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Drug delivery from hydrophobic-modified mesoporous silicas: Control via modification level and site-selective modification

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ABSTRACT

Dimethylsilyl (DMS) modified mesoporous silicas were successfully prepared via co-condensation and post-grafting modification methods. The post-grafting modification was carried out by the reaction of the as-synthesized MCM-41 material (before CTAB removal) with diethoxydimethylsinale (DEDMS). N_2 adsorption–desorption and ^{29}Si MAS NMR characterization demonstrated that different amount of DMS groups were successfully incorporated into the co-condensation modified samples, and the functional DMS groups were placed selectively on the pore openings and external pore surfaces in the post-grafting modified samples. Subsequently, the controlled drug delivery properties from the resulting DMS-modified mesoporous silicas were investigated in detail. The drug adsorption experiments showed that the adsorption capacities were mainly depended on the content of silanol group (CSG) in the corresponding carriers. The in vitro tests exhibited that the incorporation of DMS groups greatly retarded the ibuprofen release rate. Moreover, the ibuprofen release profiles could be well modulated by varying DMS modification levels and site-selective distribution of functional groups in mesoporous carriers.

1. Introduction

For the traditional drug delivery systems, typically tablet or intravenous injection, the plasma drug level may cause either toxic side effect if the drug concentration swings above the maximum level or lack of efficacy if the drug concentration falls below the minimum therapeutic level. Therefore, the maintenance of steady therapeutic drug level in plasma has been a major challenge. It is highly desirable to develop a suitable biomaterial for encapsulation of drugs with high drug loading capacity and well-controlled drug delivery profile, consequently, for enhancing the action of therapeutic agents.

Ordered mesoporous materials, which possess high surface area, large pore volume, controllable pore geometry, narrow pore size distribution, tunable pore diameter ranges between 2 and 30 nm, easily modified surface with silanes, provide potential host matrix for the applications in adsorption, separation, catalysis, sensor, drug delivery system and other microdevices [1–6]. Vallet-Regí et al. reported for the first time the use of mesoporous silica MCM-41 in ibuprofen delivery system in 2001 [5]. Since then, mesoporous materials with different pore structural parameters, pore geometry, and surface organic composition have been widely investigated as drug delivery system in order to obtain the high drug loading capacity and well-defined drug delivery profile [7–19]. It has been shown that drug release rate, a critical parameter for clinical applications, could be modulated by designing mesoporous silicas with different surface area, pore size, pore connectivity and pore geometry [14,15]. For example, it is generally accepted that the pore size has a pronounced influence on the kinetics of drug release, the drug delivery rate decreased with the decreasing pore size in mesostructures [14,15]. The previous researches also revealed that the mesoporous silica carrier modified with special functional groups is of great benefits to controlling drug release rate [7–13]. Several studies pointed out that the release rate of drug ibuprofen, which has been widely investigated as model drug, could be modulating by varying the density of the surface organic amino groups, changing the chain length of amino groups, or using different species of amino groups, e.g. aminopropyl, aminoethylaminopropyl and so on [7–9]. Our preliminary results demonstrated that mesoporous silica MCM-41 materials modified with hydrophobic groups, including methylsilyl (MS), dimethylsilyl (DMS), and trimethylsilyl (TMS), could be employed as controllable drug delivery systems [19,20]. Moreover, the DMS-modified

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MCM-41 provided better effect over delayed drug release profile than that of the MS-modified MCM-41 [19]. In addition, the drug-impregnated mesoporous MCM-41 modified with TMS groups greatly reduced the ibuprofen release rate [20].

It can be seen that organic modification of mesoporous silicas is an important strategy and feasible pathway to obtain desired drug delivery profile. Actually, organic modification of mesoporous silicas with silanes is an effective way to obtain materials with specific surface properties, which provide desired active sites or inert sites to meet with the application purposes [21–23]. With the development of organic modification technology, it is possible to precisely control over the surface properties of mesostructure via the different organic modification routes of post-grafting procedure and co-condensation procedure. Co-condensation method is currently the most common and direct synthesis route for the introduction of organic groups into mesoporous matrix with uniform surface coverage of organic groups. Post-grafting method refers to the modificaton of a pre-fabricated inorganic mesoporous material by attaching of functional groups to the mesoporous surface. By combined with the different organic modification methods, the functional groups are expected to be selectively located on the external surface or pore interior surface of mesostructures [24–26]. Thus, it is important to investigate the influences of functional groups distribution in mesoporous matrix on the drug delivery properties. Herein, we report controlled drug delivery profiles from mesoporous silica matrices modified with hydrophobic groups in detail. In order to do so, a series of mesoporous silica materials modified with different surface densities of DMS groups and different DMS distribution were prepared via co-condensation and post-grafting modification methods. The drug release experiments illustrate the ibuprofen delivery profiles can be well-modulated by varying DMS modification levels and site-selective distribution of functional groups in mesoporous carriers.

2. Experimental

2.1. Preparation of pure silica MCM-41

Pure silica MCM-41 was prepared according to the procedure described in Ref. [27], except that a different method [28] was employed to remove the surfactant $C_{16}H_{33}N(CH_3)_3Br$ (CTAB, 98%). The removal of CTAB was carried out using alcoholic solutions of ammonium nitrate. Typically, 1 g of the as-synthesized material was dispersed in 125 mL of ethanol (95%) containing 0.3 g of ammonium nitrate, and the mixture was stirred at 60 °C for 1 h. Finally, the powders were recovered by filtration and washed with ethanol and deionized water. The above treatment was repeated twice. The obtained sample was denoted as M41-p.

