Occurrence and Risk Assessment of Targeted Pharmaceuticals Active Compounds in Drinking Water Treatment Plants at Shanghai, China

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A B S T R A C T

The Occurrence of nine selected pharmaceutically active compounds (PhACs), namely Paracetamol, Carbamazepine, Sulfamethoxazole, Pentoxifylline, Gemfibrozil, Diclofenac, Ibuprofen, Tetracycline and Naproxen were investigated in influents and effluents of two drinking water treatment plants (DWTPs) across Shanghai, China. In addition, the removal of these compounds in both DWTPs with differentexisting technologies (DWTP-A: biofiltration process, activated carbon and ozonation; DWTP-B: sand filtration and coagulation, flocculation and sedimentation) was investigated.The concentrations of these compounds in the influents from the two DWTPs showed substantial variations with average concentrations ranging from 3.24ng $L^{-1}$for Tetracycline to 62.3ng $L^{-1}$for Gemfibrozil, while Naproxen and Carbamazepine were found in effluents with average concentration of 0.26 ng $L^{-1}$and 1.53 ng L^{-1}, respectively. The risk assessment based on the ''worst-case scenario'' of the monitoring data from the influents of the present study suggested that Diclofenac and Sulfamethoxazole could pose a medium risk to the aquatic organisms while other compounds showed no potential toxic risks to aquatic organisms. A screening level risk assessment implied that the concentrations of the detected PhACs are well below levels that would pose a risk to the health of consumers of drinking water at Shanghai, China. Biodegradation using ozone was found to be the most effective mechanism for removing concentrations of PhACs, while filtration appeared to be a minor process for removing all PhACs.

INTRODUCTION

Pharmaceuticals have recently raised great public attention as emerging contaminants in the aquatic environment [1-3]. PhACs are used all over the world for human beings and veterinary. The users administrating pharmaceuticals excrete them and their metabolites and utilizing personal-care products waste them after usage into wastewater. Many PhACs are, therefore, discharged into the aquatic environment via wastewater treatment plants (WWTPs), since the WWTPs have less efficiency in their removal [4]. Although research in pharmaceuticals fate is limited,

they may be deposited in the environment through improper disposal, runoff from sludge fertilizer and reclaimed wastewater irrigation, and leaky sewage [5]. Conventional treatment systems, mainly based on the use of microorganisms have proven inadequate to effectively remove these types of organic compounds, largely due to their complex molecular structure [6, 7].

Drinking water treatment and disinfection may potentially reduce these already low levels of PhACs found in streams to even lower levels [8]. Drinking Water Treatment Plants (DWTPs) use a wide range of processes, but they are not specifically designed to remove pharmaceuticals that may be present in source waters. However biodegradation on slow sand filters and/or sorption to particles removed by coagulation may

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reduce their concentrations in the treated effluent for some extend. The increasingly prevalent use of Granular Activated Carbon (GAC) and Powdered Activated Carbon (PAC) as a final finishing treatment to remove pesticides and taste and odour causing compounds may also lead to removal by sorption (or biodegradation on GAC) of some pharmaceuticals products [9]. However, there is evidence that some compounds are unaffected by such processes [10].

Although some pharmaceuticals are unlikely to be a risk to the aquatic environment because of low concentrations combined with low toxicity, other pharmaceuticals such as natural and synthetic sex hormones may pose potentially significant risks. The estimation of potential impact of human pharmaceuticals to human health fromenvironmental exposures typically uses two concepts: the predicted environmental concentration (PEC) and the predicted no effect concentration (PNEC). The PEC element is based on the physical, chemical and biological fate properties of themolecule, as well as hydrological information on STP effluent flows and surface waterflows. The PNEC element estimates concentrations at which potential effects onhuman health might occur. In general, if the PEC is less than the PNEC (PEC/PNEC <1) the risk is deemed acceptable. This approach to environmental risk assessment is called the risk characterization ratio method [11]. The human health risks associated with PhACs in the aquatic environment are largelyunknown; however, the risks are likely to be very low, especially for water supplies withprotected watersheds. Most current drinking water standards forregulated organic chemicals are in the low ranges (<5 to 0.2 parts per billion (ppb)). The levels found in the various occurrence studies tend to be in the low ng L^{-1} range in surface water and are generally some 500-10,000-fold below these limits [12].

The objectives of this study were (1) to investigate the concentration of nine commonly used PhACs (Ibuprofen, Naproxen, Diclofenac-Na, Gemfibrozil, Paracetamol, Tetracycline, Sulfamethoxazole, Carbamazepine and Pentoxifelline) in the influents and effluentsof drinking water treatment plants (DWTPs) at Shanghai, China; (2) to examine the removal and fate of these pharmaceutical materials at different treatment processes within selected DWTPs that use a range of treatment technologies (i.e. biofiltration treatment, activated carbon, ozonation, sand filtration and coagulation, flocculation & sedimentation) and assess the risks associated with target compounds on aquatic organisms and adverse health impacts on human health based on the toxicity data in the literature.

MATERIALS AND METHODS

Site selection and sampling

Effluent samples were collected after each process using a grab sampler (Forestry Suppliers, Jackson MS) from two drinking water treatment plants from Shanghai, China to assess the effectiveness of these processes inremoving PhACs illustrated in Table 1. Samples were collected in pre-washed 4 L amber glass bottles. Water samples were collected in glass bottles (4 L) that were pre-rinsed according to Ahrer et al., [13] and rinsed with sample water onsite. Water chemistries such as pH and water temperature were measured at the time of sampling. Samples, wrapped with aluminum foil, were shipped on ice and delivered to the laboratory within 4 h. Samples were stored in air-tight condition in dark cold room until the analyses but no longer than two weeks.

