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'An investigation into the occurrence and removal of pharmaceuticals in Colombian wastewater'

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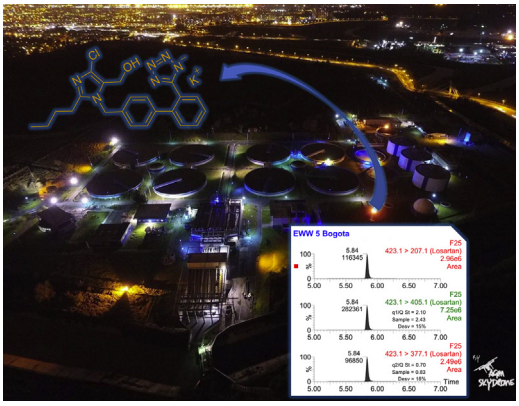
HIGHLIGHTS

- Pharmaceuticals were present at ppb levels in urban and hospital wastewaters from Colombia.
- Effluent wastewater from conventional WWTPs contained concentrations similar to raw influent wastewater.
- Both IWW and EWW are directly discharged in the aquatic ecosystem in some locations.
- Removal efficiency of pharmaceuticals in WWTPs is incomplete, therefore additional tertiary treatments are needed.
- The use of LC-MS/MS QqQ allowed reliable quantification supported by quality control analysis.

GRAPHICAL ABSTRACT



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ABSTRACT

In this work, the presence of 20 pharmaceuticals in wastewater from Colombia is investigated. Several widely consumed compounds have been detected in wastewater samples from different origins and geographical areas in Colombia. The studied pharmaceuticals included antibiotics, analgesics and anti-inflammatories, cholesterol lowering statin drugs, lipid regulators, and anti-depressants. The investigated samples were urban wastewater collected during one whole week before (influent) and after treatment (effluent) in the wastewater treatment plants (WWTPs) of Bogotá and Medellin. Raw wastewater from the Hospital of Tumaco and from the city of Florencia were also collected. Analyses performed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) revealed that most of the target analytes were present in all the wastewater samples. The highest concentrations (up to 50 μg/L) corresponded to acetaminophen, but several antibiotics, such as azithromycin, ciprofloxacin and norfloxacin, and antihypertensive drugs, such as losartan and valsartan, were commonly present in influent wastewater (IWW) at levels above 1 μg/L. Moreover, the treatment applied in WWTPs seemed to not efficiently remove the compounds under study, because most pharmaceuticals were also present in effluent wastewater (EWW) at concentrations close to those of the IWW. Special emphasis was made in this work on the quality of data reported, performing a detailed study of quality control (QC) samples.

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The analytical approach used –direct injection of 5-fold diluted samples without any additional treatment – is simpler and faster than the commonly applied solid phase extraction (SPE). The use of 12 isotope-labelled internal standards ensured the satisfactory correction of matrix effects for the corresponding analytes. For the remaining 8 compounds, no drastic matrix effects were observed, and only four compounds (cloxacillin, doxycycline, losartan, tetracycline) presented QC recoveries near or slightly below 60%, revealing ionization suppression, particularly in the IWW. Data on the occurrence of pharmaceuticals reported in this paper are the basis for current studies that aim to develop efficient systems for the degradation/removal of these compounds from the aquatic environment.

1. Introduction

Currently, there is special concern about the presence and potential hazardous effects of emerging contaminants (EC) in the aquatic environment. ECs are widely used compounds that are not regulated yet (or only a few of them); however, they are commonly found in wastewater and surface water at concentrations that may be higher than classical persistent and/or priority substances; therefore, they can be harmful to aquatic ecosystems and become a hazard for human public health (Daughton, 2004; Gracia-Lor et al., 2012a; Hernández et al., 2015a; la Farré et al., 2008). Within the wide group of ECs, pharmaceuticals are among the most frequently detected compounds in the aquatic environment (Hughes et al., 2013). Antibiotics are of particular concern due to the potential risks associated with the development of microorganisms resistant to antibiotics (Makowska et al., 2016; Manaia et al., 2016). The evaluation of the hazards of emerging contaminants, such as pharmaceuticals and personal care and disinfection by products, is a current priority in regulatory water quality monitoring (Loos et al., 2009; Brack et al., 2012; Brack et al., 2017).

It was approximately 40 years ago when pharmaceuticals were first considered environmental contaminants in the aquatic environment (Hignite and Azarnoff, 1977; Richardson and Bowron, 1985). Several pioneer works highlighted the interest in studying the occurrence and impact of pharmaceuticals in the aquatic environment (Daughton and Ternes, 1999; Daughton, 2004; Kolpin et al., 2002). From then, there has been an impressive increase in the number of publications reporting the presence of pharmaceuticals in the water environment. The development of sophisticated analytical techniques played a key role in their emergence (Hernández et al., 2015b; Richardson and Kimura, 2016). Data reported by many environmental laboratories around the world reveal that pharmaceuticals are omnipresent in the aqueous environment (e.g., wastewater influent and effluent, manure, industrial effluent, surface water, groundwater, and drinking water (aus der Beek et al., 2016; Monteiro and Boxall, 2010)). Liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) has played a prominent role in this process. LC-MS/MS is the most widely applied technique for the determination of emerging contaminants in water, due to its excellent sensitivity, selectivity and robustness, together with reliability in the identification of the compound detected. For the successful application of LC-MS/MS, at least two MS/MS transitions need to be monitored and their ion ratios evaluated (Hernández et al., 2018; García-Galán et al., 2016; Gracia-Lor et al., 2014; Bayen et al., 2014; van Nuijs et al., 2010; Pozo et al., 2006a; Pozo et al., 2006b).

As expected from the wide human consumption, the main source of pollution for pharmaceuticals is urban wastewater, and it is rather common to find high pharmaceuticals concentrations (up to hundreds of ppb) in influent wastewater (IWW). Unfortunately, conventional wastewater treatment plants (WWTP) do not efficiently remove these compounds, and they can remain in effluent wastewater (EWW) at concentrations similar, or even higher, than in IWW (Gracia-Lor et al., 2012a; Gros et al., 2010; Jelic et al., 2011; Lacey et al., 2008). In addition to the inefficient removal in WWTPs, some pharmaceuticals are also persistent and can bioaccumulate in living organisms (Daughton and Ternes, 1999; Yang et al., 2014). As a consequence, these compounds can easily reach surface water (Dai et al., 2015; Kasprzyk-Hordern et al., 2008; Fatta-Kassinos et al., 2011; Liu et al., 2015; Matamoros et al., 2012) and even drinking water (Boyd et al., 2003; Carmona et al., 2014; Kumar and Xagoraraki, 2010; Sodré et al., 2010; Vulliet et al., 2011).

Although much data are available around the world, revealing the presence of pharmaceuticals in different aquatic scenarios, little information is available from Latin America. This is a particular worry, because in some areas, the discharge of raw sewage into rivers, lakes and reservoirs is rather common (De Paula et al., 2007; Gracia-Lor et al., 2012b; Montagner and Jardim, 2011; Thomas et al., 2014). Concern over the presence of these contaminants is well founded, because these water resources not only flow through tropical areas rich in biodiversity, but surface waters are also often used as a source for human consumption (Aristizabal-Ciro et al., 2017).

Recently, we performed a wide-scope qualitative screening of organic contaminants, including pharmaceutical, veterinary drugs, X-ray agents, personal care products, sweeteners, illicit drugs, and a notable number of metabolites in wastewater and receiving surface waters from the area surrounding Bogotá (Hernández et al., 2015a). The use of high resolution MS, specifically liquid chromatography coupled to quadrupole-time-of-flight (LC-QTOF MS) allowed us to identify a notable number of pharmaceuticals in both EWW and in surface water, emphasizing acetaminophen, carbamazepine, clarithromycin, diclofenac, lincomycin, losartan and valsartan, among others, together with several metabolites. As a consequence of that work, future monitoring, based on quantitative analyses, was recommended to focus on those compounds found in the screening.

