Elsevier Editorial System(tm) for Science of the Total Environment
Manuscript Draft

Manuscript Number:

Title: PHARMACEUTICALS AND PERSONAL CARE PRODUCTS IN UNTREATED AND TREATED SEWAGE SLUDGE: OCCURRENCE AND ENVIRONMENTAL RISK IN THE CASE OF APPLICATION ON SOIL- A CRITICAL REVIEW

Article Type: Review Article

Keywords: sewage sludge, pharmaceuticals, personal care products, environmental risk, sludge-amended soil

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Abstract: This review is based on 59 papers published between 2002 and 2015, referring to about 450 treatment trains providing data regarding sludge concentrations for 169 compounds, specifically 152 pharmaceuticals and 17 personal care products, grouped into 28 different classes. The rationale of the study is to provide elements to evaluate the environmental risk posed by the spreading of treated sludge in agriculture. Following discussion of the legislative scenario governing the final disposal of treated sludge in European countries and the USA, the study provides a snapshot of the occurrence of selected compounds in primary, secondary, mixed, digested, conditioned, composted and dried sludge originating in municipal WWTPs fed mainly with urban wastewater as well as in sludge-amended soil. Not only are measured values reported, but also predicted concentrations based on Kd values. It emerges that in secondary sludge, the highest concentrations were found for fragrances, antiseptics and antibiotics and an attenuation in their concentrations occurs during treatment, in particular anaerobic digestion and composting. An in-depth analysis of the Kd values for the different compounds and treated sludge are reported. The data regarding measured and predicted concentrations of selected compounds in sludge-amended soil is then analyzed. Finally an environmental risk assessment posed by their occurrence in soil in the case of land application of sludge is examined, and the results obtained by different authors are compared. The most critical compounds found in the sludge-amended soil are estradiol, ciprofloxacin, ofloxacin, tetracycline, caffeine, triclosan and triclocarban. The study concludes with a focus on the main issues that should be further investigated in order to refine the environmental risk assessment.

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Ferrara, July 13th 2015

Dear Prof. Damia Barceló
Editor in Chief
Science of the Total Environment,

referring to the paper:

PHARMACEUTICALS AND PERSONAL CARE PRODUCTS IN UNTREATED AND TREATED SEWAGE SLUDGE: OCCURRENCE AND ENVIRONMENTAL RISK IN THE CASE OF APPLICATION ON SOIL- A CRITICAL REVIEW

by

Paola Verlicchi and Elena Zambello

in submitting it to Your international Journal, I would like to make the following remarks:

- the work described in this paper has not been previously published and it is not under consideration for publication elsewhere,

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Unique features of the study

The paper reports a review referring to the occurrence of 169 pharmaceutical and personal care products belonging to 28 different therapeutic classes in untreated (primary, secondary biological and mixed) and treated sludge (digested, composted, conditioned, dried, dewatered). The main models proposed to predict sludge concentrations are presented and critically analyzed. In doing this, the literature values of K_d are compiled for many compounds and different types of sludge.

The study then discusses the effects on PPCPs concentrations of the different treatments as well as in soil after sludge application on it for agriculture purposes.

Then, by means of the risk quotient approach, it evaluates the environmental risk connected to their presence in secondary or digested sludge-amended soil. This analysis allows to define a ranking of the most critical compounds.

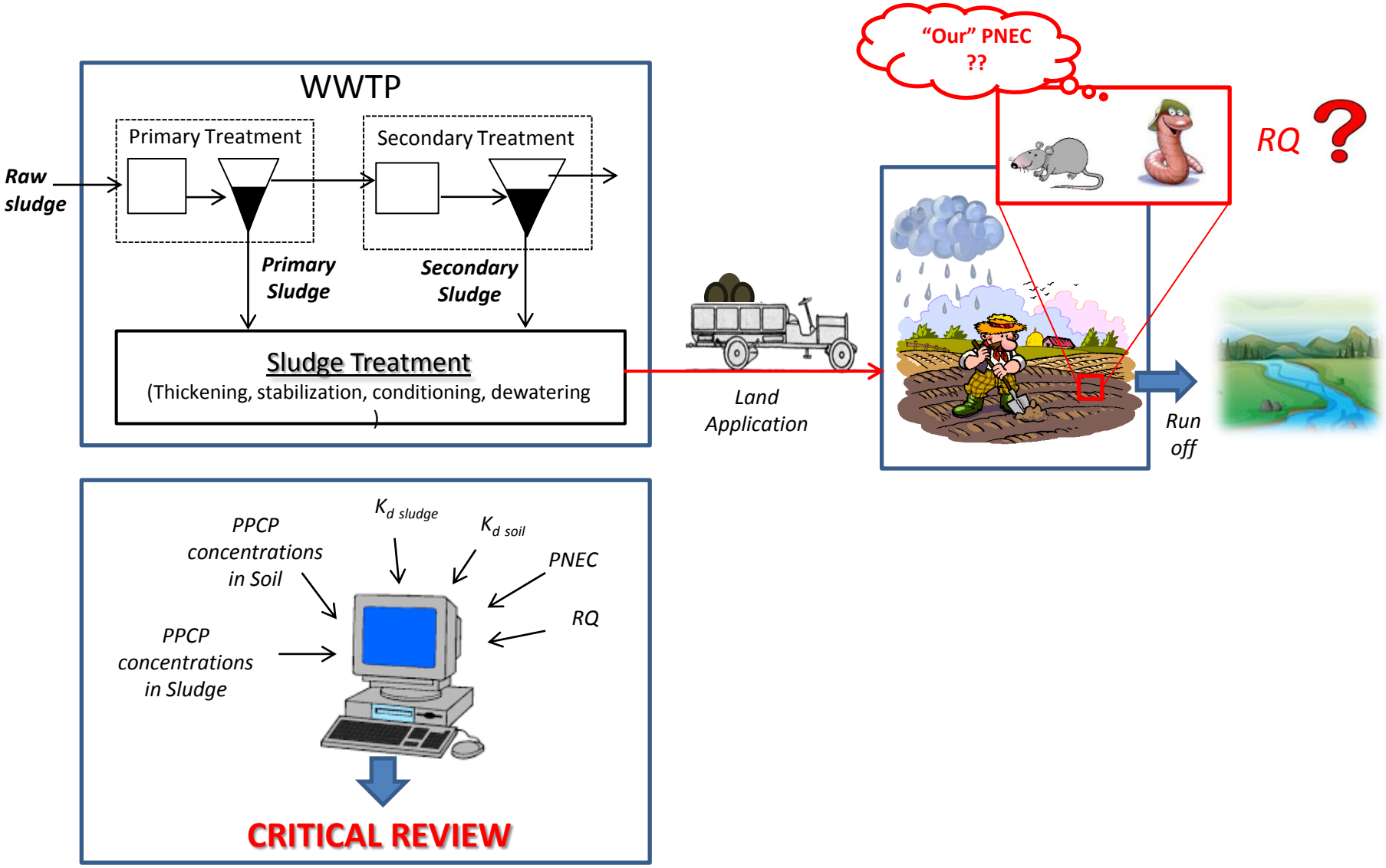
The paper finally focuses on the main research fields requiring further investigation.

To the best of our knowledge, this is the first time that such a large number of PPCPs is included in a review considering their occurrence in different kinds of sludge and in sludge-amended soil, and environmental risks.

Sincerely Yours

Paola Verlicchi

*Graphical Abstract



Highlights Review on occurrence of PPCPs in Sludge

The review refers to concentrations of 169 PPCPs in different kinds of sludge.

After digestion or composting, concentrations of most compounds reduced.

K_d values are collected for the selected compounds in the different kinds of sludge and soils.

The environmental risk due to PPCPs in case of sludge application on soil is assessed.

The most critical compounds are triclosan, triclocarban, hormones and antibiotics.

PHARMACEUTICALS AND PERSONAL CARE PRODUCTS IN UNTREATED AND TREATED SEWAGE SLUDGE: OCCURRENCE AND ENVIRONMENTAL RISK IN THE CASE OF APPLICATION ON SOIL- A CRITICAL REVIEW

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Abstract

This review is based on 59 papers published between 2002 and 2015, referring to about 450 treatment trains providing data regarding sludge concentrations for 169 compounds, specifically 152 pharmaceuticals and 17 personal care products, grouped into 28 different classes. The rationale of the study is to provide elements to evaluate the environmental risk posed by the spreading of treated sludge in agriculture. Following discussion of the legislative scenario governing the final disposal of treated sludge in European countries and the USA, the study provides a snapshot of the occurrence of selected compounds in primary, secondary, mixed, digested, conditioned, composted and dried sludge originating in municipal WWTPs fed mainly with urban wastewater as well as in sludge-amended soil. Not only are measured values reported, but also predicted concentrations based on K_d values. It emerges that in secondary sludge, the highest concentrations were found for fragrances, antiseptics and antibiotics and an attenuation in their concentrations occurs during treatment, in particular anaerobic digestion and composting. An in-depth analysis of the K_d values for the different compounds and treated sludge are reported. The data regarding measured and predicted concentrations of selected compounds in sludge-amended soil is then analyzed. Finally an environmental risk assessment posed by their occurrence in soil in the case of land application of sludge is examined, and the results obtained by different authors are compared. The most critical compounds found in the sludge-amended soil are estradiol, ciprofloxacin, ofloxacin, tetracycline, caffeine, triclosan and triclocarban. The study concludes with a focus on the main issues that should be further investigated in order to refine the environmental risk assessment.

Keywords: sewage sludge, pharmaceuticals, personal care products, environmental risk, sludge-amended soil

List of acronyms

AeD= aerobic digestion; AnD = anaerobic digestion; AOX= absorbable organically bound halogens; BAF= biological aerated filter; BNR= biological nutrient reactor; CAS= conventional activated sludge; CEC = cation exchange capacity; CFR = Code of Federal Regulations; CW = constructed wetland; DM = dry matter; D_{ow} = octanol water partition coefficient; E1 = estrone; E2 = estradiol; E3 = estriol; EE2 = ethinylestradiol; EQS = environmental quality standard; f_{oc} = fraction of organic carbon; K_a = dissociation constant; k_{biol} = biological degradation rate; K_d = solid liquid partition coefficient; K_{ow} = octanol water distribution coefficient; LAS = linear alkyl sulfonates; MAnD = mesophilic anaerobic digestion; MBR = membrane biological reactor; MEC = measured environmental concentration; NP = nonylphenol; NPnEO = nonylphenol (n) ethoxylates; OM = organic matter; PAH = polycyclic aromatic hydrocarbons; PCB = polychlorinated biphenyls; PCDD = Polychlorinated dibenzo-p-dioxins; PCP = personal care product; PEC = predicted environmental concentration; PhC = pharmaceutical compound; PNEC = predicted no effect concentration; PPCP = pharmaceutical and personal care product; RQ = risk quotient; SRT = sludge retention time; SSD = Sewage Sludge Directive; T = temperature; TAnD = thermophilic anaerobic digestion; TSS = total suspended solids; UASB = upflow anaerobic sludge blanket; WWTP = wastewater treatment plant

1 Introduction

Sludge originates during biological and chemical processes in wastewater treatment plants (WWTPs) and may contain a wide spectrum of organic and inorganic substances as well as microorganisms and viruses which are separated from the liquid phase during treatments.

Its production is expected to increase from 11.5 M tons of dry matter (DM) (2010) to over 13 M tons of DM by 2020, chiefly due to increased sewerage and treatments in East European countries (Palfrey, 2010; Eriksson et al., 2008). The main disposal routes are incineration, landfill, land application, composting, with the specific percentages varying from country to country. For instance incineration reaches 90 % in Belgium, 50 % in Germany and 45 % in Denmark, while reuse in agriculture reaches 50 % in Denmark and 25 % in Sweden, where 50 % is landfilled or allocated to construction work (Malmborg and Magnér, 2015; Kelessidis and Stasinakis, 2012). Recently Kelessidis and Stasinakis (2012) reported that 53 % of sludge in EU-27 is reused in agriculture either directly or after composting, whereas Citulsky and Farahbakhsh (2010) reported that more than 40 % is spread on land in the USA and Canada.

The interest in using sewage sludge in agriculture is due to its nutrient content and soil-conditioning properties that are useful for restoring overexploited land to agricultural use or for improving the

humus content and water-holding capacity of light-textured sandy soil as well as in cases where soils are depleted or subject to erosion.

Disposal routes of sewage sludge must fulfill specific regulations. With regard to the land application option, in the last 20 years great attention has been placed mainly on the occurrence of heavy metals in sludge and their fate once it is applied on agriculture land, and limits have been set and adopted in different countries (Stasinakis, 2012). Sometimes, additional limits have been implemented for surfactants (mainly linear alkyl sulfonates, LAS), polycyclic aromatic hydrocarbons (PAH) , nonylphenol (n)ethoxylates (NPnEO), polychlorinated biphenyls (PCB), phthalates and pesticides in sludge, and studies monitoring their fate once spread on the land are ongoing (Kelessidis and Stasinakis, 2012). No limits have been set for pharmaceuticals (PhCs) and other contaminants of emerging interest, including personal care products (PCPs) in sewage sludge.

Land disposal of sewage sludge is regulated at EU level by the so-called Sewage Sludge Directive (SSD) 86/278/EEC (CEC, 1986) and in each EU country national regulations have also been set in accordance with the SSD. Generally, they set the maximum allowable concentrations of potentially toxic elements in soil after the application of sewage sludge, and maximum annual rates of application. They do not set concentration limits for organic compounds for either sludge or soil. A draft of a working document on sludge and biowaste is under discussion within the EU, where cut-off values are set for other groups of organic compounds (EC, 2010).

There is ongoing debate within the scientific community in order to evaluate potential (environmental) risks in this kind of practice, due to the occurrence of toxic and persistent substances in sludge, such as aquifer contamination, the accumulation of pollutants in soil, and their transfer into the food chain. It has been estimated that loads of up to some kilograms per hectare may enter agricultural soils, and that concentrations of antibiotics similar to pesticides may be reached (Thiele Bruhn, 2003). The occurrence of antibiotics may cause resistance in pathogens. Moreover, antibiotic residues and resistant microorganisms can affect the natural soil microbial community and soil function and they may enter the food chain (Thiele Bruhn, 2003).

The sorption on sludge and in soil of an organic contaminant is strongly affected by many factors, including the characteristics of the compound (molecular structure, in particular the presence of amino groups or COOH groups in the molecule, and chemical properties, including K_{ow}, p*K*a, K_d) and the sludge (soil) (organic compound fraction, cation exchange capacity CEC, suspended solid size) and operating (environmental) conditions (pH, sludge retention time). As discussed in Verlicchi et al. (2012), rules of thumb have been proposed and used for a rough prediction of the behavior of pharmaceuticals and personal care products (PPCPs), but they often lead to scenarios that are quite different from the observed behavior. The distribution of sewage sludge on farmland

may result in an accumulation of persistent compounds in soil, representing a threat for the soil ecosystem and in particular, for soil living organisms. Once the sludge is amended to soil, PhCs and PCPs will still remain adsorbed or released, thus entering the soil water pore. In the water phase they may be subjected to biodegradation and/or photodegradation or remain unchanged. They could volatize, reach groundwater, surface water bodies, or be taken up by plants, crops and grass growing on the land.

In the last few years, many investigations have been carried out addressing different aspects of this complex topic. The aim of this study is therefore to provide a snapshot of the main issues related to the presence of selected PPCPs in raw and treated sewage sludge and in sludge-amended soil. Collected data will be used to carry out an environmental risk analysis based on the risk quotient approach in order to identify the most potentially critical compounds in the case of sludge-amended soil. This analysis will lead to a focus on the main critical aspects related to the acquired knowledge and the fields requiring future research.

