Supporting Information

Microfluidic array surface ion imprinted monolithic capillary microextraction chip on-line hyphenated with ICP-MS for high throughput analysis of gadolinium in human body fluids

Xiaoxiao Ou, Man He, Beibei Chen, Han Wang, Bin Hu*

Key Laboratory of Analytical Chemistry for Biology and Medicine (Ministry of Education), Department of Chemistry, Wuhan University, Wuhan 430072, China

*Corresponding author, fax: 86-27-68754067, E-mail: binhu@whu.edu.cn

Abbreviations

SIIP	surface ion imprinted polymer
SNIP	surface non-ion imprinted polymer
MCME	monolithic capillary microextraction
ICP-MS	inductively coupled plasma mass spectrometry

Apparatus and reagents

The monolithic capillary was prepared in thermostat water bath cauldron (Zhengzhou Great Wall Branch Industry & Trade Co., Ltd., China). A KW-4A spin coater (Siyouyen Electronic Technology Co., Ltd, Beijing, China) and a PDC-M plasma cleaner (Mingheng Science and Technology Development Co., Ltd, Chengdu, China) were used in the preparation of microfluidic chips. In the process of chip based extraction, TS2-60 microsyringe pumps (Baoding Longer Precision Pump Co., Ltd, Baoding, China) and sterile microsyringes were applied. A Mettler Toledo 320-S pH

meter (Mettler Toledo Instruments, Shanghai, China) supplied with a combined electrode was used to determine the pH values of samples. The samples were digested with a WX-3000 microwave accelerated digestion system (EU Chemical Instruments Co. Ltd., Shanghai, China) and evaporated by WX-4000 Microwave Digestion Analyzer (Shanghai Hao Technology Development Co., Ltd., China). A MATLAB interface (Matlab, The Maths Works Inc., USA) and a pressure controller were uesd to control the opening/closure of different gas valves of the chip-based array poly(γ-MAPS@Gd^{3+}-SIIP) MCME. Thermo Nicolet iS10 FTIR spectrometer (Waltham, MA, USA) and an X-650 scanning electron microscope (SEM) (HITACHI, Japan) were employed for the characterization of the prepared chip based monolithic capillary.

The solutions of coexisting cations (Na^+, K^+, Ca^{2+}, Fe^{3+}, Al^{3+}) were prepared from their corresponding nitrates, and those of interfering anions (Cl^-, NO_3^-, SO_4^{2-}, $H_2PO_4^-$) were obtained by their sodium salts.

γ-Methacryloxypropyltrimethoxysilane (γ-MAPS) was acquired from Chemical Plant of Wuhan University (Wuhan, China). 2,2-Azobisisobutyronitrile (AIBN), iminodiacetic acid (IDA), dimethyl sulfoxide (DMSO) and toluene were purchased from Sinopharm (Shanghai, China). Glycidylmethacrylate (GMA) and methylene bisacrylamide (Bis) were obtained from Sigma-Aldrich (St. Louis, MO). Polydimethylsiloxane (PDMS) was prepared by heating the mixture containing oligomers (component A) and crosslinking agents (component B) (GE RTV 615, Momentive Performance Materials, NY, USA) at a certain ratio. All reagents were of at least analytical reagent grade. High purity deionized water supplied by Milli-Q

Element System (18.2 MΩ cm, Mollipore, Molsheim, France) was used throughout this work.

Design and preparation of microchip

The microfluidic chip integrates eight capillary microextraction channels (Fig. 1A, orange lines M1-M8), twelve controlling "push-up" microvalve channels (Fig. 1A, green lines V1-V12), eight waste oulet channels (Fig. 1A, blue lines W1-W4), eight sample inlets (Fig. 1A, I1-I8), two gas (N_2) inlets (Fig. 1A, I9-I10) for separation of the liquid, two cleaning inlets (Fig. 1A, I11-I12) and CN which is the connector of chip to the Burgener-HP nebulizer of ICP-MS. A 3 cm length of fused-silica capillary (75 μm i.d.) with little dead volume and good leakproofness combined with capillary junction tube was used to connect the outlet of the chip with ICP-MS for online detection. Specifically, the height is 50 μm for all channals except for the orange section, in which the height and the width are 650 μm to match the size of monolithic capillary (530 μm i.d. × 680 μm o.d., 1 cm length). The width is 500 μm for microextraction channals, 800 μm for microvalve channals and 1000 μm for cross section of the microvalve channals to strengthen the quality of the microvalve. The microfluidic devices was fabricated through soft lithography and rapid prototyping with poly(dimethylsiloxane) (PDMS) technology.

