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DOI:
10.1016/j.emcon.2020.02.004

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (Harvard):
Anekwe, J, Oluseyi, T, Drage, D, Harrad, S & Abdallah, M 2020, 'Occurrence, seasonal variation and human exposure to pharmaceuticals and personal care products in surface water, groundwater and drinking water in Lagos State, Nigeria', *Emerging Contaminants*, vol. 6, pp. 124-132. https://doi.org/10.1016/j.emcon.2020.02.004

Emerging Contaminants 6 (2020) 124–132

Contents lists available at ScienceDirect

Emerging Contaminants

journal homepage: http://www.keaipublishing.com/en/journals/emerging-contaminants/

Research article

Occurrence, seasonal variation and human exposure to pharmaceuticals and personal care products in surface water, groundwater and drinking water in Lagos State, Nigeria

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ARTICLE INFO

Article history:
Received 11 November 2019
Received in revised form
15 January 2020
Accepted 18 February 2020

Keywords:
Pharmaceuticals and personal care products
PPCPs
Freshwater
Ground water
Drinking water
Seasonal variation
Human exposure
Nigeria

ABSTRACT

The occurrence of 28 pharmaceuticals and personal care products (PPCPs) was investigated in 17 surface water samples (rivers, canals, and lagoons), 12 groundwater samples (wells and boreholes, which can also be consumed for drinking) and 8 drinking water samples (bottles and sachets) during dry and rainy seasons in Lagos state, Nigeria. The most prevalent compound detected in all samples was amoxicillin (an antibiotic) at median concentrations of 1614, 238 and 358 ng/L in surface water, ground water and drinking water, respectively. This is of concern due to potential impact on development of antibiotic-resistant microbial strains. Other frequently-detected compounds include acetaminophen, nicotine, ibuprofen, and codeine with detection frequencies of more than 70%. Investigation of seasonal variability revealed that glyburide, caffeine, naproxen and diclofenac concentrations were significantly ($P < 0.05$) higher during the dry season (winter), while Nicotine and Codeine levels were higher during the rainy season (summer). The factors influencing such seasonal variability include: dilution by extensive rainfall, agricultural activity (for nicotine) and usage patterns of pharmaceuticals among the local community. Measured concentrations in drinking water samples were used to assess inadvertent human exposure to PPCPs in Nigerian adults. Results revealed average daily exposures of 81, 14 and 3 ng ΣPPCPs/kg BW/day via drinking borehole, sachet water and bottled water, respectively. While there exists no health-based limit value (HBLV) for chronic exposure to mixtures of PPCPs, our results raise concern and warrant further investigation of the potential health implications of such unintended PPCPs exposure.

1. Introduction

Pharmaceuticals and personal care products (PPCPs) are used for treatment or prevention of diseases in humans and animals, as well as to maintain and improve the quality of daily life. PPCPs have been recently identified as a group of emerging environmental contaminants and have been detected in various environmental matrices such as freshwater, marine water, wastewater, soil sediment and fish [1–3]. These emerging contaminants are extensively and increasingly used in human and animal medicine, leading to their ubiquitous presence in the environment [4]. In a previous contribution, we pointed out that the major sources of PPCPs to the environment are via wastewater treatment plants (WWTPs), which cannot completely remove PPCP residues during the treatment process, and landfill leaching [1].

In developed countries such as the United Kingdom, United States of America, Australia and Japan, several studies have been conducted to better understand the occurrence, behaviour and fate of PPCPs in the environment. However, very few studies have addressed this area of research in developing countries in Africa

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Peer review under responsibility of KeAi Communications Co., Ltd.

https://doi.org/10.1016/j.emcon.2020.02.004

and South America [1,5]. The insufficient data on the occurrence and behaviour of PPCPs in Nigeria, with a population of nearly 200 million people, compounded with an incomplete sewage treatment system (probably direct discharge into waterways) represent a cause for concern and a significant research gap. Most urban communities in Nigeria, with the exception of the capital Abuja and limited areas in Lagos, have no sewage system. Consequently, the sewage and sullage either lie stagnant or are disposed through the storm water drainage system [6]. This is supported by the scarce data available on PPCPs in the Nigerian environment, where high concentrations of 1–20 μg/L of paracetamol, chloroquine, diclofenac and ciprofloxacin were detected in four surface- and groundwater samples collected from an industrial area of Sango Ota, Ogun State, Nigeria [7]. Dilution and degradation factors were suggested as natural mechanisms capable of reducing PPCPs concentrations in Nigerian surface water in the absence of wastewater treatment processes [8]. Several studies have demonstrated that environmental conditions (weather/season), source characteristics, as well as water flow rates are significant factors that control the detection frequency and concentrations of PPCPs in natural waters [9,10]. Nigeria has only two major seasons (dry and rainy season). The dry season, known locally as the "Harmattan" is accompanied by predominant influences of dust-laden air mass from the Sahara desert. It usually starts from late October and lasts to early March with peak dry conditions between early December and late February. The rainy season starts in April and lasts until early October with peak wet conditions in June. This season is influenced by wind from the South Atlantic Ocean mostly known as the South West wind. At the peak of the rainy season, the weather in Lagos is wet about half the time [11]. Despite these stark seasonal differences in precipitation, there exists no information on the seasonal influence on the concentrations of PPCPs in Nigerian freshwater (surface and ground water). Moreover, due to the incomplete sewage treatment and water disposal systems, many Nigerian households rely upon boreholes as their main source of non-potable water and 97% of households use bottle or sachet water as their main drinking water source [12]. The use of Sachet water, which is packaged in individual units of 500 ml high density polyethylene sachets, is common in Nigeria with an estimated daily consumption of up to 60 million units [13]. Other forms of packaged water that are available in Nigeria include bottle-packaged water (patronised by citizens in the higher income brackets) and 'ice water' which is mainly consumed by lower income individuals. The 'ice water' type is usually prepared by withdrawing water from nearby piped or vended water sources, filtered over a piece of cloth and thereafter put into transparent low-density polyethylene (LDPE) plastic minibags. Therefore, 'ice water' has been almost completely phased out for hygienic reasons and due to the advent of the better packaged and purified Sachet water [14]. Therefore, Only Bottled and Sachet water were investigated in the current study. The average cost difference between sachet-packaged ($0.03) and bottled ($0.3) water is 1000%. Thus, sachet water is perceived as clean and affordable to a wide spectrum of middle and low-income earners in Nigeria [15]. It's also worth mentioning that a small fraction of low-income Nigerian households may use water from local boreholes for drinking, despite the public health advice against it [12].

