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Preparation of molecularly imprinted solid-phase microextraction fiber for the selective removal and extraction of the antiviral drug abacavir in environmental and biological matrices

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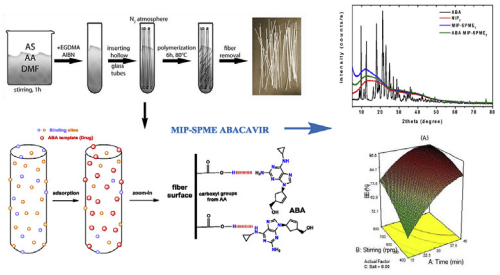
HIGHLIGHTS

- Preparation of a novel SPME MIP fiber with remarkable recognition properties.
- Selective removal and extraction of abacavir from environmental & biological media.
- Detailed adsorbent characterization and adsorption studies.
- Successful application of synthesized MIPs as SPME sorbents.
- Estimation of expanded uncertainty following a bottom-up approach.

GRAPHICAL ABSTRACT



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ABSTRACT

In the present study, a molecularly imprinted solid-phase microextraction fiber (MIP-SPME$_f$) was synthesized and applied for the selective removal and extraction of the antiviral drug, abacavir (ABA). Morphology and structure characterization of fibers were performed by scanning electron microscopy and Fourier transform infrared spectra, respectively. The effects on the adsorption behavior of the process parameters were studied and the equilibrium data were fitted by the Langmuir, Freundlich and Langmuir-Freundlich models. The maximum adsorption capability (Q_{max}) was determined by Langmuir-Freundlich model and was 149 mg/g for MIP-SPME$_f$. In the next step, SPME methodology followed by liquid desorption and liquid chromatography with mass spectrometry (LC/MS) has been developed and evaluated for the determination of the target compound in environmental and biological matrices (surface waters, wastewaters and urine). Parameters that could influence SPME efficiency were investigated. Then, optimization of stirring speed, extraction time and salt content was carried out by using a central composite design (CCD) and response surface methodology (RSM). A quadratic model between dependent and independent variables was built. Under the optimum conditions (extraction time 40 min, stirring rate 650 rpm and salt content 0.3% NaCl w/v) the validated method presented a high sensitivity and selectivity with LODs and LOQs in the range of 10.1–13.6 and 33.3–43.9 ng/L, respectively. The developed method was successfully applied to the analysis of ABA in real samples. The percentage extraction efficiency ranged from 88 to 99% revealing good accuracy and absence of matrix effects.

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1. Introduction

In recent years, there is a growing awareness of the risks related to the emission of Pharmaceuticals, Personal Care Products (PPCPs) and their Transformation products (TPs) in the aquatic environment [1,2]. The occurrence of PPCPs has been documented worldwide in various compartments of the water cycle including both natural and technical aquatic systems impacted by wastewater discharges and waste disposal sites and became a hot topic for environmental analytical chemists [3–6].

For determination of PPCPs in complicated environmental samples, suitable sample preparation could not be avoided [7,8]. It is required in order to remove interferences and preconcentrate target analytes. Among the various sample preparation methods, sorptive microextraction techniques (SμE) [8,9] such as Solid Phase Microextraction (SPME) [10], for pre-concentration and/or clean up of analytes offer new possibilities in sample treatment and superior advantages compared to conventional extraction methods.

A number of commercially available and laboratory-made SPME sorbents have proven useful for a wide variety of applications in SPME techniques [11–13]. However, the desire for even more selective phases is the current driving force in research, and various sorbents based on molecularly imprinted polymers (MIPs) have hence been explored during recent years [14–17], allowing in most cases not only pre-concentration and cleaning of the sample but also selective extraction of the target analyte, which is important, particularly when the sample is complex and impurities can interfere with quantification.

