Magnetic Fe₃O₄@mesoporous silica composites for drug delivery and bioadsorption

Shanshan Huang, Chunxia Li, Ziyong Cheng, Yong Fan, Piaoping Yang, Cuimiao Zhang, Kuiyue Yang, Jun Lin *

State Key Laboratory of Rare Earth Resource Utilization, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, PR China
Graduate University of the Chinese Academy of Sciences, Beijing 100049, PR China

Abstract

Magnetic Fe₃O₄@mesoporous silica (MS) composites were synthesized by generating Fe₃O₄ nanoparticles in the mesoporous silica matrix using the sol–gel method in nitrogen atmosphere. The mesoporous silica hosts include SBA-15 particles owning highly ordered p6mm mesostructure, siliceous mesostructured cellular foams (MCFs), and fiber-like mesoporous silica (FMS) with unique pore structures. The X-ray diffraction (XRD), transmission electron microscopy (TEM), and N₂ adsorption/desorption results show that Fe₃O₄ functionalized MCFs and FMS possess suitable mesoporous structure for the adsorption of both small-molecular drug and large biomolecules. The biocompatibility tests on L929 fibroblast cells using MTT assay reveal low cytotoxicity of these systems. These Fe₃O₄@mesoporous silica composites show sustained release properties for aspirin in vitro. The release of the aspirin molecules from the pores of the Fe₃O₄@mesoporous silica composites is basically a diffusive process. Fe₃O₄@MCFs and Fe₃O₄@FMS owning larger pore size are good candidates for the adsorption of bovine serum albumin (BSA). These magnetic composites can be potential vectors for drug delivery and bioadsorption.

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1. Introduction

Mesoporous silica based systems for drug delivery, controlled release, and bioseparation have attracted immense interests over the past few years [1–4]. The immobilization of proteins on the porous silica materials is of great potential for applications such as biosensors and biocatalysis [5]. Mesoporous silica materials have high surface areas, tunable pore sizes and volumes, high chemical and mechanical stability, and silanol groups on the surface for modification, which provides a robust framework for deposition and incorporation of guest molecules to give multifunctional capabilities [6,7]. There have been many reports concerning the use of functionalized mesoporous silica materials for the immobilization of enzymes, the enzymatic activities can be retained, and the stabilities also can be improved to some extent [8–10]. Periodic mesoporous organosilicas (PMOS) [11], SBA-15 type silicas [12–14], and organo-functionalized FDU-12 type silicas [15] have been studied as supports for enzymes. Polyelectrolyte encapsulated mesoporous silica composites have been synthesized to enhance the activity of the catalase [16]. Amine-functionalized SBA-15 with Poly (acrylic acid) has been prepared through electrostatic assembly, which has a potential application as a pH-responsive protein delivery system [17].

Magnetic mesoporous silica composite can be a promising vector for enzyme immobilization because it can be easily recovered using an external magnetic field and recycled [18–20]. Magnetically separable mesoporous silica sphere has been prepared to immobilize laccase [21]. Magnetic iron oxide/silica nanocomposites with diverse mesostructures have been synthesized, and lysozyme adsorption capacities of these composites have been studied [22]. The cytotoxicity of the carrier system is a key factor in evaluating the potential of drug delivery system. Only nontoxic carriers are suitable for drug delivery. The biocompatibility of the magnetic silica composites with iron oxide nanoparticles has rarely been discussed.

In this paper, we choose SBA-15 silica with highly ordered p6mm mesostructure, siliceous mesostructured cellular foams (MCFs), and fiber-like mesoporous silica (FMS) with pore system in the range of 10–40 nm as the matrices. These silica materials were magnetically functionalized by generating magnetic Fe₃O₄ nanoparticles onto them via the sol–gel method in nitrogen atmosphere. Fe₃O₄@MCFs and Fe₃O₄@FMS own large pore sizes that provide the possibility to host small-molecular drugs and large biomolecules. The biocompatibility tests on L929 fibroblast cells using MTT assay reveal low cytotoxicity of these systems. These composites have been studied as drug carriers by using aspirin and BSA as model drugs. Aspirin was chosen on the basis of its pharmacological activity and small molecular size, which is suitable for the pore of the mesoporous materials selected. In order to study their adsorption capabilities for large biomolecules, BSA...
was chosen as the model protein based on its comparatively large dimensions (40 × 40 × 140 Å³). BSA has a molecular weight (69 kDa), and its isoelectric point (pI) is around pH 4.7–4.9 [23].

