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Research Article

Prevalence and Detection of Pharmaceuticals in Hospital Wastewater: A Case of Referral and District Hospitals in Zanzibar

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Abstract: Despite the great efforts taken by the developed and some developing countries in managing the release of pharmaceuticals from their primary sources to the environment; the pharmaceutical wastewater management in Zanzibar-Tanzania still has not received much attention as a bulk of pharmaceuticals and their metabolites are released to the environment without proper treatment. Therefore, this study has scrutinized the incidence of pharmaceuticals in wastewater released from the referral and district hospitals in Zanzibar, to ascertain the levels of pharmaceuticals present in hospital wastewater. Purposive sampling was implemented to collect a total of seventy-two (72) wastewater samples in a period of six months (March-August 2022). Samples were collected in the effluent of wastewater-streams (Mnazi Mmoja Hospital, MMH) and pit latrines (Kivunge District Hospital (KDH) and Makunduchi District Hospitals (MDH)). The pharmaceuticals in these samples were obtained via the solid phase extraction after which they were analyzed using the LC-tandem MS (Agilent 1,290 LC coupled to 6,460-triple quadrupole MS). The limit of detections (LODs) and limit of quantitations (LOQs) for the determination of pharmaceuticals were in the range of 0.021-0.037 μg L^{-1} and 0.033-0.059 μg L^{-1}, respectively. The detected analytes belonged to antibiotics, anti-inflammatory, benzodiazepine, antipsychotic, antipyretic and anticonvulsant (anti-epileptic) drugs. Diclofenac (DIC), paracetamol (PCT), ciprofloxacin (CIP), sulfamethoxazole (SMZ) and azithromycin (AZM) were detected at higher concentrations (> 0.25 μg L^{-1}) in wastewater samples collected from KDH and MDH. Lower concentrations of pharmaceuticals (< 0.10 μg L^{-1}) were identified in MMH wastewater samples. These present findings provide estimable information on the incidence of pharmaceuticals in wastewater that can assist in strengthening the environmental strategies for the protection of marine and terrestrial life from pharmaceutical pollution in Zanzibar.

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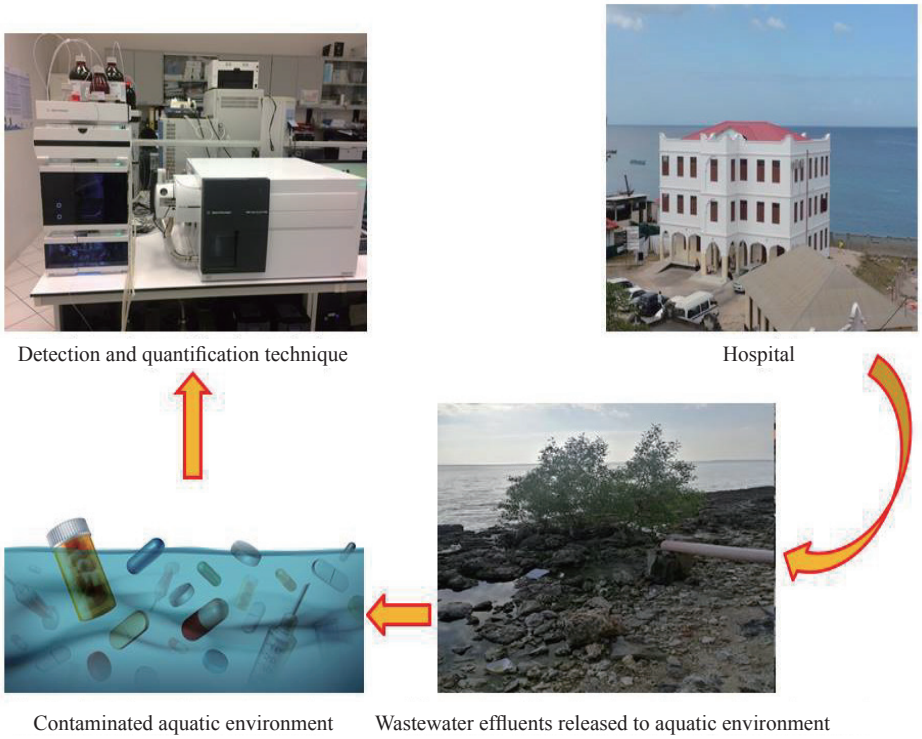


***Keywords*:** detection, pharmaceuticals, wastewater, hospital, zanzibar

1. Introduction

Water is a necessary component in the life of organisms; therefore, its consumption must be effectively managed to preclude it from contamination.[1] In recent times, the presence of pharmaceuticals in marine surroundings has garnered significant attention due to the noxious effects of these classes of contaminants on aquatic environments and human safety.[2-4] This coupled with the recent advancement in the development of analytical techniques which has enabled the detection of pharmaceuticals even at trace concentration may be a reason for the heightened interest shown by scientists on this subject.[5] Pharmaceuticals can enter water bodies directly from pharmaceutical industries, hospitals, wastewater treatment plants, and households[5] or be excreted through urine and reach the aquatic habits through sewage system[6] or atmospheric wet deposition.[7] However, the principal route for the discharge of pharmaceuticals into marine surroundings has been attributed to hospital and domestic waste.[8] This incident has rising attention to the fate of pharmaceuticals in marine environments.

The presence of raw hospital wastewater in the surroundings is of global concern due to its adverse effect on the ecosystem upon release.[9] Several treatment techniques including biological treatment[10-12], submerged aerobic fixed film reactor-coupled with tubesettler[9,13], constructed wetland[14], membrane bioreactor-coupled with ozonation[15] have been applied for the remediation of hospital wastewater. In Zanzibar, the application of advanced treatment methods for the sequestration of noxious pharmaceutical contaminants in hospital wastewater is not well implemented. Among the reasons for this observation are the high operational and maintenance costs of advanced wastewater-removal-techniques, and also the lack of practical knowledge of using low-cost methods that have proven to be most effective in removing these compounds in contaminated water.

Several wastewater-streams are discharged from Mnazi Mmoja Hospital (MMH) to the adjacent coastline. Since this wastewater is coming from hospitals, there is a possibility of being contaminated with pharmaceuticals including antibiotics; therefore prolonged exposure to these antibiotics may result in antibiotic resistance which impairs the ecological systems.[6,16,17] For instance, Amasari et al.[18] reported that organisms exposed to this condition are at health risk as they are easily prone to antibiotic resistance genes (ARG) and antibiotic resistant bacterial (ARB) infections. These

infections are affirmed to have high morbidity and mortality rates as can be inferred from the report which indicated that about 671,700 infections with 33,000 associated deaths were reported in 2015[19], which is expected to increase by 2050.[20,21]

Although, many precautions and environmental pharmaceutical monitoring have been taken from the developed and some developing countries; however, in Tanzania (including Zanzibar), the management of pharmaceuticals from their primary sources to aquatic and terrestrial environments still has not received much attention. Several pharmaceuticals and their metabolites from the hospitals are released into marine environments, trenches and pit latrines without proper management and treatment. Despite this release, no current literature is available on the kinds of pharmaceuticals and their concentrations present in influents and effluents from the hospitals in Zanzibar. Therefore, there is a need to conduct research to identify the incidence of pharmaceuticals in wastewater released from hospitals. This study seeks to identify and assess pharmaceuticals present in wastewater from the referral hospital (Mnazi Mmoja Hospital) and district hospitals (Kivunge District and Makunduchi District hospitals) and their concentration levels.