In this work, we have performed a quantitative analysis, based on LC-MS/MS with triple quadrupole, for selected pharmaceuticals in Colombian wastewater. Raw wastewater samples from the Hospital of Tumaco (Nariño), as well as from the city of Florencia (Caquetá), which are currently discharged directly in two rich biodiversity regions in Colombia (the Pacific and Amazonian regions), were analysed. In addition, influent and effluent wastewater samples collected during one week in the cities of Bogotá and Medellin (department of Antioquia) were also analysed. The aim of this work was 1) to estimate the removal efficiency of WWTPs from analysis of IWW and EWW; 2) to have better knowledge on the compounds present in effluent wastewater that potentially reaches the surface waters receiving discharges from WWTPs; 3) to allow the design of complementary treatments, such as the advanced oxidation processes, that we are investigating at present for the efficient removal of the pharmaceuticals most commonly found in wastewater.

2. Experimental

2.1. Characteristics of the wastewater treatment plants and studied areas

The analysed samples were collected in two of the main cities of Colombia (Bogota D.C. and Medellin, department of Antioquia), in the young city located in southeast Colombia (Florencia – Caquetá) and in one coastal pacific city (Tumaco). In the case of Bogotá and the department of Antioquia, a total of 28 samples were taken from the

wastewater treatment plants (WWTP). The samples included influent wastewater (IWW) and effluent wastewater (EWW). In the case of Tumaco, three raw composite samples were analysed in three different campaigns and were collected directly from the local Hospital (San Andrés - Hospital). In Florencia, two composite samples were taken from a municipal wastewater discharge.

The WWTP "Salitre" in Bogotá treats wastewater from approximately 2.5 million inhabitants. It is located in the northwest of Bogotá, and collects water from several districts (Fig. 1). After treatment, the effluent wastewater is discharged in the Bogotá River. The average flow rate of wastewater treated by the WWTP over one year is 4 m^3/s (ca. 350,000 m^3/day), with a removal efficiency of 40% BOD and 60% of suspended solids. The WWTP "Salitre" is strategically located at the entry of the "Juan Amarillo" river in order to catch wastewater from the downtown and northern areas of Bogotá. This WWTP uses assisted chemical treatment (ACT) and includes a bar screen to filter solids and large objects. Fat and grease is also removed before the primary treatment of sewage. Likewise, ACT includes a primary treatment based on the partial removal of suspended solids and organic matter through coagulation, flocculation and sedimentation (http://www.acueducto.com.co/). In the case of Antioquia, the study was carried out using wastewater samples from one WWTP of this department. The average flow rate of wastewater treated by the WWTP over 1 year is 1.8 m^3/s (ca. 150,000 m^3/day), with a removal efficiency of 80% BOD and 85% suspended solids. Due to its location, the WWTP collects wastewater from several schools, universities, hospitals, business offices, shops and clubs, and some industries. This plant has a primary treatment coupled to a stabilization process with sludge (http://www.epm.com.co/).

Tumaco does not have treatment plants for wastewater, so contaminated water (e.g., hospital water) is discharged directly to the surface water sources and to the sea. In the case of Florencia, it does not have any WWTPs and currently has 30 discharges on three rivers (Rio Hacha, Quebrada la Perdiz and Quebrada la Sardina) in the city. Quebrada la Perdiz receives a discharge of 254.31 L/s, which consists of 42.15% of the total wastewater flow of the city. The pollutant load due to domestic, agroindustrial and hospital wastewater is 3150.95 kg/day of BOD and 1418.11 kg/day of SST (SERVAF, 2013). In this way, "Quebrada la Perdiz" is affected by anthropic intervention and has become an aquatic ecosystem with poor water quality not suitable for consumption and recreation, and only after treatment can it be used for agriculture, livestock, flora and fauna (Manrique-Losada and Pelaez-Rodriguez, 2010).

Fig. 1 shows the location of the cities of Tumaco and Florencia and the catchment areas of WWTP "Salitre" – Bogotá and WWTP – Antioquia.

2.2. Sample collection

The influent (IWW) and effluent (EWW) wastewater samples (24-h composite) from Bogotá and Medellín were collected daily over seven consecutive days in 2016. In Bogotá, samples were taken using a volume-proportional sampling mode (every 2500 m^3) approximately every 10 min, starting on Wednesday, March 11th and ending on Tuesday, March 17th (auto-sampler Endress-Hauser). In the case of Antioquia, sample collection was performed using a time proportional sampling mode (every 30 min) starting on Monday, October 17th and ending on Sunday, October 23rd. In Tumaco, daily composite samples

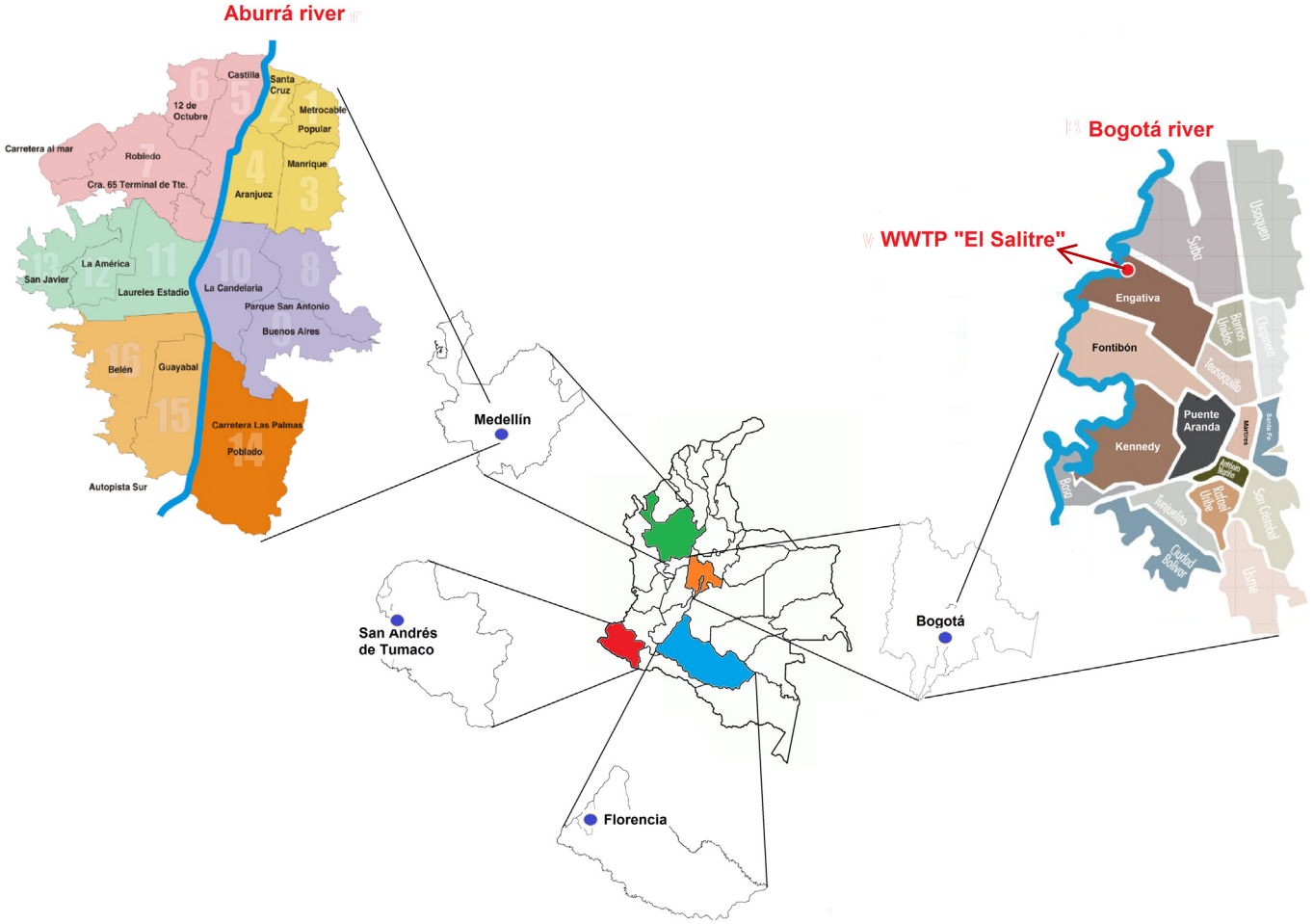

Fig. 1. Location of Tumaco and Florencia cities, and catchment areas of WWTP El Salitre – Bogotá and WWTP – Medellín, Antioquia.