TABLE 1. Physico-chemical properties of the studied PhACs.

Therapeutic Class	Compound	Structure	Chemical data
Anti-inflammatory Drug and Analgesic	Ibuprofen		MW: 206.29 MF: $C_{13}H_{18}O_2$ pKa: 4.91 log K_{ow}: 3.97
Anti-inflammatory Drug and Analgesic	Naproxen		MW: 230.27 MF: $C_{14}H_{14}O_3$ pKa: 4.15 log K_{ow}: 3.18
Anti-inflammatory Drug and Analgesic	Diclofenac		MW: 298.15 MF: $C_{14}H_{11}Cl_2NO_2$ pKa: 4.15 log K_{ow}: 4.51
Anti-inflammatory Drug and Analgesic	Paracetamol		MW: 151.17 MF: $CH_3CONHC_6H_4OH$ pKa: 9.4 log Kow: 0.46
Lipid regulators	Gemfibrozil		MW: 250.34 MF: $C_{15}H_{22}O_3$ pKa: 4.70
Antiepileptic	Carbamazepine		MW: 236.27 MF: $C_{15}H_{12}N_2O$ pKa: < 2 log K_{ow}: 2.45
blood viscosity control	Pentoxifylline		MW: 278.31 MF: $C_{13}H_{18}N_4O_3$ pKa: < 2 log K_{ow}: 0.29
Antibiotics	Tetracycline		MW: 444.44 MF: $C_{22}H_{24}N_2O_8$ pKa: 9.69 log K_{ow}: -1.19
Antibiotics	Tetracycline		MW: 444.44 MF: $C_{22}H_{24}N_2O_8$ pKa: 9.69 log K_{ow}: -1.19
Antibiotics	Sulfamethoxazole		MW: 253.28 MF: $C_{10}H_{11}N_3O_3S$ pKa: 6.1 log K_{ow}: 0.89

MF: Molecular Formula; MW: Molecular Weight; pKa: -log$_{10}$ of Ka (acid dissociation constant); log K_{ow}: Logarithm of octanol/water partition coefficient.

Sample analysis

Target compounds were extracted using the method described by Gros et al., [14].Prior to extractions, Samples were filtered through 1 µm glass fiber filters and then prepared for extraction by adding 100 µl of 40% H_2SO_4, and 0.6 g of disodium ethylene diamine

tetra acetate (Na$_2$EDTA) to the bottle containing 3000 ml of permeate samples. To achieve dissolution of the Na$_2$EDTA, the bottles were agitated on an orbital shaker for 60 minutes at 100 rpm. Target compounds were extracted using 60-mg HLB (hydrophilic-lipophilic balance) Oasis® brand cartridges from Waters (Millford, MA). Cartridges were preconditioned with 5ml of methanol; 5ml deionized water at neutral pH, at a flow rate of 1 mL min^{-1}. After the conditioning step water samples were passed through the cartridges at 10 mLmin^{-1}. Afterwards, the cartridge was rinsed with 5mL of milliQ water to remove excess Na$_2$EDTA. Elution was performed with 2×4mL of methanol at 1 mLmin^{-1}. The extract was evaporated under a gentle nitrogen stream and reconstituted with 1mL of methanol–water (25:75, v/v). Finally, 10µL of a 10 ngµL^{-1} standard mixtures of the internal standards Ibuprofen-D3, Carbamazepine-D10 and Simeton were added to the extract for internal standard calibration and to compensate possible matrix effects.

LC/MS/MS analysis

Liquid chromatography with tandem mass spectrometric detection was used to determined target compounds. These selected target PhACs compounds are summarized in Table 1. These methods have been published previously [15]. Briefly, an Agilent HPLC system consisting of a G1311A quaternary pump, a G1322A vacuum degasser, a G1316A thermostated column oven and a G1329A auto sampler (Agilent, USA) were used. The analysis was carried out on a LC-MS Column (Luna C18 (2), 2.0×150mm, 5 µm, Phenomenex Ltd., USA) and operated at room temperature; the injection volume was 1µL. A binary gradient consisting of 0.1% formic acid (v/v) in water (A) and 0.1% formic acid (v/v) in acetonitrile (B) at a flow rate of 700 µL min^{-1} was used. The gradient was as follows: 15% B held for 0-1 min; increased linearly to 80% held for 6 min; 6–8 min maintained the previous settings 80% B; and finally the instrument was immediately returned to starting conditions and maintained from 8 to 12 min. The total run time per sample was 12 min. An injection volume of 0.40 mLmin^{-1} was used for all analyses. Mass spectrometry was performed using an API 4000 triple quadrupole mass spectrometer (Applied Biosystems Ltd., USA) using MRM with electrospray ionization (ESI$^-$) negative mode for all compounds. Full LC–MS/MS method parameters have been described previously [15].

Risk assessment

The environmental risk posed by certain contaminants on aquaticecosystems was assessed through the calculation of risk quotients (RQ) as described previously [16-21]. RQ values for aquatic organisms werecalculated from the measured environmental concentration (MEC) and the predicted no effect concentration (PNEC) of the pharmaceutical compound. PNECs are calculated by dividing the lowest chronicno observed effect concentrations (NOECs) by assessment factors (AFs) chosen according to the European Technical Guidance Document [22]. The PNECs for the pharmaceuticals were adopted from Zhao et al. [23]. A commonlyused risk ranking criteria was applied: RQ<0.1 means minimal risk,0.1≤RQ<1 means median risk, and RQ≥1 means high risk [24].

