Occurrence of selected pharmaceuticals in wastewater and sludge samples from wastewater treatment plants in Eastern Cape province of South Africa

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ABSTRACT
The occurrence of pharmaceuticals in various wastewater treatment plants (WWTPs) and their discharge into the surface water are existing global challenges. However, such challenges are more detrimental in developing countries due to the aging infrastructure and its vandalism influenced by poverty, resulting in the illegal breakdown of the WWTPs. This study investigated the presence of efavirenz, ibuprofen, naproxen, sulfamethoxazole, and trimethoprim in WWTPs. Ultrasound-assisted extraction (UAE) followed by solid-phase extraction (SPE) was used to extract these pharmaceuticals in sludge samples, with wastewater extracted with only the latter. This was followed with analysis using a high-performance liquid chromatography-photo-diode array detection system. Recoveries found after spiking the samples with analytes at different concentrations ranged from 56 to 117%. An antibiotic, sulfamethoxazole, was among the prominent drugs in untreated wastewater with its concentration reaching 77 µg L⁻¹. All the analytes were detected in sludge samples, with naproxen having the highest concentration of 13.35 ng g⁻¹. The pharmaceutical with the lowest removal efficiency (2–12%) in WWTPs was efavirenz, while other drugs were fairly removed from wastewater. Overall, the findings of this study indicate the dysfunctionality of selected WWTPs in the Eastern Cape province of South Africa due to the release of high amounts of pharmaceuticals into the surface water which can be detrimental to humans, animals, and aquatic life.

KEYWORDS
solid-phase extraction; ultrasound-assisted extraction; wastewater; sewage sludge; pharmaceuticals; removal efficiency

INTRODUCTION
The occurrence of pharmaceuticals in environmental matrices represents a significant health risk to humans and aquatic species. This is because some pollutants are endocrine disruptors, while others can promote antibiotic resistance when ingested continuously at low levels by non-targeted persons.¹ Wastewater treatment plants (WWTPs) are highlighted as the dominant source of these environmental pollutants due to wastewater effluent discharges into rivers and the use of sludge as a soil enricher in the agricultural sector.²⁻³ This is due to the ineffectiveness of wastewater treatment systems in removing organics such as pharmaceuticals resulting in their disposal into the environment.⁴ Some South African municipalities have WWTPs which are not serving their purpose of preserving the environment and keeping pollutants out of rivers and oceans. This is a result of poor maintenance of WWTPs and the utility of outdated technologies in the wastewater treatment process. In addition, the steady increase in human population and the onset of climate change are putting these WWTPs under intense pressure.⁵ The global increase in medication accessibility also adds significantly to pharmaceutical dispersal in the WWTPs. For instance, non-steroidal anti-inflammatory drugs (NSAIDs) are available in numerous grocery stores as over-the-counter medications that can be purchased uncontrolled.⁶ This encourages medicine stockovering, and as a result, drugs are flushed down the toilet after their expiration dates.

WWTPs are normally located in the vicinity of rivers, thus allowing the effluent to be released into the river streams. As a result, wastewater from dysfunctional WWTPs is received by environmental waters which are sometimes used for irrigation as well as a source of drinking water in some communities.⁷ Pharmaceuticals are mostly removed from wastewater in conventional WWTPs through their adsorption into the sludge.⁸ As a result, pharmaceuticals are accumulated in high quantities in sewage sludge samples.⁹⁻¹⁰ The sewage sludge is mostly used in agricultural land for soil enrichment as a circulation practice. This may result in the occurrence of pharmaceutical residues in human food chains since crops that are grown on polluted soil can absorb pollutants.¹¹ In this regard, restrictive laws and thorough sewage sludge assessments are imperative prior to disposal in agricultural land to protect human health. However, there is still some missing information on the occurrence of pharmaceuticals in sludge samples in South Africa. Moreover, evaluating the removal efficiency of the WWTPs in terms of degrading and/or elimination of pharmaceuticals will provide an overview status on the functionality of the WWTPs.

