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Research Paper

Sensitive detection of pyrraline with a molecularly imprinted sensor based on metal-organic frameworks and quantum dots

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ABSTRACT

A novel opto-sensor was constructed by anchoring the molecularly imprinted polymers (MIPs) onto the surfaces of metal-organic frameworks (MOFs) and CdSe/ZnS quantum dots (QDs) *via* one-step reverse micro-emulsion polymerization. It was used for highly selective and sensitive detection of pyrraline (PRL) in milk powders. High selectivity was guaranteed by molecular imprinting, and sensitivity was improved by double signal amplification using the CdSe/ZnS QDs nanocrystals as fluorescent elements and MOFs as an imprinting matrix. The QDs were introduced into the molecularly imprinted sensor as a tentacle to sense bonding interactions between the MIPs and target molecules and to transduce them into fluorescent signals. The opto-sensor had a high fluorescence quantum yield because of the use of hydrophobic CdSe/ZnS QDs and the reverse micro-emulsion. Under optimized conditions, the fluorescence intensity of the opto-sensor was linear with increasing PRL concentration over the range 5×10^{-6}–1×10^{-3} mol L^{-1}, with a detection limit of 3.9×10^{-6} mol L^{-1}. Recoveries of 90–110% were achieved in direct selective detection of PRL in milk powders.

1. Introduction

Sensors report the detection of targets *via* electrical, optical, magnetic, or thermal signals according to certain criteria [1–4]. Device characteristics include miniaturization, digitization, intelligence, multi-functionality, systematic behavior, and networking. Recently, molecularly imprinted sensors have been widely used for the detection of trace materials from complex matrices [5]. Molecular imprinting usually involves polymerization in the presence of a template molecule to produce cavities in the polymer that are highly selective for that template [6]. Sensors that incorporate the high selectivity of molecularly imprinted polymers (MIPs) can also exhibit sensitivity and simplicity, and can have cost-effective instrumentation [7]. However, MIPs can only identify molecules and cannot output a signal. Signaling response elements are thus usually introduced as a tentacle to produce detectable signals when sensing bonding interactions between the MIPs and target molecules.

Fluorescent sensing elements have many advantages such as high sensitivity, selectivity, and real-time chemical analysis [8,9]. In particular, quantum dots (QDs) have attracted increasing attention because of charge or energy transfer interactions with the analyte. QD optosensing elements made from nanocrystalline semiconductor have high luminescence efficiency, good photostability and size dependent emission wavelengths [10–13]. For example, Huang et al. reported highly sensitive urea detection with mercaptosuccinic-acid-capped CdSe/ZnS QDs [14]. Cyclodextrin-modified CdSe/ZnS QDs enabled the highly sensitive detection of pollutant phenols in the environment [15]. Bai et al. prepared hydrophilic amine-functionalized nanocomposites by using hydrophobic QDs of ZnS:Mn^{2+}@allyl mercaptan as building blocks for detection of nitro-aromatics [16]. Huang et al. developed a simple and sensitive sensor for three ruthenium anticancer drugs and calf thymus DNA based on CdTe QD fluorescence [17]. A molecularly imprinted sensor based on CdSe/ZnS QDs on the surface of the

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MIPs for enabled optosensing of dicyandiamide in dairy products [18].

Here, the sensor sensitivity is improved by dual signal amplification that uses QDs as fluorescent elements and metal-organic frameworks (MOFs) as an imprinting matrix. MOFs are highly porous solids that assemble transition metal ions or clusters with poly-functional organic ligands [19,20]. They have extremely high surface areas, uniform pore sizes, powerful chemical tailoring, and good thermal stability [21]. In particular, the material from Institut Lavoisier (MIL-101) also has high chemical and hydrothermal stabilities, and a high specific surface area. These properties make it an ideal support material [22,23].

Based on the above considerations, we propose a novel strategy combined the high selectivity of molecular imprinting with the strong fluorescence of QDs and the high specific surface area of MIL-101 to fabricate a new sensor for the detection of pyrraline (PRL). PRL is an advanced glycation end products (AGEs) that accumulate in different tissues and organs of the human body [24]. It plays a significant role in aging and in the development of chronic diseases such as diabetic nephropathy, Alzheimer's disease, and atherosclerosis [25,26]. Therefore, it is very important that a simple, rapid, highly sensitive and selective method be developed for PRL detection. Recently, we have prepared a core–shell MOFs coated with a dummy template MIPs by one-pot bulk polymerization for the detection of pyrraline in food samples [27].

A molecularly imprinted PRL sensor based on MOFs and QDs (MIS@MOFs&QDs) is discussed. High selectivity is guaranteed by molecular imprinting, and high sensitivity is derived from the dual signal amplification by the QDs and MOFs. The sensor was tested for detection of PRL *via* fluorescence quenching across a wide concentration range, which was achieved *via* direct molecularly imprinted sensor-analyte interactions without complex pre-treatment steps.