Risk assessment of nine pharmaceutical compounds under study on human health was conducted according to procedure developed by Snyder et al [25]. The healthvalue applied in this study was the acceptable daily intake (ADI). Then ADIs were converted to drinking-water equivalent levels (DWELs) in micrograms per liter (or parts per billion) by multiplying it by an assumed body weight (70 kg, the U.S. EPA default body weight of an adult male) and a metric unit conversion factor, and dividing by an average daily drinking water ingestion rate (2 liters per day). Methods and examples of deriving and calculating ADIs, including DWELs, can be found in Snyder et al [25] and Schwab et al [26].

RESULTS AND DISCUSSION

PhACs levels in DWTPs influent and effluent

The occurrence of pharmaceuticals in the environment, including the water cycle, atconcentrations ranging from nanograms to low micrograms per litre has been widely discussed and published in the literature in the past decade [15, 27, 28]. In this study the concentrations of nine pharmaceuticals in the influents and effluents of two DWTPs at Shanghai, China were detected (Figure. 1). Data were consistent for triplicate samples, and the standard deviation was less than 12.5.Measured concentrations were generally in the low parts-per-trillion range, with mostconcentrations below 10 ngL^{-1}. These findings are comparable to studies in the USA that have detected very low levels of pharmaceuticals in finished drinking-water [29]. Studies have also shown several pharmaceuticals in tap water atconcentrations ranging from nanograms to low micrograms per liter in severalcountries in Europe, including Germany, the Netherlands and Italy [30]. Also in the Netherlands, traces of antibiotics, antiepileptics and beta blockers were detected in the drinking-water supply at concentrations below 100 ng L^{-1}, with most concentrations below 50 ng L^{-1} [31] .While other compounds recorded high concentration values reached to be 258 ng L^{-1} for Carbamazepine in the finished water at DWTP in southern California [30]. The drinking water processes was deferentially effective for removing PhACs from < 20 to > 90%. However, there were

sensitive concentrations of PhACs at the effluents of DWTP ranging from 2.13 ng L^{-1} for Carbamazepine to 0.04 ng L^{-1} for Naproxen. To date, between 15 and 25 pharmaceuticals have been detected in treated drinkingwaterworldwide, as reported in the peer-reviewed scientific literature [9, 28]. The occurrence of PhACs in finished water may indicate that drinking water is a source of human exposure.

Among the target PhACs, Gemfibrozil (110.39 ng L^{-1}) and Carbamazepine (26.54 ng L^{-1}) were detected in the highest levels in the influentof DWTP 1, other studied compounds were also detected in the range of 3.44 – 16.14 ng L^{-1}. Lower concentration values were observed in the second DWTP influent, since Carbamazepine, Diclofenac-Na, Gemfibrozil and Pentoxyfelline were recorded 17.03, 16.4, 14.21 and 10.35ng L^{-1}, respectively; whereas other compounds were detected in the range of 2.52 ~ 9.99 ng L^{-1}. These results are in agreement with other studies around the world, which concluded that PhACs have been detected in wastewater effluents and raw drinking source waters at concentrations of sub μgL^{-1}[1, 4, 32].

Removal of target compounds during drinking water treatment processes

Although, these processes were not specifically designed to remove pharmaceutical compounds from the water stream, the processes used in both DWTP showed significant removal for target compounds.The removal efficiency of these processes is presented in Figure. 2.

Biofiltration was simulated using biological acclimated sand. Some compounds appeared smoothly biodegraded such as Diclofenac (90.97%) and Gemfibrozil (82.74%), while Pentoxifylline (61.11%) and Carbamazepine (58.06%) were moderately removed. Other compounds were barely biodegraded. This was attributed to molecular structure, hydrophobicity, charge and molecular size of target compounds, since these factors affecting the adsorption process [33, 34].