Preparation of poly(γ-MAPS) monolithic capillary

The poly(γ-MAPS) monolithic capillary was prepared according to Ref.[1] with minor modifications. Briefly, the mixture containing γ-MAPS (575 μL) and HCl (0.12 mol L^{-1}, 100 μL) was vortexed for 30 min. Simultaneously, 30 mg of AIBN was mixed

with 420 μL toluene in a separate dark brown vial. Then, 180 μL γ-MAPS/HCl solution was added to the solution of AIBN in toluene. After vortexing for 3 min and sonicating for 3 min, the mixture was introduced into the vinylized capillary by an injector. The polymerization reaction was maintained at 80 °C for 2.5 h with both ends of the capillary being plugged with a rubber septum. Next, the capillaries were rinsed with ethanol to remove unpolymerized components, and a porous poly(γ-MAPS) monolithic skeleton was obtained.

Fabrication of monolithic capillary-embedded microchip

The monolithic capillaries (680 μm o.d., length of 1.0 cm) were embedded in the channel of PDMS microfluidic chips using a square quartz stick (length of 1.0 cm, hight of 650 μm, and width of 650 μm) as the template according to our previous work.[1] The key point for embedding a monolithic capillary into a microfluidic chip was to avoide leakage and minimize the dead volume. So PDMS oligomers was applied to fill the gap between the outer wall of monolithic capillary and the microchip channel to ensure the liquid to flow through the monolithic capillary.

Online chip-based arrary poly(γ-MAPS@Gd^{3+}-SIIP) MCME

Specifically, eight portions of sample solution were simultaneously introduced into eight array microextraction channels at a flow rate of 40 μL min^{-1} through inlets of I1-I8, respectively. The loading process was finished in 750 s. During sample loading process, the controlling microvalves of V5 and V10 were opened and the others were closed. Then, sequential elution of target Gd reteined on the monolithic capillaries was carried out. Firstly, V5 and V10 was turned off and V1 was turned on,

and the eluent was pumped into the monolithic capillary M1 through I1 at a flow rate of 25 μL min^{-1} for 35 s for elution and the eluent was directly introduced into the ICP-MS through CN. Then the microvavle V1 was switched off and V11 was switched on; 5% (v/v) of HNO_3 was pumped through inlets I11 and I12 to wash the channals for 60 s. After that, microvavle V11 was closed and V12 was opened; 0.1 L min^{-1} of N_2 was injected through inlets I9 and I10 for 10 s to separate the liquid. Then the elution on M1 microexrtaction channal was finished. The elution process was repeated for elution of other microextraction channels sequentially.

References

1 D. Gharbharan, D. Britsch, G. Soto, A. M. Weed, F. Svec, Z. Zajickova, *J. Chromatogr. A*, 2015, **1408**, 101-107.

2 J. Zhang, B. B. Chen, H. Wang, M. He, B. Hu, *Anal. Chem.*, 2017, **89**, 6878-6885.

Table S1 Operating conditions of ICP-MS (Thermo Fisher Scientific, MA, USA)

Parameters	
Rf power	1200 W
Plasma gas (Ar) flow rate	14 L/min
Auxiliary gas (Ar) flow rate	0.8 L/min
Nebulizer gas (Ar) flow	0.9 L/min
Sampling depth	150 steps
Sampler/skimmer diameter orifice	Nickel, 1.1 mm / 0.7 mm
Peak pattern	Peak hopping
Dwell time	100 ms
Integration mode	Peak area
Monitored isotope	^{157}Gd

Table S2 Pore structure parameters of poly(γ-MAPS), poly(γ-MAPS@Gd^{3+}-SIIP) and poly(γ-MAPS@Gd^{3+}-SNIP) monolithic capillaries based on measurement of nitrogen adsorption/desorption

Monolithic capillary	BET Surface area (m^2 g^{-1})	Pore volume (mL g^{-1})	Pore size (nm)
poly(γ-MAPS)	62.2	0.15	9.5
poly(γ-MAPS@Gd^{3+}-SIIP)	29.0	0.07	9.9
poly(γ-MAPS@Gd^{3+}-SNIP)	13.1	0.05	16

