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Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments

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Abstract

Pharmaceutical residues in the environment, and their potential toxic effects, have been recognized as one of the emerging research area in the environmental chemistry. The increasing attention, on pharmaceutical residues as potential pollutants, is due that they often have similar physico-chemical behaviour than other harmful xenobiotics which are persistent or produce adverse effects. In addition, by contrast with regulated pollutants, which often have longer environmental half-lives, its continuous introduction in the environment may make them "pseudopersistents".

Pharmaceutical residues and/or their metabolites are usually detected in the environment at trace levels, but, even that, low concentration levels (ng/L or μg/L) can induce to toxic effects. In particular, this is the case of antibiotics and steroids that cause resistance in natural bacterial populations or endocrine disruption effects.

In this study, an overview of the environmental occurrence and ecological risk assessment of pharmaceutical residues is presented from literature data. Risk Quotient method (RQ) was applied as a novel approach to estimate the environmental risk of pharmaceuticals that are most frequently detected in wastewater effluents, surface waters and sediments.

Keywords: Environmental risk assessment; Pharmaceuticals; Residues; Wastewaters; Surface waters; Sediments

1. Introduction

The occurrence and implications of pharmaceutical residues in the environment is an emerging concern. The presence of drugs in waterways has been concern of several publications [1–3], but increased attention is also currently focused on drug residues as potential pollutants. Drugs often have similar physico-chemical behaviour as other harmful xenobiotics that are accumulated or induce adverse effects in terrestrial or aquatic organisms.

On the other hand, because of its continuous introduction in the environment, are considered as "pseudopersistent compounds" in the environment. Human and veterinary drugs are continually being released to the environment mainly as a result of manufacturing processes, improper disposal or metabolic excretion. The most significant entry routes of drugs in the environment are related with the release from conventional sewage treatment plants (STPs) and the animal excreta [4–7]. In addition, some drugs are not completely degraded in STPs and remain in the water effluent. Examples of removal efficiency rates in STPs have been reported in recent studies [8] showing the partial removal for some drug residues. Drugs, such as carbamazepine, atenolol, metoprolol, trimethoprim or diclofenac are partiality removed (<10% for most of them and 10–39% for diclofenac). Conversely, other drugs may be release in a modified form, either hydrolysed or conjugated (e.g. ibuprofen is removed in more than 90%, and transformed in hydroxyl and carboxy transformation products). As result, drug residues or their transformation products are detected in effluents [9–16].

Pharmaceutical residues that have been detected in different environmental compartments include: antibiotics, analgesic and anti-inflammatory, lipids regulator agents, β-blockers, antiepileptics, contraceptives, steroids and related hormones. Although, the environmental concentrations are generally at trace levels (ng/L to low μg/L) in the environment, can be sufficient to induce toxic effects. A major concern has been mostly

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focused on antibiotics or steroids drugs that may cause resistance among natural bacterial populations [17] or in the case of steroids, the induction of estrogenic responses as well as alterations in the reproduction or development [17]. However, the ecological risk associated with occurrence of most of the pharmaceuticals in the environment is not sufficiently described.

In this sense, the evidence that environmental implications, of at least some drugs, can be similar to problematic regulated priority organic pollutants (POPs) indicates their consideration in comprehensive risk assessment studies. General principles and guidelines for environmental risk assessment (ERA) of new and existing chemicals have been introduced by European Medicines Evaluation Agency (EMEA) and the Food and Drug Administration (FDA), employing similar tiered system. Both are based in the comparison between the predicted environmental concentrations (PEC) and the worst-case predicted no effect concentrations (PNEC) estimated from standard toxicity assays [18,19].

A contrasted study by Bound and Voulvoulis [20], of both approaches shows the significant improvements in risk assessment guidelines in recent years, but also the proposed solutions for improvement the areas that, if modified, could reduce the effect of uncertainties and lead to a more reliable system [20]. In particular, the use of threshold values to trigger investigations, chronic and mechanism specific toxicity screening or mixture toxicity. In addition, under these approaches, most PECs are overestimated and in this sense, a more concerted monitoring effort would ensure that the relationship between predicted and measured environmental concentrations (MEC) will be in a better understood.