Activated carbon can be extremely effective for removal of PhACs. However, its removal efficacy is greatly reduced by the presence of natural organic matter, which competes for binding sites and can block pores within the activated carbon structure [35]. The adsorption of micro pollutants onto solids depends on their physico-chemical properties, most common of which are hydrophobicity, charge and molecular size [33, 34, 36]. Another important parameter is water-octanol partition coefficient (log K_{ow}). In particular, depending on log K_{ow}, hydrophobic pollutants (log K_{ow}> 4) have higher adsorption capacity [37-39]. Therefore, the activated carbon treatment was ineffective for removing studied compounds due to low log K_{ow} (< 4). In addition, adsorbate concentration also considered an important factor in evaluating the efficiency of activated carbon process. Using granular activated carbon, it was determined that higher initial contaminant concentrations resulted in higher percent removal for Estradiol [40]. Therefore, the removal efficiency of Activated carbon for the studied PhACs was quiet low. Also removal efficacy is a function of contact time, organic loading, chemical structure, solubility and carbon type [4, 8, 41]. Iopromide, Ibuprofen, Meprobamate, Sulfamethoxazole and Diclofenac were some of the compounds found to be mostresistant to activated carbon removal [41].
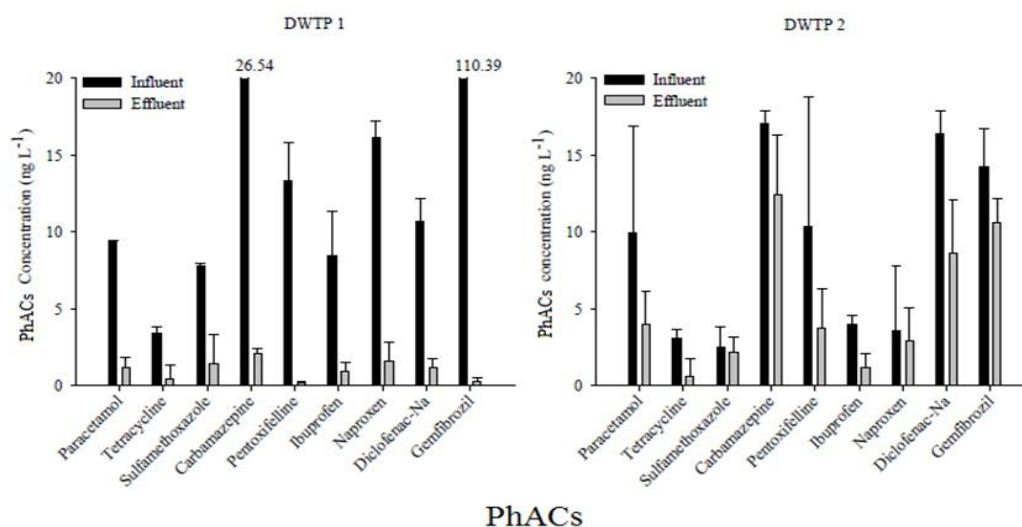

Figure 1. Occurrence of studied compounds in influents and effluents of two DWTP

Ozone has been found to be a more effective oxidizer for a large range of pharmaceuticals (Figure. 2). Ozone achieve removal of pharmaceutical via chemical destruction rather than just chemical separation from solution, this achieved by the exchange of electrons between constituents and the corresponding decrease in the overall electrical potential [42]. Westerhoff et al. [9] also concluded that ozone (O_3) is a more powerful oxidizing agent than chlorine and a very effective biocide, ozone reacts with most organic matter either by direct attack or indirectly through the formation of hydroxyl radicals (•OH) formed from ozone, meaning that the oxidation occurs mainly through reactions with OH radicals [9]. We can divide the effect of ozonation for the removal of studied pharmaceutical to high effective in case of Naproxen (99.45%), Gemfibrozil (97.55%) and Pentoxifelline (97.79%), Diclofenac-Na (85.87%), Ibuprofen (78.33%) and Tetracycline (71.52%) and moderate effect in case ofCarbamazepine (69.18%), Paracetamol (63.25%)and Sulfamethoxazole (59.48%). These results are in agreement with those obtained by McDowell et al., [43] who concluded that the spiked Rhine river water treated with O_3 (dose 1.2 mg L^{-1}) achieved 100% removal for Pentoxifelline and other compounds. Further studies reported that water treatment plants employing ozonation are capable of removing large number of PhACs compounds from water [9, 28, 44].
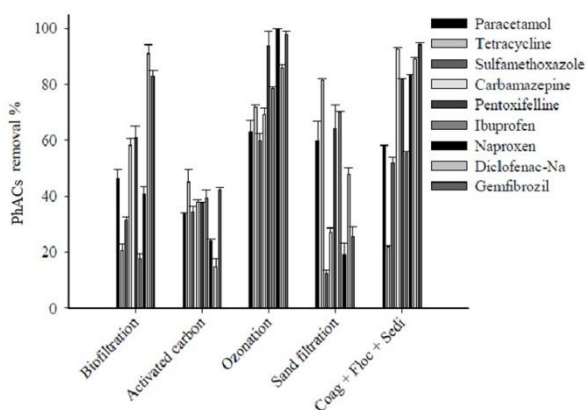

Figure 2. Removal efficacy of different DWTP processes for the removal of PhACs

Filtration occurs as the water passes through a substance that helps remove even smaller particles. One of the oldest and simplest processes used to treat water is to pass it through a bed of fine particles, generally sand. Sand filtration usually removes fine suspended solid matter as well as some other particles, such as larger microorganisms. Sand filtration was quiet effective for removing Tetracycline (81.00%) and Ibuprofen (70%), moderate removal for Pentoxifylline

(64.25%) and Paracetamol (59.9), while low removal efficiency was observed of other studied compounds.

Chemical coagulation using aluminum or iron based salts will precipitate metal hydroxides. Chemical softening removes dissolved calcium and magnesium using lime and soda-ash to precipitate calcium carbonate (pH > 9.0) and magnesium hydroxide (pH > 11). Organic compounds can co-precipitate with the metal hydroxides and carbonates or adsorb onto surfaces after precipitation. Chemical coagulation and softening aid in removing suspended solids (i.e., turbidity), colloids and some dissolved organic carbon (DOC) from water. Sedimentation and filtration follow coagulation or chemical softening to remove these newly formed particles [36].

Unexpected, Coagulation, flocculation & sedimentation showed high removal efficiency for target compounds (i.e., Gemfibrozil, Carbamazepine, Diclofenac, Naproxen and Pentoxifylline), since previous studies using both alum and ferric chloride as coagulants for natural water or pure water samples spiked with pharmaceutical target compounds showed that coagulation (with or without chemical softening) is largely ineffective in removing pharmaceutical target compounds[9, 33, 45]. Also, Awwa Research Foundation project concluded that coagulation was largely ineffective for pharmaceutical removal in bench-scale, pilot-scale and full-scale investigations [41]. This finding might be attributed to low concentration values of studied compounds resulted from sand filtration process, which were not exceed than 10 ngL^{-1}. On the other hand, these highly hydrophobic contaminants are most likely to enter a facility already bound to particles and may not be detected in the analytical protocol and is not suitable for particle analysis [36]. Nevertheless, the obtained results here are similar to some previous observation reported by Huerta-Fontela et al. [29] who concluded that coagulation/flocculation and sand filtration can remove from <33 to 100% of PhACs.