2. Materials and experimental

2.1 *Chemicals and reagents*

Ibuprofen (IBU), diclofenac (DIC), naproxen (NAP), paracetamol (PCT), ampicillin (AMP), ciprofloxacin (CIP), trimethoprim (TMP), sulfamethoxazole (SMZ), cloxacillin (CLOX), azithromycin (AZM), phenoxymethylpenicillin (PcV), amoxicillin (AMOX), diazepam (DZP), haloperidol (HAL), carbamazepine (CBZ), acetonitrile (ACN), methanol, sulfuric acid (SA) and triethylamine (TEA) used in this study were of highest purity (LC-MS or HPLC grade, > 99%) and purchased from Sigma-Aldrich (Shanghai) Trading Co., Ltd.

2.2 *Description of the study areas*

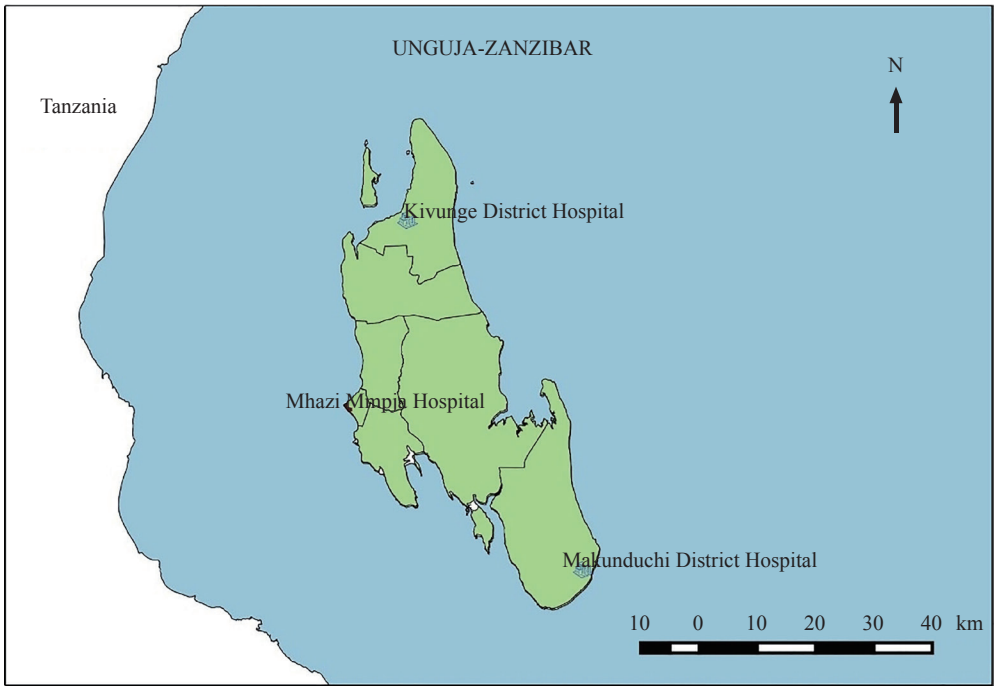


Figure 1. Location of sampling sites: Mnazi Mmoja, Kivunge District and Makunduchi District Hospitals

Mnazi Mmoja Hospital (MMH) is located on the west coast of Unguja Island (5°56'0"S 39°17'0"E), about 1 km

from Stone Town, Zanzibar (Figure 1). At MMH, the samples of wastewater were collected from the effluent discharged to the aquatic environment. However, Kivunge District Hospital (located in Unguja North Region, 5°52'44.8"S 39°17'05.9"E) and Makunduchi District Hospital (located in Unguja South Region, 6°25'00.4"S39°33'19.8"E), the wastewater samples were obtained from hospital latrines. The pictures taken from the sampling sites are shown in Figure 2. The choice of the study areas is greatly influenced by the fact that Mnazi Mmoja Hospital is the referral hospital, while Kivunge and Makunduchi hospitals both are district hospitals in Zanzibar. These hospitals usually received several in-patients and out-patients daily who consumed different pharmaceuticals for medical purposes.

Figure 2. Photos taken from sampling sites

2.3 *Preparation of stock solutions*

The standard solution (1,000 μg/mL) of each target pharmaceutical was prepared using HPLC grade methanol (CH_3OH) and stored at 4 °C in the dark chamber to increase stability and prevent photodegradation of the sensitive pharmaceuticals. The following procedures were followed to prepare a stock solution of target pharmaceuticals; approximately 0.01 g each of pharmaceuticals (IBU, DIC, NAP, PCT, AMP, CIP, TMP, SMZ, CLOX, AZM, PcV, AMOX, DZP, HAL and CBZ) was precisely weighed and added into the volumetric flask (10 mL), and then dissolved with CH_3OH up to the mark to get a stock solution of 1,000 mg/L.

2.4 *Sampling and experimental design*

Purposive sampling was considered in this study due to the nature of the study areas. Maximum samples were collected from the study areas in a specific period (six months) to assess the occurrence and concentration levels of the pharmaceuticals present in the designated hospital wastewater. The collection was done without considering the seasonal variations that might influence the hospital wastewater physicochemical properties and the studied pharmaceuticals. The samples were specifically collected from wastewater-streams (outlet) adjacent to the coastline (Mnazi Mmoja Hospital) and pit latrines (Kivunge District and Makunduchi District hospitals). Two wastewater samples were taken at each hospital every week for a period of twenty-four weeks (March-August 2022). Seventy-two (72) samples of wastewater were subjected to solid phase extraction coupled with high-pressure liquid chromatography-tandem mass spectrometry (LC-MS/MS) to assess the pharmaceuticals present. Sample collection method, solid phase extraction (SPE) and analysis of pharmaceuticals were done with minor modifications according to the procedures described by Abafe et al.[22] Herein, the LC-MS/MS method was validated with major modification according to the methods described by

Sveshnikova et al.[23]

