-Abstract-

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Determination of Drugs and Metabolites in Water by use of Liquid Membrane Systems and HPLC
-Method development and application-

Pharmaceuticals have been detected in wastewater treatment plants, rivers, and groundwater and even in drinking water. This poses potential risks for aquatic organisms and ecosystems in particular, although possible future effects on human health cannot be ruled out. Therefore, developing sensitive and selective analytical methods for monitoring of metabolites and active drugs in aqueous environments is an important task in exposure analysis.

The analytical techniques usually used e.g. HPLC-UV-MS or GC-MS, still afford an efficient sample pretreatment to enrich and separate the analytes from complex matrix. The aim of this study was to investigate the applicability of bulk liquid membranes and supported liquid membranes (SLM) to extract efficiently selected drugs of environmental concern and some of their metabolites from water samples.

The active drugs carbamazepine, diclofenac, ibuprofen and sulfamethoxazole were selected due to their high quantity applied for medical purposes and their relative high concentrations found in the aquatic environment in previous studies. The metabolites *10,11-dihydroxy*-carbamazepin*e*, *4-hydroxy*-ibuprofen, *N-4-acetyl*-sulfamethoxazole, sulfamethoxazol-*N1-glucuronide* are not commercially available, they were synthesized and also used in membrane systems. Several factors affecting the transport in the membrane chambers such as the membrane composition, pH of feed and strip phase, and enrichment time were studied.

By means of the supported liquid flat-membrane chamber (SL-FM), *4-hydroxy*-ibuprofen and *N-4-acetyl*-sulfamethoxazole were efficiently extracted by combining an organic solvent dihexyl ether (DHE), decane or undecane with tri-n-octylphosphine oxide (TOPO) as a carrier and a pH-gradient between feed and strip phases. Maximum extraction yields ~ 90% of *4-hydroxy*-ibuprofen and ~ 85% of *N-4-acetyl*-sulfamethoxazole were obtained by using DHE with 10% (w/w) of TOPO, at an analyte concentration of 1 mg/L after 8-hours of extraction.

Enrichment devices were constructed based on supported liquid bag membrane systems, to enrich trace target analytes from water samples and determine them by means of HPLC-UV. These systems contained one bag (SL-BM) or four bags (SL-4-BM).

Using the SL-4-BM equipment 45% of *4-hydroxy*-ibuprofen, 55% of *N-4-acetyl*-sulfamethoxazole, 30% of diclofenac, and 50% of ibuprofen, were extracted from 500 mL of sample volume and enriched into 0.4 µL of strip solution (0.1 mol/L NaOH). Enrichment factors in the range of 383- 727 were obtained in a concentration range from 1-100 µg/L after 4-hours of extraction.

The results of an investigation show that in comparison to solid phase extraction (SPE), the novel SL-4-BM system offers advantages due to higher enrichment factors, more efficient clean-up-effects, low consume of organic solvents and time.

To prove if the SL-4-BM is robust against interferences, the sample matrix was varied. It can be recognized that in the range of 0.3- 1.5 µg/L the type of spiked water sample (distilled, tap and surface water) had no noticeable influence in the extraction recoveries.

The SL-4-BM method was applied to real samples from the river Ruhr. The surface water sample was evidently not polluted by the target analytes as they were not detectable by means of the membrane method and HPLC (method detection limits ~ 0.07- 0.2 µg/L).