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Luminescent Porous Silica Fibers as Drug Carriers

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Abstract: Luminescent and porous silica fibers have been successfully prepared by using the electrospinning process. The obtained multifunctional silica fibers, which possess a porous structure and display blue luminescence, can serve as a drug delivery host carrier, using ibuprofen (IBU) as a model drug, allowing the investigation of storage/release properties. Scanning electron microscopy (SEM), transmission electron microscopy (TEM), Fourier-transform infrared spectroscopy (FT-IR), N_2 adsorption/desorption, photoluminescence (PL) spectra, and kinetic decay were used to characterize the structural, morphological, and optical properties of the as-obtained samples. The results reveal that the multifunctional silica materials exhibit an irregular porous structure, and display a fiberlike morphology with dimensions of several hundred nanometers in width and several millimeters in length. The obtained silica fibers exhibit an intense broad bluish emission, which might be attributed to impurities and/or defects in the silica fibers. The IBU-loaded silica fiber system shows blue luminescence under UV irradiation and controlled release behavior for IBU. In addition, the emission intensities of silica fibers in the drug carrier system vary with the released amount of IBU, thus allowing the drug release to be easily tracked and monitored by the change of the luminescence intensity.

Keywords: drug delivery · electrospinning · luminescence · porous materials · silica

Introduction

In recent years, increasing attention has been devoted to novel drug storage/release systems. These display many advantages compared with conventional forms of dosage, such as enhanced bioavailability, greater efficacy and safety, controlled and prolonged release time, and predictable therapeutic response.[1–8] In general, an efficient drug delivery system can not only deliver the therapeutic drugs to the targeted cells or tissues but also maintain the optimum concentration and rational toxicity of drugs in precise sites of the organs, which can improve therapeutic efficiency and reduce toxicity.[1,9–11] To date, many different types of systems have been successfully employed for the sustained/controlled delivery of drugs, such as biodegradable polymers,[1] hydroxyapatite (HAp),[12,13] calcium phosphate cement (CFC),[14,15] xerogels,[16] and hydrogels.[17,18] Porous silica has also been investigated as a drug carrier for the delivery of a variety of pharmaceutical molecules because of its stable porous structure, tunable pore size, high specific surface area with abundant Si–OH active bonds on the pore walls, nontoxic nature, well-defined properties, and good biocompatibility.[19–22] Up to now, a large variety of drug storage/release systems based on porous silica materials has been reported.[6,21, 23–41]

Photoluminescent porous materials have potential applications in the fields of drug delivery and disease diagnosis and therapy.[42–47] This is because these controlled drug delivery systems not only have high pore volumes for the storage and delivery of drugs, but also display photoluminescence, which can be monitored to evaluate the efficiency of the drug release. Recently, a class of stable, efficient, and environmentally friendly self-activated luminescent materials (without rare-earth or transition-metal ions as activators, and for which the emission is induced by the defects or impurities in the host lattices) has been prepared by various synthesis routes.[48–52] These novel self-activated inorganic materials may be promising as fluorescent materials for bio-

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detection due to their good optical properties, high chemical stability, and nontoxicity. Therefore, the design and development of self-activated luminescent silica materials with nano-sized and porous characteristics will play a key role in achieving this endeavor.

The electrospinning technique was developed in 1934 for the synthesis of 1D nanomaterials.[53] Electrospinning is an effective and simple method for preparing nanofibers from a wide variety of materials,[54–60] such as polymers, inorganic, and organic–inorganic hybrid compounds. It is a process that uses the strong electrostatic force that occurs when a high static voltage is applied to a polymer solution placed in a container with a millimeter diameter nozzle. Under an applied electrical force, the polymer solution is ejected from the nozzle. After the solvents have been evaporated during the course of jet spraying, the nanofibers are collected. Recently, we reported the preparation of quasi-one-dimensional beltlike and one-dimensional fiberlike HAp materials by doping Eu^{3+} during the synthesis of porous HAp by an electrospinning process. We mainly focused on the investigation of the luminescence and drug storage/release properties of the resulting multifunctional materials (bioactive, luminescent, porous).[61] Although some silica materials have been prepared by electrospinning,[62,63] to the best of our knowledge, porous silica fibers functionalized with photoluminescence (PL) by an electrospinning process have never been really tested as drug storage/release systems. As a continuation of our research on drug storage/release,[64,65] herein we describe the preparation of multifunctional silica materials as drug carriers by using the electrospinning method. These materials have a porous structure and display blue luminescence properties.

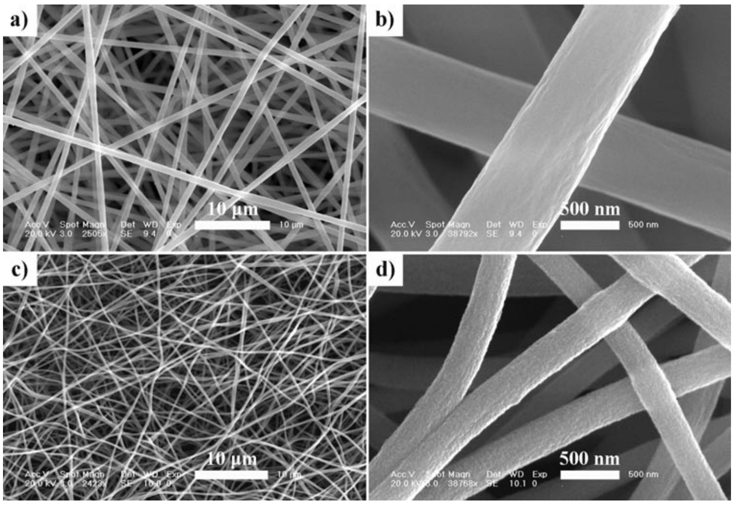

Figure 1. SEM images of the as-formed precursor for silica samples and those annealed at 600 °C. a, b) Precursor for silica fibers, c, d) silica fibers.