2 Definition and types of sludge included in this review

Sewage sludge is defined as a mixture of the residuals from WWTPs receiving urban wastewater, or other wastewater of a similar composition. In general it is a liquid or a semi-liquid phase, with a solid percentage varying from 0.25 to 12 % by weight, depending on the operations and processes used (Metcalf and Eddy, 2004). A rough distinction is made between primary, secondary and treated sludge, mainly thickened, digested, composted, conditioned, dried and dewatered. The data collected from literature and presented in this study refers to this distinction. In addition, the term *biosolids* is often used for treated sewage sludge in order to underline the fact that sludge contains nutrients and other substances that can positively contribute to the improvement of soil properties and fertility (Clarke and Smith, 2011). Table 1 clearly presents the main characteristics of all these kinds of sludges, which will be referred to in the figures and tables discussed throughout the paper .

Table 1

The data collected in this review regards the occurrence of selected PPCPs in the sludge originating from all the treatments reported in Figure 1.

Figure 1

Some studies refer to other names/types of sludge, for instance rural sludge and urban sludge in Peysson and Vulliet (2013). However, in the current manuscript we maintain its original name. In addition to the sludge compiled in Table 1, the biomass attached to gravel in constructed wetlands has also been included (Zhu and Chen, 2014) and defined "sediments (in CW)".

3 Framework of the review

The current study is mainly based on 59 papers, published between 2002 and 2015, referring to about 450 treatment trains (full scale plants for more than 90 % of the plants) operating in 24 different countries, providing data regarding sludge concentrations for 169 compounds - 152 pharmaceuticals (PhCs) and 17 personal care products (PCPs), grouped into 28 different classes (see Table 1: 23 for PhCs and 5 for PCPs). The main issues addressed in the published investigations included in the review are detailed in Table SD-1, whereas Table SD-2 compiles all the selected compounds together with their main chemical and physical properties (molecular structure, log K_{ow}, p*K*a, and molecule charge at pH 7).

Table 2.

After a discussion of the legislative scenario governing the final disposal of treated sludge in European countries and the USA, the current study provides a snapshot of the occurrence of selected PPCPs in (untreated and treated) sludge and after its application on soil. Occurrence data refers to concentrations of PhCs and PCPs in primary, secondary, mixed and differently treated sludge originating in municipal WWTPs mainly fed with urban wastewater. In a few cases, factories slightly contribute to the WWTP feeding (Golet et al., 2003, Miao et al., 2005, Radjenovic et al., 2009a). Moreover, one case (Jelic et al., 2012) deals with an anaerobic codigestion of the sewage sludge with the organic fraction of biowaste. In most studies, when the concentration was found to be less than the detection limit , it was assumed to take half the reported value, according to many Authors (among them von der Ohe et al., 2011). Data collected in spiking investigations was not included as, according to Eggen and Majcherczyk (1998), it does not represent reality because added compounds behave differently compared to "aged" compounds, which are more linked to a matrix and therefore require more energy to be degraded.

Most of the collected data refers to grab samples of sludge, and in just a few cases to composite samples. According to many authors, grab samples of treated sludge may be considered sufficiently representative of the treatment line (Lajeunesse et al., 2012; Jelic et al., 2012).

Concentrations of PPCPs in manure and sludge originating from livestock WWTPs are not reported. These may contain much higher concentrations not only of nutrients but also of estrogens (E1, E2, EE2 and E3), as shown in Sim et al. (2011).

In addition to measured concentrations, predicted concentrations in sludge were also reported and the most common models adopted for this prediction are critically discussed. They are generally based on the parameter K_d. For this reason, the current study also includes a reconnaissance of the different values of K_d referring to the different kinds of sludge.

The study then reports the data regarding the measured concentrations of PPCPs in sludge-amended soil and analyzes the main model used for predicting them. Finally, it carries out an environmental risk assessment posed by the occurrence of PPCPs in soil in the case of land application of sludge and compares the results obtained by different authors. The study concludes with a focus on the main issues that should be further investigated.

4 Legislation constraints

With regard to European countries, sewage sludge management and its final disposal have to respect specific directives related to wastewater and also waste management since sewage sludge, generated in WWTPs during wastewater treatment, is often transported elsewhere, either to a specific treatment platform or to final disposal and thus it becomes a (liquid) waste. European Directives aim to improve aquatic environment protection, by encouraging a progressive reduction of contaminants released into the aquatic environment (Directive 2000/60/EC, Council Directive 91/271/EEC) and thus promote an upgrade of the existing WWTPs, sometimes resulting in a higher production of sludge. Moreover, they encourage the reuse of sewage sludge (Directive 91/271/EEC) and, for this objective, they set qualitative and quantitative limits as in the Sewage Sludge Directive (SSD) 86/278/EEC. Moreover, they want to reduce the amount of waste to landfill, in particular biodegradable waste (that is waste capable of undergoing anaerobic or aerobic decomposition) (Directive 99/31/EC). It is possible to use sludge on agricultural land - in accordance with the SSD, Member States have established national legislations and in particular have set conditions allowing land application of sewage sludge. The SSD sets the maximum concentrations for heavy metals (Zn, Cu, Ni, Cd, Pb, Hg) in sludge, but many Member States set more stringent limits for heavy metals, organic micropollutants (including PCBs, LAS, and PAH) and pathogens (in particular Salmonella, enteric viruses and helminth eggs) (Inglezakis et al., 2014; Kelessidis and Stasinakis, 2012). No limits have been set for organic compounds and in particular for PhCs.

The SSD favors the agricultural use of sludge subjected to a "*biological, chemical or heat treatment, long-term storage or any other appropriate process*" in which "*fermentability and health risks resulting from its use*" have been significantly reduced.

At EU level, revision of the SSD is ongoing, addressing different issues concerning: (*i*) the intention to reduce the chemical content in sludge promoted by REACH (that is a regulation regarding the Registration, Evaluation, Authorization and Restriction of Chemicals), (*ii*) the possibility of increasing the treatment of *biological wastes* to produce *compost,* characterized by a lower content of hazardous substances with respect to sewage sludge, and to favor its spreading on soil and (*iii*) the interest in encouraging the use of sludge for biogas production and other forms of energy recovery. Bearing this in mind, in the coming years limits will be revised for the regulated substances and set for organic pollutants (absorbable organically bound halogens (AOX), surfactants, PCB, PCDD, etc.) and pathogens, as discussed in Inglezakis et al. (2014).

In order to avoid the risk of pathogen spread into the environment in Sweden, a new regulation is under discussion which would require a sanitation step including chemical and thermal treatments for all those sludges allocated to agriculture purposes. A comparison of the efficacy of the different sludge treatment in removing the typical pathogens contained in sludge is described in the study by Arthurson (2008). This new regulation will come into force in January 2019 (Malmborg and Magnér, 2015).

An in-depth discussion and comparison of the legislation adopted in EU-27 is reported in Kelessidis and Stasinakis (2012).

With regard to USA regulations (USA Code Part 503), Standards for the use or Disposal of Sewage Sludge (generally called biosolids) are found Part 503 of Section 40 of the Code of Federal Regulations (40 CFR 503, hereafter simply "Part 503"). US limits for heavy metals are less severe than those set by the SSD. Part 503 distinguishes between two types of biosolids (Class A and Class B) on the basis of the treatment the sludge is subjected to. The distinction is briefly reported in Table 1, while an in-depth discussion is reported in Jones-Lepp and Stevens (2007) and in McClellan and Halden (2010).

5 Results

5.1 Sorption mechanisms and attempts to predict the sorption potential of a compound

Sorption can be ascribed to two kinds of mechanisms: *absorption,* due to hydrophobic interactions of aliphatic and aromatic groups of a compound with the lipophilic cell membrane of the microorganisms and the lipid fraction of the sludge, and *adsorption,* due to electrostatic interactions

caused by contact between positively charged groups of chemicals and the negatively charged surfaces of the microorganisms (Ternes et al., 2004). In the past, many attempts have been made to predict the sorption behavior of a compound on the basis of its specific properties, in particular its lipophilicity, expressed in terms of K_{ow} (octanol water distribution coefficient) and its affinity to the solid phase, expressed in terms of K_d (solid liquid partition coefficient). Rules of thumb have been proposed in recent years (Table 2), but their application led to rough estimations that were quite often differed too much from the evidence. For instance, Jones et al. (2014) did not find any correlation between Log K_{ow} and concentration for 7 PhCs and a disinfectant for primary, secondary and mixed sludges collected in 28 different WWTPs in the UK. In Verlicchi et al. (2013) an in-depth discussion is reported.

Ambient pH may play a critical role for compounds containing functional groups which can be protonated and de-protonated. Further attempts to predict sorption behavior also tried to include the effect of pH and p*K*a (acidic dissociation constant), leading to another rule of thumb based on the parameter D_{ow} (octanol water partition coefficient). But discrepancies between predictions and measuremets still occurred for many compounds. The conclusion is that sorption mechanisms may hardly be *correlated* to the value of one parameter(K_{ow}, D_{ow}, K_d) as due to the complexity of the molecule, the fate of a PPCP depends on all of them (Table 3).

Table 3.

It is well-know that concentrations of (micro and macro) pollutants in sewage sludge are strictly affected by the characteristics of the influent wastewater, the sludge characteristics (pH, organic matter and cation concentration), the adopted wastewater and sludge treatments, and the operational conditions. In secondary sludge, microorganisms represent the greatest proportion of suspended solids, while primary sludge essentially contains fewer micro-organisms and has a large lipid fraction (Ternes et al., 2004). A characterization of the different kinds of sludge is reported in Table 4 and this can be useful in explaining the results that will be presented and discussed in the following sections.

Table 4.

5.2 Measured concentrations in different kinds of sludge

5.2.1 Raw sludge

An interesting analysis carried out by Lindberg et al. (2010) on the occurrence of antifungal agents in sludges, highlights that in raw sewage particles, ketoconazole and econazole were detected at 980 and 470 ng/g DM respectively. In raw sludge the concentrations were 1,300 and 240 ng/g DM respectively. Jia et al. (2012) found that the concentrations of some antibiotics and the antiseptic pipemic acid were similar in raw sludge and primary sludge, ranging in the interval of 10 and 70 ng/g DM. The variability range was higher for norfloxacin, ofloxacin and moxifloxacin - between 170 and 1,060 ng/g DM. Lindberg et al. (2006) found higher concentrations of norfloxacin and ciprofloxacin in raw rather than primary sludge s, occurring in the ranges of 4,700-5,800 ng/g DM and 5,700-7,700 ng/g DM in raw sludge, and 1,700-4,200 and 2,000-4,000 ng/g DM in primary sludge.

5.2.2 Primary sludge

Figures 2 and 3 refer to concentrations measured in primary sludge. It emerges that the most investigated therapeutic classes are antibiotics (20 compounds), analgesics and anti-inflammatories (7 compounds), and antifungals, hormones and psychiatric drugs (4 compounds). Moreover, the most investigated compounds are ciprofloxacin and norfloxacin (10 data), ibuprofen (9), and estradiol, ethinylestradiol and caffeine (7 values). The highest concentrations were found for the fragrances galaxolide (187,000 ng/g DW) and tonalide (183,000 ng/g DM) (Ternes et al., 2004), triclosan (14,700 ng/g DM) (McAvoy et al., 2002) and salicylic acid (13,800 ng/g DM) (Khan and Ongerth, 2002).

Figure 2

Figure 3.

5.2.3 Secondary sludge

Figures 3 and 4 refer to secondary biological (excess) sludge from activated sludge processes, including conventional systems (CAS, BNR) and MBR. The most investigated classes were antibiotics (135 data referring to 29 compounds), analgesics and anti-inflammatories (36 data regarding 7 compounds), hormones (49 data regarding 4 compounds). The most studied compounds

were ciprofloxacin (19 data), estradiol and ethinylestradiol (16), ciprofloxacin (14), ofloxacin and carbamazepine (13), sulfamethoxazole (12), and triclosan (10). Ten compounds were found at a concentration > 10,000 ng/g DM: azithromycin (64,000 ng/g DM), clarithromycin (67,000 ng/g DM), ofloxacin (21,000 ng/g DM), sulfamethoxazole (68,000 ng/g DM), trimethoprim (41,000 ng/g DM), triclosan and triclocarban (17,500 and 43,200 ng/g DM respectively), galaxolide and tonalide (131,000 and 10,2000 ng/g DM respectively). It emerges that the range of the observed concentrations may be wide up to 3-4 orders of magnitude for many compounds, namely diclofenac, azithromycin, josamycin, norfloxacin, ofloxacin, spiramycin, sulfamethoxazole, estradiol, ethinylestradiol, carbamazepine and tonalide. This can be ascribed to the adopted biological reactor configuration which may include anoxic, aerobic and anaerobic compartments, promoting C, N and P removal and different SRT values.

Figure 4

Figure 5

Jones et al. (2014) found that although the quality of the WWTP influent and of the effluent discharged may exhibit a consistent variability between different WWTPs, the sludge quality is more "homogeneous", that is the variability range is generally narrower. This could be related to the prolonged residence time of the sludge which promotes good mixing and higher degradation processes in its bulk.

With regard to the seasonal variation of the concentration of PPCPs, Gao et al. (2012a) and Martin et al. (2012a) observed a consistent variability in the concentrations of antibiotics in sewage sludge from different municipal WWTPs. The highest concentrations were found in winter, and the lowest in autumn.

5.2.4 Mixed sludge

Jones et al. (2014) provided data regarding the average concentrations for 7 PhCs, triclosan and 3 NPnEO in mixed sludges concerning different WWTPs in the UK. The highest concentrations were found for NP3EO (176,000 ng/g DM), oxytetracycline (7,630 ng/g DM), NPEO (5,000 ng/g DM) triclosan (4,900 ng/g DM), NP2EO (1,100 ng/g DM), and dicloenac, ibuprofen, propranolol, erythromycin, ofloxacin and fluoxetine (60-270 ng/g DM).

5.2.5 Digested sludge

Figures 6, 7 and 8 refer to concentrations measured in aerobically or anaerobically digested sludge. The most studied classes were psychiatric drugs (19 compounds) and antibiotics (16), followed by analgesics/antinflammatories, antifungals, hormones and non ionic surfactants (6 compounds in each class). The most investigated compounds were carbamazepine (41 values), ibuprofen (27), estradiol (26), diclofenac (22), estrone (21), ciprofloxacin (20), caffeine (19) and norfloxacin (18). Anaerobic digestion (AnD) was more frequently investigated than aerobic (AeD) (in the cited figures, circles refer to AnD, squares to AeD and stars to an undefined digestion process). The highest concentrations were found in AnD sludge with the only exceptions of galaxolide and tonalide. Compounds that occurred at concentrations higher than 10^4 ng/g DM (=10 μg/g DM) are (in descending order) galaxolide (81,000 ng/g DM), triclocarban (63,000 ng/g DM), triclosan (46,000 ng/g DM), NP2EO (25,000 ng/g DM), estrone (22,000 ng/g DM), OP2EO (20,000 ng/g DM), tresolide and tonalide (16,000 ng/g DM).

A consistent seasonal variation was also noted by Nieto et al. (2010) for acetaminophen, diclofenac and ibuprofen in AnD sludges. The authors ascribed it to higher consumption in winter than in spring-summer.

Fig 6.

Fig 7.

Fig 8.

5.2.6 Biosolids, composted, conditioned, dried and differently treated sludge

Figures 9 and 10 report literature data for selected PPCPs in biosolids, composted, conditioned, dried and other kinds of treated sludges, according to the definition in Table 1. Referring to biosolids, the most investigated class was antibiotics (27 compounds) and the most studied compounds triclosan (9 values) and triclocarban (7 values). The highest concentrations were due to triclocarban (441,000 ng/g; US EPA, 2009) and tonalide (427,000 ng/g DM; Kinney et al., 2006),

galaxolide (177,000 ng/g DM; Kinney et al., 2006), triclosan (133,000 ng/g DM; US EPA, 2009), ofloxacin (58,000 ng/g DM; US EPA, 2009), and ciprofloxacin (47,500 ng/g DM; US EPA, 2009).