2.5 *Validation of method*

The method validation was done (concerning the linearity, sensitivity and recovery) to establish the rationality of test results. Method linearity was validated from the regression analysis using nine-point calibration curves for every analyte (peak area vs. concentrations of pharmaceutical). These curves were plotted to determine the precise concentration of pharmaceuticals in a sample. As indicated in Table 1, the linearity of calibration curves of all pharmaceuticals has higher regression coefficients ($R^2 > 0.980$). The sensitivity of the method was evaluated by considering both the LODs and LOQs (equations 1 and 2, respectively). The results indicate that the LODs and LOQs are in the range of 0.021-0.037 μg L^{-1} and 0.033-0.059 μg L^{-1}, respectively. The percentage recovery was determined based on the spiked amount of pharmaceuticals in comparison to the measured concentration target matrices.

$$LOD = \frac{concentration\ of\ lowest\ spiked\ level}{average\ of\ S/N} \times 3 \quad (1)$$

$$LOQ = \frac{concentration\ of\ lowest\ spiked\ level}{average\ of\ S/N} \times 10 \quad (2)$$

Table 1. Linearity, LOD and LOQ of the pharmaceuticals

Pharmaceuticals	Linearity (R^2)	LOD (μg L^{-1})	LOQ (μg L^{-1})
Ibuprofen	0.991	0.023	0.037
Diclofenac	0.989	0.025	0.048
Naproxen	0.983	0.028	0.036
Paracetamol	0.993	0.025	0.054
Ampicillin	0.989	0.037	0.045
Ciprofloxacin	0.998	0.031	0.048
Trimethoprim	0.992	0.022	0.033
Sulfamethoxazole	0.996	0.034	0.041
Cloxacillin	0.986	0.029	0.047
Azithromycin	0.995	0.034	0.055
Penicillin	0.989	0.026	0.059
Amoxicillin	0.986	0.031	0.044
Diazepam	0.991	0.034	0.047
Haloperidol	0.997	0.021	0.052
Carbamazepine	0.984	0.026	0.038

2.6 *Physicochemical and LC-MS/MS analysis*

Physicochemical characteristics of hospital wastewater were determined with minor modifications to the standard methods performed by Haeusser et al.[15] by considering the pH, electroconductivity (EC), chemical oxygen demand (COD), total dissolved solids (TDS) and turbidity (TUR). These properties were analyzed using the respective instruments, namely, Mettler Toledo FP30-standard, Mettler Toledo conductivity S23030019034, COD digester reactor Hach Lange LT200, Mettler Toledo conductivity S23030019034 and Oakton T-100 turbidity meter. The instruments were calibrated, and the reagents and solutions used were of analytical grade and standard.

For LC-MS/MS analysis, approximately 2 L of samples from each hospital was collected and directly stored in an ice pack (at < 4 °C), then transported to the laboratory. The samples were put in amber bottles (pre-cleaned with 0.1% nitric acid) covered with aluminium foil to preclude the photodegradation of light-sensitive pharmaceuticals. At the laboratory, the samples were preserved at -20 °C until subjected to analysis. 50 mL of every sample were sieved through a 0.45 µm membrane and the filtrate was adjusted to pH 3.0 using 0.1 M H_2SO_4. Then the samples were subjected to SPE. Samples were carried through a C-18 cartridge activated with CH_3OH (5 mL), 5 mL of CH_3OH/H_2O 50/50 (v/v) and 5 mL of H_2O at pH 3.0. 5 mL of triethylamine (5% v/v) was then used to elute the cartridge in CH_3OH. The eluted solution was vaporized to 20 µL utilizing nitrogen gas at 50 °C. Finally, the volume of the samples was reconstructed to 1 mL by the addition of H_2O/TEA (95/5 v/v) and then injected into the LC-MS/MS (Agilent 1,290 LC coupled to 6,460-triple quadrupole MS). Analysis of samples was done at the Chief Government Chemist Laboratory Agency (CGCLA) and Tanzania Bureau of Standards (TBS).

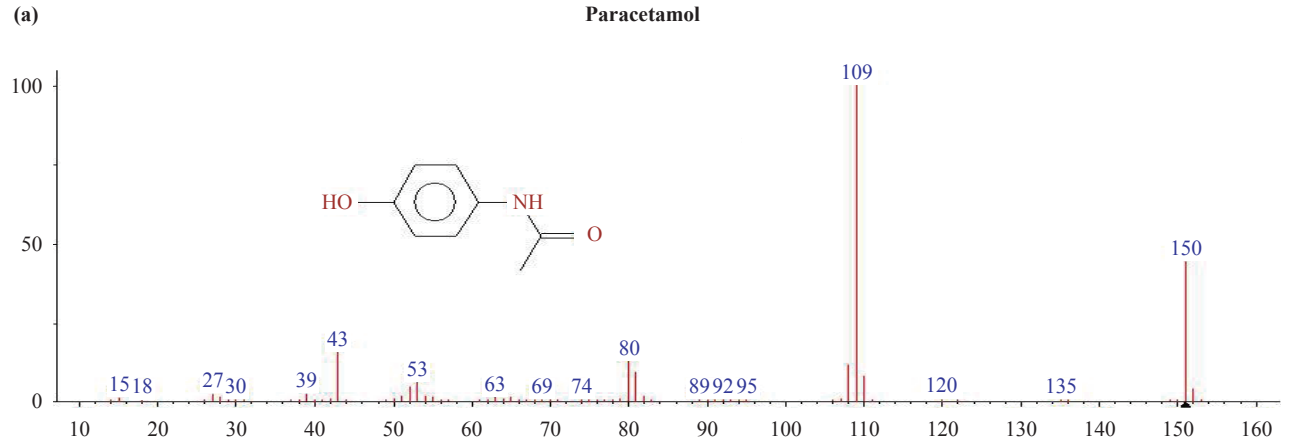
2.7 *Statistical analysis*

Hospital wastewater samples were analyzed in triplicates. Descriptive analysis was performed and the data were computed to obtain the mean and standard deviation using Origin 9.1 and presented as mean ± S.E., (n = 3). Pharmaceutical concentrations are presented in µg L^{-1}.