As one of the most widely used non-steroidal analgesic and anti-inflammatory drugs, ibuprofen (IBU) has been extensively studied as a model drug for sustained and controlled drug delivery because of its short biological half-life (2 h), good pharmacological activity, and the molecule size of about 1.0 × 0.6 nm, which allows it to pass through the pores of host porous materials.[21] Herein, we report a general strategy for the synthesis of multifunctional luminescent porous fiberlike silica materials by using the electrospinning process. More importantly, the silica fibers show a strong self-activated (without rare-earth or transition-metal ions as activators) luminescence ranging from 300 to 600 nm, and centered at 405 nm. This sample can be potentially used as a kind of environmentally friendly luminescent material. The samples were fully characterized by means of scanning electron microscopy (SEM), transmission electron microscopy (TEM), Fourier-transform infrared spectroscopy (FT-IR), N_2 adsorption, and photoluminescence (PL) spectra. Additionally, the drug storage/release properties for this system were investigated by using IBU as a model drug.

Results and Discussion

Formation and morphology: ***SEM and TEM***: The morphologies and structures of the samples were investigated by SEM and TEM. Figure 1 shows the SEM images of as-prepared precursor fibers and porous silica fibers. From the low-magnification SEM images of the as-formed precursor (Figure 1a) and those of the sample annealed at 600 °C (Figure 1c), it can be seen that the samples consist of uniform fibers with a length of several tens to hundred micrometers. From the high-magnification SEM, the as-formed precursor fibers are smooth with diameters ranging from 0.7 to 1.1 μm (Figure 1b). After being annealed at 600 °C, the fiber diameters decrease considerably due to the decomposition of the organic species. For instance, the diameters of the silica fibers annealed at 600 °C for 3 h range from 200 to 400 nm (Figure 1d).

The morphology of the porous silica fibers is further characterized by TEM techniques. Figure 2 shows the typical TEM image of silica fibers annealed at 600 °C. This indicates that the diameter of the silica fibers is about 240 nm, which is consistent with that observed from the SEM image (Figure 1d). The porous structure of the silica fibers can be seen clearly from the high-magnification TEM images due to the different electron penetrability. The triblock copolymer P123 is a nonionic surfactant, which is composed of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO).

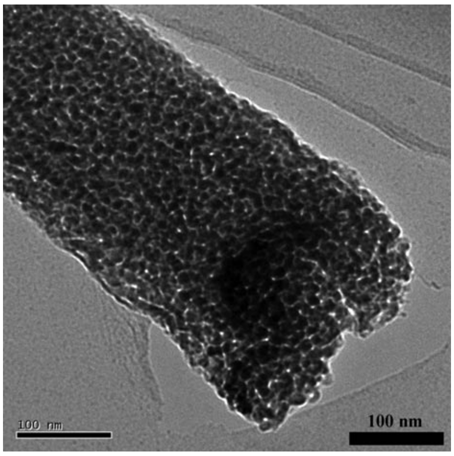

Figure 2. TEM image of silica fibers.

In dilute aqueous solutions, the PEO–PPO–PEO copolymers may self-assemble to form micelles, with a hydrophobic core containing PPO, which is protected from the surrounding water by a water swollen PEO corona. Initially, P123 formed irregular micelles and rodlike micelles in ethanol solution containing tetraethyl orthosilicate (TEOS) and 3-aminopropyltriethoxysilane (APTES). Then PVP was added to adjust the viscoelasticity of the solution, which forms the hybrid sol for electrospinning. Micelles can exist in the electrospinning precursor fibers. Under high-temperature annealing, the silica fibers formed after removing PVP, and the porous structures were retained after removal of the P123 directing agent. The possible formation process of the porous structures in silica fibers is shown schematically in Figure 3.

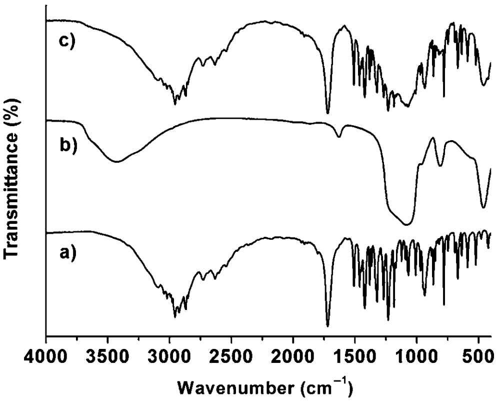

Figure 4. FT-IR spectra of IBU (a), silica fibers (b), and IBU–silica fibers (c).