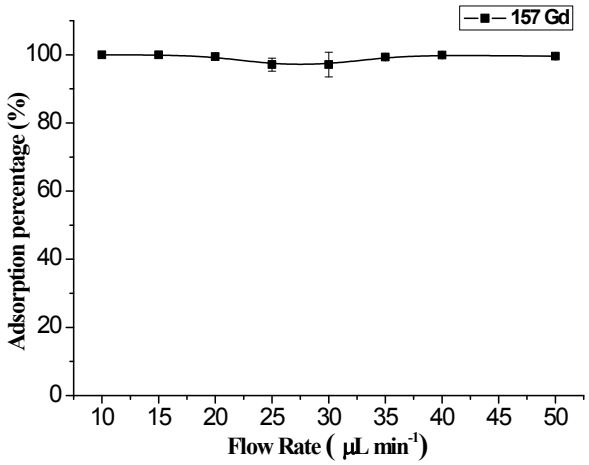

Fig. S1 Effect of sample flow rate on the adsorption percentage of Gd^{3+}; Experimental conditions:

c (Gd^{3+}) = 10 μg L^{-1}; sample volume: 0.5 mL; pH=5

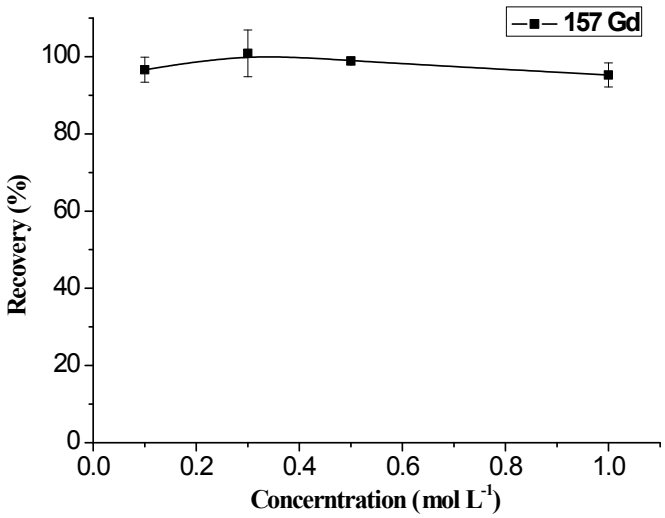

Fig. S2 Effect of eluent concentration on the recovery of Gd^{3+}. Experimental conditions: c (Gd^{3+}) = 10 μg L^{-1}; sample volume: 0.5 mL; sample pH=5; sample flow rate: 40 μL min^{-1}; eluent volume: 50 μL; elution flow rate: 40 μL min^{-1}

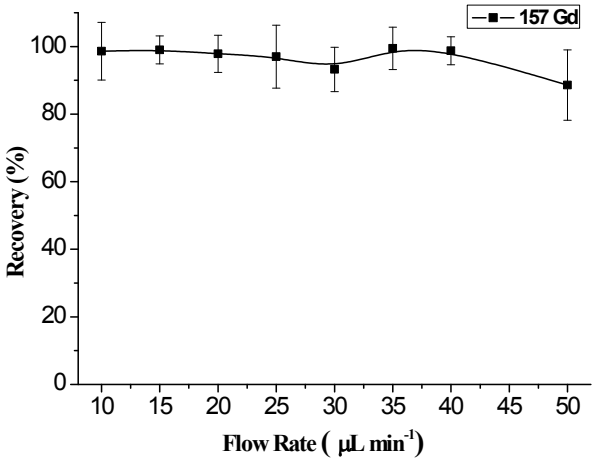

Fig. S3 Effect of eluent flow rate on the recovery of Gd^{3+}. Experimental conditions: c(Gd^{3+}) = 10 μg L^{-1}; pH=5; sample volume: 0.5 mL; sample flow rate: 40 μL min^{-1}; eluent: 0.2 mol L^{-1} HNO_3; eluent volume: 50 μL.

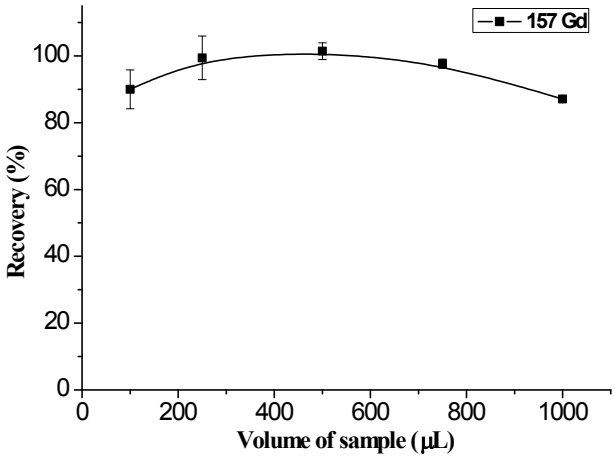

Fig. S4 Effect of sample volume on the recovery of Gd^{3+}. Experimental conditions: c(Gd^{3+}) = 10 ng; pH=5; sample flow rate: 40 μL min^{-1}; eluent: 0.2 mol L^{-1} HNO_3; elution flow rate: 25 μL min^{-1}.