Risk assessment

In Shanghai, China, most wastewater treatment plants effluents are discharged into aquatic environment, which are used as influent for drinking water treatment plants or for irrigation directly without any treatments. This might lead to negative impacts on the aquatic environment.Consequently, adverse health impacts on human health may be existed.

Environmental risks to aquatic organisms were assessed for the worst case scenario in the influent of DWTPs based on the risk quotients (RQ) calculated using MECs and PNECs (Table 2). The RQ values for Diclofenac and Sulfamethoxazolewere 0.62and 0.19, respectively, while the RQs for all the other compounds detected were below 0.1. According to the RQ classification scheme from Hernando et al. [24],

Diclofenac and Sulfamethoxazole could pose a medium risk to the aquatic organisms.Whereas, the RQ values for other compounds detected were less than 0.1, indicating no potential risks to the aquatic organisms.

Biologicaltests showed toxicological effects of Diclofenac and sulfamethoxazole on various aquatic organisms.Diclofenac as anamphiphilic acid binds to the lipid–water interphaseof cell membranes thereby inhibiting the synthesisand release of prostaglandines [46]. The histopathological examinations of diclofenac-exposed fish revealedalterations of the kidney such as an hyaline dropletdegeneration of the tubular epithelial cells and the occurrence of an interstitial nephritis. In the gills, the predominant findingconsisted in anecrosis of pillar cells leading to damage of the capillary wall within the secondary lamellae, thelowest observed effect concentration (LOEC) at which both renal lesions and alterations of the gills occurred was 5µg/L [19]. While veterinary antibiotics (e.g., Sulfamethoxazole) are designed to affect mainly microorganisms and bacteria found in animals. This therefore makes them potentially hazardous to other such organisms found in the environment [47]. Ingeneral, toxic levels of antibiotics for microorganisms, bacteriaand micro-algae present in the environment are 2–3 orders of magnitude below the toxic values for higher trophiclevels [48].

On the other hand the human health risks associated with the presence of PhACs in drinking water have been thoroughly studied.Several screening level risk assessments have concluded that no appreciable human health risk exists for the trace levels of PhACs detected in other comparable studies [25, 48]. In this study we utilize existing toxicological data on Acceptable Daily Intakes (ADIs), which converts to drinking water equivalent level (DWEL) to establish the margin of exposure (MOE), which defined as the DWEL divided by the maximum-detected water concentration.

TABLE 2. Risk quotient of studied PhACs on aquatic organisms using their PNEC data.

Pharmaceutical	MEC (influent) (ng L^{-1})	PNEC (ng L^{-1})	RQ^a
Paracetamol	9.62	9,200	0.001
Tetracycline	3.24	310	0.01
Sulfamethoxazole	5.13	26.8	0.19
Carbamazepine	21.78	4,920	0.004
Pentoxifelline	11.64	Not applicable	Not applicable
Ibuprofen	6.21	7100	0.001
Naproxen	9.85	640.0	0.015
Diclofenac-Na	61.52	100.00	0.62
Gemfibrozil	62.3	10000.00	0.006
^{a}RQ = MEC / PNEC			

Table 3 provides the results of this type of analysis. One way to understand the relationship between the DWEL and the water concentration is to numerically estimate the difference. For example, the DWEL for

Carbamazepine was calculated to be 12 µgL^{-1} and the maximum drinking water concentration was 0.0021 µgL^{-1}. Consequently, the water concentration exceed 5000-fold lower than the DWEL, although recall that the DWEL itself is not a threshold of an adverse effect. Comparing DWELs to maximum concentrations of nine pharmaceuticals in drinking water, the results demonstrate that MOE were more than 5000 fold lower than the permissible concentrations (DWEL) for all studied compounds. Thus, no adverse effects would be expected from drinking water with the reported concentrations for consumers.

These findings are in line with other studies over the past decade,which also supported the conclusion that discernible risks to health arising from trace levels of pharmaceuticals in drinking-water are extremely unlikely[10, 25, 49-53].

TABLE 3. Impact of PhACs on human health using ADI from drinking water

Pharmaceutical	ADI (µg/kg-d)	DWEL (µg/L)	Maximum drinking water conc. (µg L^{-1})*	Margin Of Exposure MOE
Paracetamol	340	12,000	0.002	<6,000,000
Tetracycline	30.0	1,050	0.0004	> 2,500,000
Sulfamethoxazole	130	4,500	0.0014	3,250,000
Carbamazepine	0.34	12.0	0.0021	> 5000
Pentoxifelline	Not applicable	Not applicable	0.0007	Not applicable
Ibuprofen	110.0	3,800	0. 0009	< 4,300,000
Naproxen	570.0	20,000	0.0005	40,000,000
Diclofenac-Na	67.0	2,300	0.0012	< 2,000,000
Gemfibrozil	1.3	45.0	0.0006	75,000

*Single highest discrete sample concentration, from finished drinking water

CONCLUSION

Although pharmaceuticals appear at relatively low concentrations ranging between ng L^{-1} and µg L^{-1} levels, they may impose serious effects on the environment. Different technologies at DWTPs were assessed for removing nine PhACs and proved that:

1-Biodegradation using ozone was found to be the most effective mechanism for removing concentrations of PhACs, especially for Naproxen (99.45%), Gemfibrozil (97.55%) and Pentoxifelline (97.79%)

2-Filtration appeared to be a minor process for removing all PhACs.

