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Pharmaceuticals in the Environment: Levels of Selected Drugs in Water in Lagos, Nigeria

[1*]Ogah C. O, [1]Adetifa I. O. and [2]Basheeru K. A.

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Lagos, Nigeria.
[2]D.K. Olukoya Central Research Laboratory, University of Lagos, Nigeria.

ABSTRACT

Pharmaceuticals are discharged daily into the environment through drug manufacturing activities and from human and animal waste. Once in the environment, they are consumed unintentionally by the general population (in sub therapeutic amounts) and may cause human health and ecological adverse consequences over time. This study determined the levels of artemether, diclofenac and ofloxacin in samples from well, borehole and treated tap water in Mushin Area of Lagos State, Nigeria. Samples were collected using standard procedures and pre-concentrated by means of solid phase extraction cartridges. Analyses were carried out using HPLC with UV detector and analytes were quantified from standard calibration curves of the three drugs. The results show that artemether and diclofenac were present in borehole water in concentrations of 0.62 and 0.39 mg/L respectively and in treated tap water in concentrations of 0.04 and 0.17 mg/L respectively. Ofloxacin was detected in all three categories of water samples and the concentrations were 0.73, 0.24 and 0.08 mg/L for well, borehole water and treated tap water respectively. It is concluded that the levels of the three drugs in the samples were higher than WHO accepted values and therefore potentially harmful to human health.

Keywords: Water, artemether, diclofenac, ofloxacin, HPLC.

INTRODUCTION

Pharmaceutical waste generation is a rising concern, especially in the developing world. Increased drug manufacturing, emerging diseases and introduction of new drugs are some of the factors that may lead to rise in the amount of active pharmaceutical substances being discharged into the environment. Disposal of unused or expired pharmaceutical products down the drain or along with municipal waste is a common practice among communities; this practice, along with excretion of drugs by humans and animals constitute a route of entry for this group of contaminants into the environment (Jonathan and Nicolaos, 2005). Many pharmaceutical ingredients go through conventional water treatment processes without being removed (Chen and Zhou, 2014). This is due to low removal efficiency of these plants for pharmaceutical as they are mostly equipped to trap and remove suspended solids, biodegradable materials and infective agents. Therefore, untreated, as well as treated sewage and waste water (including leaches from landfills) are the main channels of active pharmaceutical compounds in environmental media (Anekwe *et al*. 2017). Some pharmaceuticals are known to affect the function of the endocrine system while others cause cancers, decreased fertility, congenital malformation, drug resistance, allergic reactions and other diseases in humans, wildlife and laboratory animals (Oliver *et al*. 2003; Oaks *et al*. 2004; Ng *et al*. 2006; Novo *et al*. 2013). Adverse health effects may also occur when individuals are exposed to a mixture of these compounds. Like most chemical contaminants, the effects of this group of compounds in the environment are seen after several years of exposure, which contributes to the low level of awareness on this issue. Moreover, pharmacists and other drug handlers are not trained on hazardous waste management while safety and environmental services managers are not familiar with the active ingredients and formulations of pharmaceutical products. This encourages the practice of improper disposal of pharmaceutical waste. Once in the environment, active pharmaceutical substances are consumed unintentionally by the general population (in sub therapeutic amounts) through food and water, and some can bioaccumulate due to their persistence in the environment (Ashton *et al*. 2004; Mnif *et al*. 2011; Raghav *et al*. 2013). This, coupled with the fact that pharmaceuticals are designed and used for their biological activity increases their potential for adverse human health and ecological impact after unintentional exposure over time. Compared to other chemical environmental contaminants, active pharmaceutical substances have received relatively low attention especially in developing nations like Nigeria. There is therefore a need to monitor the levels of these chemicals in the environment. Well, borehole and treated tap water are the most common sources of water supply for domestic use and for the production of drinking water in Nigeria.

