Investigation on the Occurrence of Pharmaceutical and Personal Care Products (PPCPs) Residues in Sea Water and Fresh Water from Jakarta Bay and Lower Reach of Rivers at Jakarta Great Area

A Sudaryanto[1,*], M Ilyas[1], DB Aviantara[1], F Suciati[1], S Sulistia[1], R Tanoue[2], A Morimoto[2], and T Kunisue[2]

[1] Research Center for Environmental and Clean Technology, National Research and Innovation Agency, Kawasan Puspiptek Gedung 820, Tangerang Selatan 15314, Indonesia
[2] Center for Marine Environmental Studies (CMES), Ehime University, Bunkyo-cho 2-5, Matsuyama 790-8577, Japan

1. Introduction

Pharmaceuticals and personal care products (PPCPs) are known as an emerging class of water contaminants that are not commonly monitored but have the potential to enter the environment and cause known or suspected adverse ecological and/or human health effects. These chemicals are anthropogenic origin and could be significant sources of contamination to surface waters, such as lakes ponds, rivers and streams[1)] which then reach coastal areas, eventually entering ocean offshore. The pharmaceuticals include mainly drugs administered to humans or animals, such as antibiotics, anti-inflammatories, their metabolites as well as transformation products, which are either excreted in faces and urine, originated from wastewater treatment plants (WWTPs), clinics, hospitals, industrial effluents, and aquaculture wastewaters. Whereas for personal care products (PCPs) include diverse types of products such as lotions, sunscreen creams, soaps, cosmetics, perfumes, toothpastes, etc. Many health issues can possibly arise when such contaminants finally enter the available water resources[2)].

Indonesia is home to 273 million people and one of the fastest growing pharmaceutical markets in Asia. Indonesia's pharmaceutical market is ranked the largest market in the ASEAN regions, with the market value expected to hit USD 10.11 billion by 2021[3)]. Of the geographical area of Indonesia, the Jakarta Great Area (JGA) is the main center of Indonesian economic activity and the largest concentration of urban population in Indonesia[4)]. Many rivers end up to Jakarta Bay, of which the 13 rivers flowing through Jakarta City discharge their waters into Jakarta Bay, which thus receives waste from more than 10 million inhabitants[4)]. It has been reported that 75% of wastewater goes untreated in Jakarta, being directly discharged into rivers or open canals[5)]. As a result, the marine ecosystem in Jakarta Bay is under threat, for example a marked decline in the biodiversity has been reported, in relation to the increased anthropogenic pressure in the area[6)].

Although the effects of large number of PPCPs on the environment remain unknown, however some compounds have shown not only acute ecotoxicity but also their genotoxicity, development of pathogen resistance, and endocrine disruption[7)]. Despite worldwide concern on their environmental contamination globally, very little is known about the occurrence and fate of these pollutants in Indonesia. A study conducted by Dsikowitzky et al.[8)] analyzed very few pharmaceutical compounds and found caffeine to be present in almost all water samples collected from the rivers

flowing through Jakarta at concentrations of up to 8900 ng/L, comparable with the highest caffeine concentrations reported in US streams. Alongside caffeine, ibuprofen was also identified in most samples, at levels ranging between 30 and 1700 ng/L[9]. More recently, high concentrations of paracetamol as an antibiotic were detected in Jakarta Bay at Angke (610 ng/L) and Ancol (420 ng/L)[10]. Based on these preliminary findings, highlight further comprehensive study focuses on surface seawater contamination in Jakarta Great Area (JGA) particularly in Jakarta Bay and its watersheds, with emphasis on PPCPs contamination and their potential ecological health risk. This study would be a first scientific study to report the presence of wide range PPCPs contaminants in the marine environment and lower reaches of rivers around JGA of Indonesia.

Aims

The objectives of this study are to determine PPCPs in surface waters of JGA in order: (a) to understand the occurrence and distribution of PPCPs in Jakarta Bay and rivers that flow to Jakarta Bay, and (b) to estimate the potential health risk of selected PPCPs for aquatic ecosystems.