2. Materials and methods

2.1. Chemicals and materials

All chemicals are of analytical reagents (A.R.) and used directly without further purification, including cetyltrimethylammonium bromide (C16TAB, Yili Chemical Co., Ltd., Beijing), (EO)100(PO)270 (EO)220 (P123, Mw = 5800, Aldrich), tetraethoxysilane (TEOS, Yili Chemical Co., Ltd., Beijing), disodium metasilicate (Na2SiO3, Aldrich), ethyl acetate (CH3COOC2H5, Beijing Chemical Reagent Company, Beijing), 1,3,5-Trimethylbenzene (TMB, Sinopharm Chemical Reagent Co., Ltd., Shanghai). Iodine (III) acetylacetone (Fe(acac)3, 99.9%, Aldrich), aspirin (ASP, acetyl salicylic acid, Sigma), and BSA (Sinopharm Chemical Reagent Co., Ltd., Shanghai).

2.2. Synthesis of mesoporous silica materials

SBA-15 silica was synthesized according to the published process [24,25]. Siliceous mesosstructured cellular foams (MCFs) were prepared based on the previous report using TMB as cosolvent [26]. Fiber-like mesoporous silica (FMS) was synthesized based on the previous literature with some modifications [27]. 5.03 g of C16TABr and 2.56 g of Na2SiO3 were dissolved in 90 mL of distilled water to form clear solution, and then 5.0 mL of ethyl acetate was quickly added under stirring. After being stirred for 30 s, the mixture was allowed to stand at room temperature for 5 h. Then the mixture was kept in the conical flask stayed at 363 K for 3 days in an oven. During the aging process, organic vapor was allowed to evaporate through the cap of the flask. The resulting solid was recovered by the filtration of the warm reaction mixture, extensively washed with distilled water and ethanol, and dried at ambient temperature. The template was removed by calcination at 600 °C for 6 h.

2.3. Synthesis of Fe3O4@mesoporous silica composites in nitrogen atmosphere

A typical process used was as follows: 0.4730 g Fe(acac)3 was immersed in mixture of 4.5 mL CH3COOH and 1.5 mL HNO3, then stirred for 4 h to make sure that Fe(acac)3 was completely dissolved to form a solution. Then 0.5 g SBA-15 powder was added into the above solution. After stirring under the room temperature for another 4 h, the mixture was then left stand overnight. The sample was then subjected to heat treatment in nitrogen atmosphere up to a temperature of 500 °C with a heating rate of 4 °C min⁻¹ and maintained at 500 °C for 30 min. The final products obtained gave an iron content lower than that theoretically calculated.

2.4. In vitro cytotoxicity of the Fe3O4@mesoporous silica composite

The in vitro cytotoxicity of the Fe3O4@mesoporous silica composite was determined by MTT (3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) assays, and the Vero cell line was used here. L929 fibroblast cells (5000–6000) in 200 µL media well per well were plated in a 96-well plate for 24 h to allow the cells to attach and then exposed to different concentrations of the Fe3O4@mesoporous silica composite (1.5625, 3.125, 6.25, 12.5, 25.0, 50.0, and 100.0 µg mL⁻¹) for 24 h in 5% CO2 at 37 °C. At the end of the incubation time, the medium containing the Fe3O4@mesoporous silica was removed and MTT solution (20 µL, diluted in a culture medium to a final concentration of 5 mg/mL) was added. After incubation at 37 °C in the dark for 4 h, 100 µL of acidified isopropanol was added to each well, and the absorbance was monitored with a microplate reader at a wavelength of 570 nm. Averages and standard deviations were based on four samples, and all tests were performed in triplicate. The cell viability was calculated using the following equation: cell viability (%) = [Acondition/Acontrol] × 100.

2.5. Aspirin loading and protein adsorption

Typically, 400 mg of sample was suspended in 30 mL ether solution of aspirin with a concentration of 40 mg mL⁻¹ aspirin at room temperature under stirring for 48 h in a sealed flask to prevent the evaporation of the ether. After loading of the drug, the sample was collected by centrifugation, washed gently by ether, and dried at 60 °C under vacuum for 10 h. The amount of aspirin loaded was assessed by thermogravimetry (TG) analysis. 100 mg of the obtained samples was compressed into disk for drug release.