With regard to composted sludges, the most investigated classes were analgesics/anti-inflammatories and psychiatric drugs (8 compounds each), followed by antibiotics (5 compounds), hormones and lipid regulators (4). The most studied compounds were carbamazepine (13 values) and acetaminophen (8 values). The highest concentrations were found for galaxolide (6,800 ng/g DM; Tavazzi et al., 2013), triclosan (4,230 ng/g DM; Peysson et al., 2013), tonalide (3,500 ng/g DM; Kinney et al., 2006) and acetaminophen (920 ng/g DM; Martin et al., 2012a).

Data regarding conditioned sludge is less available and mainly refers to antibiotics (8 compounds), psychiatric drugs (7 compounds) and analgesics/antinflammatories (4 compounds). The most studied substances are carbamazepine (4 values) followed by caffeine, galaxolide, and tonalide (3 values each). The highest concentration was found for galaxolide (30,000 ng/g DM; Carballa et al., 2007b), followed by tonalide (7,000 ng/g DM, Carballa et al., 2007b) and triclosan (3,500 ng/g DM; Kinney et al.,2006).

In dried sludges, the most investigated classes were non-ionic surfactants and psychiatric drugs (6 compounds each), followed by antifungals (4 compounds). NP and NP1EO occurred at the highest concentrations (50,000 and 31,000 ng/g DM respectively, Mailler et al., 2014), followed by diphenhydramine (6,000 ng/g DM; Peysson et al., 2013), tonalide (5,000 ng/g DM; Kinney et al., 2006), triclosan (3,700 ng/g DM; Kinney et al., 2006), caffeine (2,100 ng/g DM; Malmborg and Magnér, 2015).

On the basis of the collected data and its processing (Table 5, Figures 5- 10) it emerges that concentrations of selected PhCs and PCPs may be reduced by common treatments. Digestion represents the first step in treatment, and an attenuation occurs for most compounds. Composting, conditioning and drying may reduce the variability ranges of occurrence of analgesics and anti-inflammatories, antibiotics, antiseptics by about one order of magnitude.

The most recalcitrant compounds seem to be doxycycline and tetracycline, which are still present at concentrations higher than 560 ng/g DM after conditioning; non ionic surfactants which are present at concentrations higher than 30,000 ng/g DM after thermal drying, and antiseptics and fragrances which are detected up to 5,000 ng/g DM.

Figure 9

Figure 10.

Table 5

5.2.7 Composting

Composting processes aim to accelerate the biodegradation of organic compounds thanks to a high microbial diversity and activity (mainly thermophilic organisms), abundant substrates, changing pH and redox conditions (aerobic and anaerobic microenvironments) (Xia et al., 2005). Martin et al. (2012a) found that degradation of organic matter and, at the same time, enhancement of the degradation of persistent compounds occurs under aerobic conditions. In the composted sludge a general attenuation of all the groups of compounds is observed (see Table 5 with regard to the main classes of selected compounds). The most recalcitrant substances were triclosan, galaxolide and tonalide (up to 4-5 10^3 ng/g DM; Peysson et al., 2013; Tavazzi et al., 2013; Kinney, 2006), and ibuprofen (close to 10^3 ng/g DM; Martin et al., 2012a).

5.2.8 Lagoon sludge

Martin et al. (2015) investigated the sludge from an anaerobic wastewater stabilization pond in Spain and found that most compounds occurred in a wide range of concentrations. Those exhibiting the maximum concentration of greater than 100 ng/g DM were: acetaminophen, salicylic acid, ciprofloxacin, gemfibrozil and caffeine, with naproxen, ofloxacin, carbamazepine, bezafibrate showing values of between 50 and 100 ng/g DM. Compounds always found below the corresponding limit of detection were ibuprofen, ketoprofen, norfloxacin, propranolol, ethinylestradiol, estradiol, estriol, estrone and clofibric acid.

5.2.9 Concentration in sediments (in CW)

Investigations of the concentrations of selected PhCs in sediment of subsurface flow constructed wetlands by Zhu and Chen (2014) confirmed the same tendency to sorb onto gravel for the compounds exhibiting high concentration in excess sludge, in particular for trimethoprim and triclocarban. The authors concluded that the risk of these compounds in sediments should not be neglected.

5.2.10 Attenuation of PPCP concentrations in sludge during treatment

Martin et al. (2012a, 2015) highlighted different behavior of PhCs during sludge treatment and tried to correlate it to the physico-chemical properties (namely chemical structure, p*K*a, Log K_{ow}) of the compounds, sludge composition and presence of aerobic/anaerobic conditions influencing the rate of biodegradation and its bioavailability. A higher content of organic matter in secondary sludge (see Table 3) could explain why most PhCs (naproxen, carbamazepine, the hormones E1, E2, EE2, E3, and gemfibrozil) were found at a higher concentration in secondary sludge compared to primary. The opposite trend was found by other authors (among them Stasikanis et al., 2013) - diclofenac, ibuprofen, salicylic acid, caffeine, nonilfenol and triclosan were found at higher concentrations in primary sludge than in secondary, probably due to the protonation at lower pH values of primary sludge (around 6.5) compared to secondary sludge (around 7.2) and the formation of electrostatic interactions between these compounds and the solid surface.

Jones et al. (2014) found higher concentrations of triclosan, propranolol, ibuprofen, and erythromycin in primary sludge rather than in secondary sludge samples, while they found that the type of secondary treatment (CAS, MBR, BNR, biological filtration) did not affect the concentration in the sludge.

Fernandez-Fontaina et al. (2013) remarked that the better overall performance of MBRs in the removal of PPCPs with respect to CAS is due to the typical higher biomass concentration in MBRs rather than CAS, resulting (generally) in an enhanced biodegradation of PPCPs. Collected data exhibited that PhCs tended to sorb less onto the aged MBR sludge than the primary and secondary activated sludge, possibly as a consequence of the higher biodegradation potential of the biomass within the MBR (Radjenovic et al., 2009b).

With regard to estrogens, concentrations of E2, E3 and EE2 were found to be similar in primary and excess sludges, 10-13, 2-3 and <3 ng/g DM respectively (Muller et al., 2010), whereas E1 was higher in excess sludge (43 ng/g DM) than in primary sludge (8 ng/g DM). This higher concentration may result either from the bacterial transformation of E2 to E1 or the hydrolysis of conjugated E1 forms during biological treatment. Muller et al. (2010) remarked that WWTPs with biological nitrogen treatment, and SRT in the range of 10-15 d enhance the biodegradation of estrogens, and their concentration in the excess sludge is lower than that detected in conventional activated sludge systems (12 ng/g DW *vs*. 50 ng/g DM referring to their total concentration).

Li et al. (2014) found that in conventional activated sludge systems, a longer SRT may enhance the sorption of quinolones (including ciprofloxacin and norfloxacin) onto secondary sludge, whereas Stasinakis et al. (2010) did not find any improvement in the sorption of triclosan at a longer SRT.

Sludge stabilization and conditioning involve physical, chemical, mechanical and biological processes and changes which could affect solid partitioning, degradation, adsorption and, to a lesser extent, volatilization and photolysis pathways of PhCs and PCPs in sludge matrices. Sludge chemical composition may change, resulting in different adsorption behavior of compounds. This was observed by Martin et al. (2012a) for ibuprofen, salicylic acid, caffeine and gemfibrozil, whose concentrations decreased from secondary, to digested and composted sludges, and by Miao et al. (2005) who investigated carbamazepine, whose concentration increased from untreated to treated (digested and thermally dried) sludge, from 69 to 258 ng/g DM.

With regard to fragrances, Clara et al. (2011) remarked that a good level of removal is achieved in activated sludge systems, as sorption is their principal removal method. A comparison between concentrations of fragrances in excess sludge (Fig. 4, class J) and AnD sludge (Fig. 7, class J) highlights that anaerobic biodegradation is not really effective in reducing the content of this group of compounds (see also Table 5).

An interesting analysis was carried out by Martin et al (2015) regarding 7 different kinds of sludge (primary, secondary, mixed, anaerobically digested, aerobically digested, composted, and settled in a lagoon) with regard to eight main therapeutic classes of PhCs. They found that primary sludge exhibited higher concentrations of anti-inflammatories, antiepileptics, nervous stimulants and estrogens than secondary sludge. On the contrary, higher concentrations of antibiotics, beta-blockers and lipid regulators were found in secondary sludge. Digested sludges showed lower concentrations than untreated sludges, which is often correlated to the loss of lipophilic properties during stabilization treatments (Khan and Ongerth, 2002).

Kimura et al. (2010) found that modest variations in pH may impact the removal of acidic PhCs (among them ibuprofen, naproxen, ketoprofen) by sorption, presumably due to enhancement of the affinity between the sludge surface and the PhCs subjected to protonation.

An increment in the concentrations of E1 and E2 was found during anaerobic digestion of the excess sludge (Andersen et al., 2003), specifically from 7 ng/g DM to 25.2 ng/g DM and 1.7 ng/g DM to 5.1 ng/g DM respectively.

Estrogenic compounds are hydrophobic and they have a high tendency to sorb, which can prevent them from biodegradation. The increment in the concentration of estradiol in the digested sludge is due not only to its hydrophobic nature, but also to the cleavage of conjugated steroid estrogens (Khan and Orgerth, 2002; Andersen et al., 2005) and to accumulation on the remaining digested sludge (Martin et al., 2012b).

During AnD, E1 is reduced to E2 (Paterakis et al., 2012, Carballa et al., 2007c), and biochemical reactions proceed faster in thermophilic than mesophilic conditions. Mesophilic conditions require a

higher SRT than thermophilic conditions, in order to guarantee a significant reduction of E1 to E2 (Paterakis et al., 2012).

In the digested sludge, Martin et al.(2012a) found a decrement in the concentrations of most analgesics, antibiotics and lipid regulators. They ascribe this attenuation to the fact that during anaerobic digestion, many PhCs tend to desorb and may then be involved in biodegradation reactions.

In anaerobic digestion, T and SRT greatly affect the biodegradation of NP1EO, while they do not affect the biodegradation of some PhCs, synthetic musks and estrogens (Carballa et al., 2006; Stasinakis, 2012). Biomass acclimatization improved the biodegradation of diclofenac, diazepam and estrogens (Carballa et al., 2006, 2007b).

The lab scale investigation by Carballa et al. (2007c) on the fate of a selected group of PhCs and PCPs by AnD highlights that a significant removal occurred for several PhCs (operating at a SRT equal to 10-20 d). Values were higher than 85 % for naproxen, sulfamethoxazole, roxithromycin, and E1, E2, and EE2; and between 65 and 85 % for galaxolide, tonalide, and diazepam (only mesophilic AnD). Ibuprofen and iopromide exhibited a poor removal (20-40 %) and carbamazepine was recalcitrant to degradation. They did not find consistent differences between mesophilic and thermophilic conditions.

With regard to antiseptics, Heidler et al. (2006) reported that AnD did not promote triclocarban degradation, resulting in an accumulation in the digested sludge, and McAvoy et al. (2002) reported a good level of removal of triclosan in aerobic digestion but not in anaerobic digestion.

Malmborg and Magnér (2015) investigated the correlation between lipophilicity (defined as log P for bases/neutrals and logD for acids) with the persistence of the compounds (expressed as a percentage of remaining substances) during mesophilic and thermophilic AnD and observed a direct proportionality which would correspond to high solid partitioning of lipophilic compounds, resulting in lower availability to degrading microorganisms.

Anaerobic treatments seem to be more efficient than aerobic ones in removing all PhCs, as shown in Figures 6, 7 and 8. Concentrations of PhCs in aerobically digested sludge subjected to compost are similar or higher than anaerobically digested. This could be due to the loss of organic compounds due to biodegradation and in a concentration of the residual persistent compounds. This is the case of estriol (Khan and Ongerth, 2002).

(Mechanical) dewatering treatments (centrifuge, filter press) do not affect the content of PPCPs in sludge, as they aim to reduce the water volume of the sludge and not to remove dry matter. As compound concentrations are expressed in g compound/g sludge DM, its concentration before and after a filter press or a thickener or centrifuge does not change (Mailler et al., 2014).

Braga et al. (2005) investigated concentrations of steroid estrogens (E1, E2, EE2) in excess sludge and dewatered sludge (by filter press). They found that concentrations are slightly higher in dewatered sludge than in excess sludge, but the PhC load in dewatered sludge is lower than its load in excess sludge.

With regard to chemical treatments, when a lime stabilization is performed, the increment in pH causes the desorption of estrogens (Clara et al., 2004).

Chemical and thermal (pre)treatments have been thoroughly investigated, but results are not always encouraging. Carballa et al., (2006, 2007a and 2008) investigated the influence on the removal of selected Phcs of pretreatments of anaerobic digestion of mixed sludge. They first tested a thermal pretreatment, consisting of an autoclave at 160°C for 30 mins, followed by a cooling step before AnD, and a chemical pretreatment by adding lime (CaO) to the stirred sludge up to a pH over 12, followed by neutralization, first with HCl, then AnD. They found that higher removal efficiencies were observed only for ibuprofen when thermal pretreatments were present and for roxithromycin in the presence of an alkaline pretreatment. No attenuation was found for estrogens, fragrances (tonalide and galaxolide), psychiatric drugs (carbamazepine and diazepam), sulfamethoxazole and iopromide.

They then investigated the effect of ozonation (20 kg O_3/kg TSS) of the sludge before anaerobic stabilization and found that it reduces carbamazepine by up to 60% but it does not affect the removal of other PCPs (Carballa et al., 2007a, 2008)

They remarked that neither chemical nor thermal pretreatments of the sludge prior to AnD can greatly improve the sorption potential of PhCs. This could be due to the fact that some pretreatments may decrease the bioavailability of target compounds (as is the case of thermal processes) or that target compounds are strongly adsorbed onto sludge that may not be attacked by oxidizing (as is the case of chemical retreatment).

Final sludge stabilization and dewatering by thermal pressurized treatments tends to increase the estrogen concentration from anaerobic digestion (mainly for E2 and EE2), probably by enhancing their extractability (Muller et al., 2010).

According to Malmborg and Magnér (2015), pasteurization has a slight effect on the removal of PhCs from the sludge matrix, with thermal hydrolysis reducing the concentrations of estrone (E1), estradiol (E2) and ethinylestradiol (EE2). This leads to the conclusion that in the case of thermal hydrolysis, the end-product of E2 is not E1 (as is often observed).

An attenuation in secondary sludge concentration was observed by Malmborg and Magnér (2015) for amlopidine, atenilol, caffeine, hydrochlorotiazide, and ketoconazole by means of Fenton's reaction, whereas ammonia treatments increased the concentrations of caffeine, furosemide,

naproxen and hydrochlorothiazide). An increment in concentrations was also observed in thermophilic dry digestion for caffeine, furosemide and hydrochlorotiazide.

5.3 Predicted concentrations of selected compounds in sludge

Some studies provide models to predict concentrations in sludges, the so-called predicted environmental concentrations (PEC). The authors of these studies include Carballa et al.(2007b), Cunningham et al. (2012), Khan and Ongerth (2002), Jones et al. (2002).

Frequently, PEC in sludge is evaluated on the basis of equation (1):

$$PEC_{i,\,sludge} = C_{i,\,water} \times K_{d,\,i\,sludge} \qquad \text{(eq. 1)}$$

where $C_{i,\,water}$ corresponds to MEC or PEC in water.

Another common equation is that proposed in Jones et al. (2002):

$$PEC_{i,\,sludge} = \frac{M_{c\,i}}{V_{ww}/K_d + M_{sludge}} \qquad \text{(eq. 2)}$$

where M_{ci} is the annual consumption of the compound i (kg), V_{ww} is the total annual wastewater volume (m^3), M_{sludge} is the annual sludge production (kg of dry matter) and K_d is the solid-water distribution coefficient which describes the ratio between its concentration sorbed onto sludge and its dissolved concentration S at equilibrium.