In recent decades, studies on monitoring pharmaceutical residues in both wastewater and sewage sludge have been conducted worldwide.¹²⁻¹⁵ However, the emphasis is always focused on the development of analytical procedures with great initiatives on sample preparation protocols that adhere to the green chemistry principles. For the analysis of pharmaceuticals in aqueous samples such as wastewater, the solid-phase extraction (SPE) technique is the most preferred sample preparation method. Meanwhile, ultrasonication-assisted extraction (UAE) is gaining popularity for the extraction of pharmaceuticals in solid samples due to its shorter extraction periods and physico-chemical properties of these pharmaceuticals were compiled from the literature and presented in Table 1.¹⁷⁻¹⁹ Three WWTPs were not operational during the sampling times, but sewage water from surrounding homes and hospitals was still entering the plant’s facilities and being deposited into the nearby river untreated. The other two WWTPs were operational, but not to the desired capacity. Therefore, it became imperative to examine the performance of these semi-operational WWTPs in the removal of selected pharmaceuticals in
wastewater. At the same time, the presence of the same pharmaceuticals was monitored in untreated water flowing through the WWTPs into the nearby river. The five pharmaceuticals under investigation were selected as model drugs due to their high consumption rates in South Africa. In addition, these pharmaceuticals have been previously detected in various water systems around the country and the African continent at large, which qualified them as the model drugs in this study due to their regular presence in the South African water network. This study aimed to provide a comprehensive assessment of the contribution of the selected WWTPs which seemed to be dysfunctional to release pharmaceuticals into the nearby surface water. This was done by examining the presence of pharmaceuticals in wastewater flowing from the WWTPs into the river. In addition, pharmaceuticals were determined in the sewage sludge to account for their removal due to sorption into solid particles.

EXPERIMENTAL

Chemicals and materials

The solvents (acetonitrile (99.9%), acetone (99.5%), formic acid (98%), and methanol (99.9%) used in this study were HPLC-grade and were procured from Merck Chemicals (Pty) Ltd. (Johannesburg, South Africa). The same chemical supplier provided the pharmaceutical standards which were received in white powder form. These pharmaceutical standards were efavirenz (99.8%), ibuprofen (99.6%), naproxen (≥98%), sulfamethoxazole (≥98%), and trimethoprim (99.8%). SPE was the main technique used for sample preparation. In this case, Oasis HLB 6cc/150 mg cartridges procured from Waters Corporations (Milford, MA, United States) were used as a sorbent bed to trap analytes during the extraction process.

Table 1: Physio-chemical properties of selected pharmaceuticals.

<table>
<thead>
<tr>
<th>Analytes</th>
<th>Chemical structure</th>
<th>Water solubility (mg L⁻¹)</th>
<th>Log Kow</th>
<th>pKa</th>
<th>Excretion rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td><img src="image" alt="Efavirenz" /></td>
<td>10</td>
<td>4.15</td>
<td>12.52</td>
<td>67</td>
</tr>
<tr>
<td>Ibuprofen</td>
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<td>44</td>
<td>3.97</td>
<td>5.20</td>
<td>15</td>
</tr>
<tr>
<td>Naproxen</td>
<td><img src="image" alt="Naproxen" /></td>
<td>44</td>
<td>3.18</td>
<td>4.15</td>
<td>95</td>
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<tr>
<td>Sulfamethoxazole</td>
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<td>610</td>
<td>0.89</td>
<td>5.70</td>
<td>85</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td><img src="image" alt="Trimethoprim" /></td>
<td>400</td>
<td>0.91</td>
<td>7.12</td>
<td>67</td>
</tr>
</tbody>
</table>