FT-IR spectroscopy: The FT-IR spectra of commercial IBU, silica fibers, and IBU–silica fibers are shown in Figure 4a–c, respectively. As shown in Figure 4b for as-prepared silica fibers, the FT-IR spectrum shows the –OH group (3430 cm^{-1}), H_2O (1625 cm^{-1}), the Si-O-Si group (ν_s: 1085 cm^{-1}; ν_{as}: 810 cm^{-1}), the Si–OH group (ν_s: 960 cm^{-1}), and the Si–O group (δ: 461 cm^{-1}) (where ν_s represents symmetric stretching, ν_{as} represents asymmetric stretching, and δ represents δ bending).[23] The obvious absorption bands, assigned to the –OH group and the O–H vibration from H_2O, indicate that a large number of OH groups and H_2O are present on the surface of silica fibers, which are important for bonding drug (IBU) molecules. For the IBU-loaded silica fibers (Figure 4c), the band assigned to the vibration of –COOH at 1720 cm^{-1} is clear except for a slight decrease of the intensity compared with that of IBU (Figure 4a). Furthermore, the absorption bands assigned to the quaternary carbon atom located at 1460 and 1510 cm^{-1}, the tertiary carbon atom at 1322 cm^{-1}, the O–H bending vibration at 1421 cm^{-1}, and the C–H_x bond at 2922 and 2958 cm^{-1} can also be observed (Figure 4c),[24] which confirms the successful adsorption of IBU onto the surface of the porous silica fibers.

N_2 adsorption/desorption analysis: The respective N_2 adsorption/desorption isotherms of silica fibers (a) and IBU-silica fibers (b) are shown in Figure 5. It can be seen that the silica samples show similar VI isotherms and typical H_1-hysteresis loops, demonstrating the properties of a typical porous material. The results reveal that the loading of IBU molecules has not altered the basic pore structure of porous silica fibers. For the silica fibers, the BET surface area is about 697.62 m^2 g^{-1}, the pore volume is about 0.554 cm^3 g^{-1}, and the average pore size is about 3.18 nm. After incorporation of the IBU molecules, the BET surface area, pore size, and pore volume are markedly reduced compared with those of silica fibers, the

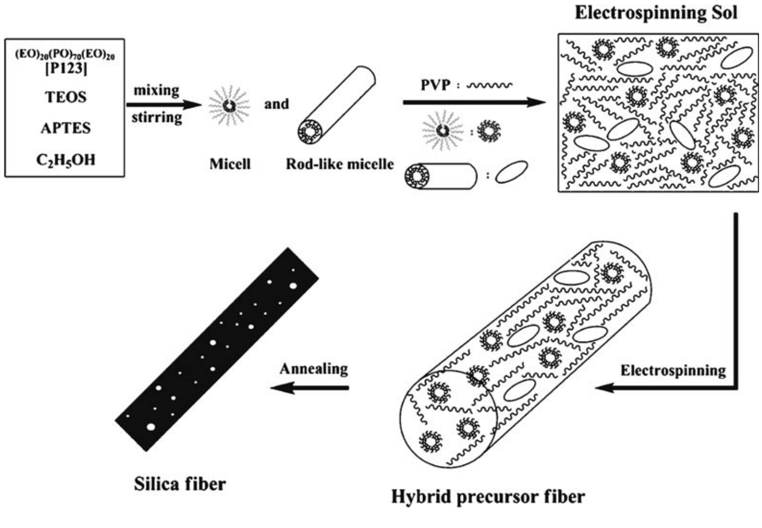

Figure 3. The possible formation process of the porous structures in silica fibers.

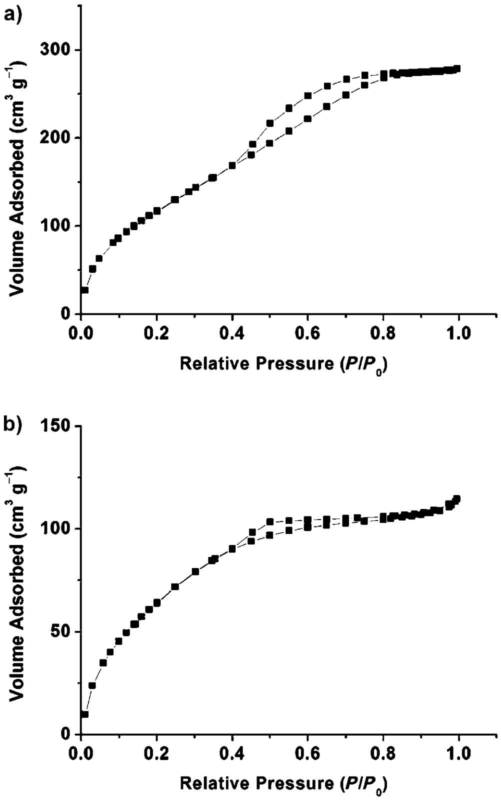

Figure 5. N_2 adsorption/desorption isotherms for silica fibers (a) and IBU–silica fibers (b).

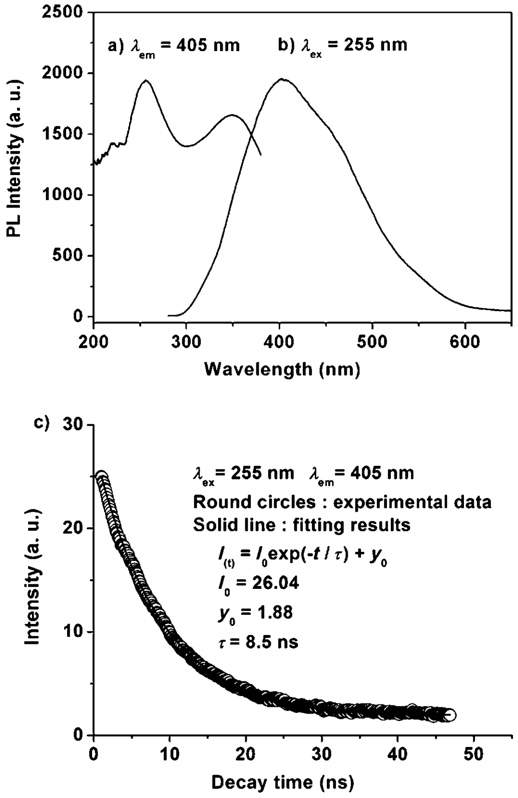

Figure 6. Excitation (a) and emission (b) spectra for silica fibers, and the decay curves (c) for the as-prepared silica fibers.

