PHARMACUTICALS AS EMERGING CONTAMINANTS: SOURCES, ENVIRONMENTAL LEVELS AND GENERAL ENVIRONMENTAL PROBLEMS

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In a vast array of contaminants of anthropogenic origin reaching our water supplies, pharmaceutically active compounds (PhACs) are among the ones with the most continuous input into the environment, especially the over-the-counter (OTC) drugs, which is raising scientific concerns of long-term consequences on human health. Due to their continuous input into the aquatic media through wastewater as a main point-source, PhACs are considered to be "pseudo-persistent". PhACs are a group of chemical substances that have medicinal properties, and they are produced worldwide on a 100 000 t scale. Most of modern drugs are small organic compounds with a molecular weight (MW) below 500 Da, which are moderately water soluble as well as lipophilic, in order to be bioavailable and biologically active. After the oral, parenteral and/or topical administration, PhACs are excreted via liver and/or kidneys as a mixture of parent compound and metabolites that are usually more polar and hydrophilic than the original drug. The metabolism of PhACs begins with phase I reactions that usually convert the parent drug into more polar metabolites by introducing a functional group or unmasking one (e.g., hydroxylation, epoxidation, reduction, and hydrolysis). The metabolites can be inactive or with modified or preserved activity, and if sufficiently polar they may be readily excreted. However, many phase I products are not eliminated rapidly and they undergo a subsequent reaction with an endogenous substrate such as glucuronic acid, sulfuric acid, acetic acid, or an amino acid, which leads to the formation of a highly polar conjugate that are excreted in the urine or bile. Also, there are some non-therapeutic medicines that are eliminated slowly from the body without biotransformation, since they are not metabolised in the human body.

Many PhACs do not exhibit acute toxicity but have a significant cumulative effect on the metabolism of non-target organisms and ecosystem as a whole. Some of the adverse effects that pharmaceuticals might have in the environment are toxicity, resistant development in pathogenic bacteria, genotoxicity, and endocrine disruption. Also, some PhACs such as antidepressants, β-blockers or lipid regulators, can be prone to bioconcentration/bioaccumulation in aquatic organisms. Cytostatic agents, immunosuppressive drugs, human and veterinary antibiotics are classes of PhACs that pose unambiguous impacts on the aquatic organisms (e.g., microorganisms, phytoplankton, plants, crustaceans, fish and insects), and soil microorganisms as well. Furthermore, there is a great lack of knowledge on whether the spread of antimicrobial agents in the environment contributes to the development of bacterial resistance, or to what extent can PhACs reach humans through food-chain biomagnification. This is of even more concern if the concentration levels in the aquatic environment increase, for instance due to demographic reasons.

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After their usage for the intended purpose, a large fraction of these substances will be discharged into the wastewater unchanged or in the form of degradation products that are often hardly eliminable in conventional wastewater treatment plants (WWTPs). Depending on the efficiency of the treatment and chemical nature of a compound, they can reach surface and ground waters. In the worst-case scenario they are encountered in the drinking water, in spite of the expensive treatment steps. They can undergo different chemical, photolytic and biological reactions that modify the structure and physical transport of a compound in the environmental media. In a proper evaluation of persistency of a certain compound both transformation of a compound in the environment and its supply rate should be taken into consideration.

Conventional wastewater treatment does not eliminate polar pollutants completely. Therefore, to avoid such contaminants, emissions with WWTP effluents would have to be reduced by the advanced treatment or by avoidance and replacement measures for the respective pollutant. Other possible ways to regulate the environmental pathways of PhACs are labeling of medicinal products, developing disposal and awareness campaigns and/or additional sewage treatments in hospitals.

Considering the potential consequences on human health, lack of knowledge about the effects of life-long exposures to pharmaceutical residues, and everyday world-wide usage of human and veterinary drugs in quantities of several thousand tons, further research needs to be encouraged and implications of global exposure to PhACs has to be evaluated. A better understanding on the fate and behaviour of PhACs in the environment will help us improve the abatement strategies and mitigate subtle environmental consequences.

This presentation will discuss general problematic of pharmaceuticals as environmental contaminants (is there a real risk?) and several specific issues such as (i) prioritization of pharmaceuticals as environmental contaminants, based on their wastewater entry routes into the environment, usage quantities, human or environmental health implications, indication of certain contamination sources or classes of compounds; and availability of analytical methods and the predicted environmental concentrations (PECs); (ii) research needs regarding their fate and behaviour in the environment; (iii) current research involving antiviral drugs (i.e. tamiflu).

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