Synthesis of sandwich-like molybdenum sulfide/mesoporous organosilica nanosheets for photo-thermal conversion and stimuli-responsive drug release

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Abstract: Sandwich-like molybdenum sulfide/mesoporous organosilica nanosheets (denoted as MoS₂@MOS) have been prepared for the first time via direct growth of ethane-bridged mesostructured organosilica on MoS₂ nanosheets by using cetyltrimethylammonium bromide (CTAB) as structure directing agent. The obtained MoS₂@MOS nanosheets possess well-defined sandwich-like structure, high surface

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area ($\sim 920 \text{ cm}^2/\text{g}$), uniform pore size ($\sim 4.2 \text{ nm}$), large pore volume ($\sim 1.41 \text{ cm}^3 \text{ g}^{-1}$). In vitro cytotoxicity assessments demonstrate that the $\text{MoS}_2@\text{MOS}$ nanosheets have excellent biocompatibility. Owing to the encapsulation of the MoS_2 , the obtained $\text{MoS}_2@\text{MOS}$ nanosheets have photo-thermal conversion capability and photo-thermally controlled drug release property. These properties make the $\text{MoS}_2@\text{MOS}$ nanosheets promising for biomedical applications.

Keywords: mesoporous organosilica, MoS_2 , sandwich structure, photo-thermal conversion, drug release

1. Introduction

Mesoporous organosilicas have attracted more and more research attention because of their combined advantages of ordered mesostructure, organic and inorganic fragments hybridized frameworks, large specific surface areas, good biocompatibility and extensive promising applications in various areas such as separation, catalysis, and biomedicine.^[1-6] Due to the hydrolysis and condensation of the organosilica precursors in solution are highly controllable. Recently, tremendous efforts have been devoted to synthesize functional organosilica composites by coating mesoporous organosilica on magnetic or luminescent particles to extend their properties and applications.^[7-11] However, to the best of knowledge, the organosilica based multifunctional materials are limited to core-shell structures with a spherical shape.^[12,13] Sheet-like mesoporous organosilica composites have not been reported so

far.

In recent years, molybdenum sulfide (MoS_2) nanosheets that resemble the 2D structure of graphene have become a hotspot of research for biomedical applications due to their remarkable photo-thermal effect in an aqueous medium.^[14–18] The single- or few-layered MoS_2 can be readily produced from bulk MoS_2 via lithium intercalation.^[19] However, newly synthesized MoS_2 generally possesses low stability and easily aggregates in aqueous solution. Therefore, modification of the MoS_2 to ensure satisfied stability and good biocompatibility is very important for their biomedical applications.^[20–22]

Herein, we successfully prepared a sandwich-like structured MoS_2 @MOS nanosheets by direct co-assembly of cetyltrimethylammonium bromide (CTAB) surfactant and organosilicates on the MoS_2 . The obtained sandwich-like MoS_2 @MOS nanosheets possess high surface area ($\sim 920 \text{ cm}^2/\text{g}$), ordered mesopores ($\sim 4.2 \text{ nm}$), large pore volume ($\sim 1.41 \text{ cm}^3 \text{ g}^{-1}$). Moreover, cytotoxicity and photo-thermal experiments show the MoS_2 @MOS nanosheets have excellent biocompatibility, photo-thermal conversion capability and photo-thermally controlled drug release properties, showing great potential for biomedical applications.

2. Experimental

2.1 Materials.

Molybdenum (IV) sulfide (MoS_2) powder ($< 2 \text{ }\mu\text{m}$, 99%) was purchased from Sigma-Aldrich; n-butyllithium (n-BuLi, 2.4 M hexane solution) was bought from

Amethyst; CTAB, concentrated ammonia aqueous solution (25 wt %), and anhydrous ethanol were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). 1,2-Bis(triethoxysilyl)ethane (BTSE) were bought from Sigma-Aldrich (St. Louis, MO, USA). Decane with a purity of >99% were purchased from Acros Organics (Merck, Germany). Millipore water was used in all experiments.

