Science of the Total Environment 710 (2020) 136347

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Pharmaceutical pollution of water resources in Nakivubo wetlands and Lake Victoria, Kampala, Uganda

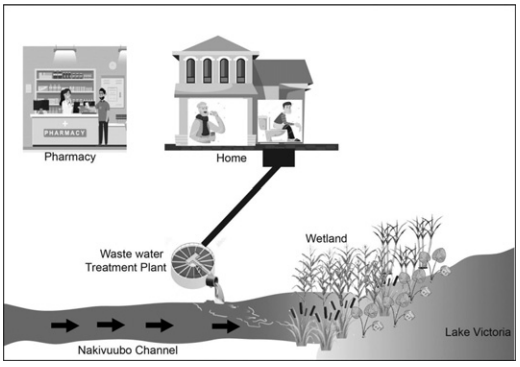
Sahar Dalahmeh [a,*], Emma Björnberg [a], Anna-Klara Elenström [a], Charles B. Niwagaba [b], Allan John Komakech [c]

[a] Department of Energy and Technology, Swedish University of Agricultural Sciences (SLU), Box 7032, SE 750 07 Uppsala, Sweden
[b] Department of Civil and Environmental Engineering, Makerere University, Box 7062, Kampala, Uganda
[c] Department of Agricultural and Biosystems Engineering, Makerere University, Box 7062, Kampala, Uganda

HIGHLIGHTS

- Pharmaceuticals assessed in wastewater and surface water in Nakivubo wetland area, Kampala Uganda.
- Wastewater treatment was ineffective in removal of pharmaceuticals.
- Trimethoprim and sulfamethoxazole (antibiotics) were predominant wetland detections.
- No pharmaceuticals were detected in the drinking water reservoir, Lake Victoria.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 13 November 2019
Received in revised form 23 December 2019
Accepted 24 December 2019
Available online 28 December 2019

Editor: Damia Barcelo

Keywords:
Kampala
Lake Victoria
Nakivubo wetland area
Pharmaceutical pollution
Sulfamethoxazole
Trimethoprim
Wastewater

ABSTRACT

This study investigated the occurrence and removal in wastewater and water bodies in Nakivubo wetland area and Inner Murchison Bay, Lake Victoria, of common prescription and non-prescription pharmaceutically-active substances (PhACs) sold in Kampala city, Uganda. A questionnaire was sent to 20 pharmacies in Kampala, to identify the most commonly sold PhACs in the city. During two sampling campaigns, samples were collected from Bugolobi wastewater treatment plant (WWTP) influent and effluent and surface water samples from Nakivubo channel, Nakivubo wetland and Inner Murchison Bay. The concentrations of 28 PhACs, organic matter, solids and nutrients in water samples were analysed. Ciprofloxacin (antibiotic), cetirizine (anti-allergy), metformin (anti-diabetes), metronidazole (antibiotic) and omeprazole (gastric therapy) were reported by pharmacies to be the PhACs most commonly sold in the study area. Chemical analysis of water samples revealed that trimethoprim (antibiotic) and sulfamethoxazole (antibiotic) were the dominant PhACs in water from all sites except Lake Victoria. Other PhACs such as atenolol (anti-hypertensive), carbamazepine (anti-epileptic) and diclofenac (anti-inflammatory) were also found at all study sites except Lake Victoria. $\sum$PhACs in effluent from Bugolobi WWTP (13000–37,600 ng L^{-1}) was higher than in the corresponding influent (4000–28,000 ng L^{-1}), indicating poor removal of PhACs within the WWTP. $\sum$PhACs decreased by a factor of 2–6 between Bugolobi WWTP effluent and Nakivubo channel (5700 ng L^{-1}), due to dilution and sorption to channel sediment, and by a factor of 1–3 between the Nakivubo channel and Nakivubo wetland (3900–5400 ng L^{-1}), due to sorption to sediment and uptake by plants in the wetland. No detectable levels of PhACs were found in water from Lake Victoria. Overall, this investigation demonstrated that PhACs in wastewater enter Nakivubo water system. Thus, Bugolobi WWTP

* Corresponding author.
E-mail address: sahar.dalahmeh@slu.se (S. Dalahmeh).

https://doi.org/10.1016/j.scitotenv.2019.136347

needs to be upgraded to improve PhACs removal from wastewater. Considering the high occurrence of antibiotics in the water system in Kampala, development and spread of antimicrobial resistance within the area should also be investigated.

1. Introduction

Urban wastewater treatment plants are one of the most important point sources of pharmaceutically active compounds (PhACs) found in surface water receiving bodies and other environments (Carmona et al., 2014). Lack of proper wastewater treatment due to limited financial and technical resources results in high prevalence and outbreaks of water-borne diseases in many low-income countries, including Uganda (Fuhrimann et al., 2015). Despite contamination with e.g. pathogens and PhACs, wastewater is widely re-used for irrigation, organics and nutrients in Uganda, Ghana and many other developing countries (Agyenim and Gupta, 2012; Rehman et al., 2013). In addition, it is often discharged into rivers, channels and lakes used as sources of drinking water.

After ingestion, unchanged forms of PhACs, metabolites or conjugates of PhACs are excreted in urine and faeces, and often end up in municipal sewage systems (Lindberg et al., 2014). The levels of pathogens and organic micropollutants, especially PhACs, present in poorly treated wastewater fractions (Fuhrimann et al., 2016) represent an important contamination pathway for the environment (Fernandes et al., 2019). A high burden of diseases, including water-borne diseases and malaria, coupled with high population density in many low-income countries, results in high excretion and disposal of some specific PhACs in wastewater (Kasule et al., 2018; Rehman et al., 2013). For example, HIV/AIDS and malaria are the second and third leading causes of death in Uganda (IHME, 2019) and high consumption of antimicrobial PhACs is likely. In Uganda, Kenya and other African countries, sulfamethoxazole combined with trimethoprim is used to treat a number of bacterial infections. The World Health Organization recommends daily doses of these drugs for children of HIV-infected mothers (Kasule et al., 2018). All of these practices increase the burden of PhAC pollution in wastewater and receiving aquatic environments in many low-income countries.

