Environmental occurrence and potential adverse effects of the residues of cytostatic drugs

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Recently concerns have been raised whether the residues of cytostatic drugs in the environment may pose threat to aquatic organisms and human health. We analysed consumption amounts of cytostatic drugs in Slovenia and calculated their predicted environmental concentrations (PEC). The investigations of consumption trends between the years 2009 and 2011 showed clear increase in the consumption of these drugs that consequently leads to increased levels released into the environment. Based on the obtained PEC values four cytostatics (5-fluorouracil, cisplatin, etoposide and imatinib mesylate) with different mechanisms of action were selected to be studied. Their ecotoxic and genotoxic properties were determined in experimental models with algae, cyanobacteria, higher plants, crustacea, mussel and zebrafish. Relatively high toxicity was observed in the reproduction assays with algae (P. subcapitata), cyanobacteria (S. leopoliensis) and crustacea (D. magna and C. dubia). Much lower toxicity was observed in the zebrafish embryo test. The genotoxicity of the compounds was determined with the comet and/or micronucleus assays. In D. magna all four cytostatics induced clear dose dependent increase in DNA damage with cisplatin and imatinib mesylate being the most potent. Similar increase in DNA damage was observed also in mussel U. tumidus, however at higher concentrations. In plants (Allium and Tradescantia assays) etoposide and cisplatin were the strongest inducers of micronuclei formation. In zebrafish that were exposed to 5-FU for 4 months an increase in DNA damage was observed in the liver, but not in gills and gonads. In blood erythrocytes a significant increase in micronuclei formation was detected. The results showed that the four cytostatics are toxic to aquatic organisms. 5-FU, cisplatin and imatinib mesylate induced genotoxic effects at concentrations that are close to PEC and those found in hospital wastewaters. These results indicate the need for further investigations of the occurrence and fate of cytostatics in the environment and investigations of their combined effects in complex environmental mixtures that will enable environmental risk assessment.

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