Journal of Chromatography A, 1572 (2018) 27–36

Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Micro-fabricated packed metal gas preconcentrator for enhanced monitoring of ultralow concentration of isoprene

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ARTICLE INFO

Article history:
Received 4 June 2018
Received in revised form 24 August 2018
Accepted 30 August 2018
Available online 31 August 2018

Keywords:
Gas preconcentrator
Breath analysis
Absorbent
Laser etching technology
Vacuum diffusion welding
Advanced fibrosis

ABSTRACT

A novel non-silicon-based micro-preconcentration device, as a pretreatment component in a portable gas chromatography system, was developed for the preconcentration one of the trace volatile organic compounds (VOCs) in the exhaled gases, which is one typical biomarker for the chronic liver disease (CLD). The device was designed as an array of manifold-shaped rectangular metal micro-channels with flat dimensions of 16 mm × 12.6 mm and the internal empty volume is 14.4 μL on the copper substrate. Instead of the non-silicon fabrication process, the traditional laser etching technology (LET) was optimized to etch micro-channels, and vacuum diffusion welding (VDW) was applied to form internal channels. The fabricated chip was filled with Carbopack X adsorbent. In the testing, the metal gas preconcentrator (MGP) was installed in a commercial GC (gas chromatography) and nitrogen was used as carrier gas and desorbed gas. With the MPG, up to 352 of concentration factor can be achieved for 10 ppb isoprene. The developed MGP, which has advantages of high strength, low cost, good thermal conductivities, can potentially be used for non-invasive screening of advanced liver fibrosis by monitoring isoprene concentrations in exhaled breath.

1. Introduction

The prevalence of CLD has steadily increased and is currently estimated to affect 14.7% of the U.S. population [1]. CLD is the 12th leading cause of death in the country and causes 4 billion dollars in hospital admissions each year [2]. In any cause of CLD, the disease spectrum ranges from no fibrosis to minimal fibrosis to advanced fibrosis and cirrhosis with complications secondary to portal hypertension. Therefore, it is crucial to identify patients with advanced fibrosis and cirrhosis as soon as possible so that appropriate treatment and screening methods can be established to prevent, diagnose, and treat complications of end-stage liver disease [3].

Liver biopsy is a gold standard test to assess the staging of fibrosis. It is an invasive procedure with a complication rate of approximately 5.9% [4], the most worrisome of which is bleeding [5]. Compared with the traditional gold standard, the exhaled breath analysis is a non-invasive diagnostic method, which has the advantages of non-invasiveness, low cost, simple operation, safety and convenience [6]. Therefore, we tried to detect isoprene, which is considered a biomarker for CLD with high specificity, by means of breath analysis techniques in order to preliminarily classify CLD and avoid liver biopsy in a large number of patients. Unfortunately, the cutoff value required for the detection of isoprene is at least a level of ~10 ppb (parts per billion) [3]. Whereas, the most commercial gas sensors are developed for measuring samples with concentrations at several tens ppm (parts per million). The concentration of isoprene in breath analysis is too low to be detected by the existing gas sensors directly.

To realize much lower detection limit of a gas analysis system, a preconcentrator can be used to amplify the concentration of the target gas. It will effectively convert a sample containing a low gas molecular concentration into a smaller volume sample with a high concentration [7]. Specifically, the preconcentrator exhibits collecting and concentrating the analyte sample over a period of time and then releasing the concentrated analyte to a sensor after application of the heating pulse [8,9]. It can be integrated at the front-end of any gas analysis system such as gas chromatographs [10,11], mass spectrometers and ion mobility spectrometers [10,12]. The conventional preconcentrators are usually made of stainless steel or silicon tubes filled with adsorbent. The high temperature required for operation of the device is obtained by coils wound on the tube.

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https://doi.org/10.1016/j.chroma.2018.08.058
0021-9673/

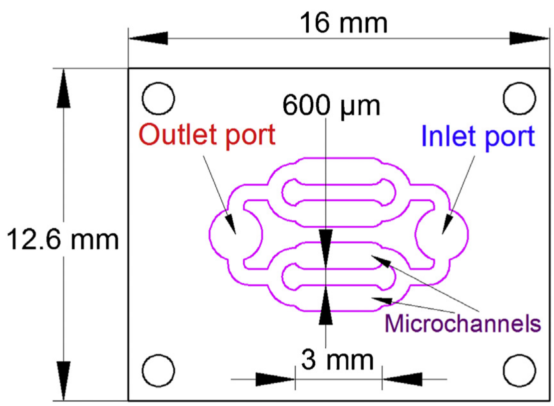

Fig. 1. Schematic of channel of MGP from top view.