Constructed wetlands can be used for removal of different wastewater pollutants, including micropollutants (Chen et al., 2016; Dalahmeh et al., 2018; Emerton, 1998). Soil microbial activity, soil adsorption, plant uptake, stable neutral pH and temperature provide favourable conditions for removal of pollutants in wetlands. Efficient removal of a number of PhACs, e.g. acetaminophen, gemfibrozil and naproxen, in wetlands has been reported (Conkle et al., 2008). Chen et al. (2016) found that degradation and absorption in the soil were the two major pathways for pharmaceutical removal in wetlands. In soil treatment systems, Liu et al. (2019) recorded removal rates of 80% and 95% for trimethoprim and sulfamethoxazole, respectively.

Kampala, the capital city of Uganda, encompasses two important ecosystems with great socioeconomic value: Nakivubo wetland and Lake Victoria. Nakivubo wetland covers 40 km^2 of Kampala's total area, but is under pressure due to urbanisation, industrial development and the establishment of slums (Kayima et al., 2008; Mbabazi et al., 2010). In addition, Nakivubo channel receives domestic and industrial wastewater from Kampala (Fuhrimann et al., 2015), which is used in the wetland for cultivation of yam (*Dioscorea* spp.) and various vegetables (Emerton, 2005; Kayima et al., 2008; Mbabazi et al., 2010). The remaining Nakivubo water flows down into Lake Victoria, which is another important ecosystem of great significance for riparian status in the area, as it is the major source of drinking water and water for agricultural and industrial purposes (Juma et al., 2014; Orata et al., 2009).

There has been intensive research on the occurrence, removal, fate and effects of PhACs in wastewater and other water resources in industrialised countries such as the US, Europe, Canada, Japan and Australia (Birch et al., 2015; Fram & Belitz, 2011; Kleywegt et al., 2011; Loos et al., 2010; Okuda et al., 2009). However, few studies have examined the occurrence and fate of PhACs in environmental samples in Africa (Madikizela et al., 2017). Information regarding PhAC pollution of water resources in developing countries such as Uganda is still scarce, partly due to the high cost of analysis and lack of laboratory infrastructure and analytical methods. The aim of this study was thus to investigate PhAC contamination in wastewater and water resources in Nakivubo wetland and Inner Murchison Bay in Lake Victoria, Kampala, Uganda. Specific objectives were to (i) identify the most common non-prescription and prescription medicines sold in Kampala and (ii) evaluate the occurrence and concentrations of these pharmaceuticals and other substances (28 PhACs) in wastewater and water resources in Nakivubo wetland area and in the water of Inner Murchison Bay.

2. Materials and methods

2.1. Description of the study area

The study area was divided into four sampling systems along the main wastewater channel of Kampala: (i) Bugolobi wastewater treatment plant (WWTP) (influent and effluent), (ii) Nakivubo channel, (iii) Nakivubo wetland and (iv) Inner Murchison Bay in Lake Victoria (Fig. 1). Nakivubo channel is a 12.3 km long drainage channel and receives discharges from stormwater, illegally discharged wastewater from communities, markets and industries and secondary-treated effluent from Bugolobi WWTP before entering Nakivubo wetland. Nakivubo wetland is located to the south-east of Kampala (00°18′N, 32°38′E), at altitude 1135 m above sea level, covers ~6.0 km^2 and has a total catchment area of over 40 km^2 (Emerton, 1998). The wetland is divided by an old railway line and consists mainly of drained farmland in the north and submerged (floating) wetland in the south. Both areas are cultivated with yams and sugarcane. The wetland acts as a buffer zone before water reaches Lake Victoria (Kansiime and Nalubega, 1999).

2.1.1. Sample collection

Wastewater, surface water and lake water samples were collected from the study area during two sampling events, on 29 April and 5 May (Fig. 1). Grab samples of wastewater were collected in duplicate from the influent and effluent of Bugolobi WWTP during both sampling events (in total $n = 8$). According to its operator, Bugolobi WWTP is extremely overloaded and the hydraulic retention time of the wastewater is <3 h. Therefore the effluent samples were collected 2–3 h later than the influent samples, to account for this hydraulic retention time Surface water grab samples (50 cm below the water surface) were collected manually (using a rope and bucket) in duplicate in Nakivubo channel and Nakivubo wetland. In addition, duplicate samples were collected at two points from the coastal water of Lake Victoria at Ggaba (in total $n = 2$) (Fig. 1; Table S1 in Supplementary information (SI)). All samples were stored in plastic bottles, which were prewashed thoroughly with distilled water and ethanol prior to use. All samples were kept frozen at −20 °C and transported to Sweden for analysis of PhACs.