(every 30 min) were collected directly from hospital effluents on three different days: 3rd October 2016, 28th April and 5th July 2017. In all cases, samples were collected in high-density polyethylene bottles and transported to the corresponding laboratories for sample treatment. Upon reception in the laboratory, samples were immediately stored in the dark at −20 °C until filtration. Concentrations of chemical oxygen demand (COD), biological oxygen demand (BOD) and total iron were routinely measured in each sample. In Florencia (Caquetá), the samples were taken from representative effluent located in the Raicero neighbourhood. They were obtained using a volume-proportional sampling mode approximately every 1 h during 24 h on two dates (August 29th and September 30th, 2016) with different weather conditions (rainy and non-rainy day).

2.3. Target compounds

In total, 20 compounds were selected for this study. The target compounds corresponded to: 1 antiepileptic drug, 3 analgesics, 12 antibiotics, 1 antidepressant and 3 antihypertensive drugs.

Table 1 shows the compounds investigated, with the LC-MS/MS conditions and the quality control (QC) recovery values.

2.4. Reagents and chemicals

Pharmaceutical reference standards were acquired from Sigma-Aldrich, LGC Promochem, Toronto Research Chemicals, Across Organics, Bayer Hispania, and Aventis Pharma. All reference standards were of 93% purity or higher.

Individual standard stock solutions were prepared at concentrations between 50 at 500 mg/L. Intermediate solutions of 10 mg/L were prepared by dilution with methanol. Mixed working solutions containing all analytes at the μg/L level were prepared weekly from intermediate solutions by appropriate dilutions with water and were used for preparation of the aqueous standard calibrations and for spiking samples used as quality control.

Isotopically labelled internal standard (ILIS) acetaminophen-d4, diclofenac-d4, valsartan-d8, erythromycin-13C-d3, irbesartan-d6, venlafaxine-d6, carbamazepine 10,11-epoxide-d10 were from CDN Isotopes (Quebec, Canada); sulfamethoxazole-13C6, azithromycin-d3, ciprofloxacin-d8, norfloxacin-d5 and trimethoprim-13C3 were from Cambridge Isotope Laboratories (Andover, MA, USA). Individual ILIS stock solutions between 50 and 500 mg/L were prepared in MeOH. Intermediate mix ILIS between 1 and 0.1 mg/L were prepared by dilution with MeOH. A working mix ILIS solution at 2 μg/L was prepared in MeOH for its use in the analysis of samples. All solutions were stored in amber glass bottles at −20 °C.

HPLC-grade methanol (MeOH), HPLC-grade acetonitrile (ACN), formic acid (HCOOH, content >98%) and ammonium acetate (NH_4AC, reagent grade), were purchased from Scharlab (Barcelona, Spain). HPLC-grade water was obtained from distilled water that was passed through a Milli-Q water purification system (Millipore, Bedford, MA, USA).

2.5. Instrumentation

A Waters Acquity UPLC system was interfaced to a triple quadrupole mass spectrometer Xevo TQS (Waters, Milford, MA, USA) equipped with an orthogonal *Z*-spray electrospray ionization interface (ESI) operated in positive mode. Nitrogen (Praxair, Valencia, Spain) was used as a cone gas as well as a desolvation gas at 250 L/h and 1200 L/h, respectively. For operation in MS/MS mode, the collision gas was argon 99.995% (Praxair, Spain) with a pressure of 4 × 10–3 mbar in the collision cell (0.15 mL/min). The capillary voltage was 3.5 kV, source temperature was 150 °C and the desolvation temperature was 650 °C. Cone voltage was selected at 10 V for all compounds. Dwell times were automatically selected in order to obtain enough points per peak and could be decreased down to 3 ms.

Chromatographic separation was performed using an Acquity UPLC BEH C18, 1.7 μm, analytical column, 100 mm × 2.1 mm (Waters). The mobile phase was A = H_2O, B = MeOH, both with 0.01% HCOOH and 1 mM NH_4Ac. The percentage of organic modifier (B) was changed as follows: 0 min, 5%; 7 min, 90%; 8 min, 90%; 8.1 min, 5%; and 10 min, 5%. The flow rate was 0.4 mL/min. The column was kept at 40 °C, and sample manager was maintained at 5 °C. The analysis run time was 10 min.

All data were acquired and processed using Masslynx v 4.1 software (Waters).

2.6. Analytical methodology

The wastewater composite samples were unfrozen and filtered under a vacuum through 0.45-μm membrane filters (mixed cellulose ester, Whatman ME 25) (Whatman, Manchester, UK). Then, aliquots of these samples were collected in centrifuge tubes of 50 mL and

Table 1
Compounds investigated and analytical LC-MS/MS conditions for determination. LOQs and Quality Control data (recovery, %).
All compounds were analysed in ESI positive mode. Q, quantification transition; q1 and q2 confirmation transitions; ILIS, isotope-labelled internal standard; LCL, lowest calibration level.

Compound	Family/Function	Q	q1	Average q1/Q ratio	q2	Average q2/Q ratio	ILIS	QC rec (%) 0.1 μg/L IWW/EWW	QC rec (%) 1 μg/L IWW/EWW	LCL (μg/L)
Acetaminophen (ACET)	Analgesic	152 > 110	152 > 65	0.11	152 > 93	0.17	YES	[a]/[a]	[a]/[a]	0.05
Azithromycin (AZIT)	Antibiotic	749 > 83	749 > 116	0.76	749 > 591	0.39	YES	[a]/[a]	[a]/[a]	0.05
Carbamazepine (CARB)	Antiepileptic	237 > 194	237 > 192	0.24	237 > 179	0.06	YES	88/91	121/87	0.001
Ciprofloxacin (CIPR)	Antibiotic	332 > 314	332 > 231	0.29	332 > 288	0.16	YES	[a]/[a]	98/93	0.05
Clarithromycin (CLAR)	Antibiotic	590 > 158	590 > 116	0.25	590 > 98	0.11		110/107	106/106	0.001
Clindamycin (CLYN)	Antibiotic	425 > 126	425 > 377	0.06	425 > 389	0.02		110/117	105/104	0.001
Cloxacillin (CLOX)	Antibiotic	436 > 160	436 > 277	0.31	436 > 114	0.27		42/51	60/81	0.05
Diclofenac (DICL)	Analgesic	294 > 250	294 > 214	0.05	294 > 178	0.01	YES	105/108	99/99	0.001
Doxycycline (DOXY)	Antibiotic	445 > 428	445 > 154	0.13	445 > 98	0.12		51/53	72/79	0.001
Erythromycin (ERYT)	Antibiotic	734 > 158	734 > 576	0.37	734 > 558	0.03	YES	94/109	83/103	0.001
Irbesartan (IRBE)	Antihypertensive	429 > 207	429 > 195	0.28	429 > 180	0.05	YES	108/104	98/134	0.001
Losartan (LOSA)	Antihypertensive	423 > 207	423 > 405	2.1	423 > 377	0.70		[a]/[a]	67/91	0.001
Metronidazole (METR)	Antibiotic	172 > 128	172 > 82	0.49	172 > 56	0.06		80/88	71/82	0.01
Naproxen (NAPR)	Analgesic	185 > 169						[a]/[a]	96/70	0.001
Norfloxacin (NORF)	Antibiotic	320 > 302	320 > 276	0.16	320 > 281	0.10	YES	[a]/83	75/91	0.05
Sulfamethoxazole (SULF)	Antibiotic	254 > 92	254 > 156	1.58	254 > 108	0.93	YES	[a]/101	124/108	0.001
Tetracycline (TETR)	Antibiotic	445 > 410	445 > 154	0.81	445 > 425	0.71		56/61	92/81	0.001
Trimethoprim (TRIM)	Antibiotic	291 > 123	291 > 230	1.14	291 > 261	0.70	YES	108/125	58/71	0.001
Valsartan (VALS)	Antihypertensive	436 > 207	436 > 235	1.04	436 > 261	0.009	YES	[a]/[a]	87/105	0.001
Venlafaxine (VENL)	Antidepressant	278 > 58	278 > 260	0.62	278 > 121	0.33	YES	101/102	86/104	0.001

[a] Recovery could not be calculated due to the presence of the analyte in the "blank" samples used for preparation of the QC at concentration above that the fortification level.

transported in cool containers to Spain, within a maximum period of 24 h. Once in the laboratory, they were frozen at ≤−18 °C. Water samples were thawed at room temperature the same day of the analysis; an aliquot was transferred to a 2-mL Eppendorf and centrifuged at 12,000 rpm for 3 min. The procedure applied for sample analysis was based on our previous work, where direct injection of the samples, without any pre-concentration step (e.g., SPE), was used. This was possible thanks to the excellent sensitivity of the LC-MS/MS instrument (Boix et al., 2015). In the present work, we included a simple dilution ×5 with Milli-Q water in order to reduce the matrix complexity; a 200 μL-aliquot of wastewater sample was taken and then 750 μL Milli-Q water and 50 μL of a mix ILIS solution (2 μg/L) were added (final ILIS concentration in the samples injected was 0.1 μg/L). Finally, 100 μL of the diluted sample was directly injected into the UHPLC-MS/MS system.