BET surface area is about 418.83 m^2g^{-1}, pore volume is about 0.248 cm^3g^{-1}, and average pore size is about 2.37 nm.

Photoluminescence properties: Under short wavelength UV irradiation, the as-prepared silica fibers exhibit blue emission. Figure 6 shows excitation (a) and emission (b) spectra for porous silica fibers annealed at 600 °C in the UV/Vis spectral region. Under excitation with 255 nm short UV light, the obtained emission spectrum consists of a broad intense band from 300 to 600 nm with a maximum at 405 nm (Figure 6b). The corresponding excitation spectrum includes a double broad band from 200 nm to 370 nm with peaks at 255 and 355 nm, as shown in Figure 6a. The decay curve for the luminescence of silica fibers is shown in Figure 6c. This decay curve can be fitted into a single-exponential function as $I=I_0\exp(-t/\tau)+y_0$, in which I_0 (initial intensity value at $t=0$) is 26.04, y_0 (offset of I, which may be caused by the instrument) is 1.88, and the lifetime (τ) is determined to be 8.5 ns.[52,66] This short lifetime (nanoseconds) is typical for the luminescence caused by defects.[67]

Because pure silica materials themselves do not emit, the observed luminescence from silica samples must be related to some chemical bond breakage resulting from some impurities and/or defects in the systems.[68–72] As reported previously, amorphous SiO_2 is well known to show luminescence generally from 350 nm to 700 nm with lifetimes of less than 10 ns. The origin of the luminescence in these silica materials is assigned to the introduction of defects and/or impurities in the hosts without a clear or exact identification of the emission centers. This assignment is based on the comparison with the much studied sol gels derived from condensation of TEOS, tetramethoxysilane (TMOS), and APTES with organic acids. For organic–inorganic hybrid silicones containing -NH_2 (-NH) groups that were obtained room temperature, Carlos et al.[73–75] proposed a mechanism based on NH_3^+/NH^- (or NH_2^+/N^-) donor–acceptor pairs to explain the blue emission from these materials. Another defect type associated with carbon impurities was proposed as being the origin of the luminescence of sol–gel derived silica gels based on TEOS and TMOS incorporating a variety of carboxylic acids.[50] Under heat treatments of up to at least about 247 °C, the carbon impurities are created in the −O−Si−O− network, leading to the formation of −O−C−O and/or −Si−C− bonds. The carbon-related defects are luminescent active only after heat treatment because these gels are not luminescent prior to this procedure.[73–75] Our results are consistent with a carbon-/oxygen-related defect center mechanism resulting from calcination of the precursor silica fibers.

It is worth noting that the characteristic emission bands are still evident in the emission spectrum for the IBU–silica fiber (Figure 7). This makes the drug loading system easily identifiable, trackable, and monitorable by using the luminescence. From the typical PL spectra (Figure 7), it can be seen that the silica fiber has a higher PL intensity than the

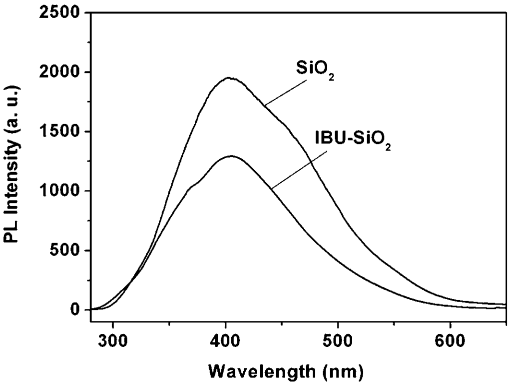

Figure 7. Emission spectra for silica fibers and IBU–silica fibers.

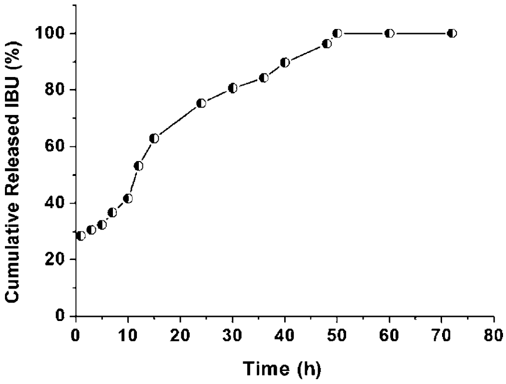

Figure 8. Cumulative ibuprofen release from IBU–silica fibers systems as a function of the release time in the release media of SBF.

IBU–silica fiber (all the experimental conditions were kept identical to avoid experimental errors). This also indicates that IBU has been successfully loaded onto the surface of the porous silica fibers. This phenomenon can be ascribed to the quenching effect of the self-activated luminescence of SiO_2 by IBU molecules, which contain large numbers of organic groups with high phonon energies. A detailed relationship between the emission intensity and the extent of IBU drug release in the IBU–silica fibers system will be discussed in the next section.