Against this backdrop, the objectives of the current study are: (a) to investigate the occurrence and concentrations of 28 commonly used PPCPs (Tables SI–1) in Lagos State waterways, groundwater and drinking water (bottled and sachet). PPCPs selection was based on priority pollutant lists developed by the European Union (EU) under the Water Framework Directive (WFD), as well as the United States Environmental Protection Agency (USEPA). Other selection criteria include: frequent environmental occurrence, persistence and toxicity to aquatic organisms [1]; (b) evaluate seasonal variability in concentrations of target PPCPs in the studied water samples during the Nigerian dry and wet seasons; and (c) use the measured concentrations in drinking water to estimate unintended human exposure to the studied PPCPs via drinking water.

2. Materials and methods

2.1. Chemicals and materials

All solvents used in this study were purchased from Fisher Scientific™ (Loughborough, UK) and were of UPLC grade. Individual standards of 28 PPCPs (Tables SI–1), in addition to isotope-labelled Caffeine-D9, Codeine-D3, Carbamazapine-D10 and 4-Chlorophenol-2,3,5,6-D4 used as surrogate standards were purchased from Sigma-Aldrich™ (Irvine, UK) at the highest available purity (>99%). ^{13}C-tetrabromobisphenol A (^{13}C-TBBPA) and tris (2-chloroethyl) phosphate-D12 (TCEP-D12) used as recovery (syringe standards) were obtained from Wellington Laboratories (Guelph, ON, Canada).

All standard stock solutions (5 mg/ml) were prepared and further diluted in methanol. Oasis MCX cartridges (6 cm^3, 150 mg sorbent per cartridge) were obtained from Waters™ (Hertfordshire, UK). Ammonium formate (NH_4COOH), Na2EDTA, ammonium hydroxide (NH_4OH, 30%), ammonium fluoride (NH_4F), Acetic acid and formic acid (HCOOH) were obtained from Sigma-Aldrich™ (Gillingham, UK). Nitrogen gas (oxygen free, 99.998%) was purchased from BOC (Birmingham, UK). Milli-Q water (Merck Millipore, Burlington, MA) was used for cleaning and sample preparation purposes.

2.2. Sampling and preparation

Water samples (1 L each) were collected at different locations comprising 17 surface water (rivers, canals, and lagoons), 12 groundwater (four wells and eight boreholes) and eight drinking water samples (four brands of sachet water and four brands of bottled water) within the mega city of Lagos, Nigeria. One sample was collected from each location during the dry season (throughout the period from December 2017–February 2018) and the rainy season (throughout the period from June–July 2018), except for the bottled water samples (n = 4), which were only collected during the rainy season sampling campaign. Surface and groundwater were collected as grab samples in screw-capped, high density polypropylene (HDPE) bottles. The sampling locations represent some of the major waterways that travel across the city and flow down into the Atlantic Ocean. Surface water samples were collected from Amuodofin River (2 locations), Anthony River, Ijora River, Ikorodu River, Iwaya Canal, Kara River, Lekki River, Lekki River drainage, Makoko River, Makoko middle river, Miletwo River (2 locations), Unilag Gate Canal (2 locations), Unilag River (2 locations). The longer waterways were sampled in 2 locations spaced at least 3 miles apart to provide a better idea on the occurrence and levels of PPCPs. Ground water samples were collected from Amuodofin Borehole, Amuodofin Well, Anthony Borehole, Ijora Borehole, Ikorodu Borehole, Iwaya Borehole, Iwaya Well, Kara well, Lekki Borehole, Makoko Adekunle Borehole, Miletwo Borehole, Miletwo Well. Bottled (n = 4) and sachet water samples (n = 4) were purchased from local super markets in the same area of the study. These sampling locations are in close proximity to both residential areas, as well as industrial and commercial activities (Fig. 1). The bottled and sachet water comprised four different commercial providers for each type of packaged water. The labelling on the sample packages indicated regional sources of water from deep wells or mangrove rain forest regions of West Nigeria