Regulatory concepts of ERA are commonly based on a set of short-term ecotoxicological studies in three to four different species, environmental behaviour and the application of assessment factors to correct inherent uncertainties. However, the application of assessment factors for deriving chronic no-observed effect concentration (NOECs) appears to be problematic. In fact, the use of a variety of long-term tests is unachievable for all the drugs and induces to deficiencies in the toxicity screening [21]. Testing regimes should adopt specific approach for each drug including chronic toxicity studies more relevant or realistic considering the mode of action of drugs and the nature of the exposure of the organisms to these drugs.

As alternative to chronic toxicity screening, other conceptual considerations make use of pharmacological and toxicokinetic information derived from mammals during drug substance development [21]. As well as for improving risk assessment guidelines, considerations for further investigation into the effects of exposure to mixtures of drugs, show that an additional tier of risk assessment would be required [20].

Under this context, this article present an preliminary approach to characterize the environmental risk for pharmaceutical residues (antibiotics, analgesic/anti-inflammatory, lipid regulator agents, β-blockers, antiepileptics and steroid hormones) that have been detected in wastewaters, surface waters and sediments, involving data from literature of occurrence and the implementation of the second-tier assessment based on acute ecotoxicity data.

2. Drug residues in the environment: occurrence in waters (surface water, wastewater effluents) and sediments

The occurrence of drug residues has been investigated in several studies showing their detection in the aquatic and terrestrial ecosystems. Drug residues have been detected in effluents from STP, as well as in the aquatic system, e.g. small creeks, big rivers [22], lakes [23], ground water [24] or in the sea [25]. Exposure in the aquatic ecosystem is of particular concern, since aquatic organisms are subject to continual introduction into surface waters from STPs. This fact, make them to be assumed "pseudopersistents", even if drugs have relatively short environmental half-lives. Moreover, the polar and non volatile nature of some drugs prevents their escape from the aquatic realm.

Positive findings of drug residues have also been reported in the terrestrial environment [26,27] pointed the disposal of biosolids from STPs and animal wastes, that is applied to land, as main inputs. Some drugs with acidic properties and high log K_{ow}, may show affinity to sludge or soil. For example, drugs, such as gemfibrocil or estrogens that are hydrophobic compounds and have low volatility, it is expected that their sorption on soil or sediments will have a significant factor in reducing their aqueous phase concentrations [27].

This section compiles data from recent literature concerning the occurrence of drug residues in STP effluents, surface waters and sediments. The aim of this section has been to extract the levels of drugs commonly detected in waters and sediments and its application as measured concentrations for later ecological risk characterization studies.

2.1. STP effluents

Among the wide variety of drug residues reported, pharmaceuticals, such as antibiotics, lipid regulator agents, anti-inflammatories, β-blockers, contrasts media and contraceptives can be assumed commonly detected in STP effluents. Table 1 compiles an average of concentrations, which have been reported in recent publications, for these therapeutical groups. The concentration levels commonly found are at ng/L or low μg/L (ppt–ppb), the higher concentrations reported has been for lipid regulator agents, which ranged between 110 and 2353 ng/L [9–12]. Concerning to the frequency that some drugs allowing to this group are detected, a relationship could be established with their wide human consumption, because actually, this group, which is mainly related with treatment of high blood cholesterol levels and hyperlipidemia, is in the top ten (first position) of prescribed therapy classes [28]. Examples of detected drugs allowing to this group, bezafibrate and gemfibrocil were founded in low μg/L level. In the lower concentration level have been reported the detection of steroid hormones, generally at low ng/L [13,14]. However, in spite of the low level (ppt), it is well documented that, estrogens can induce serious chronic effects, such as endocrine disruption [17]. Similarly to lipid regulator agents, analgesic/anti-inflammatory group is a therapeutical group with also a wide human consumption, due their common

Table 1
Occurrence of drug residues in STP effluents, surface waters and sediments