2. Materials and Methods

2.1. Study area and sampling

This study was conducted at Jakarta Great Area (JGA) including lower reach rivers and Jakarta Bay as shown in Figure 1. The field surveys were conducted at 17 stations (n=17) of Jakarta Bay and 16 stations (n=16) of lower reach rivers which end up to Jakarta Bay during September and December 2018 to collect surface water samples. Surface water were sampled using a stainless steel containers. The surface water then transferred to 100 ml of bottle sample, preserved with keep in cool box, and transferred to Center for Marine Environmental Studies (CMES), Ehime University, Japan for chemicals analysis.

Figure 1. Map showing sampling locations.

2.2. Chemical analysis

Surface water samples were analysed according to the method published elsewhere[11]. Briefly, extraction of the sample was carried out by filtering water samples (20 mL), added with internal standard (IS) and then inserted into the Oasis HLB Plus Light cartridge as a solid phase extraction for the clean-up procedure. The target PPCPs retained in the cartridge was

eluted with a solution of methanol/MTBE (3 mL, by volume ratio 7:3), and the eluate was concentrated to 0.2 mL under a stream of N_2. For identification and quantification of PPCPs, the residue was dissolved in acetonitrile/methanol/Milli-Q (1 mL, volume ratio 1:2:7).

Identification and quantification of target PPCPs was carried out using a Prominence Ultra-Fast Liquid Chromatograph equipped with a mass spectrometer. This equipment operates in positive and negative electrospray ionization (ESI) mode with dual reaction monitoring (MRM).

A total of 74 PPCPs were targeted for this study (Table 1). The identification of PPCPs in the sample was carried out by comparing their retention times with the original standard and for confirmation by comparing the peak area ratios for the two product ions. While the concentration was determined using the isotope dilution method. Furthermore, as part of quality control and quality assurance, a procedural blank sample was performed for each batch of sample analysis to check for potential contamination during sample preparation. The concentration of the sample will be subtracted from the blank sample in the same batch. The recovery rate of IS-corrected PPCP targets in the samples was determined by their triplicate analysis spiked with original standards at 4, 20, and 100 ng/L. In this study, an acceptable IS corrected recovery rate of 73%-110% and precision with a coefficient of variation (CV) of <15% were obtained for all 74 target compounds. The Minimum Detection Limit (MDL) ranges from 0.036-8.8 ng/L depending on the target compound. The concentration of each target PPCP is expressed as ng/L, otherwise it will be determined.

2.3. Potential health risk

Risk Quotients (RQs) as ratios of measured concentration to the predicted no-effect concentration (PNEC) values[12] was used to assess the potential risk of certain PPCPs to aquatic ecosystem. PNEC is the concentration of a chemical which marks the limit at which below no adverse effects of exposure in an ecosystem are measured. The measured concentrations were concentrations of PPCPs measured in each sampling locations, while the PNEC values were estimated from the chronic/sub-chronic ecotoxicity data previously reported for aquatic species at different trophic levels such as the lowest chronic/sub-chronic ecotoxicity data, no observed effect concentrations (NOECs), lowest observed effect concentration (LOEC), or 10%–25% effect concentrations ($EC_{10–25}$ values). A constant uncertainties factors (UFs) of 10 was applied for deriving PNECs of this study based on the guideline "Methods for the Risk Assessment of Priority Assessment Chemical Substances"[13]. Risk was characterized into several risk consideration i.e "high risk concern" ($RQ \geq 10$), "risk concern" ($10 > RQ \geq 1$), "no risk concern" ($RQ < 1$)[13].

3. Results and Discussion

3.1 Levels and Distribution

Among 74 target PPCPs, 20 of them were detected in at least one station of Jakarta Bay, 47 compounds in the rivers, and only 16 compounds were detected in all river stations (Table 1). Of the PPCPs analyzed, the personal care products, particularly N,N-diethyl-3-toluamide (DEET) was the most highest concentrations detected among other PPCPs at mean and range concentration of 3700(160-10000) ng/L at JGA Rivers and 51 (<8.0-170) ng/L

at Jakarta Bay, whereas other PPCPs were one or three order magnitude lower (Table 1).

Table 1. Occurrence, mean and range concentration of PPCPs (ng/L) in Jakarta Great Area during 2018.