In both equations, PEC_{sludge} implies knowledge of the coefficient K_d. Some authors have experimentally evaluated K_d values for many compounds in different kinds of sludge. A reconnaissance of these values is reported in Table SD-4 in the Supplementary Data section, along with the corresponding references.

Another approach in predicting PhC concentrations in primary and secondary sludge is proposed by Khan and Ongerth (2002) based on the fugacity model. Close correlations were observed between predicted and measured values for naproxen, ibuprofen and paracetamol in primary sludge, whereas for salicylic acid and carbamazepine, measured values were two orders of magnitude higher than predicted values. This could be ascribed to hydrophilic interactions, not included in the model, which considers lipid partitioning the main mechanism for solid sorption. On the other hand, the measured concentration for gemfibrozil was one order of magnitude less than predicted. This fact could be attributed to incomplete extraction from the solid owing to its very high lipophilicity and also to a higher biodegradation rate than that estimated in the model.

5.3.1 Considerations regarding K_d

The extent of sorption onto a solid (sludge and soil) is generally based on the distribution coefficient (K_d) which implies a linear equilibrium relationship based on the concept of solute partitioning (Sathyamoorthy and Ramsburg 2013).

K_d values are strictly correlated to different operational conditions, namely temperature, pH, SRT, sludge type, and reactor configuration. Table SD-4 compiles the measured values of K_d for each compound and for the different kinds of sludge (primary, secondary, digested and differently treated). In many cases, a wide range of variability occurs due to the fact that collected K_d values were found in different systems operating at different conditions as discussed herein.

Lower values of K_d were found at a higher temperature for most organic compounds, whose solubility increases with temperature, as reported by Lajeunesse et al. (2012). With regard to compounds presenting basic properties such as the antidepressants fluoxetine, norfluoxetine, and paroxetine, higher pH values will result in higher K_d values. On the contrary, for neutral molecules (such as carbamazepine) no significant variations in K_d were observed in the case of variation in pH.

K_d values were investigated for sludge produced in activated sludge systems with short and long SRTs (Fernandez-Fontaina et al., 2012; Horsing et al., 2011), in anoxic, aerobic and anaerobic compartments. Fernandez-Fontaina et al. (2012) and Hyland et al. (2012) found similar values of K_d in CAS with different sludge ages, while Jia et al. (2012) found that, referring to fluoroquinolone antibiotics, K_d values are slightly higher in aerobic units than anoxic and anaerobic units. Fernandez-Fontaina et al. (2012) remarked that K_d values obtained in batch experiments are significantly lower than values obtained in continuous reactors and highlighted the importance of measuring sorption coefficients under real operating conditions. Discrepancies could be due to the different acclimatization conditions of the biomass, resulting in different biodegradation rates and bioavailability.

Horsing et al. (2011) experimentally determined the values of K_d for primary and secondary sludge for 75 compounds. For most PhCs, K_d values are higher for secondary sludges than primary ones due to different factors, including better sorption onto the former, higher organic matter content in secondary sludge (Yan et al., 2014) and fast biodegradation which reduces the concentration of the compound in water (Martin et al., 2012b).

Stasinakis et al. (2010) investigated the influence of SRT (3, 10 and 20 d) on K_d values for NP and TCS in an activated sludge system fed with municipal wastewater. They found that the highest K_d values occurred at the shortest SRT (see table SD-4).

There have been many attempts to correlate K_d with properties of the compound of interest and the solid phase (sludge types, particles, sediments and soil), from single parameter to multiple parameter models. To evaluate the sorption of lipophilic compounds on secondary sludge, Matter-Muller et al. (1980) proposed the following equation:

$$K_d = 0.39 + 0.67\, K_{ow} \qquad \text{(eq. 3)}$$

In the same years, Karickoff (1981) developed a two parameter equation for K_d on the basis of K_{ow} and the fraction of organic carbon in sludge f_{oc}:

$$K_d = f_{oc}\, x\, 0.41\, x\, K_{ow} \qquad \text{(eq. 4)}$$

Eq. 4 was used by many other authors, including Jones et al. (2002). The parameter f_{oc} is frequently assumed to be equal to 0.35. Other values have been suggested for f_{oc} for different kinds of sludge - for primary sludge 0.30 (Zhu and Chen, 2014), 0.43 (Braga et al., 2005) and 0.49-0.51 (Stevens-Garmon et al., 2011); for secondary sludge 0.27 (Andersen et al., 2003) and the ranges 0.39-0.47 (Stevens-Garmon et al., 2011), and 0.45-0.55 (Hyland et al., 2012); 0.02-0.136 for differently pretreated mesophilic digested sludge and 0.032-0.152 for differently pretreated thermophilic digested sludge (Carballa et al., 2008).

An in-depth discussion of further semi-empirical expressions suggested for calculating K_d as a function of K_{ow} is reported in Andersen et al. (2005), Pomiès et al. (2013), Sathyamoorthy and Ramsburg (2013) and, as a function of D_{ow}, by Stevens-Garmon et al. (2011).

Yan et al. (2014) remarked that eq. 4 leads to an overestimation of several orders of magnitude for hydrophobic compounds and to an underestimation for ionic and polar ones.

Some authors (Golet et al., 2003,Ternes et al., 2004) remarked that for compounds, including fluoroquinolones, characterized by low K_{ow},(log K_{ow} = -1 for norfloxacin) and high K_d (log K_d = 3.9 for norfloxacin), electrostatic interactions are the main sorption mechanism. On the contrary, non-ionic compounds such as EE2 (log K_{ow} = 4.2, log K_d = 2.8) tend to be sorbed in the lipid fraction or onto organic matter at ambient pH and for them hydrophobic interactions are quite relevant.

For acidic and basic compounds different correlations have been developed. A discussion is reported in Verlicchi et al. (2013) and Vasquez-Roig et al. (2012). More complex polyparameter models are discussed in Sathyamoorthy and Ramsburg (2013) with regard to negatively or positively charged compounds.

An interesting compilation of literature data of K_d for secondary sludge obtained in different systems (CAS, MBR) can be found in the review by Sathyamoorthy and Ramsburg (2013), which correlates K_d values to pH, biomass concentration in the aeration tank, charge and pKa of the secondary treatment under consideration.

5.4 Concentration of PPCPs in soil after sludge application

Once the digested sludge is spread onto soil, occurring PPCPs may be subjected to different processes, namely fixation, mobility and transport, degradation and inactivation. Fixation depends on the nature of interaction between PPCPs and the sludge-amended soil characteristics. PPCP concentration in soils depends on many factors that will be addressed in the following section, in discussing measurements and predicted values.

MEC - Data regarding PPCP concentrations in sludge-amended soil are scarce due to the lack of appropriate instrumentation and methods to carry out accurate measurements of compounds occurring at very low concentrations in complex matrices (Li, 2014, Kinney et al., 2008). Table 6 reports the range of concentrations found in literature.

Table 6 Measured

With regard to trimethoprim, carbamazepine and triclosan, different ranges of concentrations were found by Kinney et al., (2008) and Li (2014), confirming that many factors may influence their occurrence. These factors include rate of sludge application, frequency, soil conditions and characteristics, chemical and biological characteristics of the compound (Butler et al., 2012), time between sludge application and soil sampling (Jones et al., 2014) precipitation and runoff.
Golet et al. (2002) measured the concentrations of norfloxacin and ciprofloxacin in the topsoil 8 months after sludge application. They found 0.29-0.32 mg /kg DM for norfloxacin and 0.35-0.40 mg/kg DM for ciprofloxacin. They also monitored the sludge-amended soil concentration after 21 months and noticed a slight reduction in the antibiotic levels, demonstrating that traces of fluoroquinolones persist and may accumulate in the terrestrial environment after sludge application. Butler et al. (2012) reported a slight attenuation of triclosan in soil (initially 0.8-1 mg/kg) in the first eight months following the sludge application in three different soil types. The reduction was about 80 % after one year of application. They attribute this reduction to the biodegradation of triclosan to methyl triclosan, whose concentration was found at about 0.4 mg/kg.
The sorption of PhC to soil depends on the soil pH, soil organic materials and soil minerals (Thiele-Bruhn, 2003). The most important mechanisms are association with organic matter, ion exchange, surface adsorption to mineral constituents, hydrogen bonding and the formation of complexes with ions such as Ca^{2+}, Mg^{2+}, Fe^{3+} or Al^{3+} (Thiele-Brun, 2003; Diaz-Cruz et al. 2003, Xia et al., 2005).

In this context, on the basis of the pK_a value of a compound (see Table SD-2), Monteiro and Boxall (2010) propose a scheme to predict its main sorption mechanisms, which include hydrophobic interactions; van der Waals interactions, hydrogen bonds with OM or clay, cation exchange, charge transfer, and ligand exchange with OM.

With regard to the adsorption of antibiotics to organic and mineral exchange sites, this is mostly due to charge transfer and ion interactions and not to hydrophobic partitioning. Strongly adsorbed antibiotics are subjected to transportation processes due to fast leaching through soils by macropores, or to the transportation of the dissolved soil colloids to which they are attached..

In a soil matrix, biodegradation can take place with different kinetics depending on the (micro)environment where they are located. Triclosan and triclocarban, for instance, tend to sorb onto soil and sediment and may be subjected to very low biodegradation in aerobic conditions, whereas in anaerobic conditions they are more resistant (Ying et al., 2007).

The mobility of PPCPs in soil, and consequently their potential for contaminating groundwater and surface waters, is shown to depend on the amount of substance applied, the intensity of the rain events and the soil type. Mobility of a pharmaceutical (or any other organic compound to that effect) in a heterogeneous porous medium such as soil is also influenced by the soil structure and not simply its composition (Drillia et al., 2005). Some PhCs may reach surface water due to fast preferential and macropore flow, others due to co-transportation with mobile colloids such as dissolved organic materials (Thiele-Bruhn, 2003). Photodegradation has no significant effect, whereas biodegradation may take place due to the action of enzymatic transformation reactions like oxidative decarboxylation and hydroxylation.

PPCP sorption onto soil organic matter and soil minerals or the formation of complexes may cause a loss of detectability as well as a loss in bacterial activity (Kummerer, 2009). There could be the potential for accumulation of compounds within agricultural soils characterized by very poor biodegradability or biotransformability (as is the case of some benzodiazepines, Redshaw et al., 2008).

5.4.1 Predicted concentrations of PhCs in soil

According to the European Technical Guidance Document on Risk Assessment EUR 20418 EN/2 (EC-TGD, 2003), the PhC concentration in soil may be assessed by eq.

$$PEC_{i,\,soil} = \frac{c_{i,sludge}\ x\ APP_{sludge}}{DEPTH_{soil}\ x\ RHO_{soil}} \qquad \text{(eq. 5)}$$

where c_{sludge} is the MEC (or PEC) in digested sludge (μg/kg DM), APP_{sludge} is the application rate of the dry sludge onto soil (generally the value of 0.5 kg/m^2 is used for agricultural soil; Stasinakis et al. (2008) adopted 1 kg/m^2), $DEPTH_{soil}$ is the mixing depth (generally 0.20 m is used for agricultural soils. Stasinakis et al., 2008 adopted 0.10 m) and RHO_{soil} is the bulk density of wet soil (1,700 kg/m^3 for agricultural soils; Stasinakis et al. (2008) adopted 1,300 kg/m^3).

The "depth of soil" represents the depth range for the top soil layer which is of interest. The depth of 20 cm is generally taken because this range usually has a high root density of crops, and represents the ploughing depth.

For grassland the depth is less, since grasslands are not ploughed. The average period of 180 days for crops is chosen as a representative growing period for crops. For grassland this period represents a reasonable assumption for the period that cattle are grazing on the field. For the ecosystem a period of 30 days is taken as a relevant time period with respect to chronic exposure of soil organisms (EC-TGD, 2003).

The model used to evaluate PEC_{soil} is based on the assumption that a complete mixing between sludge and soil occurs. This may not always be verified and the concentration of selected compounds could be higher (accumulation of the substance) or lower.

In McClellan and Halden (2010) a different approach for soil prediction concentration which also considers pore water contribution is proposed and discussed.

Table 7 reports predicted concentrations in soil for a selection of compounds.

Table 7

According to Drillia et al., 2005, the tendency of pharmaceuticals to move through the soil is well correlated with their sorption tendencies and for this objective a rough evaluation could be carried out by using K_d for the different kinds of soil.

Drillia et al. (2005) provide values of K_d for soils with low organic carbon and high clay content and soil with high organic carbon and low clay content. The adsorption of pharmaceuticals on the soil of the low organic carbon was not only dependent on the organic content of the matrix, but also on the other matrix properties and the dissociation degree of the compounds.

Sarmah et al. (2008) provided K_d for different soils (in New Zealand) with regard to three estrogens (E2, EE2, and E1) and noted consistent differences in the soil organic carbon content.

In the Supplementary data section, Table SD-5 reports the collected data regarding K_d for the different kinds of soils.

5.5 Environmental risk assessment due to PhCs and PCPs in sludge and in sludge-amended soil

The common equations used for evaluating the environmental risk posed by PPCPs occurring in sludge and after its application to soil for agriculture purposes is based on the risk quotient (RQ) that is the ratio between pollutant concentration and its predicted no-effect concentration (PNEC):

$$RQ_{i,j} = \frac{C_i}{PNEC_i}\Big|_j \qquad i = \text{PhC},\ j = 1\ \text{(digested sludge)},\ 2\ \text{(soil)} \qquad \text{(eq. 6)}$$

where C_i represents the concentration of the compound of interest in the solid phase (sludge or soil) and may be directly measured (MEC) or predicted (PEC) by means of literature models as already discussed above.

With regard to sludge, PEC is generally evaluated according to eq. 1 or eq. 2, whereas PEC_{soil} may be predicted after one dose of sludge application, according to eq. 5:

Due to the lack of data regarding chronic and acute toxicity for terrestrial dwelling organisms with regard to PhCs and PCPs, many authors (Martin et al., 2012a) evaluate the corresponding PNEC for sludge and soil on the basis of the known PNEC for the water and partition coefficient K_d of the compound of interest, according to eq. 7. PNEC reported in Table 7 are literature data regarding specific values of PNEC evaluated for soil by the reported Authors. In this study, values of PNEC used for environmental risk assessment are those reported in Verlicchi et al. (2012).

$$PNEC_{i,j} = PNEC_{water} \times K_{d,ij} \times 1000 \qquad \text{(eq. 7)}$$

where i =PPCPs and j = sludge or soil.

PNEC values refer to the acute toxicity data taken from literature. According to eq. 7, PNEC values for soil and sludge refer to aquatic organisms and not to terrestrial ones, as only a little data is available regarding the toxicological effects of PPCPs on terrestrial organisms (Table 7). This approach is suggested by the European Commission (EC-TGD, 2003) and is called the equilibrium partition approach.

The criteria usually applied to evaluate the risk by means of RQ values is that proposed by Hernando et al. (2006), which considers a high risk if $RQ \geq 1$, medium risk if $0.1 < RQ < 1$ and low if $RQ \leq 0.1$.

An environmental risk analysis was carried out for those PPCPs whose concentrations in digested sludge, K_d values for digested sludge and PNEC (in water) of the compound of interest are known. For this group of PPCPs, the minimum and maximum RQ values have been evaluated (eq. 6) on the

basis of their minimum and maximum concentrations found in digested sludge (Table SD-3) and the average value of K_d among those reported in Table SD-4 for the compounds.

The results are reported in Fig. 11, which provides a snapshot of the current knowledge. It shows that a high environmental risk is posed by antibiotics (sulfamethoxazole, erythromycin, roxithromycin, azithromycin, and ofloxacin), hormones (E1, E2, and EE2), analgesics and anti-inflammatories (acetaminophen, ibuprofen, naproxen and salicylic acid) and the beta-blocker propranolol.