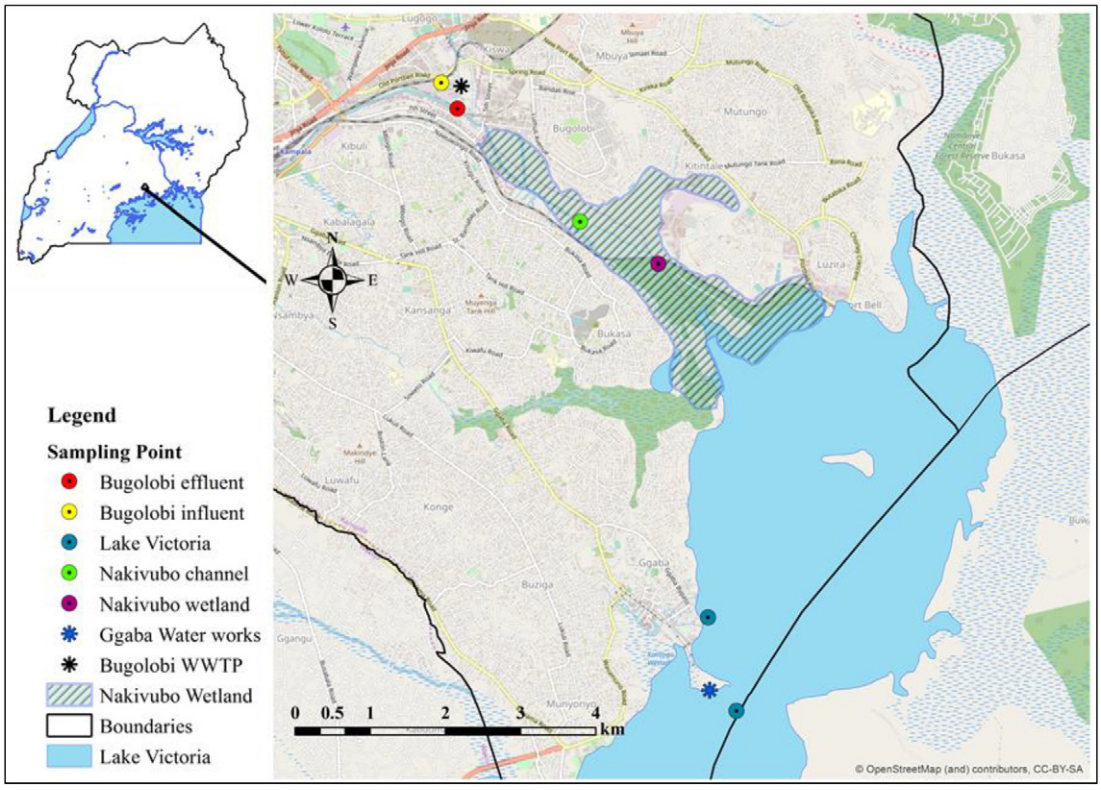


Fig. 1. (Top left) location of the study area in Kampala, Uganda, and (right) sites used for sampling influent/effluent to Bugolobi wastewater treatment plant ($n = 4$) and surface water in Nakivubo channel ($n = 4$), Nakivubo wetland and Lake Victoria ($n = 4$).

2.2. Analyses of PhACs in wastewater, surface water and lake water

2.2.1. Survey of the types of PhACs prescribed and sold in Kampala

A survey of 20 anonymous pharmacies in Kampala was conducted to identify the PhACs mostly prescribed, sold and ingested within Kampala and the disposal methods employed for old/unused medicines. The aim was to identify target PhACs for environmental samples (wastewater, surface water, lake water). Some of the questions asked were (for full questionnaire, see SI):

1. What are the most common non-prescription and prescription medicines sold at your pharmacy?
2. What quantities of these medicines are sold per year or issued per day?
3. What are the most common medicine doses prescribed/ingested per day?
4. Is any information provided to the customer on how to dispose of any unused medication?
5. How does your pharmacy handle any expired pharmaceutical stocks?
6. Where are expired/unused pharmaceutical stocks disposed of?
7. Are any instructions/restrictions provided by the relevant authority on how to handle unused or expired medication?
8. How is medication returned to the pharmacy handled/disposed of?
9. Do pharmacy staff know how pharmaceutical residues affect the environment?

2.2.2. Target analytes

In total, 28 PhACs, including common-use substances identified in the survey and other compounds representing a wide range of different therapeutic groups, were selected as target analytes (Table 1). Chemical characteristics of the substances are summarised in Tables S2 and S3 in SI.

2.2.3. Extraction of PhACs from liquid samples

Prior to extraction of PhACs, the water samples were filtered through a 0.7 μm glass-fibre filter (Whatman™, 0.7 μm). Then 500 mL of liquid sample were spiked with 50 μL of an isotope-labelled internal standard mixture containing 0.5 ng mL^{-1} of the relevant substance (Table S1). The samples were extracted using Oasis HLB cartridges (200 mg, 6 cm^3; Waters Corporation, Manchester, UK) with a solid phase extraction (SPE) vacuum manifold (Supelco, Stockholm, Sweden). Before sample loading, the cartridges were conditioned with 6 mL of methanol followed by 6 mL of MilliQ® water. After sample loading at 1 drop per second, the SPE cartridges were washed with 6 mL MilliQ® water and centrifuged for 5 min at 3500 rpm to remove excess water. The target PhACs were eluted with 2×4 mL of pure methanol at 1 drop per second without applying vacuum and the eluate was collected in 14-mL glass tubes. The eluate was evaporated under a gentle nitrogen (N_2) stream to 200 μL, transferred to a 1-mL amber glass HPLC vial and evaporated with nitrogen gas until complete dryness. Extracts were reconstituted to 0.5 mL of methanol/water (10:90, v/v). Method blank ($n = 6$) and matrix recovery samples consisting of 100 mL of the wastewater influent ($n = 3$), effluent ($n = 3$) and wetland water ($n = 3$) spiked with 200 μL PhACs standard mixture ($c = 1$ ng μL^{-1}) were extracted in the same manner as the natural samples.

2.2.4. Instrumental determination and quantification of PhACs

Analysis was carried out with an Acquity ultra-performance liquid chromatography (UPLC) system, coupled to a quadrupole-time-of-flight (QTOF) mass spectrometer (Xevo G2S QTOF, Waters Corporation, Manchester, UK). Chromatographic separation was achieved at a flow rate of 0.5 mL min^{-1} using an Acquity HSS T3 column (100 mm × 2.1 mm i.d., 1.8 μm particle size; Waters, Manchester, UK). For the mobile phases, a 5 mM ammonium formate buffer with 0.01% formic acid (A) and acetonitrile (ACN) with 0.01% formic acid (B) were used. The chromatographic gradient applied started with 95% A and these

Table 1
Therapeutic group, usage and type of pharmaceuticals (PhACs) included in the analyses.