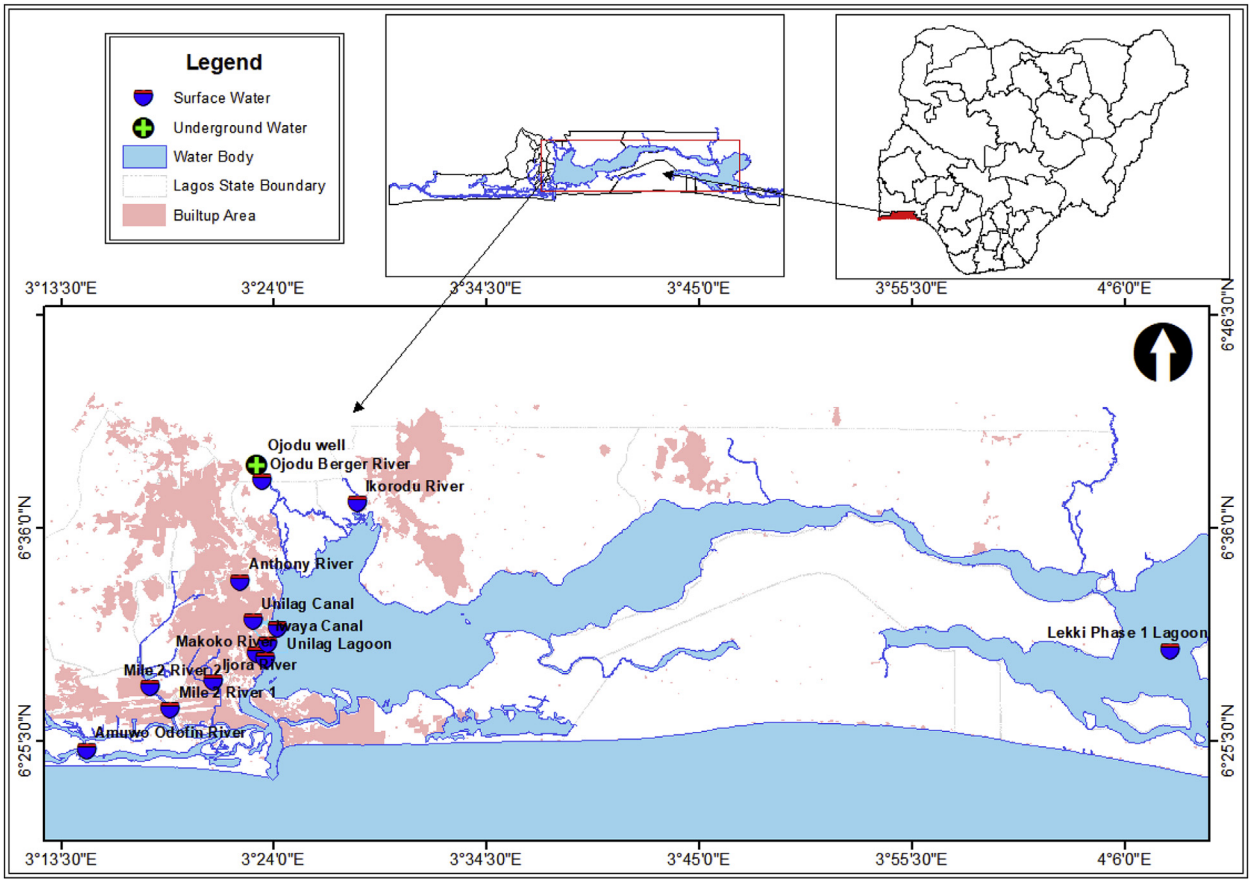

Fig. 1. Map depicting sampling locations in Lagos State Southwest of Nigeria.

followed by multi-stage filtration/purification process to comply with the National Agency for Food and Drug Administration Control (NAFDAC) water quality standards.

Collected samples were stored in ice-packed containers and transported back to the chemistry department laboratory at the University of Lagos, where they were stored at −18 °C until extraction within a maximum of 48 h from collection. Sample extraction was conducted according to a recently reported method [16]. Briefly, 500 mL of each sample were filtered through glass fibre filters (0.7 μm, Whatman®) and spiked with 50 ng of isotope-labelled surrogate standards mixture (Caffeine-D9, Codeine-D3, Carbamazapine-D10 and 4-Chlorophenol-2,3,5,6-D4) then passed onto Oasis MCX cartridges that were pre-conditioned with 2 mL of MeOH and equilibrated with 2 mL of deionized water. Each of the cartridges were carefully labelled and wrapped in aluminium foil before been couriered to University of Birmingham, UK for further extraction and instrumental analysis. On arrival, cartridges were placed in a freezer at −20 °C until further processing within 24 h of receipt. Each cartridge was eluted with 5 mL MeOH followed by 5 mL of 5% ammonium hydroxide in methanol (NH4OH). The eluate was evaporated to dryness under a gentle stream of nitrogen and reconstituted in 200 μL of 8:2 water/methanol solution containing 25 pg/μL of ^{13}C-TBBPA and TCEP-D12 used as recovery (syringe) standards for QA/QC purposes. Further details are provided as supplementary information.

2.3. Instrumental analysis

Extracted samples were analysed on an ultra-performance liquid chromatography coupled to a Q-Exactive Plus orbital trap high resolution mass spectrometer (Thermo Fisher Scientific™, Bremen, Germany) equipped with a heated electrospray ionisation (HESI) ion source according to a previously reported method [16]. Chromatographic separation was achieved on an Accucore RP-MS column (100 × 2.1 mm, 2.6 μm) using 2 mM NH_4COOH/2 mM NH_4F in water (mobile phase A) and 0.5% formic acid in methanol (mobile phase B). A gradient method at 400 μL/min flow rate was applied as follows: start at 2% B, stay for 1 min; increase to 98% B over 11 min, held for 1 min; then decrease to 2% B over 0.1 min; maintained constant for a total run time of 16 min. Injection volume was 5 μL. The Orbitrap MS parameters were set as follows: alternate switching (−)/(+) ESI full scan mode sheath gas flow rate 20 AU (arbitrary units), discharge voltage 4.5 kV, capillary temperature 320 °C, resolution 35000 FWHM, AGC target 1E6, maximum injection time (IT, the maximum time allowed to obtain the set AGC target) 50 ms and scan range 125–750 *m/z*. Quantification was performed using Xcalibur software (Xcalibur 3.0, Thermo Fisher Scientific). Further details are provided as supplementary information.