Quality control (QCs) samples consisted of IWW and EWW from Bogota (day 7), spiked with the target pharmaceuticals at 0.1 and 1 μg/L. To this aim, 650 μL of Milli-Q water were taken, and 200 μL of a sample, 100 μL of the mix standard solution (1 or 10 μg/L) and 50 μL of the mix ILIS (2 μg/L) were added.

Quantification of analytes was made using the quantification transition (Q) and external calibration with standards in solvent. In those cases in which the analyte ILIS was available (12 out of 20 compounds analysed), relative areas were used for quantification. In this way, potential matrix effects were corrected, as shown by the acceptable QC recoveries obtained.

The reliable identification of compounds in the samples was carried out by calculating the ion ratios (peak area) between the quantification (Q) and confirmation (q_1 and q_2) transitions. To this aim, three MS/MS transitions were acquired, and two intensity ion-ratios were available for confirmation of the identity (q1/Q and q2/Q). The finding was considered positive when at least one experimental ion ratio and the retention time of the compound in the sample were within the tolerance ranges (±30% for ion ratio, ±0.1 min for retention time) in comparison with the reference standards injected in the calibration (SANTE, 2015).

3. Results and discussion

3.1. Selection of target compounds

A total of 28 compounds were initially selected on the basis of the following information: 1) previous findings in a wide-scope screening performed in wastewater from Bogotá (Hernández et al., 2015a); 2) our previous experience on the determination of pharmaceuticals in effluent wastewater by direct injection of the sample (Boix et al., 2015); and 3) information on the consumption of pharmaceuticals in Colombia (Conpes, 2015; INAS, 2014; Jaramillo et al., 2005; Machado and Moncada, 2012; Mendoza-Ruiz et al., 2017; ODC, 2013;)

The selected compounds corresponded to pharmaceuticals from different therapeutic classes. Twelve of these compounds had been previously found by QTOF MS screening in effluent wastewater and surface water from Bogotá (Hernández et al., 2015a), and 11 compounds were previously tested in different water types with satisfactory analytical figures using direct injection of the samples (Boix et al., 2015). Altogether, there were 14 compounds: 9 were included in both lists, 3 were only in the screening list (Hernández et al., 2015a), and 2 were only in the second list (Boix et al., 2015). In addition, 14 more compounds were added to the target list of the present work based on the consumption data, making a total of 28 selected analytes.

The results obtained for the QCs were not satisfactory for 8 out of the 28 compounds. Some of these 8 compounds could be detected in the samples, but no quantitative data are reported in this paper due to the low recoveries of the QCs. In other cases, the low sensitivity did not allow the targets to be quantified at the concentrations present in the samples, or the method was not robust and/or reproducible. Some examples are ceftriaxone, amoxicillin and meropenem, which were identified in several samples, but could not be quantified. The 8 compounds eventually discarded due to the non-reliability of the data were: amoxicillin, ampicillin, cefotaxime, ceftriaxone, imipenem, meropenem, oxacillin and oxytetracycline.

In summary, considering the QC values, in this work we report data for the remaining 20 compounds. QCs were prepared and analysed for all of them using the "blank" samples under study, which were spiked at 0.1 and 1 μg/L. ILIS were available for 12 of the compounds selected.

3.2. Pharmaceuticals in urban wastewater

A total of 28 wastewater 24-h composite samples were collected from the WWTPs serving Bogotá (14 samples) and Medellín (14 samples). The 14 samples collected at each WWTP corresponded to 7 influent wastewater (IWW) and 7 effluent wastewater (EWW) samples, collected during one whole week. Analyses of IWW and EWW allowed us to roughly estimate the removal efficiency in the WWTP, comparing the concentrations found in the IWW with those obtained in the EWW. Although some compounds (particularly those of low polarity) can be sorbed to the solid particles, and consequently can remain in the sludge, the comparison between IWW and EWW is commonly used for an assessment of the efficiency of the WWTP to remove emerging contaminants (Gracia-Lor et al., 2012a; Bijlsma et al., 2014).

Table 2 shows the daily concentrations of the pharmaceuticals and average weekly concentrations in IWW from Bogota and Antioquia, while Table 3 shows the data obtained for the EWW. It can be seen that all compounds investigated were present in both IWW and EWW, with the exception of tetracycline in some samples, illustrating the wide presence of pharmaceuticals in wastewaters, even after treatment in the WWTPs. In general, the IWW samples from Bogotá contained higher drugs levels than those from Antioquia, with the highest concentrations being found for the widely used analgesic acetaminophen (39.2 and 9.2 μg/L for Bogotá and Antioquia) and the antibiotic azithromycin (6.3 and 5.8 μg/L for Bogotá and Antioquia). Acetaminophen is widely consumed in Colombia due to factors such as the pressure of the pharmaceutical industry, the ease of taking these medications when a pain arises due to it being sold without a prescription, and the lack of knowledge about the implications of its high consumption (Conpes, 2012; Jaramillo et al., 2005). The database (IMS) of the private national pharmaceutical market shows that between April 2010 and April 2011, the country bought USD $ 10,850 in paracetamol, which was higher than the budget for ibuprofen (USD $ 8500) and acetylsalicylic acid (USD $ 4300) (Vásquez Velásquez et al., 2010). Apart from these two major compounds, other pharmaceuticals were found at levels above 1 μg/L in the IWW, such as the antibiotics norfloxacin and ciprofloxacin, the antihypertensives losartan and valsartan, and the analgesic naproxen in the Bogotá samples. However, none of these drugs exceeded an average concentration of 1 μg/L in Antioquia.

All compounds detected in the influent samples were also present in treated EWW, which illustrates the poor removal efficiency of the WWTPs. Similarly to the IWW, the major compounds in treated wastewater were acetaminophen and azithromycin, although the former was found at low levels in the Antioquia samples. Losartan, valsartan and naproxen were at concentrations commonly above 1 μg/L (Table 3).

Daily concentrations for both IWW and EWW were rather consistent throughout the whole week, showing similar consumption patterns of pharmaceuticals, without a significant increase on the weekend. This steady behaviour differs from that of illicit drugs of abuse, which sees concentrations commonly increase on the weekend (Thomas et al., 2012; Bijlsma et al., 2014, 2016). Particularly in Bogotá, the daily levels were quite constant for each compound throughout the week, which is illustrated by coefficients of variation (CV) that were usually below 30%, with a few exceptions (e.g., valsartan). In the samples from Antioquia, the concentrations throughout the week showed the same trend as in Bogotá. Although CVs were higher in Antioquia, this was more due to

Table 2
Pharmaceuticals in 24-h influent wastewater samples collected along one week.