Therapeutic group	Use	Substance
Analgesic	Also called painkillers. A type of medicine that serves to reduce pain without affecting consciousness or blocking nerve impulses	Codeine
Antibiotic	Chemical substances produced by microorganisms that can be used to treat bacterial infections	Ciprofloxacin Trimethoprim Sulfamethoxazole Sparfloxacine Metronidazole
Anti-depressant	Mood-enhancing drugs that can be used by people who are depressed or suffer from other mental disorders	Citalopram Venlafaxine Oxazepam
Anti-epileptic	Prevents or treats epileptic seizures	Carbamazepine Diazepam Lamatrogine
Anti-hypertensive	Treats high blood pressure	Irbesartan Losartan
Anti-inflammatory agent	A type of analgesic that reduces inflammation at its source	Diclofenac
Anti-malarial	Used to treat malaria	Pyrimethamine
Anti-histamine	Used to sooth allergies	Cetirizine
Ant-iulcer agent	Treats ulcers in the stomach	Ranitidine
Beta-blocker	Reduces heart rate, myocardial contractility and blood pressure	Atenolol Metoprolol Sotalol
Diuretic	Increases production of urine in order to expel excess liquid from the body. These drugs can be used to treat cirrhosis or oedema caused by heart failure	Furosemide Hydrochlorothiazide
Lipid regulator	Primarily used to treat high cholesterol	Atorvastatin Bezafibrate Gemfibrozil
Bronchodilatory drugs	Asthma medicine	Sulbutamol
Local anaesthetic	Produces a local loss of sensation and pain. Can be used when extracting teeth, for example	Lidocaine

conditions were kept constant for 0.5 min. From 0.5 to 5 min, the organic solvent increased to 95% B and then again to 99% B over 0.2 min. The latter conditions were kept constant for 1 min, and at 7 min initial conditions were reached again (95%) and kept constant until 13 min. The injection volume was 5 μL and the column temperature was set to 40 °C and the sample manager temperature to 15 °C. The resolution of the time-of-flight (TOF) mass spectrometer was around 30,000 for a mass/charge ratio (m/z) 556 at full width half maximum (FWHM). Data were acquired over a m/z range of 100–1200 with a scan time of 0.25 s. A capillary and cone voltage of 0.35 kV and 30 V, respectively, was applied. The desolvation gas flow rate was 700 L h^{-1} and the cone gas flow was 25 L h^{-1}. The desolvation temperature was set to 450 °C and the source temperature to 120 °C. Samples were acquired with MSE mode using a low energy function with collision energy of 4 eV and a high energy function with a collision energy ramp ranging from 10 to 45 eV. The mass axis from 100 to 1200 m/z was calibrated daily with a 0.5 mM sodium formate solution prepared in 90:10 (v/v) 2-propanol/water. For automated accurate mass measurements, the lock-spray probe was employed, using as lock mass leucine encephalin solution (2 μg mL^{-1}) in ACN/water (50/50) with 0.1% formic acid, pumped at 10 μL min^{-1} through the lock-spray needle. The leucine encephalin [M + H] + ion (m/z 556.2766) and its fragment ion (m/z 278.1135) for positive ionisation mode were used for recalibrating the mass axis and to ensure robust accurate mass measurement over time. Positive identification of target PhACs in the samples was based on: (a) accurate mass measurements of the precursor ion ([M + H] + for all compounds) in the low energy function, with an error below 5 ppm, (b) the presence of at least one characteristic m/z ion in the high energy function and the exact mass of these fragment ions, with a 5 ppm tolerance, and (c) the UPLC retention time of the compound compared with that of a standard (±2%; Table S2). Further details about the analytical method can be found in Gros et al. (2013).

2.2.5. Quality control

No PhACs were detected in any of the blank samples (method blanks $n = 6$, instrumental blanks $n = 4$). Limit of detection (LOD) and limit of quantification (LOQ) were determined at the minimum detectable amount of analyte with a signal-to noise ratio of 3 and 10, respectively. The LOD of the different substances ranged from 2.0 to 169 ng L^{-1} in wastewater influent, wastewater effluent, wetland water, channel water and lake water (Table S4 in SI). The LOQ ranged from around 6 to 506 ng L^{-1}. Recovery of target PhACs in liquid samples and MilliQ® water was investigated by spiking the samples with a known concentration of the target PhACs (300 ng L^{-1}). Recovery was determined by comparing the concentrations obtained after the whole SPE procedure with the initial spiking levels. Since wastewater samples contained the target PhACs, the original samples (non-spiked wastewater) were also analysed and the detected levels were subtracted from those obtained for spiked samples. Recovery rate of the target PhACs in influent and effluent wastewater and MilliQ® water ranged from 65 to 113% for all substances except carbamazepine (120%), metoprolol (150%) and sparfloxacine (135%). Calibration standards were analysed at the beginning and end of each sequence, and one calibration standard was analysed repeatedly throughout the sequence to check for signal stability.