2.4. Quality assurance and quality control

To ensure accurate quantification of the target PPCPs, a number of quality assurance and quality control (QA/QC) measures were implemented. Both Milli-Q water spikes (n = 5, comprising Milli-Q water spiked with analytical standards of target PPCPs) and real samples (n = 5) were analysed in triplicate and the relative standard deviation in concentrations detected between all the

replicates was less than 15% (Tables SI–2). For method blanks, Milli-Q water samples were analysed in the same manner as samples and none of the target compounds were detected in the method blanks. Therefore, no blank correction of the results was required.

Recoveries of the isotope-labelled surrogate standards were calculated against the syringe standards in all environmental and QA/QC samples. High percent recoveries (>70%) of all five surrogate standards were obtained indicating good overall performance of the method.

A calibration standard containing all the target and surrogate standards (500 ng/mL) was injected at the beginning and end of each sample batch. These were used to calculate the relative response factor (RRF) used for quantification of analytes within the sample batch and fell within 10% of the average RRFs calculated over a 5-point calibration range for each target compound (1–1500 ng/ml). Peak identity was achieved mainly via accurate mass of the target analytes (Tables SI–1). In addition, the peak for each target analyte was locked to be within ±0.3 min of the average time determined in the 5-point calibration standards and within ±0.1 min of its relative retention time. Further details are provided as supplementary information.

2.5. Statistical analysis

Statistical analysis was conducted using IBM SPSS statistics 22.0 software package for Windows 10. Initially, sample distribution was investigated using the Kolmogorov-Smirnov test combined with visual inspection of the Q-Q plot for data distribution. Results revealed the generated datasets to be normally distributed. Therefore, parametric tests were further applied for comparison of sample means (student t-test to compare between two datasets) and Analysis of Variance (ANOVA). ANOVA in combination with Tukey's honestly significant difference (HSD) post-hoc test were applied for pair-wise comparison among 3–8 datasets to assess statistically significant differences. For statistical analysis purposes, concentrations below the method detection limit (MDL; Tables SI–2) were assigned a value of 0.5 MDL, except in cases of a detection frequency below 50% where a value of MDL multiplied by the detection frequency was assigned to minimise statistical bias (e.g. 0.35 MDL for compound-X with a detection frequency of 35%). P values < 0.05 were considered significant.

2.6. Results and discussion

Out of the 28 target PPCPs studied, 27 were detected in at least one sample of surface water, 24 in groundwater and 14 in sachet drinking water. The antibiotic Doxycycline was not detected in any sample.

2.7. PPCPs profiles in Lagos surface water, groundwater and sachet drinking water

The average concentrations for ΣPPCPs during the dry season were 28200 ng/L, 2070 ng/L and 382 ng/L, while the rainy season average concentrations were 10050, 2860, 708 ng/L, for surface water, groundwater and sachet drinking water samples, respectively (Table 1). Statistical analysis revealed no significant differences ($P > 0.05$) in ΣPPCPs concentrations among the three types of water samples studied.

The two most frequently detected compounds in the current study were amoxicillin and acetaminophen. Amoxicillin was detected in all surface water samples at an average concentration of 13,300 ng/L (87–272,150 ng/L). The detection of amoxicillin, a widely-used antibiotic, was not surprising as it is regularly dispensed in Nigeria as an over-the-counter drug, which does not require a prescription [17,18]. Nevertheless, this is of concern because previous studies have shown continuous input of antibiotics, such as amoxicillin, into the environment may lead to significant long term, irreversible impacts such as the development of antibiotic-resistant bacterial strains [19]. A modelling study using the public EUCAST toxicological database predicted the lowest no effect concentration for resistance development against amoxicillin in 29 bacterial strains at 250 ng/L [20]. Notwithstanding the uncertainties associated with this modelling approach and the lack of regulatory significance, the median concentration of Amoxicillin in Surface water in the present study (1610 ng/L) largely exceeds this limit. This indicates that the observed high concentrations of Amoxicillin in surface water may be contributing to the development of antibiotic-resistant strains.

Acetaminophen was detected in 90% of the samples at average concentrations of 506 ng/L (<1–12,430 ng/L), 25 ng/L (2–188 ng/L) and 3 ng/L (<1–11 ng/L) in surface, groundwater and sachet water respectively. This high detection frequency is in line with previous studies from both African and non-African countries, and is consistent with the common over-the-counter use of this analgesic to relieve fever, aches and pain. Acetaminophen was reported as the third most consumed drug (4.3 tonnes) in Kenya and was detected at relatively high concentrations up to 16000 ng/L in the Nairobi River basin [21]. It was also detected in water from the Umgeni River (South Africa) at concentrations ranging from 5800 to 58700 ng/L [22]. In the river Leine (Germany), the average acetaminophen concentration was 1992 ng/L [23], while in the river Taff (UK); acetaminophen was present at indicative concentrations of 1010–1390 ng/L [24].

DEET was also detected in 90% of the samples studied at average concentrations 192 ng/L (5–1350 ng/L), 18 ng/L (<3–60 ng/L) and 6 ng/L (<3–10 ng/L) in surface, ground and sachet water, respectively. The use of DEET as an insect repellent is common in Nigeria, as one of the recommended protective measures against malaria [25]. The number of publications reporting the presence of DEET in surface water from tropical and sub-tropical countries has increased over the last decade [26,27]. The concentration of DEET detected in surface water in the current study is similar to that reported in Australian urban waterways where concentrations ranging from 8 to 1500 ng/L were reported [28–30]; but were lower than the exceptionally high DEET concentrations reported in surface waters from Jakarta, Indonesia (30–24000 ng/L) [31].