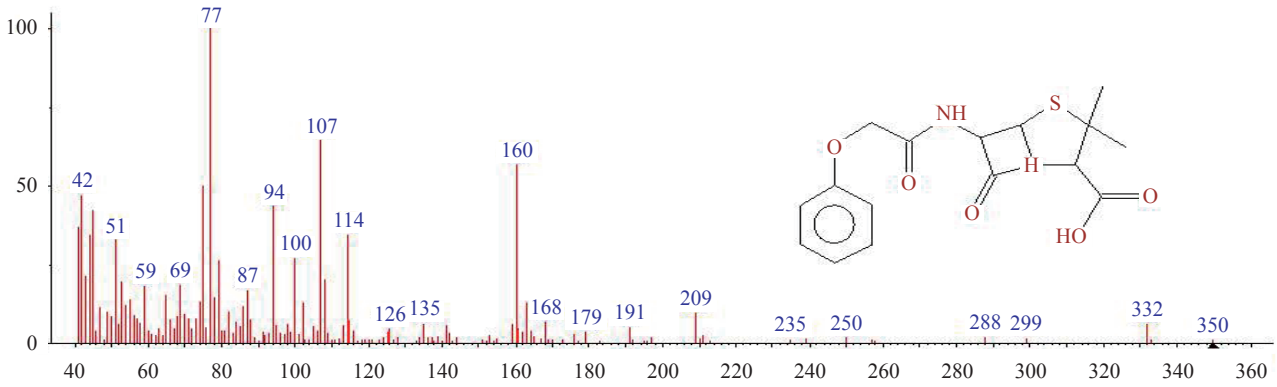
3. Results and discussion

3.1 *Mass spectra analysis*

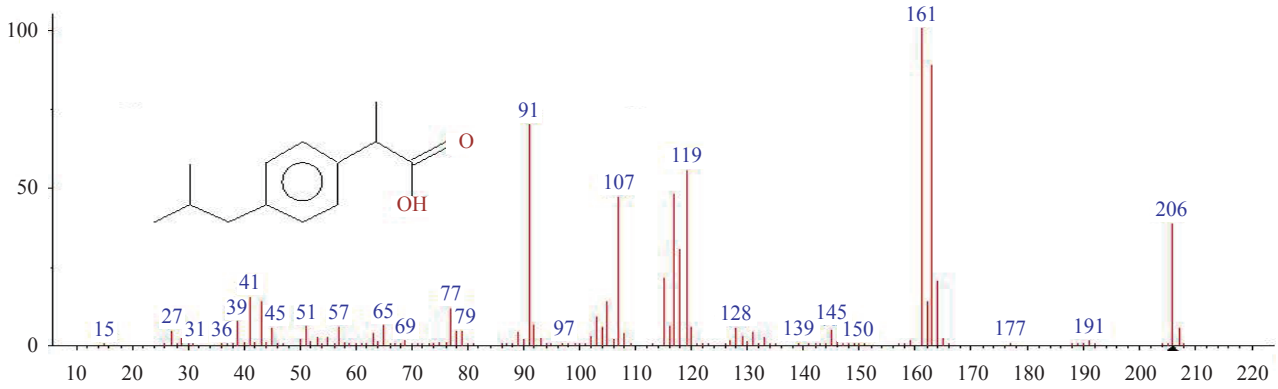
Figure 3 (a-j) shows the full scan mass spectra of the pharmaceuticals detected in the hospital wastewater samples. These spectra indicate the precursor ions and major fragments of paracetamol/acetaminophen (a), phenoxymethyl penicillin (b), ibuprofen (c), naproxen (d), ciprofloxacin (e), trimethoprim (f), sulfamethoxazole (g), diazepam (h), haloperidol (i) and carbamazepine (j).