2.2.6. Analysis of physical and chemical water pollutants

The concentrations of 5-day biochemical oxygen demand (BOD_5), chemical oxygen demand (COD), total organic carbon (TOC), pH, total solids (TS), total suspended solids (TSS), phosphorus as phosphate (PO_4-P), total phosphorus (TP), nitrogen as nitrate (NO_3-N) and total nitrogen (TN) were measured in the liquid samples. The BOD_5 was determined according to APHA 5210-BOD_5 and TS content according to APHA 2540-Solids. Chemical analysis was performed using Spectroquant® cell kits number 09772-09773 (COD), 14879.0001 (TOC) and 14848 (PO_4-P), 00683 (NH_4), 09713 (NO_3) and 14963 (Tot-N) (Merck KGaA, Darmstadt, Germany). Concentrations were determined colorimetrically using a Nova 60 photometer (Merck KGaA). The pH was measured using WTW pH/ion 340i meter (WTW, Weilheim Germany).

2.2.7. Calculations and statistical analysis

Two-way analysis of variance (ANOVA) at 95% confidence level was used to assess the difference in PhACs concentrations between sampling: (i) locations and (ii) events. All statistical analyses were performed using STATISTICA version 10 (Statsoft Inc., Tulsa, OK, USA). When a statistically significant difference was found, Tukey multiple comparison of means (95% confidence level) was performed.

3. Results and discussion

3.1. Types of PhAcs prescribed and sold in Kampala

Seventeen out of the 20 pharmacies approached responded to the questionnaire (response rate = 85%). The responding pharmacies sell a total of 57 PhACs (prescription and non-prescription) to the public in Kampala (Table 2, Fig. S1 in SI), 12 of which are antibiotics. A total of 31 PhACs were described by the pharmacies as commonly sold, with reporting rate 24–100% (Table 2). The most frequently sold PhACs reported were ciprofloxacin (antibiotic), cetirizine (anti-allergy), metformin (anti-diabetes), metronidazole (antibiotic) and omeprazole (gastric therapy). The most commonly prescribed PhACs according to the pharmacies were diclofenac (anti-inflammatory) and lamotrigine (anti-epileptic), but these two medicines were not among the most commonly sold PhACs. The most commonly sold PhACs for different types of diseases are shown in Fig. S1. Of the substances identified in

Table 2
Summary of the most sold pharmaceuticals (PhACs) in Kampala, arranged in order of reporting rate (RR) by responding pharmacies ($n = 17$).

PhAC	RR, %	PhAC	RR, %
Ciprofloxacin	100	Valproic acid	41
Cetirizine	88	Amoxicillin	41
Metformin	88	Duo-cotexine	35
Metronidazole	82	Levofloxacin	35
Omeprazole	82	Microgynon	35
Amlodipine	71	Nifedipine	35
Salbutamol	71	Cold cap[1]	35
Doxycycline	65	Amoxyl	29
Rifampicin	65	Clotrimazole	29
Coartem (artemether/lumefantrine)	76	Digoxin	29
Glibenclamide	59	Losartan	29
Cefixime	53	Prednisolone	29
Levonorgestrel	53	Cloxacillin and ampicillin	24
Loperamide	53	Ibuprofen	24
Phenylpropanolamine	47	Loratadine	24
Ketoconazole	41		

the survey, initial analyses were performed for ciprofloxacin, cetirizine, metformin, metronidazole, omeprazole, amlodipine, salbutamol, amoxicillin, amoxyl, clotrimazole, lumefantrine, ampicillin, ibuprofen, ketoconazole and other substances listed in Table 1. However, recovery rate of metformin, omeprazole, amlodipine, amoxicillin, amoxyl, clotrimazole, lumefantrine, ampicillin, ibuprofen and ketoconazole was very low and therefore these 10 PhACs are excluded from the list of analytes presented in Table 2.

Regarding management of leftover or unused drugs, 71% of pharmacies reported that they gave information to the patients on how to dispose of unused or expired medicines. Of these, 15% of pharmacies told their customers to return unused/expired medicines to the pharmacy for destruction; 10% informed customers to get rid of unused/expired medicines by throwing them in pit latrines or in dustbins; 6% (one pharmacy) advised the customers to dump them in a safe place; and the remaining 40% (seven pharmacies) said that the expired/unused medicines were collected in a separate bin and sent for destruction to the National Drug Authority (NDA) (four pharmacies) or the town of Nakasongola, 140 km north of Kampala (three pharmacies). All pharmacies reported that the relevant authority had given them instructions/restrictions on how to handle unused or expired medicines.

3.2. Physical and chemical characteristics of wastewater and water resources in the Nakivubo area

There were higher average concentrations of TS in effluent than in influent to Bugolobi WWTP, but treatment at the plant removed about 50% of TSS from incoming water (Table 3). Marginal removal of organic matter was also observed in Bugolobi WWTP (30% for BOD_5, 60% for COD and 15% for TOC). No tangible removal was observed for Tot-N or PO_4-P, while 37% removal of Tot-P was observed. These low removal efficiencies indicate poor performance of Bugolobi WWTP, where the treatment system consists of a primary treatment using sedimentation and a secondary/biological treatment using trickle filters. Wastewater has a short residence time in the plant (<3 h), which results in most pollutants in wastewater leaving the plant with the effluent. This was confirmed by the WWTP operator, who reported that the plant was overloaded and was not fully functional during the study period.

Levels of solids (TS and TSS), organics (BOD_5, COD and TOC) and Tot-N in Nakivubo channel were lower than those measured in the wastewater effluent. Apart from wastewater from Bugolobi WWTP, Nakivubo channel also collects stormwater, which results in dilution of pollutants in the channel. In addition, settling of solids and oxidation of organic matter are likely to occur while water is running in the channel. The high levels of Tot-P in channel water most likely leached from agricultural fields alongside the channel. The wetland water showed higher concentrations of most pollutants than the channel (Table 3). The free water above the soil in the wetland is shallow (<50 cm) and disturbance of the wetland sediment could not be avoided during the sampling, resulting in re-suspension of solids from the sediment.