Out of the target 28 PPCPs, Nicotine, codeine, caffeine, valsartan, tramadol, ibuprofen, naproxen, gemfibrozil and meclofenamic acid were detected in more than 70% of the surface water samples. This is of concern due to the possible adverse effects of the individual pharmaceuticals (e.g. addictive effects of tramadol [32] or endocrine-disruption by NSAIDs [33]), as well as the potential toxicological impacts of the mixture [34,35].

Codeine was detected at median concentrations of 421, 8, 48 ng/L in surface water, groundwater and sachet water, respectively (Table 2). Similar median concentrations of codeine (9–320 ng/L) were reported in surface water samples collected along the River Ely, UK [36] and the river Llobregat, Spain (30–39.5 ng/L) [37]. Archer et al. reported average concentration of 129 ng/L of codeine in the Gauteng river in South Africa [38]. Given misuse of codeine by Nigerian youth for recreational purposes has been previously highlighted [39]; its detection in sachet drinking water, albeit at low concentrations, raises concern due to the addictive nature of this chemical.

Average concentrations of caffeine in surface water, groundwater and sachet water were 115 ng/L, 4 ng/L and 8 ng/L, respectively (Table 2). Higher concentrations were reported for caffeine in South African surface water (average = 2078 ng/L [38] and range = 1170–60530 ng/L [22]), while concentrations of caffeine in

Table 1
Statistical summary of concentrations of ΣPPCPs (ng/L) detected in Nigerian surface, ground and sachet water samples collected during the dry and rainy seasons.

		Dry season	Rainy season
Surface water (n = 17 from each season)	Min	503	2480
	Median	4660	6710
	Max	283862	29803
	Average	28211	10066
	StDev	69928	7547
Ground water (n = 12 from each season)	Min	130	184
	Median	948	1161
	Max	6674	9141
	Average	2068	2860
	StDev	2242	3236
Sachet drinking water (n = 4 from each season)	Min	148	527
	Median	424	641
	Max	533	1022
	Average	382	708
	StDev	165	220

three urban rivers in the Yangpu District of Shanghai, China, ranged from 66 to 8571 ng/L [40]. Another study in California reported a maximum concentration of 290 ng/L caffeine in groundwater [41]. The relatively low levels of caffeine in the studied water samples may be attributed to the absence of caffeine-producing plants in the sampled urban area of Lagos (Fig. 1). Therefore, caffeine levels in the sampled water may principally be attributed to anthropogenic sources. This is in agreement with the results of a study from Barbados that reported low caffeine concentrations in surface water (average = 100 ng/L) sampled distant from caffeine-producing plants [42].

Another stimulant, nicotine, was detected in more than 50% of the studied samples at average concentrations of 1995 ng/L (<7–9335), 288 ng/L (<7–3533), and 30 ng/L (<7–143) in surface, ground, and sachet water, respectively. A much lower average concentration of 190 ng/L was reported in Egyptian surface water samples [16]. [38] reported an average concentration of 246 ng/L of Nicotine in water samples collected downstream of a WWTP in Gauteng Province of South Africa, while the upstream samples contained an average nicotine concentration of 154 ng/L.

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently detected pharmaceuticals in the freshwater aquatic environment due to their high consumption rate [1]. Four NSAIDs were investigated in the current study, namely Naproxen (DF = 76%), Ibuprofen (DF = 83%), Diclofenac (DF = 56%) and Meclofenamic acid (DF = 71%) (Table 2). The concentrations of Naproxen in the surface water samples is comparable to those detected in Poland (12–76 ng/L) [43] and Sweden (13–87 ng/L) [44]. Madikizela reported average concentrations (ng/L) ± standard deviations for naproxen, ibuprofen and diclofenac in South African surface water of 2770 ± 1.66, 6720 ± 1.23 and 2580 ± 1.38, respectively [45]. Olarinmoye et al. reported a broad range of concentrations for Naproxen (<20–1030 ng/L), Ibuprofen (<20–8840 ng/L) and Diclofenac (<20–270 ng/L) in surface water samples collected from Lagos, Nigeria in 2015 [46]. These are generally in line with the concentrations reported in the current study (Table 2). Meclofenamic acid was detected at concentration of 2380 ng/L in South African surface water [47], which is relatively higher than the average concentration of 226 ng/L (range; <1–2004 ng/L) in the present study.

2.8. Seasonal variation

Nigeria is located in the tropical zone, with variable rainy and dry seasons. Based on this seasonal variability, we hypothesise that the concentrations of PPCPs in surface and ground water will be lower in the rainy season than the dry season due to a dilution effect. To test this hypothesis, concentrations of target PPCPs in samples collected from the same locations in dry and rainy seasons were statistically compared (Table 3).

Results revealed seasonal variation in some PPCPs

Table 2
Concentrations (ng/L) and detection frequency (DF) of PPCPs in surface water, groundwater and sachet water in Lagos State, Nigeria.

