DETECTION OF DRUG RESIDUES IN KERAYONG RIVER, KUALA LUMPUR

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ABSTRACT

The existence of drug residues in rivers have significant influence on the aquatic eco-system such as the proliferation of antibiotic resistant bacteria, hepatic gene expression and endocrine disruption in fishes subjected to long-term exposure. This study investigates the occurrence of drugs in urban surface water. 5 samplings stations along Kerayong River, Kuala Lumpur is examined. Samples collected underwent filtration and concentration processes and are then analysed using liquid chromatography coupled with quadrupole-time-of-flight tandem mass spectrometry for the purpose of compound tracing. Results showed that several drugs of different therapeutic usage can be detected in the river water.

Keywords: drug residues; Kerayong River; Malaysia; river water.

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1. INTRODUCTION

Development in medical services and technology causes the human to be increasingly dependent on prescribed drugs for health care and treatment. However, most people are oblivious about the related risk on the environment, the water resources and more specifically on the aquatic lives. Incomplete metabolism and excretion of drug residues from human body ends up in the municipal sewage system and wastewater treatment plant. Presently, most wastewater treatment plants (WWTPs) are not particularly designed to treat disposed drugs. Most pharmaceutical compounds have low removal rate in conventional treatment process. Treatment efficiencies of the assortment of polar compounds ranges between 50-99% [1]. A number of advanced oxidization process (AOP) such as ultra-violet and H$_2$O$_2$ are able to remove these compounds, but are not widely used due to cost factor [2]. In some cases, human pharmaceuticals have resistances for the removal process in the sewage treatment system. [3]. Drugs/pharmaceutical compounds can ultimately enter the environment via 3 major routes: 1) the disposal and/or the release of these compounds through wastewater influent, 2) the discharge into the environment through wastewater effluent and 3) the direct release of compounds to the environment.

Kerayong River is located in a highly urbanized area in the middle of Kuala Lumpur city in Malaysia. It is the main tributary of Klang River which runs from Pandan Indah to Pantai Baru with a catchment size of 61 km$^2$ [4-5]. The catchment area is 74% imperviousness with over half being residential land use [6]. In this paper, 5 sampling points located along Kerayong River, labelled from SP 1 to SP 5 in the downriver direction are strategically selected to identify potential existence of drug residues. Table 1 summarizes the details for each sampling point.
2. METHODOLOGY

2.1. Materials and Standards

The analytical standard of drugs residue used is > 90% high purity grade purchased from FLUKA, USA. All the solvents including methanol and acetonitrile with HPLC-grade are
purchased from JT Baker in the USA. Ultrapure water (UPW) was produced using Milli-Q unit at Millipore city in the USA. The stock solutions of individual compounds have been dissolved in methanol at final concentration of 50 mg/mL. The mixture standard solution was prepared by diluting the stock solutions before each analysis. All the solutions are stored at 4 ℃ in the dark. Calibration curve is produced prior to the sampling.

2.2. Sampling and Sample Preparation for Drugs Analysis

The sample for each location was taken forthnightly. The samples were collected using 300 mL amber glass bottles pre-rinsed with ultra-pure water (UPW). Upon arrival at the laboratory, the samples were immediately filtered through 0.45 µm GF/C filters. They are stored in the refrigerator at temperature below 4 ℃. The samples must be extracted within 14 days of collection. The solid phase-extraction (SPE) was conducted on all samples using Hydrophile-Lipophile Balance (HLB) cartridges by Oasis HLB (200 mg bed size and 6 mL volume) was extracted for analyzing. Next, 5 mL of acetonitrile was poured into the cartridge and followed by 5 mL of Ultra pure water during the conditioning process. After the conditioning process is completed, the samples were loaded into the HLB cartridge at a flow rate of 10 ml/min, noting that higher flow rate may cause reduced recovery. After the loading process, the cartridges were dried for 15 minutes and then flush with 5 mL of acetonitrile for elution process. Finally, the samples were concentrated using nitrogen evaporator until the desired volume is archived with re-constituted of 2 mL sample. For analysis procedure, 20 µL of the samples were injected into the LC-Q-ToF/MS.

2.3. Compounds Analysis

The Agilent of 6200 HPLC system (Santa Clara, CA, USA) coupled with Agilent of 6500 series quadrupole-time-of-flight tandem mass spectrometry (LC-Q-ToF/MS) equipped with the Z-spray electrospray interface were used to perform LC analysis. The chromatographic separation was achieved with C18 column (Eurospher 5 µm; 250 x 4 mm with precolumn; Knauer, Germany). The flow rate was set to 0.1 mL/min, and the injection volume was 20 µL. The column oven temperature was set at 27 ℃. The ratio of the solution in mobile phase is estimated at 70:30 (v/v %) of acetonitrile and UPW. The runtime for each sample analysis was set to 10 min. The MS/MS data were acquired in ESI+ mode (300 ℃ capillary temperature; 4.50 KV source voltage, 8 L/min nitrogen gas flow, 35 psi nebulizer pressure, 29 V capillary voltage
and 9 to 40 Ev collision energy ranged). Multiple reactions monitoring (MRM) mode was set to the range of m/z ion between 100 to 1000. This allow several categories of compounds to be detected in the water sample.