Therapy class of drugs	Drugs	STP effluents (ng/L)			Surface water (ng/L)			Sediments (ng/L)		
		Range of concentration	Average	Reference	Range of concentration	Average	Reference	Range of concentration	Average	Reference
Antibiotics	Trimethoprim		154	13,15,			[13,15]			[26,38]
	Sulfamethoxazole		128	16,32,		50	[36]			[9,39]
	Erytromycin		886	29,30,		34				
	Roxytromycin		680	31						
	Tylosin	128–886			2–50	2.2		3 –578		
	Ofloxacin								3	
	Chlortetracycline								73	
	Flumequine								578	
	Oxytetracycline								246	
	Trimethoprim		154	13,15,			[13,15]			[26,38]
Analgesics and anti-inflammatories	Diclofenac	273–2134	1276	10,11,		225	[12,13]			
	Ibuprofen		2134	12,15,		226	[15,37]			
	Naproxen		1847	16	68–266	266				
	Ketoprofen		733							
	Mefanamic acid					68				
Lipid regulator agents	Bezafibrate		2353	9,10,	270–1100	1100	[13,15] 36			
	Fenofibrate	110–2353	110	11,12						
	Gemfibrocil		2366							
	Clofibric acid		361			270				
β-Blockers	Propanolol		676	[11,13]		25	[13,15]			
	Betaxolol		190	[35]		28	[36]			
	Bisoprolol	190–777			25–2000					
	Atenolol					145				
	Metoprolol		777			2200				
Antiepileptics	Carbamazepine			[8,11]		460	15			
		1625		[12,13]	460					
			1625	[16]						
Steroid hormones	17-α-Ethinyl estradiol		7	[7,26]		2.4		28 –51		[26]
				[38]						
	Diethylstilbestrol	18–20	20		2.4–7.5	7.5				
	Diethylstilbestrol acetate		18			7.5				

use to treat inflammation, pain, and/or fever. However, there is still considerable lack of knowledge about their spread and fate in the aquatic environment. The detection of ibuprofen, naproxen, ketoprofen or mefenamic acid, have been typically reported in concentrations between 273 and 2134 ng/L [10–12,15,16], being ibuprofen and naproxen, compounds that have been found in a higher concentration (low μg/L level). The occurrence of antibiotics in STP effluents has been also carried out in several studies [29–31]. Sulfonamides (sulfamethoxazole), macrolides (erythromycin, roxithromycin), fluoroquinolones, chloramphenicol, tylosin, trimethoprim or erythromycin are often founded at medium-high ng/L level (128 and 886 ng/L) [13,15,16,32]. β-bloquers is other group extensively used to treat angina and hypertension (included in the top 200 prescribed medications in USA [33,34]) and occurrence of β-blockers group has been concern of publications, reporting concentrations between 190 and 777 ng/L [11,13,35] being propanolol and betaxolol, compounds detected in high ng/L level. On the other hand, from the point of view of persistence in the environment, antiepiletics are considered as ubiquitous and prevalent due to poor STP removal. Thus, as example carbamazepine is a drug frequently detected and high ng/L or low μg/L levels have been reported in several publications [10–13,16].

2.2. Surface waters

Many studies have now been conducted to show that drugs and their metabolites are widely distributed in surface waters from STP effluents [32,22]. Table 1 includes concentration levels that have been reported for drug residues in surface waters (average of concentrations). Levels founded are often in the range of ng/L-μg/L. The occurrence of β-blockers have been reported in low ng/L and μg/L (i.e. bisopropol and metoprolol were detected at aproximately 2 μg/L) [13,15,36]. Reviewed publications showing also examples of lipid regulator agents identified at similar levels than β-blockers in surface waters (range of 270–1100 ng/L) [13,15,36]. From this group, bezafibrate is reported to be founded with frequency in low μg/L level. Among the analgesics/anti-inflammatories group, diclofenac and ibuprofen are the compounds that have been founded in higher concentration levels, usually in a range of 68–266 ng/L [12,13,15,37]. The presence in surface waters of antibiotics is often reported in lower concentration level (low ng/L) [13,15,36] and several publications about sulfamethoxazole, erytromicyn evidencing the frequency of both drugs in the aquatic compartment [13,15,36]. On the other hand, the ubiquitous occurrence of carbamazepine also in surface waters (average concentration aproximately of 460 ng/L), can be associated to the very low removal efficiency from STPs [13,15]. In fact, in the literature, it is recognized that STP effluents is the main input of drug residues in the aquatic ecosystem.

