Research Article

Controlled Release of Ibuprofen by Using Morphologically Modified Mesoporous Silica

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The synthesis of mesoporous silica with variable pore sizes was carried out for the purpose of controlled drug release study. Mesoporous silica containing three-dimensional cage-like structures was prepared by the simple hydrothermal method using triblock copolymer Pluronic F-127 as the template and tetraethyl orthosilicate (TEOS) as a silica source. The synthesized samples of plain and modified mesoporous silica were compared to measure the drug release ability of ibuprofen. The effect of co-surfactants, temperature, and different salts on the pore structure of the materials were also observed. The surface property enhancement of mesoporous silica was contributed by controlling its pore morphology. The materials were characterized by FT-IR, SEM, TGA, and UV-Visible spectroscopy and later used for the ibuprofen release study. The results indicated that the modified mesoporous silica with increased pore diameter showed increased storage capacity and high pH-responsive release behavior as compared to the plain mesoporous silica.

1. Introduction

Mesoporous materials are referred to as materials having a pore diameter within the range of 2–50 nm possessing a long-range order [1]. Mesoporous materials are combined with different kinds of silica and alumina that have comparably measured mesopores [2, 3]. These materials possess unique structural characteristics and offer a wide range of potential applications [4]. An exceptional regular mesoporous material is activated carbon, and its adsorption ability depends on the porosity of the carbon system. Different porous structures can be obtained by carefully choosing the template, normally a surfactant that acts as structure-directing agent [5]. By changing the chain lengths of surfactants, the pore dimensions of mesoporous silicas can be altered [6]. The pore size of mesoporous silicas can also be altered by changing the temperature, as every 10°C rise in temperature results in the increase of more than 1 nm in the pore sizes. pH change and salt addition also upset the porosity and pore order of mesoporous silica [7].

These porous materials have attracted much attention because of the wide variety of applications they are suitable for, such as eradication of water pollution [8], air cleaning, photonics, and carbon dioxide capture and in biocatalyst, sensors, and chromatographic materials, and are particularly useful for the preparation of the drug delivery system [9–11]. Well-ordered mesoporous silica materials have well-organized and continuous mesostructures [12]. In order to obtain mesoporous materials, the solgel method, solution precipitation method, hydrothermal method, vapor-phase pathway, and surface template mechanism have been used [13, 14].

In the present work, mesoporous materials were prepared via the solgel method, in which tetraethoxysilane (TEOS) was used as a precursor. Due to the suitable structure of mesoporous silica and its well-defined properties, these materials are ideal as a support for drug delivery purposes. In recent years, several researchers have described the use of mesoporous materials in the drug delivery system [15, 16]. A controlled drug delivery system can achieve temporal delivery of the drug to the target site. In addition to surface functional groups, the morphology and size of mesoporous materials also have an important influence on drug release characteristics. The influence of surface area, pore size, particle size, and morphology of silica on the drug release regime is very important.
release properties has also been discussed. The parameters that alter the morphology of mesoporous materials were proved to be beneficial for the design of drug release systems. Ibuprofen was chosen as a sample drug. It is a nonsteroidal anti-inflammatory drug widely used in the treatment of pain and inflammation in musculoskeletal disorders. The ibuprofen delivery by mesoporous materials is a crucial and ever-continuing research field. All the morphologically modified mesoporous silicas were characterized by various methods such as Fourier-transform infrared (FT-IR) spectroscopy, scanning electron microscopy (SEM), thermogravimetric analysis (TGA), and UV-Visible spectroscopy. The structural effect of the mesoporous silica (SBA-16) on ibuprofen release has been studied for the first time.

2. Experimental

Pluronic F-127 (Sigma–Aldrich), HCl (Riedal-de Haen), butanol (Riedal-de Haen), tetraethoxysiliane (TEOS) (Fulka), KCl (BDH AnaLAR), cetyltrimethylammonium bromide (CTAB) (BDH AnaLAR), and n-hexane (Merck) were purchased. Ethanol and ibuprofen were purchased from a local market. All chemicals were used as received without further purification.