3.3. PhACs in water resources in Nakivubo system

Of the 28 substances included in chemical analyses, 17 PhACs were detected in the different water resources (Fig. 2). These were: atenolol, bezafibrate, carbamazepine, cetirizine, codeine, diclofenanc, furosemiode, hydrochlorothiozide, irbesartan, lidocaine, losartan, salbutamol, sotalol, sulfamethoxazole, gemfibrozil, trimethoprim and venlafaxine. Trimethoprim and sulfamethoxazole were the most abundant PhACs in all water resources except Lake Victoria. Interestingly, these two particular PhACs were not reported by the pharmacies surveyed as being among the most commonly sold drugs in the study area.

3.3.1. Occurrence and removal of PhACs in Bugolobi wastewater treatment plant

Bugolobi WWTP had the highest combined total of PhACs ($\sum$PhACs) in influent (4000–28,000 ng L^{-1}) and effluent (13000–37,600 ng L^{-1}) (Table S5 in SI). Trimethoprim (antibiotic and chemotherapeutic agent) was the PhAC present in the highest concentration in both influent (1300–22,600 ng L^{-1}) and effluent (8600–31,000 ng L^{-1}) (Fig. 2). Other PhACs which contributed strongly to $\sum$PhACs in influent and effluent were atenolol (β-blocker; 550–2000 ng L^{-1}), diclofenac (anti-inflammatory; 100–500 ng L^{-1}) carbamazepine (anti-epileptic; 200–1300 ng L^{-1}), furosemide (diuretic; 160–1300 ng L^{-1}), hydrochlorothiazide (diuretic; 230–1350 ng L^{-1}), losartan (antihypertensive; 100–160 ng L^{-1}) and sulfamethoxazole (antibiotic; 660–800 ng L^{-1}).

According to the Ugandan Institute for Health Metrics and Evaluation (IHME), infections of HIV/AIDS and malaria are the second and third leading causes of death in Uganda (IHME, 2019). The high concentrations of trimethoprim and sulfamethoxazole in Kampala water resources can be attributed to the fact that the area is a malaria pandemic region and there is a high prevalence of HIV/AIDS, and thus high consumption of PhACs is likely. In Uganda, Kenya and other African countries, sulfamethoxazole combined with trimethoprim is

Table 3
Physical and chemical quality of Bugolobi wastewater treatment plant (WWTP) influent and effluent and of surface water from Nakivubo channel, Nakivubo wetland and Lake Victoria. Values shown are mean ± standard deviation. All concentrations are expressed in mg L^{-1}. $n = 2$ for [a], $n = 1$ for [b] and $n = 4$ for all other samples. For parameter abbreviations, see Section 2.2.6.

Parameter	Bugolobi WWTP influent	Bugolobi WWTP effluent	Nakivubo channel	Nakivubo wetland	Lake Victoria
TS	480 ± 220	680 ± 70	570 ± 80	1190 ± 1220	130 ± 60
TSS	210 ± 80	100 ± 30	480 ± 430	250 ± 390	10 ± 5
BOD_5	540 ± 40[a]	370 ± 20	190	120 ± 6	20 ± 10
COD	980 ± 150	390 ± 40	150 ± 10	550 ± 320	14 ± 7
TOC	3770 ± 40	3190 ± 240	2870 ± 1200	3280 ± 620	270 ± 50
Tot-N	56[b]	50 ± 4	18 ± 1	30 ± 9	2 ± 0
PO_4-P	4.40 ± 0.30	4.00 ± 0.10	5.40 ± 0.10	5.20 ± 0.20	0.05 ± 0.00
Tot-P	9.90[b]	6.28[b]	10.52 ± 0.10	8.32 ± 0.70	0.16 ± 0.03

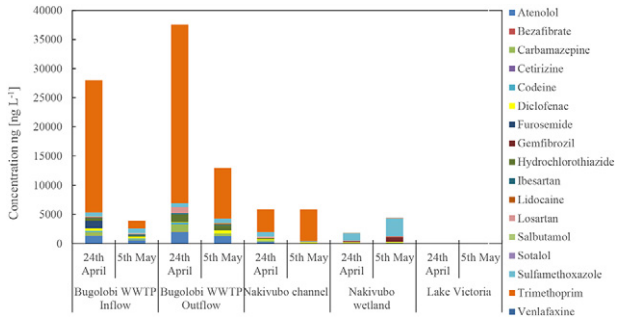


Fig. 2. Average concentrations (ng L^{-1}) of individual pharmaceuticals (PhACs) in Bugolobi wastewater treatment plant (WWTP) influent and effluent and in surface water samples from Nakivubo channel, Nakivubo wetland and Lake Victoria collected on 29 April and 5 May.

prescribed to people living HIV/AIDS (Kasule et al., 2018; Thera et al., 2005). The high concentrations of these antibiotics detected are alarming and attention should be paid to health risks related to trimethoprim/sulfamethoxazole-resistant bacteria in the area. In fact, bacterial resistance to these antibiotics has been already reported in Africa for two decades, with treatment of urinary tract infections and respiratory infections failing due to drug resistance (Feikin et al., 2000; Huovinen, 2001). Wastewater pathogenic bacteria, e.g. different strains of *Escherichia coli*, *Salmonella typhi* and *Shigella* spp. are among the trimethoprim/sulfamethoxazole -resistant bacteria found in Africa (Feikin et al., 2000).