No	Compounds	Conc. (ng/L) / Occurrence (%)		No	Compounds	Conc. (ng/L) / Occurrence (%)	
		Jakarta Bay	Rivers			Jakarta Bay	Rivers
A	**Pharmaceuticals**			38	Chlorpromazine	<1.5/(0)	<1.5/(0)
1	Diclofenac	<0.60/(0)	38(<0.60-94)/(94)	39	Aripiprazole	<0.56/(0)	<0.56/(0)
2	Indomethacin	<0.84/(0)	<0.84/(0)	40	Zotepine	<0.13/(0)	<0.13/(0)
3	Mefenamic acid	4.8(<0.44-13)/(82)	540(16-1500)/(100)	41	Carbamazepine	0.13(<0.068-0.37)/(65)	5.9(0.76-17)/(100)
4	Ibuprofen	6.9(<1.0-22)/(77)	400(12-1400)/(100)	42	Phenytoin	0.40(<0.18-1.1)/(77)	9.2(0.73-26)/(100)
5	Bezafibrate	<0.20/(0)	0.20(<0.20-1.6)/(13)	43	Clonazepam	<0.26/(0)	<0.26/(0)
6	Fenofibric acid	<0.34/(0)	4.8(<0.34-23)/(81)	44	Diazepam	<0.23/(0)	0.35(<0.23-1.1)/(44)
7	Clofibric acid	<0.28/(0)	<0.28/(0)	45	Zolpidem	<0.037/(0)	<0.037/(0)
8	Gemfibrozil	0.61(<0.036-1.5)/(88)	37(1.0-130)/(88)	46	Nitrazepam	<0.32/(0)	<0.32/(0)
9	Atorvastatin	<0.33/(0)	3.7(<0.33-21)/(81)	47	Oxazepam	<0.60/(0)	<0.60/(0)
10	Pravastatin	<0.1.5/(0)	<0.1.5/(0)	48	Flunitrazepam	<0.21/(0)	<0.21/(0)
11	Diltiazem	<0.76/(0)	0.48(<0.76-1.6)/(38)	49	Lorazepam	<2.0/(0)	<2.0/(0)
12	Amlodipine	<0.80/(0)	2.7(<0.80-7.3)/(56)	50	Alprazolam	<0.088/(0)	0.07(<0.09-0.49)/(19)
13	Propranolol	<0.23/(0)	0.33(<0.23-1.3)/(44)	51	Etizolam	<0.044/(0)	<0.044/(0)
14	Carvedilol	<0.40/(0)	<0.40/(0)	52	Sulfadiazine	0.45(<0.34-2.0)/(53)	6.6(0.64-17)/(100)
15	Losartan	0.016(<0.24-0.28)/(5.9)	5.9(<0.24-20)/(94)	53	Sulfathiazole	<1.4/(0)	1.3(<1.4-8.2)/(31)
16	Telmisartan	0.13(<0.14-0.51)(47)	10(<0.14-36)(88)	54	Sulfapyridine	<0.40/(0)	4.4(<0.40-25)/(75)
17	Irbesartan	0.18(<0.84-0.63)/(65)	29(<0.84-77)/(94)	55	Sulfamerazine	<0.24/(0)	0.26(<0.24-1.7)/(25)
18	Valsartan	0.81(<0.30-2.7)/(77)	71(1.2-180)/(100)	56	Sulfamethizole	<0.64/(0)	<0.64/(0)
19	Rebamipide	<0.12/(0)	10(0.24-41)/(100)	57	Sulfamethazine	<0.44/(0)	3.4(<0.44-10)/(68)
20	Diphenhydramine	<0.40/(0)	12(<0.40-66)/(81)	58	Sulfamonomethoxine	<0.48/(0)	<0.48/(0)
21	Chlorpheniramine	<1.1/(0)	5.6(<1.1-19)/(50)	59	Sulfamethoxazole	2.2(<0.44-6.1)/(88)	110(5.7-310)/(100)
22	Cetirizine	0.36(<0.24-1.1)/(53)	28(<0.24-81)/(94)	60	Sulfadimethoxine	<0.19/(0)	<0.19/(0)
23	Fexofenadine	0.025(0.15-0.43)/(5.9)	12(<0.15-56)/(94)	61	Trimethoprim	0.13(<0.60-0.85)/(18)	23(<0.60-58)/(93)
24	Warfarin	<0.16/(0)	0.07(<0.16-0.64)/(19)	62	Lincomycin	1.4(<0.21-4.0)/(82)	110(1.3-240)/(100)
25	Crotamiton	<4.4/(0)	<4.4/(0)	63	Erythromycin	<0.21/(0)	4.2(<0.21-16)/(50)
26	Tramadol	1.9(<0.048-4.8)/(88)	110(0.81-410)/(100)	64	Clarithromycin	<0.076/(0)	2.8(<0.076-14)/(75)
27	O-desmethyl tramadol	6.5(<0.092-31)/(82)	130(1.3-290)/(100)	65	Roxithromycin	<0.23/(0)	0.79(<0.23-3.8)/(44)
28	N-desmethyl tramadol	0.53(<0.10-1.3)/(77)	21(0.72-53)/(100)	66	Florfenicol	<0.30/(0)	<0.30/(0)
29	Sertraline	<0.96/(0)	<0.96/(0)	67	Chloramphenicol	<0.80/(0)	9.3(<0.80-37)/(69)
30	Norsertaline	<1.2/(0)	<1.2/(0)	**B**	**Personal Care Products**		
31	Fluoxetine	<0.64/(0)	<0.64/(0)	68	Triclosan	<1.40/(0)	180(3.4-760)/(100)
32	Norfluoxetine	<0.84/(0)	<0.84/(0)	69	Triclocarban	1.5(<0.56-3.9)/(77)	180(3.4-490)/(100)
33	Paroxetine	<1.2/(0)	<1.2/(0)	70	Methyl paraben	<8.8/(0)	120(<8.8-530)/(56)
34	Fluvoxamine	<1.3/(0)	<1.3/(0)	71	Ethyl paraben	<4.4/(0)	8.6(<4.4-49)/(44)
35	Haloperidol	<0.064/(0)	<0.064/(0)	72	Propyl paraben	<2.1/(0)	77(<2.1-250)/(81)
36	Risperidone	<0.56/(0)	<0.56/(0)	73	Butyl paraben	<1.1/(0)	3.4(<1.1-11)/(56)
37	Quetiapine	<0.12/(0)	<0.12/(0)	74	N,N-diethyl-3-toluamide	51(<8.0-170)/(77)	3700(160-10000)/(100)

