Environmental Pollution 235 (2018) 312–321

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Monitoring the occurrence of pharmaceuticals in soils irrigated with reclaimed wastewater☆

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ARTICLE INFO

Article history:
Received 18 September 2017
Received in revised form
18 December 2017
Accepted 22 December 2017
Available online 4 January 2018

Keywords:
Pharmaceuticals
Wastewater
Soil
Environmental risk assessment

ABSTRACT

The use of reclaimed wastewater for irrigation is foreseen as a possible strategy to mitigate the pressure on water resources in dry regions. However, there is the risk of potential accumulation of contaminants of emerging concern (CECs) in the edaphic environment, their percolation and consequently contamination of aquifers. In the present study, we measured the levels of a wide range of commonly used pharmaceutically active compounds (PhACs) in sewage from a local wastewater treatment plant (WWTP) and in soils irrigated with treated wastewater. Analysis of target compounds showed total concentrations between 73 and 372 $\mu g\,L^{-1}$ in WWTP influents, and from 3 to 41 $\mu g\,L^{-1}$ in effluents. The total concentrations of PhACs detected in surface soil samples were in the range of 2 and 15 $ng\,g^{-1}$, with predominance of analgesics and anti-inflammatories (maximum concentration = 10.05 $ng\,g^{-1}$), followed by antibiotics and psychiatric drugs (maximum concentration = 5.45 $ng\,g^{-1}$ and 3.78 $ng\,g^{-1}$, respectively). Both effluent samples and irrigated soils shared similar compositional patterns, with compounds such as hydrochlorothiazide and diclofenac being predominant. Additionally, PhACs were also detected in soil samples at a depth of 150 cm, indicating that these chemical undergo leaching associated with heavy-rain episodes. Their occurrence in soils was affected by temperature too, as maximum concentrations were measured in colder months (up to 14 $ng\,g^{-1}$), indicating higher persistence at lower temperatures. Finally, the ecotoxicological risk of PhACs in soil was evaluated by calculating their risk quotients (RQs). The risk was very low as RQ values ranged between <0.01 and 0.07. However, this initial assessment could be improved by future works on toxicity using specific terrestrial organisms.

1. Introduction

Pharmaceutically active compounds (PhACs) are regarded as emerging environmental contaminants as many of them are ubiquitous, persistent and biologically active substances (Daughton and Ternes, 1999; Jelić et al., 2012; McEneff et al., 2015). Pharmaceuticals such as antibiotics or analgesics have frequently been found in surface waters at the ng L^{-1} level (Baena-Nogueras et al., 2016; Jelić et al., 2012; Loos et al., 2013; López-Serna et al., 2011). There are several direct and indirect pathways through which PhACs can be introduced into the aqueous environment. Treated and untreated wastewater discharges are identified as the major route responsible for surface water contamination with pharmaceuticals (Castiglioni et al., 2006; Gros et al., 2010; Jelić et al., 2012; Li, 2014; Loos et al., 2010; Santos et al., 2009). A considerable number of studies have reported the presence of PhACs in influent and effluent samples from wastewater treatment plants (WWTPs). For instance, and just in Spain, Gros et al. (2010) reported the occurrence of 73 pharmaceuticals in seven municipal WWTPs in the Ebro River basin, whereas Santos et al. (2009) measured concentrations of four anti-inflammatory drugs, an antiepileptic drug and a nervous stimulant up to 353 $\mu g\,L^{-1}$ in four WWTPs in Seville. In Europe, 21 different PhACs were found in 6 WWTPs in Italy (Castiglioni et al., 2006), including ciprofloxacin, ofloxacin, sulfamethoxazole, ibuprofen, atenolol, furosemide, hydrochlorothiazide, ranitidine, and bezafibrate, whereas in Czech Republic, similar results were achieved by Golovko et al. (2014). Other recent studies in the United States (Lara-Martín et al., 2014; Subedi and Kannan, 2015) have evaluated the removal efficiencies of many other WWTPs. Overall, and after treated wastewater discharge, many of

☆ This paper has been recommended for acceptance by Klaus Kummerer.

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https://doi.org/10.1016/j.envpol.2017.12.085
0269-7491/

these chemicals can not only be detected in the receiving surface waters but also in sediments and even in drinking water (Ternes, 1998; Petrović et al., 2003; Carballa et al., 2004; Gros et al., 2006). Additionally, and due to the enormous pressure on water supplies, treated wastewater from WWTPs can also be used to supplement irrigation on golf courses, crops, parks and gardens. This raises a safety concern as such supplemental irrigation can lead to the potential contamination of soils and groundwater resources. While disease-causing pathogens and heavy metals are often routinely monitored in these cases, contaminants of emerging concern (CECs), especially pharmaceuticals, are not, resulting in very limited information on their occurrence and fate.

Compared to aquatic systems, pharmaceuticals have hardly been studied in soil environmental matrices, and the very limited data on their presence in the terrestrial environment mostly consist of some investigations on the pharmaceutical removal following effluent irrigation onto land (Kinney et al., 2006; Ternes et al., 2007; Gielen et al., 2009). Previous studies have also reported the presence of pharmaceutical compounds in European aquifers (Teijon et al., 2010; Cabeza et al., 2012). The likelihood of soil and groundwater contamination by PhACs as a result of the discharge of WWTP effluents depends on several factors such as the physicochemical properties of these pollutants, the type of wastewater treatment technology implemented, and climatic conditions (e.g., dilution of wastewater effluent, rainfall, temperature, and irradiance) (Kasprzyk-Hordern et al., 2009). As many of these compounds are ionizable, soil hydraulic properties (e.g. hydraulic conductivity, soil moisture content, etc.) and environmental conditions (e.g., pH) also strongly influence their transport (Schaffer and Licha, 2015). So far, occurrence of 5 PhACs has been reported in volcanic sandy loam soils irrigated with treated wastewater in New Zealand (Gielen et al., 2009), whereas Durán-Alvarez et al. (2009) detected pharmaceuticals and potential endocrine disruptor compounds at concentrations bellow 1 ng g^{-1} in agricultural Mexican soils irrigated with untreated wastewater for approximately 90 years. Leaching and contamination of groundwater by bisphenol-A, triclocarban, triclosan, 4-nonylphenol, salicylic acid, oxytetracycline, tetracycline, trimethoprim and primidone have been also recently observed in irrigated soils in China (Chen et al., 2011). Regarding our previous work, we have reported up to 7 out of 64 target PhACs in SW Spain after analysis of 21 sludge-amended surface soil samples (Pérez-Carrera et al., 2010) and soil cores at different depths (Corada-Fernández et al., 2015), showing values for individual components up to 1.3 ng g^{-1}.