*Corresponding Author: Email – onotsec@yahoo.com Phone – +234802 314 8053

Surface and ground water have been reported to be contaminated with active pharmaceutical substances in different countries (Kolpin *et al*. 2002; Nikolaou *et al*. 2007; Fick *et al.* 2010, Randir and Rolf, 2013; Lindholm-Lehto *et al.* 2015, Shraim *et al*. 2017). The type of pharmaceuticals detected depends largely on the pattern of drug use and drug development activities in the studied environment (Tauxe-Wuersch *et al.* 2005). In a densely populated area like Mushin in Lagos state of Nigeria, many people are bound to use medicines to treat common ailments on a regular basis. Also, a number of medical centers and hospitals are located in Mushin Local Government Area. Pain and bacterial infections are common, and malaria is still endemic in Nigeria. Antimalarials, analgesics and antibiotics have been reported to be among the commonly prescribed drugs in medical facilities in Lagos (Oshikoya and Ojo, 2007; Olaitan *et al*. 2014). Other countries (Malaysia, Canada, Switzerland, England, USA, Italy, etc.) have available data on pharmaceuticals in various types of water samples (Golet *et al*. 2002; Kolpin *et al.* 2002; Anekwe *et al.* 2017). Similar data for Nigeria is scanty. This study analysed water samples from three sources for presence of commonly used drugs in a selected location in Lagos, Nigeria.

MATERIALS AND METHODS

Materials and Equipment

HPLC (Agilent technologies 1200 series) with UV detector; Methanol (HPLC grade), all other chemicals and reagents were of analytical grade. Artemether and Diclofenac standards were sourced from Sigma Aldrich (Steinheim, Germany) while Ofloxacin was a USP reference standard.

Collection of Samples

Water samples were collected from wells, boreholes and Water Corporation taps into one litre amber glass bottles with Polytetrafluoroethylene (PTFE)-lined screw caps. Five samples each, from wells and boreholes were collected from different locations in Mushin Local Government while tap water samples were collected at the Water Corporation plant serving the area. Water from the tap was allowed to flush for 2 minutes for the water temperature to stabilize before collecting into bottles. Samples were maintained below 10 ^{o}C by means of ice packs and transported to the laboratory. At the laboratory, the samples were stored below 6 ^{o}C and protected from sunlight until analysis.

Preparation of Samples

Samples were extracted and pre-concentrated using solid phase extraction cartridges (C-18). HPLC grade water was used as conditioning solvent while 10% methanol and 100% methanol were used as washing and eluting solvents respectively. EDTA was added to remove any dissolved heavy metals from the eluates.

Preparation of Standard Solutions

Stock solutions (1 mg/ mL) of the standard artemether, diclofenac and ofloxacin were prepared in acetonitrile and working solutions of 50, 25, 12.5 and 6.25 µg/mL were prepared each day by serial dilution.

HPLC Analysis

Analyses were carried out using HPLC (Agilent technologies 1200 series) with UV detector (Fatta *et al*. 2007; Cesar and Pianetti, 2009). The analytes were separated under their respective chromatographic conditions as stated in Table 1. Concentrations of the test drugs in the water samples were calculated from their respective standard calibration line equations.

Table 1: Chromatographic Conditions for the Three Drugs

	Diclofenac	Ofloxacin	Artemether
Stationary Phase	YMC C18 (150 x 4.6 mm, 5µ)	YMC C18 (150 x 4.6 mm, 5µ)	YMC C18 (150 x 4.6 mm, 5µ)
Mobile Phase	$^{+}$Buffer : CAN (40:60)	$^{+}$Buffer : ACN (30:70)	Distilled water: CAN (40:60)
Flow Rate	0.7 ml/min	0.6 ml/min	1.5 ml/min
UV Detector Wavelength	210 nm	274 nm	216 nm
Injector Volume	10 µl	10 µl	10 µl
Acquisition Time	6 minutes	7 minutes	10 minutes

Key: ACN-Acetonitrile; $^{+}$0.01 M potassium hydrogen phosphate, adjusted to pH 3.1 with formic acid.