Protein adsorption experiments were carried out by contacting 50 mg of silica composites with 50 mL of solution containing 1 mg mL⁻¹ BSA in pH 4.7 and 50 mM acetate buffer. The adsorbent and solution were shaken at 160 rpm and 20 °C until equilibrium was reached. The amount of protein adsorbed was calculated by subtracting the amount found in the supernatant liquid after adsorption from the amount of protein present before the addition of the adsorbent Fe3O4@mesoporous silica, by UV absorption at 278 nm for BSA. The adsorbed amount of BSA was calculated according to the following equation: q = V(C0 − C)/W, where q is the equilibrium adsorbed amount in the particles, C0 and C are the protein concentrations at initial and equilibrium solution, respectively, V is the volume of the initial protein solution, and W is the weight of the adsorbent.

2.6. Aspirin and BSA release in vitro

After drug loading, the ASP-loaded disks were soaked into 30 mL simulated body fluid (SBF, pH = 7.4) maintained at 37 °C. In order to avoid the limitation of the delivering rate by external diffusion constraints, continuous mild stirring was maintained during the assays. At predetermined time intervals, 0.5 mL of the sample was withdrawn and immediately replaced with an equal volume of preheated SBF buffer to keep the volume constant. The withdrawn samples were properly diluted and monitored by UV–vis spectrophotometer at a wavelength of 296 nm. For the release of BSA, protein–loaded composites from the above step were immersed in 20 mL of phosphate buffer solution (pH ~ 7.3). At selected time points, slurries were centrifuged and the released protein in the supernatant was measured by UV absorption at 278 nm.

2.7. Characterization

X-ray power diffraction (XRD) was performed on a Rigaku Dmax 2500 diffractometer using Cu Kα radiation (λ = 0.15405 nm). Fourier transform infrared (FTIR) spectra were recorded on a Bruker Vertex 70 IR spectrophotometer using KBr pellet technique. N2 adsorption/desorption isotherms were obtained at 77 K on a NOVA-1000 apparatus. The specific surface areas were calculated based on the Brunauer–Emmett–Teller (BET) method, and the pore size distributions were derived from the desorption branches of the isotherms by the Barrett–Joyner–Halenda (BJH) method. The morphology of the sample was inspected using a field emission
scanning electron microscope (FESEM, XL30, Philips). Transmission electron microscopy (TEM) was obtained from a FEI Tecnai G2 S-Twin transmission electron microscope with a field emission gun operating at 200 kV. Inductively coupled plasma (ICP) measurement (Thermo iCAP 6000 ICP-OES) was performed on the sample to determine the exact loading level of iron oxide. Magnetization measurements were performed on an MPMS-XL-7 SQUID (superconducting quantum interference device) magnetometer. Thermogravimetry (TG) was carried out between 40 and 800 °C in air using a Perkin Elmer 7 Series Thermal Analysis System. The UV–vis absorption spectra values were measured on a U-3310 spectrophotometer.

3. Results and discussion

3.1. XRD analysis

Fig. 1 shows the low-angle XRD patterns of the silica hosts and Fe3O4 loaded samples. SBA-15 (Fig. 1A) exhibits a strong (100) diffraction peak with two small (110) and (200) peaks associated with a 2D hexagonal mesostructure (p6mm), confirming the highly ordered mesostructure of the silica host [24,25]. MCFs (Fig. 1B) display an obscure (100) peak that indicates the presence of a mesoporous structure with less order [21]. For FMS (Fig. 1C), the XRD patterns show one (100) peak for silica matrix and iron oxide loaded sample, which indicates that these samples possess less ordered mesopores. After the generation of iron oxide nanoparticles, the characteristic diffraction peaks of the pristine silica still exist, while the diffraction intensity decreased apparently. These results indicate that the mesoporous phase of the composites has been maintained, while the integrity of the mesopore structure was affected by the incorporation of iron oxide nanoparticles.

Fig. 2 shows the wide-angle XRD patterns of iron oxide loaded samples. The broad band centered at 2θ = 22° can be assigned to the characteristic reflection from amorphous SiO2 (JCPDS 29-0085). The wide-angle XRD patterns show (220), (311), (440) diffraction peaks, which are in accordance with that of magnetite (Fe3O4, JCPDS 19-0629). The broad nature of the XRD patterns can be ascribed to the small size of Fe3O4 [28].