Sampling and sample pre-treatment

Wastewater and sludge samples were sampled from wastewater treatment facilities located in the Eastern Cape province of South Africa. All the sampled WWTPs serve different communities in the outskirts of King Williams Town and East London. Figure 1 illustrates the locations of the five WWTPs that treat domestic, industrial, and hospital wastewater. WWTP 1 is located within 5 km of the central business district in King Williams Town. This WWTP receives wastewater from the town which is a home for the Grey Provincial Hospital, and its residential areas known as Fort Hill and Schornville. During the sampling period, the WWTP was not operational, with its sewage bypassing all the treatment stages (flowing untreated) to the nearby Buffalo River. Therefore, only one sampling spot was considered in this WWTP (which was the same case for WWTPs 3 and 5). 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wastewater from Reeston and Scenery Park communities. The sludge samples were collected from the septic tanks of operational WWTPs and stored in aluminium foil while being transported to the laboratory. The wastewater samples were collected using a grab sampling approach in a 1 L glass bottle. The collected samples were placed in an ice-filled box for preservation and delivered to the laboratory. In the laboratory, Whatman grade 1 qualitative filter papers from Merck Chemicals (Pty) Ltd. (Johannesburg, South Africa) of a diameter of 125 mm were used to filter wastewater samples upon arrival to remove any particle content, and sludge samples were left to dry in the fume hood overnight. The dried sludge samples were then ground into powder using Ball Mill BM40 equipment from the POWTEQ Planetary (Beijing, China). This was followed by sieving the powdered samples through a <150 µm sieve. Ultimately, the filtered wastewater samples and sieved sludge samples were kept at 4 °C in refrigerator until the extraction process.

Sample preparation

Water samples

Pharmaceutical contaminants in wastewater were extracted using a modified procedure described by Madikizela and co-workers. In brief, the extraction was carried out with an automated Dionex Auto Trace™ 280 SPE instrument purchased from Thermo Fisher Scientific (Waltham, United States). The SPE cartridges (Oasis HLB 6cc/150 mg) were first conditioned and equilibrated with 5 mL of methanol and 5 mL of ultra-high purity water at a flow rate of 1 mL min⁻¹. The cartridges were then loaded with 250 mL of wastewater at a flow rate of 5 mL min⁻¹. The cartridges were rinsed with 2 mL of ultra-high-purity water at 1 mL min⁻¹ to remove the impurities. This was followed by drying the cartridges with a gentle stream of nitrogen gas for 5 min. Afterward, the retained analytes were eluted with 10 mL of methanol at a flow rate of 0.8 mL min⁻¹. The eluted methanol fraction was preconcentrated through evaporation to near dryness, followed by the reconstitution of analytes in 1 mL of 0.1% formic acid in methanol. Thereafter, the resulting solution was subjected to HPLC for analysis.

Sludge samples

The extraction of pharmaceuticals from sewage sludge was carried out using a modified approach described by Gago-Ferrero and co-workers. Briefly, a 100 mg of dried sludge sample was precisely weighed into a 15 mL centrifuge tube. The centrifuge tube was then filled with 5 mL of a mixture of methanol and acetonitrile, and vortexed to allow the solvent to come into contact with the entire sample. The homogenized solution was ultrasonically treated for 30 minutes and centrifuged at 3000 rpm for 5 minutes. This procedure was executed three times, and the extracts were combined. The organic solvent was subsequently reduced to 1 mL by vaporization and replaced with 250 mL of deionized water for sample cleanup using the SPE procedure described for wastewater samples.

