Toxicity of selected cytostatic drugs and their mixtures to alga *P. subcapitata* and cyanobacterium *S. Leopoliensis*

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Due to rapid advances in medical science and the associated growth of pharmaceutical industry, pharmaceuticals represent new emerging pollutants in the aquatic environment. The residues of cytostatic drugs, that due to their mechanism of action may affect any growing cell, and in general all organisms might be susceptible to their toxicity, are of particular concern.

Our study provided new ecotoxicological experimental data for four widely used cytostatics: 5-fluorouracil (FU), cisplatin (CP), etoposide (ET) and imatinib mesylate (IM). In the growth inhibition test with two phytoplankton species; alga *P. subcapitata* and cyanobacterium *S. leopoliensis* the four cytostatics showed very different toxic potential and also differences in the susceptibility of the two species to the same compound. FU was the most toxic compound (with EC50 at 0.13 mg/l) for *P. subcapitata* and CP was the most toxic compound (with EC50 at 0.67 mg/l) for *S. leopoliensis*. IM was more toxic for *P. subcapitata* (EC50 at 2.26 mg/l) then for *S. leopoliensis* (EC50 at 5.36 mg/l). ET showed very low toxicity.

It is expected that in the aquatic environment residues of cytostatics occur in combinations, thus combined effects were studied as well. Binary mixtures of FU/CP and CP/ET were selected due to their combined use in cancer treatment and mixture of FU/IM was selected due to relatively high consumption amounts of this two drugs. We first calculated predicted effects of mixtures from the responses obtained with single compounds. The mixtures were then tested and the observed effects were compared to calculated values. In *P. subcapitata* synergistic effects were observed with mixtures of FU/CP and FU/IM, and additive effect was observed with the mixture of CP/ET. In *S. leopoliensis* antagonistic effects were observed with mixtures of CP/ET and FU/IM, whereas the effect of the mixture FU/CP was additive at low dose range to synergistic at high dose range. The synergistic effect of the mixture of FU/IM is of particular concern, because their predicted environmental concentrations (PEC-s) are relatively high.

The obtained experimental data contribute to currently very scarce ecotoxicological data for cytostatic drugs needed for scientifically based risk assessment.

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