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Selective detection and controlled release of Aspirin over fluorescent amino-functionalized metal–organic framework in aqueous solution

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ABSTRACT

Aspirin, as a traditional anti-inflammatory drug, also leads to some side-effect due to inapposite dose. Simple and sensitive sensors capable of detecting Aspirin would have a significant relevance for human bodies. In this work, a highly selective and sensitive fluorescence probe for detecting Aspirin has been developed based on luminescent Zr-based metal–organic frameworks (MOFs) with accessible channels and functional sites (free amino group). The MOFs show excellent luminescence and good fluorescence stability in aqueous environment. In the presence of Aspirin, the fluorescence would enhance dramatically (~20.77 times as much as that of without Aspirin) due to the intermolecular hydrogen-bonding interaction between free-NH_2 in MOFs and Aspirin. The proposed detecting system shows a low detection limit (0.02 μM) and a broad liner range (0.02–200 μM) for Aspirin detection. Most importantly, it also expresses good capacity for controlled release of Aspirin in PBS buffer solution (pH 7.4), which has a higher loading content (46%) than some Aspirin loading system. Considering its simple, cost-effective, environmental-friendly as well as combining detection and controlled release, we expect the system will have great potential for biological analysis.

1. Introduction

Aspirin (A) is a traditional antipyretic analgesic anti-inflammatory drug, which has good curative effect on prevention and control of diseases such as cardiovascular disease (CVD) [1,2], acute coronary syndromes (ACS), percutaneous coronary interventions (PCI), *etc.* [3]. It has produced a huge role since the first time Aspirin (A) was applied to human bodies. However, the contraindicated use of Aspirin (A) may lead to psychotomimetic effects [4], gastroduodenal ulcers [5,6], hepatic or renal lesion as people discovered. Thus, it appears that no risk-free dose of aspirin exists and the side-effect to different age groups or different organs of one people has not defined clearly thus far [7]. Therefore, designing a detector with specificity for Aspirin (A) will have a significant sense for exploring the bad effects of various doses to human bodies.

Recently, fluorescence-based chemosensors have been of immense importance with remarkable advantages over the other newly developed detection technologies owing to high sensitivity, portability, short response time, low cost and dual compatibility in solid and solution media [8–11]. Among fluorescent chemosensors, of particular interest are metal–organic frameworks (MOFs) which are a new class of porous conjugated materials with diversity of structural characteristics, nature of the pore surface [12–14]. It is generally known that MOFs have shown a variety of potential applications, such as gas storage [15,16], separation [17,18], heterogeneous catalysis [19,20]. Due to the diverse pore topologies, accessible channels and functional sites (Lewis basic/acidic sites and open metal sites) make MOFs well suitable for developing fluorescence detector. To date, luminescent MOFs have been constructed to detect metal ions [21], solvent small molecules [22], explosives [23], DNA [24] and so on. For another the all advantages of MOFs above are also the necessary elements for drug delivery systems (DDSs) [25,26] and they have been used for drug carrier successfully which indicated that MOFs possess significant advantages over conventional DDSs in obtaining high drug loadings and facile controlled release kinetics. Horcajada et al. have chosen MIL-53(Fe) as a matrix for the adsorption and *in vitro* delivery of ibuprofen [27]. 5-Fluorouracil (5-Fu), which is a wide-used anticancer drug, have been loaded into Cu(pi)-PEG5k successfully by Zhou group [28]. MOFs leading DDSs have the characters of a high drug loading and a controlled release of therapeutic agents to targeted areas of body [29]. Unfortunately, fluorescence-monitored DDSs have gained less attention until now and to the best of our

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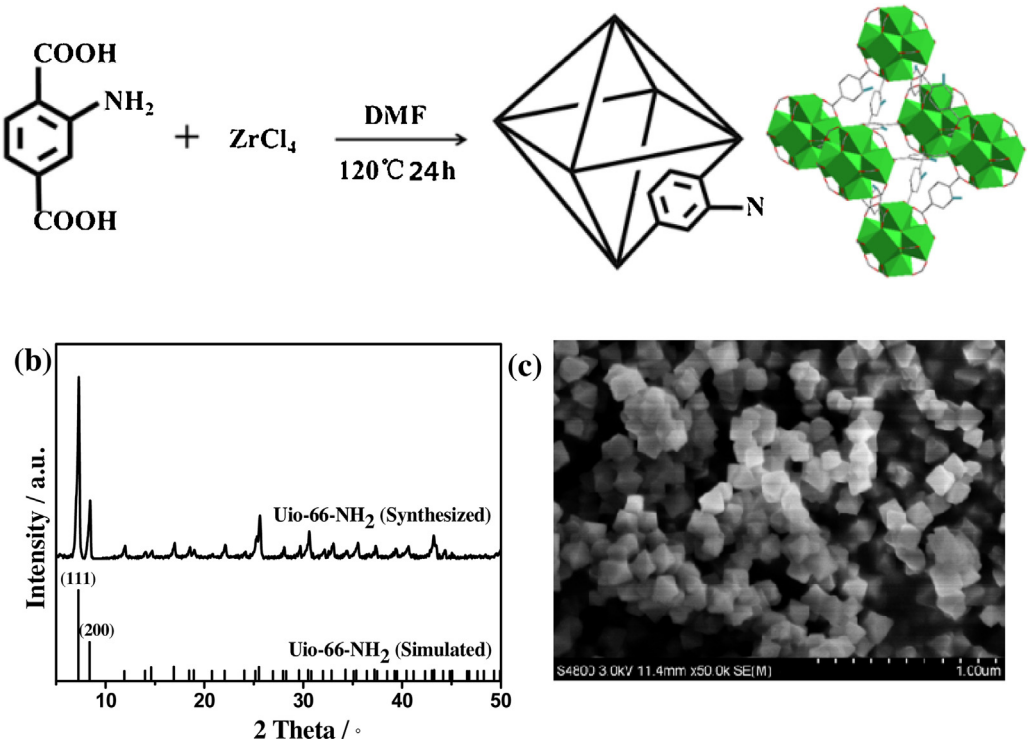