Drug loading and release properties: During the loading and release process, the IBU molecules can be adsorbed onto the surface of porous materials in the impregnation process and liberated by a diffusion-controlled mechanism. The OH groups on the surface should be the reaction sites for the formation of hydrogen bonds with the carboxyl group of IBU when IBU is adsorbed on the surface. During the release process, the solvent enters the IBU–matrix phase through the pores. The drug is then slowly dissolved into simulated body fluid (SBF) from the surface and diffuses from the system along the solvent-filled irregular capillary channels. The respective degree of loading of IBU for silica fibers is 26 wt% determined by thermogravimetric analysis. The cumulative drug release profiles in IBU–silica fibers systems as a function of release time in SBF are shown in Figure 8. From Figure 8 it can be seen that the IBU–silica fibers delivery system exhibits a drug-pronounced initial burst release of about 29 wt% within 1 h. The amount released from the IBU–silica fibers delivery system reaches about 53 wt% in 12 h and 84 wt% within 36 h. The release time of the systems can last for more than 48 h. The initial release may be attributed to the IBU weakly adsorbed on the outer surface of porous silica fibers, and the slow release of the rest of the IBU can be ascribed to the strong interaction between IBU molecules and the silica fiber surface.

The PL emission intensity of IBU–silica fibers as a function of the cumulative amount of IBU released is given in Figure 9. The PL intensity increases with the cumulative amount of IBU released, and reaches a maximum when IBU is completely released. The reason might be that the

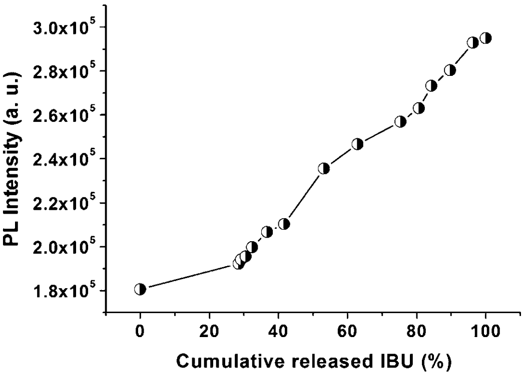

Figure 9. The PL emission intensities of IBU–silica fibers as a function of the cumulative amount of ibuprofen released.

IBU molecules can be adsorbed onto the surface of porous silica fibers and quench some luminescent centers. With the increase of release time, more and more IBU molecules can be released from the IBU–silica fibers system and the number of quenched luminescent centers would decrease, resulting in the increase of emission intensity. This relationship between the luminescence properties and the extent of drug release has potential as a probe for monitoring or tracking drug release.

Many molecules show auto-fluorescence under UV radiation, which leads to a decrease in the sensitivity of detection. Herein, silica fibers with luminescent and porous properties are prepared without doping with any toxic luminescent materials. The drug storage/release test indicates that the luminescent silica fibers show drug loading and controlled release properties for ibuprofen (IBU). Additionally, the emission intensity (excitation at 255 nm) of silica fibers in the drug-carrier system increases with the cumulative amount of IBU released, indicating that the drug release might be easily tracked and monitored by measuring the change of the luminescence intensity. Following this principle, the next step for us will be to introduce infrared-to-visible up-conversion nanophosphors into porous SiO_2 as labels for drug carriers. The up-conversion phosphors can emit higher visible photons after being excited by lower near-infrared (NIR) photons, and excitation with the NIR only results in a very weak auto-fluorescence background because the UV-excitable biomolecules that interfered with normal phosphor luminescence can no longer be excited by NIR radiation.

Conclusion

In summary, the electrospinning process for making luminescent porous silica fibers is described, which results in the formation of a multifunctional material. The obtained silica material retains its regular fiberlike morphology, and exhibits a porous structure, which is suitable for drug (IBU) release as a drug carrier. Furthermore, a strong blue emission peaking at about 405 nm can be observed at room temperature under UV excitation, and the PL intensity increases with the cumulative amount of IBU released, which can be easily tracked and monitored in the drug release process by the change in the intensity of the PL emission. These studies indicate that electrospinning is a facile and novel route for the development of functionalized silica materials that have potential for application in the fields of drug delivery and disease therapy based on their bioactive, luminescent, and porous properties.

Experimental Section

Chemicals and materials: Polyvinylpyrrolidone (PVP, $M_w=1,300,000$) was purchased from Aldrich. Tetraethyl orthosilicate (TEOS, analytical reagent, A. R.) was purchased from Beijing Yili Fine Chemicals Co., Ltd. 3-Aminopropyltriethoxysilane (APTES, 99%) was purchased from Acros. $(EO)_{20}(PO)_{70}(EO)_{20}$ (P123, $M_w=5800$) was purchased from Aldrich. Ibuprofen (IBU) was purchased from Nanjing Chemical Regent Co., Ltd. All the initial chemicals in this work were used without further purification.

Synthesis of luminescent mesoporous hydroxyapatite: Luminescent porous silica fibers were prepared by employing an electrospinning process using P123 as the structure-directing agent and TEOS as silicon source. Typically, P123 (0.25 g) was dissolved in C_2H_5OH (6.3 mL) with stirring at room temperature for 0.5 h. Then a mixture of TEOS (0.8 mL) and APTES (0.025 mL) was added dropwise to the solution with stirring at room temperature for 0.5 h. Finally, PVP (0.59 g) was added to adjust the viscoelastic behavior of the solution. The solution was stirred for 3 h to obtain a homogeneous precursor sol for further electrospinning. The distance between the spinneret (a metallic needle) and collector (a grounded conductor) was fixed at 20 cm and the high-voltage supply was maintained at 8 kV. The spinning rate was controlled at $1.0\,mL\,h^{-1}$ by a syringe pump (TJ-3A/W0109–1B, Boading Longer Precision Pump Co., Ltd, China). The as-prepared hybrid precursor samples were annealed at 600 °C with a heating rate of $1\,°C\,min^{-1}$ and held there for 3 h in air.