2.3. Sediments

Even though, several publications compile occurrence data of drug residues in aquatic ecosystem, limited publications concern the occurrence in terrestrial ecosystem. In sediments, most of the drug residues data found in literature concerns the occurrence of estrogens and antibiotics. Given the relatively low polarity, in particular for estrogens with K_{ow} (2.5–5) [26], sorption to sediments appears quite likely to be cumulative process. Steroid hormones typically reported in literature are 17 α-ethinyl estradiol, diethylstilbestrol and diethylstilbestrol acetate. All of them have been identified at low ng/kg level [26]. As well as some antibiotics, because of its elevated lipophilicity, has already found in sediments. Antibiotics like ofloxacin, chlortetracycline, flumequine or oxytetracycline have been also detected at low-medium μg/kg [26,38]. The detection of tetracyclines in sediments because of their precipitation with cations, such as calcium and accumulation in sewage sludge's or sediments is also documented [9,39]. Table 1 includes also the occurrence of estrogens and antibiotic residues in sediments.

3. Toxicity studies: application of bioassays

In general, the literature shows that most drugs, when detected, are in ppt–ppb range [40,41]. Although ppt–ppb concentrations may not induce adverse effects or represent ecological risk, it is not well documented whether other receptors in non-target organisms are sensitive. On the other hand, it is also recognized that even though individual concentrations of any drug might be low, the combined concentrations from drugs sharing a common mechanism of action could be induce additive or synergistic effects [42]. In these sense, there is an increasing demand of information on the potential toxicity of drug residues. However, there is a lack of data concerning their effects on terrestrial or aquatic fauna.

To date, most of the literature related to toxic effects of drug residues is focused on representative organisms of the chain food. Standard ecotoxicity methods (including e.g. algae, bacteria, invertebrate, fish) defined by OECD guidelines for testing chemicals, are of common application in the reported studies [43].

The available ecotoxicity data reported on different representative species is often complicated by variability arising from the differences in experimental procedures and conditions. In ecotoxicity literature, some authors make use of EU Directive 93/67/EEC to interpret the toxicity data, which classifies substances according to the measured effective concentrations (EC_{50} value) in a scheme with different risk classes [44]. An $EC_{50} < 1$ mg/L would entail the classification "very toxic to aquatic organisms"; from 1 through 10 mg/L "toxic" and from 10 through 100 mg/L "harmful to aquatic organism". Substances with an $EC_{50} > 100$ mg/L would not be classified [44].

This section presents a compilation of acute ecotoxicological data to taxonomic groups (algae, bacteria, invertebrate and fish), which are interpreted on the scheme base proposed in this guideline, for therapeutical groups (antibiotics, analgesics/anti-inflammatories, lipid regulators and β-blockers, antiepiletptics and steroid hormones) included in Section 2 related to the occurrence of drugs residues in the environment.

3.1. Antibiotics

Among therapeutical groups, more attention has been directed towards the antibiotics. It is well documented the spreading resistance among bacterial pathogens due the widespread (and some times indiscriminate) use of antibiotics [13]. Recent publications on representative organisms showing EC_{50} values of streptomycin, flumequine or oxytetracycline, indicating that could have harmful effects or even, very toxic effects as example in the case of oxofloxacin for bacteria [47,38,45]. Exposure of antibiotics, such as tylosin, oxytetracycline, chlortetracycline or erythromycine induces high toxicity to algae [38,45,46]. Biossays performed with sulphadimethoxine or oxytetracycline showing the toxic character to invertebrates [47,48], conversely, flumequine presents harmful or not toxic effects as well as tylosin to invertebrates [47,48]. In consequence, sufficiently low concentrations could altered community structures (even microbial community) and thereby affect the food chain. In Fig. 1 are represented EC_{50} values from bibliography for different antibiotics to taxonomic groups (bacteria, invertebrate and algae).

3.2. Analgesics/anti-inflammatories

Despite the increasing environmental significance of this therapeutical group, investigations concerning their adverse effects are lacking up to now. The current investigations reported in bibliography reveal, at first, the high toxicity ("very toxic class") of anti-inflammatories, such as diclofenac, ibuprofen, naproxen or ketoprofen to bacteria [11,13,49]. Other authors have also reported toxic effects of diclofenac or ibuprofen to invertebrate [47,11,50] and algae [11,50]. However, differences concerning the effects of diclofenac and ibuprofen have been observed using different species from the same taxonomic group, leading EC_{50} values >100 mg/L, and therefore, indicating the absence of toxic effects [47,11,44]. The same situation has been observed in results reported for the toxicity of Naproxen to algae [11,50]. Fig. 1 shows also the EC_{50} reported in bibliography for different analgesics/anti-inflammatory to the three taxonomic groups.