In this study, SEM (an EVOLS-10 instrument operated at an accelerating voltage of 20 kV) was used to observe the morphology of all samples. FT-IR (Shimadzu, IR-Tracer 100) was used for spectral analysis of samples within the range of 4000 cm$^{-1}$–500 cm$^{-1}$. UV-Visible absorption was measured by using an UV-Visible spectrophotometer (BMSUV-2600). Thermogravimetric analysis was performed by using TGA (SDTQ-600) to check the thermal stability of the samples.

2.1. Synthesis of Mesoporous Silica (SBA-16). Mesoporous silica (SBA-16) was prepared by the hydrothermal method. First, 1 g of pluronic acid (F127) was added in 8 mL of distilled water and mixed gently. Then, 32 mL of HCl (2 M) was added to it, and the above solution was stirred continuously on a hot plate for one hour at 40°C. After that, 3.36 mL of tetraethoxysiliane (TEOS) was added to it, and the solution was again stirred on a hot plate for 30 minutes at 45°C. The synthesized material was then put in a Teflon-lined stainless steel vessel and heated at 100°C for 24 hours. After centrifugation, the gel was washed with water two to three times and then washed with C$_6$H$_{12}$OH. The gel was dried in an oven for three hours at 80°C, and finally, the obtained powder was calcined in furnace at 550°C for 6 hours. The white powder of plain mesoporous silica was obtained and characterized.

2.2. Synthesis of SBA-16 (120°C). The same procedure was repeated as mentioned in Section 2.2 except that the resulting mixture was put in a Teflon-lined stainless steel vessel in an oven at 120°C for 24 h.

2.3. Synthesis of SBA-16+CTAB. The composites were synthesized with the same procedure as described in Section 2.2 except that CTAB was used as the surfactant instead of Pluronic F-127. A white powder of SBA-16+CTAB was obtained at the end of the reaction.

2.4. Synthesis of SBA-16+KCl. Mesoporous silica (SBA-16) was prepared in the same way as mentioned in Section 2.2 except that KCl was used in the place of Pluronic F-127. As a result, a white powder of SBA-16+KCl was obtained in the end.

2.5. Synthesis by the Microwave Method. Mesoporous silica was also prepared by the microwave method. First, water and 0.2 g Pluronic F-127 were mixed under constant stirring at 40°C, and 2 M HCl and TEOS were added as silica sources to it. The solution was stirred for 30 min at 45°C. The resulting mixture was then heated in a microwave oven at 10 W for 5, 10, and 15 min, respectively. After gel formation, it was dried in an oven for 3 h at 80°C and calcined in the furnace at 550°C for 6 h. The final appearance of the material was a white-colored powder. A similar procedure was performed with cosurfactant CTAB under similar conditions.
2.6. Ibuprofen Adsorption Process. 0.05 g of the prepared composite was mixed with 5 mL of hexane containing different concentrations of ibuprofen (0.005, 0.015, 0.025, and 0.035 g) in a closed vial to prevent evaporation of hexane and stirred for 48 hours. The concentration of ibuprofen in hexane was determined through an UV-Visible spectrophotometer at 235 nm by collecting a small amount of the solution.

2.7. Ibuprofen Release Process. To obtain the release profile, a 0.01 g drug (IBU)-loaded sample was added separately into PBS saline at a pH of 7.4 and 2, respectively, under continuous stirring at 37°C. The sample was extracted time to time to analyze for ibuprofen concentration in the sample by using an UV-Visible spectrophotometer. The effect of control drug release was also analyzed by changing different factors such as time effect, pH, and concentration effect.