Fig. 1. (a) Schematic illustration of the synthesis of Uio-66-NH_2 (b) the powder X-ray diffraction (PXRD) pattern and (c) SEM image of Uio-66-NH_2.

knowledge, very rare MOFs have been studied for the detection of drug molecules. Therefore, to design a chemosensory base on luminescent MOFs which can be used to drug detection and delivery, simultaneously, may be a great challenge.

Among the tens of thousands of known MOFs, the Uio (University of Oslo) type can be considered as one of the most promising frameworks for various applications due to its combination of high thermal and chemical stability and its important porosity [30–32]. Together with its versatile organic composition which has pivotal effects on luminescence producing and the fact that zirconium is a low toxic metal (oral lethal dose LD50 (zirconyl acetate) ~4.1 g kg^{-1}, human daily requirement 0.05 mg per day), makes this material without any doubt an interesting candidate for drug detection and delivery. According to this, we demonstrate a nanoscale luminescent MOFs (Uio-66-NH_2) as a detector to achieve the detection of anti-inflammatory drug Aspirin (A) with high selectively. Uio-66-NH_2 can be reasonably able to recognize Aspirin (A) molecules *via* fluorescence enhancement. As a binding site in the pore of Uio-66-NH_2, amino group is the key to performance the process. Then, we explored the delivering behavior of Uio-66-NH_2 for Aspirin (A) which showed a high loading content and good controlled release.

2. Experimental

2.1. Chemicals

All of the chemicals are commercially available and used without further purification. Zirconium chloride (ZrCl4, 98%) and 2-aminoterephthalic acid (bdc-NH2) were used to synthesize compound Uio-66-NH2. Aspirin (A), Ibuprofen (B), Acetaminophen (C), 5-Flurouracil (F) were used for target drug candidate for fluorescence detection experiment.

2.2. Instrumentation

Powder X-ray diffraction patterns (PXRD) were recorded with a Bruker D8 diffractometer using CuKα radiation with 40 mA and 40 kV and the dates were collected within the 2θ range of 5–50°. Scanning electronic microscope (SEM) images were recorded with a Hitachi S-4800. Nitrogen adsorption/desorption isotherms were performed at liquid nitrogen temperature using a Nova 1000 analyzer. Thermal gravimetric analysis (TGA) were carried out on a Netzsch STA 449C system at a heating rate of 5 K min^{-1} from 40 °C temperature to 800 °C under nitrogen atmosphere in the Al_2O_3 crucibles. Fourier transform infrared (FTIR) spectra were recorded in the range 4000–400 cm^{-1} on a Nexus 912 AO446 spectrophotometer using KBr pellets. UV–vis diffuse reflectance spectrum was taken with BWS003. Luminescence excitation and emission spectra of the samples are obtained on Edinburgh FLS920 spectrophotometer using a 450 W xenon lamp as excitation source.

2.3. Synthesis of Uio-66-NH_2

Uio-66-NH_2 was synthesized according to the synthesis method and conditions (molar ratio, time and temperature) in the literature [33,34]. 133.2 mg of $ZrCl_4$ (0.634 mmol) were dissolved in 36.6 mL of *N*,*N*-dimethylformamide (DMF, 475.5 mmol). 114.8 mg of 2-aminoterephthalic acid (0.634 mmol) were added and mixture was sonicated for 10 min before heating in oven at 120 °C for 24 h. After cooling to room temperature, the obtained precipitate was separated by centrifugation at 13,000 rpm for 5 min and washed three times with DMF and three times with EtOH. Finally, the yellow power was dried at 100 °C for 24 h before further characterization. Similar reaction conditions but using H_2BDC as linker were tried to synthesize pure phase unfunctionalized Uio-66 [33].