Analysis of Data

Concentrations of the drugs in the water samples were expressed as mean ± standard deviation. They were compared with WHO reported values using Student t-test at $p < 0.05$.

RESULTS

Mean retention times for Artemeter, Diclofenac and Ofloxacin were determined as 7.53, 4.18 and 2.80 minutes respectively as reflected in Figure 1. Artemeter was detected in borehole and treated tap water in concentrations of 0.62 µg/mL and 0.04

µg/mL respectively. Diclofenac was found at lower concentrations of 0.39 µg/mL and 0.17 µg/mL in borehole and treated tap water samples respectively. Both drugs were not detected in well water samples. The concentrations of Ofloxacin were 0.73, 0.24 and 0.08 µg/mL in well, borehole and treated tap water samples respectively. The results are presented in Table 2. A comparison of levels of the drugs in water samples from the three sources is presented in Figure 2.

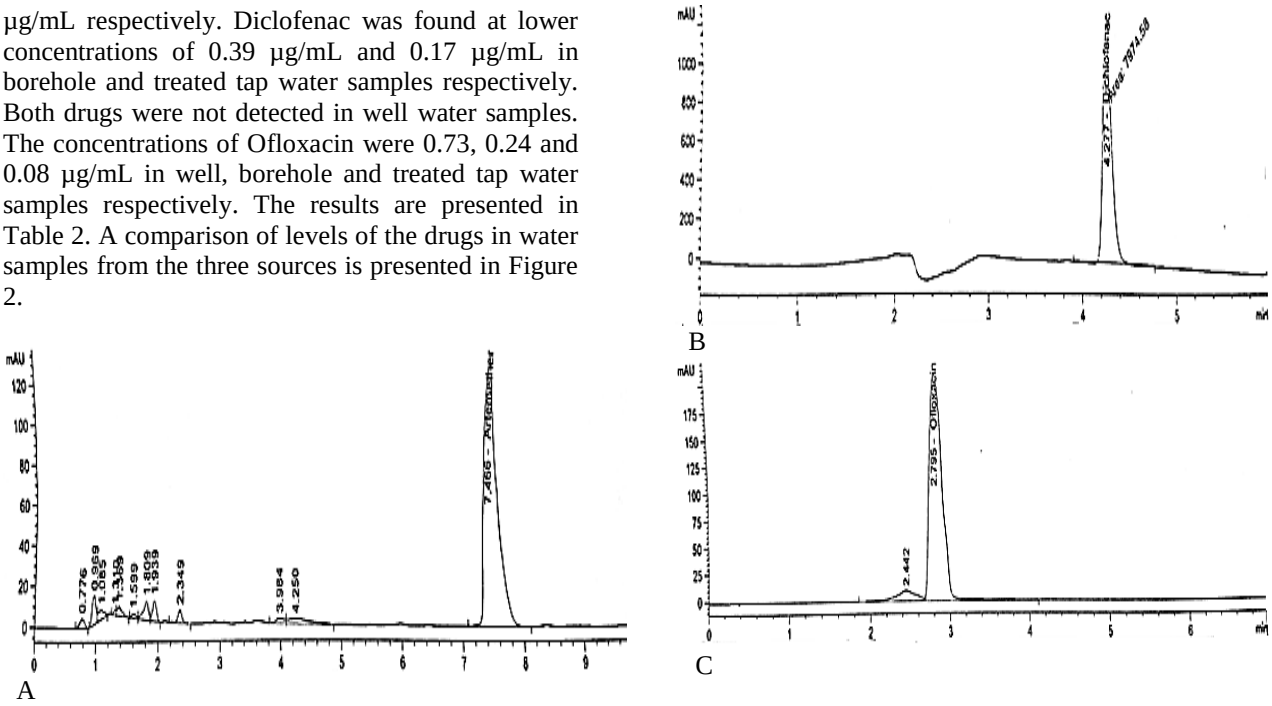

Figure 1: HPLC chromatograms for Standard Artemether (A), Diclofenac (B) and Ofloxacin (C) at 50 µg/mL