Compound	IWW 1	IWW 2	IWW 3	IWW 4	IWW 5	IWW 6	IWW 7	Average	CV (%)
Bogotá IWW (conc. in μg/L)									
Acetaminophen	38.5	45.7	44.2	36.7	34.1	29.1	46.6	**39.25**	**17**
Azithromycin	6.41	6.13	5.92	6.81	6.37	6.27	6.31	**6.32**	**4**
Carbamazepine	0.073	0.073	0.085	0.060	0.046	0.043	0.082	**0.07**	**25**
Ciprofloxacin	3.35	2.74	2.56	2.09	2.14	1.49	1.69	**2.29**	**28**
Clarithromycin	0.432	0.313	0.393	0.268	0.242	0.212	0.377	**0.32**	**26**
Clindamycin	0.031	0.025	0.023	0.018	0.016	0.013	0.024	**0.02**	**28**
Diclofenac	0.368	0.437	0.717	0.289	0.245	0.331	0.427	**0.40**	**39**
Doxycycline	0.159	0.157	0.136	0.110	0.082	0.092	0.093	**0.12**	**27**
Erythromycin	0.039	0.050	0.051	0.036	0.027	0.032	0.056	**0.04**	**26**
Irbesartan	0.184	0.499	0.140	0.105	0.071	0.110	0.121	**0.18**	**83**
Losartan	2.89	2.41	2.44	1.90	1.36	1.50	2.73	**2.18**	**27**
Metronidazole	0.385	0.363	0.327	0.264	0.264	0.186	0.378	**0.31**	**24**
Naproxen	3.72	3.32	3.28	2.85	2.41	2.21	3.07	**2.98**	**18**
Norfloxacin	2.01	1.53	1.58	1.28	1.13	1.07	0.983	**1.37**	**26**
Sulfamethoxazole	0.729	0.704	0.827	0.609	0.442	0.439	0.662	**0.63**	**23**
Tetracycline	–	0.383	0.341	–	0.276	–	–	**0.33**	**16**
Trimethoprim	0.432	0.315	0.341	0.375	0.241	0.211	0.345	**0.32**	**24**
Valsartan	5.09	1.50	1.33	0.853	0.757	0.702	1.11	**1.62**	**96**
Venlafaxine	0.038	0.034	0.034	0.030	0.030	0.032	0.032	**0.03**	**9**
Medellin IWW (conc. in μg/L)									
Acetaminophen	5.37	11.6	4.65	5.85	1.39	8.20	27.2	**9.19**	**93**
Azithromycin	5.68	5.68	6.21	6.15	5.82	6.07	5.24	**5.84**	**6**
Carbamazepine	0.095	0.041	0.026	0.069	0.451	0.161	0.226	**0.153**	**98**
Ciprofloxacin	1.37	1.04	0.921	0.827	0.898	0.766	1.03	**0.980**	**20**
Clarithromycin	0.238	0.136	0.103	0.123	0.076	0.143	0.172	**0.141**	**37**
Clindamycin	0.009	0.005	0.004	0.003	0.003	0.008	0.007	**0.006**	**45**
Diclofenac	0.556	0.212	0.205	0.081	0.128	0.214	0.256	**0.236**	**65**
Doxycycline	0.159	0.111	0.089	0.095	0.063	0.067	0.075	**0.094**	**35**
Erythromycin	0.056	0.033	0.025	0.020	0.016	0.035	0.028	**0.030**	**44**
Irbesartan	0.045	0.027	0.006	0.012	–	0.032	0.048	**0.028**	**60**
Losartan	1.45	0.941	0.543	0.664	0.434	0.789	0.975	**0.828**	**41**
Metronidazole	0.232	0.267	0.096	0.156	0.072	0.184	0.346	**0.193**	**50**
Naproxen	1.08	1.32	0.735	0.622	0.519	0.847	1.31	**0.919**	**35**
Norfloxacin	1.15	0.799	0.729	0.633	0.714	0.715	0.898	**0.806**	**22**
Sulfamethoxazole	0.441	0.558	0.227	0.203	0.123	0.160	0.379	**0.299**	**54**
Tetracycline	–	–	–	–	–	–	–	–	–
Trimethoprim	0.125	0.110	0.078	0.026	0.013	0.065	0.108	**0.075**	**57**
Valsartan	0.179	0.164	0.062	0.111	0.049	0.114	0.220	**0.128**	**49**
Venlafaxine	0.074	0.052	0.039	0.044	0.052	0.057	0.072	**0.056**	**23**

Average concentration for the seven days (EWW1-EWW7). CV is the variation coefficient in percentage.

the low concentrations present than to the very different concentration levels (see Tables 2 and 3).

In addition to the samples from Bogotá and Antioquia, two samples of raw wastewater were collected from the city of Florencia, Caquetá Province (August and September 2016). The aim was to confirm the presence of the compounds under study in these samples that are directly discharged to the river La Perdiz. The results of analyses (Supporting information, Table S1) revealed high concentrations of acetaminophen (12 and 15 μg/L) and the antibiotic azithromycin (6.5 and 7.0 μg/L) as the major compounds in these samples. All the remaining target compounds were also found, with the exceptions of clindamycin, doxycycline, tetracycline and irbesartan, supporting the wide consumption of most of the compounds investigated in this work.

The data obtained in this work are in general agreement with other papers that have reported the presence of pharmaceuticals in influent and effluent wastewater around the world (Alder et al., 2010; Alidina et al., 2014; Anumol and Snyder, 2015; Campanha et al., 2015; Carmona et al., 2014; Ghoshdastidar et al., 2015; Gracia-Lor et al., 2012a; Gros et al., 2010; Jelic et al., 2011; Lacey et al., 2008; Liu and Wong, 2013; van Nuijs et al., 2015; Wu et al., 2015), although concentrations of acetaminophen and the antibiotic azithromycin in the samples from Colombia seem slightly higher, revealing the high consumption of these compounds in this country.

3.3. Removal efficiency in WWTPs

Removal efficiencies (RE) were estimated by comparing effluent concentrations (C_{EWW}) from day (x + 1) with influent concentrations (C_{IWW}) from day (x), considering a residence time of 24 h (Bijlsma et al., 2014). RE were calculated as:

$$RE(\%) = \left(1 - \frac{C_{EWW}\ (x+1)}{C_{IWW}\ (x)}\right) \times 100$$

In this way, daily RE were calculated, as well as the average RE for the whole week, estimated from the daily values. Using this approach, the lower levels commonly found in effluents are assumed to be the result of removal in the WWTP, due to microbial degradation, or other transformation processes (Gracia-Lor et al., 2012a). However, the analysis of suspended particulate matter (SPM) has also been suggested to prevent under-reporting. The analysis of both aqueous phase (influent and effluent) and SPM would surely provide a better estimation of the removal and environmental impact of compounds by WWTPs, since removal from wastewater does not necessarily imply degradation (Baker et al., 2012; Baker and Kasprzyk-Hordern, 2013). Some micropollutants can be notably sorbed to SPM, especially those of low polarity, and thus, even good removal rates obtained in the aqueous phase (i.e., comparison of influent and effluent wastewater concentrations)

Table 3
Pharmaceuticals in 24-h effluent wastewater samples collected along one week.

