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Occurrence and ecological risk of pharmaceuticals in river surface water of Bangladesh

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ABSTRACT

Pharmaceutical contamination in the aquatic environment is a global issue that affects aquatic animals, microorganisms and human health. The occurrence and preliminary ecological risk of 12 (11 antibiotics and 1 antiepileptic drug) pharmaceuticals were investigated for the first time in the surface water of the old Brahmaputra River, where open-water-fed aquaculture activities are being practiced in Bangladesh. The pharmaceuticals were quantified by high-performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS), operated with positive electrospray ionization (ESI^+) and a multiple reaction monitoring (MRM) mode. Nine pharmaceuticals were detected in the river surface water, whereas three were below the limit of detection (LOD). Metronidazole was detected in all the samples with concentrations ranging from 0.05 to 13.51 ng L^{-1}. Trimethoprim had the second highest frequency of detection (95%) with the highest concentration (17.20 ng L^{-1}). The ranges of concentration and detection frequency of sulfonamides and macrolides were < LOD-11.35 and < LOD-16.68 ng L^{-1}; 35–70 and 60–85%, respectively, whereas carbamazepine was in the range of < LOD-80 ng L^{-1} and had a detection frequency of 65%. The concentrations of sulfamethoxazole, trimethoprim, erythromycin-H_2O and tylosin were distinctly higher in the fed aquaculture areas. The principal component analysis confirmed that fed aquaculture activities contributed most of the pharmaceutical contamination in the river surface water. Hospitals, nursing homes, sewage wastewater or surface runoff from the surrounding areas might all contribute to the presence of metronidazole and carbamazepine. The preliminary ecological risk assessment revealed that sulfamethoxazole, erythromycin-H_2O and tylosin showed medium risk, and carbamazepine displayed low risk to sensitive aquatic organisms for maximum measured concentrations. Thus, this study suggests that pharmaceutical contamination in different rivers and seasons needs to be quantified, and ecological as well as human health risks need to be assessed in Bangladesh.

1. Introduction

Pharmaceuticals are, in general, a frequently discussed global issue as an emerging contaminant in aquatic environments (Välitalo et al., 2017). The continuous release of pharmaceuticals into the aquatic environments and their pseudo-persistent characteristics have become a concerning issue of research (Roberts and Thomas, 2006). Pharmaceuticals are biologically active substances generally applied for preventive or curative measures and as growth promoters to target organisms. They might accumulate in water bodies and, subsequently, affect non-target organisms in the aquatic ecosystem and bioaccumulate in mollusks and fishes, even at low concentrations (Moreno-González et al., 2016; Sangion and Gramatica, 2016). Some of the pharmaceuticals partially degrade by photooxidation, microbial action or hydrolysis (Batchu et al., 2014; Vila-Costa et al., 2017; Yamamoto et al., 2009). However, others may be quite persistent (Batchu et al., 2014; Bu et al., 2016). In some instances, they may remain in their unchanged form, even after treatment in a conventional sewage treatment plant (Clara et al., 2004), and in sludge liquor in wastewater treatment plants (Ivanová et al., 2017), and finally find their way into the aquatic environments.

Pharmaceuticals, such as sulfamethoxazole, trimethoprim, erythromycin, penicillin, metronidazole and carbamazepine, used as essential drugs for humans in Bangladesh (DGDA, 2016). Metronidazole (MNZ), is an antibacterial and antiprotozoal drug, belongs to nitroimidazole group, used in humans and widely used in veterinary and

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aquaculture practices (Wagil et al., 2015). Carbamazepine (CAB), one of the antiepileptic drugs used in humans, has been detected in the sewage effluents, surface waters, drinking waters and even in ground waters in China, Japan, South Korea, Europe, USA and Canada (Zhang et al., 2008). Several studies reported that the half-life of CAB, found either in lab or field based studies, has exceeded its persistence criteria of 60 days in water compartment (Yamamoto et al., 2009; Zou et al., 2015). The repeated release of MNZ and CAB into the aquatic environment may have significant, long-term effects on the stability of ecosystems, because MNZ and CAB and their metabolites possess mutagenic, carcinogenic and toxic properties (Capitan-Valley et al., 2007; Chiron et al., 2006). For this reason, the application of MNZ in animals used as human food is strictly prohibited in the EU and USA (Wagil et al., 2015). However, despite the use of MNZ as human drug, it is still being used as a veterinary drug, particularly in the poultry industry of Bangladesh.

In many developing countries, there are insufficient health services for all the people; people can generally buy drugs from a drug store without a physician's prescription. Therefore, peoples' misuse of pharmaceuticals is normally higher in developing countries than in the developed countries. The wastewater treatment facilities for hospital wastewater are very limited or even absent in most of these countries, particularly in the semi-urban areas of Bangladesh. As a result, wastewater that is directly or indirectly released into the river, and the regular discharge of pharmaceuticals from hospitals and nursing homes, might be contaminating the river water. In their recent review, Välitalo et al. (2017) reported that pharmaceuticals have been widely detected in river surface waters in the USA, UK, Spain, Sweden, Japan, Korea, China, Hong Kong, Vietnam, and Kenya. Concentrations vary from nanograms to micrograms per liter and their occurrence in waters varies greatly across regions and by seasons. Larsson et al. (2007) have shown that the highest levels (up to 31,000 $\mu g\,L^{-1}$) of pharmaceutical concentrations are in the effluents of wastewater plants that treat the wastewater from 90 drug manufacturers in India. The consequences of pharmaceutical compounds that are discharged in rivers have resulted in severe negative effects and sometimes the threat of extinction of the native fish species due to over exposure (Sanchez et al., 2011).