2.2 Characterization.

Transmission electron microscopy (TEM) images were obtained on an HT7700 microscope (Hitachi, Tokyo, Japan) operated at an accelerating voltage 100 kV. Energy dispersive X-ray (EDX) analyses and dark-field scanning TEM (DF-STEM) were performed on a JEOL JEM-2100F electron microscope (200 Kv) equipped with an energy dispersive X-ray spectrometer. X-ray power diffraction (XRD) was measured on a Bruker model D8 focus diffractometer with Cu K α radiation (0.154 nm) operated at 40 kV and 40 mA. Fourier transform infrared (FT-IR) spectra were obtained on a Nicolet NEXUS870 spectrometer (USA), using KBr pellets of the solid samples. Nitrogen sorption isotherms were measured using a Micromeritics Tristar 3000 analyzer at $-196\text{ }^{\circ}\text{C}$. The samples were degassed at $150\text{ }^{\circ}\text{C}$ for 10 h before the measurements. The specific surface area was calculated with the Brunauer-Emmett-Teller (BET) method by using the adsorption data. The pore size distribution was obtained by applying proper nonlocal density functional theory (NLDFT) methods from the adsorption branch of isotherms. The total pore volume was evaluated from the adsorbed amount at a relative pressure (p/p_0) of 0.994.

2.3 Preparation of MoS₂ nanosheets.

MoS₂ nanosheets were synthesized by lithium intercalation-exfoliation and exfoliation method.^[23,24] Briefly, a mixture of 0.2 g MoS₂ and 6.25 mL n-BuLi hexane solution was stirred at room temperature for 48 h under Ar atmosphere, then allowed to settle for several hours. Excess n-BuLi solution in the reaction mixture was removed by a syringe, and the black solid was collected in a tube. Ar saturated water was carefully introduced into the tube to avoid sputtering under the protection of Ar, since lots of hydrogen gas are released at that moment. The MoS₂ nanosheets aqueous suspension was sonicated for 1.5 h to thoroughly complete the exfoliation process and then centrifuged at 1200 rpm for 30 min. After centrifugation, the precipitates were discarded. Further purification by centrifugation was repeated at least two times. Finally, the precipitated MoS₂ nanosheets were dispersed in water and the concentration of the MoS₂ nanosheets aqueous solution was 1.308 mg mL⁻¹.

2.4 Preparation of sandwich-like MoS₂@MOS nanosheets.

The MoS₂@MOS nanosheets were prepared by co-assembly of CTAB and ethane-bridged organosilicates on MoS₂. In a typical experiment, CTAB (0.0386 g) was dissolved in 11.9 mL water, 3.3 mL MoS₂ nanosheets aqueous solution (1.308 mg mL⁻¹), 0.72 mL of concentrated ammonia aqueous solution (25 wt %), and 0.12 mL of decane. The mixture was stirred 20 min at 50 °C and a mixed solution containing 0.08 mL BTSE and 0.32 mL ethanol was then added. After 12 h, the products were collected by centrifugation and washed with water three times. Finally, CTAB templates were removed from the products by three solvent-extractions in 30 mL ethanol (containing 0.06 mL HCl) at 60 °C for 3 h. After washing with ethanol for

three times and dried under a high vacuum, the sandwich-like MoS₂@MOS nanosheets were obtained.

2.5 Cell viability assay.

Cell viability is assessed by the MTT method. First, 1×10^4 MCF-7 cells were plated in a 96-well culture plate, then incubated with the MoS₂@MOS nanosheets at various concentrations (100, 200, 400, 600, 700, 800, 900 and 1000 $\mu\text{g mL}^{-1}$) for 24 h in a humidified incubator. The absorbance at 570 nm was measured with a microplate reader (BioTek Instruments, Winooski, VT) after dissolving the precipitates with DMSO (150 μL). Each experiment was repeated three times, and six wells were treated in parallel for each concentration. The cell viability (%) was calculated according to our previous work.^[25]

2.6 Measurements of photo-thermal property.

The MoS₂@MOS nanosheets dispersed in water with concentrations from 0 to 1000 $\mu\text{g mL}^{-1}$ were irradiated with a power density of 2 or 5 W cm^{-2} for 5 min from an 808 nm laser system (Hi-Tech Optoelectronics Co., Ltd., China).