3. RESULTS AND DISCUSSION

The compounds analysis was achieved using QTOF-LCMS. A number of drug classifications are as shown in Fig. 2. The MS spectrum peak of the detected compounds from the samples of Kerayong River are shown in Fig. 3.

![Diagram of drug types and categories]

**Fig.2.** The list of drugs detected in river water classification based on their therapeutic usage

<table>
<thead>
<tr>
<th>Sampling Location 1</th>
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<td><img src="image_a" alt="Graph (a)" /></td>
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(a)  
(b)
Fig. 3. The MS Spectrum Peak for each compound detected including (a) Metoprolol, (b) Ranitidine, (c) Ketamine, (d) Tramadol, (e) Alprenolol, (f) Sulpiride, (g) Tramadol, (h) Metoprolol, (i) Ketamine, (j) Telmisartan and (k) Ketamin

3.1. Metoprolol

Metoprolol was detected at the sampling location 1 and 2. It is used to treat Angina (chest pain) and hypertension (high blood pressure). It is also used to treat or prevent heart attack. The highest expenditure incurred in the public and private sectors was RM 22.4 million [7]. The occurrence of metoprolol on water surface maybe due to the low removal efficiency in waste-water treatment plant. In [8] reported that 23% metoprolol has been only removed in the conventional waste-water treatment plant. However, in [9] discovered 38% of the removal
efficiency for metoprolol meanwhile in the waste-water treatment plant, the most dominant compounds were 83.3% atenolol and 83% metoprolol.

3.2. Ranitidine
In this study, the ranitidine has been detected at the first sampling location (up-stream). It is commonly used in the treatment of ulcer, gastro-intestinal and gastro-esophageal refluxes. According to Malaysia Statistics on Medicine 2006, the ranitidine is among the top 40 drugs utilized in Malaysia at 1.71 (defined daily dosage/1000 population/day) [7]. The occurrence of ranitidine in water surface and waste-waters have been previously reported [10]. Ranitidine was discovered in the effluents of sewage treatment plants in Greece at the median level of 1059 ng L$^{-1}$ and in river water of Spain at the median concentration of 396.5 ng L$^{-1}$ [11]. Furthermore, in [12] showed that 39% and 84% of ranitidine had been removed at the winter and summer in sewage treatment plants, respectively.

3.3. Ketamine
Ketamine was detected for twice times along Kerayong River, which was at the sampling location 1 and 4. Ketamine is a type of drug starting and maintaining general anesthesia. It is not completely metabolized in humans and other organisms [13]. Ketamine was consistently detected in waste-water effluents in United State of America [14] and China [15]. Recently, most studies associated the urinary tract dysfunction with the prolonged exposure using ketamine. In [16] achieved one of these studies, Ketamine was detected in drinking water with 49% of frequency in Canada.

3.4. Tramadol
From the data analyzed, the results illustrated that the tramadol was detected at the sampling location 1 and 2. Tramadol commonly was used to relieve moderating to severe pain. In [17] showed that the tramadol has low removal efficiency during activated sludge treatment with 36%. The average removal from waste-water treatment in the central and east of Europe achieved by Yi Chen [18]. They only indicated to 70% for removal of tramadol. This drug also gives the highest level of the concentrate ion detected in five rivers in Sweden with range 157 to 3015 pg/L [19].
3.5. Alprenolol

Alprenolol as detected at the sampling location 2 located at Cheras Town with a high population of residential. Beta-blocker is one of the alprenolol under the group of chiral pharmaceuticals which was used in the treatment of hypertension, cardiac diseases and glaucoma. They are prescribed world-wide as common drugs residue in river water. Normally, they monitored their occurrences and fate in the environment [20].

3.6. Sulpiride

As reported by [21] for River Thames basin, the sulpiride was detected at 99% frequency and average of concentration at 58 ng/L. In [22] completed the study for sulpiride, carbamazepine and metoprolol. They showed the relatively high concentrations (84–117 ng/L⁻¹) detected in waste-water treatment plant in Beijing, China. The removal efficiency of sulpiride during the conventional treatment in WWTPs was low ranging from 0 to 30%. Similar to finding by [23] also found that the removal efficiency of sulpiride was from 7% to 25%.

3.7. Telmisartan

Statistic from National Malaysian Use Survey on Medicine 2006 reported that the telmisartan was among highest usage of antihypertensive medicine with 0.41 defined daily dosage/1000 population/day [7]. Telmisartan was detected in the sewage system, as reported by [24] with the range of concentration from 1.3 to 2.3 ug/L. Also, the detected in effluent for waste-water treatment plant in Uppsala, Sweden was with concentration of 170 ug/kg.

4. CONCLUSION

7 types of the drugs have been detected along Kerayong River including Metoprolol, Ketamine, Ranitidine, Sulpiride, Telmisartan, Alprenolol and Tramadol. The drugs are potentially contributed from various sources. Further analysis is required to evaluate the quality of the river water to determine the hazards posed.

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