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New Methods

The usage of micellar extraction for analysis of fluvastatin in water and wastewater samples

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ABSTRACT

This work illustrates the development of new procedures for the isolation and preconcentration of fluvastatin (FLU) from aqueous solutions. Micellar extraction (ME) combined with high performance liquid chromatography (HPLC-UV) has been successfully applied for this purpose. It was found that the analyte created micelle with anionic sodium dodecylsulfate (SDS) and/or with the binary mixture of surfactants nonionic triton X114 (TX114) and cationic tetra-*n*-butyloammonium bromide (TBAB).

The optimal analytical conditions for the proposed extraction procedures (solution pH, concentration of surfactants, centrifugation time and electrolyte type) were ascertained. The calibration curves were recorded. The linearity ranges for FLU, isolated by SDS and the mixture of TX114/TBAB, were 0.21–28.79 $\mu g\,mL^{-1}$ and 0.21–16.45 $\mu g\,mL^{-1}$ with limit of detection (LOD) 0.19 $\mu g\,mL^{-1}$ and 0.14 $\mu g\,mL^{-1}$, respectively. The recoveries afforded by the proposed methods were high, approximately 97%. These preconcentration procedures were applied for the isolation of the statin from water and wastewater samples taken from the local rivers and wastewater treatment plants.

1. Introduction

Pharmaceuticals are widespread contaminants which enter the environment from many points [1]. Residues of drugs have been detected in various aquatic environments [1,2]. The most common occurring in aquatic ecosystems are: drugs available without prescriptions, antibiotics, lipid regulators, anti-inflammatory drugs, steroids and related hormones, cancer therapeutics and others [2]. The number of publications devoted to their assay in environmental samples increases each year [3]. Concentrations of pharmaceuticals in the water samples are found at the level of $ng\,L^{-1}$ to $\mu g\,L^{-1}$. Pharmaceuticals are not completely removed in the wastewater treatment process [4]. The literature data shows that lowering lipid drugs are eliminated from wastewater only in 34–50% [5]. Medications and their metabolites can get into drinking water and accumulate in plants, animals as well as in humans. Therefore, continuous monitoring and control of water quality should be a priority in environmental analysis.

Fluvastatin ($pK_a = 4.27$, $\log K_{o/w} = 3.76$) became the subject of this study because it belongs to the most widely used group of pharmaceuticals which lowers blood level of lipids. The total expenditure for the Belgian statin market (number of patients 1,138,804) in 2011 was €285,320,000 wherein only for fluvastatin was €2,910,000 in the same year [6].

The first generation drug derived from the fungus *Aspergillus terreus* was lovastatin. Other compounds from this therapeutic group are produced by semi-synthetic (simvastatin, pravastatin) or totally synthetic (fluvastatin, atorvastatin) processes [7]. Chemical structure of statin, which was examined in this research, with the absorption spectrum is showed in Fig. 1.

There are many literature data on methods for isolation and determination of statins in biological samples [8–13], pharmaceutical formulations [8,14–17] and waters samples as well [18–21]. According to literature, statins are found in waters samples at a very low level. Assayed level of atorvastatin in urban wastewaters samples was 10.3 $ng\,L^{-1}$ [22] and 45.0 $ng\,L^{-1}$ [23]. The presence of lovastatin was recorded in Canadian wastewaters at concentration 49 $ng\,L^{-1}$ [24].

A review of the cited examples of literature suggests that the most frequent method used for determination statins and their derivatives in different samples is chromatographic [10–12,16,18,22–24], rarely electrochemical [25] and spectrophotometric [17]. Moreover, solid phase extraction mainly on different sorbents especially HLB (strongly hydrophilic, water–wettable polymer with a unique hydrophilic–lipophilic balance) [22–24,26] and liquid–liquid extraction [16] were mainly used for isolation these compounds from different matrixes.

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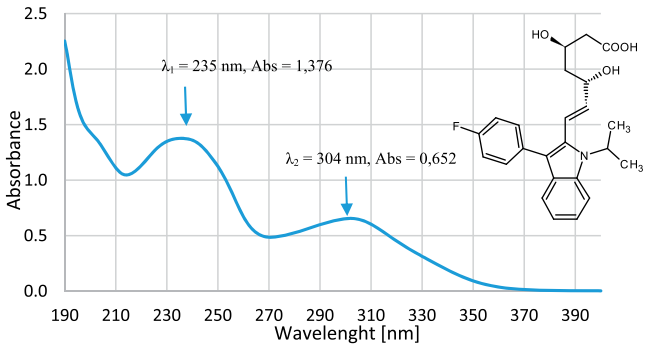

Fig. 1. The absorption spectrum of the FLU solution in methanol (C_{FLU} = 16.45 μg mL^{-1}) with the molecule structure of FLU ($C_{24}H_{26}FNO_4$, MW = 411.28 g mol^{-1}).

Due to the complexity of the matrix, the analysis of environmental samples is a major challenge to the analyst. Determination of analyte in the presence of interfering substances requires the development of specific and selective methods of sample preparation before analysis. Therefore, the aim of presented studies is to develop efficient and selective extraction procedures for isolation of fluvastatin from aqueous samples. For this purpose, micellar extraction (ME) was used. This preconcentration technique involves introducing a suitable surfactant solution to an aqueous sample containing an analyte followed by the binding of a particular compound in the hydrophobic core of the surfactant. The addition an electrolyte solution into the sample causes cloudiness of the solution, by increasing the amount of aggregates formed. Surfactant rich phases are dissolved in a small amount of solvent and such a prepared sample is ready for the final determination. ME is mainly used for metal analysis and rarely organic compounds [27], but until now there are exceptionally few articles describing the applications of ME for drugs analysis.