Compounds	Surface water			Groundwater			Sachet water		
	Range	Median	DF (%)	Range	Median	DF (%)	Range	Median	DF (%)
Metformin	<0.5–1760	4	41	<0.5–349	<0.5	8	<0.5	<0.5	0
Acetaminophen	1–12430	24	100	<1-188	7	71	<1-11	1	25
Gabapentin	<1-67	9	59	<1-41	1	21	<1	<1	0
Nicotine	<7-9340	912	85	<7-3530	12	50	<7-143	11	50
Codeine	<2-1780	421	85	<2-2440	8	50	<2-305	48	50
Sulfamethoxazole	<1-3180	6	59	<1-64	<1	25	<1-7	<1	25
Caffeine	<4-1080	115	74	<4-166	<4	33	<4-51	8	63
Trimethoprim	2–388	34	79	<1-21	<1	33	<1	<1	0
Amoxicillin	87–272150	1610	100	44–6490	238	100	86–495	358	100
Tramadol	<2-852	56	79	<2-883	14	71	<2-6	<2	25
Metoprolol	<1-168	8	50	<1-54	<1	21	<1-4	<1	13
Propranolol	<1-12	<1	12	<1	<1	0	<1	<1	0
Carbamazepine	<1-342	9	53	<1-50	<1	29	<1	<1	0
Hydrocortisone	<3-471	<3	9	<3	<3	0	<3	<3	0
Erythromycin-H2O	<1-275	<1	3	<1	<1	0	<1	<1	0
DEET	5–1350	82	91	<4-63	11	54	<4-10	6	50
Oxazepam	<2-1220	<2	38	<2-27	<2	13	<2-7	<2	13
Mefloquine HCl	<1-58	<1	12	<1-56	<1	4	<1	<1	0
Naproxen	<3-2120	19	76	<3-17	<3	38	<3-17	<3	13
Valsartan	<1-3330	27	74	<1-84	<1	13	<1	<1	0
Diazepam	<0.3–42	<0.3	18	<0.3–26	<0.3	8	<0.3	<0.3	0
Glyburide	<3-326	18	53	<3-39	<3	33	<3-34	<3	25
Diclofenac	<1-200	12	56	<1-42	<1	13	<1	<1	0
Ibuprofen	<4-2740	298	85	<4-2250	32	63	<4-50	12	50
Clotrimazole	<1-618	<1	26	<1-191	<1	4	<1	<1	0
Meclofenamic acid	<1-2000	76	71	<1-43	<1	13	<1	<1	0
Gemfibrozil	<4-552	158	79	<4-730	90	83	<4-32	<4	25

concentrations between the dry and rainy season samples. Concentrations of Glyburide (an antidiabetic) in groundwater were significantly higher during the dry season ($p = 0.03$). Similarly, Caffeine was detected at higher concentrations ($p = 0.02$) in surface water samples collected in the dry season (average = 342 ng/L) than rainy season (average = 152 ng/L). Likewise, the non-steroidal anti-inflammatory drugs, Naproxen and Diclofenac, displayed significantly higher concentrations in groundwater and surface water, respectively during the dry season, which is in agreement with our initial hypothesis of dilution by the extensive rainfall during the wet season in Nigeria.

In contrast, the average concentration of nicotine in surface water was significantly higher ($p = 0.002$) in the wet season (3340 ng/L) than in the dry season (654 ng/L). This was in contrast with the expected reduction in PPCPs concentration due to dilution during the rainy season. Further inspection of potential sources revealed that nicotine is predominantly found in tobacco and coca as well as in lower quantities in plants such as tomatoes, potatoes and capsicum. The high concentrations of nicotine observed in this case could thus be due to the presence of tobacco cultivation areas around the sampling locations [48]. The heavy flooding during the rainy season could wash out nicotine from tobacco plants to the nearby waterways; therefore contributing to the high concentrations observed in surface water sampled during the rainy season. Another factor that may contribute to the higher concentrations of nicotine during the rainy season is less photodegradation due to the

Table 3
Concentrations (ng/L) of target PPCPs in water samples collected during the dry (D) and wet (W) seasons in Lagos, Nigeria.

