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Millifluidic chip with a modular design used as a sample pretreatment cartridge for flour and flour food products

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ABSTRACT

The integration of sample pretreatment remains one of the hurdles towards a rapid, automated micro total analytical system (μ-TAS) for real samples. In this paper, a modular design, which was used for sample preparation, has been developed as the polydimethylsiloxane (PDMS) millifluidic chips with channels at a millimeter level. Multiple functional units, including extraction, filtration, mixing and solid phase extraction (SPE), for sample pretreatment were integrated in one chip. In this chip, each functional unit was connected by pump tubings and one-way valves in series to form a fully automated system. Based on the modular design, multiple functional units have been combined in different sequences according to practical needs. In addition, the proposed system has characteristics of miniaturization, portability, and real-time application. Herein, spiked benzoyl peroxide (BPO) in flour samples was used as a model compound to study the system's performances. With a portable integrated Raman spectrometer for detection, the detection limit of BPO was 0.017 g kg^{-1}, with a linear relationship from 0.025 to 0.5 g kg^{-1}. This modular design was demonstrated to be effective and it can be expanded for pretreatment of other food samples.

1. Introduction

Automation of as many steps as possible in a process has been the goal of analytical chemists over the years [1]. Human error and contamination can potentially be reduced through the integration of sample pretreatment, separation and detection [2]. Miniaturization of traditional analyses is helpful to enable their automation and integration by using a reduced amount of sample and in a short analysis time [1]. Hence, the micro total analysis system or μ-TAS has been developed quickly ever since Manz et al. first proposed such a concept in 1990 [3]. Various conventional techniques have been successfully developed in miniaturized systems. μ-TAS have been widely used in biological, food and environmental analysis [4–6], especially in the form of the integrated device, and it has emerged as a promising technique because of its low fabrication and reagent cost, rapid analysis, and high portability [7,8]. However, the integration of sample pretreatment into the μ-TAS is still one of the remaining hurdles towards achieving the real miniaturized systems [9]. Although several sample pretreatment steps, such as filtration [10,11], liquid-phase microextraction [12,13], liquid-liquid extraction [14,15], solid-phase extraction [16,17], cell lysis [18,19], and pre-column derivatization [20], have been integrated into the microfluidic chip, such an integration is often not sufficient for analysis of real samples because the isolation of target analyte from real samples is often accompanied with multiple sample-processing steps. In addition, the protocols for sample pretreatment were usually different according to the detection method and sample matrices involved. So, the integration of different sample pretreatments into one system is still difficult, and the optimized protocol may only be suitable for limited samples or some similar kinds of samples. Such protocols reduced the efficiency of the analysis greatly and hindered their application in detection in real samples.

Benzoyl peroxide or BPO, due to its bleaching and sanitizing properties, is commonly used as a food additive in flour [21]. However, excessive BPO not only degrades nutrients in flour but also induces

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allergic reactions, and BPO is also a weak carcinogen [21]. In wheat flour, the decomposed product of BPO, such as benzoic acid and biphenyl, may further cause tissue damage and diseases [22,23]. Therefore, the amount of BPO used as a flour additive is strictly controlled by food safety regulations of various countries [24]. In the US and UK, the maximum BPO concentration regulated is 0.05 g kg^{-1}. In China, the maximum concentration regulated is 0.06 g kg^{-1}. From 2011, BPO has been strictly forbidden as a flour additive in European Union and China [24]. Therefore, analysis of BPO in wheat flour is required for regulation enforcement. Analysis includes chromatography methods [25–32], flow injection analysis (FIA) [33,34], chemiluminescence [35], electrochemistry [36,37], spectrophotometry [38] and fluorescence [24]. Compared with chromatographic methods, spectroscopic methods can offer rapid detection, but these methods always require sample pretreatments, such as purification, derivatization and preconcentration, but automation of sample preparation is rarely seen. In short, most of the existing methods are still difficult to meet the requirements of on-site rapid detection.

Here, a modular-based millifluidic chip system for sample pretreatment was proposed using BPO as a model compound, and a portable SERS detection was integrated with the sample pretreatment to accomplish a full automation of the system. The modular approach was proposed in order to accommodate different pretreatment protocols. Modular design is a new concept, and it has only emerged in recent years. This technique increases analytical capabilities, simplifies the whole analytical process, and broadens the access to valuable technologies [39]. Modular design has been successfully used in integrating PCR and CE for genetic analysis [40], immunodetection with an automated point-of-care system [39], cultivation and delivery of mammalian cells [41], and coupling magnetic capturing and detection [42]. Furthermore, the millifluidic chip system has several advantages over microfluidic chips such as low cost for fabrication, ease of assembly [43], which can provide different assembly sequence or partly satisfy different demands from different samples, in accordance with the modular design of the millifluidic system. The whole system proposed here enables high levels of integration, automation, and flexible assembly ability, with advantages of low cost and small sizes and has the potential to be expanded into a combination of multi-functional systems. The modular design was successfully used for sample pretreatment and detection of BPO in flour and flour products.

