Effects of pharmaceuticals on natural microbial communities

Tolerance development, mixture toxicity and synergistic interactions

SARA BROSCHÉ, 2010

UNIVERSITY OF
GOTHENBURG

FACULTY OF SCIENCE

DEPARTMENT OF PLANT AND ENVIRONMENTAL SCIENCES

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Examinator: Professor Göran Dave, Institutionen för växt- och miljövetenskaper, Göteborgs universitet

Fakultetsopponent: Dr Alistair Boxall, Environment Department, University of York, Great Britain

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Abstract

Due to our extensive use of pharmaceuticals, low concentrations (picomol-nanomol/L) end up in the aquatic environment. Antibiotics comprise a group of pharmaceuticals specifically designed to disrupt microbial biochemical processes, and might therefore in particular have detrimental effects on microbial communities in the environment. However, current environmental risk assessment strategies of pharmaceuticals do not necessarily suffice for protecting environmental microbes. Therefore, the ecotoxicity of pharmaceuticals were assessed on natural bacterial communities to provide ecologically more realistic data and to improve the knowledge about their environmental hazard.

Paper I, III and IV in the thesis focussed on the effects of antibiotics. It was shown that in particular chlortetracycline, but potentially also ciprofloxacin, is clearly toxic already at concentrations currently detected in the environment, hence posing an environmental risk to environmental bacteria. In paper II, attached microbial communities were exposed to 5 pharmaceuticals and personal-care products (PPCPs) (fluoxetine, propranolol, triclosan, zinc-pyrithione and clotrimazole), which all showed to be toxic towards the algae, however only at concentrations below currently detected.

Many pharmaceuticals are often simultaneously present in sewage treatment plant effluents. Hence, the exposed microbial communities in the recipient are subjected to a mixture of active substances. Mixtures do generally cause higher effects than each of their comprising substances alone, and it is therefore also important to consider also their combined toxicity. Based on the experimentally determined effects of the individual substances, two mathematical concepts have been suggested for predicting toxicity of mixtures comprised of similarly and dissimilarly acting substances: Concentration Addition (CA) and Independent Action (IA). Their applicability is generally accepted for single species assays, and the results in paper I and II in the thesis supports their validity also at a community level of biological complexity. However, both concepts are based on the assumption that no interactions occur between the mixture components.

One such interaction would be the effect of chemosensitizing substances that inhibit bacterial efflux of antibiotics, thus increasing their toxicity beyond the predicted. Therefore, the combined effects of 3 proven chemosensitizers and the antibiotic ciprofloxacin on natural bacterial communities were investigated in paper IV. As opposed to results from clinical studies, no increased effects beyond what was predictable by IA were seen. Chemosensitization seems therefore be of low importance in natural bacterial communities.

Poorly controlled pharmaceutical production facilities have recently been shown to release extremely high amounts antibiotics. Apart from the high toxicity of this pollution, concerns were raised with respect to bacterial resistance development in the receiving river. Therefore, the potential for tolerance development in microbial communities were assessed in paper III, using either treated effluent from an Indian production site or ciprofloxacin at corresponding concentrations. Both exposures induced tolerance of the bacterial communities towards ciprofloxacin, the effluent to the highest extent. However, whether this was due to resistance development or not needs to be further investigated.

To conclude, this thesis shows that current environmental hazard assessment strategies for pharmaceuticals and antibiotics might not be realistic enough to protect natural microbial communities, and should therefore be extended accordingly. The results also emphasize the need to take complex environmental exposure situations into account, and to especially consider the combined toxicity of pharmalceuticals in the environment.

Keywords: antibiotics, pharmaceutical mixtures, microbial community ecotoxicology, Concentration Addition, Independent Action, community tolerance development, chemosensitization