3.2. SEM and TEM

Fig. 3 shows the SEM images of calcined silica and the corresponding Fe3O4 loaded samples. The SBA-15 exhibits oval morphology about 500 nm in width, with length about 1 μm (Fig. 3a). MCFs (Fig. 3b) display an obscure (100) peak that indicates the presence of a mesoporous structure with less order [21]. For FMS (Fig. 3c), the XRD patterns show one (100) peak for silica matrix and iron oxide loaded sample, which indicates that these samples possess less ordered mesopores. After the generation of iron oxide nanoparticles, the characteristic diffraction peaks of the pristine silica still exist, while the diffraction intensity decreased apparently. These results indicate that the mesoporous phase of the composites has been maintained, while the integrity of the mesopore structure was affected by the incorporation of iron oxide nanoparticles.

Fig. 2. Wide-angle XRD patterns of Fe3O4@SBA-15 (a), Fe3O4@MCFs (b), Fe3O4@FMS (c).

Fig. 1. Low-angle XRD patterns of SBA-15 (A), MCFs (B), FMS (C): (a) calcined silica matrices, (b) Fe3O4 loaded samples.
Fig. 3. SEM images of the calcined SBA-15 (a), Fe₃O₄@SBA-15 (b), MCFs (c), Fe₃O₄@MCFs (d), FMS (e), Fe₃O₄@FMS (f).

Fig. 4. TEM images of SBA-15 (a), Fe₃O₄@SBA-15 (b), MCFs (c), Fe₃O₄@MCFs (d).
Fig. 5. TEM images of FMS (a) ordered pores, (b) disordered pores, Fe\textsubscript{3}O\textsubscript{4}@FMS (c and d).

Fig. 6. N\textsubscript{2} adsorption/desorption isotherms of SBA-15 (A), MCFs (B), and FMS (C): (a) calcined samples, (b) Fe\textsubscript{3}O\textsubscript{4}-loading samples, (c) ASP-loaded samples.
of mesoporous cellular foams (MCFs) reported previously [Fig. 4c] [26]. As shown in Fig. 5a and b, FMS shows ordered arrays of mesopore channels and disordered foam like pores. The Fe₃O₄ nanoparticles appear as dark spots inside the pore channels and on the outer surface of the silica (Figs. 4b, d and 5c, d), while the porous structure of the silicas was retained after the introducing of the Fe₃O₄ nanoparticles.

3.3. N₂ adsorption/desorption

The nitrogen adsorption/desorption isotherms and the corresponding pore size distributions of silica hosts and Fe₃O₄@MS are shown in Figs. 6 and 7, respectively. The data of the BET surface area, pore volume, and pore size of the corresponding samples are listed in Table 1. The isotherms of SBA-15 and MCFs (Fig. 6) exhibit type IV isotherms and steep hysteresis loops of type H1 at high relative pressures, which is typical for mesoporous materials that exhibit capillary condensation and have large pore sizes with narrow size distributions [26]. The pore size distribution curves shown in Fig. 7 further confirm that the pore sizes of SBA-15 and MCFs are 7.7 nm and 16.7 nm, respectively. For FMS, the isotherm displays a pronounced hysteresis loop, and the pore size distribution plot shows pores in the range of 2–4 nm and larger pores ranging from 10–40 nm (Fig. 7C), which is consistent with the TEM results. It could be observed that the iron oxide loaded samples have the similar nitrogen sorption curves compared with their corresponding silica hosts. Therefore, it could be deduced that the pore dimensions of the silica matrices still remained. These results coincide with the XRD results, while the adsorption capacities decreased due to the incorporation of the Fe₃O₄ nanoparticles. It can be seen clearly that the surface area and pore volume reduced markedly after the generation of Fe₃O₄ particles. The pore volume values of the composites, which are 0.89, 1.42, and 1.01 cm³/g for Fe₃O₄@SBA-15, Fe₃O₄@MCFs, and Fe₃O₄@FMS, respectively, show that a high internal volume is available for drug storage. The pore volume values decreased further after the adsorption of aspirin, which confirmed the introduction of the drug molecules into the pores of the composites.

3.4. Magnetic properties

The magnetic properties of Fe₃O₄ loaded composites were characterized using a superconducting quantum interference device (SQUID) magnetometer with fields of up to 5 T. The hysteresis

![Figure A](imageA.png)

![Figure B](imageB.png)

![Figure C](imageC.png)

Fig. 7. Pore size distribution curves of SBA-15 (A), MCFs (B), FMS (C): (a) calcined samples, (b) Fe₃O₄-loading samples, (c) ASP-loaded samples.

