Endocrine Disrupting Chemicals in the Pearl River: Is There A Potential Hazard to Local Human Health?

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Abstract. Endocrine-disrupting chemicals (EDCs) serve as agents that could damage the endocrine systems in human bodies. The EDCs can be introduced into an aquatic system via physicochemical reactions by nature and anthropogenic activities mainly including pharmaceuticals and industrial discharges. Generally, concentrations of EDCs in the Pearl River fall in higher ranges than those in other lakes and rivers in China and around the world. The potential hazards of the EDCs in the Pearl River have been thoroughly assessed in the last two decades but not comprehensively compared. This review aimed to discuss the detected concentration levels of EDCs in the surface water and sediment of the Pearl River respectively and conducted the risk assessment for residents along the Pearl River. Among EDCs, six important groups of chemicals (estrone, 17β-estradiol, nonylphenol, octylphenol, bisphenol A, and triclosan) were selected for analysis in this review due to their environmental ubiquity and toxicity in the Pearl River. The risk assessment indicated there was no potential negative impact of target EDCs on human health via water ingestion.

1. Introduction
Endocrine-disrupting chemicals (EDCs) are dispersed in water and sediment by natural reactions and anthropogenic activities, and thus may cause civilization diseases, especially in highly industrialized areas such as the Pearl River Delta (PRD). EDCs can be divided into natural compounds and anthropogenic products based on the origin (Hampl et al., 2016; Metzler & Pfeiffer, 2001). EDCs can also be classified into short-life and persistent compounds based on their duration in the environment (Hampl et al., 2016). Natural EDCs originate from humans, animals, and plants whereas anthropogenic EDCs can leach as pharmaceutical compounds from municipal wastewater, or industrial chemicals from industrial products (Richardson et al., 2005; Weigel et al., 2002). However, there are still limited systematic studies on the concentration levels and distribution of EDCs in river waters and sediments in the Pearl River, which is a representative area with a great number of factories and pharmaceutical industries in a developing country (i.e. China). The objectives of this present study were to offer a comprehensive analysis on concentration levels of EDCs in the surface water and sediment from the PRD, and ultimately conduct a risk assessment via comparison with previous studies all over the world.

2. Concentrations of primary EDCs in surface water
The present study summarized levels of primary EDCs detected from surface waters along the Pearl River (Table 1). Based on the worldwide research in recent two decades, Nonylphenol (NP), octylphenol (OP), bisphenol A (BPA), and triclosan (TCS) are the four most studied EDCs with...
relatively high concentrations ranging from not-detected to 332, 31, not-detected to 2470, 1 to 1030, and 0.6 to 1023 ng/L, respectively. Besides, estrone (E1) and 17β-estradiol (E2) with relatively low concentrations or rarely detected are also taken into consideration, and their levels in surface water samples ranged from not-detected to 75 and not-detected to 7.5 ng/L.

Generally, the levels of total EDCs presented unevenly in different sections of the Pearl River. This is characterized by the ascent from west to east (Diao et al., 2017; Xie et al., 2020; Xu et al., 2014). Riverine sections along the eastern areas which are close to highly populated cities such as Guangzhou and Dongguan showed high EDCs levels, thus might be related to approximately the same contents of downstream outlets (Xie et al., 2020; W. Xu et al., 2014). For instance, NP and OP both presented high concentrations in the Humen outlet; levels of BPA were found to be highest in the Jiaomen outlet.

The contents of NP, OP, BPA, TCS and E1 in the samples of Pearl River were slightly higher than those reported in the studies regarding other rivers in China, whereas the concentrations of E2 showed great resemblance in those rivers in China (Jiang et al., 2012; Li et al., 2013; Ma et al., 2018; Sun et al., 2016; B. Wang et al., 2013; L. Wang et al., 2012; L. Wang et al., 2011; Wu et al., 2013). Moreover, the contents of NP, BPA, TCS, and E1 in the samples of Pearl River were higher than those in previous studies on rivers around the world. Nevertheless, the concentrations of OP and E2 were comparable with those in previous worldwide studies (Esteban et al., 2016; Heemken et al., 2001; Isobe et al., 2001; Pojana et al., 2007; Rocha et al., 2013; Salgueiro-González et al., 2015; Stasinakis et al., 2012; Ying et al., 2008; Yoon et al., 2010; Zhang et al., 2007).