Table 2: Concentrations of drugs in the water samples

Pharmaceuticals	Water source	Area (mAU*s)	Concentration (mg/L)
Artemether	Well water	0.000	Nd
	Bore hole water	23.245	0.62 ± 0.03
	Treated tap water	8.900	0.04 ± 0.01
Diclofenac	Well water	0.000	Nd
	Bore hole water	26.932	0.39 ± 0.05
	Treated tap water	6.215	0.17 ± 0.01
Ofloxacin	Well water	65.605	0.73 ± 0.04
	Bore hole water	34.736	0.24 ± 0.05
	Treated tap water	7.452	0.08 ± 0.01

Nd = Not detected; Concentrations are expressed in mean ± standard deviation (n = 5).

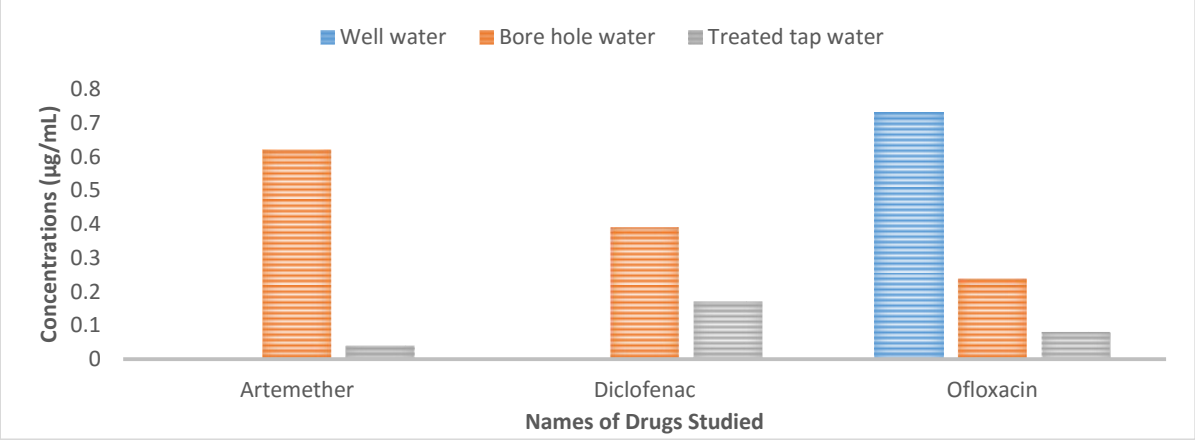

Figure 2: Comparison of drug levels in water samples from the three sources.