Chromatographic analysis

Pharmaceutical residues in wastewater and sludge samples were identified and quantified using the Agilent 1260 Infinity high-pressure liquid chromatography (HPLC) system procured from Agilent Technologies (Waldbroon, Germany). The chromatographic system consisted of a degasser unit, binary pump, autosampler, auto-injector, thermostatic column compartment, and diode array detector. The chromatographic column that was kept at 30 °C was Waters Xterra® C18 5 µm 3.9 × 150 mm column obtained from Waters Corporation (Milford, MA, United States). The sample injection volume was 10 µL. The chromatographic separation was achieved using the mobile phase flowing at 1 mL min⁻¹ which consisted of acetonitrile and 0.1% formic acid in water, operated in the gradient elution mode. The gradient elution began with 45% of acetonitrile which was held for 3.5 min, then increased to 60% for 2 min, and reverted to the initial conditions for 1 min. The ChemStation offline program was used for data collection and processing. Except for ibuprofen, which was detected at a wavelength of 230 nm, all other analytes were monitored at 254 nm.

Method validation

Initially, a stock solution containing a mixture of all analytes at a concentration of 10 mg L⁻¹ was prepared in acetonitrile. The calibration
standards (0.1 to 10 mg L\(^{-1}\)) were then prepared from this solution via serial dilution using acetonitrile. The calibration curves were constructed for each analyte by plotting the concentration of each pharmaceutical against the HPLC instrument response in the form of the surface area attained for the chromatographic peak. The sensitivity of the analytical method was determined based on the limits of detection (LODs) and limits of quantitation (LOQs) which were computed as 3 and 10 times the signal-to-noise ratio, respectively. The validation of the analytical method included spiking deionized water and samples from WWTPs with all analytes at different concentration levels. Prior to the spiking process, the samples were extracted and analyzed for the existence of analytes. Wastewater and sludge samples were spiked with 5 and 15 µg L\(^{-1}\), and 5 and 15 ng g\(^{-1}\), respectively. The samples were then subjected to the sample preparation procedures and analyzed using HPLC. Recoveries were computed for each analyte and used as a measure of the accuracy of the analytical method. All analyses were conducted in triplicate, resulting in the determination of the relative standard deviations (RSD) values as a measure of precision.

RESULTS AND DISCUSSION

Quality assurance

The quality of the analytical method and attained analytical data was measured in terms of accuracy, precision, sensitivity, and linearity. The results are provided in Table 2. As seen in Table 2, the calibration curves were linear over the calibration range for all the analytes with \( R^2 \) values exceeding 0.99. Initially, deionized water was spiked with 5 and 15 µg L\(^{-1}\) of all compounds. The LODs and LOQs attained for all analytes were ranging from 0.1–0.8 µg L\(^{-1}\), and 0.3–2.7 µg L\(^{-1}\), respectively (results not shown). Also, as a measure of the accuracy of the analytical method, recoveries varied from 75–107%, with RSD values below 13% (results not shown). To determine the influence of the matrix in the extraction of analytes in wastewater and sludge, samples collected from WWTPs were spiked with different concentrations of analytes, followed by their extraction and analysis processes. It was observed that the LODs and LOQs varied across the different sample matrices due to the influence of the sample matrix (Table 2). In this case, the sensitivity of the analytical method was comparable to the other existing methods reported in the literature.\(^{14,24,25}\) The accuracy of the applied analytical method was evaluated through recovery studies performed for each analyte at different spiking concentrations. For all the sample matrices, recoveries of all analytes ranged from 56 to 117% (Table 2), suggesting the acceptance of the analytical method. Similarly, the RSD values of less than 15% indicated the precision of the analytical method. Therefore, these results qualified the applied analytical method as a fit-for-purpose procedure.