Figure 11

Previous studies provided a risk analysis based on the RQ approach for a limited group of compounds in secondary, digested sludges and after sludge application on soil. These are briefly compiled in Table 8. With regard to digested sludge, the most critical compounds are antibiotics (sulfamethoxazole, sulfadiazine, ofloxacine, erythromycin andazithromycin), hormones (ethinyestradiol andestradiol), ibuprofen and triclosan and triclocarban. After sludge application on soil, the high risk is due to the residual of estradiol, ciprofloxacin, ofloxacin, tetracycline, caffeine, triclosan and triclocarban.

Table 8.

Martin et al. (2012b) compare the risk in untreated and treated sludge and remark that the environmental risk due to PhC occurrence in sludge decreases from digested sludge and after application on land (digested sludge-amended soil) and is lower still in the case of compost applied to land.

Land application represents a viable environmental route to enter the food chain, even if PPCP concentrations in the sludge remain very low.

Different criteria for environmental risk assessments have recently been proposed and are under discussion. Eriksen et al. (2009) suggest assuming a cut-off of 100 μg/kg as the PNEC of PhCs for soil and that PhC levels below this limit should be regarded by the European Medicine Agency as posing a negligible environmental risk. With regard to hormones, the cut-off is set at 10 μg/kg as this group of compounds is considered to pose a higher environmental risk. This approach implies refining steps in order to identify the group of compounds which requires special attention. Munoz et al. (2009) based their environmental risk assessment on the half-life in soil for the compounds of interest and assume it to be equal to twice the value obtained for the water compartment. In

addition, they consider that in 6 half-lives complete degradation of the compound will occur, assuming first-order kinetics.

6 Future fields of research

Future investigations should focus on the occurrence of some groups of PPCPs that have a high sorption potential (such as antimycotics) in treated sludge, and their fate in the case of sludge-amended soil. Special attention should also be paid to the ability of the compound to sorb onto the dissolved organic matter fractions. They can affect the mobility of PPCPs in soils influenced by intensive irrigation with reclaimed wastewater or amended with treated sludge (Maoz and Chefetz, 2010).

Moreover, future investigations should also deal with the reduction of the total estrogenic activities measured after treatment due to transformation products, mainly for those treatments able to attenuate the content of the PPCPs of interest.

Improvements in environmental risk assessment are highly recommended in particular research on PNEC referring to soil-dwelling organisms, especially plants and fauna in soil, rather than to aquatic ones, as has already been done for other groups of compounds, including anionic surfactants (LAS) (Kloepper-Sams et al., 1996, Ying et al., 2006).

Very little data is available regarding the chronic toxicity and effects of mixtures of PPCPs on different organisms. Moreover, studies refer to the effects of the contemporary occurrence of sub-therapeutic concentrations of antibiotics on soil microbial community structures, as well as the spreading of antibiotic resistant bacteria.

The environmental risk assessment should be carried out in a global perspective and include potential leaching due to the rain water runoff of sludge-amended soil onto surrounding surface water, the contribution of irrigation by means of reclaimed wastewater reuse, which represents an additional exposure route for the target compounds in terrestrial ecosystems. In this context, Munoz et al. (2009) developed a method to carry out this evaluation and Vasquez-Roig et al. (2012) have already addressed some interesting issues.

There is a further element of risk posed by the wash-off of sewage sludge into water courses. Whilst concentrations of contaminants in sludges reported here were low in relation to the sludge/soil concentration criteria, the presence of a relatively small quantity of sludge in suspension in a watercourse could exceed the much more stringent EQS values that have been set for surface waters.

7 Supplementary Data:

Supplementary material is provided online and includes a summary of the main issues addressed in the papers included in the review (Table SD-1); a list of the main chemical and physical characteristics of the compounds under review (Table SD-2); tables with all the concentrations (Table SD-3) and K_d (Table SD-4) found in the different kinds of sludge together with the corresponding references, and finally a table reporting K_d for the different kinds of soil (Table SD-5).

8 Acknowledgements

This work was financially supported by the Technopole 'Terra&AcquaTech' of the University of Ferrara (Funding: POR-FESR 2007–2013).

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Table 1 Types of untreated and treated sludge included in the review

Sludge type	Description
Untreated sludge	
Raw	It contains suspended solids collected by filtering raw sewage (Jia et al., 2012, Lindberg et al., 2010) or in a grit chamber (Miao et al., 2005).
Primary	It derives from primary clarifiers which may also be chemically enhanced (for instance with $FeCl_3$, Lajeunesse et al., 2012) and contains about 2- 8 % of total dry solids. Water content can be easily reduced by thickening or dewatering. It has a larger particle size than secondary sludge.
Secondary	It is generated in secondary biological treatments - conventional activated sludge systems (CAS), membrane biological reactors (MBR), biological nutrient reactors (BNR), or attached biological systems, such as trickling filters, and biological aerated filters (BAF). Sludge produced in UASB has also been included in this type of sludge.
Mixed	It is the mixture of primary and secondary sludges.
Lagoon sludge, SF	Sludge produced and settled in deep anaerobic stabilization ponds or in aerobic surface flow basins.
Treated sludge	
Digested sludge	Stabilized sludge produced in aerobic or in anaerobic digesters. The main aim of digestion is to reduce organic content and pathogens and also eliminate odors. Anaerobic digestion may occur both at a low temperature (mesophilic digestion, around 37 °C) and at a high temperature (thermophilic digestion, around 55 °C).
Composted sludge	Stabilized sludge resulting from the decomposition of organic compounds by microorganisms under aerobic conditions ensuring proper aeration by regularly turning sludge.
Biosolids	This term reflects the fact that the solids ("sludge") are organic products that can be beneficial after treatment with processes such as biological stabilization and/or digestion of primary and secondary sludges and composting. In the USA a distinction is made between Class A and B on the basis of the treatment the sludge is subjected to. In a Class A sewage sludge treatment has greatly reduced pathogens below detectable limits and thus can be distributed as a soil amendment without any restriction. Class B sewage

	sludge may contain pathogens and therefore restrictions on crop harvesting, animal grazing and public access are requested after sludge application on land (Jones-Lepp and Stevens, 2007; Citulsky and Farahbaksh, 2010).
Conditioned sludge	Sludge from systems aiming to reduce its water content by chemical and physical processes (for instance by addition of $FeCl_3$).
Dried sludge	Sludge from systems aiming to reduce its water content by thermal processes.
Thickened and Dewatered sludge	Sludge from systems aiming to reduce its water content by mechanical and physical processes.
Other types of treated sludges	Sludges obtained by disinfection (aiming to reduce the pathogen concentration), pasteurization (aiming to eliminate most pathogens by heating the sludge at 70 °C for 60 min), thermal hydrolysis (aiming to improve biodegradation of organic content by heating the sludge at 165 °C, at 6 bar for 30 min), advanced oxidation (adopted to treat or stabilize the organic material in the sludge) in particular Fenton's reaction (by adding sulfuric acid and hydrogen peroxide to the sludge), and ammonia treatment (by mixing dissolved ammonia or urea to the digested sludge) (Malmborg and Magnér, 2015; Arthurson, 2008)

Table 2. Groups of classes of PhCs and PCPs included in the review and, in brackets, their corresponding symbol and number of compounds.

Class	Class	Class	Class
Analgesics/antinflam. (A, 11)	Anti-histamines (I, 2)	Hormones (Q, 6)	Antiseptics (a, 2)
Antianginals (B, 1)	Anti-hypertensives (J, 6)	Hypnotics (R, 1)	Insect repellents (b, 1)
Antiarrhythmics (C, 2)	Anti neoplastics (K, 2)	Lipid regulators (S, 6)	UV filters (c, 1)
Antibiotics (D, 45)	Antiplatelets (L, 3)	Psychiatric drugs (T, 31)	Synthetic musks (d, 6)
Anticoagulants (E, 1)	Antiprotozoals (M, 1)	Contrast Media (U, 1)	Non ionic surfactants (e, 7)
Antidiabetics (F, 2)	Beta-agonists (N, 3)	Receptor antagonists (V, 5)	
Antiemetics (G, 1)	Beta-blockers (O, 10)	Stimulants (W, 3)	
Antifungals (H, 7)	Diuretics (P, 1)		

Table 3. Rules of thumb in predicting the sorption behavior of a compound

Parameter	Conditions	Rule of thumb	Reference
Log K_{ow}	< 2.5	Low sorption	Rogers (1996)
Log K_{ow}	> 4	High sorption	Rogers (1996)
K_d	> 500 L/kg	High sorption	Ternes and Joss (2006)
Log K_d	> 2.67		
K_d	< 500 L/kg	Low sorption	Ternes and Joss (2006)
Log K_d	< 2.67		
Log D_{ow}	< 1	Low sorption	Cunningham (2008)
Log D_{ow}	>3	High sorption	Cunningham (2008)

Table 4. Characterization of the main characteristics of the sludges

Property	**Primary**	**Secondary**	**Mixed**	**AnD**	**AeD**	**Dew**	**SOIL**
pH	6.6-7	6-8		5.8-7.5	7-7.5		4-8
OM %				31-48 (MAnd)			1-8
				24-51 (TAnD)			
C %	70	7-72		18-28 (MAnD)			0.4-7
				14-30 (TAnD)			
f_{oc} %	37.7	12.2		5.8-14 (MAnD)		36.7	
		42-47		3.2-15 (TAnD)			
N tot %		5.1-5.9		2-3 (MAnD)			
				1.4-2.5 (TAnD)			
P %		0.7-5		2.1-4.3 (MAnD)		0.26	
				0.29-4.4 (TAnD)			
TSS, g/L	50-125	10-35	30-95				
CEC, meq/100 g		54-75					16-28

Data from: Butler et al., 2011; Carballa et al., 2007c, 2008; Drillia et al., 2005; Gao et al., 2012b, Golet et al., 2003; Horsing et al., 2011; Hyland et al., 2012, Jelic et al., 2012; Li et al., 2014.

Table 5 Ranges of observed concentrations for the principally investigated groups (ng/g DM)

Class	Analgesics	Antibiotics	Hormones	Psychiatric drugs	Antiseptics	Fragrances	Non ionic surfactants
Primary	3-10 ^{4}	5-4 10^3	4-4 10^2	5-2 10^3	40-1.5 10^4	10^3-10^5	10^2
Secondary	1-10^3	10^{-1}-7 10^4	10^{-1}-3 10^2	1-6 10^2	10^2-2 10^4	10-10^5	--
Digested	4-10^3	1-8 10^3	1-10^4	10^{-1}-3 10^3	10^2-7 10^4	10-8 10^4	10-2 10^4
Composted	10^{-1}-10^3	8 10^{-1}-2 10^2	2 10-2 10^2	10^{-1}-9 10^2	10^1-8 10^3	--	--
Biosolids	10-10^4	4 10^{-1}-6 10^4	8 -10^3	1-6 10^3	10^2-4 10^4	10^3-4 10^4	--
Conditioned	1-10^2	10-5 10^2	2-3 10	10-10^3	8 10^1-3 10^3	8 10^2-3 10^4-	--
Dried	5-3 10^2	8-10^2	3-10^3	1-10^3	7 10^2-4 10^3	10^3-7 10^3	10-5 10^4

Table 6 Measured concentrations of PhCs in soil and corresponding references

Compound	**Measured concentrations [ng/g]**	**References**
Diclofenac	n.d.[1]-1.16	Li, 2014
Ibuprofen	n.d.-5.03	Li, 2014
Ciprofloxacin	350-400 After 8 months	Golet et al., 2002;
	280-270 After 21 months	
	450 (2.5 cm depth)	Golet et al., 2003
Norfloxacin	320-290 After 8 months	Golet et al., 2002;
	270-300 After 21 months	Golet et al., 2002;
	350 (2.5 cm depth)	Golet et al., 2003
Sulfadiazine	n.d.-3.82	Li, 2014
Trimethoprim	0.64	Kinney et al., 2008;
	n.d.	Kinney et al., 2008;
	n.d.-60.1	Li et al., 2014
Diphenhydramine	n.d.	Kinney et al., 2008;
	n.d.	Kinney et al., 2008;
Carbamazepine	n.d.	Kinney et al., 2008;
	n.d.	Kinney et al., 2008;
	0.02-7.5	Li, 2014
Caffeine	n.d.	Kinney et al., 2008
	n.d.	
Triclosan	833	Kinney et al., 2008;
	96;160	Kinney et al., 2008;
	n.d.-16.7	Li, 2014
	774-949	Butler et al., 2012
Galaxolide (HHCB)	633	Kinney et al., 2008
	1,050;2,770	
Tonalide (AHTN)	113	Kinney et al., 2008
	287;773	Kinney et al., 2008;
NP1EO	n.d.	Kinney et al., 2008
	n.d.	Kinney et al., 2008;
NP2EO	n.d.	Kinney et al., 2008

		n.d.		Kinney et al., 2008;

[1] n.d. = not detected

Table 7 PEC in soil available in literature and PNEC for some compounds

Class	Compound	PEC Soil [ng/g DM]	PNEC Soil [ng/g DM]	Referneces
	Diclofenac	0.21 (0.14)		Jones et al., 2014;
			0.013	Munoz et al., 2009
A	Ibuprofen	1.42 (0.58)		Jones et al., 2014;
			0.73	Munoz et al., 2009
B	Ciprofloxacin	40 (60 t/ha of sludge)	2,6000	Eriksen et al., 2009;
		1,400-6,000 (2.5 cm depth)		Golet et al., 2003;
		180-750 (20 cm depth)		
			0.29	Munoz et al., 2009
	Erythromycin	0.34 (0.12)		Jones et al., 2014;
			0.0041	Munoz et al., 2009
	Norfloxacin	1,400-6,000 (2.5 cm depth)		Golet et al., 2003
	C16H18FN3O3	180-750 (20 cm depth)		
	Ofloxacin	1.23 (0.46)		Jones et al., 2014
	Oxytetracycline	91.65 (16.43)		Jones et al., 2014
	Sulfamethoxazole		0.025	Munoz et al., 2005
	Tetracycline	10 (60 t/ha of sludge)	8,800	Eriksen et al., 2009
J	Hydrochlorothiazide		2,400	Munoz et al., 2009
O	Atenolol		440	Munoz et al., 2009
	Metoprolol	20 (60 t/ha of sludge)	58,9000	Eriksen et al, 2009
	Propranolol	0.81 (0.31)		Jones et al., 2014
	Sotalol	20 (60 t/ha of sludge)	4,095,000	Eriksen et al, 2009
S	Atorvastatin	50 (60 t/ha of sludge)	11,000	Eriksen et al, 2009
	Gemfibrozil		0.061	Munoz te al., 2009
	Carbamazepine		0.05	Munoz et al., 2009
T	Fluoxetine	0.52 (0.28)		Jones et al., 2014;
			44	Munoz et al., 2009
V	Ranitidine	40 (60 t/ha of sludge)	5,277	Eriksen et al, 2009
W	Caffeine		37	Munoz et al., 2009
a	Triclosan	80		Stasinakis et al., 2013;
			2.1	Munoz et al., 2009;
			0.096	Ying and Kookana, 2007

Table 8. Review of the published investigations on the Risk quotient due to PPCPs in sludge and in the case of sludge-amended soil

