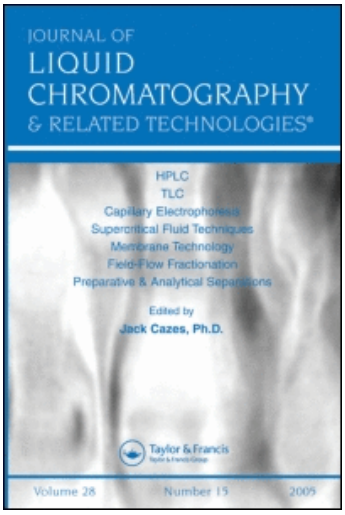

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Study of the Preparation Conditions of Silica Monoliths for HPLC

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ABSTRACT

Preparation conditions of silica monoliths for high performance liquid chromatography (HPLC) were systematically studied. The monoliths eventually formed were examined in many aspects, including mechanical strength, skeleton size, through pore size, BET surface area, pore volume, etc. The mechanism of mesopore formation and parameters affecting mesopore structures, such as cytyltrimethylamine bromide (CTAB) in the reaction mixture and after-treatment with ammonium hydroxide, were also studied in detail.

Key Words: Preparation conditions; Silica monolith; Cytyltrimethylamine bromide (CTAB).

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INTRODUCTION

For nearly two decades, columns packed with spherical silica particles of 5 μm have been widely used in high performance liquid chromatography (HPLC).[1] But, with the progress in separation science and technology, high column efficiency and fast analysis becomes increasingly necessary. Though high column efficiency may be realized by reducing the particle size, it is sometimes not adopted in actual applications due to the accompanying high backpressure. So, particles of 5 μm act as a compromise between column efficiency and backpressure for the time being.

Fast analysis necessitates an increase in velocity of mobile phase, but simultaneously generates an increase in plate height and backpressure. This was partly overcome by perfusion particles whose perfusion pores make convective mass transfer possible. Convective mass transfer can set up a balance between stationary phase and mobile phase quickly, which permits raising the velocity of mobile phase without sharply decreasing the column efficiency, and realizing fast analysis. But, due to the high porosity of perfusion particles, the backpressure is so low that most of the mobile phase flows around the particles rather than through the perfusion pores, diminishing the convection effect. And then, fast analysis is not so practical by using such packings. Therefore, advancement in HPLC seemed to be hindered until the emergence of the silica monolith.

Silica monoliths were introduced as HPLC stationary phases by Nakanishi et al. in the last decade,[2–12] and then it was commercialized by Merck KGaA. The most distinguishing character of silica monolith lies in its bimodal pore structure, namely mesopores and through pores. The former, existing on the surface of the silica skeletons, provide sufficient phase ratio for the chromatographic adsorption–desorption process, while the latter offers a network through which the mobile phase would flow. This novel pore structure enables fast separation while keeping high column efficiency. This has already been demonstrated by Cabrera et al.[13] In their report, baseline separation of three parabens was achieved in 1 min at a flow rate of 9 mL/min of the mobile phase, while the backpressure was just 100 bar. Tanaka also reported the fast separation of nine polypeptides within 5 min.[14] Their research demonstrates that silica monoliths integrate fast analysis as well as high column efficiency, and they naturally attracted increasing attention in recent years.[15,16]

Silica monoliths are synthesized by means of sol–gel technology in which hydrolysis and polycondensation of alkoxysilane take place in the presence of water-soluble polymer. The water-soluble polymer induces phase separation in the process, forming a silica phase and a solvent phase. After washing and calcination, the former becomes the silica skeleton while the latter forms the through pores. Mesopores could be obtained by eroding the silica skeletons with bases. Tanaka et al. have demonstrated that silica monoliths with different

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skeleton sizes and through pore sizes could be acquired by altering the polymer additive.[6] Nakanishi et al. reported that mesopore size of silica monoliths could be tailored by urea treatment, ranging from 3 to 500 nm.[9]

In this paper, we explored the relationship between microstructure of a silica monolith and its mechanical strength, and the effect of cytyltrimethylamine bromide (CTAB), which was widely used in the synthesis of ordered mesoporous materials, on the mesopore formation of the silica monolith. Moreover, the conditions for preparing of silica monoliths were also investigated systematically.