Compound	EWW 1	EWW 2	EWW 3	EWW 4	EWW 5	EWW 6	EWW 7	Average	CV (%)
Bogotá EWW (conc. in μg/L)									
Acetaminophen	35.1	32.8	30.7	32.7	27.5	19.5	29.2	**29.66**	**17**
Azithromycin	4.12	3.95	4.09	4.66	3.55	3.68	3.91	**3.99**	**9**
Carbamazepine	0.078	0.068	0.071	0.067	0.058	0.041	0.069	**0.065**	**19**
Ciprofloxacin	1.07	0.822	0.824	0.766	0.839	0.677	0.668	**0.81**	**17**
Clarithromycin	0.402	0.299	0.271	0.284	0.257	0.216	0.406	**0.31**	**24**
Clindamycin	0.032	0.021	0.014	0.016	0.014	0.009	0.020	**0.018**	**40**
Diclofenac	0.446	0.312	0.332	0.338	0.296	0.225	0.415	**0.34**	**22**
Doxycycline	0.079	0.075	0.062	0.064	0.063	0.059	0.058	**0.066**	**12**
Erythromycin	0.050	0.046	0.036	0.043	0.041	0.031	0.062	**0.044**	**23**
Irbesartan	0.172	0.663	0.167	0.110	0.091	0.077	0.100	**0.20**	**106**
Losartan	2.76	2.14	2.05	1.92	1.66	1.27	2.01	**1.97**	**23**
Metronidazole	0.450	0.372	0.293	0.308	0.297	0.187	0.358	**0.32**	**25**
Naproxen	2.81	3.16	2.42	2.38	2.02	1.69	2.33	**2.40**	**20**
Norfloxacin	0.606	0.453	0.482	0.430	0.504	0.394	0.417	**0.47**	**15**
Sulfamethoxazole	0.831	0.767	0.640	0.680	0.542	0.446	0.624	**0.65**	**20**
Tetracycline	0.126	0.107	0.167	0.106	0.090	0.079	0.090	**0.11**	**27**
Trimethoprim	0.417	0.328	0.456	0.358	0.318	0.168	0.315	**0.34**	**27**
Valsartan	1.42	1.65	0.963	0.894	0.900	0.619	0.889	**1.05**	**34**
Venlafaxine	0.019	0.015	0.012	0.013	0.011	0.011	0.013	**0.014**	**22**
Medellin EWW (conc. μg/L)									
Acetaminophen	0.025	0.058	0.134	0.072	0.410	0.165	0.249	**0.16**	**84**
Azithromycin	4.57	4.10	4.00	3.02	4.08	3.80	3.57	**3.88**	**13**
Carbamazepine	0.102	0.033	0.049	0.054	0.342	0.212	0.179	**0.14**	**81**
Ciprofloxacin	0.654	0.446	0.579	0.758	0.685	0.692	0.526	**0.62**	**17**
Clarithromycin	0.165	0.082	0.117	0.089	0.060	0.078	0.081	**0.096**	**36**
Clindamycin	0.010		0.003	0.004		0.003	0.006	**0.004**	**87**
Diclofenac	0.359	0.127	0.131	0.149	0.111	0.134	0.152	**0.17**	**52**
Doxycycline	0.133	0.086	0.062	0.076	0.069	0.064	0.060	**0.078**	**33**
Erythromycin	0.050	0.021	0.029	0.027	0.021	0.020	0.024	**0.028**	**38**
Irbesartan	0.041	0.006	0.028	0.040	0.006	0.016	0.040	**0.025**	**62**
Losartan	1.41	0.820	1.08	1.15	0.761	0.848	0.945	**1.00**	**23**
Metronidazole	0.381	0.187	0.301	0.315	0.164	0.205	0.272	**0.26**	**30**
Naproxen	0.480	0.502	0.653	0.540	0.477	0.432	0.459	**0.51**	**14**
Norfloxacin	0.529	0.350	0.499	0.540	0.503	0.515	0.429	**0.48**	**14**
Sulfamethoxazole	0.348	0.279	0.358	0.434	0.311	0.348	0.357	**0.35**	**14**
Tetracycline	0.231	0.095	0.185	0.152	0.084	0.079	0.104	**0.13**	**44**
Trimethoprim	0.155	0.051	0.090	0.119	0.066	0.065	0.089	**0.091**	**40**
Valsartan	0.086	0.044	0.085	0.089	0.051	0.049	0.056	**0.066**	**30**
Venlafaxine	0.049	0.021	0.034	0.040	0.030	0.032	0.039	**0.035**	**26**

Average concentration for the seven days (EWW1-EWW7). CV is the variation coefficient in percentage.

might not imply degradation to the same extent (Jelic et al., 2011). In the particular case of pharmaceuticals studied in the present work, it is expected that poor sorption on SPM is due to the medium-high polar nature of most of the selected compounds.

The results obtained in this paper for average removal efficiencies are shown in Fig. 2. Most of the compounds were partially removed (Fig. 2, left), while five drugs were not removed and/or their concentrations in EWW were even higher than in IWW, leading to a negative RE.

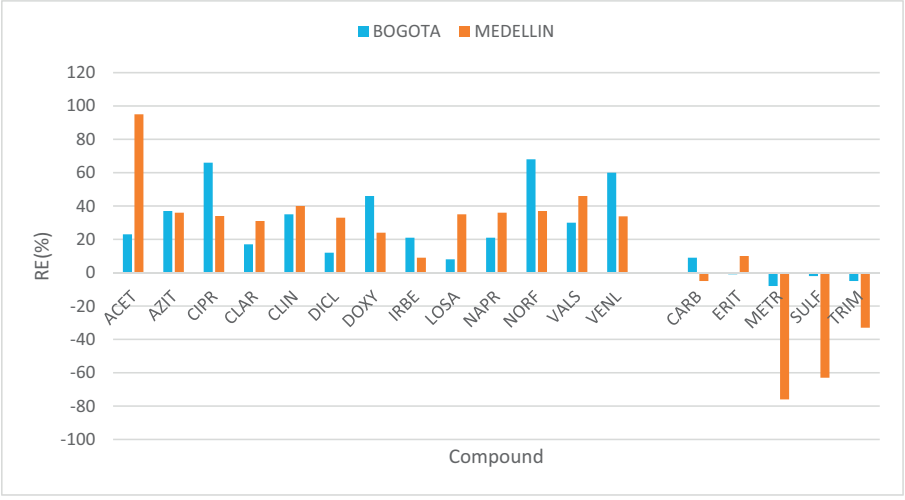

Fig. 2. Estimated removal efficiency of pharmaceuticals in the WWTPs of Bogotá and Medellin. Average values for one week.

The latter was only observed for 3 compounds, all being antibiotics (metronidazole, sulfamethoxazole, trimethoprim) (Fig. 2, right). This is in agreement with previous studies where some compounds were reported to be more abundant in effluents than in influents (Lacey et al., 2008; Gros et al., 2010; Jelic et al., 2011; Gracia-Lor et al., 2012a). The higher complexity of the influents leads to strong matrix effects (commonly ionization suppression), which would lead to reporting lower concentrations if the correction for the matrix effects is not fully satisfactory. In addition, the enzymatic cleavage of the compound glucuronides and other conjugated metabolites and the subsequent release of the parent compound during the treatment process might also lead to higher levels in the effluent samples (Vieno et al., 2007; Lacey et al., 2008; Gros et al., 2010).

In general, the results for the two WWTPs were rather coherent, showing similar trends in the RE, although acetaminophen seemed to be almost completely removed in the Medellin WWTP (RE, 95%) and just partially removed in Bogotá (RE, 23%). This difference might be due to the treatment applied in these plants: only physico-chemical processes in Bogotá, and physico-chemical plus biological processes were applied in Medellin (see Experimental section). The data obtained in this paper in relation to RE are consistent with previous works, which reported that the majority of emerging contaminants were partially or not removed in WWTPs (Gros et al., 2010; Heberer, 2002; Jelic et al., 2011; Gracia-Lor et al., 2012a; Bijlsma et al., 2014).

3.4. Pharmaceuticals in raw hospital wastewater

The analysis of raw wastewater from the Hospital San Andrés in Tumaco revealed the presence of high concentrations of several pharmaceuticals (Table 4). In total, 3 composite samples were analysed in three different campaigns (see "Experimental"). The results showed a high variability in concentrations, which might be explained by the different treatments applied to patients during the days of sampling. With the exception of acetaminophen, the highest levels were generally found for antibiotics, specifically azithromycin, ciprofloxacin, clarithromycin, clindamycin and norfloxacin, with concentrations above 10 μg/L in several samples. This is of particular concern due to the negative effects that antibiotics may have on ecosystems, even leading to bacterial resistance (Boxall et al., 2012; Marti et al., 2013; Marti et al., 2014). Ceftriaxone, amoxicillin and meropenem were also detected in some raw samples from Tumaco hospital, but no quantification was made due to the problems observed in the QC samples.

Table 4
Concentrations of pharmaceuticals (μg/L) in raw wastewater samples from the hospital of Tumaco, Nariño.

Compound	Raw hospital wastewater 3-Oct-16	Raw hospital wastewater 28-April-2017	Raw hospital wastewater 5-July-2017
Acetaminophen	50.9	78.1	10.8
Azithromycin	6.93	d	26.1
Carbamazepine	1.39	–	0.07
Ciprofloxacin	5.56	14.9	20.2
Clarithromycin	11.8	0.11	26.8
Clindamycin	8.34	17.5	24.1
Diclofenac	3.04	1.08	1.72
Doxycycline	–	–	–
Erythromycin	1.85	–	0.31
Irbesartan	1.41	0.24	0.03
Losartan	1.19	4.79	7.65
Metronidazole	3.54	2.40	n.c.
Naproxen	5.74	2.66	n.c.
Norfloxacin	0.853	1.34	10.1
Sulfamethoxazole	0.415	1.30	d
Tetracycline	–	–	–
Trimethoprim	1.71	0.93	0.06
Valsartan	1.93	0.04	2.34
Venlafaxine	0.018	0.07	d

n.c. not confirmed, the identity could not be confirmed by q/Q ratio agreement.
d: detected, concentration below LCL.

