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An integrated microfluidic chip for formaldehyde analysis in Chinese herbs

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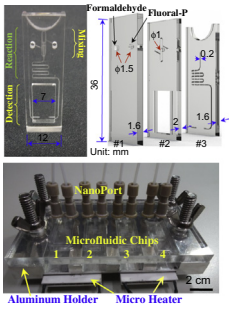
HIGHLIGHTS

- A novel integrated microfluidic chip is proposed for formaldehyde analysis.
- The validity of the proposed device is confirmed with formaldehyde concentrations ranging from 1 to 50 ppm.
- The real-world applicability is then demonstrated by measuring the formaldehyde concentration in commercial Chinese herbs.
- The measurement results deviate by no more than 3.7% from those results obtained using colorimetric method.

GRAPHICAL ABSTRACT



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ABSTRACT

A novel integrated microfluidic chip with a three-layer polymethyl methacrylate (PMMA) structure is proposed for formaldehyde concentration detection applications. In the proposed device, the sample and a fluorescence derivatization reagent (Fluoral-P) are mixed in a circular mixing chamber and then flow through a serpentine reaction channel heated to a temperature of 30 °C by an integrated hotplate. Following a reaction time of 4 min, the microchip is removed from the hotplate and placed in the microscope stage of a laser-induced fluorescence (LIF) detection system. The formaldehyde concentration of the sample is then inversely derived from the measured value of the fluorescence intensity. The validity of the proposed device is confirmed by comparing the detection results obtained for standard samples with known formaldehyde concentrations ranging from 1 to 50 ppm with those obtained using a traditional UV/VIS absorption spectrometry. The real-world applicability of the proposed device is then demonstrated by measuring the formaldehyde concentration in ten commercial Chinese herbs. It is shown that the measurement results deviate by no more than 3.7% from those results obtained using colorimetric method by CAAPIC. Overall, the results presented in this study show that the proposed microchip provides a rapid and reliable tool for formaldehyde concentration measurement purposes.

1. Introduction

Microfluidic devices are widely used throughout the health, food, environmental monitoring, medicine and chemical industries [1–14]. Compared to their macroscale counterparts, such devices not only offer the advantages of a lower cost and a more rapid

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throughput time, but also facilitate the automation of the measurement process; thereby minimizing the risk of human error and improving the reproducibility of the measurement results. Typically, microfluidic devices are designed to carry out specific tasks such as capillary electrophoresis (CE), species mixing, flow cytometry, polymerase chain reaction (PCR), sample pre-treatment and injection [15–29].

Many researchers have demonstrated the feasibility of integrating multiple microfluidic devices on a single chip so as to realize Lab-on-Chip (LoC) systems for a variety of chemical and biological analysis applications [30–49]. For example, Lin et al. [31,32] presented an integrated microfluidic chip for rapid DNA digestion and time-resolved capillary electrophoresis analysis comprising two gel-filled chambers, a micromixer, a serpentine channel and a CE channel. The time-resolved electropherograms showed that the device was capable of concentrating and analyzing Φx-174 DNA samples comprising 11 fragments within 24 min. Ju et al. [37] presented an integrated system for the distillation and detection of SO_2 composed of a microfluidic distillation chip, a power control module and a carrier gas pressure control module. The experimental results showed that a correlation coefficient of $R^2 = 0.9981$ and a distillation efficiency of as much as 94.6% were obtained for H_2SO_3 solutions with SO_2 concentrations ranging from 100 to 500 ppm. Rosenauer and Vellekoop [39] presented a novel silicon-based microflow cytometer incorporating an integrated three-dimensional adjustable optofluidic lens system for biochemical analysis applications. It was shown that the device was capable of detecting particles with a diameter of as little as 4 μm at a nominal flow rate of 600 beads/s.

Formaldehyde occurs naturally in air and the human body and is widely used as a preservative in processed food; particularly dried food and frozen food. However, many countries have now banned the use of formaldehyde as a food additive due to concerns regarding its potential adverse effects on human health, e.g., headaches, abdominal pain, vomiting, breathing difficulties, and so on. Many different macroscale techniques have been proposed for formaldehyde concentration detection, including colorimetric methods [50,51], spectrophotometric detection methods [52,53], fluorometric methods [54,55], gas chromatography or high-performance liquid chromatography (HPLC) methods [56,57], and kinetic methods [58]. However, while such methods enable the formaldehyde concentration to be reliably measured, they have a number of drawbacks. For example, colorimetric methods are relatively slow and have a limited sensitivity, while fluorometric methods require the use of large, complex and expensive instrumentation. Furthermore, gas chromatography and HPLC methods have poor specificity and are easily interfered with by carbonyl substances, such as acetaldehyde or acetone.