3. Results and Discussion

3.1. Materials and Characterization. FT-IR of the photocatalysts was recorded by using IR tracer-100 SHIMADZU at a room temperature in the region of 400–4000 cm⁻¹. FT-IR measurements were performed in order to identify the structural differences between the morphologically modified silicas (Figure 1). All samples showed absorption peaks of Si–O–Si asymmetric stretching vibration at 1055 cm⁻¹, symmetric stretching vibration of the Si–O–Si group at 812 cm⁻¹, Si–O group vibration at 982 cm⁻¹, and water molecules retained by siliceous materials at 1690 cm⁻¹.

Similar results were shown by the mesoporous silica samples, which were prepared by the microwave method (Figure 2). Mesoporous silicas retained their siliceous structure even when prepared in microwave oven, demonstrating that no significant changes occurred in the formation of the framework. The main IR-absorption peaks were shown by asymmetric stretching vibration of the Si–O–Si group at 1055 cm⁻¹ and Si–O group and Si–O–Si symmetric vibration at 983 and 818 cm⁻¹, respectively. It was observed that the relative band of the Si–O–Si group at 1055 cm⁻¹ intensified as the time increased.

Although four samples were prepared by the microwave method, their FT-IR results showed some irregularities in the samples and hence only samples prepared by conventional heating were used for drug loading and release studies. IBU-loaded samples of the mesoporous silica showed the absorption peaks of both silica and IBU, confirming that IBU is successfully loaded on mesoporous silica surfaces (Figure 3). By increasing the IBU loading, intensified bands at 1058 cm⁻¹ of symmetric vibration of Si–O–Si and at 1720 cm⁻¹ of the carboxylic group of IBU were observed. The other IR peak of CH bands of the alkyl functional group in IBU at 2850 cm⁻¹ was also observed.

Figure 4 shows the thermal gravimetric analysis (TGA) of morphologically modified mesoporous silicas. All the samples were heated up to 1000°C in air, but only a small weight loss up to 200°C was observed in all the samples, which can be attributed to the removal of solvent molecules.
After 200°C, no weight loss indicated that the samples are thermally stable.

The morphology of all the modified silicas was examined by means of SEM; the results are shown in Figure 5. The SEM images of the plain mesoporous silica in Figures 5(a) and 5(b) show spherical particles of about 6–7 µm. However, images of SBA-16 in Figures 5(c) and 5(d) (120°C) show no big clusters or rocks, but they show spherical particles with a rough surface. Moreover, Figures 5(e) and 5(f) exhibit spherical particles of the mesoporous silica modified by CTAB with a smooth surface. All samples exhibited almost similar morphology with the exception of their pore size.

3.2. Proposed Mechanism. On the basis of characterization results, the mechanism for the preparation of modified mesoporous silicas using the hydrothermal method is preferred compared to the microwave method. The use of microwave having the maximum power (10 W) with less time produced irregular and poorly crystalline mesoporous structures. The irregularities in mesoporous structure were observed because of “hot spots” at certain points during microwave synthesis [16]. On the other hand, the samples prepared by the hydrothermal method possessed homogeneous and uniform structure. The phenomena of “hot spots” also occurred in this method, but it was assumed that this thermal supply helped to arrange the micelles faster as compared to above method [17]. Uniform silica structures with a large surface area showed better loading and release results with IBU.

3.3. Ibuprofen Absorption Isotherm. IBU was selected as a model drug to observe the loading capacity and storage of the drug on ordered mesoporous silica materials. The first step in the absorption process is the migration of IBU...
molecules on the mesoporous surface from the bulk solution. The second step is the diffusion of these molecules into the interior part of the silica. More IBU concentrations allowed more diffusion inside the pores until equilibrium is reached. Drug loading is also correlated with structural parameters of the modified mesoporous materials. The loading rate increases by increasing the pore size of the sample materials.

It can be seen in Figure 6 that IBU was absorbed rapidly in first 3 h and a slow absorption was observed up to 9 h. SBA-16 showed the highest absorption even with maximum ibuprofen loading. CTAB + SBA-16 showed less absorption rate as compared to all samples and completed its loading after 9 h. This process was observed with different concentrations of IBU, and it showed that by increasing IBU concentrations, loading and storage of drug on the mesoporous silica surface also increased. The above results showed the variable IBU absorption behavior due to different morphologies of prepared samples.