Concentration of DEET measured during 2018 of the Jakarta Bay still lower to those study by Dsikowitzky *et al.* during October 2012 at concentration range of <10-1100 ng/L which was considered among the highest found so far in surface seawater worldwide [8] Concentrations of DEET in the Jakarta Bay however higher than those observed for Qinzhou Bay, China at concentrations of 8,3 (0,12-34) ng/L[14], North Sea at concentrations of 0.36 (nd-1.1 ng/L)[15] and Tromso, Norway at 4.6 (0.40-13) ng/L[16] as well as other Norwegian coastal waters at 23 (14-240) ng/L[17]. Our study confirmed previous study[8] that Jakarta Bay has DEET among the highest worldwide seawater. As for other similar detected PPCPs, Ibuprofen, Sulfamethoxazole, Triclocarban, Gemfibrozil, Carbamazepine and Trimethoprim were in the same order magnitude or even higher than those detected in Xiamen Bay, China during August 2019[18]. Triclocarban and

Carbamazepine were higher compared to those in Qinzhou Bay, China[14] and Ibuprofen was higher than in Tromso, Norway[16]. Overall, high concentration of DEET in Jakarta Bay indicate the extensive application of this compound in Jakarta great area. JGA Rivers as well as reported in previous study indicate that freshwater rivers which flow to Jakarta Bay showed high concentration of DEET indicate that the rivers input was an essential source of PPCPs[8]. In Indonesia, DEET is massively used as an active ingredient for insect repellents such as to protect against the dengue fever, which is transmitted by mosquitoes[8].