EXPERIMENTAL

Reagents and Materials

Tetramethoxysilane (TMOS) was obtained from the Chemical Factory of Wuhan University (Wuhan, China). Acetic acid, CTAB, methanol, and poly(ethyleneglycol) (PEG, $M_w = 10{,}000$) were purchased from Shanghai General Chemical Reagent Factory (Shanghai, China). Water was distilled from a quartz apparatus. Disposable plastic syringes of 5 mL were purchased from Nanchang Medical Instrumental Company (Jiangxi, China).

Preparation of Silica Monoliths

Silica monoliths were prepared by a sol–gel process as in previous work, with modifications.[6] Generally, TMOS, PEG, acetic acid, and CTAB (when necessary) were mixed together. After the mixture was vigorously stirred at 273 K for 20 min, it was drawn into a syringe and put into an oven at 313 K for reaction. Twenty hours later, gelation took place within the syringe, forming the wet silica gel. After remaining at room temperature for 2 days, the wet gel was washed, sequentially, with water and methanol. Then, it was dried at 313 K for 3 days. Finally, the monolith was placed in a crucible and sintered at 873 K for 2 h. The ratio of the reactants is summarized in Table 1.

Mechanical Strength Evaluation

To evaluate the mechanical strength of the silica monoliths, external pressure experiments were performed. Briefly, silica monoliths were packed together with silica particles (ca. $1 \sim 2\,\mu m$) in a stainless steel column, and then flushed with methanol at $100\,kg/cm^2$ for 24 h. Afterwards, the monoliths were taken out to observe their integrity.

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Table 1. The starting compositions of reactants and assigned codes for monoliths.

TMOS (mL)	PEG (g)	CH_3COOH (0.01 mol/L)	CTAB (g)	Assigned codes
4	1.0	10 mL	—	Monolith 4
5	1.0	10 mL	—	Monolith 5
6	1.0	10 mL	—	Monolith 6-10
7	1.0	10 mL	—	Monolith 7
6	0.8	10 mL	—	Monolith 6-8
6	1.1	10 mL	—	Monolith 6-11
6	1.2	10 mL	—	Monolith 6-12
6	1.0	10 mL	0.7	Monolith CTAB-07
6	1.0	10 mL	2.4	Monolith CTAB-24

Ammonium Hydroxide Treatment

In order to obtain suitable mesopores, some of the monoliths underwent ammonium hydroxide treatment. Usually, the monoliths were put into a container filled with different concentrations of ammonium hydroxide, and then heated to 313 K for 8 h. After washing away the ammonium hydroxide with water, the monoliths were thoroughly dried for measurement of surface area and pore size. Table 2 gives the concentrations of ammonium hydroxide in detail.

Characterization

A Hitachi Model X-650 scanning electron microscope was used for SEM observations (Tokyo, Japan). Slices of cross-section were cut off from the

Table 2. The starting compositions of reactants, treating conditions, and assigned codes for monoliths.

TMOS (mL)	PEG (g)	CH_3COOH (0.01 mol/L)	$NH_3 \cdot H_2O$ (mol/L)	Assigned codes
6	1.0	10 mL	0	Monolith 6-10
6	1.0	10 mL	0.01	Monolith NH_3-001
6	1.0	10 mL	1	Monolith NH_3-1

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monoliths and vapor deposited with gold for scanning electron microscope analysis at 25 kV.

Surface area and pore size analyses were carried out on a Coulter SA 3100 Plus surface area and pore size analyzer (Florida, USA). Briefly, monolithic samples were ground into pieces and heated at 573 K in vacuum for 3 h to remove any physically adsorbed substances before analysis. Nitrogen adsorption–desorption isotherms were determined at 77 K.