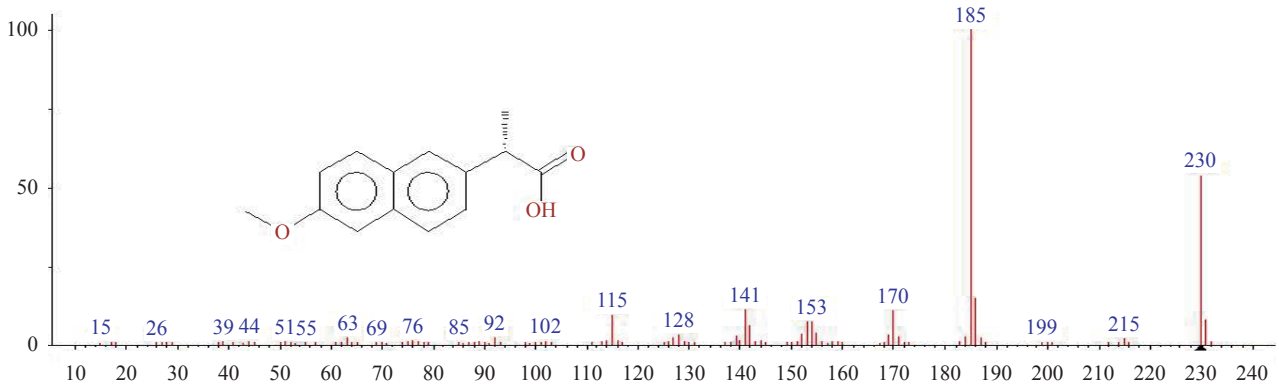
(b) **Phenoxymethyl penicillin**



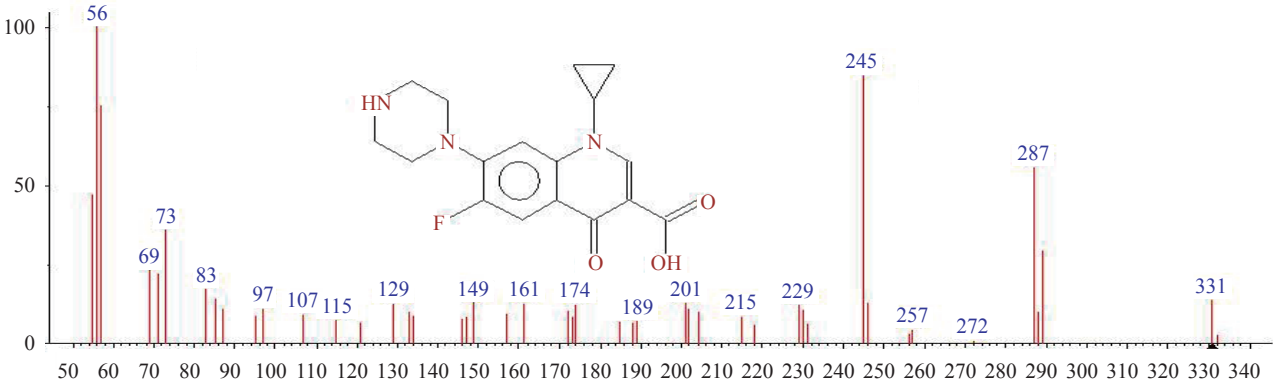
(c) **Ibuprofen**



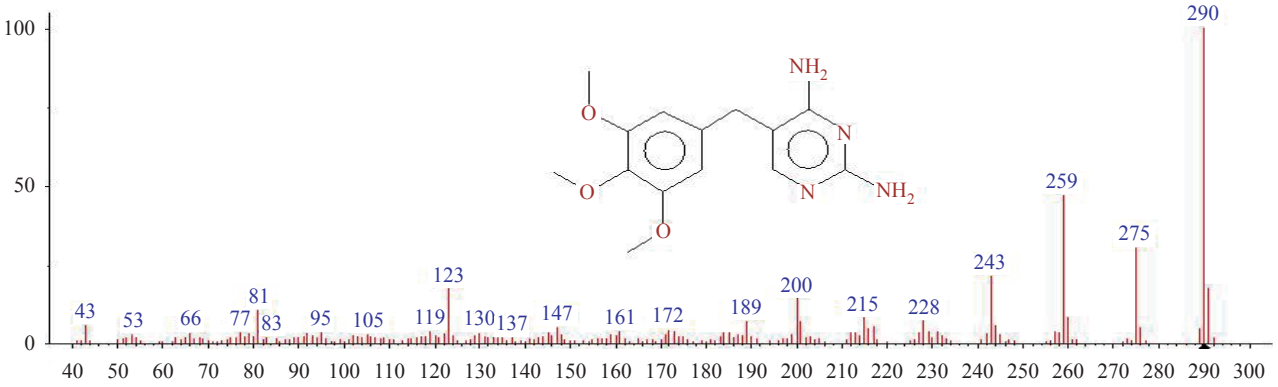
(d) **Naproxen**



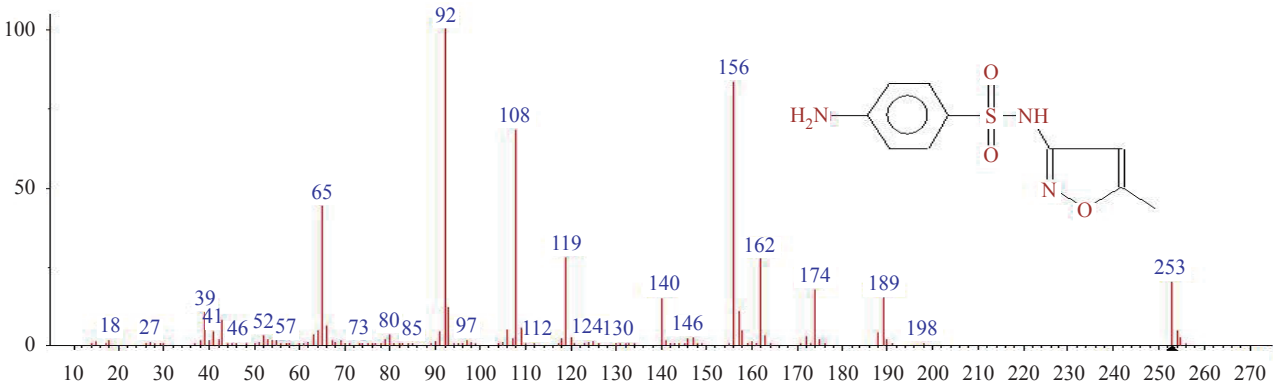
(e) **Ciprofloxacin**



(f) **Trimethoprim**



(g) **Sulfamethoxazole**



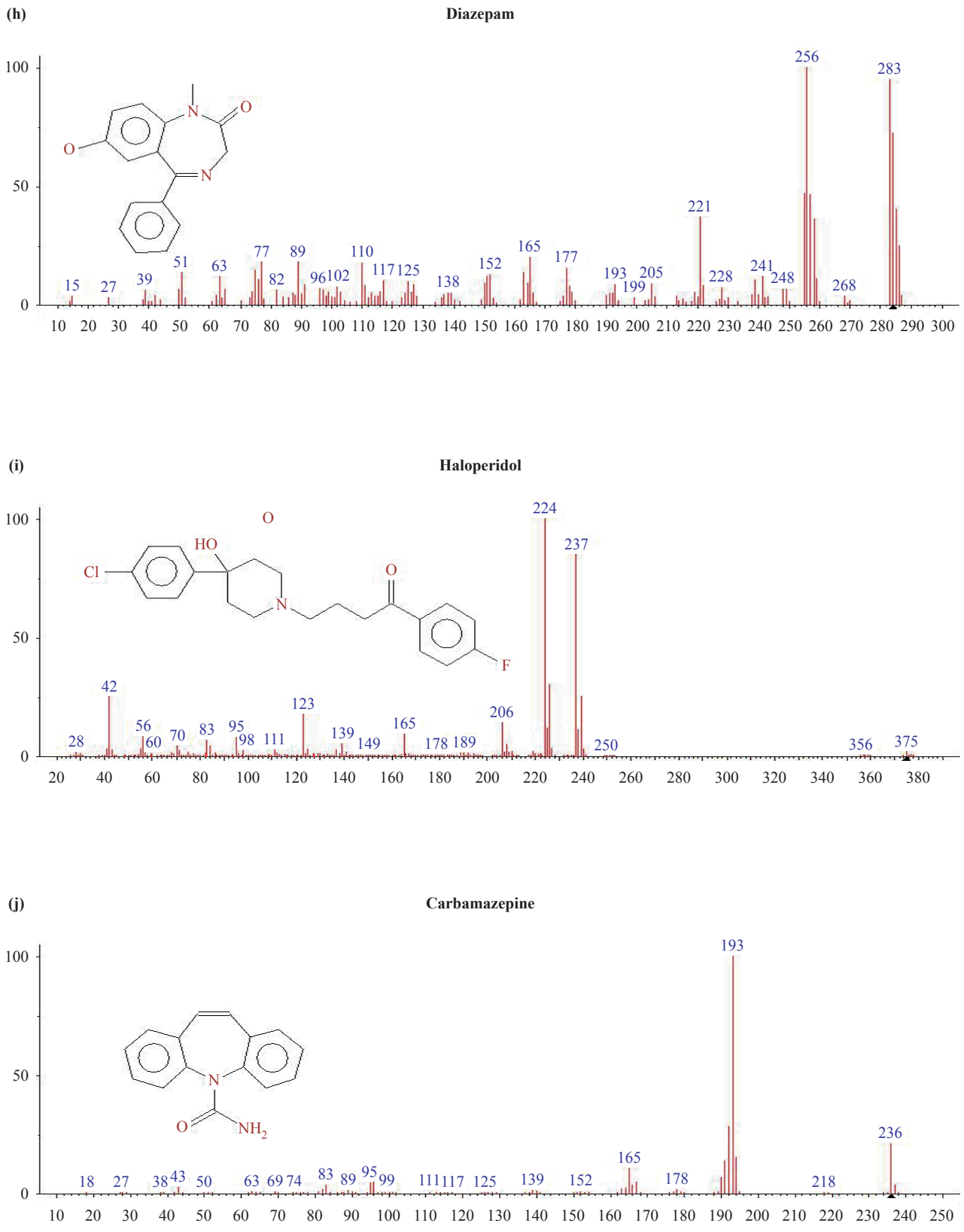


Figure 3. Full scan mass spectra of the pharmaceuticals detected in wastewater samples