When treated wastewater is used for irrigation, contaminants in reclaimed water may transfer to soil through water leaching onto the vadose zone, potentially negatively affecting organisms inhabiting this zone (e.g., earthworms, plants, etc.). However, information on the accumulation of PhACs in soils and their environmental risks towards terrestrial species is scarce (Muñoz et al., 2009; Martín et al., 2012; Jones et al., 2014; Verlicchi and Zambello, 2015). Among the few available examples, Amorim et al. (2010) assessed the toxicity of triclosan in the terrestrial environment using several soil species including invertebrates (*Eisenia andrei*, *Enchytraeus albidus* and *Folsomia candida*) and the plants *Triticum aestivum* and *Brassica rapa*. Another study investigated the ecotoxicological risk of carbamazepine on species the macrophyte genus *Typha* (Dordio et al., 2011) by measurements of relative growth rates (RGR). For most of the PhACs, however, information is not available and the equilibrium partitioning method, relying on the use of toxicity data towards aquatic species and the partition coefficients of chemicals, has been used to predict toxicity data (ECB, 2003).

In order to gain novel information on the distribution and fate of CECs, we monitored a wide number of PhACs in wastewater ($n = 78$) and soil ($n = 45$) samples taken along a period of two years from a WWTP and its adjacent garden (irrigated with effluent water) in Jerez de la Frontera (SW Spain). The target compounds were selected taking into account the agricultural, urban and industrial activity of the area and the results from previous studies (Pérez-Carrera et al., 2010; Corada-Fernández et al., 2015; Baena-Nogueras et al., 2016) on the distribution of PhACs in receiving surface waters and sludge-amended agricultural soils. Some of the analyzed chemicals (e.g., diclofenac and several macrolide antibiotics) are also included in the first watch list and EC list of priority substances from the European Parliament and the Council of the European Union (European Commission, 2015). The main objectives of this research were: a) to monitor the concentrations of different classes of PhACs (analgesic/anti-inflammatories, antibiotics, antiepileptics, beta-blocker drugs, lipid regulating agents, etc.) in influent and effluent wastewater samples and in soils, b) to evaluate the effects on the vadose zone of utilizing this type of water by taking samples at different times of the year and analyzing the vertical distribution of PhACs in soil cores, and c) to perform a preliminary environmental risk assessment towards terrestrial species considering the measured PhAC concentrations and the current available ecotoxicity data.

2. Materials and methods

2.1. Chemicals and materials

All the pharmaceutical standards for target compounds (Table S1, Supporting information) were of high purity grade (>95%) and were obtained from Sigma–Aldrich (Madrid, Spain). Isotopically labelled compounds, used as internal standards, were atenolol-d_7, phenazone-d_3, acetaminophen-d_4, ibuprofen-d_3 from LGC Standards (Barcelona, Spain), carbamazepine-d_{10}, gemfibrozil-d_6, glyburide-d_3 from CDN Isotopes (Quebec, Canada) and sulfadimethoxine-d_6, ofloxacin-d_3, trimethoprim-d_9, naproxen methoxy-d_3, albuterol-d_3, hydrochlorothiazide $^{13}C_6$ from Sigma–Aldrich.

LC-MS grade methanol and water were purchased from Scharlau (Barcelona, Spain), formic acid (98%), ammonia (25%), ammonium formate (97.8%), ammonium acetate (97%) and acetic acid (99%) were purchased either from Sigma Aldrich (Madrid, Spain) or Panreac (Barcelona, Spain). Water was Milli-Q quality and the cartridges used for solid phase extraction were Oasis HLB (200 and 500 mg) from Waters Corporation (Barcelona, Spain).

Standard solutions of pharmaceuticals and isotopically labelled internal standard were prepared in methanol or methanol-water, depending on the compound, at concentrations of 250 mg L^{-1} and 1000 mg L^{-1}, respectively, and stored at −20 °C. Stock solutions of pharmaceuticals were prepared every six months, except for antibiotics, which were prepared monthly due to their limited stability. Before analysis, a calibration curve was prepared by appropriate dilution of the aforementioned standards in methanol–water (25:75, v/v).

2.2. Wastewater samples

The municipal WWTP serves 215 000 inhabitants from Jerez del Frontera city and is designed to treat up to 103 000 cubic meters of water per day. Water treatment consists in three main stages: a primary physicochemical treatment followed by a secondary biological treatment, comprising nitrification and denitrification zones, and finally an elimination step by disinfection through ultraviolet radiation. Most of the Jerez de la Frontera sewage (between 50 000–65 000 m^3 day^{-1}) is treated at this WWTP and, after secondary treatment, discharged into the Guadalete River and also used for irrigation of the WWTP gardens. Additionally, a fraction of

the WWTP effluent (60 000–70 000 m^3 $year^{-1}$) undergoes tertiary treatment and is transferred to the local golf course for irrigation and/or discharged into the Torrox pond. Sludge is composted (4500 tons $year^{-1}$) and used by local farmers as fertilizer, covering a surface of up to 10 km^2.

One-liter influent and effluent wastewater samples (n = 22) were collected monthly from the secondary treatment between July 2014 and July 2015 considering the hydraulic retention time in the treatment plant (24 h). Daily-composite samples were obtained by mixing sample volumes collected every hour during 24 h by an automatic device. The sewage samples were taken once per month, on a weekday the second week of each month. Then, aliquots of each type of sample were extracted (n = 4) within 24 h after collection after filtration through Whatman glass fiber filters (1 μm pore size), which were combusted at 450 °C for 4 h in an oven prior use.

Removal rates (%R) of individual pharmaceuticals were calculated using the following equation (1):

$$\%R = \frac{C_{inf} - C_{eff}}{C_{inf}} \cdot 100 \quad (1)$$

where C_{inf} is the concentration measured in the influent wastewater and C_{eff} is the concentration measured in the effluent wastewater.

2.3. Soil sample collection and characterization

Soil samples were collected from the garden of Jerez de la Frontera WWTP, which covers an area of approximately 7.5 m^2. These soils are covered by *St. Agustine* (*Stenotaphrum secundatum*) and are irrigated with treated wastewater from the plant after physicochemical and biological treatments. The irrigation rate is 9.17 L min^{-1}. During summers, the garden is irrigated with pulses of 20–30 min roughly five times per week, whereas during the rest of the year the irrigation frequency decreases at approximately twice per week because of intermittent rainfalls and lower temperatures (see Fig. S1, Supporting information). Surface soil samples were collected at 20 cm depth to avoid the radicular grass zone (considered constant, 10 cm). All samples were taken seasonally in the second half of each season over two years to determine the concentration of PhACs in the soil from winter 2014 to autumn 2015. Additionally, disturbed soil samples were vertically collected from the top surface using a soil auger (Eijkelkamp) and stainless steel rings (5 cm length; 5 cm inner diameter) inserted by percussion with a hammer in the second half of summer and winter months and sectioned to analyze 6 specific depths (20, 40, 60, 90, 120 and 150 cm). All these samples were transported at 4 °C to the laboratory, where they were frozen at −20 °C. Later, soil samples were freeze-dried, milled and stored in sealed plastic bags at room temperature until analysis. The main physicochemical properties of these soils are shown in Table S2 (Supporting information). Briefly, the soil of our sampling area was characterized by having high clay + silt content (on average, 86%), low hydraulic conductivity, K_S (on average, 4.45E-09 m s^{-1}) and average porosity of 34% (Biel-Maeso et al., 2015).