2. Experimental

2.1. Materials

All chemicals were of analytical reagent grade, and deionized (DI) water was used for the preparation of reagent and sample solutions. Anhydrous benzoyl peroxide or BPO (98%) was purchased from J&K Scientific Co., Ltd. (Beijing, China). Acetone and methanol were bought from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). The solid phase extraction (SPE) disk was bought from Aumi technology Co, Ltd. (Shandong, China). The flour samples were bought from the local supermarkets. The stock solution of BPO were prepared by dissolving 0.10 g BPO in 100 mL acetone, and the stock was then gradually diluted to 0.1, 0.05, 0.025, 0.01, 0.005, 0.0025, 0.001 g kg^{-1} by acetone. All solutions were freshly prepared from the stock solution prior to the experiments. The gold nanoparticles (50 nm in diameter) used in SERS detection was prepared as in a previous report [44] and they were stored in a 4 °C refrigerator.

2.2. Instrumentation

A UV–visible spectrophotometer (model UV-1800 from Shimadzu, Japan) was used to characterize the gold nanoparticles and optimize the system. A commercial portable Raman spectrometer (PT6010, from Photop Technoglogis, Inc. Fuzhou, China) was used to collect the SERS signal of BPO from the samples. The laser wavelength was 785 nm, and the laser beam diameter was approximately 3 mm. The spectral resolution was 8 cm^{-1}, and the integration time was set at 10 s. All measurements were performed at room temperature.

2.3. Chip design and fabrication

The schematic diagram of the millifluidic chip, as shown in Fig. 1, consisted of three functional units (sample chamber, mixing pool and SPE unit), and had three inlets (A, B and C) and one outlet (D). Inlet A was connected with a hollow pipe, which acted as the sample chamber. Pieces of sieve plate were mounted at the bottom of the chamber and acted as filters. After the sample chamber, there was the mixing pool. Inlet B was connected to the mixing pool and used as a breath hole. The mixing pool was then connected to the SPE unit. Input C, which was also connected with the SPE unit, was used to introduce the effluent solution. A membrane, which was cut from the SPE disk was fixed on the bottom of a pipe and acted as the SPE unit. After the SPE unit, there was the outlet D, from where the waste was discarded or the eluant collected. There were several one-way valves in the design to ensure the solution can only flow forward in one direction. All of the three functional units and valves were connected by pump tubings.

As shown in Fig. 1b, the millifluidic chip was fabricated by the following 4 steps: preparation of PMMA mold, construction of channels, PDMS casting and curing, and removal of mold. First, polymethyl methacrylate (PMMA) (Shandong Zhangqiu organic glass Co., China) plates were cut and combined to form a mold with a size of 70 mm × 60 mm × 23 mm (length × width × thickness). Second, the 3 functional units and 4 valves were connected by the tubing and form an integrated flow path. Third, the flow path was put and fixed in the mold and PDMS was poured into the mold. Finally, after the curing of PDMS, the mold was removed, and a millifluidic chip with the size of 70 mm × 60 mm × 23 mm (length × width × thickness) was obtained.

2.4. Integrating instrument for liquid flow control and Raman detection

An integrated instrument was constructed to operate the millifluidic chip. This instrument was used to pump reagent solutions to flow through the millifluidic chip, to achieve SERS detection of BPO and to display results. The integrated instrument (Fig. 1c) which comprised a fluid-pumping system, a Raman spectrometer and a display screen, had a size of 26.5 cm × 16.5 cm × 10 cm. As shown Fig. 1c, three reagent reservoirs were designed at the right of the instrument; four peristalsis pumps (model TT-10A from Tianli Fluid Industrial Equipment Factory, Wuxi, China) were installed on the back of the instrument, such that the flow rate was controlled at 0–10 mL min^{-1} precisely; a chip holder was installed beside the reagent reservoirs, where a millifluidic PDMS chip has been mounted. The front main body of the instrument is a 7-in. touch LCD display screen, with a resolution of 800 × 600 dpi. The parameters of the peristalsis pumps and the Raman spectrometer were set through the display screen, and the results of the SERS detection was also displayed on the screen. The control circuit of the instrument and a portable Raman spectrometer were sequentially arranged under the touch screen.

2.5. Pretreatment of flour food samples and SERS detection

First, 3 mL DI water and 1 g flour or flour food sample were loaded into the mixing pool (via Inlet B) and the sample chamber (via Inlet A after removing the stopper), respectively. Then, 1 mL acetone was injected from Inlet C to rinse the SPE membrane at a flow rate of 0.43 mL min^{-1}. Second, 3 mL acetone was pumped through the sample