3.2 *Physicochemical properties of hospital wastewater*

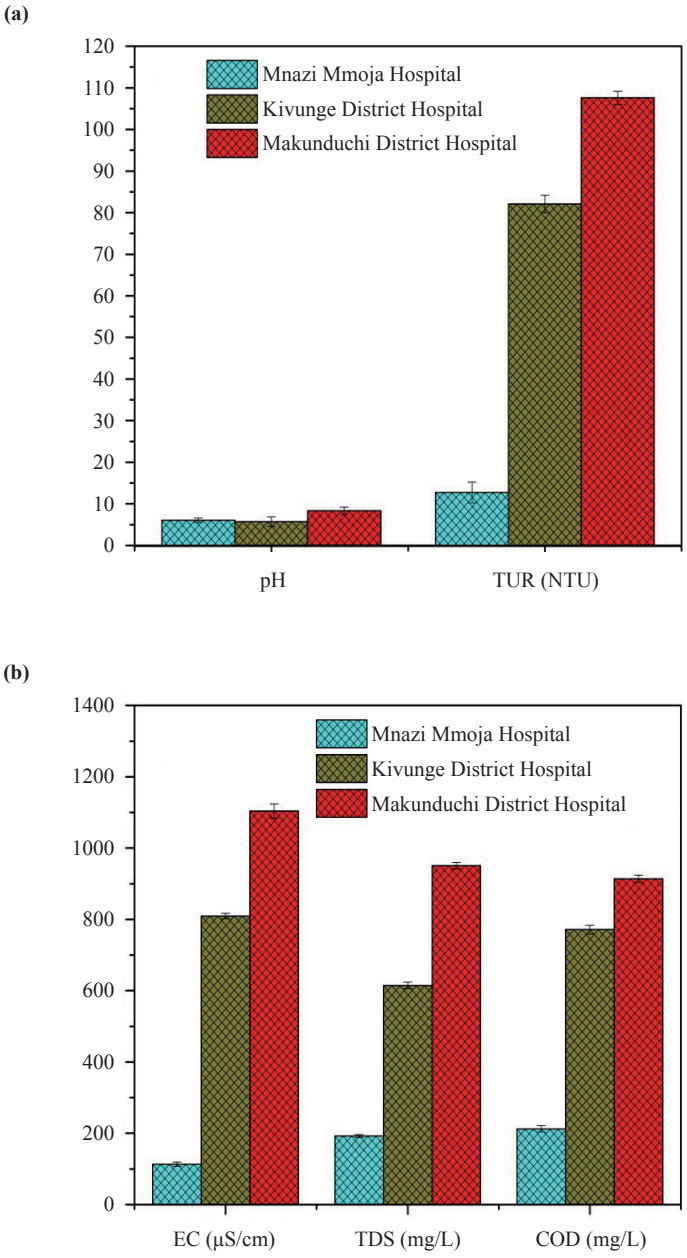


Figure 4. Physicochemical properties of hospital wastewater; (a) pH and turbidity (TUR), (b) Electroconductivity (EC), Total Dissolved Solids (TDS) and Chemical Oxygen Demand (COD)

Physicochemical characteristics of hospital wastewater effluent (MMH) and influents (KDH and MDH) are presented in Figure 4. The results indicate that the pH values of samples taken from MMH and KDH were slightly acidic (6.05 ± 0.24 and 5.72 ± 1.15, respectively) while that of MDH was in an alkaline medium (8.31 ± 0.92). Moreover, KDH and MDH samples have higher levels of EC (809.4 ± 7.8 and 1,103.6 ± 20.2 µS/cm), TDS (614.7 ± 8.7 and 950.3 ± 9.3 mg L^{-1}), COD (771.2 ± 12.4 and 913.0 ± 10.5 mg L^{-1}) and TUR (82.1 ± 2.1 and 107.6 ± 1.6 NTU) compared to MMH samples (113.2 ± 6.3 µS/cm, 192.1 ± 4.2 mg L^{-1}, 212.3 ± 9.1 mg L^{-1}, 12.7 ± 2.5 NTU, respectively) (Figure 4). This indicates that KDH and MDH wastewater have large inputs of nutrients and organic matter. These

constituents can reduce the dissolved oxygen in aquatic surroundings; consequently, promoting the growth of pathogenic microorganisms and aquatic weeds.[24] The presence of higher amounts of organic matter and nutrients in wastewater can impair water quality and result in adverse effects on the ecological systems[25], due to the presence of potential noxious compounds. The lower levels of EC, TDS, COD and TUR in Mnazi Mmoja hospital effluents could be explained by the fact that some organic matters and nutrients were degraded or removed in the wastewater treatment plant (membrane filtration process) before the effluents were released into the aquatic environment.

The average COD concentrations (212.3-913.0 mg L^{-1}) in the wastewater effluents/influents of MMH, KDH and MDH are relatively lower compared to the ones reported from hospital wastewater in Brazil (2,480 mg L^{-1}), Spain (2,464 mg L^{-1}), India (1,142 mg L^{-1}) and South America (1,074 mg L^{-1}).[26-28] In addition, the TDS of wastewater effluents/influents (192.1-950.3 mg L^{-1}) found in this study was lower than that reported by Rehman et al.[29] in Faisal Hospital (2,710 mg L^{-1}). Table 2 presents the physicochemical characteristics of wastewater of MMH, KDH and MDH compared to the Environmental Protection Agency (EPA) standards. It is very obvious that some of the parameters for MMH, KDH and MDH wastewater do not comply with EPA standards.

Table 2. Comparison of physicochemical properties of wastewater from MMH, KDH and MDH, and that of EPA standards

Parameters	MMH	KDH	MDH	EPA standards*
pH	6.05	5.71	8.31	6.0-9.0
EC (µS/cm)	113.2	809.4	1103.6	750
TDS (mg/L)	192.1	614.7	950.3	1500
COD (mg/L)	212.3	771.2	913.7	250
TUR (NTU)	12.7	82.1	107.6	75

* = Owusu-Ansah et al.[30]

3.3 *Detection of common pharmaceuticals in hospital wastewater*

According to the results of this study, the wastewater samples collected were observed to contain six (6) classes of pharmaceuticals, viz. antibiotics (AMOX, AMP, AZM, CIP, CLOX, PcV, SMZ, TMP), anti-inflammatory (IBU, DIC, NAP), antipyretic (PCT), antipsychotic (HAL), anticonvulsant/anti-epileptic (CBZ) and benzodiazepine (DZP). As can be seen from Figure 5, wastewater from KD and MD hospitals have a higher concentration of pharmaceuticals compared to that of MMH.