2.4. Sample treatment and analysis of the pharmaceutically active compounds

The analytical procedure used for wastewater sample analysis was based on that previously reported by Baena-Nogueras et al. (2016), whereas soil samples were measured according to the protocol described by Biel-Maeso et al. (2017). Briefly, PhACs were extracted from soil (4 g) using pressurized hot water (40 mL) extraction (PHWE) at 100 °C. Soil extracts and wastewater samples (100 mL) were purified and preconcentrated by solid phase extraction (SPE) using Oasis HLB columns. These cartridges were pre-conditioned with 8 mL of methanol followed by 8 mL of Milli-Q water at a flow rate of 1 mL min^{-1}. After passing the samples, the cartridges were then rinsed with 8 mL of Milli-Q water and dried under vacuum for 10 min to remove excess of water. Analytes were finally eluted from the HLB sorbent with 10 mL of methanol at 1 mL min^{-1}. The final extract was evaporated under a gentle stream of nitrogen and reconstituted with 1 mL methanol-water (25:75, v/v) and filtered using PTFE filters (0.22 μm from Teknokroma Corporation, Spain). Extraction recovery percentages, previously published by Baena-Nogueras et al. (2016), were between 17 and 146% for wastewater samples, being higher than 70% for 47 target analytes, and between 50% and 124% for most of the analytes (60%) in the case of soil samples (Table S1).

Chromatographic analyses were performed by ultra-performance liquid chromatography – mass spectrometry (UPLC-MS/MS) using a Bruker EVOQ Elite system (Bruker, Billerica, MA), equipped with a C18 chromatographic column (100 mm × 2.1 mm with 2 μm particle size) and an electrospray interface. For aqueous samples, the method limits of detection (LOD) were below 1 ng L^{-1} for most compounds (>90%), whereas for soil samples they were between <0.01 and 0.83 ng g^{-1} (Table S1). In general, the precision of the method, calculated as the relative standard deviation (RSD) of replicate extractions and analyses, was less than 20%. More specific details on both analytical methods is presented elsewhere (Baena-Nogueras et al., 2016; Biel-Maeso et al., 2017).

2.5. Ecotoxicological risk assessment

The potential environmental risk of the target PhACs was assessed based on the "worst case scenario" in accordance with the Technical Guidance Document on Risk Assessment of the European Union (ECB, 2003). Ecotoxicological risk assessment was evaluated in wastewater irrigated soils by means of risk quotient values (RQs). The RQ value of each pharmaceutical in soil was calculated as the ratio between its measured environmental concentration (MEC) in soil and the concentration below which no adverse effect is expected to occur (predicted no-effect concentration: PNEC) (ECB, 2003). Different risk levels were then established following the recommendation by Hernando et al. (2006): insignificant risk (RQ < 0.01), low risk (0.01 > RQ > 0.1) and moderate risk (0.1 > RQ > 1).

The equilibrium partitioning method was used to calculate PNEC values as toxicity data were not available for soil organisms. This method relies on the use of toxicity data towards aquatic species and the partition coefficients of contaminants (ECB, 2003). Therefore, $PNEC_{soil}$ values were estimated from $PNEC_{water}$ values applying the following equation (ECB, 2003):

$$PNEC_{soil} = \frac{K_d}{RHO_{soil}} \cdot PNEC_{water} \cdot 1000 \quad (2)$$

where K_d is the soil-water partition coefficient, and RHO_{soil} is the bulk density of wet soil (see Table S3 and Table S2, respectively, for more information). $PNEC_{water}$ values were estimated from the lowest acute toxicity data reported in literature (EC_{50}) for algae, invertebrate and fish species as target organisms and applying an assessment factor of 1000. These values were derived from the existing literature (Table S4, Supporting information).

3. Results and discussion

3.1. Concentrations and removal of PhACs in Jerez de la Frontera WWTP

The concentration of pharmaceuticals (minimum, maximum and mean) in influent and effluent wastewater, as well as detection frequencies and removal efficiencies, calculated for samples collected over a one-year period, are presented in Table 1. In total, 44 out of 78 target PhACs (Table S1) were found in influent and effluent samples. On average, 220 $\mu g\,L^{-1}$ of pharmaceuticals were measured in the influent to the WWTP, ranging between 39 and 397 $\mu g\,L^{-1}$ depending on the sampling month. The total pharmaceutical concentration discharged through the WWTP effluent was significantly lower, approximately 17 $\mu g\,L^{-1}$ (ranging 3–41 $\mu g\,L^{-1}$). Acetaminophen showed the highest levels in influent samples, with a mean concentration of 83 $\mu g\,L^{-1}$, followed by caffeine, ibuprofen and salicylic acid (with mean concentrations of 55, 29 and 17 $\mu g\,L^{-1}$, respectively). All of them, except caffeine, were analgesic and anti-inflammatories which do not need medical prescription. These results are in agreement with previous studies (Santos et al., 2009; Lara-Martín et al., 2014) reporting the predominance of these therapeutic class. Regarding the wastewater effluent samples, ranitidine, hydrochlorothiazide and gemfibrozil were identified as the most abundant PhACs, with mean concentrations of 2.8, 2.3 and 1.9 $\mu g\,L^{-1}$, respectively. Here, 33 out of the 44 detected compounds had concentrations lower than 500 $ng\,L^{-1}$ on average, and 8 PhACs had low detection frequencies (<50%). The hydrochlorothiazide concentrations in the present study were quite similar to those previously measured by Lara-Martín et al. (2014) at Stony Brook WWTP (United States). However, these authors found lower levels for ranitidine (30 $ng\,L^{-1}$) and gemfibrozil (42 $ng\,L^{-1}$). Our values might be also different from those reported in effluents from other treatment plants (Petrović et al., 2003; Gros et al., 2006; Kasprzyk-Hordern et al., 2009; Kosma et al., 2010), although within the same order of magnitude, reflecting different wastewater

Table 1
Concentration ranges of pharmaceuticals ($ng\,L^{-1}$) in influent and effluent wastewater from Jerez de la Frontera WWTP, detection frequencies (%) and removal efficiencies (R) over one-year period (July 2014–July2015).

