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Review

Ecotoxicology of human pharmaceuticals

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Abstract

Low levels of human medicines (pharmaceuticals) have been detected in many countries in sewage treatment plant (STP) effluents, surface waters, seawaters, groundwater and some drinking waters. For some pharmaceuticals effects on aquatic organisms have been investigated in acute toxicity assays. The chronic toxicity and potential subtle effects are only marginally known, however. Here, we critically review the current knowledge about human pharmaceuticals in the environment and address several key questions. What kind of pharmaceuticals and what concentrations occur in the aquatic environment? What is the fate in surface water and in STP? What are the modes of action of these compounds in humans and are there similar targets in lower animals? What acute and chronic ecotoxicological effects may be elicited by pharmaceuticals and by mixtures? What are the effect concentrations and how do they relate to environmental levels? Our review shows that only very little is known about long-term effects of pharmaceuticals to aquatic organisms, in particular with respect to biological targets. For most human medicines analyzed, acute effects to aquatic organisms are unlikely, except for spills. For investigated pharmaceuticals chronic lowest observed effect concentrations (LOEC) in standard laboratory organisms are about two orders of magnitude higher than maximal concentrations in STP effluents. For diclofenac, the LOEC for fish toxicity was in the range of wastewater concentrations, whereas the LOEC of propranolol and fluoxetine for zooplankton and benthic organisms were near to maximal measured STP effluent concentrations. In surface water, concentrations are lower and so are the environmental risks. However, targeted ecotoxicological studies are lacking almost entirely and such investigations are needed focusing on subtle environmental effects. This will allow better and comprehensive risk assessments of pharmaceuticals in the future.

Keywords: Pharmaceuticals; Ecotoxicological effects; Environmental toxicity; Chronic effects; Environmental risk assessment

Contents

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1. Introduction

It came as a surprise when an unusually high death rate among three species of vulture in India and Pakistan was reported in 2004 to be caused by diclofenac, a widely used analgesic and antiinflammatory drug (Oaks et al., 2004). The oriental white-backed vulture (*Gyps bengalensis*) is one of the most common raptors in the Indian subcontinent and a population decline of >95% makes this species as being critically endangered. Whereas a population decline has started in the 1990s, recent catastrophic declines also involve *Gyps indicus* and *Gyps tenuirostris* across the Indian subcontinent (Prakash et al., 2003; Risebrough, 2004). High adult and subadult mortality and resulting population loss is associated with renal failure and visceral gout, the accumulation of uric acid throughout the body cavity following kidney malfunction. A direct correlation between residues of diclofenac and renal failure was reported both by experimental oral exposure and through feeding vultures diclofenac-treated livestock. Hence, the residues of diclofenac were made responsible for the population decline (Oaks et al., 2004). This drug has recently come into widespread use in