Table 1

<table>
<thead>
<tr>
<th>Samples</th>
<th>$D_{pore}$ (nm)</th>
<th>Pore volume (cm³/g)</th>
<th>$S_{BET}$ (m²/g)</th>
<th>Aspirin loading (%)</th>
<th>Fe loading (%)</th>
<th>BSA loading (mg/g)</th>
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<tr>
<td>SBA-15</td>
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<td>1.25</td>
<td>646</td>
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<td>Fe₃O₄@SBA-15</td>
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<td>0.89</td>
<td>435</td>
<td></td>
<td>11.80</td>
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<td>ASP–Fe₃O₄@SBA-15</td>
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<td>0.67</td>
<td>332</td>
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<tr>
<td>MCFs</td>
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<td>2.13</td>
<td>508</td>
<td></td>
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<tr>
<td>Fe₃O₄@MCFs</td>
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<td>1.42</td>
<td>379</td>
<td></td>
<td>12.44</td>
<td>305</td>
</tr>
<tr>
<td>ASP–Fe₃O₄@MCFs</td>
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<td>0.36</td>
<td>140</td>
<td>33%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FMS</td>
<td>2–4, 10–40</td>
<td>1.03</td>
<td>642</td>
<td></td>
<td>12.87</td>
<td>191</td>
</tr>
<tr>
<td>Fe₃O₄@FMS</td>
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<td>1.01</td>
<td>411</td>
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<tr>
<td>ASP–Fe₃O₄@FMS</td>
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<td>0.57</td>
<td>220</td>
<td>22%</td>
<td></td>
<td></td>
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</table>

loops of these samples were registered at temperature of 300 K, as shown in Fig. 8. The ICP results reveal that the Fe ratio of these samples was 11.80%, 12.44%, and 12.87% for Fe$_3$O$_4$@SBA-15, Fe$_3$O$_4$@MCFs, and Fe$_3$O$_4$@FMS, respectively. The curves of Fe$_3$O$_4$@MCFs and Fe$_3$O$_4$@FMS present a very small hysteresis loop, which indicate ferromagnetic characteristic at room temperature. The Fe$_3$O$_4$@MCFs shows coercivity (Hc = 35 Oe, 1 Oe = 1000/4π Am$^{-1}$) and remanence (Mr = 0.20 emu/g). The Fe$_3$O$_4$@WMS exhibits a low coercivity (Hc = 7.2 Oe) and remanence (Mr = 0.13 emu/g). The magnetization curve of Fe$_3$O$_4$@SBA-15 presents negligible coercivity and remanence, which indicates that the sample shows superparamagnetic property. Fig. 9 displays the ZFC (zero-field cooling) and FC (field cooling) curve of Fe$_3$O$_4$@SBA-15. It can be seen that the ZFC magnetization showed a broad maximum at about 180 K, which is a typical characteristic of superparamagnetic behavior, and the FC magnetization increased with the decreasing temperature. The broad peak of ZFC curve reveals the wide range of particle size distribution [29]. The saturation magnetization of these composites is 3.86 emu g$^{-1}$ (Fe$_3$O$_4$@SBA-15), 5.12 emu g$^{-1}$ (Fe$_3$O$_4$@MCFs), and 5.78 emu g$^{-1}$ (Fe$_3$O$_4$@FMS), respectively. It is important to note that the magnetic moments are given per total mass of the sample (emu/g), that is, the total weight of iron oxide and silica used [30]. The images shown in Fig. 10 demonstrate that the composite can be separated from the solution under the external magnetic field.

3.5. FT-IR spectra

FT-IR spectra are demonstrated to understand the change of the functionalized process and the interaction between the drug and composites. The FTIR spectra of silica hosts, Fe$_3$O$_4$-loading, and ASP-loading samples were similar, so only the spectra of MCFs and its corresponding Fe$_3$O$_4$-loaded and ASP-loaded magnetic samples are shown in Fig. 11. For the Fe$_3$O$_4$@MCFs, a band at 561 cm$^{-1}$ ascribed to the Fe–O was found after the formation of iron oxide nanoparticles [31]. After the loading of the aspirin molecules, the phenyl system band from aspirin at 666, 1456, and 1485 cm$^{-1}$ was detected. The carboxylate band at 1397 and 1565 cm$^{-1}$ was detected, which illuminates that proton transfer from the carboxylic acid of aspirin to silanol group and iron oxide on the silica surface has occurred. A carboxylic acid band at 1754 cm$^{-1}$ is still observed in the spectrum of Fe$_3$O$_4$ loaded samples, suggesting that the aspirin has not decomposed [32,33].