2.7 DOX loading and releasing.

In the loading experiments, DOX was loaded by mixing various concentrations of drug with MoS₂@MOS in PBS (pH 7.4) for 5, 24, 48, and 72 h at 37 °C. The unloaded DOX was separated by centrifugation at 13,200 rpm for 5 min. The DOX concentration in the supernatant was determined to calculate the loading efficiency and capacity.

In the releasing experiments, 0.5 mg mL^{-1} MoS₂@MOS was mixed with 0.1 mg

mL^{-1} DOX in PBS for 72 h. Then the obtained DOX/MoS₂@MOS was centrifuged and redispersed in PBS with a concentration of 0.5 mg mL^{-1} . The solution was then irradiated by an 808 nm laser at power density of 5 W cm^{-2} for 60 min. A sample of the solution was centrifuged every 10 min during the irradiation to determine the DOX concentration in the supernatant and calculate the released percentage of DOX. The releasing behavior of DOX/MoS₂@MOS in PBS without irradiation was also measured as control.

3. Results and discussion

The preparation process of the sandwich-like MoS₂@MOS nanosheets is illustrated in Scheme 1. First, MoS₂ nanosheets were prepared via lithium intercalation-exfoliation method. Then the MoS₂ nanosheets were dispersed in an aqueous solution containing ammonia, CTAB, and small amount of decane. The CTAB micelles were adsorbed on the MoS₂ through electrostatic interaction. It should be pointed out that the introduced decane has a swelling behavior for the CTAB micelles and results in relatively large mesopores. After the organosilica precursor BTSE is added, they are hydrolyzed to form negatively charged oligomeric organosilicate species and co-assemble with the CTAB micelles on the MoS₂ nanosheets. With the reaction proceeding, the organosilicates were cross-linked each other on the MoS₂ nanosheets, and the CTAB-organosilicate composites grow gradually and form ordered mesostructures. After removal of surfactants by solvent extraction, sandwich-like MoS₂@MOS nanosheets with MoS₂ located in interlayer

and mesoporous organosilica at upper and lower layers are finally obtained.

Scheme 1. Illustration of the preparation process of the sandwich-like MoS₂@MOS nanosheets.

TEM images show that the obtained MoS₂@MOSs possess sheet structure and excellent dispersibility in aqueous solution owing to the coating of the ethane-bridged mesoporous organosilica (Figure 1A). In contrast, the naked MoS₂ aggregates easily in aqueous solution (Figure S1). Also, TEM observation demonstrates that no free PMO nanoparticles or naked MoS₂ nanosheets are presented. The MoS₂@MOS nanosheets have an average lateral size of 200 nm. The DF-STEM image shows that the MoS₂@MOS nanosheets have well-defined sandwich-like structure (Figure 1B). High magnification TEM image further indicates the mesopores are oriented to surface of the MoS₂ nanosheets (Figure 1C). Top-view TEM image further demonstrates the radially oriented mesopores with openings at surface (Figure 1D). The radially oriented mesochannels favor the adsorption and release of guest

molecules, such as anticancer drugs. EDX line scanning (Figure 2) clearly reveals the sandwich-like structure with MoS₂ sheets between the organosilica layers. The integrated energy dispersive X-ray spectroscopy (EDX) analysis further confirms the presence of Si, O, S, and Mo (Figure S2).

Figure 1. (A, C, D) TEM images and (B) DF-STEM of the sandwich-like MoS₂@MOS nanosheets prepared by co-assembly of CTAB micelles with hydrolyzed BTSE on MoS₂.

Figure 2. (B-F) EDX line scanning profiles of S, Mo, Si, and O recorded from the MoS₂@MOS nanosheets shown in (A).

