TG instrument.

Results and Discussion

Low angle XRD patterns (Figure 1) of SBA-15 showed well-resolved patterns with a prominent diffraction peak at 2θ value of 0.92 indexed to (100) reflection characteristic of well-ordered hexagonal mesostructures in the symmetry group *P6 mm*. Two additional peaks

were indexed to 110 and 200 reflections. The d-value (d_{100}) was calculated to be 8.2 nm and the unit cell size was calculated (using the formula $a_0 = \sqrt{(4/3)}d$) to be 9.5 nm. The N_2 adsorption-desorption shows Type IV isotherm according to IUPAC[22] with H1 hysteresis loop which are characteristic of mesoporous materials (Figure 2). The SBA-15 samples shows a high specific BET[23] surface area of 662 m^2/g. The TEM images (Figure 3) shows the hexagonal porous structures of the silica materials. FT-IR spectra of pure and drug loaded SBA-15 show characteristic Si-OH stretching at 975 cm^{-1} in pure SBA-15 and at 972 cm^{-1}. The C=O stretching frequency can be observed in drug loaded SBA-15 materials at 1735 cm^{-1} and a peak at 3750 cm^{-1} can be assigned to alcoholic-OH without hydrogen bonding. The amount of drug loaded calculated from the weight loss percentage from TG analysis and was found to be 28%. The drug release profile is shown in Figure 4. From the release profile graph, it can be seen that around 30% of the drug released instantaneously and then drug releases slowly (~9%). In about 2.5 h almost all of the drug (>90%) is released from SBA-15 support.

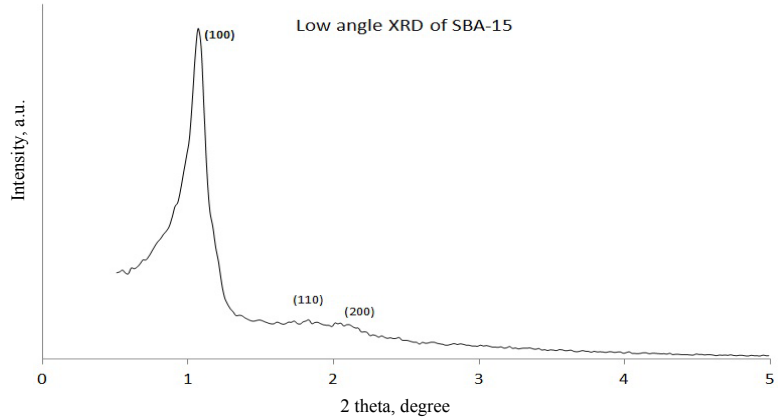

Figure 1. Low angle XRD of SBA-15

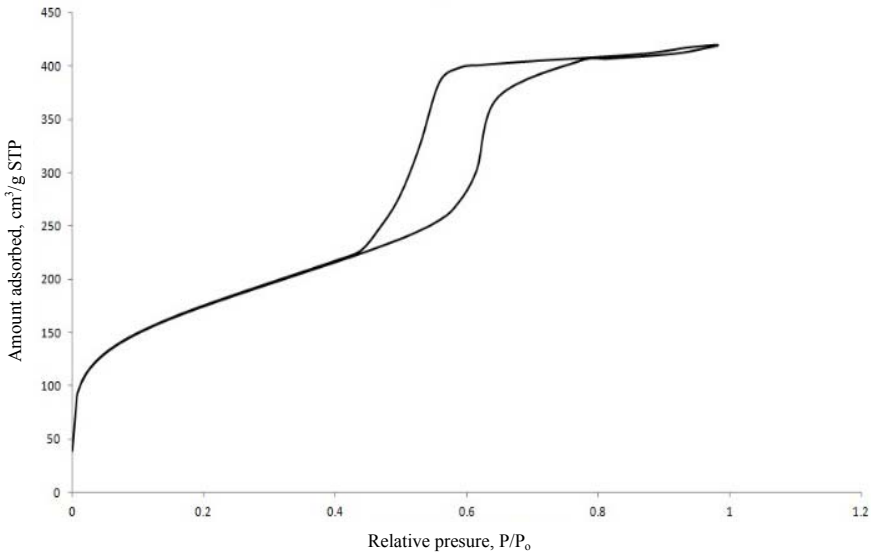

Figure 2. Nitrogen adsorption-desorption (BET) isotherm of SBA-15

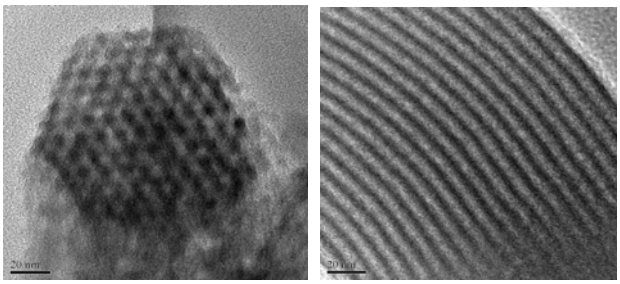

Figure 3. TEM images of SBA-15

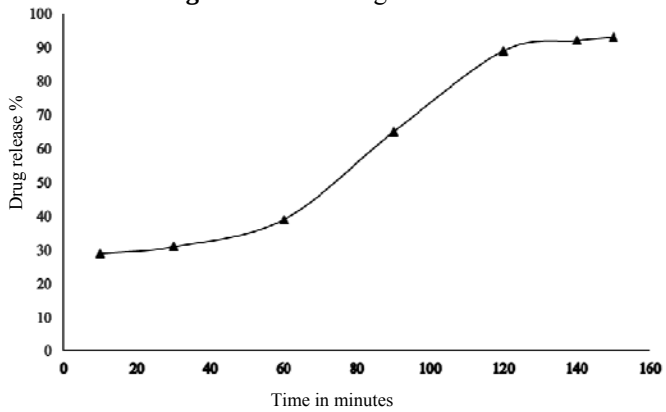

Figure 4. Aspirin release profile from SBA-15

Conclusion

The mesoporous SBA-15 materials present a novel carrier material for aspirin drug release under biological pH. The high surface area and mesoporous character of the materials provide ample opportunities for drug molecules like aspirin to be loaded on both onto the surface and inside the mesopores of SBA-15 and thereby providing controlled release of the drug. Sustained aspirin release using SBA-15 can prove beneficial for many patients.

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