3. Concentrations of primary EDCs in sediment

The pollution situation of primary EDCs in sediments of the Pearl River was also summarized in this research (Table 2). The concentrations of OP and BPA ranged from not-detected to 463 and 0.6-428 ng/g dry weight, respectively. Although E1 and E2 were detected in some studies, the concentrations of them fluctuated around the limit of quantitation (Gong et al., 2011; Peng et al., 2006). TCS would not be taken into consideration in this study due to its uncertainty of whether TCS is present at levels sufficient to threaten the survival of dwelling organisms based on limited data (Miller et al., 2008; Wilson et al., 2008).

The general distribution of EDCs could be related to the sediment organic carbon, which plays a critical role in the sorption of EDCs (Ferguson et al., 2001; Jonkers et al., 2003; Rice et al., 2003). Specifically, Gong et al. (2011) suggested that there was a positive correlation between NP, OP, E2 and TOC, indicating that these EDCs might be largely related to organic-rich sediments via hydrophobic interaction, due to their higher hydrophobicity with logKow values of 4.48, 4.12, and 3.94, respectively (Ahel & Giger, 1993; Lai et al., 2000). Nevertheless, there was a moderate correlation between BPA, E1 and TOC, which could be associated with their smaller logKow values of 3.32 and 3.43, respectively (Lai et al., 2000; Staples et al., 1998). Many studies indicated that sediment EDCs were found to be at high levels in Humen outlet and Hongqimen outlet. This could be associated with high EDCs concentrations detected along the water courses across Foshan with large-scale farmlands and Guangzhou with sewage treatment plants adjacent to the riverine sections (R. Chen et al., 2014; L. Xu et al., 2007).

Compared to other rivers in China, the concentrations of NP and OP in the sediments of the Pearl River were gently higher whereas that of BPA was almost consistent (Bian et al., 2010; Li et al., 2013; B. Wang et al., 2013; L. Wang et al., 2012; L. Wang et al., 2011; Wu et al., 2013). Moreover, compared to the rivers around the world, such as Danube River (Germany), Elbe River (Germany), Osaka Bay (Japan), Bay of Biscay (Spain), etc., the ranges of NP, OP and BPA were approximately comparable (Grund et al., 2011; Heemken et al., 2001; Isobe et al., 2001; Koyama et al., 2013; Labadie & Hill, 2007; Puy-Azurmendi et al., 2010; Uguz et al., 2003).
Table 1. Concentrations of EDCs in surface waters of the Pearl River (ng/L).

| Location                        | Analysis methods | E1       | E2       | NP     | OP     | BPA    | TCS    | References                                      |
|---------------------------------|------------------|----------|----------|--------|--------|--------|--------|------------------------------------------------|
| China                           |                  |          |          |        |        |        |        |                                                 |
| Pearl River Delta               |                  |          |          |        |        |        |        |                                                 |
|                                | HPLC/MS          | 1.45     | 1.28     | 23.4   | 1.02   | 12.7   | 48.0   | (Xie et al., 2020)                              |
|                                | GC-MS            | 1.29     | 1.07     | 23.0   | 1.24   | 12.5   | 48.0   | (Xie et al., 2020)                              |
|                                | HPLC/MS          | 1.20     | 0.95     | 23.0   | 1.31   | 12.5   | 48.0   | (Xie et al., 2020)                              |
|                                | GC-MS            | 1.20     | 0.95     | 23.0   | 1.31   | 12.5   | 48.0   | (Xie et al., 2020)                              |
| China                           |                  |          |          |        |        |        |        |                                                 |
| Dalian River Estuary            |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Yangtze River                   |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Portugal                        |                  |          |          |        |        |        |        |                                                 |
| Sado River                      |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Portugal                        |                  |          |          |        |        |        |        |                                                 |
| Minho River                     |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Spain and Portugal              |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Greece                          |                  |          |          |        |        |        |        |                                                 |
| Aisonas River                   | HPLC/MS          | 4.56     | 3.61     | 115.5  | 4.56   | 115.5  | 4.56   | (Stasinakis et al., 2012)                       |
| South Korea                     |                  |          |          |        |        |        |        |                                                 |
| Van River                       |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Spain and Portugal              |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Austria                         |                  |          |          |        |        |        |        |                                                 |
| Four sewage treatment plants   |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Italy                           |                  |          |          |        |        |        |        |                                                 |
| Venice lagoon                   | HPLC/MS          | 4.56     | 3.61     | 115.5  | 4.56   | 115.5  | 4.56   | (Stasinakis et al., 2012)                       |
|                                |                  |          |          |        |        |        |        |                                                 |
| USA                             |                  |          |          |        |        |        |        |                                                 |
| Mississippi River              |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Germany                         |                  |          |          |        |        |        |        |                                                 |
| Elbe River                      |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
| Sumidagawa and Tamagawa Rivers |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |

a Concentration range: minimum to maximum (mean).
b NQ: Detected but too low to be quantified.
c ND: Not detected.

Table 2. Concentrations of EDCs in sediments of the Pearl River (ng/L dw).

| Location                        | Analysis methods | E1       | E2       | NP     | OP     | BPA    | TCS    | References                                      |
|---------------------------------|------------------|----------|----------|--------|--------|--------|--------|------------------------------------------------|
| China                           |                  |          |          |        |        |        |        |                                                 |
| Pearl River Delta               |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |
|                                |                  |          |          |        |        |        |        |                                                 |

a Concentration range: minimum to maximum (mean).
b NQ: Detected but too low to be quantified.
c ND: Not detected.
LC-MS/MS   31-21885(3686) 1-463(40.3)  (Jian Gong, Xu, Yang, Chen, & Ran, 2011)
GC-MS   ND(ND) ND(ND) 204.2-664.5(366.2) 1.0-12.0(3.4) (X. Peng, Wang, Yang, Chen, & Mai, 2006)
HPLC-MS/MS   ND(ND) ND(ND) 702.7(182.4) ND(ND) (<217.7(27.7) (Xianhui Peng et al., 2017)
Yangtze River GC-MS   ND(ND) ND(ND) 1.56-35.8(12.2) 0.72-13.2(3.28) (Bian et al., 2010)
Daihao River Estuary GC-MS   ND(ND) ND(ND) 16.6-203.8(27.8) ND-7.7(ND) (L. Wang et al., 2012)
Dianchi Lake GC-MS   ND(ND) ND(ND) 2-18(7) 1-106(18) 16-849(165) (Li et al., 2013)
Liao River GC-MS   ND(ND) ND(ND) 2-18(7) 1-106(18) 16-849(165) (Li et al., 2013)
Huangpu River GC-MS   ND(ND) ND(ND) 10.34-337.73(119.44) 0.54-27.41(9.49) 0.96-14.44(7.13) (Wu et al., 2013)
Germany Upper Danube River LC-MS/MS NQ-0.240(0.86) NQ(ND) 10.34-337.73(119.44) 0.54-27.41(9.49) 0.96-14.44(7.13) (Grund et al., 2011)
Japan Osaka Bay LC-MS/MS ND-0.9 NQ-1.57 ND-119 0.63-43(1.22) (Koyama et al., 2013)
Spain Urdaibai, Bay of Biscay GC-MS ND-0.9 NQ-1.57 ND-119 0.63-43(1.22) (Puy-Arzamendi et al., 2010)
UK River Ouse catchment LC-MS/MS NQ-0.4-3.3 NQ-1.2 1.2-22.6(8.3) (Labadie & Hill, 2007)
Germany Elbe River HPLC-GC-MSD 367-975(552) 21-86(41) 66-343(182) (Heemken et al., 2001)
Japan Sumidagawa and Tamagawa Rivers GC-MS 520-13000 (910) 50-670(193) (Isobe et al., 2001)
Turkey Deyizmenderes Rivers HPLC 3150-4460(880) (Uguz et al., 2003)

a Concentration range: minimum to maximum (mean).
b NQ: Detected but too low to be quantified.
c ND: Not detected.

