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**Separation and determination of selected organic pharmaceuticals in waters by means of natural flat membranes, GC, HPLC and mass spectrometry**

Undesired immissions of pharmaceuticals into ecosystems from human and animal applications are of increasing relevance for the water quality. In this study the attention was focussed on the investigation of the possibility to apply particular animal intestines as natural membranes for the depletion of target drugs in water treatment and for sample preparation prior to laboratory analysis. In addition, analytical methods for the simultaneous qualitative and quantitative determination of the selected analytes and for further identification of unknown products should be developed based on LC-ESI/MS and GC/MS. Moreover, long-term biodegradation of the analytes at particular conditions in batches and biofilm reactors should be investigated to estimate their fate in the aquatic environments. The target drugs were *carbamazepine (CBZ)*, *diclofenac (DCF)*, *ibuprofen (IBU)* and *sulfamethoxazole (SFM)*. Furthermore, some of their main metabolites *10,11-dihydro-10,11-dihydroxycarbamazepine (Diol-CBZ)*, *N-1-glucuronidesulfamethoxazole (Glucu-SFM)*, *N-4-acetylsulfamethoxazole (Ac-SFM)* and *2-hydroxyibuprofen (OH-IBU)* were chosen as representative compounds based on high amounts consumed in medicine and relative high concentrations detected in aquatic environment so far.

Different types of intestine parts of cattle, sheep, and pig were applied. The permeation is mainly influenced by the concentration gradient, surface area and stirring velocity. Water ingredients such as surfactants can interfere the permeation process but only at unusual high concentrations. But humic substances must be of a young genesis in order to interfere the permeation process. The depletion of the drugs can reach > 90 % by combination with additional solid or liquid phase extraction. When comparing the animal intestines to technical membranes, no clogging effects could be observed during the permeation through the natural membrane, even if the water sample contained a complex mixture of other water ingredients. The stability of the natural membranes was not valid for all matrices with high bioactivity, such as wastewater. So, they might only be applied to technical application in combination with disinfection or filtration steps. Treatment with formaldehyde extended the lifetime up to 10 days. Due to slow permeation kinetics the natural membranes cannot be recommended for analytical purpose, such as clean-up procedures.

Analytical methods were developed for determination of the analytes based on a pre-concentration step by solid phase extraction and derivatization followed by GC/MS or LC-ESI/MS. In term of linearity, reproducibility, accuracy and sensitivity all developed methods are succeeding to the intended aims. For the final methods the detection limits were 1-5 ng/L in GC/MS except for SFM and its metabolites and 3-5 ng/L in LC-ESI/MS for all the analytes. The developed methods were applied to the analysis of surface water samples from the river Ruhr. All the target analytes, except Glucu-SFM, were detected in a concentration range from 100 to 320 ng/L.

Long-term biodegradation experiments in batch and in biofilm reactor in pilot scales were carried out at particular conditions. In the batches the drugs showed different behaviour depending on the type of water matrices and bioactivity as well. IBU and SFM were degraded significantly but in different rates, whereas CBZ and DCF were resistant. The main metabolites were also degraded except for Diol-CBZ. The biofilm reactor experiments significantly revealed a decline in the concentration of all target drugs - except CBZ - in different rates. Both types of reactors have been proved to be suitable model systems in order to investigate the pathways of biological degradation of active drugs and their metabolites by means of GC- or LC/MS.