RESULTS AND DISCUSSION

The Influence of TMOS Concentration on Mechanical Strength of Silica Monoliths

The silica monoliths, prepared with different ratios of reactants according to the same procedure, are listed in Table 1. Figure 1 shows the photos of Monolith 4, Monolith 5, Monolith 6-10, and Monolith 7 after pressure application. Under an external pressure of about 100 kg/cm^2, Monolith 4 collapsed quickly into small pieces, and Monolith 5 split into two parts; while Monolith 6-10 and Monolith 7 kept their integrity well. The collapse of Monolith 4 indicates that its skeleton was not well interconnected and, thus, could not withstand external pressure. The fracture of Monolith 5 suggests that its skeleton was just partly connected. However, Monolith 6-10 and Monolith 7 could withstand the applied pressure and eventually kept their integrity. Obviously, the skeletons of Monolith 6-10 and Monolith 7 were uniform and highly interconnected. These results illustrated that the concentration of

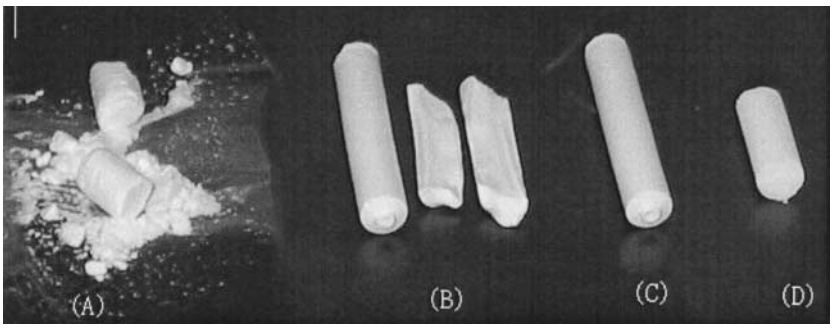

Figure 1. Photographs of monoliths. (A) Monolith 4; (B) Monolith 5; (C) Monolith 6-10; (D) Monolith 7.

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TMOS can affect the mechanical strength of the silica monoliths. From Monolith 4 to Monolith 7, as shown in Table 1, the concentration of TMOS gradually increased. A higher concentration of TMOS, after hydrolysis, could generate more silanol groups in the reaction solution, which would further react and establish a skeleton with a high level of interconnections. Therefore, the mechanical strength of the monolith increases with the increase in TMOS concentration.

Influence of TMOS Concentration on Pore Structure of Silica Monolith

In the above section, we have presented that only Monolith 6-10 and Monolith 7 possessed favorable mechanical strength for HPLC, so the influence of TMOS concentration on pore structures was studied on these two monoliths. When several drops of water were put onto Monolith 6-10 and Monolith 7, simultaneously, it can be found that water was adsorbed by Monolith 6-10, while it made Monolith 7 crack into pieces, as shown in Figure 2.

Ågren et al.[17] have reported that inorganic clusters first formed in TEOS sol, then, the small clusters aggregated together to form large skeletons, which were responsible for micropores and mesopores of the final ceramic material.[17] Likewise, in our experiment, the silica monolith skeletons resulted from condensation of primary particles (namely inorganic clusters) that were produced by hydrolysis of TMOS. Gaps between primary particles are the embryonic forms of micropores or mesopores. Smaller primary particles