Preparation of the drug storage/release system: The drug storage/release system using luminescent porous silica fibers as a carrier was prepared according to the previous report.[29] Ibuprofen was selected as the model drug. Typically, silica samples (0.12 g) were added to a hexane solution (30 mL) with an IBU concentration of $60\,mg\,mL^{-1}$ at room temperature, and soaked for 24 h with stirring in a vial which was sealed to prevent the evaporation of hexane. The IBU-loaded silica fibers, denoted as IBU–silica fibers, were separated by centrifugation, and then dried at 60 °C for 12 h.

The in vitro delivery of IBU was performed by immersing 0.12 g of the sample in the release media of simulated body fluid (SBF) with slow stirring under an immersing temperature of 37 °C. The ionic composition of the as-prepared SBF solution was similar to that of human body plasma with a molar composition of 142.0/5.0/2.5/1.5/147.8/4.2/1.0/0.5 for $Na^+/K^+/Ca^{2+}/Mg^{2+}/Cl^-/HCO_3^-/HPO_4^{2-}/SO_4^{2-}$ (pH 7.4).[29a] The ratio of SBF to adsorbed IBU was kept at $1\,mL\,mg^{-1}$. The amount of IBU adsorbed onto the porous silica fibers was monitored by thermogravimetric (TG) analysis. At predetermined time intervals, 1.0 mL of the sample was withdrawn and immediately replaced with an equal volume of fresh SBF buffer to keep the volume constant. The withdrawn samples were filtered, properly diluted, and the amount of IBU released at certain set times was determined by UV/Vis spectroscopy at a wavelength of 220 nm.

Characterization: FT-IR spectra were performed on a Perkin–Elmer 580B infrared spectrophotometer using the KBr pellet technique. The morphology of the samples was inspected by using a field-emission scanning electron microscope (Philips XL 30). Transmission electron microscopy (TEM) images were obtained from a FEI Tecnai G2 S-Twin transmission electron microscope with a field-emission gun operating at 200 kV. The nitrogen adsorption/desorption analysis was performed by using a Micromeritics ASAP 2020M apparatus. The specific surface area was determined by the Brunauer–Emmett–Teller (BET) method by using the data between 0.05 and 0.35. The pore volume was obtained from the t-plot method. Thermogravimetric measurement (Pyris Diamond PerkinElmer Thermal Analysis) was used to determine the degree of loading of IBU on the materials. The photoluminescence (PL) measurements were performed on a Hitachi F-4500 spectrophotometer equipped with a 150 W xenon lamp as the excitation source. The luminescence decay curves were obtained from a Lecroy Wave Runner 6100 digital oscilloscope (1 GHz) using a tunable laser (pulse width = 4 ns, gate = 50 ns) as excitation source (Continuum Sunlite OPO). The UV/Vis adsorption spectral values were measured on a TU-1901 spectrophotometer. All the measurements were performed at room temperature.

Acknowledgements

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[1] K. E. Uhrich, S. M. Cannizzaro, R. S. Langer, K. M. Shakesheff, *Chem. Rev.* **1999**, *99*, 3181.
[2] R. Cortesi, C. Nasturzzi, S. S. Davis, *Biomaterials* **1998**, *19*, 1641.
[3] T. Chandy, C. P. Sharma, *Biomaterials* **1996**, *17*, 61.
[4] W. Paul, C. T. Sharma, *J. Mater. Sci: Mater. Med.* **1999**, *10*, 383.
[5] Q. Yang, S. C. Wang, P. W. Fan, L. F. Wang, Y. Di, K. F. Lin, F. S. Xiao, *Chem. Mater.* **2005**, *17*, 5999.
[6] F. Y. Qu, G. S. Zhu, H. M. Lin, J. Y. Sun, D. L. Zhang, S. G. Li, S. L. Qiu, *Eur. J. Inorg. Chem.* **2006**, 3943.
[7] B. G. Trewyn, C. M. Whitman, V. S. Y. Lin, *Nano Lett.* **2004**, *4*, 2139.
[8] A. Rosler, G. W. M. Vandermuelen, H. A. Klok, *Adv. Drug Delivery Rev.* **2001**, *53*, 95.
[9] I. I. Slowing, B. G. Trewyn, S. Giri, V. S. Y. Lin, *Adv. Funct. Mater.* **2007**, *17*, 1225.
[10] X. Guo, F. Szoka, *Acc. Chem. Res.* **2003**, *36*, 335.
[11] K. Kataoka, A. Harada, Y. Nagasaki, *Adv. Drug Delivery Rev.* **2001**, *47*, 113.
[12] M. Itokazu, W. Yang, T. Aoki, A. Ohara, N. Kato, *Biomaterials* **1998**, *19*, 817.
[13] M. A. Rauschmann, T. A. Wichelhaus, V. Stirnal, E. Dingeldein, L. Zichner, R. Schnettler, V. Alt, *Biomaterials* **2005**, *26*, 2677.
[14] R. P. Del Real, J. G. C. Wolke, M. Vallet-Regi, *Biomaterials* **2002**, *23*, 3673.
[15] M. Bohner, *Injury* **2000**, *31*, D37.
[16] H. H. Yang, Q. Z. Zhu, H. Y. Qu, X. L. Chen, M. T. Din, J. G. Xu, *Anal. Biochem.* **2002**, *308*, 71.