3.2 Spatial distributions

Spatial distribution of detectable PPCPs in JGA including Jakarta Bay are shown in Figure 2. There was variation in concentration of PPCPs among locations in which higher concentration of them were found in the surface water from rivers that cross to Jakarta City (R4-R11). Concentrations of PPCPs according to transect from west to east indicate that the eastern part of the bay has higher concentrations with the highest generally found in station S13 (Figure 2a).

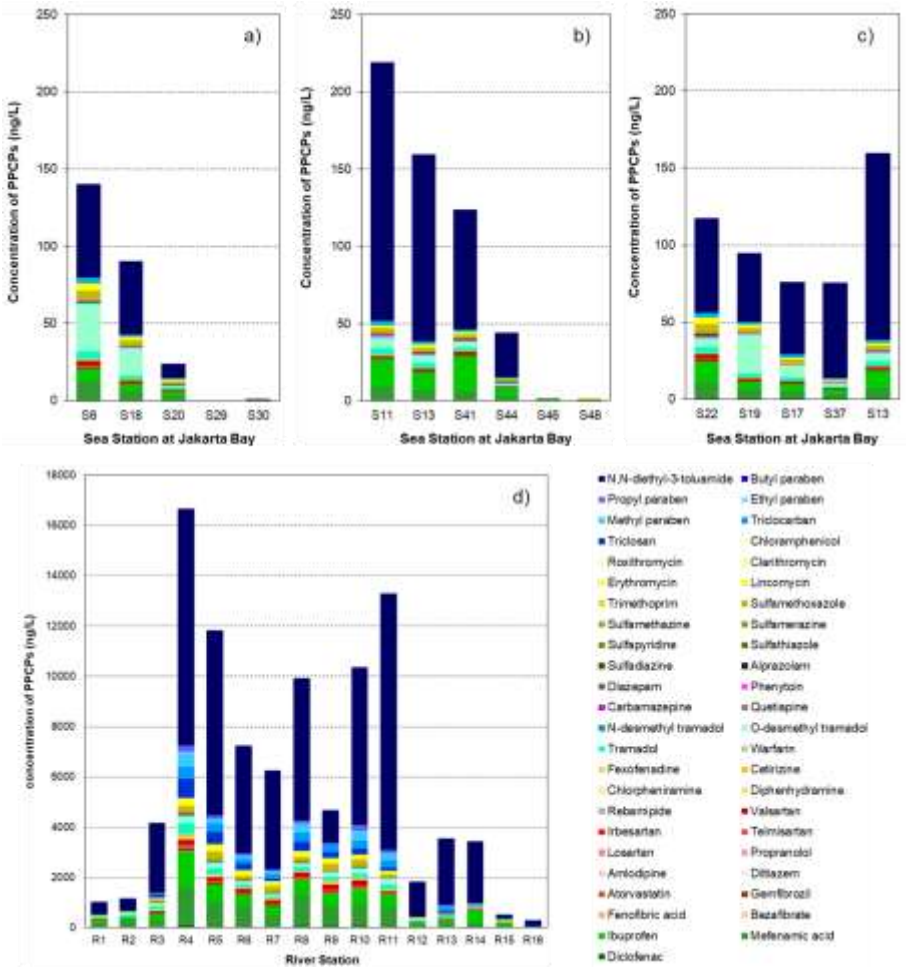

Figure 2. Spatial distribution of PPCPs in JGA during 2018, a) west to east, b) central of the bay from coastal to offshore, c) eastern part of the bay from coastal to offshore, and d) lower reach of rivers at JGA.

For example, DEET in station S13 was at 170 ng/L as compared to S22 (62 ng/L) in the western part. It has been indicated that the rivers input

was an essential source of PPCPs in Jakarta Bay (Figure 2d) as also suggested by[8]. Thus high rivers discharge in eastern part of the bay may contributed to this pattern. Moreover, spatial distribution from coastal to offshore also indicate higher concentrations of PPCPs in coastal where close to sources from rivers discharge (Figure 2b, 2c and 2d).