DISCUSSION

Water is an indispensable resource in any human community. In Lagos, Nigeria, many households do not have access to treated tap water from government Water Corporation. They have to sink boreholes or dig wells to obtain adequate water for domestic use; in some cases, water from these sources serves as drinking water and for production of packaged water. In this study, artemether was found in bore hole and treated tap water in concentrations of 0.62 mg/L and 0.04 mg/L respectively, but was not detected in well water. The drug is a common component of WHO recommended artemisinin-based combination therapy (ACT), often used in combination with lumefantrin for treatment of acute uncomplicated malaria. Artemether is only slightly soluble in water and so may not be easily degradable in aquatic environment. Concentrations up to 32 mg/L in wastewater have been reported in a study in Tanzania (Miraji *et al*. 2016). From waste and effluent water, residues of pharmaceutical active substances can find their way into ground and surface water, appearing in much lower concentrations. Not much has been reported of the levels of this drug in well, borehole and tap water. Diclofenac is a non-steroidal anti-inflammatory agent, commonly used in the treatment of arthritis and other inflammatory diseases. In this study, it was found in concentrations of 0.39 mg/L and 0.17 mg/L in borehole and treated tap water respectively. Diclofenac is a known endocrine disruptor (Anekwe *et al*. 2017), that is, it has the ability to interfere with the functions of endocrine glands (such as thyroid, adrenal and reproductive glands) and their hormones. Other studies in Europe, US and the United Kingdom have found residues of this drug in wastewater, river and ground water in varying concentrations ranging from 0.0005 mg/L to 1.2 mg/L (Kasprzyk-Hordern *et al*. 2008; Varga *et al.* 2010; Randhir and Rolf, 2013; Zhou and Broodbank, 2014). In Nigeria, Olaitan *et al.* (2014) have detected diclofenac (17 mg/L) in well water close to the effluent discharge point of a pharmaceutical company in Ogun State. Diclofenac in concentrations of 5-50 mg/L has been reported to adversely affect the kidney, gill integrity and immune system of fish (Hoeger *et al*. 2005; Ng *et al.* 2006). It has also been associated with nephrotoxicity in humans (Hickey *et al*. 2001). Ofloxacin was detected in all the samples tested, in concentrations of 0.73, 0.24 and 0.08 mg/L for well, borehole and treated tap water respectively. This broad spectrum quinolone antibiotic has also been detected in the sediments of some rivers in China (Zhou *et al*. 2011) at concentrations of 1.3 mg/Kg and in well water in India at much lower concentrations ranging from 26 – 480 ng/L. An important concern about ofloxacin in water is its potential to cause antibacterial resistance, a situation in which usually susceptible bacteria develop resistance to ofloxacin and related antibiotics due to frequent exposure of the populace to sub-therapeutic doses of the drug. This may pose a threat to effective treatment of various infectious diseases. WHO acceptable values for concentrations of pharmaceuticals are less than 0.1 µg/L in surface water and groundwater; and below 0.05 µg/L concentrations in treated water (World Health Organization, 2012). These are based on values obtained from studies in some developed nations which have formed the yard stick in the absence of current guideline values. Although the concentrations of drugs found in this study seem low in absolute terms, they are much higher than the WHO accepted values stated above. This may be indicative of excessive discharge/disposal of these pharmaceuticals in the environment around the studied location. For each of the drugs studied, concentrations in treated tap water were lower than in borehole and well water, an indication that the treatment method was able to remove these chemicals to some extent. This is also in tandem with values accepted by WHO. In the case of ofloxacin, concentration was higher in the well than in borehole water; proximity to the source of the contaminant could explain this, though the source of ofloxacin could not be established in this study. Another factor is that for domestic use, boreholes are usually deeper than wells and this means longer travel distances of contaminants through the aquifer, with longer time and possible opportunities for degradation of some of the contaminants before they enter borehole water.

Extensive and increasing use of human and veterinary medicines expectedly results in continuous discharge of these agents into the environment. This may lead to pseudopersistence, a situation in which pharmaceuticals that are degradable would eventually and effectively behave as persistent compounds because of replenishment due to their constant release into the environment (Loffler *et al*. 2005). These factors are contributory to high levels of pharmaceuticals in environmental media, such as water and may have contributed to the high values obtained in this study. New strategies need to be devised to reduce the quantities of pharmaceuticals in these sources of water in order to minimize human exposure to these chemicals.

CONCLUSION

Artemether and Diclofenac were detected in borehole water in concentrations of 0.62 and 0.39 mg/L respectively and in treated tap water in concentrations of 0.04 and 0.17 mg/L respectively. Ofloxacin was

detected in all three categories of water samples and the concentrations were 0.73, 0.24 and 0.08 mg/L for well, borehole water and treated tap water respectively. The concentrations found in the study were higher than WHO accepted values and some previously reported values from studies in other countries. There is therefore a high potential for adverse human health impact. The study has contributed to data on environmentally relevant pharmaceutical contaminants in Nigeria but studies of broader scope are required to establish a pattern of contamination in water and other environmental media.

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