2.2. Post-grafting synthesis of DMS-modified MCM-41

The post-grafting modification was carried out by the reaction of the as-synthesized MCM-41 material (before CTAB removal) with diethoxydimethylsinale (DEDMS). Four grams of the as-synthesized MCM-41 contained in a 200 mL round-bottom flask was dried at 120 °C for 24 h in a vacuum oven. Then 100 mL of dry toluene was added into the flask, followed by the addition of 1.15 mL (0.99 g, 6.7 mmol) or 2.30 mL (1.98 g, 13.4 mmol) of DEDMS under gentle stirring. The resulting mixture was stirred for 10 min at room temperature and then heated to refluxing for 24 h. A drying tube was attached to the reflux apparatus to minimize the influence of moisture. The product was filtered and washed with dry toluene several times. To remove unreacted DEDMS, the sample was dried at 120 °C for 24 h in a vacuum oven. The removal of CTAB was carried out by the same method described above. The obtained two samples were named as P-M41-1 and P-M41-2 corresponding to the addition of 1.15 and 2.30 mL of DEDMS in the original synthesis system, respectively.

2.3. Co-condensation synthesis of DMS-modified MCM-41

The preparation of DMS-modified MCM-41 materials via co-condensation method was essentially similar to the procedure used in the synthesis of the M41-p, except for the addition of a mixture of TEOS and DEDMS. The pre-mixture of DEDMS and TEOS was poured to the surfactant solution under vigorously stirring. The resulting mixture was stirred at room temperature for 1 h and then heated at 90 °C for 24 h under static conditions. The resulting powders were filtered and dried. The removal of CTAB was carried out by the same method described above. The designations of the obtained samples were made according to different molar ratios of DEDMS/(TEOS+DEDMS) in preparation procedures. C-M41-10, C-M41-20 and C-M41-30 represent the samples synthesized with a ratio of DEDMS: (TEOS+DEDMS) =1:10, 2:10 and 3:10, respectively.

2.4. Impregnation and release of drug

Ibuprofen was adsorbed from a hexane solution as already reported procedure [6,14]. Ibuprofen was dissolved in hexane (33 mg/mL), and the mesoporous sample was soaked in the solution (33 mg/mL silica/hexane), stirring for 48 h in a closed batch to prevent evaporation of hexane. Subsequently, the suspension was centrifugated and ibuprofen that remained in the liquid phase was determined using UV/vis spectroscopy reading at a wavelength of 264 nm. The amount of ibuprofen adsorbed (A_t: with respect to the 1 g of original mesoporous silica) was calculated using the depletion method. The ibuprofen-impregnated powders were carefully washed with hexane to remove the drug adsorbed on the external surface of the mesoporous material. The final retained ibuprofen amount (A_e: with respect to the 1 g of original mesoporous silica) in the mesoporous sample was calculated by subtracting the amount of ibuprofen removed in the washing step from the total amount adsorbed (A_t). Moreover, the amount of the ibuprofen impregnated was investigated by thermogravimetric analysis (TGA). The ibuprofen release profile was obtained by adding 0.3 g of the drug-impregnated powders in a 200 mL round-bottom flask containing 100 mL of simulated body fluid (SBF) at 37 °C under continuous stirring (100 rpm). SBF has a composition similar to the human body plasma [29] (pmm: 142.0/5.0/2.5/1.5/147.8/4.2/1.0/0.5 for $Na^+/K^+/Ca^{2+}/Mg^{2+}/Cl^-/HCO_3^-/HPO_4^{2-}/SO_4^{2-}$). The drug concentration in the release fluid for the different release time was determined using UV/vis spectrophotometer. In each case, 3 mL of release fluid was taken out for analysis of the drug concentration, and then 3 mL of fresh SBF was added into the release system.

2.5. Characterization

X-ray diffraction (XRD) was performed on a Bruker Axs (Germany) diffractometer using Cu$K\alpha$ radiation. The data were recorded from 1.0° to 7.0° (2θ). N_2 adsorption/desorption isotherms of the samples were measured at −196 °C on a Micromeritics Tristar 3000 sorptometer. Prior to the measurement, all samples were outgassed at 80 °C and 10^{-6} mmHg overnight. The specific surface areas of the samples were calculated using the multiple-point Brunauer–Emmett–Teller (BET) method. The pore

diameter distributions were determined from the adsorption branches of the isotherms using BJH method. Transmission electron microscopy (TEM) images were obtained with a JEOL-2010 microscope. The ^{29}Si MAS NMR spectra were recorded on a Varian Infinityplus-400 spectrometer at 79.5 MHz using 5.5 mm zirconia rotors and a magic-angle spinning speed of 8.0 KHz. The pulse delay of 20 s was applied. The concentration of ibuprofen in release solution was determined on a Shimadzu UV-2501PC UV/vis spectrometer. Thermogravimetric analysis (TGA) was performed on a Setaram TGA-92 thermogravimetric analyzer with a heating speed of 10 °C/min under argon gas with flow rate of 100 mL/min.

