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The relevance of antibiotics in the environment: Spotlight on ciprofloxacin, clindamycin & ceftriaxone

Abstract

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The global prescription of antibiotics for the treatment of infectious diseases in humans and animals is leading to a continuous release into the environment. This is raising enormous concerns regarding multifaceted effects which need to be further understood. In this thesis, the relevance of antibiotics for human use for the environmental health was studied. The investigations were focused on the medical use of the three antibiotics ciprofloxacin, clindamycin, its metabolite clindamycin sulfoxide as well as ceftriaxone in Europe. As the European regulatory landscape for environmental risk assessments of medicinal products is currently changing, the evaluation was performed according to the new draft guideline of the European Medicines Agency (EMEA/CHMP/SWP/4447/00 Rev. 1) using available literature data.

The assessment showed that the metabolite clindamycin sulfoxide and also ceftriaxone do not represent a risk to the environment according to the applied pattern of use. In contrast, a risk for surface water organisms was detected for ciprofloxacin and clindamycin. The finding related to ciprofloxacin is supported by the fact that the antibiotic is already part of the second EU watch list and is thus to be monitored in surface water by EU member states. The differing outcome regarding the risk assessment for clindamycin and its metabolite for the surface water compartment can be attributed to a 48-fold higher sensitivity of green algae to the parent compound.

The gap analysis of literature data demonstrated that most data were available for ciprofloxacin whereas the data density was lowest for clindamycin sulfoxide. Aquatic ecotoxicity data were available for all substances whereas sediment ecotoxicity data were missing. This is reflecting the changing regulatory requirements in Europe as sediment effect toxicity testing was newly added to the draft EMA guideline for a Tier A assessment. Taken together, a holistic environmental risk assessment for the four compounds cannot be performed with the data publicly available. There is still a lack of fundamental data on the fate and effects of antimicrobials in the environment despite their use for the treatment of infectious diseases since decades.

The evaluation in this thesis demonstrates that there is a risk of ciprofloxacin and clindamycin for surface water organisms in Europe with the applied pattern of use. Thus, adequate precautionary and safety measures to protect surface water ecosystems are needed. Furthermore, the creation of more information on the environmental fate and effects of antibiotics via performance of higher Tier tests could enable a better translatability of results to the complex environment. This additional knowledge would help to decide if clindamycin should be added to the EU watch list for routine monitoring in surface waters as it already is the case for ciprofloxacin.