3-Adsorption onto activated carbon was least efficient in the removal of the target PhACs, while Coagulation, flocculation & sedimentation appeared to be an effective process for most PhACs.

A risk assessment study was conducted to evaluate the RQ of PhACs to aquatic environment and minimum

margin of safety for PhACs on consumers of drinking water:

4-Based on the measured influent concentrations from this study and limited ecotoxicity data available in the literature, a potential risk assessment was conducted for the ''worst case scenario'' (100% of stream flow derived from influent and using the highest measured concentrations of target PhACs). The RQ values of Diclofenac and Sulfamethoxazole could pose a medium risk to the aquatic organisms, while for other compounds detected were less than 0.1, indicating no potential risks to the aquatic organisms.

5-The maximum-detected concentrations in finished drinking water were used to calculate drinking water equivalent levels (DWELs) for each of the target compounds. The maximum-detected concentrations used are the single highest discrete sample concentrations observed in this study, providing a conservative "worst-case" scenario approach. Using this approach, none of the pharmaceuticals detected in drinking water exceeded their corresponding ADI.

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REFERENCES

1. Heberer, T., 2002. Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: a review of recent research data. Toxicology Letters, 131(1): 5-17.

2. Kolpin, D.W., E.T. Furlong, M.T. Meyer, E.M. Thurman, S.D. Zaugg, L.B. Barber and H.T. Buxton, 2002. Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999-2000: a national reconnaissance. Environmental Science and Technology, 36(6): 1202-1211.

3. Harrison, E.Z., S.R. Oakes, M. Hysell and A. Hay, 2006. Organic chemicals in sewage sludges. Science of the Total Environment, 367(2): 481-497.

4. Ternes, T.A., 1998. Occurrence of drugs in German sewage treatment plants and rivers. Water Research, 32(11): 3245-3260.

5. Doerr-MacEwen, N.A. and M.E. Haight, 2006. Expert stakeholders' views on the management of human pharmaceuticals in the environment. Environmental Management, 38(5): 853-866.

6. Kümmerer, K., A. Al-Ahmad and V. Mersch-Sundermann, 2000. Biodegradability of some antibiotics, elimination of the genotoxicity and affection of wastewater bacteria in a simple test. Chemosphere, 40(7): 701-710.

7. Carballa, M., F. Omil, J.M. Lema, M.a. Llompart, C. García-Jares, I. Rodríguez, M. Gomez and T. Ternes, 2004. Behavior of pharmaceuticals, cosmetics and hormones in a sewage treatment plant. Water Research, 38(12): 2918-2926.

8. Ternes, T.A., M. Meisenheimer, D. McDowell, F. Sacher, H.-J. Brauch, B. Haist-Gulde, G. Preuss, U. Wilme and N. Zulei-Seibert, 2002. Removal of pharmaceuticals during drinking water treatment. Environmental Science and Technology, 36(17): 3855-3863.

9. Westerhoff, P., Y. Yoon, S. Snyder and E. Wert, 2005. Fate of endocrine-disruptor, pharmaceutical, and personal care product chemicals during simulated drinking water treatment processes. Environmental Science and Technology, 39(17): 6649-6663.

10. Jones, O.A., J.N. Lester and N. Voulvoulis, 2005. Pharmaceuticals: a threat to drinking water? Trends in Biotechnology, 23(4): 163-167.

11. E.C., Technical Guidance Document on Risk Assessment in support of Commissions Directive 93/67/EEC on Risk Assessment for new notified substances and Commissions Regulations (EC) No. 1488194 on risk assessment for existing substances, Ispra, Italy, European Chemicals Bureau. 1996.

12. New York Code, Rules, and Regulations (NYCRR).Chapter 1, State Sanitary Code. Part 5: Drinking Water Supplies. Subpart 5-1: Public Water Systems, New York State Department of Health,Title 10.

13. Ahrer, W., E. Scherwenk and W. Buchberger, 2001. Determination of drug residues in water by the combination of liquid chromatography or capillary electrophoresis with electrospray mass spectrometry. Journal of Chromatography A, 910(1): 69-78.

14. Gros, M., M. Petrović and D. Barceló, 2006. Development of a multi-residue analytical methodology based on liquid chromatography–tandem mass spectrometry (LC–MS/MS) for screening and trace level determination of pharmaceuticals in surface and wastewaters. Talanta, 70(4): 678-690.

15. Vanderford, B.J., R.A. Pearson, D.J. Rexing and S.A. Snyder, 2003. Analysis of endocrine disruptors, pharmaceuticals, and personal care products in water using liquid chromatography/tandem mass spectrometry. Analytical Chemistry, 75(22): 6265-6274.

16. European agency for the evaluation of medicinal products. Committee for medicinalproducts for human use (CHMP). Guideline on the environmental riskassessmentof medicinal products for human use. Ref EMEA/CRMP/SWP/4447/00. London, UK; 2006.

17. Stuer-Lauridsen, F., M. Birkved, L. Hansen, H.-C.H. Lützhøft and B. Halling-Sørensen, 2000. Environmental risk assessment of human pharmaceuticals in Denmark after normal therapeutic use. Chemosphere, 40(7): 783-793.

