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Transformation products of antibiotic and cytostatic drugs in the aquatic cycle that result from effluent treatment and abiotic/biotic reactions in the environment: An increasing challenge calling for higher emphasis on measures at the beginning of the pipe

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ABSTRACT

Pharmaceuticals may undergo transformation into new products during almost all possible processes along their life-cycle. This could either take place in the natural water environment and/or during water treatment processes. Numerous studies that address the issue of such transformation products (TPs) have been published, describing selected aspects of TPs in the environment and their formation within effluent and water treatment processes. In order to exemplify the number and quality of information published on TPs, we selected 21 active pharmaceutical ingredients from the groups of antibiotics and antineoplastics, and assessed the knowledge about their TPs that has been published until the end of May 2012. The goal of this work was to demonstrate, that the quality of data on pharmaceutical TPs greatly differs in terms of the availability of chemical structures for each TP, rather than to provide an exhaustive database of available TPs. The aim was to point out the challenge going along with so many TPs formed under different treatment and environmental conditions. An extensive review in the form of a table showing the existing data on 158 TPs for 15 compounds, out of 21 investigated, was presented. Numerous TPs are the result of different treatments and environmental processes. However, also numerous different TPs may be formed within only one type of treatment, applied under sometimes even very similar treatment conditions and treatments times. In general, the growing number of elucidated TPs is rationalized by ineffective removal treatments. Our results demonstrate a severe risk of drowning in much unrelated and non-assessable data, both from a scientific and from a technical treatment-related point of view. Therefore, limiting the input of pharmaceuticals into effluents as well as improving

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their (bio) degradability and elimination behavior, instead of only relying on advanced effluent treatments, is urgently needed. Solutions that focus on this "beginning of the pipe" approach should minimize the adverse effects of parent compounds by reducing and formation of TPs and their entrance into the natural environment.

1. Introduction

The research on the presence of pharmaceuticals in the environment gained momentum in the 1990s; since then, it has been growing. Until today, a considerable number of review articles and several thousand original research articles on pharmaceuticals concerning their sources, their occurrence in different compartments of the environment, their fate and elimination by natural or human-driven processes, and possible effects on humans and organisms in the environment have been published (Halling-Sørensen et al., 1998; Ternes, 1998; Kümmerer, 2001; Heberer, 2002; Boreen et al., 2003; Bendz et al., 2005; Xia et al., 2005; Fent et al., 2006; Kümmerer, 2008; Onesios et al., 2009; Ding and He, 2010; Fatta-Kassinos et al., 2011a). In addition, the evaluation of analytical methods used for detection and quantification of pharmaceuticals in the environment has also developed further (Steger-Hartmann et al., 1996; Diaz-Cruz and Barceló, 2005; Kim and Carlson, 2005; Petrović et al., 2005; Fatta et al., 2007; Hao et al., 2007; Hernández et al., 2007; Hernando et al., 2007; Rodil et al., 2012; Masiá et al., 2014). As the knowledge on pharmaceuticals and their fate in the aquatic environment, together with more accurate and sensitive methods of their detection and analysis, increased, new questions and issues started to emerge. In the meantime, the focus in this area is not only on the parent compounds themselves, but also on the molecules resulting from incomplete mineralization in the body of treated organisms (metabolites) or abiotic reactions that can take place within advanced effluent treatment and once the parent compound is released into the environment (transformation products). However, research started to improve the knowledge on this new kind of micro-pollutants, i.e. transformation products (TPs), only recently. Knowledge on sources, properties, fate, and effects of TPs on human health and the natural environment is one such research focus with a tremendously increasing number of publications.

The sources of TPs are directly connected to the fate of parent compounds. Depending on their sources, TPs are described in the literature by different terms (Table 1). TPs are being formed in different processes in the environment as well as in waste water and potable water treatment (Zwiener, 2007; Schmidt and Brauch, 2008). After being administrated to humans or animals, pharmaceuticals may be metabolized by a variety of mechanisms and pathways within the body. The rate and extent of these processes are specific to each compound and may sometimes even be different between species. In the case of human pharmaceuticals, once these compounds and/or metabolites are excreted, they reach wastewater treatment plants (WWTPs), if such plants are in place, or directly reach surface water. In the case of veterinary pharmaceuticals, they are directly disposed in fields or used in biogas plants. In WWTPs, a further transformation of pharmaceuticals and metabolites may take place, for instance, by activated sludge during aerobic wastewater treatment or anaerobic digestion of sludge, which results in bacterial metabolites, also known as biotransformation products (bio-TPs) (Längin et al., 2009; Trautwein and Kümmerer, 2011). Hydrolysis and non-biotic oxidation reactions may also play a role in the transformation of pharmaceuticals in WWTPs (Kümmerer, 2009a). Additionally, so called advanced oxidation methods are under discussion for the treatment of wastewater and WWTP effluents in order to improve the removal rate of micro-pollutants such as pharmaceuticals. Processes used for these purposes are for example chlorination and advanced oxidation processes (AOPs), such as H_2O_2/

Table 1 – Examples of terms that have been used in the literature to describe transformation products according to their source.

Processes	Transformation products	Compartment
Biodegradation	Bio-transformation products, bacterial metabolites, biodegradation products, metabolites	Wastewater treatment plant, surface water bodies, anaerobic digesters, soils as far as related to bacteria or fungi
Photolysis, photocatalysis	Photo-transformation products, photoproducts	Surface water bodies, effluent treatment, drinking water treatment/disinfection
Chlorination, ozonation and advanced oxidation processes	Chlorination products, oxidation products, photo-oxidation products (if treatment by UV light is included), by products	Wastewater treatment plant, water treatment works, pre- and/or post- treatment of wastewater, drinking water treatment and disinfection
Other	Transformation products, intermediates, degradation products, stable transformation products	Used in general to all types of transformation products

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