Occurrence of selected pharmaceuticals

Wastewater samples

The established analytical method was used to monitor the selected pharmaceuticals in wastewater samples from five WWTPs. The presence of the investigated pharmaceuticals in wastewater was determined by comparing the retention times in the sample solutions to those in the standard solutions. In addition, the photodiode array spectra emanating from the chromatographic peaks corresponding to the analyte in standard and sample solutions were used to confirm the identity of the respective target compounds. As illustrated in Table 3, all the analytes were found at higher concentrations in influent samples compared to the effluents except for naproxen which was not detected in wastewater from WWTP 3. This observation was expected as the influent samples were collected in the entry point of the WWTPs and represent wastewater that has not undergone any treatment. The highest detected concentrations in the influent samples were from sulfamethoxazole which ranged from 9.11 to 77.33 µg L\(^{-1}\), followed...
by naproxen, ibuprofen, trimethoprim, and efavirenz ranging from 8.21 to 73.11 µg L\(^{-1}\), 3.55 to 59.84 µg L\(^{-1}\), 18.73 to 53.60 µg L\(^{-1}\), 4.08 to 10.09 µg L\(^{-1}\), respectively. The consumption rates in the study area may have an impact on these high concentrations in the influent samples. A combination of sulfamethoxazole and trimethoprim is known to treat bacterial infection in both humans and animals,\(^{26}\) with these drugs being constantly detected in other South African waters.\(^{27,28}\) As illustrated in Table 1, these drugs have high excretion rates, thus, they are excreted in unchanged form at excessive amounts resulting in their occurrence in WWTPs. The detection of efavirenz in the influent could be due to South Africa having the largest group of people in the world who are on HIV treatment.\(^{29}\) This is in addition to the high amounts of efavirenz used in the formulation of ARV medications with its contents mostly exceeding the amounts of other drugs used in the combination therapy.\(^{30}\) The high detection frequency for NSAIDs (ibuprofen and naproxen) is common in South African water systems as these are over-the-counter medications.\(^{31,32}\)

The decreased concentrations of these analytes in effluent samples indicated that certain amounts were eliminated during the wastewater treatment processes. For instance, neither ibuprofen nor naproxen were detected in effluent samples from WWTP 4. Notably, the same analytes were found at higher concentrations in effluent samples from WWTP 2 compared to those from WWTP 4. Both NSAIDs were detected at the highest concentrations in the effluent samples in WWTP 2, whereas sulfamethoxazole was found at the lowest concentration compared to other analytes. This was an interesting observation since all the studied NSAIDs have low water solubility compared to sulfamethoxazole. Analytes with low water solubility tend to adsorb easily onto solid particles such as sludge and sediments which means there could be other driving mechanisms for the limited removal of such compounds in WWTPs. Hydraulic retention times could influence such results as these were not considered during the time of sampling. Similar findings were reported in a different South African-based study.\(^{33}\) In their case, sulfamethoxazole in effluent samples was detected at low concentrations (34.93–504.4 ng L\(^{-1}\)) when compared to ibuprofen and efavirenz which ranged from <LOD–7652 ng L\(^{-1}\) and 210.1–2042 ng L\(^{-1}\), respectively. These findings suggest that these pharmaceuticals are not eliminated from wastewater as they are discharged as part of effluents into the nearby river.

**Sludge samples**

The analyses of sludge samples showed the presence of all the investigated analytes and their concentrations are presented in Table 3. The highest detected concentration in WWTP 2 was for efavirenz which was found to be 11.52 ng g\(^{-1}\), whereas naproxen reported the highest concentration of 13.35 ng g\(^{-1}\) in WWTP 4. This suggested that these analytes were sorbed onto the sludge probably due to their physio-chemical properties presented in Table 1. Both naproxen and efavirenz have high octanol-water partition coefficient (log \(K_{ow}\)) and pKa values which influence their sorption onto the organic material of the sludge matrix.\(^{34}\) Similarly, ibuprofen was also found at relatively high concentrations in all sludge samples ranging from 6.92–7.11 ng g\(^{-1}\). Sulfamethoxazole was detected at the lowest concentrations compared to other analytes in both WWTPs. This might be influenced by its limited extractability as observed in Table 2. This means the complexity of this sample matrix hinders the extraction efficiency of this drug prior to its analysis.