3. Results and discussion

3.1. Material characteristics

Fig. 1a displays the XRD patterns of the samples M41-p, P-M41-1 and P-M41-2. All samples show three well-resolved diffraction peaks that can be indexed as (100), (110) and (200) reflections associated with well-ordered hexagonal arrays of mesopores [1]. It indicates that the post-grafting modification with DEDMS did not change the original pore structure. For samples prepared via co-condensation method, the XRD patterns show a characteristic intense low (100) reflection at 2θ angles between 2° and 3°, whereas (110) and (200) reflections are not distinguishable (see Fig. 1b), which is an indication that these samples have low ordered pore system [23]. Indeed, the TEM image shown in Fig. 2 confirms that the C-M41-20 has a low ordered pore system (see Fig. 2), which is consistent with the XRD analysis.

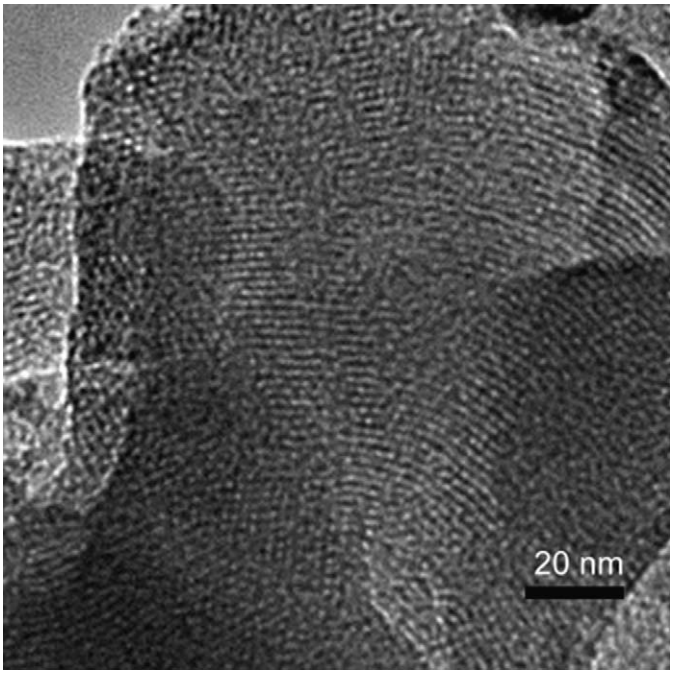

Fig. 2. HRTEM image of C-M41-20.

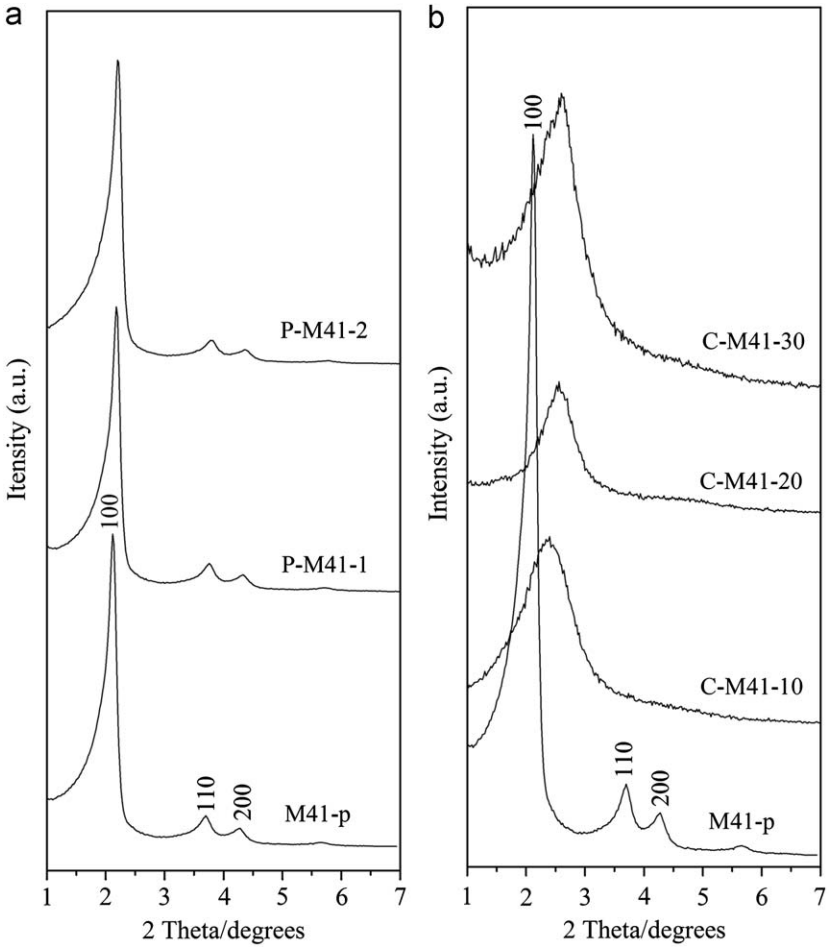

Fig. 1. Powder XRD patterns of the samples: DMS-modified samples via post-grafting method (a) and DMS-modified samples via co-condensation method (b).