3.5. Quality control data

In this work, special emphasis was made on the quality of analysis. To ensure the reliability of the data reported, several quality control samples (QCs) were included in every sample sequence. QCs consisted of IWW or EWW samples spiked at two concentrations, 0.1 and 1 μg/L. They were prepared randomly by selecting one of the "blank" wastewater samples analysed within the batch and were analysed following the same analytical procedure as the samples. When the sample used for QC preparation contained any of the compounds under study, the concentration calculated in that "blank" sample was subtracted from that calculated in the spiked sample. Percentage recoveries for QCs were calculated, and a tolerance range between 60 and 140% was applied to consider recovery as acceptable for individual recoveries, similarly to other analytical fields, such as pesticide residue analyses (SANTE, 2015). When the concentration in the "blank" sample was similar or even higher than the QC, the calculation was subjected to high error, and the recovery could not be reported. In addition to the analysis of QCs, the calibration curve was injected twice, at the beginning and the end of the sample batch.

The confirmation of positive findings was carried out by evaluating q1/Q and q2/Q ion ratios and the retention time of the compound in the sample in comparison with the reference standard (for more details see "Analytical Methodology").

The results obtained for the analysis of QCs are summarized in Table 1. Most QC recoveries were satisfactory, in both IWW and EWW, with the wide majority within the range 70–120% at the 0.1 and 1 μg/L levels. The fact that up to 12 ILIS were used for 20 target analytes was undoubtedly of help in order to get satisfactory quantification for most of the compounds. It is well-known that the use of analyte-labelled internal standards is one of the best ways to correct matrix effects in this type of complex sample.

In contrast, analyte-ILIS was not available at our laboratory for 8 out of 20 pharmaceuticals, which might compromise their quantification. However, acceptable recoveries were obtained for three of them (clarithromycin, clindamycin, metronidazole), as shown in Table 1. Another four compounds (cloxacillin, doxycycline, losartan, tetracycline) presented recoveries at approximately or slightly below 60%, revealing ionization suppression. The matrix effect for these four compounds was more marked in IWW, as illustrated by the lower recoveries in comparison with EWW. A special case was naproxen, for which only one transition was available, compromising its reliable identification in samples. This compound was considered as tentatively identified, and would need additional analysis for unequivocal confirmation.

QC recoveries could not be calculated for two compounds at any of the two levels tested, due to the high analyte concentration in the "blank" sample used for QC preparation (sample 7 from Bogotá). This was the case for acetaminophen (47 μg/L IWW; 27 μg/L EWW) and azithromycin (6.3 μg/L IWW; 4.0 μg/L EWW). Similarly, for some other compounds, QCs could not be calculated at the lowest level tested due to the presence of the analyte at concentrations notably higher than 0.1 μg/L (Table 1).

In the light of our data, it can be concluded that direct injection of 5-fold diluted wastewater samples helps to lowering matrix effects and is a satisfactory approach for most analytes in wastewater samples. This is interesting, since our strategy is the opposite to the most widely applied based on pre-concentration of samples by SPE. The excellent sensitivity of modern LC-MS/MS instruments allows the use of this approach, making sample treatment by SPE unnecessary. It is clear that SPE leads to the pre-concentration of analytes, but not necessarily to a minimization of matrix effects. In our opinion, SPE does not always eliminate or minimize matrix effects, as only those matrix components co-eluting with the analytes would be able to produce ionization suppression or

ionization enhancement, and therefore, they might not easily be removed by SPE. With the direct injection of 5-fold diluted samples, it was possible to determine the pharmaceuticals under study in a reliable way, supporting the usefulness of the approach selected for quantification of frequently consumed drugs. Surely, after SPE it would have been possible to determine lower concentrations, which would have been of help in order to quantify less consumed pharmaceuticals, with the drawback, however, of more sample manipulation and potential losses in the SPE step.

As an illustrative example, Fig. 3 shows selected chromatograms for several compounds identified in IWW and EWW, including the 3 transitions acquired and the q/Q ion ratios.

3.6. Selection of target compounds for future degradation studies

In the light of data reported in this work, we selected some model compounds to evaluate the feasibility of complementary degradation studies in the near future. We considered those compounds present at higher concentrations in EWW as well as those that were less removed by conventional treatments plants (i.e., with lowest elimination percentages).

The highest amounts discharged in the effluents of WWTP "Salitre"-Bogotá (Table 3) corresponded to: a) analgesics: acetaminophen and naproxen, with average concentrations of approximately 30 and 2.5 μg/L, respectively; b) antihypertensives: valsartan and losartan, with concentrations between 1.0 and 2.0 μg/L; and c) antibiotics: azithromycin (4.0 μg/L), and ciprofloxacin, clarithromycin, norfloxacin and sulfamethoxazole, the last four in the range of 0.3 to 0.8 μg/L. In the effluents of Antioquia (Table 3), the antibiotic azithromycin and the antihypertensive losartan, with average concentrations of 3.9 and 1.0 μg/L, respectively, were the compounds present at the highest concentrations; the antibiotics ciprofloxacin, norfloxacin and sulfamethoxazole were also found at concentrations similar to the EWW from Bogotá (0.6, 0.5 and 0.4 μg/L, respectively). The results of hospital raw wastewater showed that the antibiotics azithromycin, clindamycin and ciprofloxacin were in all samples at concentrations above 5 μg/L, and in some cases, reached values higher than 20 μg/L.

In relation to the elimination percentages, we found that none of the 20 compounds tested was completely removed by the treatment plants (Fig. 2), even when biological treatment was applied, as in the WWTP of Antioquia. Losartan, valsartan and irbesartan were among the most difficult compounds for WWTP to eliminate, and no removal was observed for carbamazepine, erythromycin, metronidazole, sulfamethoxazole