Therapeutic groups	Compounds	Influent		Effluent		R (%)
		Min-Max (Mean)	Freq.	Min-Max (Mean)	Freq.	Min-Max (Mean)
Analgesic/Anti-inflammatories	Acetaminophen	9220-170000 (83100)	100	17-441 (228)	91	98-100 (100)
	Diclofenac	38-1510 (731)	100	38-1020 (642)	100	0-68 (10)
	Ibuprofen	2630-60000 (28600)	100	95-751 (269)	73	71-100 (97)
	Ketoprofen	314-6010 (3410)	100	210-5480 (1820)	100	0-89 (45)
	Naproxen	363-17700 (8470)	100	40-1630 (247)	100	65-99 (94)
	Phenazone	8-148 (54)	91	4-683 (158)	100	0-50 (5)
	Salicylic Acid	535-52800 (16900)	100	23-419 (138)	82	90-100 (98)
Lipid regulators/Antihypertensives	Bezafibrate	27-1040 (297)	100	9-179 (73)	100	21-92 (72)
	Fenofibrate	2-422 (78)	82	1-146 (24)	82	14-95 (54)
	Gemfibrozil	987-7010 (2870)	100	518-3720 (1910)	100	0-70 (30)
	Pravastatin	406-406 (406)	9	138-138 (138)	9	66-66 (66)
	Atenolol	275-3030 (1620)	100	134-2110 (1140)	100	1-55 (30)
	Nadolol	5-103 (37)	100	1-72 (14)	100	0-93 (59)
	Propanolol	15-511 (123)	100	9-235 (73)	100	0-88 (33)
	Timolol	2-37 (13)	100	0.4–50 (12)	100	0-83 (30)
Psychiatric drugs/Stimulants	Amitriptiline	9-199 (75)	100	4-59 (23)	100	32-86 (64)
	Carbamazepine	31-906 (291)	100	21-657 (232)	100	2-37 (18)
	Fluoxetine	7-1760 (326)	55	4-1570 (326)	45	10-100 (67)
	Caffeine	14000-116000 (54700)	100	63-1950 (459)	100	97-100 (99)
Antibiotics	Ciprofloxacin	173-2610 (1130)	100	48-1450 (586)	100	0-80 (49)
	Danofloxacin	49-319 (140)	36	2-74 (35)	27	42-100 (73)
	Norfloxacin	33-468 (215)	64	5-350 (160)	64	3-86 (37)
	Ofloxacin	57-1610 (765)	100	37-1470 (631)	100	0-56 (24)
	Flumequine	1-73 (22)	45	0-24 (8)	45	0-86 (55)
	Clarithromycin	145-21700 (5790)	100	7-7640 (903)	100	18-99 (80)
	Erythromycin	40-549 (272)	91	18-359 (149)	91	16-79 (48)
	Spiramycin	374-2400 (1160)	100	181-2790 (908)	91	0-100 (44)
	Clindamycin	5-114 (42)	100	10-42 (27)	100	0-79 (27)
	Lincomycin	3-921 (132)	100	3-120 (51)	100	0-87 (28)
	Sulfadiazine	5-164 (70)	100	1-46 (18)	100	49-96 (71)
	Sulfamethizole	18-562 (256)	100	11-480 (186)	100	0-67 (26)
	Sulfamethoxazole	55-1300 (571)	100	26-633 (254)	100	19-79 (49)
	Metronidazole	7-257 (61)	100	8-117 (40)	100	0-55 (24)
	Ornidazole	3-12 (7)	27	0.4–3 (2)	27	15-93 (65)
	Trimethoprim	59-1310 (297)	100	33-788 (198)	100	0-63 (33)
Other PhACs	Famotidine	20-130 (75)	100	9-187 (58)	100	0-78 (34)
	Ranitidine	457-9870 (3410)	100	499-7500 (2770)	91	0-100 (21)
	Furosemide	527-2410 (1370)	100	161-1990 (764)	100	0-88 (45)
	Hydrochlorothiazide	1090-5000 (2970)	100	280-4430 (2270)	100	0-92 (24)
	Glyburide	1-47 (12)	91	0.4–30 (7)	82	0-100 (42)
	Albuterol	22-30 (26)	36	15-23 (18)	36	7-49 (28)
	Σ PhACs	39100-397000 (220000)	–	3100-41300 (17100)	–	87-96 (92)

treatment conditions and pharmaceutical consumption patterns in other countries.

Focusing on the removal efficiency of Jerez de la Frontera WWTP towards pharmaceuticals, more than half of the compounds detected had average poor removal efficiencies (<50%), and only 5 of them were efficiently eliminated (>85%). The most abundant compounds measured in the WWTP influent (acetaminophen, ibuprofen, naproxen, salicylic acid, and caffeine) showed the highest removal efficiencies, so the total average removal of PhACs in Jerez de la Frontera WWTP was 92%. Moderate removal efficiencies (between 30 and 75%) were observed for lipid regulators and antihypertensives. However, nearly no removal was observed for other chemicals such as diclofenac, phenazone and carbamazepine (<20%), regardless of the time of year. The removal efficiency for the psychiatric drug carbamazepine was from 0 to 30%, in accordance with previous studies (Golovko et al., 2014; Subedi and Kannan, 2015). In terms of different therapeutic classes of PhACs, the highest removal efficiencies throughout the year corresponded to analgesics and anti-inflammatories such as acetaminophen, ibuprofen, naproxen and salicylic acid, with values close to 100%. Within this group, ketoprofen showed an average removal efficiency of 45%, and the nonsteroidal anti-infammatory diclofenac and the analgesic phenazone did not show appreciable elimination. Fenoprofen, indomethacin, mefenamic acid and phenylbutazone were never detected. These data are comparable to those previously reported where removal rates of 97, 94, and 10% were measured for ibuprofen, naproxen and diclofenac, respectively (Gros et al., 2007; Kasprzyk-Hordern et al., 2009; Santos et al., 2009; Lara-Martín et al., 2014). The poor removals obtained for other substances such as hydrochlorothiazide and some antibiotics were consistent with recent studies (Gros et al., 2007; Santos et al., 2007; Lara-Martín et al., 2014), although discrepancies were observed for specific compounds such as phenazone. This pharmaceutical was reported to be eliminated between 66 and 98% in other WWTPs (Gros et al., 2007; Kosma et al., 2014), where in our case we measured higher concentrations in the effluent compared to the influent. Possible explanations could be its desorption from the sludge after secondary treatment and/or the transformation of the conjugated forms of this and other PhACs showing negative removal efficiencies into the free form by microorganisms (Radjenović et al., 2009). Regarding the antibiotic group of sulfonamides, one of the most abundant in terms of concentration, it showed removal efficiencies between 26 and 71% (on average), and these results comparable to available data from Golovko et al. (2014) (removal from 44 to 70%).