Figs. 3a and b show the N_2 adsorption–desorption isotherms and pore size distribution curves of the samples M41-p, P-M41-1 and P-M41-2, respectively. All the samples exhibit the type IV isotherms with the H1 hysteresis loops, characteristic of the ordered mesoporous structures. For the P-M41-1 and the P-M41-2, the BET surface areas, pore volumes and pore sizes decrease slightly compared with those of the M41-p (see Table 1). Although different amounts of DEDMS were added during the post-grafting process, the two modified samples possess the similar BET surface areas, pore volumes and pore sizes. It could be assumed that the functional DMS groups are mainly located on the external pore surfaces and pore openings in the P-M41-1 and the P-M41-2. About the possible site-selective modification via post-grafting procedure, some former researches have proved this strategy [24,26,30]. In order to verify our assumption, further N_2 adsorption–desorption characterization was carried out on the sample P-M41-2 before removal of the template CTAB. The very low BET surface area (63.8 m^2/g) and pore volume (0.06 cm^3/g) suggest that the template occluded the pore channels even after the post-grafting process in the present study. These results confirmed that the DMS groups are indeed attached on the external pore surfaces and pore openings in the post-grafting modified samples. In comparison with the M41-p, the samples C-M41-10, C-M41-20, C-M41-30 display the adsorption isotherms gradually changed from type IV to I, as the content of the DMS groups increased (see Fig. 4a). Type I isotherms are often characteristic for materials with micropores or pore sizes on the borderline between the micropore and the mesopore ranges [31,32], as illustrated in Fig. 4b. In addition, it can be seen that the pore sizes decrease with increasing amounts of functional DMS groups in the mesostructures (see Fig. 4b). These observations indicate that the DMS groups are on the pore surface of the samples prepared via co-condensation method. Interestingly, the BET specific surface areas of the samples C-M41-10, C-M41-20 and C-M41-30 are much higher than that of the M41-p (see Table 1). This is probably caused by the facts that the appearance of micropores in these samples and the regions between organic groups are spacious enough to accommodate nitrogen molecules when organic groups are anchored onto the pore surfaces of the mesostructures [27,33].

The ^{29}Si MAS NMR spectra of all samples are shown in Fig. 5. Relative intensities of peaks are detailed in Table 2. The spectrum

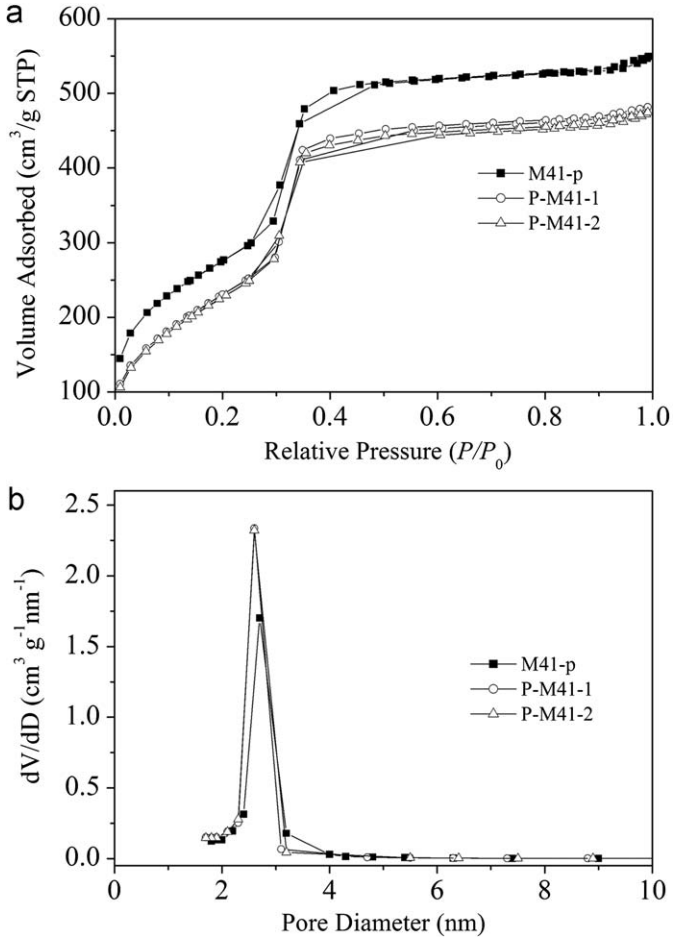

Fig. 3. Nitrogen adsorption isotherms (a) and pore size distribution curves (b) of the samples modified via post-grafting method.

Table 1
Pore structure parameters of the samples.

Sample	d(100) (nm)	D_p (nm)[a]	S_{BET} ($m^2 g^{-1}$)	V_p ($cm^3 g^{-1}$)
M41-p	4.3	2.7	953	0.78
P-M41-1	4.1	2.6	872	0.75
P-M41-2	4.0	2.6	860	0.73
C-M41-10	3.7	2.5	1197	0.65
C-M41-20	3.4	2.3	1637	0.77
C-M41-30	3.4	2.1	1389	0.66

[a] The pore size corresponding to the peak value in the pore size distribution curve.