At KDH and MMH, diclofenac, paracetamol, ciprofloxacin, sulfamethoxazole and azithromycin were detected at higher concentration levels (> 0.25 µg L^{-1}) in wastewater influent. The concentrations of DIC, PCT, CIP, SMZ and AZM in KDH were found to be 0.527 ± 0.018 µg L^{-1}, 0.481 ± 0.009 µg L^{-1}, 0.356 ± 0.009 µg L^{-1}, 0.307 ± 0.011 µg L^{-1} and 0.297 ± 0.021 µg L^{-1} whereas that for MD hospital were 0.588 ± 0.022 µg L^{-1}, 0.623 ± 0.017 µg L^{-1}, 0.571 ± 0.015 µg L^{-1}, 0.452 ± 0.023 µg L^{-1} and 0.382 ± 0.014 µg L^{-1}, respectively. These results are consistent with the findings reported by Patrolecco et al.[31], Gracia-Lor et al.[32] and Peñafiel et al.[33] whereby CIP, SMZ and AZM were found at higher concentrations in wastewater. This could be due to their higher consumption in humans for the management of a number of bacterial infections. In addition, DIC and PCT were also present in higher concentrations; this might be due to their consumption for reducing human body pain and curing fever. Other antibiotics (AMOX, AMP, CLOX, PcV and TMP) were detected at concentration levels below 0.25 µg L^{-1}. The concentration of AMOX, AMP, CLOX and PcV was 0.182 ± 0.007 µg L^{-1}, 0.201 ± 0.011 µg L^{-1}, 0.158 ± 0.013 µg L^{-1} and 0.202 ± 0.009 µg L^{-1} for KD hospital, and 0.215 ± 0.008 µg L^{-1}, 0.176 ± 0.009 µg L^{-1}, 0.148 ± 0.005 µg L^{-1} and 0.173 ± 0.011 µg L^{-1} for MD hospital, respectively. However, trimethoprim (TMP) was detected in the wastewater of KD hospital at a level of 0.095 ± 0.004 µg L^{-1}. Anti-inflammatory

drugs (ibuprofen and naproxen) were also detected in KD and MD hospitals wastewater at concentrations below 0.20 μg L^{-1}. IBU and NAP were spotted in wastewater at levels of 0.124 ± 0.003 μg L^{-1} and 0.166 ± 0.016 μg L^{-1} for KDH, and 0.116 ± 0.004 μg L^{-1} and 0.184 ± 0.006 μg L^{-1} for MDH, respectively. Antipsychotic (HAL), anticonvulsant (CBZ) and benzodiazepine (DZP) were detected in wastewater samples at concentrations of 0.066 ± 0.001 μg L^{-1}, 0.123 ± 0.003 μg L^{-1} and 0.084 ± 0.005 μg L^{-1} for KDH while 0.083 ± 0.002 μg L^{-1}, 0.107 ± 0.004 μg L^{-1} and 0.091 ± 0.007 μg L^{-1} for MDH.

On the other hand, wastewater effluents from MMH had lower pharmaceutical concentrations (< 0.10 μg L^{-1}). IBU, DIC, NAP, PCT, AMP, CIP, TMP, SMZ, CLOX, AZM, PcV and AMOX were identified in MMH wastewater at concentration levels of 0.061 ± 0.002 μg L^{-1}, 0.072 ± 0.003 μg L^{-1}, 0.053 ± 0.008 μg L^{-1}, 0.092 ± 0.005 μg L^{-1}, 0.075 ± 0.002 μg L^{-1}, 0.061 ± 0.004 μg L^{-1}, 0.054 ± 0.002 μg L^{-1}, 0.059 ± 0.003 μg L^{-1}, 0.089 ± 0.007 μg L^{-1}, 0.086 ± 0.004 μg L^{-1}, 0.093 ± 0.006 μg L^{-1} and 0.068 ± 0.009 μg L^{-1}, respectively. However, diazepam (DZP), haloperidol (HAL) and carbamazepine (CBZ) were not detected in the effluent samples of MMH. This signifies that their concentrations could be either at trace levels (below the LOQs) or removed during the treatment process.

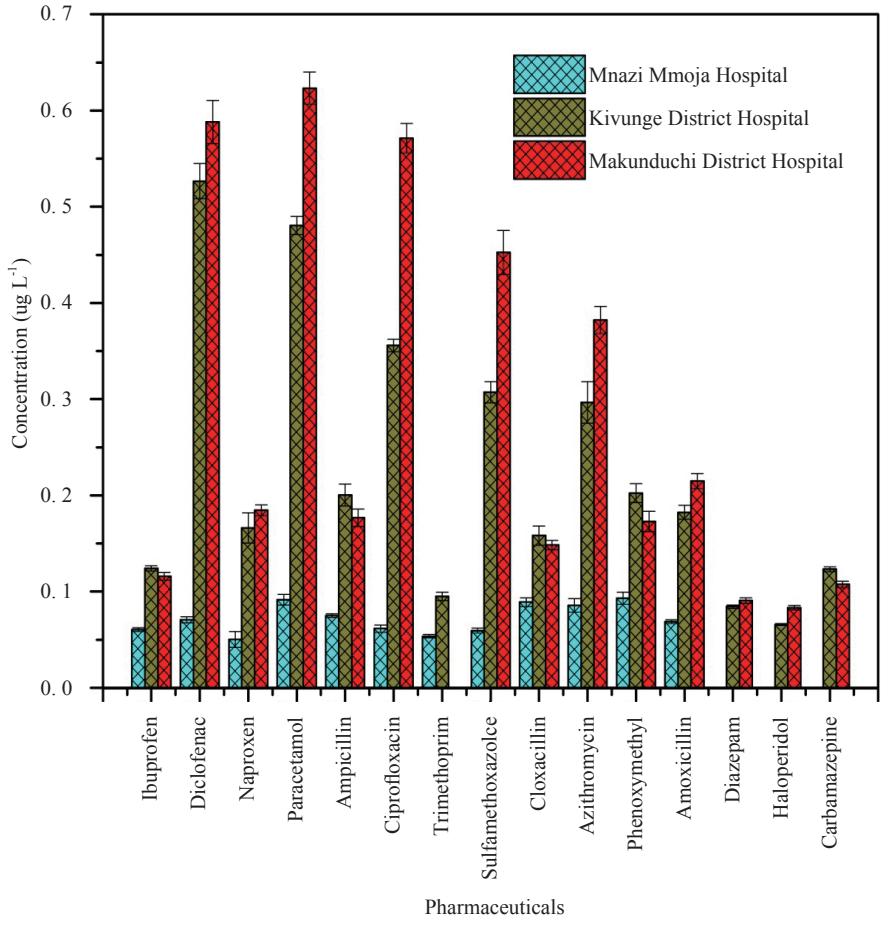


Figure 5. Concentration levels of common pharmaceuticals present in hospital wastewater

According to the results, antibiotics are the most dominant pharmaceuticals detected in the selected hospital wastewater samples followed by anti-inflammatory and antipyretic drugs (antibiotics > anti-inflammatory > antipyretic > anticonvulsant/anti-epileptic > benzodiazepine > antipsychotic). This gives the impression that antibiotics and anti-inflammatory drugs are widely consumed by the patients in Zanzibar whereby they are usually excreted or discarded in

lavatories and accumulated into the common hospital wastewater. Generally, pharmaceuticals that were administered to human beings were eliminated as active compounds (30-90%) via faeces and urine.[34] These pharmaceuticals are emerging pollutants that give rise to noxious effects on the aquatic surroundings and human health; consequently, must be appropriately treated in the water systems to safeguard the living organisms and ecosystems.[35]

3.4 *Comparison of pharmaceuticals wastewater incidence between Zanzibar and other countries*

In general, the incidence of pharmaceuticals and their concentration levels detected in Zanzibar through hospital (MMH, KDH and MDH) wastewater are quite lower compared to the pharmaceuticals reported in water resources in other countries including the United States[36], Egypt[37], Costa Rica[38], Kenya[39], Sweden[40], Netherlands[41], Jordan[42] and Uganda[43]. Table 3 shows the comparison of pharmaceuticals found in wastewater/water from different studies.

