Talanta 165 (2017) 496–501

Contents lists available at ScienceDirect

Talanta

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

A simple and fast Double-Flow microfluidic device based liquid-phase microextraction (DF-μLPME) for the determination of parabens in water samples

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ARTICLE INFO

Keywords:
Microextraction
Sample preparation
Microfluidic
Parabens
Water samples

ABSTRACT

A fast double-flow microfluidic based liquid phase microextraction (DF-μLPME) combined with a HPLC-UV procedure using diode array detection has been developed for the determination of the four most widely used parabens: Ethyl 4-hydroxybenzoate (EtP), Propyl 4-hydroxybenzoate (PrP), Butyl 4-hydroxybenzoate (BuP) and IsoButyl 4-hydroxybenzoate (iBuP) in water samples. Parabens have successfully been determined in environmental (lake and river water) samples with excellent clean up, high extraction efficiency and good enrichment factor using double-flow conditions. The microfluidic device consists of two micro-channels, which contain the acceptor and sample solution separated by a flat membrane (support liquid membrane). The sample (0.32 mM HCl) and acceptor phase (5.6 mM NaOH) are delivered to the μLPME at 10 μL min^{-1} and 1 μL min^{-1} flow rate, respectively. The extraction efficiencies are over 84% for all compounds in water samples with enrichment factors within the range of 9–11 and recoveries over 80%. The procedure provides very low detection limits between 1.6 and 3.5 μg L^{-1}. The extraction time and the volume required for the extraction are 5 min and 50 μL, respectively; which are greatly lower compared to any previous extraction procedure for parabens analysis. In addition, this miniaturized DF- μLPME procedure significantly reduces costs compared to not only the existing methods for paraben detection, but also to the existing analytical techniques for sample preparation.

1. Introduction

Sample treatment procedures and methodologies of analysis are in continuous development in order to overcome adverse influences of matrix components on target analyte signals in real sample analysis. In recent years, the miniaturization of analytical chemistry techniques is becoming a dominant trend as it removes limitations presented by current analysis technologies. Microfluidic devices present significant environmental and economic advantages since the consumption of sample, solvent and reagent are lower. In addition, it has been demonstrated their used on sample pretreatment resulting in high selectivity, sensitivity, a good clean-up and short time of analysis.

Parabens are alkyl esters of p-hydroxybenzoic acid which are a group of compounds widely used as antimicrobial agent in food and drinks [1–3]; as well as preservatives and bactericides in cosmetics, personal care and pharmaceuticals [4]. Methylparaben and ethylparaben are the most commonly used due to their shorter ester chain and higher solubility in water [4]. There is a trend to reduce their use since their endocrine disrupting potential, along with the discovery of these chemical compounds in the breast tissue of patients with breast cancer, raised wide discussion about parabens impact and safety [5,6]. Therefore, they have been regulated by the European Union (EU) countries [7–9]. Parabens are continuously released in the aquatic environment and methyl, ethyl, propyl and butylparabens have been detected in water samples at the ng L^{-1} level [10] and more recently in soils and sediments at the ng kg^{-1} range [11,12], being the domestic and industrial wastewater vias which contribute the most to their direct introduction into aquatic media.

Up to date, paraben have been mostly extracted by using traditional solid phase extraction (SPE) from aqueous samples [13–16] and in the last years, solid phase microextraction (SPME) was also used for parabens determination [17–19]. Paraben have also been extracted by liquid phase microextraction (LPME) procedures, one of the most known examples of sample preparation, as for example hollow fiber LPME in two [20] and three phases [21], dispersive liquid-liquid microextraction (DLLME) [22], membrane-assisted liquid–liquid ex-

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http://dx.doi.org/10.1016/j.talanta.2016.12.059
Received 13 November 2016; Received in revised form 15 December 2016; Accepted 22 December 2016
Available online 23 December 2016

traction (MALLE) [23], dynamic hollow fiber liquid phase microextraction (DHF-LPME) [24], single drop microextraction (SDME) [25]. All those procedures use low solvent volumes, are low-cost and offer high enrichment factor. Recently, we published a brief review of the literature concerning the traditional determination of parabens and new developments in cosmetic and environmental samples [26]. Recently, parabens have been extracted using electromembrane extraction (EME) [27] based on a LPME where the analytes are extracted through the membrane due to an electrical field applied to both sides. The authors completed the extraction of parabens in 40 min from 10 mL of sample increasing the enrichment factor obtained compared to a previous HF-LPME procedure.

However, there is a major trend in recent years towards the development of new analytical miniaturized technologies able to perform faster, more powerful and versatile analysis. When the LPME is down-scaled in a microfluidic device, the diffusion path is shorter and the transport phenomena is faster. Very few contributions can be found in the literature for miniaturized LPME [28,29] and there is none of them related to the extraction of parabens. LPME into microfluidic devices is still under development. This microfluidic device is a modification of our previous system where the depth has been decreased 40 μm in order to accelerate the transport phenomena by passive diffusion.

In this work, for the first time a DF-μLPME procedure into a chip combined with HPLC-DAD (diode array) detection has been developed for the determination of the four most commonly used parabens in water samples. Compared to the last article published for paraben determination, this new miniaturized microfluidic device significantly reduce the extraction time and sample consumption by a factors of eight and 100 respectively. Furthermore, the organic solvent amount is decreased and DF-μLPME provides very high extraction efficiencies and good enrichment factor. The proposed DF-μLPME-chip procedure is the easiest method up to date, it can be considered as a "green method", is low-cost and simple handling, it can be reusable and allow to change the membrane a number of arbitrary times. In addition, compared to our previous μLPME device, this new geometry accelerated transport phenomena and offered higher enrichment factors together with high extraction efficiencies.