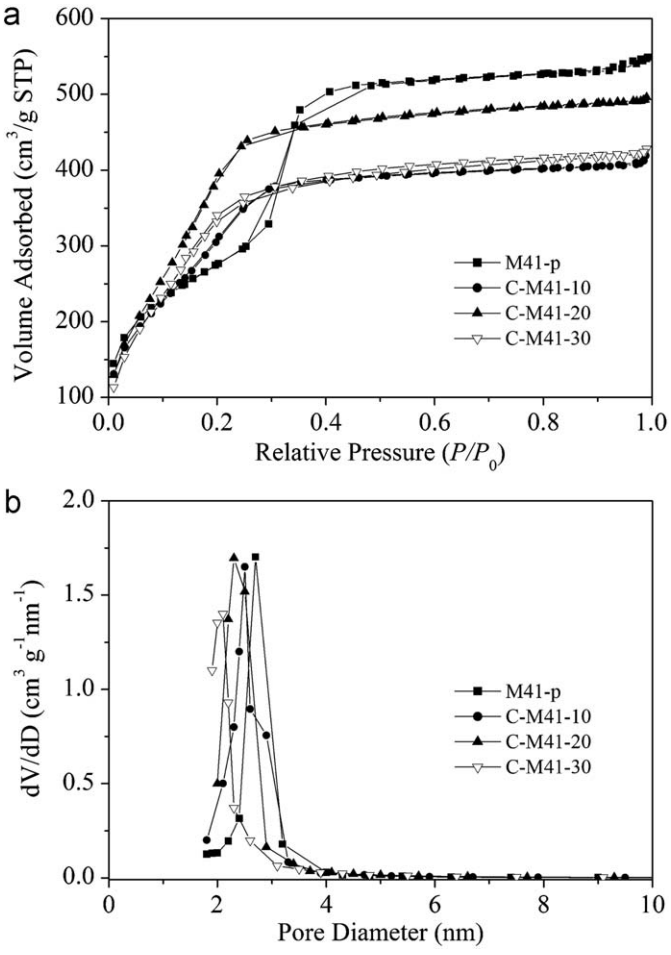

Fig. 4. Nitrogen adsorption isotherms (a) and pore size distribution curves (b) of the samples modified via co-condensation method.

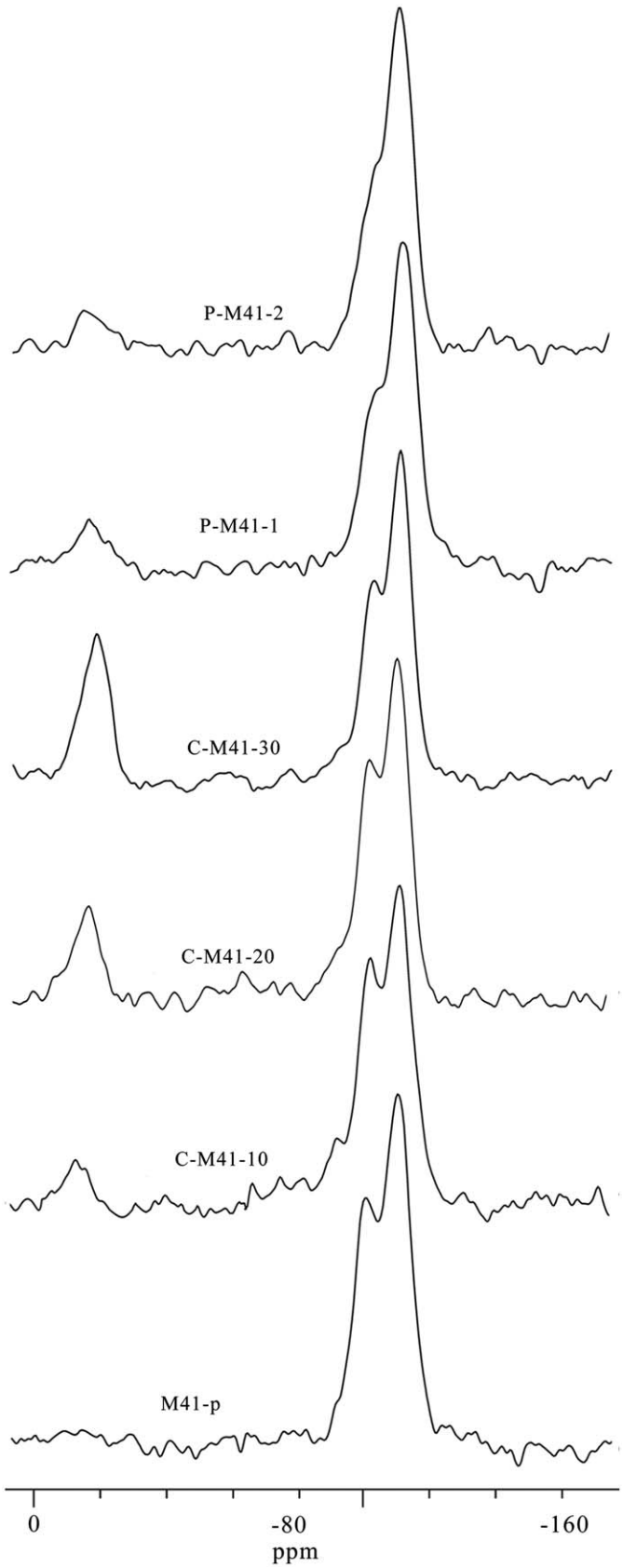

Fig. 5. ^{29}Si MAS NMR spectra of all the samples.