Regardless of the detection of lower concentrations of pharmaceuticals at MMH, KDH and MDH wastewater, their discovery gives a picture of the prevalence and potential of having adverse effects on the ecosystem as well as on humans. Several pharmaceuticals (including those detected in this study i.e. AMOX, AMP, AZM, CIP, CLOX, PcV, SMZ, TMP) can imitate the endogenous steroid hormones activity in humans thereby resulting in severe effects including diabetes, abnormal reproductive growth, obesity, cancer and endometriosis[55]. Moreover, the incidence of antibiotics in the wastewater might result in the dissemination of antibiotic resistant bacterial infections and antibiotic resistance genes in Zanzibar. These outcomes can alter the human microbiome and promote bacteria resistance to the human body.[2,56] In addition, exposures to pharmaceuticals can alter the behaviour and biological traits of living organisms[57], induce men infertility[58], increase the formation of testicular and breast cancer[58-61], and result in embryonic and teratogenic effects on the offspring and pregnant women.[62]

Table 3. Assessment of pharmaceuticals concentrations detected in wastewater/water: Comparison of the current work from the previous studies

S/N	Pharmaceuticals	Sources	Concentration (μg L^{-1})	Reference
a.	Carbamazepine	Wastewater effluent	3.138-3.352	42
		Wastewater influent	0.107-0.123	This study
		Wastewater influent	1.1	44
		Wastewater effluent	0.85	44
		Municipal WWTP influent	0.135	45
		Wastewater effluent	1,170	43
b.	Paracetamol	Wastewater effluent	0.1936	46
		Wastewater influent	14.891-24.309	42
		Wastewater influent/effluent	0.092-0.623	This study
		Wastewater influent	36.7	44
c.	Sulfamethoxazole	Wastewater influent	1.86-2.146	36
		European wastewater treatment plant effluents	1.691	47
		Wastewater influent/effluent	0.059-0.452	This study
		River water	13.8	39

Table 3. (cont.)

S/N	Pharmaceuticals	Sources	Concentration (μg L^{-1})	Reference
c.	Sulfamethoxazole	Wastewater effluent	1,370	43
		River water	0.509	39
		Wastewater influent/effluent	0.061-0.571	This study
d.	Ciprofloxacin	Wastewater effluent	42.8	48
		European wastewater treatment plant effluents	0.264	47
		Wastewater effluent	14,000	49
		River water	2.65	49
		Wastewater influent/effluent	0.054-0.095	This study
		Wastewater effluent	0.0504	46
e.	Trimethoprim	Wastewater effluents-East Aurora and the Netherlands	120-160	40
		Hospital wastewater-Sweden	600-760	40
		Wastewater influent	0.407-1.021	36
		Wastewater effluent	0.1223	46
f.	Naproxen	Wastewater influent/effluent	0.053-0.184	This study
		Wastewater influent	11-217	50
		Wastewater influent	4,750	43
		Wastewater influent/effluent	0.072-0.588	This study
		Wastewater stabilization ponds	5.52-98.85	51
g.	Diclofenac	Wastewater effluent	3.91	52
		Wastewater effluent	0.412	53
		Wastewater effluent	0.812	54

WWTP = Wastewater Treatment Plant

Despite the availability of a wastewater treatment plant at Mnazi Mmoja Hospital, the findings have shown the presence of trace levels of antibiotics, anti-inflammatory and antipyretic drugs in the effluents released to the marine environment. This signifies that the treatment plant at Mnazi Mmoja Hospital is not removing all pharmaceuticals from wastewater. It could be explained by the physicochemical nature of pharmaceuticals (including high lipophilicity, volatility and persistence) which interfere with their decontamination rate during treatment in plants[63] or due to the ineffectiveness of single-treatment technique (membrane method) to completely remove all pharmaceuticals in the influents. Therefore, there is a necessity for the wastewater released from hospitals to be treated using a combination

(integrated) processes such as biological-ozone-biological process, nanofiltration coupled with catalytic oxidation, adsorption coupled with microwave irradiation, UV photolysis coupled with ozonation, submerged aerobic fixed film reactor-coupled with tubesettler, membrane bioreactor-coupled with ozonation. These processes are promising techniques[10,14,16,64-66] as they can improve the unit operation and performance in eliminating pharmaceuticals in wastewater.

4. Conclusions

This current study provides a more comprehensive and informative analysis of the occurrence of pharmaceuticals in hospital wastewater and their likely potential impact on the marine and terrestrial environments in Zanzibar. Kivunge District Hospital and Makunduchi District Hospital wastewater samples were found to contain higher concentrations of EC, TDS, COD and TUR compared to Mnazi Mmoja hospital samples. This could be due to the existence of a large amount of nutrients and organic matter in Kivunge District Hospital and Makunduchi District Hospital wastewater; whereby these constituents could be partially removed or degraded by the treatment plant at MMH. Six (6) pharmaceutical classes (antibiotics, anti-inflammatory, benzodiazepine, antipsychotic, antipyretic and anticonvulsant) were detected in the wastewater samples. Despite the presence of lower levels of pharmaceuticals in the sampled Zanzibar hospital wastewater compared to the findings reported from the previous studies, there is still the need to regulate their disposal as they are likely to increase in the coming years due to ongoing construction of a number of hospitals (Regional and District hospitals) in Zanzibar. Therefore, it is compulsory to establish effective wastewater treatment plants with combined techniques at hospitals for effective wastewater remediation. These current findings are expected to provide knowledgeable information and reinforce the environmental guidelines and approaches to protecting marine and terrestrial life from pharmaceutical pollution in Zanzibar. Future studies should focus on assessing the wastewater influents and effluents, and compare the effectiveness of the existing treatment plant at Mnazi Mmoja Hospital in removing pharmaceuticals, organic matter and nutrients, and chemical contaminants present in wastewater. Also, the studies should consider the seasonal variations as these might influence the physicochemical characteristics and the pharmaceuticals present in hospital wastewater.

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Data availability

All data generated and analyzed in this study are included in the manuscript.

Conflict of interest

The authors declare no competing financial interest.

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