Biotransformation of the antiepileptic drug Gabapentin in the aquatic environment

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Gabapentin is an anticonvulsant drug that is used for the treatment of epilepsy and neuropathic pain since 1995.[2] High prescriptions of defined daily doses (41.8 Mio DDDs in 2013, Germany)[2] and an unmetabolized excretion of gabapentin lead to high concentrations in wastewater treatment plant (WWTP) influents of up to 18.5 µg L^{-1}.[1] Two studies showed very different removal efficiencies of gabapentin in WWTPs ranging from no removal to a high elimination of over 99 %.[1,4] In surface waters gabapentin has been measured in concentrations between 0.2 µg L^{-1} to 1.9 µg L^{-1}.[1] As for the fact that the European Chemicals Directive REACH characterizes gabapentin as potential teratogen and toxic to reproduction [3] it is of environmental concern to elucidate the fate of gabapentin.

Aerobic batch experiments were used to get a more close insight into the biodegradability and transformation pathway of gabapentin in water-sediment systems. Sediment spanning various particle size distributions and different organic carbon contents from three different rivers were used. Gabapentin concentrations were monitored during the incubation experiments by LC-tandem-MS with positive electron ion spray ionization (ESI) in MRM mode, searching for potential transformation products (TPs) was accomplished by LC-HRMS. Results revealed a degradability of gabapentin > 99 % within 14 to 50 days within the three different sediments. In sterile controls, the concentration of gabapentin was almost stable over a time span of 23 days. Hence, both sorption and abiotic transformation processes can be excluded as major transformation pathways for gabapentin. Thus, the dissipation of gabapentin is caused by biotic transformation processes and the formation of several TPs was observed. The predominant TP was identified as the γ-lactam of gabapentin (up to 20 % of the initial concentration of gabapentin) which is a known impurity during the production of gabapentin. Supplemental monitoring campaigns of WWTPs revealed an elimination of gabapentin by 44 % and a formation of the γ-lactam during conventional wastewater treatment up to concentrations of 0.4 µg L^{-1} in the effluent (influent: no detection) . Furthermore, both gabapentin (0.6 µg L^{-1}) and the γ-lactam (0.1 µg L^{-1}) have been measured in drinking water.

Currently, additional biologically formed TPs of gabapentin and the γ-lactam are identified, transformation pathways are elucidated and the stability of reducing conditions is tested.

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