2. Experimental section

2.1. Materials

CdSe/ZnS QDs with a fluorescence emission wavelength of 605 nm were purchased from Jiayuan (Wuhan, China). Chemicals used for the MIL-101 synthesis were the chromium (III) nitrate nonahydrate (99%, Strem Chemicals, Inc., Massachusetts, USA), hydrofluoric acid (40%, Xilong Chemical Co., Ltd., Guangdong, China), and terephthalic acid (99%, Sinopharm Chemical Reagent Co., Ltd.). 3-Aminopropyl triethoxysilane (APTES, 98%; Sinopharm Chemical Reagent Co., Ltd., Beijing, China), tetraethyl orthosilicate (TEOS, 98%; J&K Scientific, Ltd.), and acetic acid (99.5%, Sinopharm Chemical Reagent Co., Ltd.) were used for the MIP synthesis. Pyrraline was obtained from Toronto Research Chemicals Incorporated (Toronto, Canada). L-glutamic acid (GA), N^{ε}-carboxymethyllysine (CML), 3-pyrroline (3-PROL), pyrrole (PYR), and pyrrolidone (PRD) were purchased from J&K Scientific, Ltd. (Beijing, China). Zinc nitrate, Calcium chloride anhydrous, Magnesium sulfate, Iron(III) chloride, Iron(II) sulfate heptahydrate, Potassium chloride, Manganese chloride, Sodium chloride, D-Fructose, D-Galactose were purchased from J&K Scientific, Ltd. (Beijing, China), D-Glucose, β-Lactoglobulin, Casein, L-Phenylalanine, L-Tryptophan and L-Lysine were purchased from Sinopharm Chemical Reagent Co., Ltd. (Beijing, China). Doubly de-ionized water (DDW, 18.2 MΩ cm^{-1}) was obtained from a Water Pro water purification system (Labconco, Kansas, MO, USA). Other solvents and starting materials were used as received.

Samples of milk powders for children, students, women, and middle- and old-age peoples, were collected from a local market. They were protected from light and kept at 4 °C prior to analysis.

2.2. Instrumentation

Fourier-transform infrared (FT-IR) spectra (4000–400 cm^{-1}) were acquired by the KBr pressed-disc method on a Bruker Vertex 70vxrd spectrophotometer (Bruker, Germany). Fluorescence spectra were acquired on a multifunctional microplate (Biotek, USA), while scanning electron microscopy (SEM; S-4800, Hitachi, Japan) was used to observe the surface morphologies. Thermo gravimetric analysis (TGA) was performed under air on a PTC-10A analyzer (Rigaku, Japan) from room temperature to 700 °C at a ramp rate of 26 °C min^{-1}. X-ray diffraction (XRD) patterns were obtained using a Rigaku D/max-2500 diffractometer (Rigaku, Japan), with Cu Kα radiation.

2.3. Preparation of MIS@MOFs&QDs

MIL-101 was prepared as reported previously methods [27]. A PRL-imprinted sensor based on MIL-101 and CdSe/ZnS QDs was fabricated in the following one-step polymerization. At room temperature, 1.80 mL of Triton X-100 was dispersed in 7.5 mL of cyclohexane under vigorous magnetic stirring for 15 min. Then 1 mL of CdSe/ZnS QDs, 1 mg of MIL-101, 50 μL of TEOS, and 100 μL of aqueous ammonia solution (25 wt%) were added. After the mixture had been stirred for 2 h, 19 μL of APTES and 0.5 mg of PRL dissolved in 100 μL of DDW were added. The mixture was sealed and kept for 24 h. After polymerization, the product was washed with acetone and centrifuged at 5000 × *g* for 10 min to remove the supernatant. The precipitate was washed with DDW and successively washed with acetone and DDW twice. The polymer was extracted with acetonitrile at room temperature for 26 h. The MIS@MOFs&QDs was obtained after drying in a vacuum oven at 40 °C for 10 h. As a control, polymers were prepared in the absence of the PRL template molecule using the same procedure.

2.4. Fluorescence measurement

All the fluorescence measurements were performed under the same conditions. The excitation wavelength was 460 nm for emission over the range 500–700 nm. The MIS@MOFs&QDs was mixed thoroughly for 80 min and then scanned on the multifunctional microplate.

The MIS@MOFs&QDs (1 mg) was added to a Labsystems 96-well plate, and a specific concentration of analyte standard solution (200 μL) was added to each well. After thorough mixing, scanning was performed using the microplate reader. L-glutamic acid (GA), N^{ε}-carboxymethyllysine (CML), 3-pyrroline (3-PROL), pyrrole (PYR), and pyrrolidone (PRD) were used as competing analytes to test specificity.

2.5. Sample preparation

Protein-bound PRL was prepared as follows. Milk powder (10 mg) was homogenized in 0.5 mL of sodium borate buffer (0.2 M, pH 9.2) prior to sodium borohydride reduction. The suspensions were reduced overnight at 4 °C. Then TCA solution (60%) was added to produce a final TCA concentration of 20% in the sample. This was centrifuged at 5000 × *g* for 10 min to precipitate the protein. The retentate was hydrolyzed in 6 M HCl (1 mL) at 110 °C for 24 h. The acid was removed under vacuum and the dried protein hydrolysate was redissolved in DDW (3 mL) for detection. Free PRL in milk powder (10 mg) was used in 0.5 mL of methanol (75%) to remove the protein, and then centrifuged at 5000 × *g* for 10 min. The precipitate was added to DDW (3 mL) for the fluorescence detection.

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