of the M41-p shows three resonances at −111, −101, and −92 ppm corresponding to Q^4, Q^3, and Q^2 species of the silica framework [Q^n=Si(OSi)$_n$(OH)$_{4-n}$, n=2–4] [24,34]. In the case of DMS-modified samples, an additional resonance appears between −15 and −17 ppm, corresponding to D^2 [D^2=(CH$_3$)$_2$Si(OSi)$_2$], indicating that DMS groups are successfully incorporated into the mesostructures [35]. Moreover, the lack of well-defined D^1 signal in all modified samples implies that there is almost no DMS bound to the silica walls through single siloxane bond. Based on the distinct D^2 signal in the ^{29}Si MAS NMR spectra for the DMS-modified samples, the ratios of the relative integrated intensities of $(D^2)/[(D^2)+\sum(Q^n)]$ allow the quantitative assessment of the DMS modification levels. The samples P-M41-1 and P-M41-2 possess close amounts of DMS groups although the two samples were synthesized by adding different amounts of DEDMS. This observation supports the conclusion about the site-selective distribution of DMS groups in the P-M41-1 and the P-M41-2 for the limited amounts of active silanol groups available on the external pore surfaces and pore openings. In contrast, the amounts of DMS groups in the samples synthesized via co-condensation method increase as a function of the amounts of DEDMS used in the preparations. The DMS contents of the C-M41-10, the C-M41-20 and the C-M41-30 are 7.0%, 14.9% and 24.6% (referred to the total silicon), respectively, indicating that about 70%–75% of DEDMS in the initial synthetic system was successfully introduced into the mesostructures.

From the relative integrated intensities, the content of silanol groups (CSG) related to the total silicon of the mesostructures was calculated by using the following equation:

$$CSG = (2Q^2 + Q^3)/(D^2 + Q^2 + Q^3 + Q^4) \quad (1)$$

where the $2Q^2$ represents the hydroxy amounts derived from Q^2 sites. As presented in Table 2, the CSG in DMS-modified samples are associated with not only the DMS modification levels but also the preparation methods. The CSG of the samples prepared via co-condensation method decrease with increasing amounts of DMS incorporated. On the other hand, in comparison to the C-M41-10 with DMS content of 7.0%, the P-M41-1 (or P-M41-2) possessing the close amounts of DMS groups shows a lower CSG, which can be attributed to the reaction between DEDMS and the free (≡Si–OH) and geminal silanol (=Si(OH)$_2$) groups during the post-grafting procedure [36–38].

3.2. Adsorption of ibuprofen

Table 2 displays the amounts (A_t and A_e) of the adsorbed ibuprofen in the mesoporous silica matrices. Compared with the amount of A_t, less amount of A_e is obtained, revealing that a small portion of the adsorbed ibuprofen was removed in the washing process with hexane.

The adsorption experiments show that 1 g of the M41-p can adsorb 0.29 g of ibuprofen (see Table 2), which is in a good agreement with the result reported [6]. The adsorbed ibuprofen amounts of 0.20 and 0.17 g are obtained in the P-M41-1 and the P-M41-2, respectively. It seems that the incorporation of DMS groups prevents the adsorption of ibuprofen. Similarly, the adsorption capacities decrease with increasing DMS modification levels for the samples C-M41-10, C-M41-20 and C-M41-30. However, it should be noted that the samples C-M41-10, P-M41-1 and P-M41-2 with the quite close DMS modification levels of 7%–8% exhibit different adsorption capacities for ibuprofen. Furthermore, the maximal adsorbed ibuprofen amount of 0.32 g is obtained for the C-M41-10, rather than for the M41-p, which suggest that the incorporation of DMS groups is not the dominant factor for the adsorption capacities of these mesoporous silica carriers.

It has been shown that the driving force for the inclusion of ibuprofen inside the channels is the hydrogen bond interaction

Table 2
The ^{29}Si MAS NMR data and the adsorbed ibuprofen amounts of the samples.

Sample	δ (relative integrated intensity (%))					CSG (%)	A_t ($g\,g^{-1}$)	A_e ($g\,g^{-1}$)
	Q^4	Q^3	Q^2	D^2	$D^2/(D^2+\sum Q^n)$			
M41-p	63.3	35.0	1.7	–	–	38.4	0.29	0.22
P-M41-1	60.0	32.2	–	7.8	7.8	32.2	0.20	0.17
P-M41-2	60.8	31.0	–	8.2	8.2	31.0	0.17	0.16
C-M41-10	52.0	32.8	7.5	7.7	7.7	47.8	0.32	0.24
C-M41-20	50.1	29.3	5.7	14.9	14.9	40.7	0.23	0.19
C-M41-30	47.1	25.4	2.9	24.6	24.6	31.2	0.21	0.15

between the carboxyl groups in ibuprofen and the silanol groups on the surface of the mesoporous silica carriers [6,14]. Indeed, the reduction of the adsorption capacities in the P-M41-1 and the P-M41-2 can be well explained by the decrease of CSG in these two samples. The decrease trend of the adsorption capacities in the C-M41-10, the C-M41-20, and the C-M41-30 can be well associated with the different CSG amounts in these samples (see Table 2). Although, the C-M41-10 was modified with a certain amount of DMS groups, its higher CSG should be partly responsible for its higher adsorption capacity than the other samples. However, no linearly proportional dependency of the adsorbed ibuprofen amount on the CSG is observed for all the mesostructures, suggesting that CSG is not the unique factor affecting the ibuprofen adsorption. Obviously, the variations of the pore textural parameters (including the BET surface areas, pore sizes, pore volumes) should also play important roles in the ibuprofen adsorption [14,15].