Lipid regulator agents and β-blockers. The effects of the lipid regulators are heterogeneous, on the basis of the EC_{50} values reported for bacteria [11,20,51] and invertebrate [11,51,42]. The lipids regulators, gemfibrocil and clofibric acid are very toxic to bacteria, and most of the tested lipid regulators are not harmful to invertebrate, with the exception of fenofibrate, which is harmful. Even though, reported toxicity data is lack for most of drugs, there is more complete information on toxic effects of clofibric acid for four taxonomic groups, including fish, probably due to its interest because of extensive information about its occurrence in the environment [41,42,52,53]. The effects of clofibric acid are also heterogeneous, showing high toxicity on bacteria and absence of toxicity on invertebrate and fish, depending of the tested fish species [11,51]. Experiments on algae have showed harmful effects. Similar heterogenicity is showed on the effects of β-blockers to algae [50] and invertebrate [47,37,50]. Different effects have been observed for propanolol that show toxicity to algae, in contrast with metoprolol, atenolol or betaxolol that are not toxic. Dates of propanolol and metoprolol reveal different effects on different species from the same taxonomic group. Fig. 2 include EC_{50} values founded in bibliography for some lipid regulators and β-bloquers to the taxonomic groups.

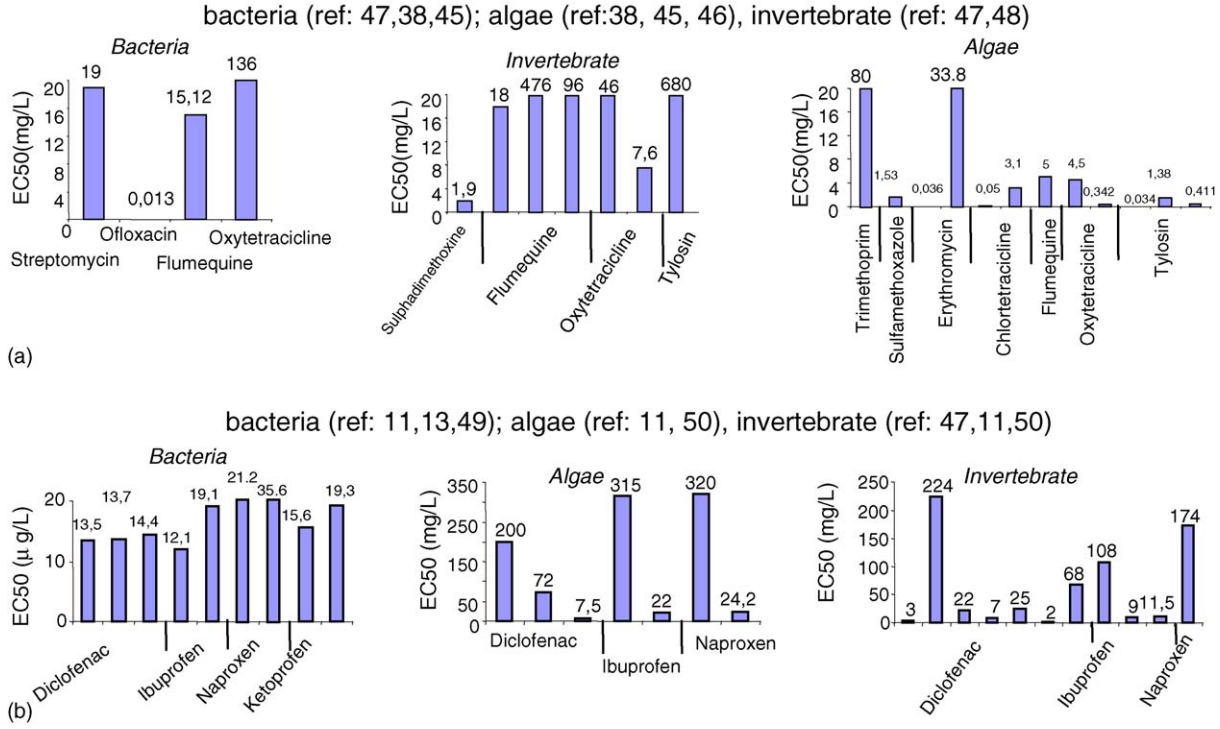

Fig. 1. Toxicity of therapeutical groups on bacteria invertebrate, algae: (a) toxicity of antibiotics to taxonomic groups; (b) toxicity of analgesics/anti-inflammatories to taxonomic groups.