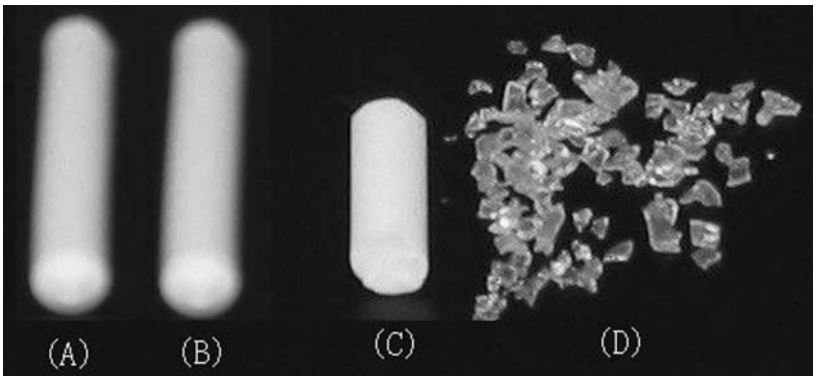

Figure 2. (A) Monolith 6-10 before water treatment; (B) Monolith 6-10 after water treatment; (C) Monolith 7 before water treatment; (D) Monolith 7 after water treatment.

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produce smaller gaps and, thus, smaller initial pores. Since the concentration of TMOS for preparation of Monolith 7 was greater than that for Monolith 6-10, smaller primary particles and smaller pores in Monolith 7 should be obtained.

The gaps between primary particles in the silica monolith are related to the capillary pressure. A small decrease in the gap size would result in a striking increase in capillary pressure. When water was introduced into Monolith 7, the capillary pressure increased and was over the strength limitation of Monolith 7, leading to its collapse. The same observation was found in aerogels. When aerogel was exposed to a moist atmosphere, the small pores in it adsorb water, leading to the increase in capillary pressure and collapse of the aerogel.[18] For Monolith 6-10, gaps between primary particles are relatively large, and the capillary pressure is relatively small. Therefore, Monolith 6-10 could keep its form well when adsorbing water, due to the small capillary pressure.

Influence of PEG Quantity on Mechanical Strength of Silica Monolith

To evaluate the influence of PEG quantity on the mechanical strength of silica monolith, the amount of TMOS and acetic acid were kept constant while PEG quantity increased gradually. The results show that PEG quantity also plays an important role in the mechanical strength of a silica monolith. Under the pressure application, Monolith 6-8 easily became a pile of slices, while Monolith 6-10, Monolith 6-11, and Monolith 6-12 kept their original shapes, as shown in Fig. 3. A similar experiment has been carried out by Nakanishi et al.,[2] but they have not focused research on mechanical strength of the monolith.

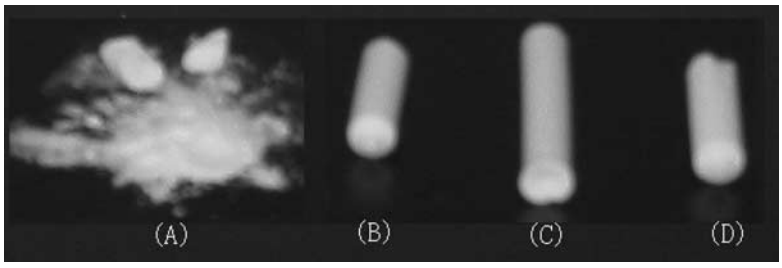

Figure 3. Photographs of monoliths. (A) Monolith 6-8; (B) Monolith 6-10; (C) Monolith 6-11; (D) Monolith 6-12.

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Many researchers have verified that the phase separation takes place during the sol–gel transition reaction.[2–5] In a homogeneous system consisting of polymers and small molecules capable of polymerization, as the polymerization of small molecules progresses, the Gibbs free energy of the system increases. According to the lowest energy principle, phase separation takes place to compensate the increase in Gibbs free energy of the system. In the system we investigated, because of hydrolysis and condensation reaction, the Gibbs free energy of the system increased and induced spinodal decomposition and then caused phase separation. The spinodal decomposition resulted in the formation of transient co-continuous phase domains that coarsened with an elapse of time, and, simultaneously, the inorganic composition underwent sol–gel transition. The gel finally froze the transient co-continuous domains as permanent gel morphology and, thus, formed silica monoliths containing through pores.[2,5] Therefore, the phase separation speed and sol–gel transition speed are responsible for the mechanical strength and morphology of the final monoliths. The increase in PEG quantity reduces the speed of Gibbs free energy increase, resulting in a relatively slow phase separation. The postponement of phase separation leads to the formation of fine silica skeletons that provide abundant cross-linking sites for reaction and they strengthen the monolith. Monolith 6-10, Monolith 6-11, and Monolith 6-12 are in that situation. However, in the case of Monolith 6-8, due to a decrease in the amount of PEG, the phase separation took place more quickly, resulting in formation of a bulky skeleton and bulky solvent phases. Bulky skeletons cannot offer the same degree of cross-link between skeletons as fine skeletons do, leading to low mechanical strength. Therefore, Monolith 6-8 collapsed under the pressure application.