Regarding possible seasonal variations within the time frame of the sampling campaign, significant changes were detected in the WWTP influent and were attributed to a combination of the PhAC seasonal consumption patterns and the influence of precipitation. That is, most of the rainfall (see Fig. S1, Supporting information) occurred in November 2014, and this corresponded to lower levels of PhACs (about one order of magnitude less than usual) registered during that month in both influent (73 $\mu g\,L^{-1}$) and effluent (3 $\mu g\,L^{-1}$) samples (Tables S5 and S6, respectively). Previous studies in this area have shown that during heavy rain events most of the wastewater is mixed with rainwater and discharged via combined sewer overflows (CSOs) directly into Guadalete River (Corada-Fernández et al., 2017), therefore increasing the levels of pollutants in the receiving waters. Among the different therapeutic classes, antibiotic showed highest concentrations in autumn and winter and lowest concentrations in spring and summer in the WWTP influent (Table S5, Supporting information). As antibiotics are mainly used to cure infections of the respiratory tract, which occur more frequently during colder months, the consumption of these chemicals is expected to be significantly higher during winter. On the other hand, relevant increases (+50%) in the concentration of analgesics and anti-inflammatories were measured during both summer seasons in 2014 and 2015. The same was observed for blood lipid regulators. As these drugs are used all year, their rising concentrations in wastewater may be associated to the increase in the population of the region during the touristic season. Another example was albuterol, a pharmaceutical used to prevent and treat asthma and chronic obstructive pulmonary diseases which was found in wastewater predominantly during spring and summer seasons, when associated diseases increase due to highest levels of pollen in air (Castiglioni et al., 2006).

The removal efficiencies of many compounds (e.g., ibuprofen and caffeine) were quite stable over the entire sampling campaign but, in some cases, significant variations were observed among different seasons and/or specific months. As an example, gemfibrozil removal was on average 30% but varied from 0 to 70% depending on the sampling period. The antibiotics trimethoprim and metronidazole were quite persistent throughout the entire year, showing low removal efficiencies that occasionally increased to up to 63%. Changes in the removal efficiency of the WWTP also had a direct effect on the concentrations of PhACs in the effluent. Overall, lower levels were measured for most compounds during the summer season and higher levels in winter and autumn (Table S6, Supporting information). This trend was expected as higher temperatures in summer contribute to increased activity of microorganisms responsible for the biodegradation of contaminants in the WWTP. Additionally, higher irradiance can also lead to faster photodegradation rates for those PhACs sensitive to sunlight (Baena-Nogueras et al., 2017).

3.2. Occurrence, distribution and ecotoxicological risk of PhACs in sewage-impacted soils

3.2.1. Surface soil samples

Table 2 shows the concentrations in soils (0–20 cm) of the PhACs that were detected during the seasonal sampling campaigns performed in 2014 and 2015. The measured total concentrations of PhACs in soil samples were generally between 2 and 15 $ng\,g^{-1}$, with highest values for analgesics and anti-inflammatories, which represented the most predominant therapeutic class (maximum concentration = 10.05 $ng\,g^{-1}$, mean concentration = 4.02 $ng\,g^{-1}$). They were followed in abundance by antibiotics (maximum concentration = 5.45 $ng\,g^{-1}$, mean concentration = 0.97 $ng\,g^{-1}$) and psychiatric drugs (maximum concentration = 3.78 $ng\,g^{-1}$, mean concentration = 1.76 $ng\,g^{-1}$). Overall, we detected 17 out of 45 target PhACs belonging to different therapeutic classes. Diclofenac, acetaminophen and caffeine were measured at relatively higher concentrations than other PhACs (1.89, 1.33 and 1.33 $ng\,g^{-1}$ on average, respectively), while hydrochlorothiazide, mefenamic acid, flumequine, and carbamazapine were present at intermediate concentrations (from 0.43 to 0.71 $ng\,g^{-1}$). The remaining drugs detected were found to be below 0.20 $ng\,g^{-1}$ on average. The occurrence of some of these compounds (mainly analgesics/anti-inflammatories) and other PhACs (e.g., omeprazole) has been confirmed in previous works reporting polluted soils and sediments within the same study region (Corada-Fernández et al., 2015; Pérez-Carrera et al., 2010; Biel-Maeso et al., 2017). For instance, diclofenac was also previously detected at concentrations between 0.1 and 15.4 $ng\,g^{-1}$ (Corada-Fernández et al., 2015; Biel-Maeso et al., 2017) in soil columns from nearby crops amended with sludge. Several other studies have also reported the presence of these and/or other PhACs in soils irrigated with reclaimed water. For example, Kinney et al. (2006) found carbamazepine, fluoxetine, erythromycin and diphenhydramine as the most commonly detected pharmaceuticals at three locations from a medium-sized

Table 2
Concentration of PhACs (ng g^{-1}) detected in superficial soil samples from Jerez de la Frontera experimental-plot. Only the PhACs detected are shown here.

	Winter 14	Spring 14	Summer 14	Autumn 14	Winter 15	Spring 15	Summer 15	Autumn 15	Min-Max (Mean)	Freq.
Analgesic/Anti-inflammatories										
Acetaminophen	5.95 ± 0.13	n.d.	0.70 ± 0.02	0.46 ± 0.03	0.32 ± 0.01	2.87 ± 0.03	0.85 ± 0.25	n.d.	n.d.-5.95 (1.39)	75
Diclofenac	0.54 ± 0.05	0.09 ± 0.01	n.d.	0.13 ± 0.00	4.73 ± 0.27	5.06 ± 0.20	3.58 ± 0.08	0.44 ± 0.07	n.d.-5.06 (1.82)	88
Ibuprofen	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	100
Mefenamic acid	0.62 ± 0.02	0.08 ± 0.00	0.15 ± 0.03	0.09 ± 0.01	1.60 ± 0.04	1.97 ± 0.25	1.05 ± 0.05	0.10 ± 0.00	0.08–1.97 (0.71)	100
Phenazone	n.d.	n.d.	0.18 ± 0.01	0.07 ± 0.00	0.36 ± 0.01	0.15 ± 0.06	n.d.	n.d.	n.d.-0.36 (0.10)	50
Σ group	7.11	0.17	1.04	0.75	7.01	10.05	5.48	0.54	0.17–10.05 (4.02)	–
Lipid regulators/Antihypertensives										
Bezafibrate	0.38 ± 0.00	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.-0.38 (0.05)	13
Gemfibrozil	0.06 ± 0.00	n.d.	0.03 ± 0.00	n.d.	0.06 ± 0.01	0.03 ± 0.00	0.02 ± 0.00	n.d.	0.02–0.06 (0.04)	100
Σ group	0.43	0.00	0.03	0.00	0.06	0.03	0.02	0.00	0.00–0.43 (0.07)	–
Psychiatric drugs/Stimulants										
Carbamazepine	0.08 ± 0.01	0.33 ± 0.00	1.36 ± 0.13	0.33 ± 0.02	0.21 ± 0.03	0.57 ± 0.06	0.33 ± 0.00	0.23 ± 0.01	0.08–1.36 (0.43)	100
Caffeine	0.51 ± 0.01	0.83 ± 0.03	1.18 ± 0.04	0.62 ± 0.02	1.73 ± 0.05	3.21 ± 0.03	1.12 ± 0.07	1.41 ± 0.03	0.51–3.21 (1.33)	100
Σ group	0.59	1.16	2.54	0.95	1.95	3.78	1.45	1.64	0.59–3.78 (1.76)	–
Antibiotics										
Flumequine	5.31 ± 2.00	n.d.	n.d.	0.14 ± 0.01	n.d.	n.d.	n.d.	n.d.	n.d.-5.31 (0.68)	25
Lincomycin	n.d.	0.03 ± 0.01	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.-0.03 (0.00)	13
Sulfamethoxazole	n.d.	n.d.	0.25 ± 0.03	0.09 ± 0.01	0.18 ± 0.01	0.12 ± 0.00	0.08 ± 0.01	0.05 ± 0.00	n.d.-0.25 (0.10)	75
Ornidazole	0.10 ± 0.00	0.34 ± 0.02	0.47 ± 0.03	n.d.	n.d.	0.28 ± 0.07	0.11 ± 0.01	0.03 ± 0.00	n.d.-0.47 (0.17)	75
Trimethoprim	0.04 ± 0.00	0.01 ± 0.00	0.03 ± 0.01	0.01 ± 0.00	n.d.	0.02 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	n.d.-0.04 (0.02)	88
Σ group	5.45	0.39	0.75	0.24	0.18	0.41	0.21	0.10	0.10–5.45 (0.97)	–
Other PhACs										
Hydrochlorothiazide	0.68 ± 0.03	0.97 ± 0.06	1.20 ± 0.04	0.40 ± 0.02	0.43 ± 0.05	0.95 ± 0.00	0.80 ± 0.02	0.38 ± 0.06	0.38–1.20 (0.73)	100
Glyburide	0.02 ± 0.00	n.d.	n.d.	n.d.	n.d.	<LOQ	n.d.	n.d.	n.d.-0.02 (0.01)	75
Σ group	0.71	0.97	1.20	0.40	0.43	0.95	0.80	0.38	0.38–1.20 (0.73)	–
Σ Total PhACs	14	3	6	2	10	15	8	3	2-15 (8)	–