2. Experimental

2.1. Chemicals and solutions

All chemicals were of analytical-reagent grade. Ethyl 4-hydroxybenzoate (EtP), Propyl 4-hydroxybenzoate (PrP), Butyl 4-hydroxybenzoate (BuP), IsoButyl 4-hydroxybenzoate (iBuP), 1-octanol, dihexyl ether, 2-nitrophenyl octhyl ether (NPOE), 1-heptanol, formic acid, sodium hydroxide, chloride acid, methanol were purchased from Fluka–Sigma–Aldrich (Madrid, Spain). All solutions and dilutions were prepared using ultrapure water from a Milli-Q Plus water purification system (Elga, purelab option S-R 7–15 (Madrid, Spain)).

Aqueous working solutions of parabens were daily prepared by adequate dilutions from methanolic 100 mg L^{-1} stock solutions stored at 4 °C. A membrane (Celgard 2500) of 25 μm thickness, 55% porosity, and 0.21 μm x 0.05 μm pores was obtained from Celgard (Charlotte, NC, USA).

2.2. Fabrication of the DF-μLPME

Fig. 1 shows a scheme of the reusable DF-μLPME. As well known, LPME works under passive diffusion of the compounds. This new geometry of the micro-device pretends to improve our previous microchip devices in order to decrease the diffusion path and accelerate the transport phenomena. In this case, the channels (composed of two symmetrical patterned plates of poly(methyl methacrylate)) had a length of 15 mm, depth of 40 μm and a width of 2 mm. The front side

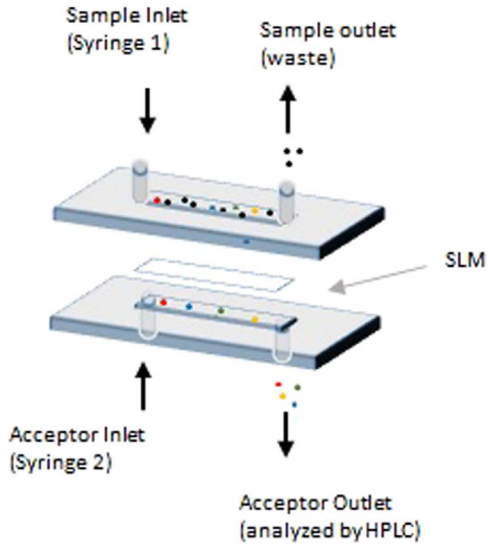

Fig. 1. Schematic of a double-flow liquid phase microextraction on a microfluidic device (DF-μLPME).

used a channel as donor (sample) solution, whereas the channel on the back side was used as acceptor phase. For the ease of fluidic handling, 1.5 mm diameter size in/outlets were drilled in both plates and Teflon sleeves were fixed.

A polypropylene membrane piece of 17 mm length×3 mm width was placed carefully over one of the channels, and it was impregnated with 1 μL of dihexyl ether using a micropipette. As a result of capillary forces, the solvent was immediately immobilized into the polypropylene membrane turning its appearance from white to transparent. This process was visually inspected. Afterwards, both methacrylate plates of the μLPME were aligned and fixed together using four screws, resulting in a new geometry for the μLPME with the dimensions for a single channel of 29×25×6 mm. An arbitrarily large number of extraction channels can be implemented and independently addressed by increasing the size of both plates.

A laser cutter (Epilog Mini 24–30 W) was used to fabricate this chip. Given the different polymer plates that can be patterned with this laser, poly(methyl methacrylate) (PMMA) was selected for its facet quality (i.e. low roughness) and processing speed. A writing speed of 45%, power of 18%, a resolution of 1500 and a frequency of 5000 provided with the best quality.

After the μLPME was closed, two separate micro-syringe pumps (Cetoni GmbH, Korbussen, Germany), each operated with a 1000 μL gastight syringe (Hamilton SYR 1 mL 1001 TLL-SAL) were used to pump the sample and acceptor solutions to the μLPME. A 0.32 mM HCl donor solution was continuously distributed to the μLPME at 20 μL min^{-1}. Additionally, a 5.6 mM NaOH aqueous solution as acceptor phase was continuously delivered to the μLPME at 1 μL min^{-1}. The polypropylene membrane separated both solutions in the μLPME. A micropipette was used to collect the acceptor solution after each extraction and the extract was analyzed by HPLC.

This microchip-device gives the possibility to be used as many times as necessary allowing the membrane exchange when it is needed.

2.3. Chromatographic conditions

The HPLC system consisted of an Agilent 1100 series (Barcelona, Spain) liquid chromatograph equipped with a G1312A Bipump systems. The injector was an autosampler G1313A allowing an injection volume of 5 μL. Separations were carried out at 25 °C using a LiChroCART1 75-4 Purosphere STAR RP-18e 3 mm (75 mm×4.0 mm i.d.) (VWR, Barcelona, Spain) proceeded by a guard column Kromasil1 100 Å, C18, 5 mm (20 mm×4.6 mm i.d.) (Scharlab S.L., Barcelona,