The only PhAC found to be removed in Bugolobi WWTP was cetirizine (anti-histamine; 75–88%). In fact, most of the substances commonly detected (e.g. atenolol, carbamazepine, codeine, hydrochlorothiazide, irbesartan, lidocaine, losartan, pyrimethamine, salbutamol and trimethoprim) were present in higher mean concentrations in effluent than in influent. Moreover, ∑PhACs in influent and effluent samples collected on 24 April was significantly higher than ∑PhACs in corresponding samples collected on 5 May. It should be noted that some biological treatment systems combining activated sludge, lagoons and wetlands can partially remove PhACs, especially biodegradable substances (Baresel et al., 2015; Hey et al., 2012; Li et al., 2013; Verlicchi et al., 2013). Bugolobi WWTP was overloaded and not functioning effectively during the sampling period, which partly explains the lack of removal of PhACs in the wastewater. Reverse transformation of the some PhACs to their parent compound and desorption from particulate matter during the treatment might explain the increased concentrations of a number of PhACs. This process is not unusual, even in well-functioning plants. The TS concentration in effluent from Bugolobi WWTP (680 ± 70 mg L^{-1}) was also higher than that in the influent (480 ± 220 mg L^{-1}) during the sampling periods (Table 3). However, only PhACs in the liquid phase were analysed in this study.

It is well known that the physical and chemical properties of PhACs play an important role in their transport and removal in the wastewater treatment process. Atenolol has low lipophilicity and a low affinity for sorption to sediment, which could explain its persistence throughout the wastewater treatment process (Küster et al., 2010). Beta-blockers (such as atenolol) are generally difficult to remove from wastewater (Baresel et al., 2015). Carmona et al. (2014) found an increase in concentration in WWTP effluent for several different PhACs, e.g. diclofenac and gemfibrozil. Poor or variable removal has been reported for carbamazepine and hydrochlorothiazide in WWTPs in Spain (Gros et al., 2013). Other studies investigating removal of PhACs in middle-income countries (e.g. Jordan) report low removal efficiencies (<50%) for a number of PhACs, including carbamazepine and sulfamethoxazole (Al-Mashaqbeh et al., 2019). In a study on a WWTP in Switzerland, Göbel et al. (2007) found an increase in trimethoprim concentration between influent and effluent.

3.3.2. Distribution and fate of PhACs in Nakivubo water resources in Kampala

Nakivubo channel contained ∑PhACs of 5700 ng L^{-1}, with trimethoprim being present in the highest concentration (3900–5400 ng L^{-1}), followed by sulfamethoxazole (170–800 ng L^{-1}) (Fig. 2). Atenolol was also present in high concentrations in the channel water (270–1300 ng L^{-1}). However, the PhAC concentrations in Nakivubo channel were generally much lower than those in effluent from Bugolobi WWTP (Fig. 2). Carbamazepine (70–240 ng L^{-1}) and losartan (β-blocker) (60–190 ng L^{-1}) were also detected in the channel water. For Nakivubo wetland, ∑PhACs was 1800–4400 ng L^{-1}, with the highest concentration recorded for sulfamethoxazole (1300–3000 ng L^{-1}). Gemfibrozil (190–800 ng L^{-1}), carbamazepine (100–120 ng L^{-1}) and diclofenac (100–150 ng L^{-1}) were also detected in wetland water (Fig. 2). The poor removal of PhACs from wastewater meant that high concentrations of trimethoprim and sulfamethoxazole in particular were transported to Nakivubo channel. This transport of PhACs substances into the channel and then to the wetland system is alarming. In particular, the high occurrence of antibiotics poses a risk of development and spread of antimicrobial resistance within the area. For this trend to be halted, it is essential that the authorities urgently stop the unethical practice at most pharmacies of dispensing any drug to their customers without a doctor's prescription.

Trimethoprim and sulfamethoxazole were also the most common substances found by K'Oreje et al. (2016) in a study of surface waters in Kenya, together with a high detection frequency of diclofenac and carbamazepine in river water. Globally, sulfamethoxazole, trimethoprim, diclofenac, naproxen and ibuprofen are the five most commonly detected PhACs in aquatic environments (Aus der Beek et al., 2016).

Interestingly, the concentration of trimethoprim in Nakivubo wetland water (20–70 ng L^{-1}) was significantly lower than that in Nakivubo channel water (4000–5400 ng L^{-1}) (Fig. 2). This can be explained by (i) degradation of PhACs along the channel, (ii) adsorption/accumulation in sediments of the channel and the wetland and (iii) uptake by wetland plants. For degradation along Nakivubo channel, factors such as length of flow path, retention time and sediment characteristics may have influenced the removal of PhACs. The flow path between the WWTP discharge point in Nakivubo channel and the beginning of the wetland is approximately 3 km, and the retention time, roughly estimated in computer simulations, is about 3.2 days in the central flow path (Kansiime and Nalubega, 1999). According to Kadlec and Wallace (2008), the longer the retention time, the longer the time for interaction between PhACs and sediment/sunlight and the more degradation will occur. In addition, accumulation of some PhACs in wetland soil and uptake by wetland occurred. We analysed PhACs concentrations in soil and plants in Nakivubo wetland area during the study period (data not shown), and found significant accumulation of trimethoprim in the soil (4.9 ng g^{-1}) and in yam root (1.1–2.5 ng g^{-1}) (Figs. S2 and S3 in SI). This clearly confirms soil accumulation and plant uptake of this substance. Other substances present in low concentrations in Nakivubo wetland water compared with channel water were atenolol, carbamazepine and diclofenac (Fig. 3). This was also explained by adsorption of the substances to the sediments of Nakivubo channed and wetland. In fact, carbamazepine accumulated in the soil of Nakivubo wetland at a concentration of 9.4 ± 2.9 ng g^{-1} (unpublished data, see SI). Interestingly, we found a significant negative correlation between the concentration of carbamazepine and the TSS content in water samples, i.e. the concentration of carbamazepine in water decreased as the TSS content in the water increased. Adsorption of carbamazepine and diclofenac to river sediment has been reported elsewhere (Carmona et al., 2014; Yang et al., 2015). Efficient removal of a number of PhACs, e.g. acetaminophen, gemfibrozil and naproxen, in wetlands was observed by Conkle et al. (2008). According to Chen et al. (2016), degradation and absorption to soil are the two major mechanisms of PhAC removal in wetlands. In artificial composite soil treatment systems fed reclaimed water containing trimethoprim and sulfamethoxazole, Liu