n.d. (not detected), <LOQ (below limit of quantification).

city in United States. Gielen et al. (2009) reported two compounds (carbamazepine and caffeine) in surface soils at significantly higher concentrations (217 and 2.9 ng g^{-1}, respectively) than those reported in our study (1.36 and 3.21 ng g^{-1}, respectively).

Some target compounds that were found in the WWTP effluent were not detected in the surface soil samples due to the different methodologies used (the validated protocol for solid samples is only suitable for 45 compounds, whereas up to 78 can be analyzed in aqueous samples) (see Table S1 for more information on specific PhACs). Nevertheless, all those PhACs detected in the receiving soils were also present in wastewater, with the exception of mefenamic acid (found in soils at concentrations up to 0.71 ng g^{-1}). Fig. 1 represents a direct comparison between the top 10 most abundant compounds in the WWTP effluent and those detected in superficial soil samples. Seven of the 10 PhACs (hydrochlorothiazide, diclofenac, caffeine, sulfamethoxazole, carbamazepine, acetaminophen, and phenazone) were found in both matrices, confirming the direct influence of the treated wastewater used for irrigation on the PhAC pattern found in soil. These compounds that were detected in both matrices at the highest concentrations are key information for future studies on their distribution and behavior, as their presence in sewage-impacted terrestrial environments is foreseen. More into detail, and although less irrigation using recycled wastewater occurred in winter, highest concentrations in soil were generally found in this season, between 10 and 14 ng g^{-1} (Table 2), when mean temperature was about 11 °C. Lower temperatures therefore likely had a significant effect on minimizing biodegradation processes compared to summer months, when values over 25 °C are often measured. The potential photodegradation in surface soils of those highly light-sensitive PhACs (e.g., antibiotics such as fluoroquinolones) (Baena-Nogueras et al., 2017) is also minimized in winter due to lower irradiation. All year round, six compounds (caffeine, carbamazepine, hydrochlorothiazide, mefenamic acid, gemfibrozil, and ibuprofen) were the most frequently detected (100%), whereas the detection frequencies (<25%) and concentrations (<0.50 ng g^{-1}) were significantly lower for three compounds, i.e, bezafibrate, nadolol, and lincomycin. Lastly, ibuprofen concentration levels in all the superficial soil samples were below the limit of quantification (LOQ). The occurrence of all these PhACs in soils is not only a consequence of their relatively high abundance in effluent wastewater (e.g., hydrochlorothiazide) but is also related to their physicochemical properties (Table S8) and those in the receiving soils (Table S2). For instance, those pharmaceuticals with high log K_{OW} values such as gemfibrozil, and/or net positive charge at the environmental pH (e.g., betablockers such as nadolol) are expected to be relatively strongly bonded to the soils (via hydrophobic interactions with the organic matter or hydrophilic interaction with negatively charged clays, respectively) and, therefore, be less available for biodegradation. These compound-soil interactions would enhance the retention and/or persistence of these contaminants in our soils, as it has been previously reported in laboratory experiments (Maszkowska et al., 2014). On the other hand, we can expect than compounds negatively charged at environmental pH, such as ibuprofen and sulfamethoxazole, tend to interact less with soil clays so their percolation towards deeper soil layers is expected to be higher.

3.2.2. Vertical distribution of PhACs in soil

Soil columns were sampled at four different seasons (winter-summer 2014 and winter -summer 2015) in the WWTP garden to study the vertical distributions of PhACs in the vadose zone