Compound		Surface water				Groundwater				Sachet water			
		Range		Median	Average	Range		Median	Average	Range		Median	Average
Metformin	D	<0.5-	26	3	4	<0.5-	3	<0.5	3	<0.5		<0.5	<0.5
	W	<0.5-	1760	37	264	<0.5-	349	<0.5	52	<0.5		<0.5	<0.5
Acetaminophen	D	3-	273	18	61	<1-	188	8	31	<1-	3	<1	3
	W	7-	12430	55	951	<1-	95	4	19	<1-	11	2	4
Gabapentin	D	<1-	49	11	14	<1-	10	<1	3	<1		<1	<1
	W	<1-	67	2	14	<1-	41	2	10	<1		<1	<1
Nicotine	D	<7-	4950	67	654	<7-	73	9	14	<7-	11	9	9
	W	108-	9340	2080	3340	9-	3530	66	562	<7-	143	21	51
Codeine	D	<2-	447	18	99	<2-	5	3	3	<2-	3	3	3
	W	68-	1780	770	898	13-	2440	87	487	<2-	305	130	164
Sulfamethoxazole	D	<1-	3180	8	326	<1-	64	<1	10	<1-	7	<1	3
	W	<1-	132	6	30	<1-	16	<1	3	<1-	5	<1	3
Caffeine	D	<4-	1080	283	341	<4-	163	<4	35	<4-	51	9	18
	W	<4-	482	51	151	<4-	166	<4	22	<4-	48	6	16
Trimethoprim	D	<1-	144	53	49	<1-	21	<1	4	<1		<1	<1
	W	<1-	388	19	62	<1-	10	<1	3	<1		<1	<1
Amoxicillin	D	87-	272150	460	23950	44-	6490	138	1310	86-	441	341	302
	W	229-	7630	1820	2710	58-	6470	315	1330	334-	495	408	411
Tramadol	D	<2-	852	56	240	<2-	883	44	150	<2-	6	<2	4
	W	<2-	482	30	138	<2-	323	10	56	<2-	5	<2	3
Metoprolol	D	<1-	1	<1	1	<1-	8	<1	2	<1-	1	<1	1
	W	<1-	168	70	73	<1-	54	<1	11	<1-	4	<1	2
Propranolol	D	<1-	9	<1	2	<1		<1	<1	<1		<1	<1
	W	<1-	1	<1	1	<1		<1	<1	<1		<1	<1
Carbamazepine	D	<1-	342	36	71	<1-	46	<1	8	<1		<1	<1
	W	<1-	20	1	7	<1-	50	<1	6	<1		<1	<1
Hydrocortisone	D	<3-	471	<3	34	<3		<3	<3	<3		<3	<3
	W	<3-	70	<3	7	<3		<3	<3	<3		<3	<3
Erythromycin-H2O	D	<1-	275	<1	17	<1		<1	<1	<1		<1	<1
	W	<1-	1	<1	<1	<1		<1	<1	<1		<1	<1
DEET	D	<4-	1350	87	237	<4-	63	7	19	<4-	13	6	7
	W	<4-	636	67	146	<4-	60	13	18	<4-	10	6	6
Oxazepam	D	<2-	1220	19	126	<2-	27	<2	5	<2-	7	<2	3
	W	<2-	12	<2	2	<2-	11	<2	<2	<2-	3	<2	<2
Mefloquine HCl	D	<1-	31	<1	7	<1-	2	<1	2	<1		<1	<1
	W	<1-	58	<1	5	<1-	56	<1	7	<1		<1	<1
Naproxen	D	<3-	2120	8	139	<3-	9	<3	4	<3-	3	<3	3
	W	<3-	129	22	33	<3-	17	<3	7	<3-	17	<3	6
Valsartan	D	<1-	3330	43	321	<1-	84	<1	12	<1		<1	<1
	W	<1-	106	17	28	<1-	10	<1	5	<1		<1	<1
Diazepam	D	<0.3-	42	<0.3	6	<0.3-	26	<0.3	3	<0.3		<0.3	<0.3
	W	<0.3-	1	<0.3	<0.3	<0.3-	5	<0.3	<0.3	<0.3		<0.3	<0.3
Glyburide	D	<3-	326	33	57	<3-	39	10	17	<3-	30	<3	12
	W	<3-	238	6	28	<3-	14	<3	7	<3-	34	<3	13
Diclofenac Na	D	<1-	1930	131	389	<1-	42	<1	9	<1		<1	<1
	W	<1-	34	<1	9	<1-	4	<1	4	<1		<1	<1
Ibuprofen	D	<4-	1680	290	490	<4-	2250	48	258	<4-	34	13	17
	W	<4-	2740	356	907	<4-	1140	19	132	<4-	50	22	25
Clotrimazole	D	<1-	618	<1	63	<1-	3	<1	1	<1		<1	<1
	W	<1-	122	<1	15	<1-	191	<1	18	<1		<1	<1
Meclofenamic acid	D	<1-	2000	136	402	<1-	43	<1	10	<1		<1	<1
	W	<1-	165	21	49	<1-	5	<1	<1	<1		<1	<1
Gemfibrozil	D	<4-	435	179	154	<4-	730	107	182	<4-	31	<4	16
	W	<4-	552	84	160	<4-	483	79	111	<4-	32	<4	16

cloudy weather [49].

Similarly, the average concentration of codeine was also significantly higher ($p < 0.05$) in the wet season (898 ng/L) than the dry season (100 ng/L) in surface water samples. This is difficult to explain but may be attributed to the increased use of cold and flu medication during the wet season [50]. Most of the cold and flu medicines dispensed in Nigeria contain codeine combination products (such as codeine combined with aspirin) or Codeine linctus (up to 2 mg/mL) and are sold over-the-counter without a medical prescription [51].

No statistically significant seasonal variability was observed in the concentrations of other target PPCPs in the studied surface and ground water samples. This may be attributed to several factors including the small sample size and the low detection frequency for some of the target PPCPs. However, it is evident that factors other than dilution by rain water contribute to the concentrations of some PPCPs in the Nigerian aquatic environment (e.g. agricultural sources for Nicotine). To our knowledge, this is the first study to investigate seasonal variation of PPCPs in the Nigerian freshwater environment, while only limited information is available on the factors affecting seasonal variation of PPCPs in surface and ground water worldwide. A recent study investigated the seasonal variation of 11 PPCPs in the Huangpu River, Shanghai, China. The results indicated that most target PPCPs exhibited higher frequencies of detection and concentrations during the dry season than those during the wet season, which was mainly attributed to the influence of rainfall [52]. Similarly, a study of five PPCPs in six Indian lakes, reported higher concentrations of Ciprofloxacin and Caffeine in summer (April to June) and winter seasons (October to February) compared to the rainy season (July to September) [53]. While these two studies focused mainly on investigating the influence of meteorological conditions (i.e. rain and temperature), another study from California attributed some of the observed PPCPs seasonal variation in surface water to increased use of insect-repellents and sunscreens in the summer. Other factors affecting PPCPs temporal variability in California included rainfall and the flow rates in both the Colorado River and the San Joaquin Delta [54]. Therefore, further investigation of both environmental and anthropogenic factors influencing seasonal variability of different PPCPs in different geographical locations is recommended.