References	Sludge RQ≥1	Sludge 0.1 <	Sludge RQ ≤ 0.1	Digested sludge-amended soil RQ≥1	Digested sludge-amended soil 0.1 <	Digested sludge-amended soil RQ ≤ 0.1
Martin et al., 2012b (digested sludge)	Ibuprofen, ethynilestradiol, estradiol	Salicylic acid, carbamazepine	Naproxen, propranolol, caffeine, estriol	Estradiol	Ethynilestradiol	Ibuprofen
McClellan and Halden 2010[(1)] (digested sludge)				Ciprofloxacin, ofloxacin, tetracycline, caffeine, triclosan, triclocarban		
Zhu and Chen, 2014 (mixed sludge)	Sulfamethoxazole Triclocarban triclosan	Carbamazepine, diclofenac	DEET, trimethoprim, caffeine, ibuprofen			
Yan et al., 2014, (secondary sludge)	Sulfadiazine, sulfamethoxazole, ofloxacine, erythromycin, azithromycin	Norfloxacin, roxithromycin, clfobric acid	Trimethoprim, sulfametazine, diclofenac, bezafibrate, metoprolol, amlodipine, simvastatin, carbamazepine			
Clark and Smith (2011)[(1)]				Triclosan and triclocarban		

(1) McClellan and Halden (2010) and Clark and Smith (2011) follow different approaches in assessing environmental risk

Figure
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FIGURES

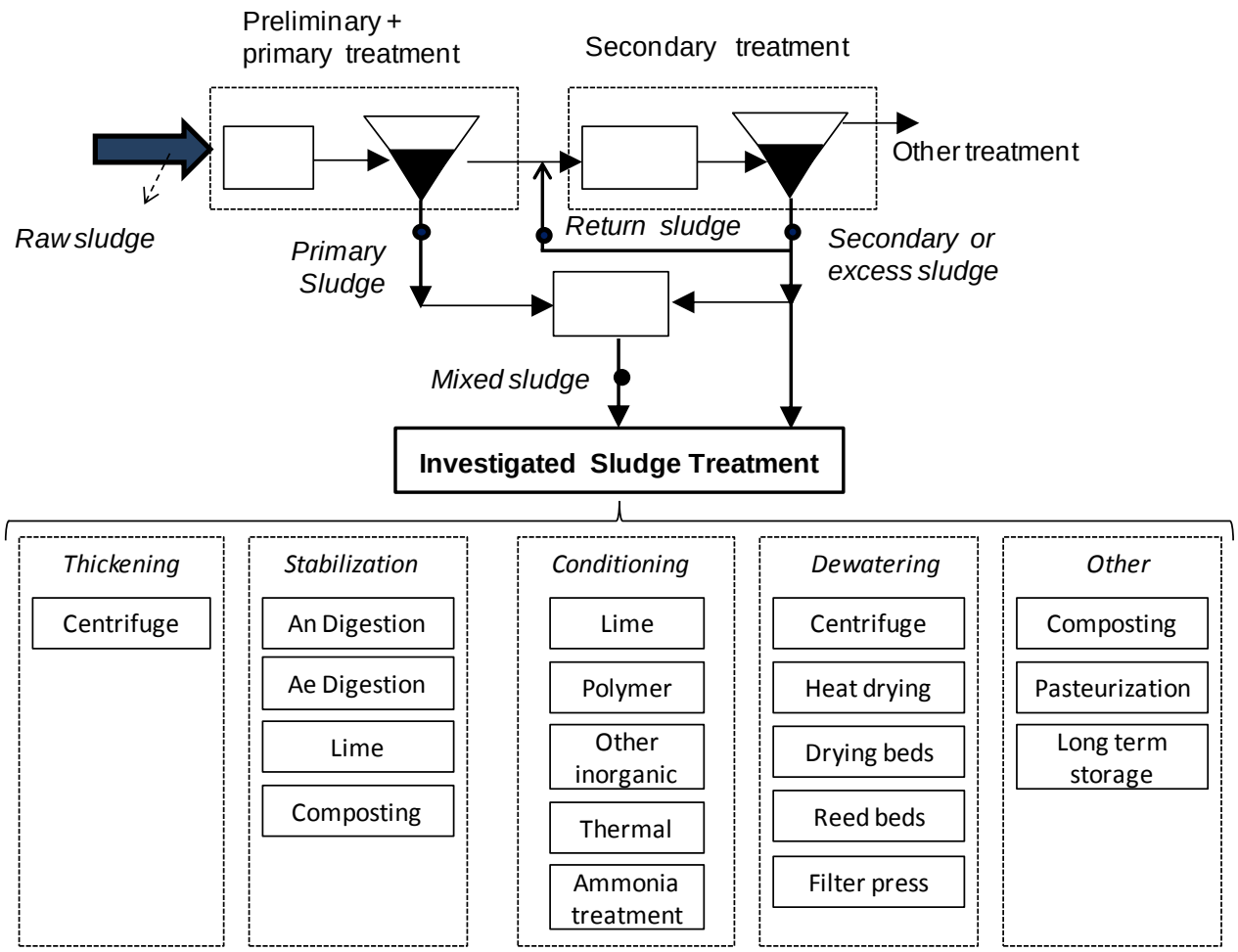

Figure 1

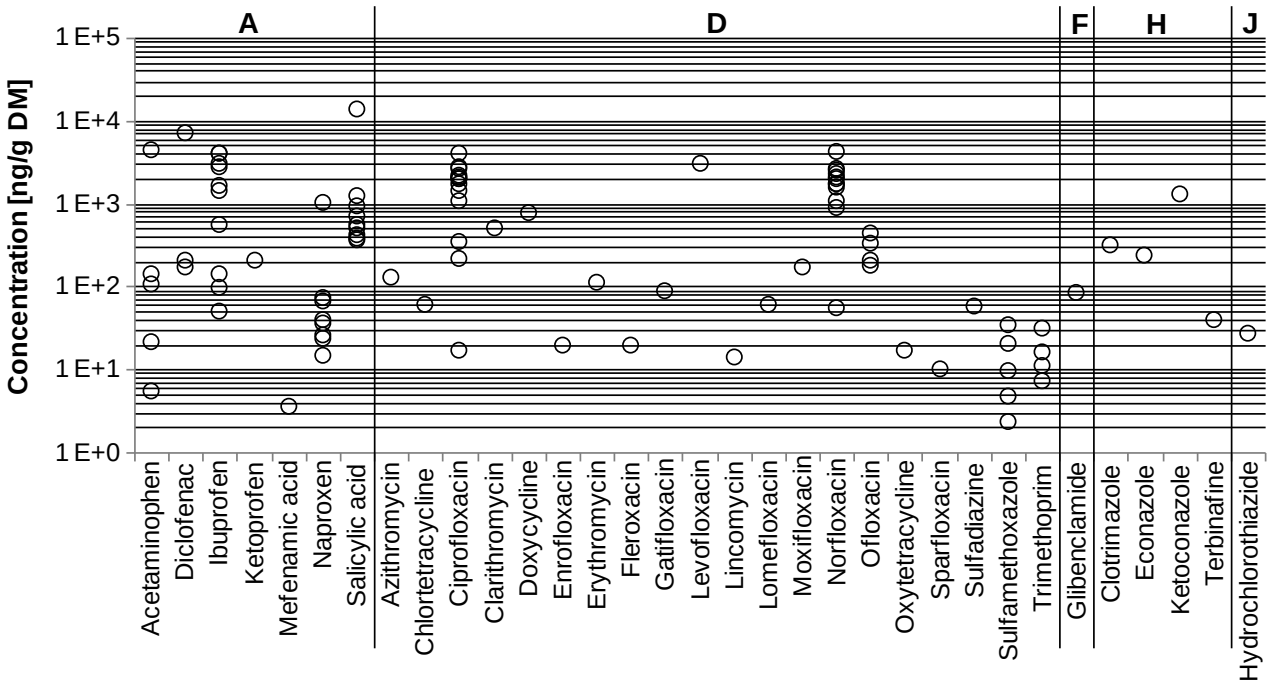
A
D
F
H
J
Concentration [ng/g DM]
1 E+5
1 E+4
1 E+3
1 E+2
1 E+1
1 E+0
Acetaminophen
Diclofenac
Ibuprofen
Ketoprofen
Mefenamic acid
Naproxen
Salicylic acid
Azithromycin
Chlortetracycline
Ciprofloxacin
Clarithromycin
Doxycycline
Enrofloxacin
Erythromycin
Fleroxacin
Gatifloxacin
Levofloxacin
Lincomycin
Lomefloxacin
Moxifloxacin
Norfloxacin
Ofloxacin
Oxytetracycline
Sparfloxacin
Sulfadiazine
Sulfamethoxazole
Trimethoprim
Glibenclamide
Clotrimazole
Econazole
Ketoconazole
Terbinafine
Hydrochlorothiazide

Figure 2

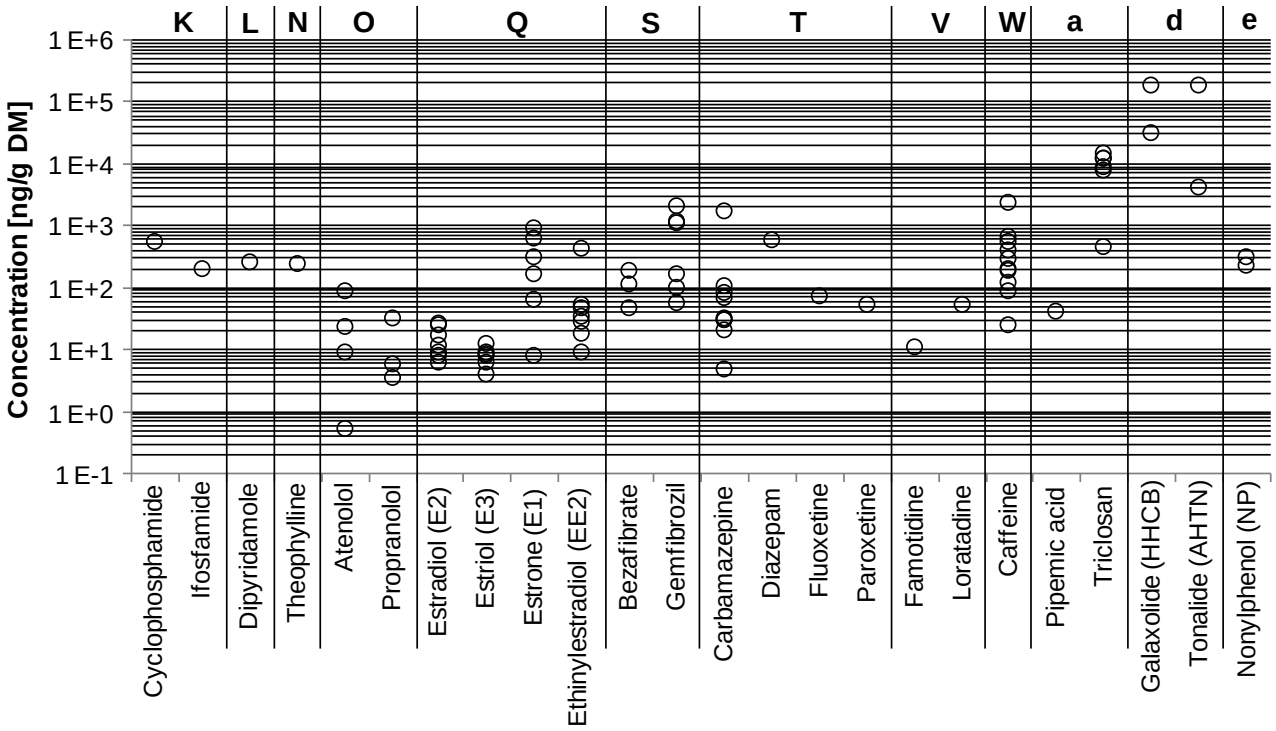
Concentration [ng/g DM]
1 E+6
1 E+5
1 E+4
1 E+3
1 E+2
1 E+1
1 E+0
1 E-1
K
L
N
O
Q
S
T
V
W
a
d
e
Cyclophosphamide
Ifosfamide
Dipyridamole
Theophylline
Atenolol
Propranolol
Estradiol (E2)
Estriol (E3)
Estrone (E1)
Ethinylestradiol (EE2)
Bezafibrate
Gemfibrozil
Carbamazepine
Diazepam
Fluoxetine
Paroxetine
Famotidine
Loratadine
Caffeine
Pipemic acid
Triclosan
Galaxolide (HHCB)
Tonalide (AHTN)
Nonylphenol (NP)