[17] P. Caliceti, S. Salmaso, A. Lante, M. Yoshida, R. Katakai, F. Martellini, *J. Controlled Release* **2001**, *75*, 173.
[18] M. Changez, K. Burugapalli, V. Koul, V. Choudhary, *Biomaterials* **2003**, *24*, 527.
[19] C. Y. Lai, B. G. Trewyn, D. M. Jeftinija, K. Jeftinija, S. Xu, S. Jeftinija, *J. Am. Chem. Soc.* **2003**, *125*, 4451.
[20] C. Barbé, J. Bartlett, L. Kong, K. Finnie, H. Q. Lin, M. Larkin, *Adv. Mater.* **2004**, *16*, 1949.
[21] Y. F. Zhu, J. L. Shi, W. H. Shen, X. P. Dong, J. W. Feng, M. L. Ruan, *Angew. Chem.* **2005**, *117*, 5213; *Angew. Chem. Int. Ed.* **2005**, *44*, 5083.
[22] J. Andersson, J. Rosenholm, S. Areva, M. Lindén, *Chem. Mater.* **2004**, *16*, 4160.
[23] S. W. Song, K. Hidajat, S. Kawi, *Langmuir* **2005**, *21*, 9568.
[24] C. Tourné-Péteilh, D. A. Lerner, C. Charnay, L. Nicole, S. Begu, J. M. Devoisselle, *ChemPhysChem* **2003**, *4*, 281.
[25] B. Muňoz, A. Rámila, J. Pérez-Pariente, I. Díaz, M. Vallet-Regí, *Chem. Mater.* **2003**, *15*, 500.
[26] F. Y. Qu, G. S. Zhu, S. Y. Huang, S. G. Li, J. Y. Sun, D. L. Zhang, S. L. Qiu, *Microporous Mesoporous Mater.* **2006**, *92*, 1.
[27] F. Y. Qu, G. S. Zhu, H. M. Lin, W. W. Zhang, J. Y. Sun, S. G. Li, S. L. Qiu, *J. Solid State Chem.* **2006**, *179*, 2027.
[28] F. Y. Qu, G. S. Zhu, S. Y. Huang, S. G. Li, S. L. Qiu, *ChemPhysChem* **2006**, *7*, 400.
[29] Y. F. Zhu, J. L. Shi, H. G. Chen, W. H. Shen, X. P. Dong, *Microporous Mesoporous Mater.* **2005**, *84*, 218.
[30] P. Horcajada, A. Rámila, J. Pérez-Pariente, M. Vallet-Regí, *Microporous Mesoporous Mater.* **2004**, *68*, 105.
[31] A. Rámila, B. Munǒz, J. Pérez-Pariente, M. Vallet-Regí, *J. Sol-Gel Sci. Technol.* **2003**, *26*, 1199.
[32] Q. Fu, G. V. Rama Rao, L. K. Ista, Y. Wu, B. P. Andrzejewski, L. A. Sklar, T. L. Ward, G. P. Lopez, *Adv. Mater.* **2003**, *15*, 1262.
[33] C. Tourné-Péteih, D. Brunel, S. Bégu, B. Chiche, F. Fajula, D. A. Lerner, J. M. Devoissele, *New J. Chem.* **2003**, *27*, 1415.
[34] N. K. Mal, M. Fujiwara, Y. Tanaka, T. Taguchi, M. Matsukata, *Chem. Mater.* **2003**, *15*, 3385.
[35] M. Vallet-Regí, A. Rámila, R. P. Del Real, J. Pérez-Pariente, *Chem. Mater.* **2001**, *13*, 308.
[36] S.-B. Cho, K. Nakanishi, T. Kokubo, N. Soga, C. Ohtsuki, T. Nakamura, T. Kitsugi, T. Yamamuro, *J. Am. Ceram. Soc.* **1995**, *78*, 1769.
[37] T. Kokubo, H. Kushitani, S. Sakka, T. Kitsugi, T. Yamamuro, *J. Biomed. Mater. Res.* **1990**, *24*, 721.
[38] H. H. P. Yiu, P. A. Wright, *J. Mater. Chem.* **2005**, *15*, 3690.
[39] J. C. Doadrio, E. M. B. Sousa, I. Izquierdo-Barba, A. L. Doadrio, J. Pérez-Pariente, I. M. Vallet-Regí, *J. Mater. Chem.* **2004**, *14*, 462.
[40] A. L. Doadrio, E. M. B. Sousa, J. C. Doadrio, J. Pérez-Pariente, I. Izquierdo-Barba, I. M. Vallet-Regí, *J. Controlled Release* **2004**, *97*, 125.
[41] M. Vallet-Regí, J. C. Doadrio, A. L. Doadrio, I. Izquierdo-Barba, J. Pe'rez-Pariente, *Solid State Ionics* **2004**, *172*, 435.
[42] D. L. Shi, J. Lian, W. Wang, G. K. Liu, P. He, Z. Y. Dong, L. M. Wang, R. C. Ewing, *Adv. Mater.* **2006**, *18*, 189.
[43] Y. S. Lin, S. H. Wu, Y. Hung, Y. H. Chou, C. Chang, M. L. Lin, C. P. Tsai, C. Y. Mou, *Chem. Mater.* **2006**, *18*, 5170.