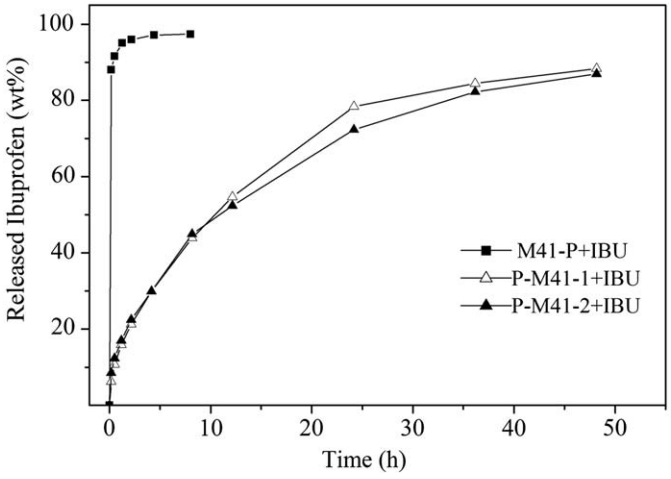

Fig. 6. Ibuprofen release profiles for the ibuprofen impregnated mesostructures of (■) M41-p+IBU, (△) P-M41-1+IBU and (▲) P-M41-2+IBU.

3.3. Drug delivery

The results of the ibuprofen release from the different mesoporous matrices are plotted in Figs. 6–8. It can be seen that the ibuprofen delivery can be controlled to a long release time period by the modification of mesoporous silicas with DMS. Sustained ibuprofen release from DMS-modified mesoporous carriers could be prolonged for release time period up to 100 times than that from pure silica mesoporous carrier under the same release conditions.

The ibuprofen release equilibrium from the M41-p is reached only after about 0.5 h. It should be noted that the ibuprofen delivery rate from the M41-p is much faster than the previous report, where the ibuprofen delivery equilibrium needed tens of hours with the comparable mesoporous matrix [6,14]. The great difference would be attributed to the different forms (disk or powder) of the ibuprofen-impregnated mesostructures and the different release conditions. As depicted in the former researches [6,14], the powders of the ibuprofen-impregnated mesostructures were compressed to disks to evaluate the drug release profiles, and the release experiments were carried out without stirring. Therefore, the powder form of the ibuprofen-impregnated mesostructures and the release processes under a stirring rate of 100 rpm are considered to be very beneficial to accelerating the ibuprofen release rate in this work.

The ibuprofen release rates from the P-M41-1 and the P-M41-2 are much slower than that from the M41-p (see Fig. 6). Even after in vitro assay for 48 h, only about 85 wt% of the impregnated ibuprofen is released from the P-M41-1. In addition, two similar ibuprofen release profiles are observed from the P-M41-1 and the P-M41-2, which would be due to the close DMS modification levels. Since the samples M41-p, P-M41-1 and P-M41-2 possess the close pore volumes, pore sizes, and BET surface areas (see Table 1), it can be concluded that the decrease of the drug delivery rate is caused by the incorporation of DMS groups in the mesostructures. Fig. 7 shows the ibuprofen delivery profiles from DMS-modified mesoporous materials obtained via co-condensation procedure. In the case of the C-M41-10, 60 wt% of the impregnated ibuprofen is released after 1 h of assay, whereas the C-M41-20 and the C-M41-30 need almost 10 and 20 h to reach that percentage, respectively, suggesting that the drug delivery rates decrease with increasing DMS modification levels in the mesostructures. On the other hand, in comparison with the ibuprofen release rate from the M41-p, the decrease of the impregnated ibuprofen release rate could be partly ascribed to the decreasing pore sizes in the modified samples [14].

Generally, in the case of the porosity matrix, release of the impregnated drug occurs through penetration of solvent into the pores of the matrix, and then the drug slowly dissolves into the permeating fluid phase and diffuses from the system along the solvent-filled channels. The modification of mesoporous silicas with DEDMS makes part pore surface attached with hydrophobic DMS groups. Consequently, hydrophobic DMS groups on the surface of the mesostructures retard the penetration of the SBF fluid into the pores and delay the diffusion of drug from the pore systems. Therefore, controlled drug release profiles are obtained from these DMS-modified carriers. For the DMS-modified samples prepared via co-condensation synthesis method, the DMS coverage on the pore surface is increased with increase of the amount of DEDMS in the silica sources. Consequently, the resistance for penetration of solvent into the pores and the diffusion of drug from the pore systems is increased, resulting in the slower drug release rate.