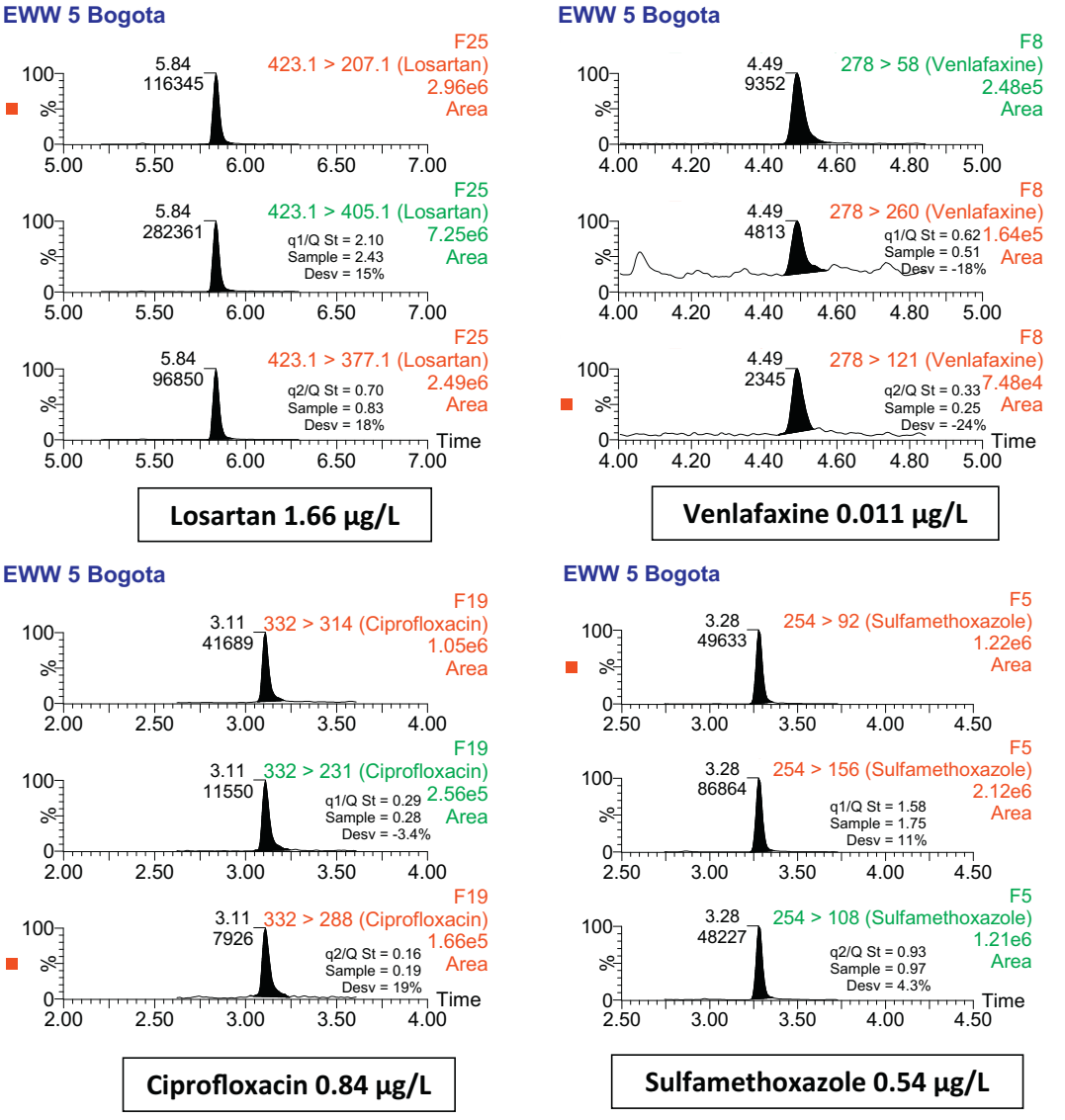

Fig. 3. LC-MS/MS chromatograms of positive effluent (EWW 5 from Bogota) and influent (IWW 6 from Medellin) samples. Ion ratios q1/Q and q2/Q are shown (deviations tolerance ± 30%).

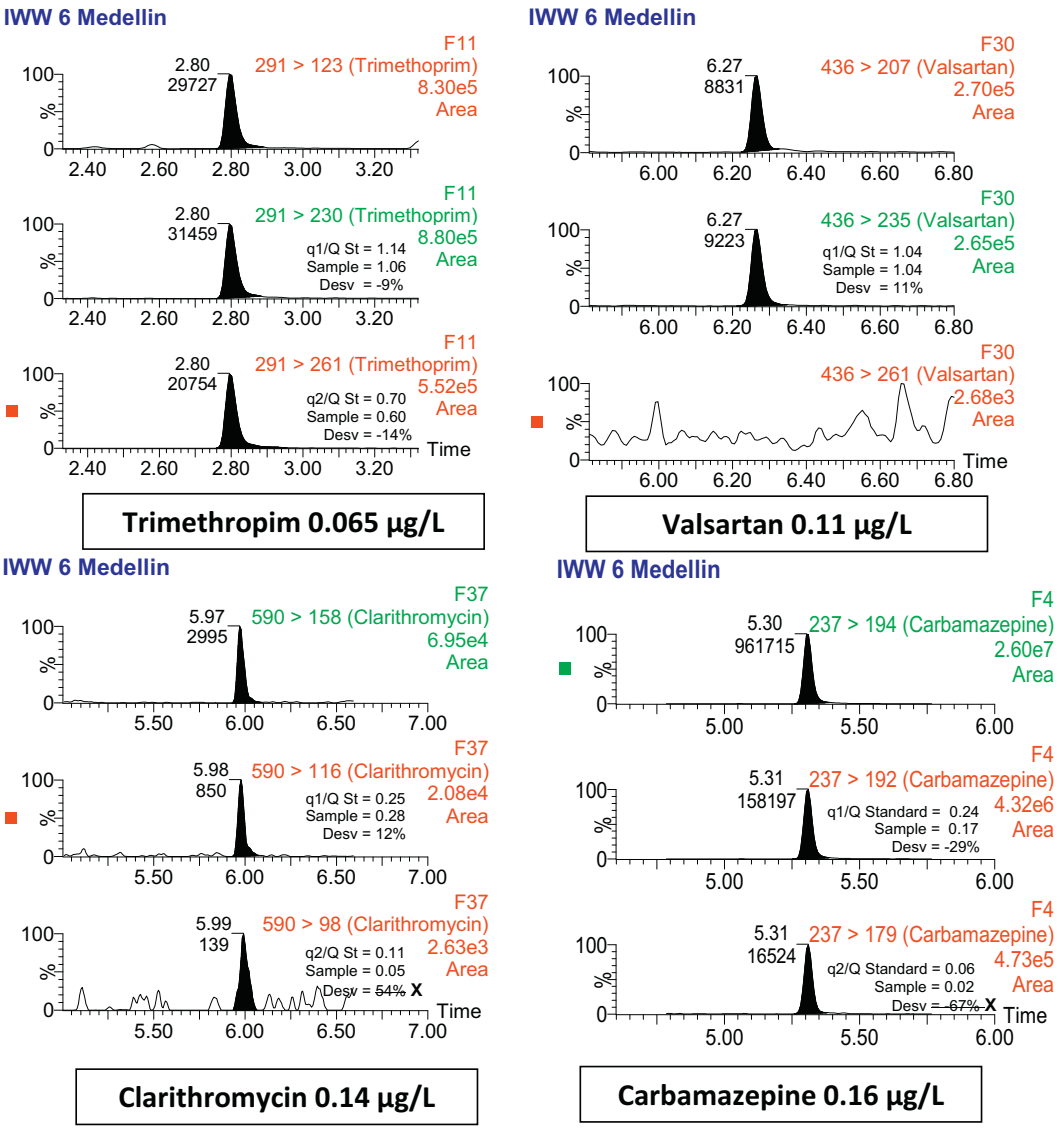

Fig. 3 (*continued*).

and trimethoprim. These results confirm that additional tertiary treatments are required for the elimination of pharmaceuticals. Some studies have shown similar results, where despite having activated sludge treatments in the WWTP, these were not sufficient for the complete elimination of emerging contaminants (de la Cruz et al., 2012). Advanced oxidation processes (AOP) have been shown to be suitable for the degradation of some of these compounds at the laboratory and pilot scales (Liu et al., 2013; Padilla-Robles et al., 2015). As illustrative examples, AOP have been applied to acetaminophen (de Luna et al., 2012), ciprofloxacin (An et al., 2010), norfloxacin (Jojoa-Sierra et al., 2017), carbamazepine, (Komtchou et al., 2015), and penicillin antibiotics (Serna-Galvis et al., 2016).

Our current research is focused on the optimization of AOPs using processes such as electro-Fenton, photo-electro-Fenton and ultrasounds, applied to real-world wastewater matrices, where pharmaceuticals are present at ppb levels and competition may occur between the degradation of organic matter and microorganisms. The data obtained in the present work reveal that most studied compounds are present in influent and effluent wastewater, with poor removal efficiency of WWTPs. Thus, the elimination of pharmaceuticals in wastewater seems a general need and is not limited to only a few compounds. Therefore, the vast majority of compounds studied in the present work are being evaluated in AOP processes applied to wastewater samples, as well as under laboratory controlled conditions. The final objective is to seek more sustainable wastewater management, safeguarding the aquatic environment by minimizing harmful impacts, and fulfilling future legal requirements that will surely be stricter in terms of the maximum pharmaceutical concentrations allowed in water.

4. Conclusions

In this work, the presence of pharmaceuticals, particularly antibiotics such as azithromycin, ciprofloxacin, norfloxacin, has been detected in different types of wastewater from Colombia. Raw wastewater from the cities of Bogotá, Medellín and Florencia contained levels of several pharmaceuticals above 1 µg/L. After treatment in the WWTPs, most of the compounds were not completely removed, still remaining at significant concentrations in the effluents. Raw hospital wastewater was also analysed from the city of Tumaco. As expected, the concentrations for several compounds, usually antibiotics (e.g., azithromycin, ciprofloxacin, norfloxacin, erythromycin and clindamycin), were commonly above 5 µg/L, higher than those found in urban wastewater. The fact that raw wastewater is sometimes directly discharged to surface waters

(the case of Florencia and Tumaco), and the presence of most pharmaceuticals investigated in the treated wastewater (Bogotá and Medellín), may suppose a risk for the aquatic environment, provoking bacterial resistance, among other effects. Therefore, there is an urgent need to implement efficient treatments that are able to remove pharmaceuticals in wastewater. Our current research is directed towards the degradation of pharmaceuticals, selected in the light of data reported in this paper, using advanced oxidation systems, such as photo-Fenton, electro-Fenton, photo-electro-Fenton or ultrasonic cavitation, which have demonstrated high removal percentages at the laboratory scale and under controlled conditions.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2018.06.088.

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