3.4. Ibuprofen Release Profile. 10 mL of PBS pH 7.6 was taken in 4 separate vials, and different samples of the drug, SBA-16, SBA-16 (120°C), SBA-16 CTAB, and SBA-16+KCl, were loaded in it. The release of ibuprofen was studied by using an UV-Visible spectrophotometer after 3h intervals.

The drug release rate depends on the pore size and morphology of the materials. The amount of drug released from the loaded materials is proportional to time, and release speed decreases gradually. Two steps were observed for the release process; the first one is a fast release called the burst effect, which is related to the release of IBU molecules attached to the silica surface of materials, and the second one is a slow release, related to the desorption of the IBU molecule that adsorbs further inside the pores by macropore channels. It can be seen in Figure 7 that after 15 h, SBA-16 CTAB showed the least drug release while the maximum release was observed for SBA-16 and SBA-16 (120). The rate of release depended on the nature of the mesoporous silica and its synthesis process. The drug release rate from the silica surface was fast at first and then it gradually decreased because firstly the molecules on the external surface were released, followed by the molecules in the deeper structure. Therefore, we can conclude that during drug release, the drug molecules must overcome two barriers; one is release from the macropore channels, and other is the diffusion from the material into the fluid.

Figure 6: Drug loading of different IBU concentrations on mesoporous silica samples. (a) Loading of 0.015 g IBU. (b) Loading of 0.025 g IBU. (c) Loading of 0.035 g IBU.
Figure 7: IBU release from different mesoporous silica samples. (a) Release of ibuprofen at 0.015 g. (b) Release of ibuprofen at 0.025 g. (c) Release of ibuprofen at 0.035 g.

Figure 8: Release of IBU at acidic pH. (a) Release of IBU at 0.015 g. (b) Release of IBU at 0.035 g.
3.5. pH Effect. IBU release from all mesoporous silica samples was analyzed at acidic pH, as well as both acidic and basic environments present in the human gastrointestinal tract. The pH in human body changes from 1 to 2 in the stomach (acidic) and 7 to 8 in the proximal intestine. The release of IBU was observed at pH 2 by using 0.015 g and 0.035 g IBU-loaded mesoporous silicas. The release profiles are shown in Figure 8. It was observed that the release of IBU from modified silicas was slow in acidic pH (2) and less than 50% of the adsorbed drug was released after 9 h. Hence, better drug release efficiency was observed at pH 7.6 than in acidic pH.

From these results, it can be concluded that at basic pH, IBU exhibited faster release than in acidic media. At pH 2 (pH > pKa), the molecule of IBU was ionized and less amount was left in the stationary phase. Thus, at basic pH, the samples showed faster release when solubility of IBU molecules was high. The other reason was that at pH 7, the surface molecules of the mesoporous silica repelled the anionic-COOH group of IBU and thus showed a high release rate.

4. Conclusion

The loading capacity and the release rate of ibuprofen from different morphologically modified mesoporoussilicas were investigated. SEM, FT-IR, TGA, and UV spectroscopical analyses indicated that ibuprofen molecules were absorbed within the pores of mesoporous silica materials. The absorption capacity and dissolution rate of IBU were found to be strongly related to the mesopores of silica materials. The materials with a larger mesopore size showed the higher IBU loading and release rate because of the low resistance for moveable IBU molecules to adsorb on the unoccupied surface of the mesoporous silica and the higher diffusivity of PBS solution and IBU molecules. The mesoporous materials also showed pH-responsive controlled release behavior for IBU due to its porous structure and high surface area.

Data Availability

Data are available on request to Sana Ahmad (drsanahmad@yahoo.com).

Conflicts of Interest

The authors declare no conflicts of interest.

References