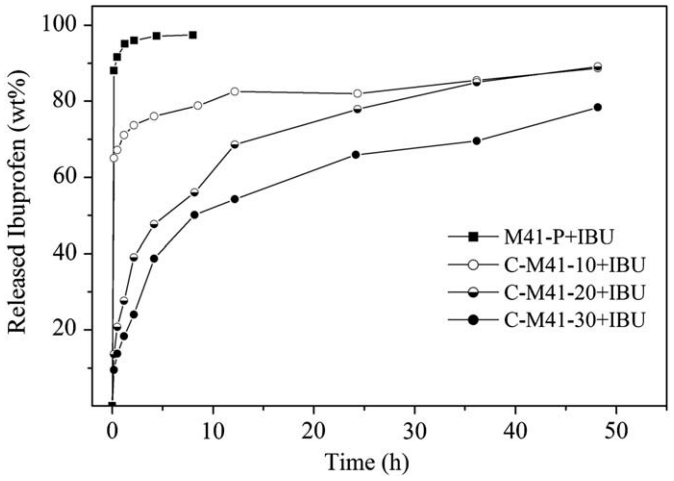

Fig. 7. Ibuprofen release profiles for the ibuprofen impregnated mesostructures of (■) M41-p+IBU, (○) C-M41-10+IBU, (◒) C-M41-20+IBU and (●) C-M41-30+IBU.

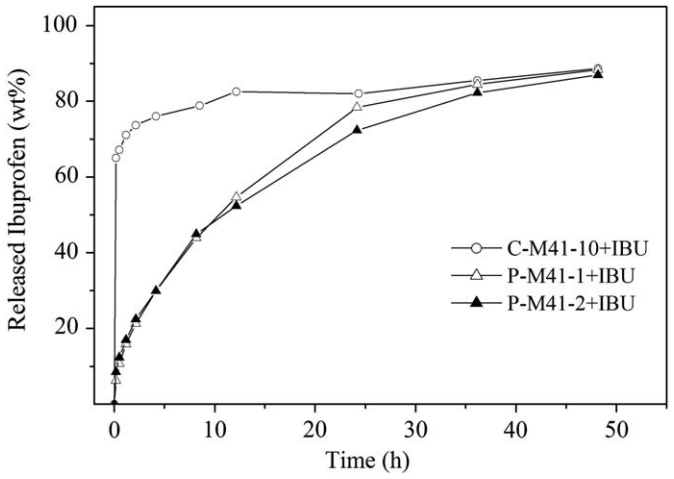

Fig. 8. Ibuprofen release profiles for the ibuprofen impregnated mesostructures of (○) C-M41-10+IBU, (△) P-M41-1+IBU and (▲) P-M41-2+IBU.

Interestingly, the distribution of DMS groups on the pore surfaces of the mesostructures strongly affects the drug release rate (see Fig. 8). The P-M41-1 and the P-M41-2 possess the close DMS modification levels as the C-M41-10, but the ibuprofen release rates from the P-M41-1 and P-M41-2 are much slower than that from the C-M41-10. The organic groups are uniformly distributed on the pore surface of the C-M41-10 synthesized via co-condensation method, whereas DMS groups in the P-M41-1 and the P-M41-2 are mainly distributed on the external pore surfaces and pore openings. Because the external pore surfaces and pore openings are the first inevitable gateway for SBF fluid entering into the pores to take out the drugs, closed-packing of DMS groups on the external pore surfaces and pore openings strongly retard the ibuprofen release, resulting in a long time drug release compared to that from the C-M41-10. Previous reports indicated that the drug delivery rate decreased with the decreasing pore size [14,15]. However, the C-M41-10 with the smallest average pore size exhibits the fastest ibuprofen release rate among the samples C-M41-10, P-M41-1 and P-M41-2, further confirming the discussion mentioned above. Even for the C-M41-20 with higher coverage of DMS groups, the drug release rate is still faster than that from the P-M41-1 and the P-M41-2. The release of 60 wt% of impregnated ibuprofen from the samples C-M41-20, P-M41-1 and P-M41-2 can be obtained after 9.5, 15 and 16 h of assays, respectively. Thus, the site-selective distribution of functional DMS groups derived from the different organic modification methods strongly affected the ibuprofen release rate from mesoporous carrier.

4. Conclusions

The results presented demonstrate the potential application of hybrid mesoporous materials modified with DMS groups for the controlled drug delivery. The ibuprofen adsorption shows that the adsorption capacities of the investigated mesostructures depend mainly on the CSG in the samples. The incorporation of DMS groups in the mesostructures strongly retards the drug delivery rate. Sustained ibuprofen release from DMS-modified mesoporous carriers could be prolonged for release time period up to 100 times than that from pure silica mesoporous carrier under the same release conditions. For mesoporous carriers with close pore size, similar pore structure and synthesized via the same organic modification procedure, the drug release rate could be well modulated by varying DMS modification levels. Moreover, at the close amount of functional DMS groups, the site-selective distribution of functional groups in mesoporous carrier strongly affected the ibuprofen release rate. The post-grafting modified material, where the DMS groups were placed selectively on the pore opening and external pore surface, showed a long release time in comparison with the co-condensation modified material. Essentially, the modification of mesoporous silicas with DEDMS makes the partial pore surfaces attached with the hydrophobic DMS groups. The hydrophobic surface of the mesostructures retards the penetration of solvent into the pore channels, and consequently delays the diffusion of drug from the pore systems, finally, resulting in the effective control of the ibuprofen delivery rate.

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