This type of preconcentrator is physically large, slow response, high power consumption during the thermal desorption cycles, and expensive [13,14]. It is not suitable for the portable instruments and rapid detection. The micro preconcentrator fabricated by MEMS process, can overcome these limitations by significantly reducing its size, thermal mass and power consumption [10,15]. Extensive research works on the micro preconcentrator have been carried out, and they mainly focus on structural forms, adsorbent materials and analyzed gas types [16–27]. However, all of above are based on the silicon substrate. It is well known that the thermal characteristic parameters (thermal conductivity and specific heat capacity) have a significant influence on the concentration factor. The high thermal conductivity, the low specific heat capacity can make the heating rate faster, and the power consumption lower. Furthermore, good temperature uniformity can make the desorption peak narrower. Hence a substrate with the expected thermal properties is beneficial to improve the concentration factor. Copper (C11000) has better thermal properties than the silicon then it is used as substrate material. The thermal conductivity of C11000 is about 2.6 times that of silicon, and the specific heat capacity of C11000 is only 0.56 times that of silicon. Moreover, C11000 has good chemical stability, adequate hardness, enough strength, as well as easy fabrication with traditional manufacturing methods.

For reasons above, we proposed a non-silicon-based micro preconcentrator. The C11000 was applied as substrate and the micro-channel was fabricated by laser etching technology. In addition, VDW was used to form the channels. Adsorbents were filled in the channel, and the carrier gas pushed the desorbed highly condensed gas into the detector. Our target minimum detection concentration was 10 ppb. In the following, the design, manufacturing, characterization and the pre-concentration results of the metal preconcentrator were presented.

2. Experimental

2.1. Preconcentrator structure

In design of the MGP, many factors should be considered, such as gas flow uniformity, high capacity, small size, simple integration and low-cost manufacturing process. Previous works mainly concerning the micro silicon-based gas preconcentrator were usually fabricated by the deep plasma etching to form the grooves and by anodic bonding to form the cavities [21]. However, for the non-silicon MGP, LET and VDW were used to fabricate micro-channels and seal them. The MGP mainly consists of 4 copper micro-channels (each is 1 mm width, 3 mm long and 500 μm depth) on the copper substrate, as shown in Fig. 1. The walls of the copper micro-channels served as heat conductor during heating while the micro-channels accommodate the adsorbent in the trenches. The internal volume of the micro-channels is 14.4 μL when no adsorbent is filled. Furthermore, in order to minimize fluctuations or delay of the desorption signal, a symmetrical manifold fluid system was designed at the inlet and outlet, which lead the original gas sample to be equally distributed at the inlet, and uniformly collected at the outlet in the concentrated form. In the VDW process, the metal plate, which is the same material as that of substrate, was covered on the copper substrate to form the cavity. The design was beneficial to form a good seal and bonding strength, avoid interfacial stress during the temperature cycles, and eventually improve the ability of withstanding high pressure and leaking. In addition, a stainless steel sieve (mesh size 100) was installed at the outlet of the MGP to prevent the sorbent from escaping. Meanwhile a micro-ceramic heater (Youpusi Technology Co., Ltd, Beijing, China) was integrated on the bottom of the copper substrate for the thermal desorption of the adsorbent. The micro-ceramic heater was fixed to the MGP by very fine stainless steel wire in good contact with underside of the copper substrate. The deactivated fused silica capillary tubes were connected with the inlet and outlet of the MGP through the customized polyimide adapter column which can operate stably for 2 h at 300 °C. And the overall size of the MGP is approximately 16 mm × 12.6 mm × 2.5 mm.

Table 1
Thermal properties of C11000 and silicon.

Materials	Thermal conductivity W/(m·K)	Specific heat capacity J/(kg·K)
Si	148	700
C11000	386.4	394

2.2. Materials

C11000 is used as a structural substrate of the micro-preconcentrator, because of its higher thermal conductivity and lower specific heat capacity than silicon (Table 1). Moreover, C11000 is a very common, cheap copper alloy, and its processing technology is available in many factories. The C11000 preconcentrator substrate is a new attempt of realizing micro preconcentrator by the traditional fabrication process.

Adsorbent material is an important factor in the performance of micro gas preconcentrators. The adsorbent must have strong affinity with the target gas, low desorption activation energy. The activation energy of an adsorbent is characterized by its desorption temperature and the adsorption capacity is related to its specific area. Although there are many adsorbents available, it is not easy to choose the most appropriate adsorbent for a certain application [13,14,28–31]. In the CLD breath diagnosis, for concentrating the ppb level low-concentration isoprene, Carbopack X (supplied by Sigma-Aldrich) with a specific surface area of 240 m^2/g and 60–80 mesh was selected. The adsorbents are small particles as show in Fig. 2a and b.

Before testing MGP, the adsorbent material Carbopack X must be activated by program heating. The stepwise temperature-time profiles for sorbent activation were: 100 °C-1 h, 200 °C-1.5 h, 300 °C-1.5 h, and nitrogen was applied as the carrier gas. In addition to the stainless steel sieve at the left outlet, deactivated glass wool (from Shimadzu, Kyoto, Japan) was inserted at the right inlet to prevent the adsorbent escaping from inlet. Furthermore, this superfine glass wool could help the analytes uniform gasification and play a role in filtering impurities. Fig. 3 shows the cross-section of the gas micro preconcentrator and simplified concentrator work process schematic. Fig. 4a and b show 3D structures from top and backside views respectively.