Influence of PEG Quantity on Skeleton Size and Through Pore Size of Silica Monolith

As discussed in the above section, the variation of PEG quantity can influence the mechanical strength and the structure of the silica monolith. So, SEM experiments were performed on Monolith 6-10, Monolith 6-11, and Monolith 6-12 to observe their skeletons and through pores. Figure 4 depicts that skeleton size and through pore size decreased with an increase in PEG quantity. The skeleton size and through pore size of Monolith 6-10 were found to be ca. 2 and 3.5 μm, while those of Monolith 6-11 and Monolith 6-12 were ca. 1.3, 1.6, 1.0, and 1.2 μm, respectively. The variation in skeleton size and through pore size with the varying PEG quantity can be explained by a "phase separation" mechanism.[2–5] As discussed above, the domain size (sum of skeleton size and through pore size) depends on how far it can coarsen before

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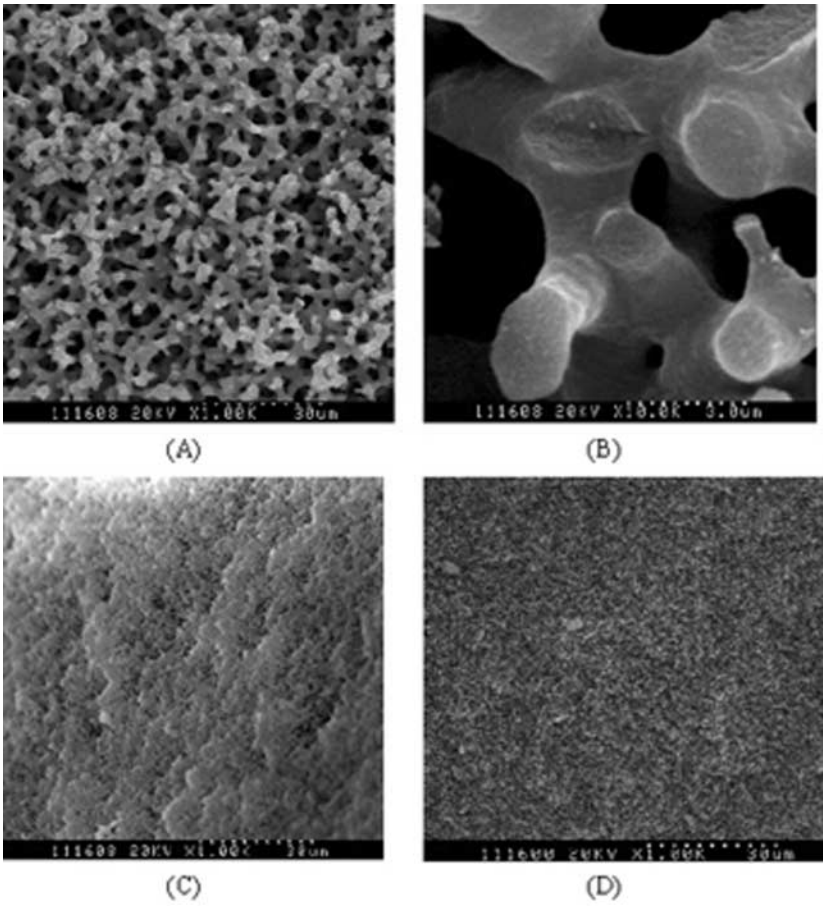

