دراسة تلوث المياه السطحية والجوفية من
متبقيات المركبات الدوائية

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Introduction

Pharmaceuticals and endocrine disrupting compounds (EDCs) are a structurally diverse class of emerging contaminants that have been detected throughout the world, especially in wastewaterimpacted surface water, groundwater, and drinking water. Pharmaceuticals include prescription drugs, over the counter medicines and veterinary drugs. The most common route by which these compounds enter the environment is via treated and untreated wastewater. Selected pharmaceuticals and EDCs may also enter the environment via other routes, such as urban or agricultural runoff. Once in the environment, pharmaceuticals and EDC concentrations attenuate by processes such as dilution, adsorption to solids, microbial biodegradation, photolysis, or other abiotic transformation.

Scientists demonstrated the presence of pharmaceuticals in the environment more than 30 years ago, with studies in the United States of America (USA) in the 1970s that reported the presence of heart medications, pain relievers and birth control medications in wastewater (1). The most cited reference in the peer-reviewed literature on the occurrence of pharmaceuticals in surface waters is the survey by the United States Geological Survey, in which more than 50 pharmaceuticals in 139 streams across 30 states in the USA were investigated during 1999 and 2000 (2).

Many peer-reviewed and published studies have shown that the primary sources of pharmaceuticals entering surface water are from excretion and bathing through treated or untreated municipal wastewater effluent discharges into receiving surface water bodies (3-10) and improper disposal of pharmaceutical waste and excess medication by consumers and health-care and veterinary facilities into sewers and drains.

Pharmaceuticals have been measured in water for more than forty years. Within the past decade, the number of papers on analysis of pharmaceuticals in water has increased significantly, concomitant with improvements in analytical instrumentation and isolation procedures, and the increased ability to detect trace levels of pharmaceuticals.

Analytical detection method

Determination of pharmaceuticals can be performed by various techniques, including highperformance liquid chromatography (HPLC) [11, 12] and gas chromatography-mass spectrometry (GC-MS) [13,14]. HPLC is the most common method used for separation and determination of these compounds because most pharmaceuticals are non-volatile. In general, sample preparation and concentration of the target analytesare often needed before analysis. Up to now, several procedures have been developed for preconcentration of pharmaceuticals from sample matrices including liquid-liquid extraction (LLE) [15] and solid-phase extraction (SPE) [16].

LC-MS/MS analysis is more suitable for measuring target compounds that are more polar and highly soluble in water, whereas GC-MS/ MS is better for more volatile target compounds.

Occurrence of pharmaceuticals in surface water

A monitoring study focused on 8 pharmaceutical compounds or their metabolites in surface waters. The results showed that a range of pharmaceuticals from different therapeutic classes were present. The values reported were within the same range as those reported in continental Europe and the USA, where more extensive monitoring has been conducted. Results in the published literature for studies conducted in the USA and Europe also suggest that usage data are positively associated with concentrations of pharmaceuticals measured in effluent and in surface water bodies receiving the treated effluent. The table below shows examples of pharmaceuticals that have been found.

Acetylsalicylic acid	7.23 µg/L
Cyclophosphamide	10.61 µg/L
Doxycycline	2.7µg/L
Tetracyline	1.9µg/L
Oxytetracycline	3.3µg/L

17α-ethinylestradiol	0.11µg/L
Phenoxymethyl-penicillin	17011µg/L
Clofibrate	8024µg/L

Table. Concentrations of selected pharmaceuticals found surface waters

The Table below shows theSummary of previous studies using different acceptable daily intake (ADI) values for the same pharmaceutical compound.

Pharmaceutical name	**Webb *et al.* {12} (assumed body weight = 60 kg)**	**Schwab *et al.* {3}**	**Schulman *et al.* {11} (assumed body weight = 60 kg)**	**Christensen {7}**
Acetylsalicylic acid	8.3 µg/kg/d (30 mg/day therapeutic dose as anticoagulation therapy)	Not applicable	16.67 µg/kg/d	Not applicable
Cyclophosphamide	16.67 µg/kg/d (1 mg/d based on immunobullous skin disorders)	Not applicable	0.017 µg/kg/d (1 µg/d based on no-significant-risk-level)	0.01 µg/d (for rat)
Doxycycline	3 µg/kg/d (100 mg/day therapeutic dose based on bacterial infection)	30 µg/kg/d (value established from WHO representing antimicrobial sensitivity of human intestinal microflora)	Not applicable	Not applicable
Tetracyline	3 µg/kg/d (1.000 mg/day therapeutic dose based on bacterial infection)	30 µg/kg/d (value established from WHO representing antimicrobial sensitivity of human intestinal microflora)	Not applicable	Not applicable
Oxytetracycline	3 µg/kg/d	30 µg/kg/d	Not	Not

	(1.000 mg/day therapeutic dose based on bacterial infection)	(value established from WHO representing antimicrobial sensitivity of human intestinal microflora)	applicable	applicable
17α-ethinylestradiol	0.167 µg/kg/d (0.010 mg/d therapeutic dose based on menopausal symptoms)	Not applicable	Not applicable	6 µg/d (prepubescent boys)
Phenoxymethyl-penicillin	16666 µg/kg/d (1.000 mg/day therapeutic dose based on bacterial infection)	Not applicable	Not applicable	5.9 µg/d
Clofibrate	8333 µg/kg/d (500 mg/d therapeutic dose based on hyperlipoprotcinacmia)	Not applicable	278 µg/kg/d	Not applicable

In addition, the table below shows the literature-reported mixture effects of pharmaceuticals

Reference	**Components chemicals of mixture**	**Testing approach**	**Observed mixture effects**
Silva *et al.* {34}	Eight chemicals of environmental relevance: 2', 3', 4', 5'-tetrachloro-4-biphenylol, 2', 5'-dichloro-4biphenylol, 4'-chloro-4-biphenylol, genistein, 2,4-dihydroxybenzophenone, benzyl-4-hydroxyparabene, bisphenol A, resorcinol monobenzoate.	Recombinant yeast estrogen screen (YES)	There were substantial mixture effects even though each chemical was present at levels well below its NOEC and EC01.
Cleuvers {33}	Diclofenac, ibuprofen, naproxen, acetylsalicylic acid	Acute *Daphnia* and algal tests	Toxicity of the mixture was considerable, even at concentrations at which the single substances showed no or only very slight effects.
Pomati*et al.* {35}	Aixture of 13 different drugs at environmentally relevant	*In vitro* cytotoxicity in *Exherichia coli*, human	

	concentrations: atenolol, bezafibrate, carbamazepine, ciprofloxacin, cyclophosphamide, furosemide, hydrochlorothiazide, furosemide, hydrochlorothiazide, ibuprofen, lincomycin, ranitidine, salbutamol, sulfamethoxazole.	embryonic HEK293, and estrogen-reponsie OVCAR3 tumor cells

Conclusion

There are few comprehensive, systematic monitoring studies on pharmaceuticals in surface water, and limited occurrence data are a challenge in assessing potential human health risks from exposure to trace concentrations of pharmaceuticals in water. In addition, there is no standardized protocol for the sampling and analytical determination of pharmaceuticals. More systematic studies, using comparable methods, will help further research on the transport, occurrence and fate of these compounds in various environmental media, and standardization of protocols for their sampling and analytical determination would help to facilitate the comparison of data.