2.9. Human exposure to PPCPs

There has been a considerable interest regarding inadvertent human exposure to PPCPs as an emerging class of environmental contaminants. Such exposure can occur via drinking water with detectable concentrations of various PPCPs. It is worth mentioning that wastewater treatment processes are not sufficient to completely remove PPCPs even in developed countries like the United Kingdom, Canada, Australia and USA, which utilise advanced water treatment methods such as ozone or granular activated carbon (GAC) [1]. In developing countries like Nigeria, the supply of water by the state water board is not always reliable; therefore some households rely on borehole water that in most cases does not undergo any treatment [12]. Using our concentrations of target PPCPs in borehole water, as well as in bottled and sachet drinking water, equation (1) was applied to estimate inadvertent adult exposure to ΣPPCPs via drinking water in Nigeria

$$\text{Daily exposure} = \frac{\sum \text{PPCPs concentration x estimated daily water intake } (2L)}{\text{Average body weight of adult } (80kg)} \quad (1)$$

It is often presumed by the public that commercially-vended water (bottled or sachet) is highly purified and free from environmental pollutants. However, several target PPCPs were detected in bottled and sachet water samples bought from local shops in Lagos, Nigeria (Table 4, Tables SI–9). This includes amoxicillin (DF = 100%, average = 164 ng/L), glyburide (DF = 41%, average = 10 ng/L), caffeine (DF = 41%, average = 13 ng/L), nicotine (DF = 33%, average = 25 ng/L) and DEET (DF = 33%, average = 3 ng/L). Erythromycin, carbamazepine, propranolol, tramadol, hydrocortisone and trimethoprim were not detected in any of the studied commercially-vended water samples (Tables SI–9).

A study in Shanghai also detected an antibiotic (Florfenicol) used for veterinary purpose in bottled water purchased from supermarkets at concentrations of 0.6 ng/L, 0.76 ng/L and 1 ng/L in the same brand of bottled water [55].

The average concentrations of ΣPPCPs in the current study were 3240, 562, 110 ng/L resulting in average estimated adult exposures to Σ*PPCPs* of 81, 14 and 3 ng kg BW^{-1} day^{-1} via consumption of borehole, sachet water and bottled water, respectively (Table 4).

The concentrations of PPCPs identified in drinking-water in the current study are typically orders of magnitude less than the lowest therapeutic doses. While this may indicate low risk from exposure to single compounds, there are no toxicity endpoints or tolerable daily intakes of regulatory standing for inadvertent exposure to mixtures of PPCPs via drinking water or other exposure pathways [56]. This raises concern because while the estimated exposure may be lower than the reported toxic dose for a single pharmaceutical compound, concurrent exposure to such a complex cocktail of pharmaceutically active ingredients may result in unexpected toxic effects resulting from potential drug-drug interactions. More

Table 4
Statistical summary of ΣPPCPs (ng/L) in Bottled water, Sachet water and Borehole water and the resulting estimates of inadvertent Nigerian adult exposure to ΣPPCPs via drinking water.

Parameter	ΣPPCPs concentrations (ng/L)		
	Bottled water (n = 4[a])	Sachet water (n = 8[b])	Borehole water (n = 16[c])
Average	110	562	3240
Median	99	549	2450
Min	61	170	155
Max	183	1040	9170
Estimated adult exposure (ng ΣPPCPs/kg BW/day)			
Average	3	14	81
Median	2	14	61
Min	2	4	4
Max	5	26	229

[a] Collected during the rainy season.
[b] 4 samples collected in each of the rainy and the dry seasons.
[c] 8 samples collected in each of the rainy and the dry seasons.

toxicological research into the potential adverse effects of such inevitable exposure to PPCPs is urgently required for accurate risk assessment of this emerging class of environmental contaminants.

2.10. Study limitations

It is important to recognise the limitations associated with the limited sampling resources for the PPCPs seasonal variation study. One sample was collected from each location during the sampling campaign period comprising one month in each season. Single sampling events that represent an entire seasonal behaviour might have some bias in the results. This may be attributed to daily- and/or sub-daily variation in chemical concentrations in contaminated waterways, especially during the rainy season. Therefore, the current study findings provide useful "snapshot" information on seasonal variability, rather than a continuous monitoring programme. Nevertheless, our results provide first evidence on seasonal variation of PPCPs concentrations in Nigerian surface, ground and drinking water. This may be a necessary initial step to establish long monitoring programmes with multiple sampling events over several years to further investigate such seasonal variability in different countries.

3. Conclusion

The current study provides novel information on the concentrations and seasonal variability of 28 PPCPs in surface water, ground water and drinking water samples collected from Lagos, Nigeria. Although there were no significant differences ($P > 0.05$) in ΣPPCPs concentrations present in the three types of water studied; median concentrations of ΣPPCPs were in the order: surface water (4660 ng/L) > ground water (948 ng/L) > drinking water (424 ng/L). Amoxicillin was the most prevalent compound detected, which is of concern owing to the potential impact of such widespread occurrence on developing antibiotic-resistant bacterial strains. Seasonal variation in concentrations of some target PPCPs was observed between samples collected in the rain season (summer) and the dry season (winter). This could be attributed to several factors characteristic to the studied local environment, including: dilution by extensive rainfall, agricultural activities and usage patterns of pharmaceuticals among the local community. The presence of PPCPs in Nigerian drinking water leads to inadvertent human exposure. Average estimates of Nigerian adult exposure to ΣPPCPs in this study were: 81, 14 and 3 ng ΣPPCPs/kg BW/day via drinking borehole, sachet water and bottled water, respectively. While there exists no health-based limit value for chronic exposure to mixtures of PPCPs, our results raise concern and warrant further investigation of the potential health implications of such unintended exposure to PPCPs.

Declaration of competing interest

I hereby declare that none of the authors of this manuscript have any known conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.emcon.2020.02.004.

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