Recently, several successful molecular imprinting SPME pharmaceutical applications have been reported by changing the SPME extraction phase and using different configurations [18]. For example, a new temperature-sensitive MIP with ofloxacin (OFL) as template for the SPME coating was synthesized by Zhao and Guan [19]. The authors demonstrated that the synthesis could be repeated well with multiple capillaries put in the same reaction solution. In another study, Prieto and Schrader prepared a MIP with ciprofloxacin (CIP) as template by using a precipitation polymerization strategy [20]. This MIP material was packed as sorbent in a device for microextraction by packed sorbent (MEPS) combined with LC-MS/MS for the analysis of selected fluoroquinolone antibiotics. The findings of the study revealed that sample preparation time and organic solvent consumption are reduced with this process which can be fully automated and coupled on-line to GC or HPLC. Finally, Qiu and Liu developed a selective, chemically- and physically-robust SPME fiber in a simple way (through a thermal radical copolymerization procedure) with a testosterone-imprinted polymer for selective extraction and analysis of anabolic steroids coupled with gas chromatography-mass spectrometry (GC–MS) [21].

Despite the fact that knowledge of MIP-SPME is steadily increasing and a number of studies have appeared in the last few years, most of the studies have been limited to antibiotics, anti-inflammatory and analgestic drugs, and studies on other groups of pharmaceuticals are scarce. For example, antivirals are among the most widely used pharmaceutical compounds. However, although the environmental release of antiviral drugs to aquatic environment is of considerable concern due to potential ecosystem alterations and the development of viral resistances, very little research has been conducted focusing on the determination of antiviral drugs in aqueous samples [22–24]. It is worth to point out that according to the study of Sanderson et al. [25], antiviral drugs are among the predicted most hazardous therapeutic classes with regard to their toxicity toward algae, daphnids and fish. Therefore, their selective and sensitive determination in surface waters and wastewaters is challenging.

In this light, in the present work a new synthesized MIP material was developed and evaluated as a MIP-SPME fiber for the selective screening of antiviral drugs in environmental and biological samples. Abacavir (ABA) which is a nucleoside human immunodeficiency virus (HIV) reverse transcriptase (RT) inhibitor and thus a key component of antiretroviral therapy (cART) regimes, was chosen as template molecule [26]. Numerous analytical methods have been developed for the quantification of ABA and other antiviral drugs in different biological matrices such as plasma, urine, hair etc [26]. Nevertheless, until recently information on their determination in water samples was scanty. As regards the MIP process, only two studies [27,28] have been published for selective determination of ABA in waters. However, both of them are focused on solid-phase extraction (SPE) extraction and to our best knowledge this is the first report in which the study of an effectively designed MIP SPME fiber was evaluated for the selective isolation and determination of ABA in aqueous and biological media. Based on the aforementioned remarks the adsorption properties of ABA MIP-$SPME_f$ were evaluated by adsorption experiments and kinetic model analysis. The retention and molecular-recognition properties of MIP-$SPME_f$ for ABA was also evaluated. The analytical performance and the uncertainty assessment of the proposed MIP-SPME methodology for the determination of ABA in surface waters and wastewater samples, as well as in urine, is also addressed. The present method had obviously improved the selectivity and purification effect and it can be proposed as an alternative clean-up procedure in place of the commonly used extraction procedures such as liquid–liquid extraction and SPE.

2. Materials and methods

2.1. Materials

Abacavir sulfate (ABA) and Adefovir-Dipivoxil (ADE) were kindly supplied by Pharmathen Pharmaceuticals SA (Greece). Acrylic acid (AA) was used as monomer form MIP preparation, ethylene glycol dimethacrylate (EGDMA) as cross-linker, azobisisobutyronitrile (AIBN) as initiator for polymerization beginning and dimethylformamide (DMF) as solvent. All of them were supplied by Sigma–Aldrich (Germany). Ethanol and methanol (EtOH and MeOH were the extraction solvent of template molecules) and Acyclovir (ACY) were also supplied by Sigma–Aldrich Germany). The chemical structures of the drugs used are given in Fig. 1.

2.2. Synthesis of MIP-$SPME_f$

The molecularly imprinted polymeric SPME fibers of abacavir sulfate (denoted as ABA MIP-$SPME_f$) was synthesized with free radical polymerization of acrylic acid for 6 h at 80 °C [29]. 1.24 mmol of ABA were dissolved in 25 mL of DMF and then 12.4 mmol of AA were added to the solution. Stirring was continued for 1 h. 72 mmol of EGDMA and 0.75 mmol of AIBN were also added and the polymerization mixture was transferred in a test tube which contained homemade glass tubes of fixed dimension (5 cm length and 2 mm diameter). The whole procedure was taken place under nitrogen sparging. The test tube was sealed and placed in oven, where the polymerization took place. The obtained fibers