Figure 3

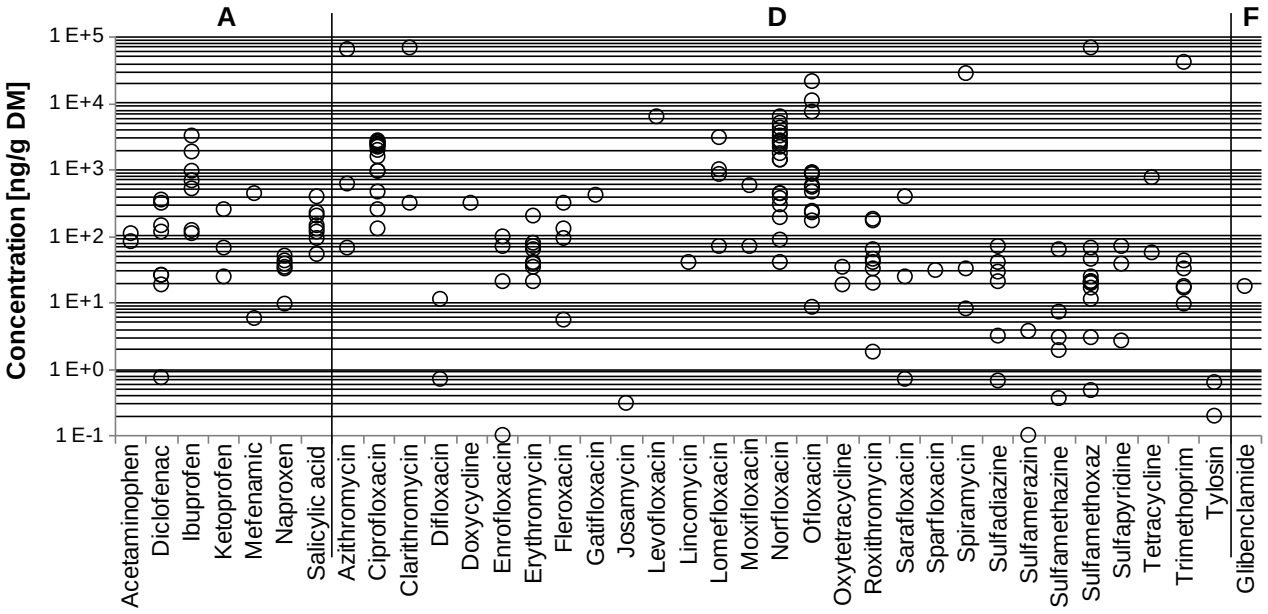

Figure 4

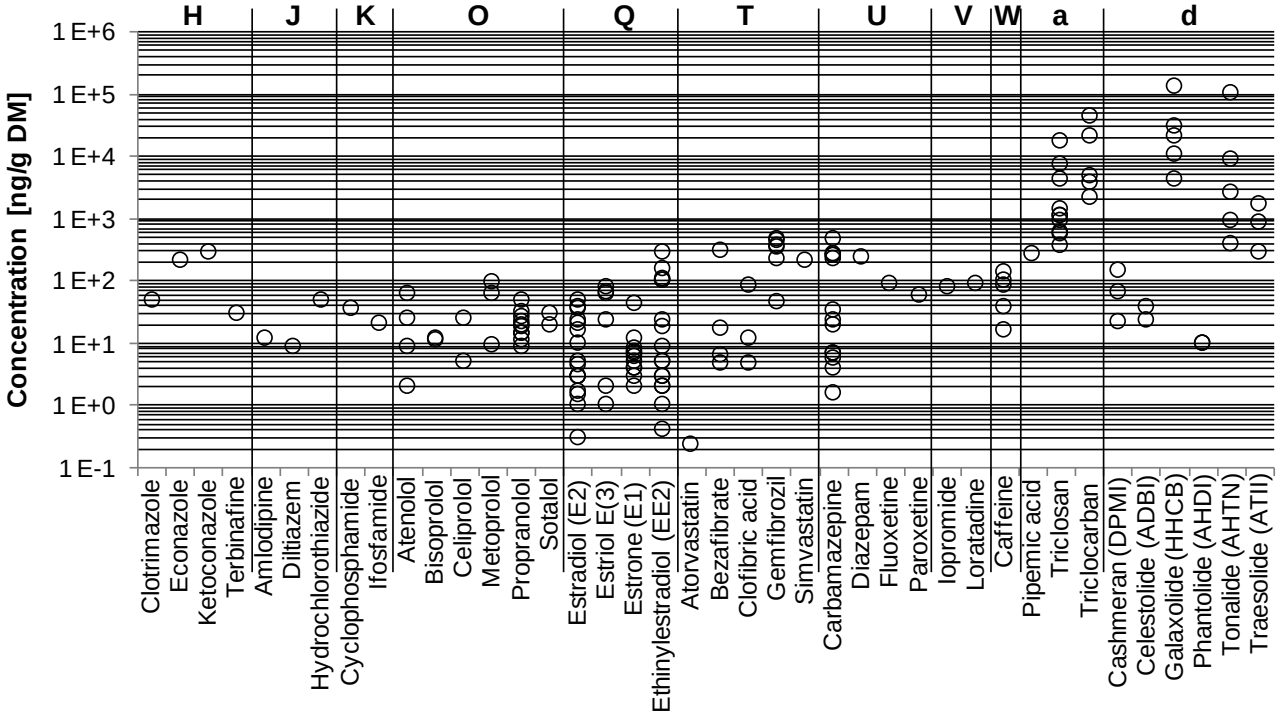

Figure 5

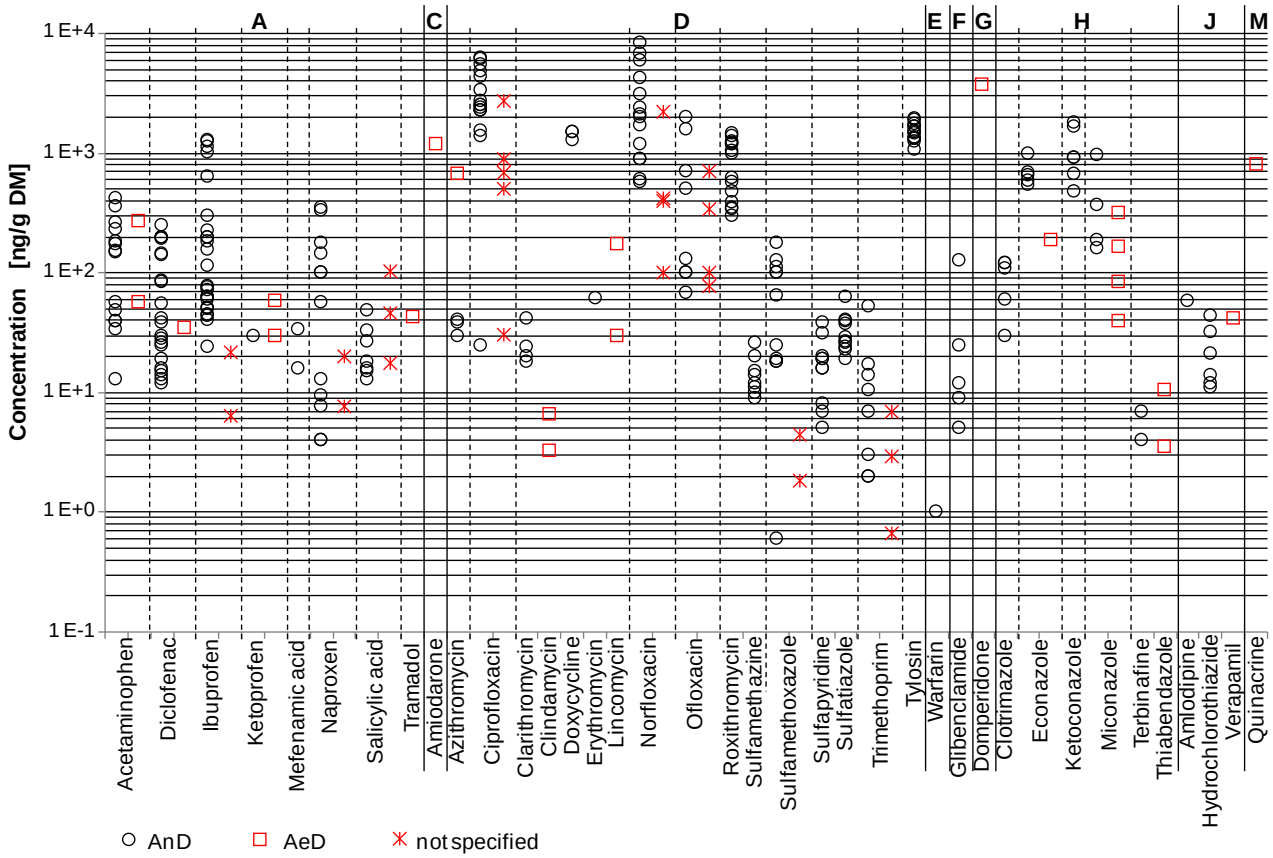

Figure 6.

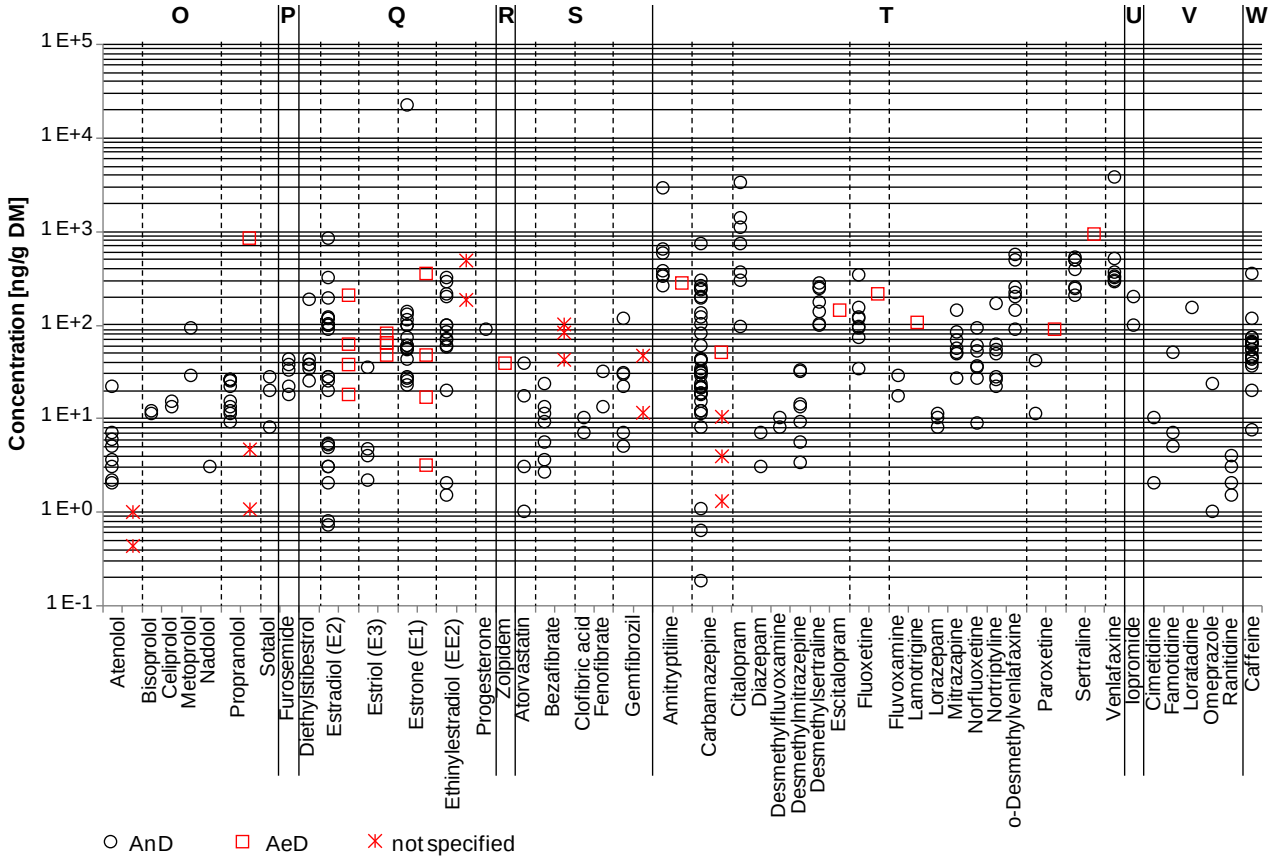

Figure 7.

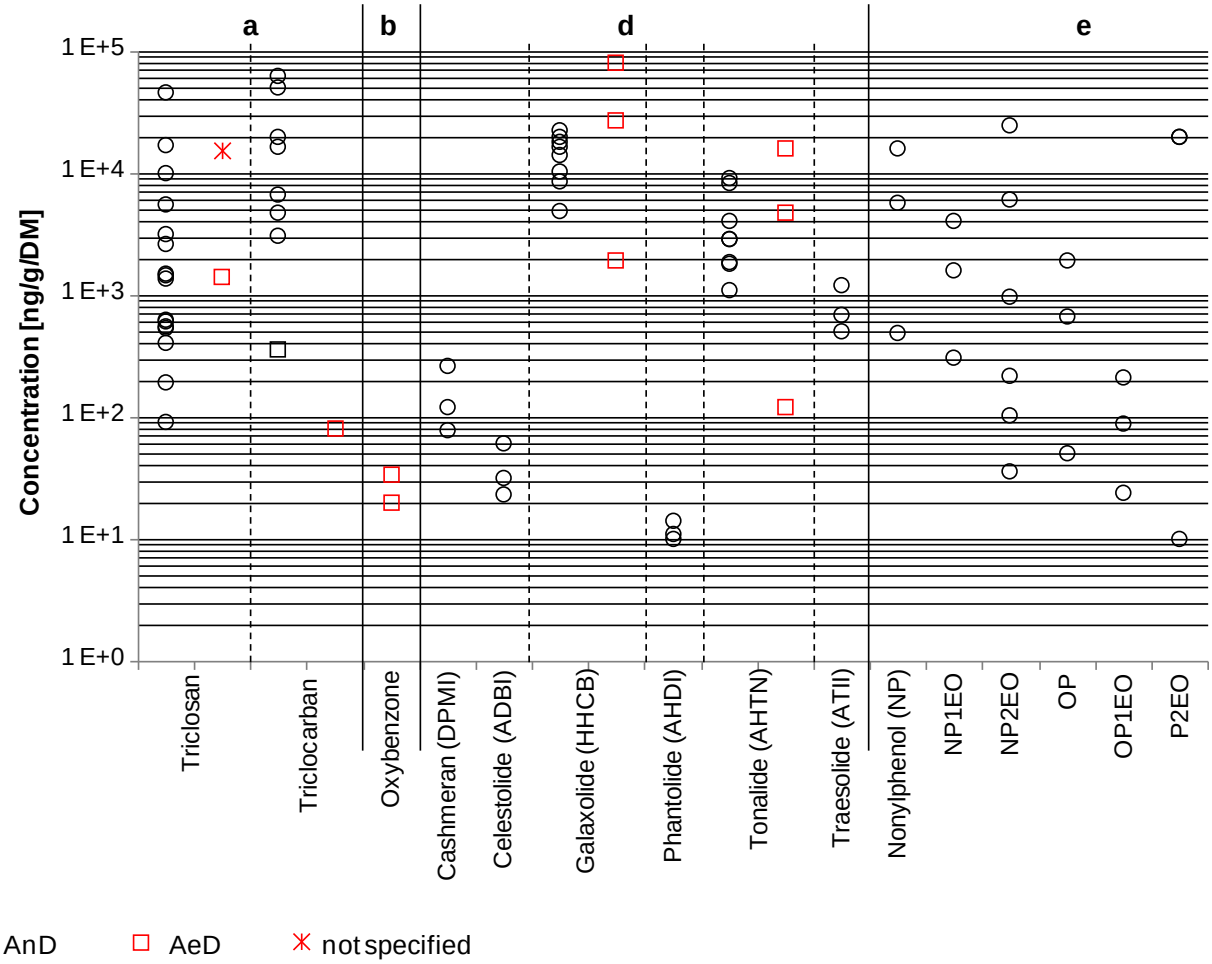
a
b
d
e
1 E+5
1 E+4
1 E+3
1 E+2
1 E+1
1 E+0
Concentration [ng/g/DM]
Triclosan
Triclocarban
Oxybenzone
Cashmeran (DPMI)
Celestolide (ADBI)
Galaxolide (HHCB)
Phantolide (AHDI)
Tonalide (AHTN)
Traesolide (ATII)
Nonylphenol (NP)
NP1EO
NP2EO
OP
OP1EO
P2EO
AnD
AeD
not specified

Figure 8

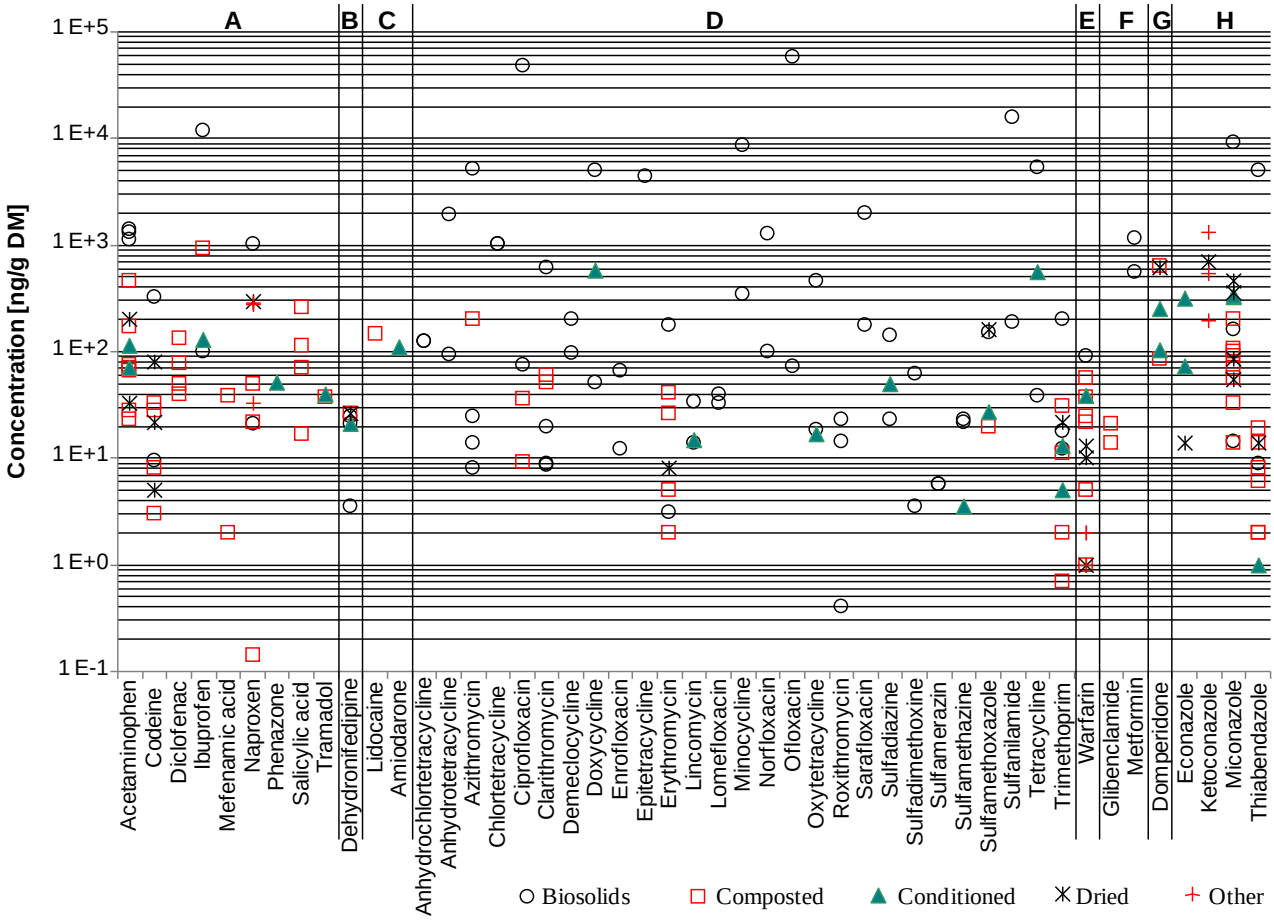
A
B
C
D
E
F
G
H
1 E+5
1 E+4
1 E+3
1 E+2
1 E+1
1 E+0
1 E-1
Concentration [ng/g DM]
Acetaminophen
Codeine
Diclofenac
Ibuprofen
Mefenamic acid
Naproxen
Phenazone
Salicylic acid
Tramadol
Dehydronifedipine
Lidocaine
Amiodarone
Anhydrochlortetracycline
Anhydrotetracycline
Azithromycin
Chlortetracycline
Ciprofloxacin
Clarithromycin
Demeclocycline
Doxycycline
Enrofloxacin
Epitetracycline
Erythromycin
Lincomycin
Lomefloxacin
Minocycline
Norfloxacin
Ofloxacin
Oxytetracycline
Roxithromycin
Sarafloxacin
Sulfadiazine
Sulfadimethoxine
Sulfamerazin
Sulfamethazine
Sulfamethoxazole
Sulfanilamide
Tetracycline
Trimethoprim
Warfarin
Glibenclamide
Metformin
Domperidone
Econazole
Ketoconazole
Miconazole
Thiabendazole
Biosolids
Composted
Conditioned
Dried
Other