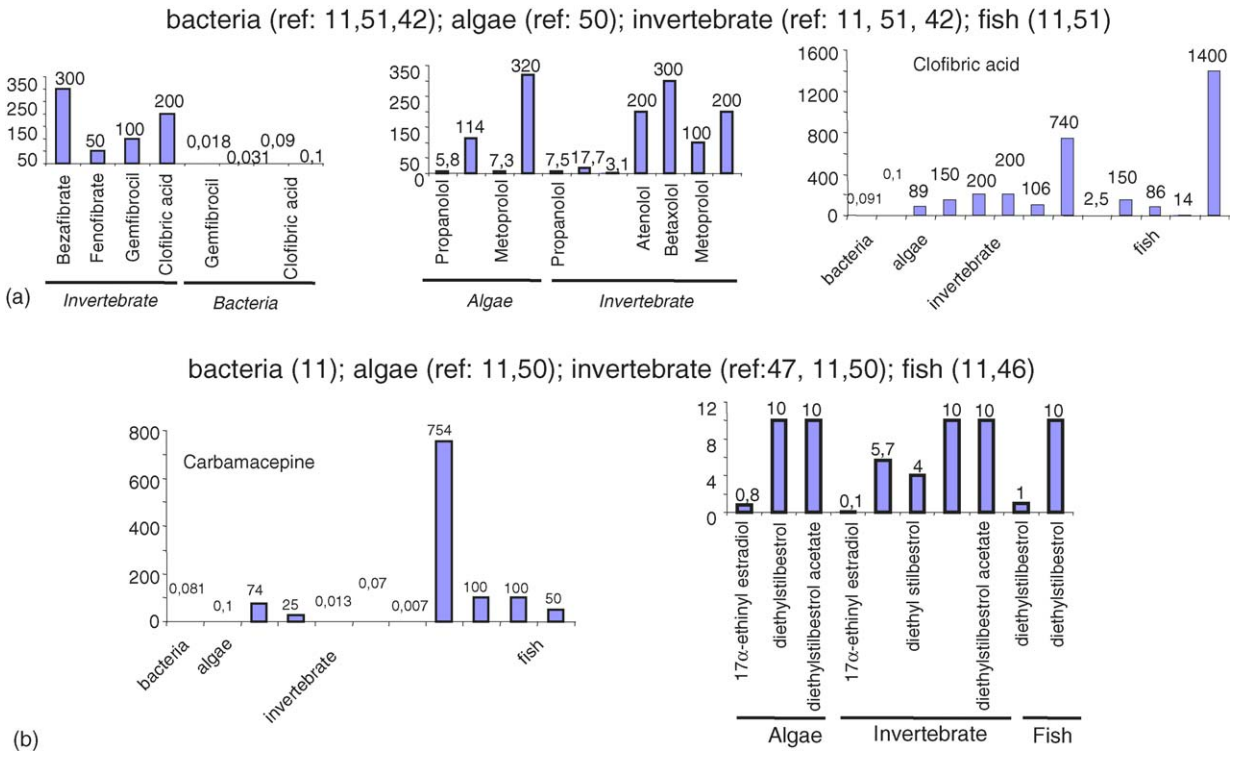

Fig. 2. Toxicity of therapeutical groups for bacteria, invertebrate, algae and fish: (a) toxicity of lipid regulator agents and β-blockers to taxonomic groups; (b) toxicity of antiepileptics and steroid hormones to taxonomic groups.

3.3. Antiepileptics and steroid hormones

There are very few reports available on the effects of carbamazepine on aquatic organisms [50,54]. This compound, according to published EC_{50} values, is considered very toxic ($EC_{50} < 1$ mg/L) for bacteria [11], algae [11,50], and most of the tested invertebrates species [11,50], and non-toxic ($EC_{50} \geq 100$ mg/L) for most of tested fish species [11,46].

The majority of toxicity data about steroids hormones are related to 17 α-ethinyl estradiol, diethylstilbestrol and diethylstilbestrol acetate [47]. Endocrine disruption of these compounds is documented in literature such in the case of norethindrone that is known to develop mammary glands in male mice [55]. Recent literature is increasing respect to the adverse effects on aquatic organisms. The reported data shows that 17 α-ethinyl estradiol, diethylstilbestrol and diethylstilbestrol acetate can be considered toxic to algae [47], invertebrate and fish [47]. In the particular case of 17 α-ethinyl estradiol, different sensitivities were also observed for different alga and invertebrate species with higher toxicity [47]. Fig. 2 shows EC_{50} values of carbamazepine and steroid hormones to taxonomic groups.