Today, many small rivers in Bangladesh are being used for open-water-fed aquaculture purposes. The fish production in rivers is mainly dependent on the use of formulated and handmade feeds and, in some cases, poultry droppings, which contain different pharmaceuticals particularly antibiotics. Recently, Ali et al. (2016) reported that 7 different types of antibiotics used in aquaculture of Bangladesh. The rapid development of intensive aquaculture and the feeding of antibiotic drugs has become a necessity in the aquaculture sector (Xu et al., 2006). The increasing use of antibiotics as human and animal drugs and in the fed aquaculture is influencing the speeding up of resistant bacterial strains that can cause adverse ecological and human-health effects (Kümmerer, 2009; Le Page et al., 2017; Sapkota et al., 2008; Shah et al., 2014). Many developed and developing countries of the world are continuously monitoring the contamination of pharmaceuticals in river surface waters and their risks to aquatic organisms as well as human health (Cunningham et al., 2009; Välitalo et al., 2017). However, in Bangladesh, the present study reports for the first time the occurrence and risk of 12 pharmaceuticals in the surface water of the old Brahmaputra River, which is being used for open-water-fed aquaculture activities in Bangladesh.

2. Materials and methods

2.1. Chemicals and standards

Target compounds of pharmaceuticals were selected based on their uses in human and veterinary medicine as well as in the aquaculture of Bangladesh. The physico-chemical properties of the target pharmaceuticals for this study are shown in Table 1. Sufamethazine-$^{13}C_6$ (SMT-$^{13}C_6$), azithromycin-d3 (AZM-d3) and carbamazepine-d10 (CAB-d10) were used as internal standards and were obtained from Cambridge Isotope Labs (Andover, MA, USA), Santa Cruz Biotechnology, Inc. (Dallas, TX, USA) and CDN Isotopes Inc. (Pointe-Claire, QC, Canada), respectively. All pharmaceuticals were dissolved in methanol and their stock and working solutions were stored at − 20 °C and 4 °C, respectively. Methanol and acetonitrile (> 99%, LC/MS grade) and formic acid (> 98%, LC/MS grade) were purchased from Wako Pure Chemical Industries (Osaka, Japan). Milli-Q (> 18.2 MΩ) water was used throughout the experiment and was generated by using an ultrapure water purification system (Millipore, Billerica, MA, USA). In addition, oasis HLB cartridges (6 mL/500 mg, Waters, USA), 0.45-μm filter membranes (ADVANTEC®, Tokyo, Japan), disposable PP syringes (NORM-JECT®, Henke-Sass Wolf GmbH, Germany) and 0.22-μm MS® PP nylon syringe filters (13 mm diameter) (Membrane Solution, Tokyo, Japan) were used.

2.2. Sampling, samples enrichment and extraction

Surface water samples (n = 20) were collected in February 2017 from the old Brahmaputra River in Bangladesh (see Fig. S1). Sampling points were ordered as BR1 to BR20 and consisted of two distinct subgroups, such as BR1-BR4 and BR17-BR20 (aquaculture adjacent areas) and BR5-BR16 (aquaculture activity areas where BR5 and BR9 are the feed-applying points; aquaculture fish species are shown in the general description of the supplementary materials). A sampling map with sampling points is shown in Fig. 1(a detailed description of the study area is presented in the supplementary materials, and the coordinates of sampling points and, sample IDs are listed in Table S1). Surface water samples (1 L) from individual sampling points were taken in precleaned polypropylene (PP) bottles. The bottles were rinsed with river water prior to use. The collected samples were immediately sent to the laboratory in the Department of Fisheries, University of Dhaka, and water samples were filtered through 0.45-μm filters to remove suspended particles. The enrichment and extraction of pharmaceuticals from water samples were performed following previous methods (Hossain et al., 2017; Li et al., 2014). Briefly, the samples were enriched by using solid-phase extraction (SPE) with Oasis HLB cartridges (6 mL/500 mg, Waters, USA). The cartridges were sequentially preconditioned with 10 mL of methanol, 5 mL of Milli-Q water and 5 mL of a 0.1% (v/v) formic acid solution. The internal standards (100 $ng\,L^{-1}$ of each) were mixed with filtered water samples and passed through the HLB cartridges at a flow rate of 10 $mL\,min^{-1}$, followed by a rinse with 5 mL of Milli-Q water. Then, the HLB cartridges were vacuum-dried for 30 min. All the cartridges were brought to the Department of Risk Management and Environmental Sciences, Yokohama National University, Japan, for pharmaceutical analysis. Each cartridge was eluted separately with 12 mL of methanol and concentrated to 1 mL and filtered by using disposable PP syringes fitted with 0.22-μm disposable filters. Finally, the eluate was transferred to an amber auto-sampler vial for analysis.

2.3. Instrumental analysis

Instrumental analysis of pharmaceuticals was performed by following our previous study (Hossain et al., 2017). Briefly, pharmaceuticals in the extracted solution were analyzed by high-performance liquid chromatography tandem mass spectrometry (HPLC–MS/MS) system that included an Agilent 1100 series (Agilent, Palo Alto, USA). Separation was achieved on an Agilent Zorbax Eclipse XDB-C18 column (150 mm × 2.1 mm, particle size 5 μm). The injection volume was 10 μL and the column temperature was maintained at 30 °C during sample analysis. The mobile phase consisted of eluent A (Milli-Q water with 0.1% formic acid) and eluent B (acetonitrile with 0.1% formic acid). The flow rate was maintained in 0.4 $mL\,min^{-1}$. The separation of target pharmaceuticals was achieved with the gradient program as follows: 5% B (0.5 min); 95% B (13.5 min); 95% B (15 min); 50% B