3.6. In vitro cytotoxicity of the Fe$_3$O$_4$@mesoporous silica composites

In order to evaluate the biocompatibility of the storage and release properties, an MTT assay was performed on these Fe$_3$O$_4$@mesoporous silica composites. This method is based on the formation of dark red formazan by the metabolically active cells after their exposure to MIT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide). Cell viability is directly proportional to the amount of formazan produced monitored by the absorbance

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![Fig. 8](image8.png)

**Fig. 8.** Magnetization curves as a function of applied magnetic field measured at 300 K. Fe$_3$O$_4$@SBA-15 (a), Fe$_3$O$_4$@MCFs (b), Fe$_3$O$_4$@FMS (c).

![Fig. 9](image9.png)

**Fig. 9.** Temperature dependence of ZFC and FC magnetic moments of Fe$_3$O$_4$@SBA-15 measured at an applied field of 100 Oe.

![Fig. 10](image10.png)

**Fig. 10.** Photograph of magnetic separation using Fe$_3$O$_4$@MCFs loaded with BSA.

![Fig. 11](image11.png)

**Fig. 11.** FT-IR spectra of (a) MCFs, (b) Fe$_3$O$_4$@MCFs, (c) ASP–Fe$_3$O$_4$@MCFs, (d) aspirin.
at 570 nm. The magnetic composites were delivered over a wide range of dosages (1.5625–100 μg/mL/C0). Fig. 12 shows the cell viability of L929 fibroblast cells incubated with the composites. The difference in cell viabilities after 24 h of incubation is negligibly small, and there is little cytotoxicity after incubation at a high concentration of 100 μg/mL/C0. These results suggest that these Fe3O4@mesoporous silica composites have good biocompatibility.

3.7. Aspirin and BSA adsorption

The TG curves of the aspirin loaded Fe3O4@mesoporous silica are shown in Fig. 13. Fe3O4@SBA-15 with a BET surface area of 435 m2/g and pore volume of 0.89 cm3/g has an ASP-loading amount of 13 wt.%. Fe3O4@MCFs with surface area of 379 m2/g and the largest pore volume of 1.42 cm3/g has a biggest uptake amount of 33 wt.%. Fe3O4@FMS owning a BET surface area of 411 m2/g and a large pore volume of 1.01 cm3/g has a drug loading amount of 22 wt.%. The drug loading degree was affected by the BET surface area, pore size, pore geometry, pore volume, and surface properties of the composites [34–36].

The results of the protein adsorption of the materials are shown in Table 1 and Fig. 14. For adsorption measurements, pH 4.7 (near the pI of BSA) was chosen because the adsorption capacity can be maximized near the pI [23,37–39]. Fe3O4@SBA-15 with an average pore size of 8.2 nm exhibits a low adsorption capacity of BSA in the first 1 h (64 mg/g composite), and then the BSA molecules desorbed from the composite. The dimensions of the BSA molecule

Fig. 12. Cell viability of L929 fibroblast cells incubated with (A) Fe3O4@SBA-15, (B) Fe3O4@MCFs, (C) Fe3O4@FMS.

Fig. 13. TG curves of (a) Fe3O4@SBA-15, (b) Fe3O4@FMS, (c) Fe3O4@MCFs, (d) ASP–Fe3O4@SBA-15, (e) ASP–Fe3O4@FMS, (f) ASP–Fe3O4@MCFs.

Fig. 14. BSA adsorption curves of (a) Fe3O4@MCFs, (b) Fe3O4@FMS.
are reported to be $40 \times 40 \times 140 \text{ Å}^3$. Since the largest dimension of BSA is larger than the average pore size of Fe$_3$O$_4$@SBA-15, the BSA molecules can be expected to be excluded from the pores, and the small amount adsorbed in the first 1 h is expected to be located on the external surface of the particle or at the pore mouths. Fe$_3$O$_4$@FMS owning pore system in the range of 10–40 nm shows BSA adsorbed amount of 191 mg/g composite. The saturation capacity for Fe$_3$O$_4$@MCFs with larger mesopores (15.0 nm) reaches 305 mg/g composite. For Fe$_3$O$_4$@FMS and Fe$_3$O$_4$@MCFs owning bigger pore size, larger amount of BSA molecules entered into the mesopore of these composites. As shown in Fig. 14, Fe$_3$O$_4$@MCFs shows a faster adsorption rate and higher adsorption amount due to its relatively large pore size and pore volume.