18. Santos, J., I. Aparicio and E. Alonso, 2007. Occurrence and risk assessment of pharmaceutically active compounds in wastewater treatment plants. A case study: Seville city (Spain). Environment International, 33(4): 596-601.

19. Schwaiger, J., H. Ferling, U. Mallow, H. Wintermayr and R. Negele, 2004. Toxic effects of the non-steroidal anti-inflammatory drug diclofenac: Part I: histopathological alterations and bioaccumulation in rainbow trout. Aquatic Toxicology, 68(2): 141-150.

20. Tauxe-Wuersch, A., L.F. De Alencastro, D. Grandjean and J. Tarradellas, 2005. Occurrence of several acidic drugs in sewage treatment plants in Switzerland and risk assessment. Water Research, 39(9): 1761-1772.

21. Ying, G.-G., R.S. Kookana and D.W. Kolpin, 2009. Occurrence and removal of pharmaceutically active compounds in sewage treatment plants with different technologies. Journal of Environmental Monitoring, 11(8): 1498-1505.

22. European Commission, 2003. Technical guidance document in support of commission directive 93/67/EEC on risk assessment for new notified substances and commission regulation (EC) No 1488/94 on Risk Assessment for Existing Substances, Part II.Brussels, Belgium. .

23. Zhao, J.L., G.G. Ying, Y.S. Liu, F. Chen, J.F. Yang, L. Wang, X.B. Yang, J.L. Stauber and M.S.J. Warne, 2010. Occurrence and a screening-level risk assessment of human pharmaceuticals in the Pearl River system, South China. Environmental Toxicology and Chemistry, 29(6): 1377-1384.

24. Hernando, M.D., M. Mezcua, A. Fernández-Alba and D. Barceló, 2006. Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments. Talanta, 69(2): 334-342.

25. Snyder, S. A., Trenholm, R. A., Bruce, G. M., Snyder, E.M., Pleus, R.C. 2008. Toxicological Relevanceof EDCs and Pharmaceuticals in Drinking Water, Awwa Research Foundation, Denver, CO.

26. Schwab, B.W., E.P. Hayes, J.M. Fiori, F.J. Mastrocco, N.M. Roden, D. Cragin, R.D. Meyerhoff, J. Vincent and P.D. Anderson, 2005. Human pharmaceuticals in US surface waters: a human health risk assessment. Regulatory Toxicology and Pharmacology, 42(3): 296-312.

27. Stackelberg, P.E., E.T. Furlong, M.T. Meyer, S.D. Zaugg, A.K. Henderson and D.B. Reissman, 2004. Persistence of pharmaceutical compounds and other organic wastewater contaminants in a conventional drinking-water-treatment plant. Science of the Total Environment, 329(1): 99-113.

28. Snyder, S.A., S. Adham, A.M. Redding, F.S. Cannon, J. DeCarolis, J. Oppenheimer, E.C. Wert and Y. Yoon, 2007. Role of membranes and activated carbon in the removal of endocrine disruptors and pharmaceuticals. Desalination, 202(1): 156-181.

29. Benotti, M.J., R.A. Trenholm, B.J. Vanderford, J.C. Holady, B.D. Stanford and S.A. Snyder, 2008. Pharmaceuticals and endocrine disrupting compounds in US drinking water. Environmental Science and Technology, 43(3): 597-603.

30. Huerta-Fontela, M., M.T. Galceran and F. Ventura, 2011. Occurrence and removal of pharmaceuticals and hormones through drinking water treatment. Water Research, 45(3): 1432-1442.

31. Mons, M.N., Hoogenboom, A.C., Noij, T.H.M. 2003. Pharmaceuticals and drinking watersupply in theNetherlands. Nieuwegein, Kiwa Water Research (Kiwa Report No. BTO 2003. 040).

32. Halling-Sørensen, B., S.N. Nielsen, P. Lanzky, F. Ingerslev, H.H. Lützhøft and S. Jørgensen, 1998. Occurrence, fate and effects of pharmaceutical substances in the environment-A review. Chemosphere, 36(2): 357-393.

33. Yoon, Y., P. Westerhoff, S.A. Snyder and M. Esparza, 2003. HPLC-fluorescence detection and adsorption of bisphenol A, 17β-estradiol, and 17α-ethynyl estradiol on powdered activated carbon. Water Research, 37(14): 3530-3537.

34. Carballa, M., F. Omil and J.M. Lema, 2005. Removal of cosmetic ingredients and pharmaceuticals in sewage primary treatment. Water Research, 39(19): 4790-4796.

35. Savransky, N., Goldin, L. , 2010. Pharmaceuticals in the Water: A look at an emerging and pressing issue, Mass Government. (www.mass.gov/eea/docs/dep/toxics/stypes/pharmh2o.pdf)

36. Snyder, S.A., Wert, E. C., Lei, H. X., Westerhoff, P., Yoon, Y. 2007. Removal of EDCs and pharmaceuticals in drinking water and reuse treatment processes. AWWA Research Foundation Denver, CO.

37. Bertanza, G., R. Pedrazzani and V. Zambarda, 2009. I microinquinanti organici nelle acque di scarico urbane: presenza e rimozione. Ingegneria Ambientale, 48:1-6

38. Choi, K.J., S.G. Kim, C.W. Kim and S.H. Kim, 2005. Effects of activated carbon types and service life on removal of endocrine disrupting chemicals: amitrol, nonylphenol, and bisphenol-A. Chemosphere, 58(11): 1535-1545.

