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Determination of widely used non-steroidal anti-inflammatory drugs in water samples by in situ derivatization, continuous hollow fiber liquid-phase microextraction and gas chromatography-flame ionization detector

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Dedicated to my supervisor Professor Ali Sarafraz Yazdi, whose guidance, patience and encouragement helped me during several years I worked in his laboratory.

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ABSTRACT

The aim of this study was to develop an analytical procedure which allows the quantification of pharmaceuticals in water at the ng L^{-1} level. Hence, it is reported research on the application of a rapid, inexpensive and simple continuous hollow fiber liquid-phase micro extraction (CHF-LPME) for the preconcentration and determination of non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (IBP), naproxen (NAP), and ketoprofen (KEP), in wastewater. In this method, a 2.50 cm end sealed piece of a polypropylene hollow fiber was immersed into the organic solvent, octanol, for 30 s. After solvent impregnation with the pores of the fiber, the excess amounts of solvent were removed from inside the fiber, and 4.0 μL of octanol, as the acceptor phase, was injected into the fiber carefully. The fiber was settled using a microsyringe into a 10.0 mL glass test tube, and 20.00 mL of the aqueous solution (the donor phase), was circulated by a pump around it. After analyte extraction for an optimized period of time (20 min), 2 μL of the organic solvent was withdrawn into the microsyringe and injected into the GC-FID for further analysis. Finally, based on the optimized analytical conditions, the method was linear in the range of 2.5–500 ng L^{-1}. The limits of detection were 1–2 ng L^{-1}. Repeatability of this method on an intra-day scale was 3.4–10.2% (RSD%). NSAIDs have been detected in several municipal wastewater samples, and the concentration range was 9.0–19.0 ng L^{-1}.

1. Introduction

Pharmaceuticals are produced and used in great annual increasing volumes. This growth leads to a drastic fear about the effects of these compounds on the environment. Although the concentration of these residues in the aquatic environment is too low to pose a very severe risk, it is unknown whether other receptors in non-target organisms are sensitive to individual residues or whether the combination of drugs that share a common mechanism of action exhibit synergistic effects [1,2]. Due to the rising risks from toxication of pharmaceuticals, the quantitative evaluation of these compounds demands sensitive and reliable analytical methods. Furthermore, there is a lack of methods permitting the detection of the low-level contaminants present in biologically significant matrices. Hence, it is necessary to develop a convenient analytical technique to study the occurrence and conclusion of these residues in an aquatic environment.

Model compounds were selected among the pharmaceuticals which predominate in the analyses of environmental samples, as well as from the lists gathered from prescription data. Most of these pharmaceuticals belong to the class of analgesics (non-steroidal anti-inflammatory drugs; NSAIDs). The following three pharmaceuticals from the class of NSAIDs were chosen as model compounds: ibuprofen, naproxen, and ketoprofen (see Fig. 1 and Table 1). The investigated drugs belong to a group of customarily prescribed drugs among NSAIDs [3].

Pharmaceutical residues are usually present in environmental water samples in trace levels (ng L^{-1}) [4]. Therefore, a sample isolation and pre-concentration technique is required for the analysis of these drugs. Hollow fiber liquid-phase microextraction (HF-LPME) is an attractive and novel pretreatment method qualified with a high enrichment factor, rapid analysis time, simple setup and low cost. As an environmental-friendly technique, it has been successfully employed for the determination of a wide range of environmental and biological contaminants [5–7]. During recent years, several different technical developments have been presented for one step LPME [8–11] and for two-step LPME [12]. In another study, Rasmussen, Pedersen-Bjergaard et al. demonstrated

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Table 1
Physical properties of the target compounds [27].

Compound	Solubility in water	pK_a/pK_b	$pK_{O/W}$
Ibuprofen	16.0 g L^{-1}	5.20 (pK_a)	4.50
Naproxen	Very low	4.15 (pK_a)	3.24
Ketoprofen	85.0 mg L^{-1}	4.23 (pK_a)	2.77

a practical technique with the use of large sample volume, and they achieved a 25,000-fold pre-concentration in a single step [13].

In general, it can be concluded that increasing the sample volume has the advantages of a higher contact area between the hollow fiber and the sample and consequently larger enrichment factors in the smaller extraction times. Therefore, in this work, a novel and simple continuous hollow fiber liquid-phase microextraction (CHF-LPME) technique is introduced for the purification and extraction of NSAIDs in environmental water samples; additionally, with recycling of the aqueous sample, this technique can provide higher pre-concentration in a shorter period of time.