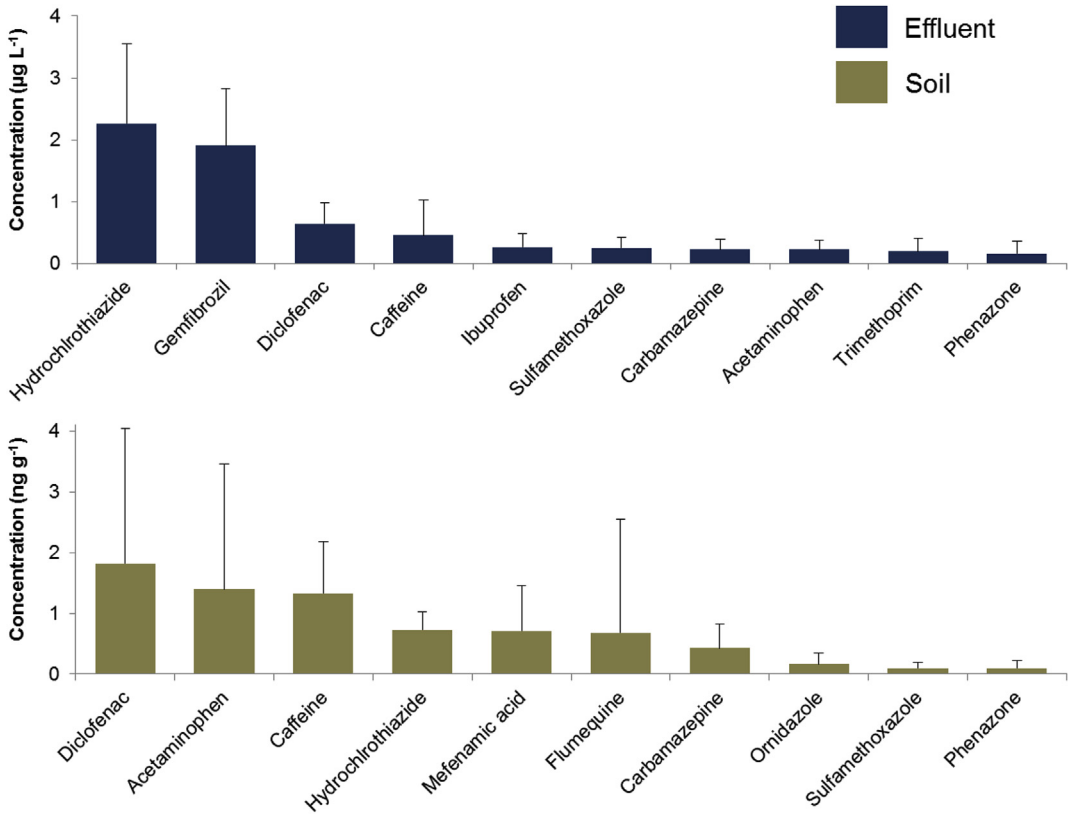

Fig. 1. Top 10 most abundant pharmaceuticals in the WWTP effluent (µg L^{-1}) and in the receiving soils (ng g^{-1}). Mean concentrations and standard deviations are shown.

between the surface down to 3 m depth. Fig. 2 shows the total concentrations of these compounds at 6 different depths (20, 40, 60, 90, 120 and 150 cm). Data on individual compounds are presented in Table S7. PhAC levels ranged from 1 to 14 ng g^{-1} and from 2 to 8 ng g^{-1} in winters and summers, respectively. This is in agreement with the results presented in the previous section and suggests that, despite more irrigation during summer months, the accumulation of pharmaceuticals was more accentuated in winter.

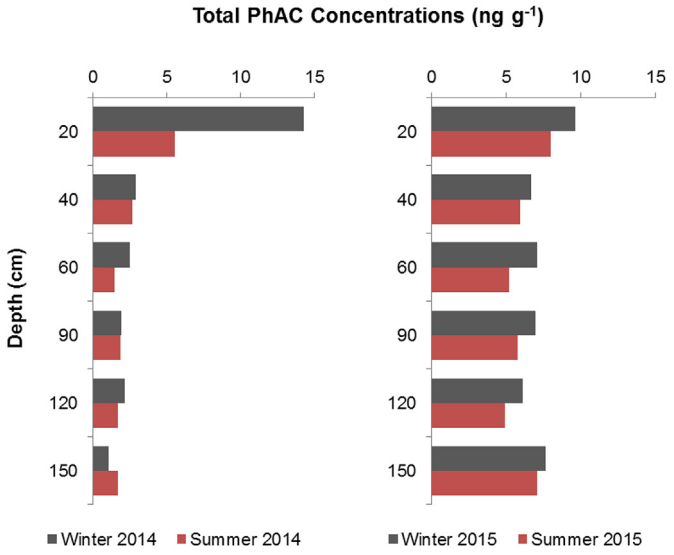

Fig. 2. Vertical concentration profiles (ng g^{-1}) for PhACs in soil columns from Jerez de la Frontera WWTP garden.

Lower PhAC concentrations in warm periods can be explained through biotransformation by enhanced microbial activity along the soil column (Baena-Nogueras et al., 2017) and, to a lower extent as the soil is covered by grass, more effective photodegradation in the surface due to higher irradiance. This last process, however, might be relevant enough for some highly photodegradable chemicals such as many antibiotics, for which very short half-life times (<5 min) have been reported (Baena-Nogueras et al., 2017) at 500 W m^{-2}, the annual average irradiance in our sampling area. The vertical profiles were also significantly different between 2014 and 2015. During the first year the highest concentrations of pharmaceuticals were clearly detected in the soil surface in both winter and summer periods. The vertical distribution of PhACs was more uniform in 2015. These differences between both years could be explained by accumulation of contaminants from the WWTP effluent during 2014 and later percolation after the precipitation events at the end of that year (see Table S6 and Fig. S1, Supporting information). The occurrence of short and intense heavy rain episodes is typical from these Mediterranean regions and can induce a rapid leaching of substances through the vadose zone, inhibiting adsorption onto soil particles and therefore promoting transport of PhACs towards deeper horizons in soils (Candela et al., 2010). In fact, the resulting vertical distribution profiles have also been previously observed in laboratory and field experiments and are described as typical mass transport movements in soil media when a pulse of chemical compound (pollutant or a tracer) is applied on the ground surface (Candela et al., 2007; Corada-Fernández et al., 2015). Additionally, there was a secondary maximum measured for PhACs at 150 cm depth in winter 2015. The same vertical profile was recently reported by our research group in other soil columns from the same region during the analysis of synthetic surfactants, linear alkylbenzene sulfonates (LAS) and alcohol polyethoxylates

(AEOs). These compounds, also sewage-derived, were detected at highest concentrations in the capillary fringe between 1.25 and 1.75 m depth and their presence here was attributed to migration and later adsorption from the aquifer beneath after rain episodes due to fluctuations in the water level (Corada-Fernández et al., 2015).

Regarding the vertical distribution of specific compounds (Table S7, Supporting information), diclofenac and mefenamic acid, having log K_{OW} 4.51 and 5.12, respectively, were found at the highest concentrations in the soil columns, with maximum values up to 4.95 and 1.60 ng g^{-1}, respectively, occurring during the winter season. The occurrence and distribution of the rest of PhACs, however, cannot be entirely described by hydrophobicity as the organic carbon content of the soil was relatively low (on average 0.73 ± 0.12%), and substances such as caffeine, also found at relevant concentrations in the column (1.73 ng g^{-1} in winter), have extremely log K_{OW} values (e.g., −0.07). Their adsorption to the soils could then be associated with their high cationic exchange capacities (CECs, see Table S2, Supporting information). In the case of caffeine, its cationic form may prevail at the soil conditions (pKa value of 10.40, Table S8) and could interact with the negatively charged surface of clays. The same behavior could be expected for nadolol (with pka values over 9 and therefore positively charged at the environmental pH), for which cation exchange is the main interaction mechanism as it has been previously described for this antihypertensive and other beta-blockers by Kodešová et al. (2015). Nevertheless, another recent study (Maszkowska et al., 2014) that investigated the sorption capacity of these drugs using different soils and environmental conditions such as pH and ionic strength concluded that beta-blockers showed a limited ability to be immobilized and thus, can be considered mobile in the soil and have potential to reach the groundwater. This is confirmed by our results as nadolol was found down to 120 cm depth. Compounds with negative net charge (see Table S8 for specific PhACs) such as ibuprofen, mefenamic acid, gemfibrozil or sulfamethoxazole, adsorb less strongly to soils containing high clay percentages (up to 50% in our sampling area) mainly because of the electrostatic repulsion between the negatively charged compounds and the negatively charged soil particle surfaces, whereas carbamazepine, ornidazole, trimethoprim and hydrochlorothiazide, remaining mostly neutral at pH 7.30, would represent an intermediate case and their main interactions with soil particles could be via hydrogen bonding and Van der Waals-forces interactions (Kočárek et al., 2016; Kodešová et al., 2015). There are, therefore, many physicochemical variables such as temperature, pH, clay content and type, etc., that can influence the vertical concentration profiles of these compounds. In that sense, previous studies have reported that pharmaceutical mobility may be more closely correlated to their D_{OW} (pH-dependent n-octanol-water distribution ratio, the combination of K_{OW} and pKa) rather than to the K_{OW} of their neutral forms (Wells, 2006). This and other key factors must be considered in ongoing and future studies to obtain a better knowledge on the fate of PhACs and other ionizable chemicals during their transport through the vadose zone.