The XRD pattern of the sandwich-like MoS₂@MOS nanosheets show an obvious peak at 1.58° (Figure 3A), suggesting a ordered mesostructure.^[26,27] The FT-IR spectrum of the MoS₂@MOS nanosheets display the stretch vibrations of the C–H bond around 2896 cm^{−1} and bending vibration of the C–H bond in the –CH₂–CH₂– moieties at 1412 cm^{−1} (Figure 3B), which suggests that the ethane-bridged organosilica are successfully deposited on the MoS₂ nanosheets.^[28, 29] Nitrogen sorption isotherms of the MoS₂@MOS nanosheets show a type IV curve with capillary condensation at relative pressures of 0.5–0.85 and 0.85–1.0 (Figure 3C), suggesting typical mesoporous structure. The surface area and pore volume are calculated to be as high as 920 m² g^{−1} and 1.41 cm³ g^{−1}, respectively. The high surface

area and large pore volume is attributed to the coating of the mesoporous organosilica layer. The pore size distribution calculated based on the nonlocal density functional theory (NLDFT) reveals that the MoS₂@MOS nanosheets have a uniform pore size of about 4.2 nm (Figure 3D). The yield of the MoS₂@MOS nanosheets with the size of 200 nm is 71%.

Figure 3. (A) XRD, (B) FT-IR spectrum, (C) Nitrogen sorption isotherms and (D) pore size distribution curve of the sandwich-like MoS₂@MOS nanosheets.

The biocompatibility of the MoS₂@MOS nanosheets were further assessed with MCF-7 cell. It is observed that the cell viability is retained about 100% when they are incubated with the MoS₂@MOS nanosheets at concentrations ranging from 100 to 1000 µg mL⁻¹ for 24 h (Figure 4). The results demonstrate that the MoS₂@MOS nanosheets have excellent biocompatibility.

Figure 4. MCF-7 cell viability after incubating with different concentrations of the sandwich-like MoS₂@MOS nanosheets for 24 h.

The photo-thermal performance of the sandwich-like MoS₂@MOS nanosheets was further investigated. Obviously, the temperature of the aqueous solution is increased with the MoS₂@MOS concentrations (Figure 5A). The temperature of the MoS₂@MOS solution with a concentration of 1 mg mL⁻¹ rapidly increases to 44.1 °C after irradiation at 5 W cm⁻² for 60 s, then reaches to 65.7 °C at 600 s. Moreover, 0.125, 0.25 and 0.5 mg mL⁻¹ of MoS₂@MOS nanosheets raised the temperatures to 40.2 °C, 45.4 °C and 54.6 °C at 600 s, respectively. When decreasing the power density of the 808 nm laser at 2 W cm⁻² (Figure S2), the temperature of 1 mg mL⁻¹ of MoS₂@MOS nanosheets increased to 33.6 °C at 60 s, then reached 44.4 °C at 600 s (Figure S3). All these results demonstrate that the MoS₂@MOS nanosheets has a photo-thermal transformation capability, which can be used for thermal treatment of cancer.^[30] Furthermore, the photo-thermally responsive drug release property of the

MoS₂@MOS nanosheets is investigated. In order to evaluate the stimulus drug release of DOX loaded MoS₂@MOS nanosheets, the drug release curves were measured with or without laser irradiation. Around 7.34% of DOX was release upon laser irradiation at 5 W cm⁻² for 60 min whereas less than 1.22% leaked out without irradiation (Figure 5B). The results confirm that the MoS₂@MOS nanosheets possess photo-thermally responsive drug release property.

Figure 5. (A) Photo-thermal curves of the MoS₂@MOS nanosheets irradiated with a power density of 5 W cm⁻² for 5 min; (B) DOX release profiles from DOX/MoS₂@MOS with or without laser irradiation.

4. Conclusions

In summary, well-dispersed sandwich-like MoS₂@MOS nanosheets have been first prepared by directly growth of mesostructured organosilica on MoS₂ nanosheets. The resultant MoS₂@MOS nanosheets possess an ordered mesopores (~4.2 nm), high surface area (~920 cm²/g), and large pore volume (~1.41 cm³ g⁻¹). Besides, the sandwich-like MoS₂@MOS nanosheets have excellent biocompatibility, photo-thermal conversion capability and photo-thermally controlled drug release

property. It is believed that such novel nanosheets provide a promising strategy for cancer treatment.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jcis>.

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Graphical Abstract

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