39. Stackelberg, P.E., J. Gibs, E.T. Furlong, M.T. Meyer, S.D. Zaugg and R.L. Lippincott, 2007. Efficiency of conventional drinking-water-treatment processes in removal of pharmaceuticals and other organic compounds. Science of the Total Environment, 377(2): 255-272.

40. Fuerhacker, M., A. Dürauer and A. Jungbauer, 2001. Adsorption isotherms of 17β-estradiol on granular activated carbon (GAC). Chemosphere, 44(7): 1573-1579.

41. Khiari, D., 2007. Endocrine disruptors, pharmaceuticals, and personal care products in drinking water: an overview of AwwaRF Research to Date. Awwa Research Foundation, Denver, CO, 238.

42. Crittenden, J.C., Trussell, R.R., Hand, D.W., Howe, K.J., Tchobanglous, G. 2005. Water treatment: principles and design, 2ed., John Wiley & Sons, Inc.: Hoboken, New Jersey. 1948.

43. McDowell, D.C., M.M. Huber, M. Wagner, U. von Gunten and T.A. Ternes, 2005. Ozonation of carbamazepine in drinking water: identification and kinetic study of major oxidation products. Environmental Science and Technology, 39(20): 8014-8022.

44. Shahram, T., Y. Paul, Z. Xiaoming, H. Chunyan, S. Rajesh, S. Linda and J. Taher, 2010. Occurrence and removal of PPCPs and EDCs in the Detroit River watershed. Water Practice and Technology, 5(1):1-8.

45. Yoon, Y., P. Westerhoff, S.A. Snyder and E.C. Wert, 2006. Nanofiltration and ultrafiltration of endocrine disrupting compounds, pharmaceuticals and personal care products. Journal of Membrane Science, 270(1): 88-100.

46. Kuschinsky, G., üllmann, H.L., 1981. Kurzes Lehrbuch der Pharmakologie und Toxikologie. 9. Auflage, Georg ThiemeVerlag Stuttgart, New York.

47. Warman, P., 1980. The effect of amprolium and aureomycin on the nitrification of poultry manure-amended soil. Soil Science Society of America Journal, 44(6): 1333-1334.

48. Wollenberger, L., B. Halling-Sørensen and K.O. Kusk, 2000. Acute and chronic toxicity of veterinary antibiotics to Daphnia magna. Chemosphere, 40(7): 723-730.

49. Pleus, R. C. 2009. Pharmaceuticals & Endocrine Disrupting Chemicals (EDCs) in Water:Development of Health Risk-Based Screening Levels, Presentation at the 2009 ACWA Spring Conference "Water Infra structure 911,"Sacramento, CA.

50. Wilson, L., P. O'Keefe, P. Palmer, R. Sheridan, R. Briggs and T. King, 2003. Survey of the New York City Watershed for the Presence of Pharmaceuticals.

51. Webb, S., T. Ternes, M. Gibert and K. Olejniczak, 2003. Indirect human exposure to pharmaceuticals via drinking water. Toxicology Letters, 142(3): 157-167.

52. Snyder, S.A. 2010. Occurrence of pharmaceuticals in U.S drinking water. ACS Symposium Series, 1048(2010):69-80.

53. Bercu, J.P., N.J. Parke, J.M. Fiori and R.D. Meyerhoff, 2008. Human health risk assessments for three neuropharmaceutical compounds in surface waters. Regulatory Toxicology and Pharmacology, 50(3): 420-427.

Persian Abstract

چکیده

وجود ۹ ترکیب فعال دارویی (PhAcs) به نام های پاراستامول،کاربامازپین،سولفامتاکسازول،پنتوکسی فیلین،جمفیبروزیل،دیکلوفناک،ایبو پروفن،تترا سایکلین و ناپروکسن در آب های ورودی و خروجی از دو واحد تصفیه آب شرب (DWTPs) در شانگهای چین مورد بررسی قرار گرفت.علاوه بر این،جداسازی این ترکیبات از هر دو واحد تصفیه با تکنولوژی های متفاوت (واحد A: بیو فیلتراسیون، واحد B: رسوب دهی) نیز مورد بررسی قرار گرفت.غلظت این ترکیبات در آب های ورودی هر دو واحد تصفیه اختلاف قابل توجهی را با میانگین غلظت ۳/۲ ng L^{-1} برای تتراسایکلین تا ۶۲/۳ ng L^{-1} برای جمفیبروزیل نشان می دهد در حالیکه غلظت ناپروکسن و کاربامازپین در آ بهای خروجی به ترتیب ۰/۲۶ و ۱/۵۳ ng L^{-1} اندازه گیری شد.انالیز خطر بر اساس "بدترین حالت ممکن" از مشاهده اطلاعات از آب های ورودی بیان می کند که دیکلوفناک و سولفامتاکسازول دارای سطح خطر متوسط برای ارگانیزم های ابزی می باشند در حالیکه سایر ترکیبات خطرات سمی برای ارگانیزم های آبزی ندارند.آزمایش آنالیز سطح خطر بیان میکند که غلظت PhAC ها زیر سطح خطر برای مصرف به عنوان آب شرب در شانگهای چین است. زیست تخریب پذیری با ازون موثرترین مکانیزم برای جداسازی PhAc هاست در حالیکه فیلتراسیون در رده بعدی برای جداسازی همه ی PhAC ها قرار میگیرد