After more microextraction methods, analytical techniques such as liquid chromatography have enabled scientists to determine the concentrations of NSAIDs in real samples like environmental waters [14–20]. More recently, capillary electrophoresis and isotachophoresis have also been used to analyze NSAID pharmaceuticals [21,6]. The analysis of NSAIDs through high performance liquid chromatography is used worldwide for the determination of pharmaceuticals. However, the pre-treatment of the sample might be difficult if the excipients or the active ingredients are non-soluble in the mobile phase. Thus some scientific reports are focused on the use of gas chromatography for analysis of these drugs [22–25]. The present investigation shows the development and validation of the quantitative analysis of NSAIDs through a sensitive and solvent-minimized liquid-phase microextraction procedure, CHF-LPME, followed by gas chromatography-flame ionization detection (GC-FID).

2. Experimental

2.1. Chemicals and reagents

The drugs, ibuprofen (IBP), naproxen (NAP), and ketoprofen (KEP), were obtained from Daroupakhsh Co. (Tehran, Iran) (Fig. 1). Acetone was purchased from Fluka (Buchs SG, Switzerland). Stock solutions of 2 mg mL^{-1} were prepared in methanol, stored in the dark at 4 °C, and diluted to the desired concentration with ultrapure water. The other compounds were from Merck (Darmstadt, Germany). These compounds were all of analytical grade.

The Accurel Q 3/2 polypropylene hollow fiber membrane used here was obtained from Membrana (Wuppertal, Germany). The wall thickness of the fiber was 200 μm, the inner diameter was 600 μm, and the pore size was 0.2 μm.

2.2. Instrumentation

Analysis was performed with a Varian 3400 (Varian Associates, Sunnyvale, USA) gas chromatograph (GC) system with a flame ionization detector (GC-FID). The analytical column was the capillary column, HYDRODEX β-6TBDM (Varian Associates, Sunnyvale, USA), 25 m × 0.25 mm ID, maximum temperature 250 °C. Helium (99.999%) was used as the carrier gas. The GC conditions were as follows: injector temperature 210 °C; initial oven temperature 135 °C for 2 min, programmed to 200 °C a rate of 2 °C min^{-1}, then maintained at 200 °C for 1 min. The injector was operated in the split mode at 1:10 ratio. The detector temperature was held at 220 °C. The pump used was a simple washing car windows pump.

2.3. Calculation of recovery and enrichment factors

Theoretical recovery % (R%) was calculated according to the following equation for each analyte [5–9]:

$$R = \frac{n_{a,final}}{n_{s,initial}} \times 100\% = \left(\frac{V_a}{V_s}\right) \times \left(\frac{C_{a,final}}{C_{s,initial}}\right) \times 100\% \quad (1)$$

where $n_{s,initial}$ and $n_{a,final}$ are the number of moles of analyte present in the initial sample and the number of moles of analyte finally collected in the acceptor solution, respectively. V_a is the volume of the acceptor solution, V_s is the volume of sample, $C_{a,final}$ is the final concentration of analyte in the acceptor solution, and $C_{s,initial}$ is the initial analyte concentration within the sample. The concentration experimental enrichment (EF) was calculated by the following formula [5–9]:

$$EF = \left(\frac{C_{a,final}}{C_{s,initial}}\right) = \left(\frac{V_s}{V_a}\right) \times \frac{R}{100} \quad (2)$$

3. Results and discussion

Various parameters were investigated to determine the optimal sample extraction procedure. All the optimization experiments were performed on the analytes ibuprofen, naproxen, and ketoprofen at a concentration of 10.0 ng L^{-1}.

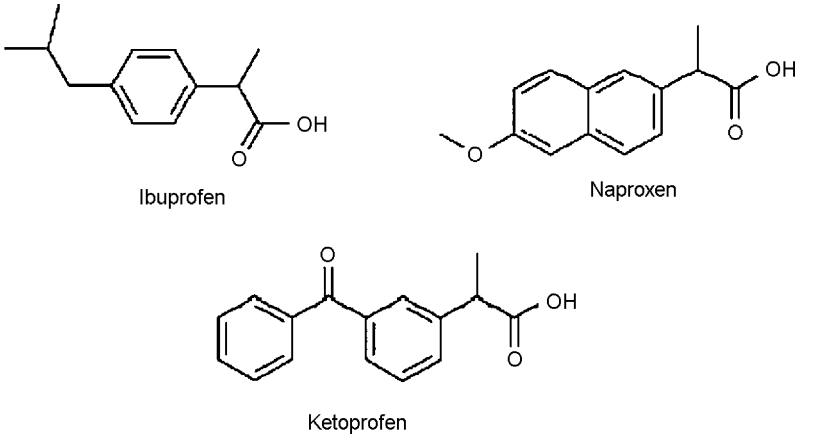

Fig. 1. Structures of the selected pharmaceuticals. Aromatic rings make NSAIDs candidates for separation through π–π interactions.