2. Experimental

2.1. Instrumentation

Thermo Separation chromatographic system with 2D Spectra System UV3000, a low-gradient pump P2000 and a vacuum membrane degasser SCM Thermo Separation were used (San Jose, California, USA). The phase-separation process was accelerated by the centrifuge MPW-251 (MPW-Med. Instruments, Warsaw, Poland). A Hitachi U-1900 spectrophotometer (Tokyo, Japan) equipped with the deuterium discharge lamp and quartz cuvette was used for the measurements. Vibrating platform shaker (Heidolph, Vibramax 110, Germany) and magnetic stirrer hotplate (Heidolph MR3001K, Germany) were also applied.

2.2. Chromatographic conditions (HPLC-UV)

The column RP-18 (LiChrospher 125 mm × 4.6 mm, 5 μm) was used in the assay of a drug. Column temperature was maintained at 25 ± 2 °C. Mobile phase consisted of a mixture of methanol:water (90:10; v:v) was used. The flow rate of a mobile phase was 0.8 mL min^{-1}.

The detection of the measurements was performed at 304 nm. Under these chromatographic conditions retention time of FLU after extraction with SDS was 1.89 min and after extraction with TX114 and TBAB was 1.67 min. Moreover, there were appeared peaks of surfactants on the chromatograms: retention time for SDS was 1.48 min, for TBAB 2.36 min and 2.64 min for TX114. The reason for a slight retention time shift is to use one or two surfactants. In the systems described may overlap slightly different

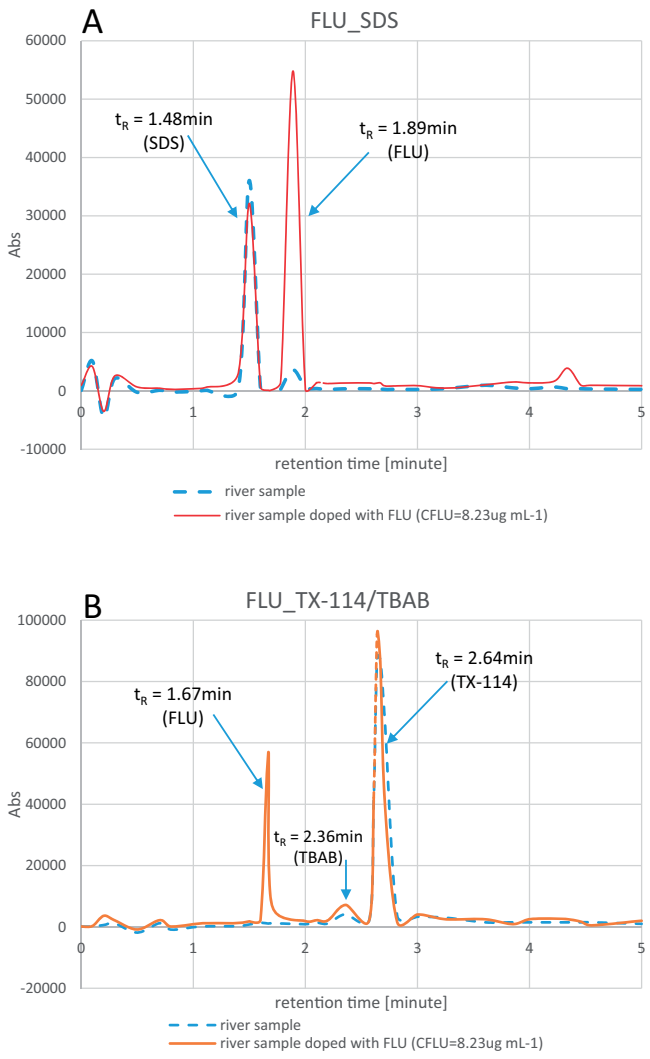

Fig. 2. The typical chromatograms of the real sample without FLU and doped with FLU after micellar extraction with SDS (A) and after extraction with the mixture of TX114/TBAB (B).

interactions between the analyte and the surface active substances, which can result in slightly different retention time for FLU in both the proposed procedures (Fig. 2).

2.3. Chemicals

Fluvastatin sodium hydrate (FLU) was bought from Sigma–Aldrich (Steinheim, Germany). Stock solutions of FLU containing 10^{-3} mol L^{-1} of an analyte were prepared in Milli-Q water. Working solution of this drug was prepared freshly every day before analysis by diluting the standard solution with Milli-Q water and then it was stored in a dark bottle at the room temperature.

Surfactants such as: tetra-*n*-butyloammonium chloride (TBAC), cetyltrimethylammonium bromide (CTAB), tetra-*n*-butyloammonium bromide (TBAB), chloride dodecylpyridine (CDP), sodium dodecylsulfate (SDS), 1-octanesulfonic acid sodium salt (OSAS), triton X114 (TX114), triton X100 (TX100) or genapol X-080 (GEN080) were bought from Sigma–Aldrich (Steinheim, Germany). An ionic micellar solutions (10^{-1} mol L^{-1}) were prepared by dilution with Milli-Q water an appropriate weight. Other solutions: TX114, TX100 and GEN080 were used as a 5% aqueous solution.

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