Figure 9

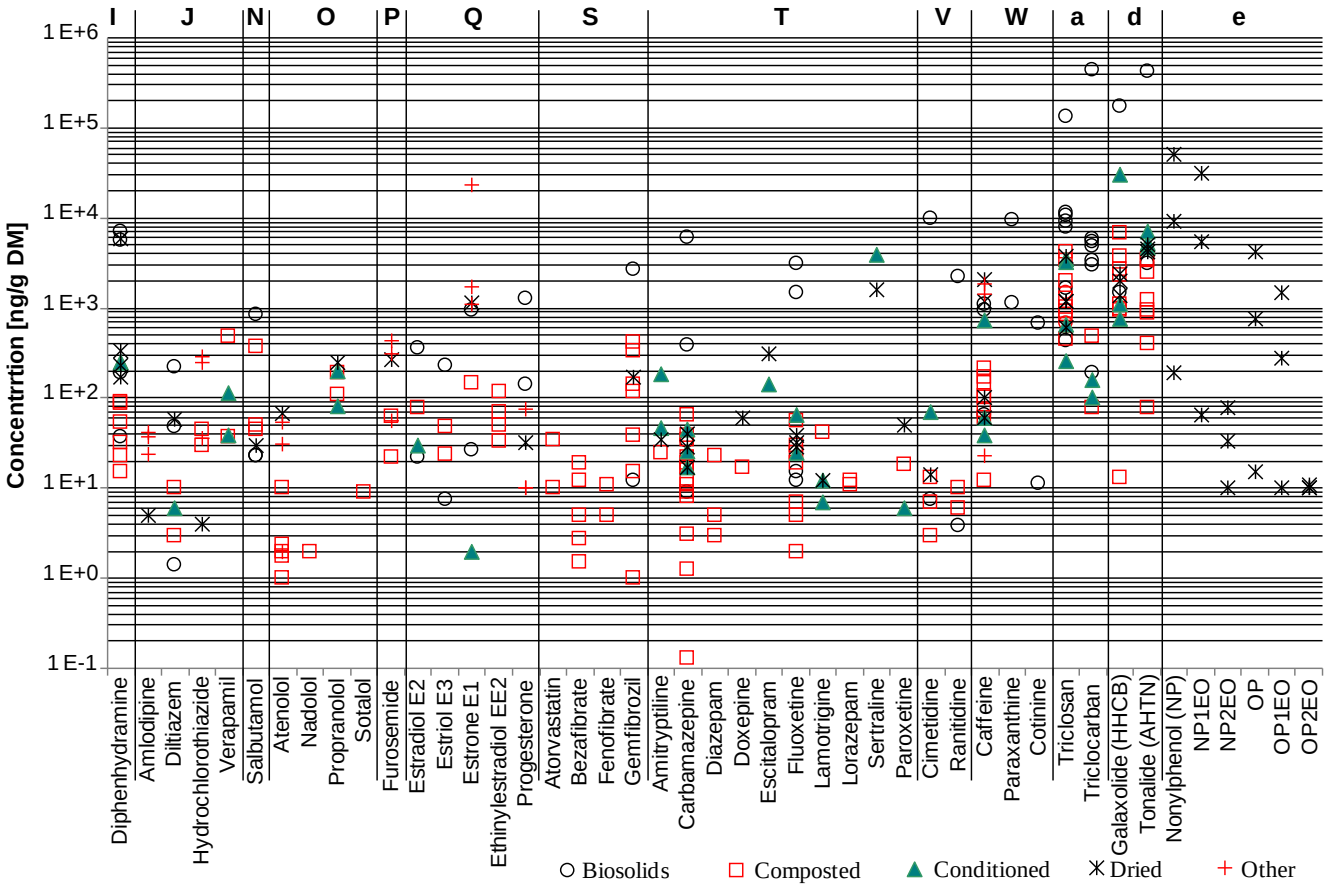
I
J
N
O
P
Q
S
T
V
W
a
d
e
1 E+6
1 E+5
1 E+4
1 E+3
1 E+2
1 E+1
1 E+0
1 E-1
Concentrtion [ng/g DM]
Diphenhydramine
Amlodipine
Diltiazem
Hydrochlorothiazide
Verapamil
Salbutamol
Atenolol
Nadolol
Propranolol
Sotalol
Furosemide
Estradiol E2
Estriol E3
Estrone E1
Ethinylestradiol EE2
Progesterone
Atorvastatin
Bezafibrate
Fenofibrate
Gemfibrozil
Amitryptiline
Carbamazepine
Diazepam
Doxepine
Escitalopram
Fluoxetine
Lamotrigine
Lorazepam
Sertraline
Paroxetine
Cimetidine
Ranitidine
Caffeine
Paraxanthine
Cotinine
Triclosan
Triclocarban
Galaxolide (HHCB)
Tonalide (AHTN)
Nonylphenol (NP)
NP1EO
NP2EO
OP
OP1EO
OP2EO
Biosolids
Composted
Conditioned
Dried
Other

Figure 10

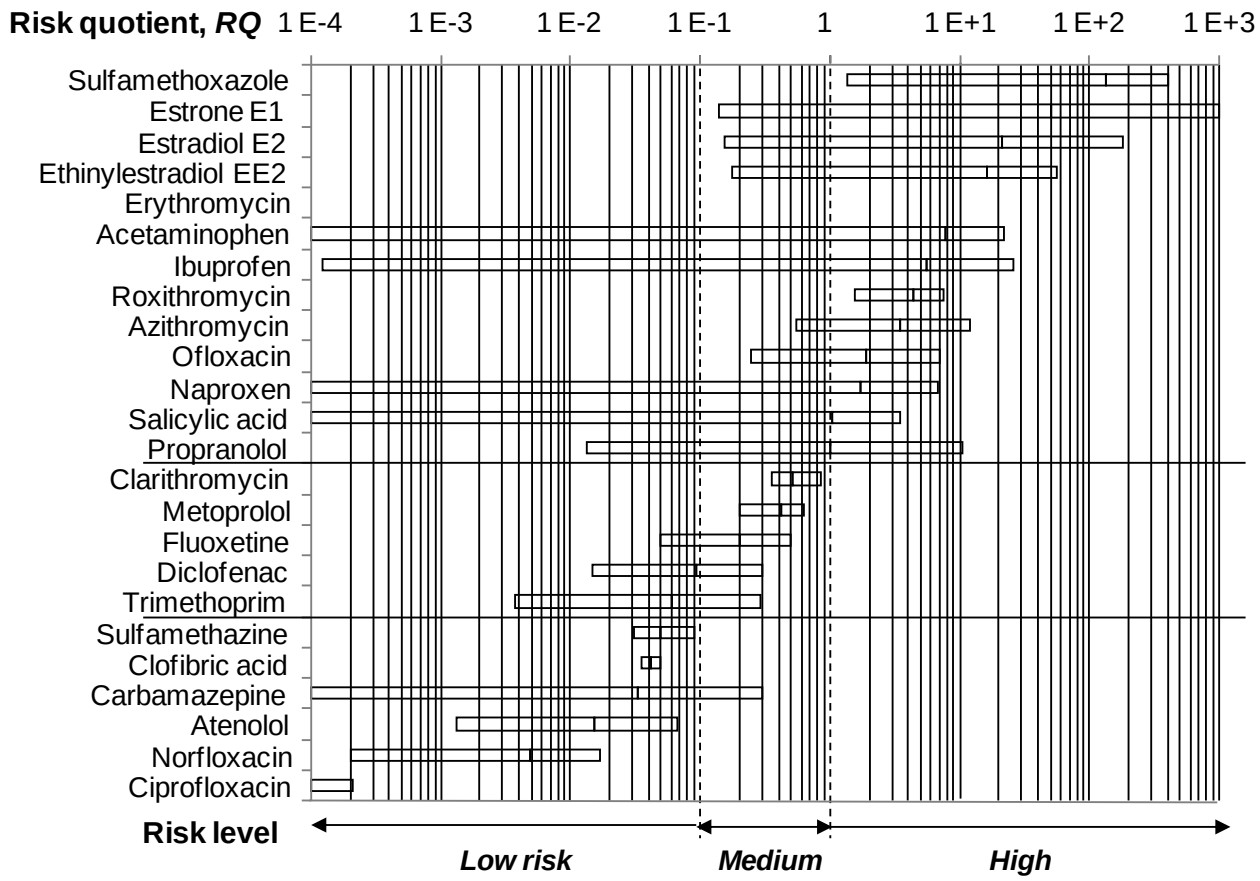
Risk quotient, RQ
1 E-4
1 E-3
1 E-2
1 E-1
1
1 E+1
1 E+2
1 E+3
Sulfamethoxazole
Estrone E1
Estradiol E2
Ethinylestradiol EE2
Erythromycin
Acetaminophen
Ibuprofen
Roxithromycin
Azithromycin
Ofloxacin
Naproxen
Salicylic acid
Propranolol
Clarithromycin
Metoprolol
Fluoxetine
Diclofenac
Trimethoprim
Sulfamethazine
Clofibric acid
Carbamazepine
Atenolol
Norfloxacin
Ciprofloxacin
Risk level
Low risk
Medium
High

Figure 11

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Figure 1 Diagram of the types of sludge included in this review with regard to the occurrence of a wide spectrum of PhCs and PCPs.

Figure 2 Occurrence of compounds belonging to classes A, D F, H and J in primary sludge.
Data from: Carballa et al., 2007b; Gao et al., 2012b; Golet et al., 2002; 2003; Jia et al., 2012; Khan and Ongerth, 2002; Lindberg et al., 2006, 2010; Martin et al., 2012a,b; Okuda et al., 2009; Radjenovic et al., 2009a; Stasinakis et al., 2013; Ternes et al., 2004.

Figure 3 Occurrence of compounds of classes K, L, N, O, Q, S, T, U, V, W, a, d and e in primary sludge.
Data from: Andersen et al., 2003; Carballa et al., 2007b; Gao et al., 2012b; Jia et al., 2012; Khan and Ongerth, 2002; Martin et al., 2012a, b; McAvoy et al., 2002; Muller et al., 2010; Okuda et al., 2009; Peterakis et al., 2012; Radjenovic et al., 2009a; Stasinakis et al., 2013; Ternes et al., 2004.

Figure 4 Occurrence of compounds belonging to classes A, D and F in secondary sludges.
Data from: Carballa et al., 2007b; Gao et al., 2012a, b; Gobel et al., 2005; Golet et al., 2003; Jia et al., 2012; Lindberg et al., 2006; Martin et al., 2012a,b, 2015; Okuda et al., 2009; Radjenovic et al., 2009a; Stasinakis et al., 2013; Ternes et al., 2004; Xu et al., 2007; Yan et al., 2014.

Figure 5 Occurrence of compounds of classes H, J, K, O, Q, T, U, V, W, a and d in secondary sludges.
Data from: Andersen et al., 2003; Braga et al., 2005; Carballa et al., 2007b; Chu and Metcalfe, 2007; Clara et al., 2011; Gao et al., 2012b; Heidler et al., 2009; Jia et al., 2012; Lindberg et al., 2010; Martin et al., 2012a, b, 2015; McAvoy et al., 2002; Muller et al., 2008, 2010; Okuda et al., 2009; Radjenovic et al., 2009a; Scheurer et al., 2010; Stasinakis et al., 2013; Ternes et al., 2004; Yan et al., 2014.

Figure 6. Occurrence of compounds belonging to classes A, C, D, E, F, G, H, J and M in biologically digested sludges.
Data from: Carballa et al., 2007c; Golet et al., 2002; Jelic et al., 2011, 2012; Khan and Ongerth, 2002; Lillenberg et al., 2009; Lindberg et al., 2005, 2006, 2010; Malmorg and Magnér., 2015; Martin et al., 2012a,b,2015; Nieto et al., 2010; Peysson et al., 2013; Radjenovic et al., 2009a; Stasinakis et al., 2013; Subedi et al., 2014.

Figure 7. Occurrence of compounds of classes O, P, Q, R, S, T, U, V and Z in biologically digested sludges.
Data from: Andersen et al., 2003; Carballa et al., 2007c; Jelic et al., 2011, 2012; Khan and Ongerth, 2002; Lajeunesse et al., 2012; Lindberg et al., 2010; Malmorg and magnér, 2015; Martin et al., 2012a,b,2015; Miao et al., 2005; Muller et al., 2010; Nieto et al., 2010; Peysson et al., 2013; Radjenovic et al., 2009a; Scheurer et al., 2010; Sim et al., 2011; Subedi et al., 2014

Figure 8 Occurrence of compounds belonging to classes a, b, d and e in biologically digested sludges.
Data from: Carballa et al., 2007c; Clara et al., 2011; Heidler et al., 2006, 2009; Mailler et al., 2014; McAvoy et al., 2002; Osemwengie et al., 2006; Peysson et al., 2013; Stasinakis et al., 2008, 2013; Stevens et al., 2003; Subedi et al., 2014; Ying and Kookana, 2007.

Figure 9 Occurrence of compounds of classes A-H in other types of treated sludge (mainly biosolids, composted, chemically conditioned, and dried).
Data from: Carballa et al., 2007b; Gao et al., 2012b; Jelic et al., 2011; Jones-Lepp et al., 2007; Kinney et al., 2006; Malmborg and Magnér, 2015; Martin et al., 2012a, 2015; Peysson et al., 2013; US EPA, 2009.

Figure 10. Occurrence of compounds of different classes of PhCs and personal care products in other types of treated sludge (mainly biosolids, composted, chemically conditioned, and dried).
Data from: Carballa et al., 2007b; Chu and Metcalfe, 2007; Gao et al., 2012b; Jelic et al., 2011; Kinney et al., 2006; Mailler et al., 2014; Malmborg and Magnér, 2015; Martin et al., 2012a, 2015; Peysson et al., 2013; Tavazzi et al., 2013; US EPA, 2009.

Figure 11 Risk quotient posed by the residue of PhCs in digested sludge

Table Sd-1

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Table Sd-2-5

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