3.3 Assessment of health risk

Characterization of health risk to aquatic ecosystem has been estimated based on PNEC of certain PPCPs which available information of their individual-level end point health risk[19] to derive RQs (Figure 3). As indicate in Figure 3, RQ was estimated for N,N-diethyl-3-toluamide, Ibuprofen, Mefenamic acid, Triclocarban, Lincomycin, Phenytoin, Gemfibrozil, Carbamazepine and Trimethoprim. Considering the risk on standard individual-level endpoints (e.g., growth, reproduction, development, and survival) for aquatic organisms, there is a risk concern due to concentration of some PPCPs showed RQs>1 which may indicate affect likely to occur, in particular for Carbamazepine, Triclocarban, Mefenamic acid, and Ibuprofen at river sampling stations. The concentrations of Ibuprofen in four locations in Jakarta Bay also showed RQs ≥1. For example, in laboratory experiments, Ibuprofen has been reported to cause decreased survival of Japanese medaka (LOEC: 1,000 ng/L, NOEC: 100 ng/L) with chronic exposure of 120 days at 1,000 ng/L[20].

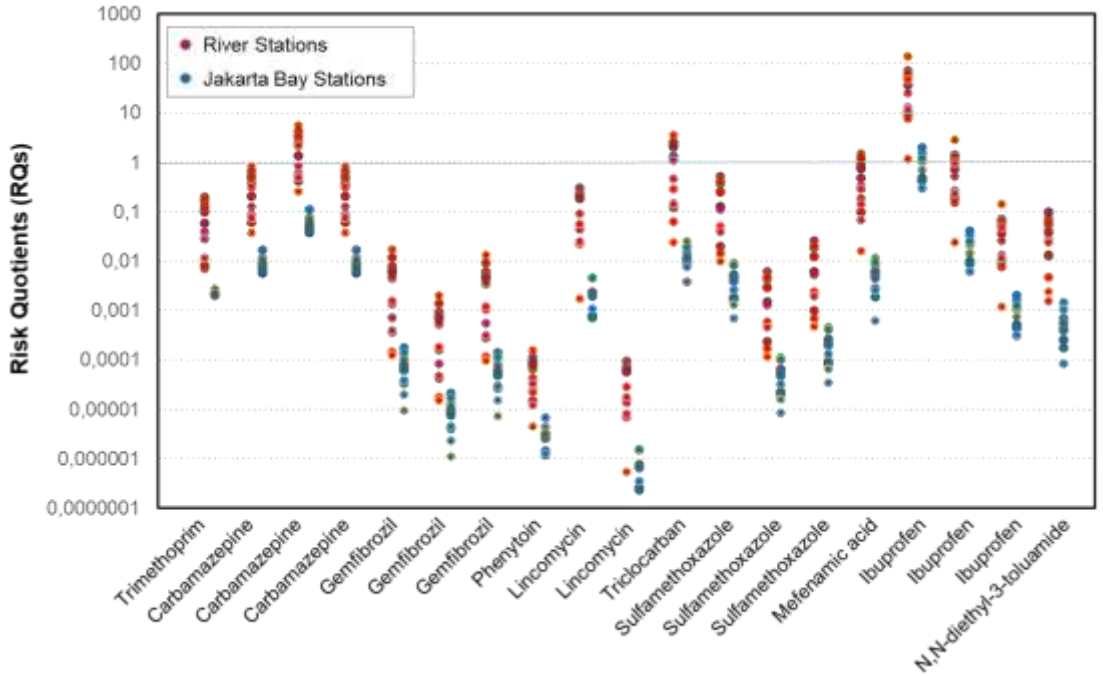

Figure 3. Risk Quotients (RQs) for certain PPCPs detected in surface water of Jakarta Great Area Rivers including Jakarta Bay during 2018.

4. Conclusion

74 PPCPs have been screened and show ubiquitously detected of 47 compounds in JGA and 20 compounds of them in Jakarta Bay. DEET was the highest compound at levels one to three order of magnitude higher compared to other detectable PPCPs. The highest levels of DEET is relevant with previously reported for this compound in Jakarta Bay and considered among highest worldwide. Spatial distribution with higher found in coastal areas

indicated that the rivers input was an essential source of PPCPs. There is risk concern due to contamination of some PPCPs in JGA Rivers and Jakarta Bay as their concentration showed RQs>1. Further study is needed to ascertain temporal variation of wide range PPCPs as well as understanding their further toxic effects.

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