3.2.3. Environmental risk assessment

Risk quotients (RQs) for terrestrial organisms were calculated from the measured environmental concentrations (MEC_{soil}) (Table 2) and the predicted no-effect concentrations ($PNEC_{soil}$) of each individual chemical (Table S3, Supporting information). For all PhACs detected in soils, their RQ values were calculated (Eq. (2)) on the basis of their measured concentrations in soil samples over a period of two years (Table S9, Supporting information). The resulting RQs (minimum, maximum and mean values) are reported in Fig. 3. The vertical line at RQ = 0.01 represents the limit between insignificant and low risk. This figure shows that no high environmental risk (RQ > 1) is posed by pharmaceuticals in the WWTP garden, so no immediate effects on terrestrial species are foreseen. All detected compounds in soil showed low risk (RQ < 0.1), and 4 out of 10 PhACs (trimethoprim, flumequine, caffeine and acetaminophen) presented insignificant risk (RQ < 0.01) during the sampling period. The maximum RQ was observed for phenazone (RQ = 0.07), followed by diclofenac (RQ = 0.06).

To the best of our knowledge, no studies have calculated RQ values for soils contaminated by PhACs. The majority of previous studies focused on the study of risk quotients in digested sludge or sludge-amended soils. As an example, Martín et al. (2012) provided the ecotoxicological risk of sixteen PhACs in sewage sludge from wastewater treatment plants. They found that the ecotoxicological risk significantly decreased after the application of digested sludge or compost to the soils. More specifically, they reported RQs ranged between 0.04 and 252 in digested sludge and between 0.002 and 37.8 in compost, which decreased below 1.92 and 0.23, respectively, after they were applied to soils. Other studies focused on the calculation of PNEC values for a limited group of compounds in the soil after sludge application (Muñoz et al., 2009; Jones et al., 2014; Verlicchi and Zambello, 2015). Nevertheless, all results, including ours, are preliminary and must be interpreted cautiously due to the limitations of the approach used. First, ecotoxicological risk assessments are currently performed using toxicity data derived from aquatic species due to the lack of information on the impact of PhACs and other emerging contaminants towards terrestrial species. Second, applying the equilibrium partitioning method recommended by Technical Guidance Document on Risk Assessment of the European Union (ECB, 2003) may not be suitable for lipophilic compounds (e.g., mefenamic acid or gemfibrozil) and does not consider the effects on soil organisms of chemicals that are adsorbed to soil particles and taken up by ingestion.

4. Conclusions

This study establishes a baseline of the presence, quantity, and seasonal distribution of a wide variety of PhACs in wastewater and sewage-impacted receiving soils. More than half of the target compounds (n = 78) could be detected in urban wastewater samples at concentrations from 73 to 372 μg L^{-1} in the influent and from 3 to 41 μg L^{-1} in the effluent. Conventional wastewater treatment based on activated sludge could not efficiently remove 24 target PhACs (removal efficiencies <50%). As a result, up to 17 of these chemicals were later detected in soils irrigated with treated wastewater. The most abundant compounds here were diclofenac, acetaminophen and caffeine, which had significantly higher concentrations (>1.3 ng g^{-1}) than the rest. Differences could be observed when comparing summer and winter vertical concentration profiles in soils. PhACs were predominant in colder months (up to 14 ng g^{-1}), indicating higher persistence of these chemicals at lower soil temperatures. The occurrence of intense heavy rain episodes was also confirmed to have a strong impact on the vertical distribution of pharmaceuticals in soil columns. A preliminary environmental risk assessment suggests, however, that the concentrations measured at any period of the year pose no risk towards terrestrial organisms inhabiting these sewage-impacted soils. This is, however, a first approximation as PhAC ecotoxicity data towards terrestrial species is almost non-existent. Additionally, other negative effects such as the generation of microbial resistances and endocrine disruption cannot be discarded, highlighting the need for further studies on the fate and effects of PhACs and other emerging contaminants in soils.

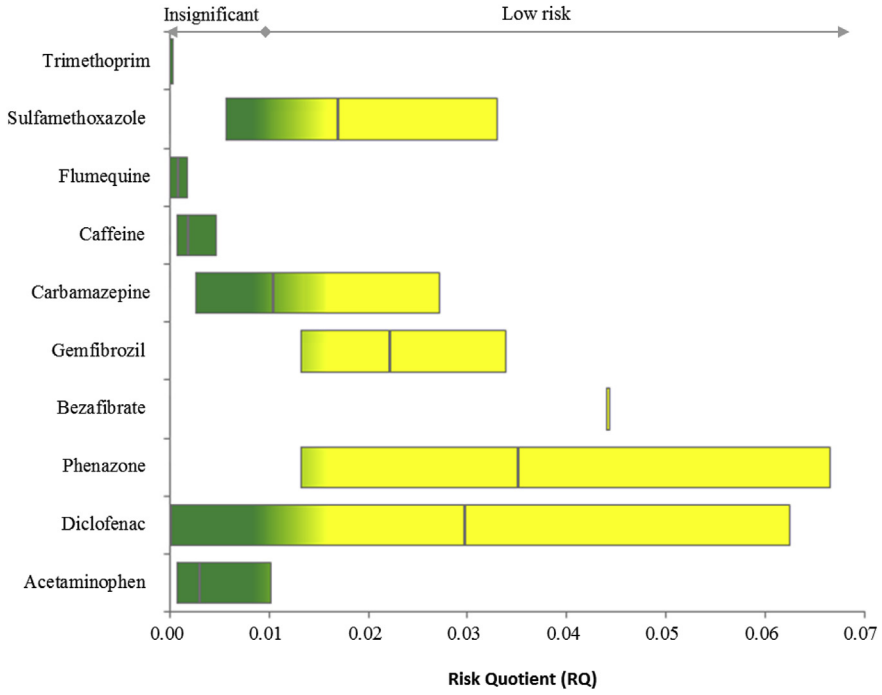

Fig. 3. Risk quotient (RQ) intervals (minimum, mean, and maximum) for those PhACs detected in soil samples.

Acknowledgements

This study has been supported by CGL2011-27349 Project and FPI fellowship, financed by the Spanish Ministry of Economy and Competitiveness.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.envpol.2017.12.085.

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