Figure 4. (A) SEM of Monolith 6-10 (×1000); (B) SEM of Monolith 6-10 at high magnification (×10,000); (C) SEM of Monolith 6-11 (×1000); (D) SEM of Monolith 6-12 (×1000).

it is frozen by the final gel. In the present case, the increase in PEG quantity retarded the onset of phase separation, but had little effect on sol–gel transition, indicating that transient co-continuous phase domains were frozen by sol–gel transition in the early stage of phase separation, resulting in the formation of small domain size, and then small skeleton size and through-pore size. So, if the amount of TMOS and acetic acid were kept constant, more PEG quantity caused the smaller skeleton size and through pore size.

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An SEM image of Monolith 6-10 at high magnification is shown in Fig. 4 (B). The clear profile and straight cross section indicate that the monolith has reasonable mechanical strength because, if the monolith were soft, the cross section would be irregular rather than straight.

Effect of CTAB on Mesopore Size of Silica Monolith

Since ordered mesoporous silica was successfully synthesized by using quaternary ammonium surfactants as templates,[19,20] CTAB was widely used in the preparation of different mesoporous oxides.[21] We introduced CTAB in the preparation of monolithic columns and evaluated its effect on mesopore formation of silica monolith.

As shown in Table 1, Monolith CTAB-07 and Monolith CTAB-24 were prepared by addition of CTAB of 0.7 and 2.4 g, respectively, into the reaction mixtures. Their nitrogen adsorption–desorption isotherms are shown in Fig. 5.

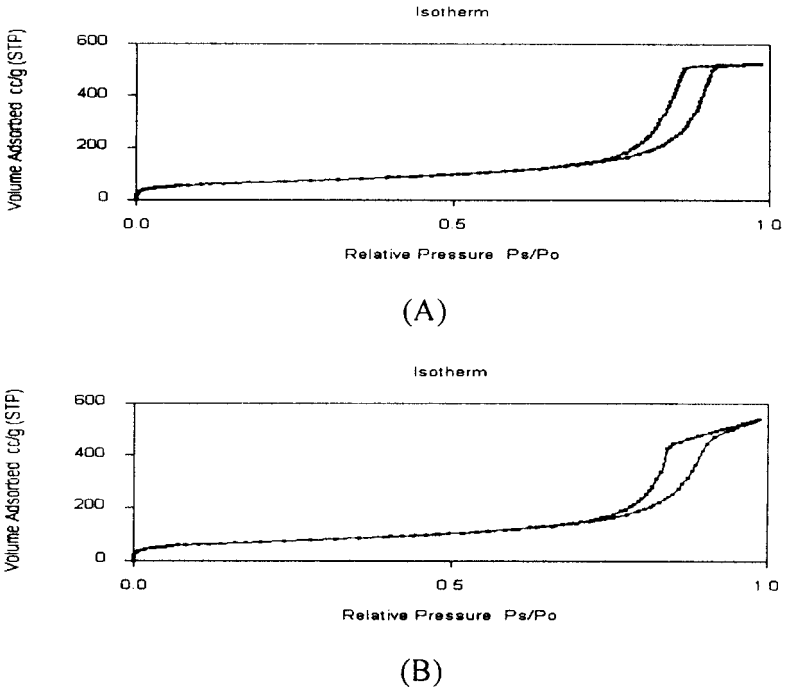

Figure 5. Nitrogen adsorption–desorption isotherms for Monolith CTAB series. (A) Monolith CTAB-07; (B) Monolith CTAB-24.

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It can be seen that they exhibit Type IV adsorption characteristic with H1 hysteresis loop, suggesting the mesopores of the silica monoliths with cylindrical shapes.[22,23] The isotherms show no remarkable adsorption uptake at pressures below 0.05 p_0, suggesting no presence of micropores; and thereafter, a monotonous increase in amount adsorbed until 0.75 p_0, indicating the occurrence of multilayer adsorption; a sharp increase in adsorption represents the emergence of capillary condensation; and finally, a small increase in adsorption until p_0 shows no macropores existing in the monoliths.