Overall, the investigated pharmaceuticals were detected at lower concentrations compared to other studies. For instance, Ademoyegun and colleagues reported the detection of ibuprofen and trimethoprim in sewage sludge from three WWTPs in the Eastern Cape province of South Africa.\(^{35}\) In their study, the concentrations of the pharmaceuticals are presented by box and whisker plots, with ibuprofen and trimethoprim reporting approximately 100 and 60 ng g\(^{-1}\), respectively. A study by Jelić and co-workers recorded high detection of the very same compounds within the range of 4.27–5.9 µg g\(^{-1}\) and 9.2–117 µg g\(^{-1}\), respectively.\(^{36}\) However, naproxen was found at lower concentrations within the range of 4.27–5.9 µg g\(^{-1}\). Another study reported the highest detection of efavirenz ranging from 17.7 to 43.6 mg kg\(^{-1}\) in WWTPs in southern Gauteng Province.\(^{37}\) The findings of the present study are indicative of dysfunctional wastewater systems where wastewater is not efficiently treated, with limited provisions to allow the settling of solids during the treatment process. The detection of these pharmaceuticals in the investigated samples is a concern as the sludge is mostly used in agricultural activities as a soil enricher which could subsequently result in the transfer of these pharmaceuticals into human food chains.\(^{38}\)

**Removal of pharmaceuticals in selected wastewater treatment plants**

During the time of sampling, two investigated WWTPs were operational. Therefore, in this case, sampling was carried out for both the influent and the effluent. This allowed for the evaluation of the performance of these two WWTPs in removing the investigated pharmaceuticals during the wastewater treatment process. This was done by computing the removal efficiency of each pharmaceutical based on the concentrations found in both the influents and the effluents. The attained results are given in Table 3. In the cases where the analytes were not detected in the effluent, the removal efficiency was considered as 100%. This was the case for both NSAIDs in WWTP 4 which could be influenced by their physio-chemical properties presented in Table 1. Literature suggests that the compounds with log \(K_{ow}\) values between 2.5 and 5 and high pKa values result in higher removal due to the excess sludge withdrawals.\(^{34}\) As seen in Table 1, the log \(K_{ow}\) values of the selected NSAIDs fall within these thresholds as a result they have registered high removals. Notably, ibuprofen and naproxen were detected at high concentrations in sludge samples which indicates that their removal was influenced more by sorption to sludge rather than biological degradations. These removals correspond with the ones reported in the study conducted by Madikizela and his colleagues wherein 97% removal efficiency of naproxen and ibuprofen was reported in Kingsburgh WWTP (South Africa).\(^{39}\) Kanama and co-workers also reported a 99% removal of ibuprofen from WWTP in the southern North West Province in South Africa.\(^{40}\) In contrast, the removal efficiency of efavirenz was reported within the range of 2 to 12% in both WWTPs which is the lowest despite having higher log \(K_{ow}\) value compared to ibuprofen and naproxen. However, it should be noted that the removal efficiency also depends on environmental conditions and operational parameters involved in the activated sludge system. The highest detection of naproxen in sludge samples from WWTP 4 indicates that its removal was based on sorption rather than biological degradation. Sulfamethoxazole and trimethoprim have low log \(K_{ow}\) as a result, they have higher mobility in the aqueous phase than in the solid phase.\(^{38}\) This explains their lower removal efficiencies compared to naproxen and ibuprofen in WWTP 4. However, WWTP 2 reported higher removal efficiencies for both sulfamethoxazole and trimethoprim compared to NSAIDs. Overall, these results indicate that conventional WWTPs are not capable of eliminating these emerging pollutants during the wastewater treatment process resulting in the direct release into surface waters.