4. Risk assessment
The estrogenicity of an EDC should be associated with that of E2 and is expressed as 17β-estradiol equivalency quotient (EEQ) (Dan et al., 2017; N Salgueiro-González et al., 2016; W. Xu et al., 2014). In this study, estrogenic activity in terms of EEQ values was calculated, employing the following equations:

$$EEQi = Ci \times EEFi$$ and $$EEQt = \sum EEQi$$

Where i refers to the pollutant i with concentration C, and EEFi is the corresponding estradiol equivalency factor. In the present study, literature EEF values of E1, E2, NP, OP, BPA, and TCS are set at 0.1, 1.0, 9.0×10⁻⁴, 1.0×10⁻⁵, 6.0×10⁻⁵, and 0, respectively (Giudice & Young, 2011; Sun et al., 2016; Xu et al., 2014).

Figure 1 shows the average EEQ values in the Pearl River were approximately consistent to those in the other lakes and rivers in China. In comparison with other Chinese lakes and rivers, the average EEQ values of other overseas lakes and rivers were evidently higher. Figure 2 indicates the total EEQ values in the sediment of the Pearl River and other regions. Noticeably, the average EEQ values in the Pearl River were generally higher than those in other Chinese riverine sediment. Nevertheless, the average EEQ values in other worldwide lakes and rivers were generally comparable to that in the Pearl River.

As shown in Figure 1, E1, E2, and NP could be major contributors to the estrogenic activity in the surface water of the Pearl River; Figure 2 indicates that NP was apparently the predominant contributor to the total EEQ values of the Pearl River.

In the present study, the ingestion of water by the population of the PRD would serve as the worst case. It was estimated that daily water intake of EDCs for adults was 1.4 L/d (USEPA, 2000). Accordingly, the exposure level through the ingestion of water from the Pearl River for adults was predicted to range from 1.6×10⁻³ to 13.9 ng/d. The reference value for acceptable daily intake (ADI) of E2 for humans was set at 0.05 μg/kg bw by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 1999). Thus, assuming an adult with the weight of 70 kg, ADI should be set at 3.5 μg/d. Basically, the highest levels of exposure via water ingestion from the Pearl River in the present study presented two or three orders of magnitude lower than this standard ADI value. Thus, this result could
suggest that there are still no potential adverse effects of detected EDCs on health of local residents via water intake.

5. Conclusion

EDCs in the PRD were found to be ubiquitous in municipal and industrial wastewaters, thus flowing into the Pearl River. The concentrations of selected EDCs (E1, E2, NP, OP, BPA, and TCS) in surface water of the Pearl River were found to be higher than or fall in the high ranges of those in the other
lakes and rivers of China and other countries. The relatively high levels were detected in Guangzhou and Dongguan due to large amounts of domestic and industrial discharge, thus could lead to approximately the same EDCs contents in the Humen and Jiaomen outlet. The contents of NP and OP in the sediment of the Pearl River were generally higher than those in other places whereas the levels of other EDCs were basically consistent in each study. Sedimental EDCs along metropolitan Guangzhou and agriculture-oriented Foshan showed relatively high concentrations, which might be responsible for the similar amount of EDCs in the Humen outlet and Hongqimen outlet. According to risk assessment, NP and E2 serve as the main contributor to the estrogenic activity in surface water of the Pearl River; and NP tended to primarily contribute to the sediment estrogenicity. Surprisingly, EEQ values in the Pearl River did not indicate a harmful effect on human health via water ingestion. Taking into account the fast-growing populations and rapidly developing industrialization, further monitoring needs to be conducted to control the amount of wastewater discharge containing EDCs into the Pearl River system.

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