Figure 6 shows pore size distribution curves of Monolith 6-10, Monolith CTAB-07, and Monolith CTAB-24. It can be seen that the mean pore size increased by the introduction of CTAB. It is interesting that Monolith CTAB-07 exhibited two peaks, resulting from two kinds of pores with different diameters [Fig. 6(B)]; one similar to that of Monolith 6-10 and another one at higher pore size, while Monolith CTAB-24 gave one peak that is between those of Monolith CTAB-07. These results imply that the mesopore

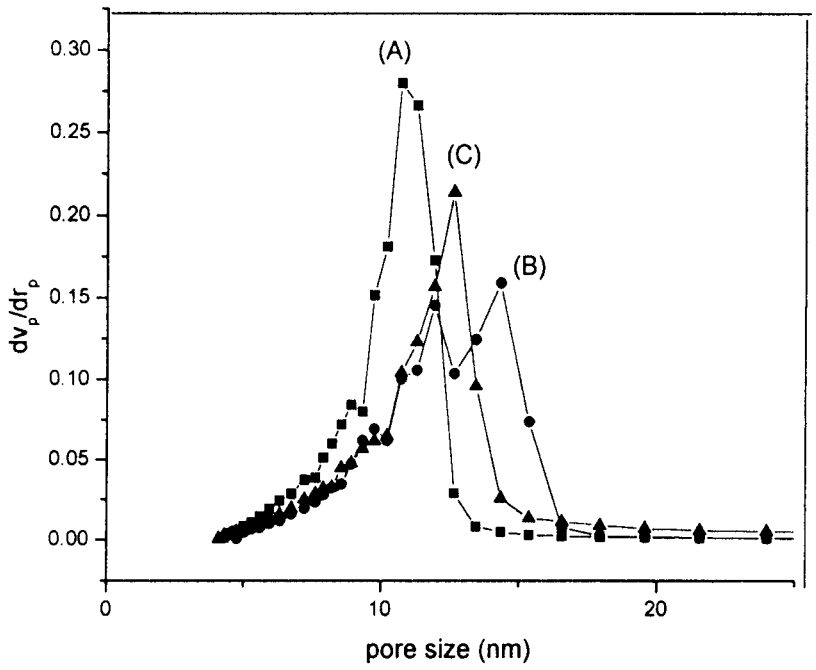

Figure 6. Pore size distribution of Monolith 6-10 and Monolith CTAB series. (A) Monolith 6-10; (B) Monolith CTAB-07; (C) Monolith CTAB-24.

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structure of the silica monoliths can be controlled by the addition of CTAB at different concentrations into the reaction mixture. In the preparation of mesoporous silica film, by using cetyltrimethylammonium chloride (CTAC) as a templating agent, Nagamine et al. found that the pore diameter increased as the ratio of CTAC/tetraethoxysilane (TEOS) decreased. They attributed the result to the intermediation between a silica wall and a CTAC micelle by a water layer whose thickness increases with the increase in the H_2O/CTAC ratio.[24] The mesopore sizes of the resulting Monolith CTABs in our experiment are greater than that of the mesoporous silica film prepared by Nagamine et al., but they have the same varying trend in the mesopore size with the variation in the concentration of CTAB or CTAC. Therefore, the first peak, as shown in Fig. 6(B), similar to that of Monolith 6-10 obtained in the absence of CTAB, is contributed from PEG; while the second peak might be ascribed to the synergetic effect of CTAB and PEG. However, only one broad peak in Fig. 6(C) might result from the overlap of the two peaks due to the shift of the second peak to small pore size.

