A novel GC-MS-method for the determination of metformin in water samples

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For years there have been more and more reports on the presence of drugs in the aquatic environment. Due to the demographic change, the consumption of pharmaceuticals has risen sharply. After taking the drugs, they are partly metabolized in the human body.

However, the metabolism is not complete so that both the metabolites and non-metabolized amounts of the parent compounds are excreted. These compounds reach the waste water and afterwards the sewage treatment plants. In sewage treatment plants transformation products can be formed by the oxidative conditions during wastewater treatment processes. The transformation products may have a higher toxicity than the actual environmental pollutants and are often only partly removed during the waste water treatment. Since a lot of these compounds are still unknown, the transformation products are not detected by target analysis used in sewage treatment plants and are often released undetected in the aquatic ecosystems. Other sources of exposure of pharmaceuticals in the environment come from their release during the production process (especially in the past), and their incorrect disposal.[[1](#_ENREF_1)] The released substances may be subject to additional transformation processes in the environment. Pharmaceuticals produced in high amounts can be already detected in the µg/L range in water bodies worldwide. More than half of the total amount of pharmaceuticals in the environment are the antidiabetic agent metformin and its major transformation product guanylurea.[[2](#_ENREF_2)] Metformin is the drug of choice for treating type 2 diabetes. The drug therapy for diabetes mellitus has increased significantly in recent years. Metformin causes an increased glucose intake and a decrease in the gluconeogenesis and glucose output. In the year 2013 598 million defined daily doses of metformin were prescribed in Germany.[[3](#_ENREF_3)] Many questions about the behavior of metformin in the environment and during the water treatment have not yet been sufficiently clarified and the long-term consequences for humans and the environment have also not been adequately studied. First indications are that metformin could potentially act as an endocrine disruptor in male fish under chronic exposure.[[4](#_ENREF_4)]

For the analysis of metformin and the potential emerging unknown transformation products reliable analytical methods are required that allow both a quantitative determination of metformin in the environment and a structural identification of potential transformation products. The first results of a novel GC-MS method are presented which allows a quantitative analysis of metformin from water samples.

[1] T. Heberer, *Toxicology Letters Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data*, *131*, 5-17*,* **2002**.

[2] T. ter Laak, K. Baken, *Water Research Institute The occurrence, fate and ecological and human health risks of metformin and guanylurea in the water cycle - A literature review,* **2014**.

[3] U. Schwabe, D. H. Paffrath, *Arzneiverordnungs-Report DOI 10.1007/978-3-642-43487-1\_11,© Springer-Verlag Berlin Heidelberg,* **2014***.*

[4] N. J. Niemuth, R. Jordan, J. Crago, C. Blanksma, R. Johnson, R. D. Klaper, *Environmental toxicology and chemistry / SETAC Metformin exposure at environmentally relevant concentrations causes potential endocrine disruption in adult male fish*, *34*, 291-296*,* **2015**.