**Comparison of detected concentrations in wastewater effluents**

Three WWTPs investigated in the present study were not operational while the other two were semi-operational. Their effluents are channelled to the Buffalo River (Eastern Cape, South Africa) with its water mostly being used for irrigation. Fishing activities are common in this river system which pours into the Indian Ocean via its estuary in East London. Therefore, the treatability of wastewater from the investigated WWTPs remains a concern due to the potential influence of their effluents on the quality of the Buffalo River and health risks. In this regard, a detailed comparison of the effluent concentrations with the levels found across other South African WWTPs is provided in
Table 4. Based on the presented data in Table 4, all the selected analytes have been detected in other effluent samples across different parts of South Africa. Although Table 4 provides a snapshot of analytical data emanating from South Africa, it was observed that the concentrations of investigated NSAIDs were mostly higher when compared to other monitoring studies. For example, Mhuka and colleagues identified ibuprofen and naproxen at LOD–7.65 µg L⁻¹ and 0.01–0.35 µg L⁻¹, respectively. Statistically, KwaZulu-Natal (KZN) and Durban are known to have a high number of people benefiting from HIV treatment programs,⁵⁴ this explains the high detections of efavirenz from these two locations. Overall, the detection of pharmaceuticals in wastewater effluents indicates that there are several dysfunctional WWTPs in South Africa that necessitate immediate intervention to protect the environment and human health from pharmaceutical pollution as well as other emerging pollutants. Furthermore, the dysfunctionality of these WWTPs is contributing significantly to the degradation of freshwater, thus hindering the government from achieving sustainable development goal (SDG) number 6.⁶

CONCLUSIONS

This study examined the role played by dysfunctional WWTPs in the release of pharmaceuticals into nearby rivers. The ignorance to adequately maintain WWTPs and vandalism are the basic causes of the dysfunctionality of WWTPs in South Africa, as is the use of outdated technologies in the wastewater treatment process. As a result, dysfunctional WWTPs are unable to remove pharmaceuticals from wastewater, instead, they are constantly released into the environment. Hence, high concentrations of all the investigated drugs in this study were found in untreated and treated wastewater flowing through the investigated WWTPs into the receiving water body. Also, all the selected pharmaceuticals were found in sewage sludge which is mostly used as soil enricher in the agricultural sector. This presents potential health risks to humans, animals, and aquatic species. The findings of this study call for immediate upgrade and fixing of the investigated dysfunctional WWTPs as well as constant inspections to protect the environment from further pharmaceutical pollution.

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DATA AVAILABILITY

The datasets resulting from the current study are available from the corresponding author in the case of reasonable scientific request.

REFERENCES

Table 4: Comparison of concentrations detected for the selected pharmaceuticals across various WWTP effluents in South Africa.

<table>
<thead>
<tr>
<th>Study site (sampling period)</th>
<th>Detected concentration ranges (µg L⁻¹)</th>
<th>Reference</th>
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<tr>
<td></td>
<td>Efavirenz</td>
<td>Ibuprofen</td>
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<td>Pretoria (undisclosed)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Undisclosed</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>KwaZulu-Natal (undisclosed)</td>
<td>0.21–2.04</td>
<td>LOD–7.65</td>
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<tr>
<td>Pretoria (December 2016 and March 2018)</td>
<td>1.22–9.15</td>
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<tr>
<td>Western Cape (April and July 2016)</td>
<td>20–34</td>
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<td>KwaZulu-Natal (August 2016)</td>
<td>3.9–68</td>
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<td>Northwest (August and December 2015)</td>
<td>0.02–1.46</td>
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<td>Gauteng (undisclosed)</td>
<td>40–112</td>
<td>-</td>
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<tr>
<td>Durban (October 2018)</td>
<td>1.15–3.30</td>
<td>-</td>
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<tr>
<td>Western Cape (undisclosed)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>KwaZulu-Natal (January to March 2016)</td>
<td>1.02–37.3</td>
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<tr>
<td>Durban (undisclosed)</td>
<td>4.00–6.00</td>
<td>Nd–26.96</td>
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26. Kosma CI, Kapsi MG, Konstas P-SG, et al. Assessment of multiclass pharmaceutical active compounds (PhACs) in hospital WWTP influent and effluent samples by UHPLC-Orbitrap MS: Temporal variation, removals