Influence of Ammonium Hydroxide Treatment on Physical Characteristics of Silica Monolith

In addition to organic additives, base eroding was a common means for improving the pore structures of silica materials. In order to evaluate the effect of base treatment on silica monoliths, Monolith 6-10 was treated with ammonium hydroxide of different concentrations, as listed in Table 2. The isotherms of the base-treated Monolith 6-10 obtained from nitrogen adsorption–desorption (not shown) were similar in shape to those in Fig. 5. But, with the increase in the base concentration, the hysteresis loop shifted to higher relative pressure gradually. Figure 7 shows the pore size distribution curves of the base-treated monoliths. It can be seen that, from Monolith 6-10 to Monolith NH_3-1, the mean pore size shifts to higher values with the increase in the concentration of ammonium hydroxide, accompanied by spread of pore size distribution.

The treatment with ammonium hydroxide induces a dissolution-reprecipitation process in the monolith, as shown in Table 3, which increases the mean pore size and the pore volume, but decreases the specific surface area. These results are consistent with that reported by Tanaka et al.[6–9] However, we used different treatment procedures from those of their work. In their research, the monoliths were treated at the wet gel status by using urea or ammonium hydroxide, while we did it after calcinations, avoiding the deformation of the monolith.

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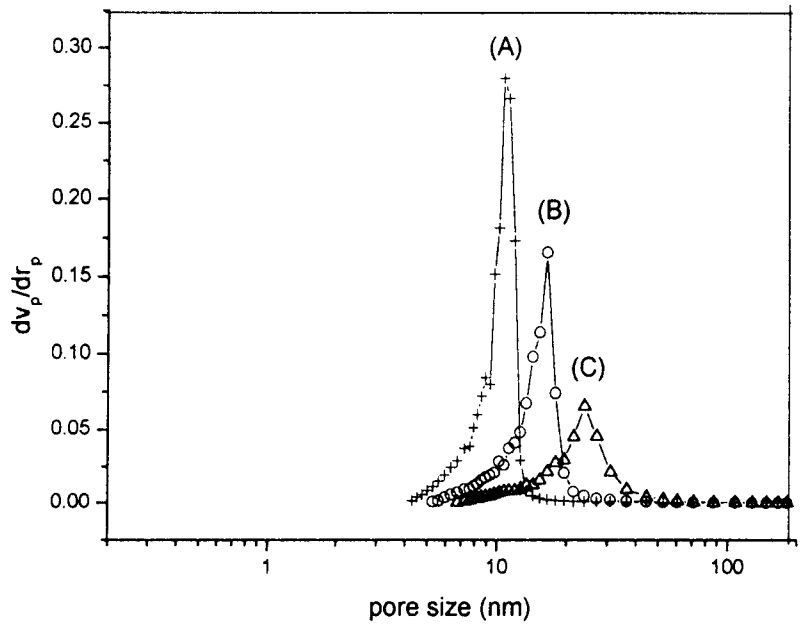

Figure 7. Pore size distribution of Monolith NH_3 series. (A) Monolith 6-10; (B) Monolith NH_3-001; (C) Monolith NH_3-1.

CONCLUSION

Silica monoliths were prepared by sol–gel technology. The results show that monolithic columns suitable for different HPLC applications can be easily obtained by altering the starting composition of reactants or after-synthesis treatment. Methods for increasing the mesopore size were studied. Treatment

Table 3. Characteristics of several monoliths.

Samples (nm)	BET surface area (sq m/g)	Pore volume (mL/g)	Mean pore size
Monolith 6-10	285.84	0.84799	11.32
Monolith NH_3-001	196.05	0.87261	16.56
Monolith NH_3-1	140.86	0.9251	24.00
Monolith CTAB-07	249.57	0.83008	11.95/14.35
Monolith CTAB-24	257.12	0.8445	12.66

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with ammonium hydroxide was a powerful means to increase the mean pore size, but with sacrifice of the pore size distribution. Introduction of additives such as CTAB is another practical way to widen the pore size without notable increase in pore size distribution.

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