The complexity and heterogenicity of the reported data for the reviewed therapeutical groups, with very different effects, depending to the methods, test conditions or time exposure, shows that the consideration of a single bioassay to get toxicity information, does not provide a full picture of the quality of the environment. On the other hand, until now the mode of action of pharmaceuticals is not well enough understood to make general statements about potential environmental effects caused by these substances. A battery of tests is suggested in ecotoxicity publications for providing a more complete situation with the evaluation of adverse effects from a wide range of representative organisms [56–60].

4. Potential impact of drug residues: RQ approach to characterize the ecological risk of drug residues in environmental compartments (waters and sediments)

This section presents a preliminary risk characterization in different environmental compartments (waters and sediments), from the data collection of drug residues (occurrence and acute toxicity) and under the two-tiered procedure of EMEA for ERA. According to this procedure, risk assessment studies [61,20] have been reported. Under EU legislation context, guidelines have been developed for new or existing substances as well as compounds, such as biocides or hazard substances [62–67]. The RQ or HQ is the basic principle internationally accepted and adopted in the development of ERA guidelines. For PEC derivation several factors, including the predicted market volume [68], the water consumption of the target population or a dilution factor accounting for dilution of effluent when reaching the surface waters are common parameters for this approach [69,70]. Other approach for the first-tier procedure, using levels of concern or measured environmental concentrations (MEC) has been also taking account in publications to derivate RQ approach [71,72]. Other key piece of information needed in risk assessment, is the concentration range at which a chemical produces adverse effects on organisms. In second-tier procedure,

PNEC for the aquatic compartment is estimated from EC_{50} values obtained with acute toxicity tests (algae, daphnia, fish) and by application of an assessment factor. Following this procedure, the assessment of whether a substance presents a risk to organisms in the environment is based on a comparison of PEC or MEC of the substance with its PNEC to organisms in ecosystems. When risk is suspected from this comparison, further considerations on a case-by-case bases are subjected to third tier-procedure, including chronic toxicity tests, micro-organism specific test, bioaccumulation study, PEC revision or assessment factor reduced with additional tests [18].

The present approach is an estimation of the incidence of adverse effects occurring in water and sediment compartments, as result of MEC of drug residues. Under second-tier procedure, environmental effects of drug residues have been characterized by extrapolating PNEC based on mean EC_{50} or LC_{50} values obtained from a set data of acute toxicity tests. A standard assessment factor (1000) has been introduced to account for extrapolation from intra- as well as inter-species variability in sensitivity. The PNEC in water compartments ($PNEC_{wat}$) have been determined following the formula (1):

$$\mathrm{PNEC_{wat}} = \frac{\mathrm{EC_{50}\ or\ LC_{50}}}{1000} \quad (1)$$

For sediments, the equilibrium partitioning method was applied to estimate $PNEC_{sed}$ according to the Eq. (2):

$$\mathrm{PNEC_{sed}} = \left[\frac{\mathrm{PNEC_{wat}} \times K_p}{d}\right] \times 1000 \quad (2)$$

where $PNEC_{wat}$ is the PNEC calculated for the water compartments; K_p, the sediment–water partition coefficient calculated according technical guidance document [28], and d is the sediment density. When ratio (exposure concentration) equals or exceeds (the effect concentration) to 1, then an ecological risk is suspected (MEC/PNEC $\geq$ 1).

Common criteria for interpreting the ratio or RQ (PEC or MEC/PNEC), in risk assessment studies, establishing different risk levels ("low risk" from 0.01 through 0.1; "medium risk" from 0.1 through 1, and "high risk" >1) [18,72], have been also applied in the present approach.

4.1. Risk characterization in STP effluents

The data set from occurrence in STP effluents (Section 2) have evidenced that reported mean MEC values of drug residues, frequently exceeded the 10-ng/L cutoff value, established in the tiered-procedure for further considerations in the second-tier assessment based on ecotoxicity data.