[44] L. N. Sun, H. J. Zhang, C. Y. Peng, J. B. Yu, Q. G. Meng, *J. Phys. Chem. B* **2006**, *110*, 7249.
[45] J. Sauer, F. Marlow, B. Spliethoff, F. Schüth, *Chem. Mater.* **2002**, *14*, 217.
[46] W. Xu, Y. T. Liao, D. L. Akins, *J. Phys. Chem. B* **2002**, *106*, 11127.
[47] L. M. Xiong, J. L. Shi, J. L. Gu, L. Li, W. M. Huang, J. H. Gao, M. L. Ruan, *J. Phys. Chem. B* **2005**, *109*, 731.
[48] S. Angelov, R. Stoyanova, R. Dafinova, K. Kabasanov, *J. Phys. Chem. Solids* **1986**, *47*, 409.
[49] W. H. Green, K. P. Le, J. Grey, T. T. Au, M. J. Sailor, *Science* **1997**, *276*, 1826.
[50] A. M. Jakob, T. A. Schmedake, *Chem. Mater.* **2006**, *18*, 3173.
[51] T. Ogi, Y. Kaihatsu, F. Iskandar, W. N. Wang, K. Okuyama, *Adv. Mater.* **2008**, *20*, 3235.
[52] C. M. Zhang, J. Yang, Z. W. Quan, P. P. Yang, C. X. Li, Z. Y. Hou, J. Lin, *Cryst. Growth Des.* **2009**, *9*, 2725.
[53] A. Formhals, US Patent Specification, **1934**, 1 975 504.
[54] S. Madhugiri, A. Dalton, J. Gutierrez, J. P. Ferraris, Jr., K. J. Balkus, *J. Am. Chem. Soc.* **2003**, *125*, 14531.
[55] L. Yao, T. W. Haas, A. Guiseppi-Elie, G. L. Bowlin, D. G. Simpson, G. E. Wnek, *Chem. Mater.* **2003**, *15*, 1860.
[56] G. Larsen, R. Velarde-Ortiz, K. Minchow, A. Barrero, I. G. Loscertales, *J. Am. Chem. Soc.* **2003**, *125*, 1154.
[57] H. Q. Hou, D. H. Reneker, *Adv. Mater.* **2004**, *16*, 69.
[58] J. Wu, J. L. Coffer, *Chem. Mater.* **2007**, *19*, 6266.
[59] J. J. Ge, H. Hou, Q. Li, M. J. Graham, A. Greiner, D. H. Reneker, F. W. Harris, S. Z. D. Cheng, *J. Am. Chem. Soc.* **2004**, *126*, 15754.
[60] M. J. Li, J. H. Zhang, H. Zhang, Y. F. Liu, C. L. Wang, X. Xu, Y. Tang, B. Yang, *Adv. Funct. Mater.* **2007**, *17*, 3650.
[61] Z. Y. Hou, P. P. Yang, H. Z. Lian, L. L. Wang, C. M. Zhang, C. X. Li, R. T. Chai, Z. Y. Cheng, J. Lin, *Chem. Eur. J.* **2009**, *15*, 6973.
[62] L. F. Zhang, Y. L. Hsieh, *Nanotechnology* **2006**, *17*, 4416.
[63] Y. Y. Zhao, H. Y. Wang, X. F. Lu, X. Li, Y. Yang, C. Wang, *Mater. Lett.* **2008**, *62*, 143.
[64] P. P. Yang, S. S. Huang, D. Y. Kong, J. Lin, H. G. Fu, *Inorg. Chem.* **2007**, *46*, 3203.
[65] P. P. Yang, Z. W. Quan, L. L. Lu, S. S. Huang, J. Lin, H. G. Fu, *Nanotechnology* **2007**, *18*, 235703.
[66] C. K. Lin, Y. Luo, H. You, Z. W. Quan, J. Fang, J. Lin, *Chem. Mater.* **2006**, *18*, 458–464.
[67] A. Pifferi, P. Taroni, A. Torricelli, G. Valentini, P. Mutti, G. Ghislotti, L. Zanghieri, *Appl. Phys. Lett.* **1997**, *70*, 348–350.
[68] T. Hayakawa, A. Hiramitsu, M. Nogami, *Appl. Phys. Lett.* **2003**, *82*, 2975.
[69] T. Brankova, V. Bekiari, P. Lianos, *Chem. Mater.* **2003**, *15*, 1855.
[70] V. Bekiari, P. Lianos, *Langmuir* **1998**, *14*, 3459.
[71] B. E. Yoldas, *J. Non-Cryst. Solids* **1992**, *147–148*, 614.
[72] J. Lin, K. Baerner, *Mater. Lett.* **2000**, *46*, 86.
[73] L. D. Carlos, R. A. Sá Ferreira, R. N. Pereira, M. Assuncão, V. de Zea Bermudez, *J. Phys. Chem. B* **2004**, *108*, 14924.
[74] L. Fu, R. A. Sá Ferreira, N. J. O. Silva, L. D. Carlos, V. de Zea Bermudez, J. Rocha, *Chem. Mater.* **2004**, *16*, 1507.
[75] L. D. Carlos, V. de Zea Bermudez, R. A. Sá Ferreira, L. Marques, M. Assuncão, *Chem. Mater.* **1999**, *11*, 581.

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