3.8. Aspirin and BSA release

Fig. 15A displays the release behavior of aspirin from these magnetic drug delivery systems in simulated body fluids over 60 h. According to the previous reports [35,36,40–42], the drug-charged material was confirmed in disk to improve the drug release process. When the powered material is charged with drug molecules, the compression of the drug-matrix mixture leads to a narrowing of the pore cavity. This could induce a slow release of drug molecules due to diffusion constraint. All the composites show sustained release property. The drug release rate was affected by the mesopore structure, morphology, and surface property of these composites. The Fe$_3$O$_4$@MCFs with largest average pore size exhibit fastest release rate, the initial burst release reaches 29% in first 1 h and 80% in 48 h. The initial burst release is mainly caused by the drug molecules dispersed on the outer surface and near the entrance of the channel of the composites. The release rates become slower afterward, probably due to the diffusion of aspirin molecules from the channels of these composites. Fe$_3$O$_4$@SBA-15 with narrow pore size shows a relatively slower release rate (70% in 48 h), comparing with Fe$_3$O$_4$@FMS owning disordered pore system in the range of 10–40 nm (77% in 48 h). Furthermore, the kinetics of the drug release by the Higuchi model showed a good linear fitting between the amount of guest released and the square root of the release time (shown in the inset in Fig. 15A), indicating that the release of the aspirin molecules from the pores of the Fe$_3$O$_4$@mesoporous silica composite is consistent with a Fickian diffusion mechanism. Because only part of aspirin molecules interact with pore wall through the hydrogen bonding, which is so weak that aspirin molecules can be relatively easy to be cleaved from the carriers. Most of aspirin molecules loaded in the Fe$_3$O$_4$@mesoporous silica composites are physical state. Therefore, the release of the aspirin molecules from the pores of the Fe$_3$O$_4$@mesoporous composite is basically a diffusive process.

Protein carrier is required to have appropriate release kinetics in addition to having high capacity of protein adsorption. Protein should be released continually over a certain period of time during the healing process. As shown in Fig. 15B, the releases of protein are at relative low rate, $\leq$50% in 48 h. BSA–Fe$_3$O$_4$@MCFs shows faster release rate. The initial burst release is caused by the proteins adsorbed on exterior surface. As proteins are also confirmed to enter into mesoporous structure, the entrapped proteins diffuse slowly from the pores of the composites. This results in the sustained release kinetics over a certain period of time.

4. Conclusions

In this article, magnetic mesoporous silica/iron oxide composites were synthesized by generating magnetic Fe$_3$O$_4$ nanoparticles into the mesoporous silica matrices using the sol–gel method in nitrogen atmosphere. Magnetic measurements reveal that these composites show sufficient reactivity under external magnetic field. These composites possessing various morphology and mesopore structure were studied as vectors for drug delivery system. The biocompatibility tests on L929 fibroblast cells using MTT assay reveal low cytotoxicity of these systems. These composites show sustained release behaviors for aspirin in vitro. The release of the aspirin molecules from the pores of the Fe$_3$O$_4$@mesoporous silica composites is basically a diffusive process. For the adsorption and release of BSA, Fe$_3$O$_4$@MCFs with average pore diameter of 15.0 nm demonstrates the highest adsorption amount and faster release rate. Fe$_3$O$_4$@MCFs and Fe$_3$O$_4$@FMS can be candidates for the adsorption and carriers for large biomolecules. These magnetic composites can be potential vectors for drug delivery and bioadsorption.

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Fig. 15. (A) Cumulative release of aspirin from (a) ASP–Fe$_3$O$_4$@SBA-15 (–○–), (b) ASP–Fe$_3$O$_4$@MCFs (–□–), (c) ASP–Fe$_3$O$_4$@FMS (–△–). Inset: the Higuchi square root of time plot. (B) Cumulative release of BSA from (a) BSA–Fe$_3$O$_4$@MCFs (–○–), (b) BSA–Fe$_3$O$_4$@FMS (–▲–).