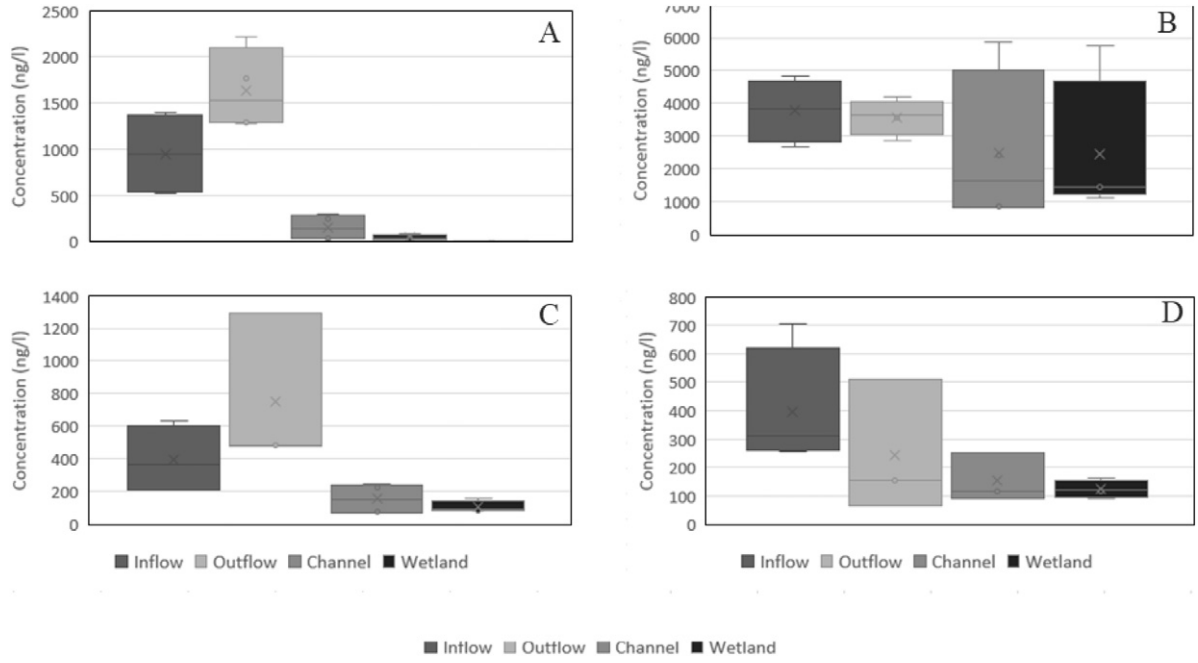


Fig. 3. Concentrations (ng L^{-1}) of the pharmaceuticals atenolol (A), sulfamethoxazole (B), carbamazepine (C) and diclofenac (D) in Bugolobi wastewater treatment plant influent and effluent and in samples from Nakivubo channel and Nakivubo wetland. Mean (line) and median (cross) concentrations, boxes extend between the 75% and 25% quartiles and bars indicate standard deviation.

et al. (2019) obtained removal rates of 80% for trimethoprim and 95% for sulfamethoxazole.

In contrast, the concentration of sulfamethoxazole was higher in Nakivubo wetland water (1300–3000 ng L^{-1}) than in channel water (200–800 ng L^{-1}0) (Fig. 3), indicating accumulation of this substance in the wetland water from other sources. Desorption of previously sorbed sulfamethoxazole from wetland soil to water could have occurred, leading to the high concentration in wetland water compared with channel water. In contrast, sulfamethoxazole has been found to decompose during transport within wetland systems in studies by Kadlec and Wallace (2008). No PhACs were detected in Lake Victoria water, probably because of dilution in the lake.

4. Concluding remarks

Pharmaceutical contamination of wastewater and surface water resources in Kampala, Uganda, was demonstrated in this study. The highest concentrations of PhACs were found in Bugolobi WWTP influent and effluent. The PhACs present in the highest concentrations in WWTP influent and effluent and in Nakivubo channel water were trimethoprim and sulfamethoxazole. Atenolol, carbamazepine and diclofenac, which were reported to be among the most commonly sold PhACs in the area, were also commonly detected in water samples from the different sites. Bugolobi WWTP acted as a point source of PhACs in the study area, due to its poor performance in wastewater treatment in general and in PhAC removal in particular.

There was significant transport of high concentrations of trimethoprim and sulfamethoxazole from Bugolobi WWTP to Nakivubo channel, but Nakivubo wetland contributed to removal of PhACs from the water through sediment adsorption and plant uptake. Lake Victoria water contained no detectable levels of PhACs.

The transport of antibiotics within the Nakivubo water system is alarming and poses a risk of development and spread of antimicrobial resistance within the area. Upstream measures are needed to reduce the levels of PhACs in wastewater, particularly antibiotics, and to limit the load entering the water system and the environment. Such measures could include limiting prescription and sales of antibiotics and increasing awareness among the public and pharmacists regarding the consequences of antimicrobial resistance. Downstream measures could include upgrading Bugolobi WWTP to enhance its capacity in wastewater treatment and PhAC removal.

Declaration of competing interest

We, the authors, declare no competing interests, nor financial or personal relationships with other people or organizations that could inappropriately influence this work.

Acknowledgments

The study was funded by the Swedish Research Council (FORMAS) through the project 'Pharmaceutical Pollution in Use of Wastewater in Crop Production' grant number 2013-01963. Special thanks go to all members at Makerere University for their assistance during sample collection in Kampala.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.136347.

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