Therefore, comparing the concentrations in STP effluents and the toxicity data, in these studies, most of the drugs residues including: antibiotics (erythromycin), anti-inflammatories (ibuprofen, naproxen, diclofenac, ketoprofen), lipid regulators agents (gemfibrocil, clofibric acid), β-blockers (propanolol, metoprolol) as well as antiepileptics (carbamazepine), are suspected to produce high ecological risk on representative species of the food chain typically used in acute toxicity tests (bacteria, algae and invertebrate), under these circumstances. Low risk would predicted for steroids hormones in the aquatic biota, but chronic effect related with endocrine disruption by long-term exposition, cannot be excluded. Table 2 summaries the potential risk of the different therapeutical groups in both environmental compartments (waters and sediments).

4.2. Risk characterization in surface waters

In a similar mode, when MEC in waters exceeding 10 ng/L, PNECs derived from acute data were estimated for each group of drug residues. In surface waters, the dilution factor makes more habitual that some drug residues are not considered in the second-tier. Under this situation, reported MEC of some antibiotics (oxytetracycline, flumequine), lipid regulators agents (gemfibrocil, clofibric acid), β-blockers (metoprolol), or steroid hormones, do not represent an ecological risk, at least, when combined concentrations of drugs is excluded from this procedure of risk assessment. Different situation have been extracted

Table 2
Potential ecological risk (RQ) of different therapeutical groups in environmental compartments (water–sediment)

Therapeutical groups of drugs	Pharmaceuticals	RQ in STP effluents	RQ in surface waters	RQ in sediments
Antibiotics	Erythromycin	High		
	Oxytetracycline			Medium
	Flumequine			Medium
Analgesic/anti-inflammatories	Ibuprofen	High	High	
	Diclofenac	High	High	
	Naproxen	High	High	
	Ketoprofen	High	High	
Lipid regulador	Gemfibrocil	High		
Agents	Clofibric acid	High		
β-Blockers	Propanolol	High	Medium	
	Metoprolol	High		
Antiepileptics	Carbamezepine	High	High	
Steorid hormones		Low		

for analgesic-anti-inflammatories (ibuprofen, diclofenac, naproxen, ketoprofen) and antiepileptics (carbamazepine), that, in general, are present in surface waters in high-medium ng/L level (or even low μg/L), in the case of anti-inflammatories or are ubiquitous and prevalent, such as carbamazepine. For these drugs residues, the risk is suspected to be high. In addition, the presence in surface of β-blockers (metoprolol) at reported concentration levels, would represent medium risk (see Table 2).

Risk characterization in sediments. Even though, some steroids hormones, anti-inflammatories (e.g. ibuprofen) or lipid regulator agents (gemfibrocil) have K_{ow}, values mostly between 2.5 and 5 [26], and sorption to sediments appears to be a cumulative process, reported concentrations in sediments for these drug residues is not suspected to induce risk in this compartment. However, comparing the reported MEC of specific antibiotics, such as oxytetraclycline and flumequine, with the toxicity data, the presence of both drugs would represent medium risk in sediments. Table 2 compiles also the risk of the different therapeutical groups in sediments.

5. Conclusions

In general, the data collected have evidenced that occurrence levels for the target drug residues of this study, have exceeded frequently the 10-ng/L cutoff value in STP effluents, which requires, therefore, the implementation of the second-tier assessment based on ecotoxicity data.

High risk is suspected to be induced in STP effluents for the following drugs: antibiotics (erythromycin), anti-inflammatories (ibuprofen, naproxen, diclofenac, ketoprofen), lipid regulators agents (gemfibrocil, clofibric acid), β-blockers (propanolol, metoprolol) and antiepileptics (carbamazepine). Conversely, steroids hormones have low risk on STP effluents. On these preliminary risk characterization results, drug residues may cause adverse effects on the aquatic ecosystem, if effluents are discharged without dilution or without the use of appropriate removal technologies in STPs that should be an adequate approach for limiting risk.

High risk is also suspected in surface waters for anti-inflammatory (ibuprofen, naproxen, diclofenac, ketoprofen) and antiepileptics (carbamacepine). As well as medium risk is suspected in sediments for antibiotics (oxytetracycline, flumequine) and for β-blockers (propanolol) in surface waters.

For further risk considerations, characterization would need to be refined in third-tier procedure, with data concerning to long-term exposition (e.g. chronic toxicity tests or bioaccumulation study).

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