To resolve these problems, many microfluidic systems for formaldehyde concentration detection have been proposed in recent years. For example, Weng et al. [59] developed a PDMS microfluidic chip in which the formaldehyde concentration was detected by illuminating the reaction region with UV light (410 nm) and measuring the absorption rate as the reaction proceeded. Zhang et al. [60] presented a miniaturized electrophoretic method for determining the concentration of formaldehyde and acetaldehyde in food using a 2-thiobarbituric acid derivatization method. The results showed that the proposed capillary electrophoresis–electrochemical detection (CE–ED) device was capable of separating the formaldehyde-2-thiobarbituric acid and acetaldehyde-2-thiobarbituric acid adducts with a detection limit of as low as 9.10×10^{-9} g/mL. Pang and Lewis [61] presented a microfluidic derivatization technique for the measurement of gas phase formaldehyde using a Pyrex micro-reactor comprising three inlets and one outlet, gas and fluid splitting/combining channels, mixing junctions, and a 2.0 m long, 620 μm internal diameter reaction microchannel. The feasibility of the proposed technique was demonstrated by measuring the formaldehyde concentration in ambient air.

The present study develops a three-layered PMMA microchip for formaldehyde concentration detection comprising two inlet ports, a mixing column, a serpentine reaction column and a rectangular collection chamber. In the proposed device, the formaldehyde sample is mixed with a fluorescence derivatization reagent (4-amino-3-penten-2-one; Fluoral-P) and then enters the serpentine reaction column. The reaction column is maintained at a temperature of 30 °C by a hotplate positioned beneath the microchip and induces a reaction between the formaldehyde sample and the Fluoral-P to produce 3,5-diacetyl-1,4-dihydrolutidine (DDL). Following a predetermined reaction time (4 min), the microchip is moved to the microscope stage of a laser-induced fluorescence (LIF) detection system and the formaldehyde concentration is inversely derived by measuring the fluorescence intensity signal of the reactant in the collection chamber. The validity of the proposed approach is demonstrated by comparing the detection results obtained for samples with known formaldehyde concentrations in the range of 1–50 ppm with those obtained using a traditional UV/VIS absorption spectrometry. Finally, the real-world applicability of the proposed device is evaluated by measuring the formaldehyde concentration in ten commercial Chinese herbs.

2. Fabrication and experimental details

2.1. Chip configuration and fabrication

Fig. 1(a) illustrates the major components within the proposed microfluidic chip, namely the mixing column, the reaction column and the detection column. As shown in Fig. 1(b), the microchip comprises a PMMA substrate with a thickness of 2 mm sandwiched between two PMMA substrates with a thickness of 1.6 mm. The upper substrate (substrate #1 in Fig. 1(b)) was drilled with two via holes with a diameter of 1.5 mm to serve as inlets for the formaldehyde sample and derivatization reagent, respectively. Meanwhile, the middle substrate (substrate #2) was patterned with a circular mixing chamber with a diameter of 1.0 mm and a rectangular collection chamber with dimensions of 7 mm × 12 mm. Finally, the lower substrate (substrate #3) was patterned with a serpentine reaction column with a width of 200 μm and a depth of 200 μm in order to connect the mixing chamber and the collection chamber.

The microchannels and reservoirs in the PMMA substrates were designed using commercial AutoCAD (2010) software and were ablated using a defocused CO_2 laser beam system. (Note that a full description of the laser ablation process is provided in a previous study by the current group [37]). The pattern and thickness of each layer of the microchip are defined by the PMMA substrates and

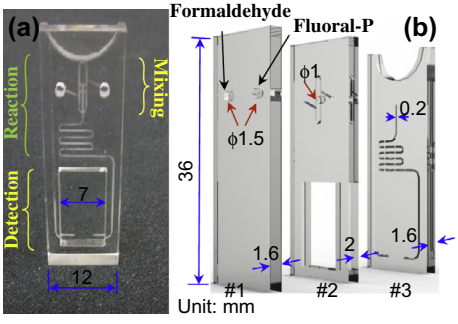

Fig. 1. (a) Photograph of assembled microfluidic chip showing major components. (b) Schematic illustration showing configuration of each PMMA substrate in three-layered structure.