

Occurrence of Common Pollutants and Pharmaceuticals in Hospital Effluents

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Abstract This chapter summarizes the current knowledge on the occurrence of common pollutants and pharmaceuticals in hospital effluents. These common pollutants include a myriad of biological, inorganic and organic pollutants. Daily and weekly concentration variability is presented for many of the covered pollutants. Particular attention is given to heavy metals (gadolinium and platinum) and pharmaceuticals commonly used in hospitals. For pharmaceuticals, the prevalent therapeutic categories are presented and are found to be dependent on the type of healthcare facility – general hospital, specialized hospitals, wards, and units.

Keywords Common pollutants, Heavy metals, Hospital effluent, Microbiological indicators, Pharmaceuticals

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1 Introduction

Hospital activities have an important role in the population well-being and healthcare research advancements. During these activities, unwanted generated by-products are treated following country-specific regulations and by using, in most cases, established management systems.

In the last decades, the scientific community has been focusing on the characterization of hospital effluents in terms of their biological, physical, and chemical properties to assess potential risks associated with discharges into aquatic ecosystems.

Pollutants such as coliforms (total and fecal), chemical residues (e.g., detergents), pathogens (e.g., *E. coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella* and *Vibrio*), pharmaceutical residues, radioelements (e.g., ^{131}I), and other heavy metals and toxic chemical compounds (e.g., Cd, Cu, cyanide, Fe, Gd, Hg, Ni, Pb, Pt, Zn, phenol, etc.) have been quantified in hospital effluents [1, 2]. Many of these pollutants are commonly classified based on their detected concentrations as micropollutants (10^{-6} – 10^{-3} mg L $^{-1}$) or macropollutants ($>10^{-3}$ mg L $^{-1}$) and the majority has no regulatory status.

Hospital activities generate variable quantities of effluent, being dependent on numerous factors (e.g., number of beds; facility age and maintenance practices; existent general services – kitchen, laundry, temperature control systems; number and type of wards and units; number of inpatients and outpatients; institution management policies, geographic location, hour of the day and season) [1, 3–5].

The water demand typically observed in hospitals has been estimated between 200 and 1,200 L bed $^{-1}$ day $^{-1}$ with the highest values reported from industrialized countries and the lowest from developing countries (200–400 L bed $^{-1}$ day $^{-1}$) [1, 5, 6]. In industrialized countries, estimates of total effluents produced from hospitals range between 250 and 570 m 3 day $^{-1}$ and the percentage of hospital effluent flow rate of the total discharge treated in municipal WWTP ranges between 0.2 and 65% [1, 6, 36].

The removal efficiency of common pollutants originated in hospital effluents is compound specific (being dependent on biodegradability and physicochemical properties – water solubility, adsorption, and volatilization) and is dependent on the WWTP characteristics (primary, secondary, and tertiary treatments), operational conditions (hydraulic and sludge retention time, pH, temperature), reactor type and its configuration (mainly conventional activated sludge system, membrane biological reactor, sequencing batch reactor), and environmental characteristics (irradiation, precipitation, temperature) [7–9]. Most municipal WWTPs have been designed to remove easily or moderately biodegradable carbon, nitrogen and

phosphorous compounds, and microbiological organisms but not micropollutants such as pharmaceutical residues and other chemical residues [8].

The assessment of pharmaceutical residues presence in hospital effluents has been performed either by using predicted concentrations or measured concentrations [37]. The calculation of predicted concentrations is based on parameters such as active ingredient consumption, water consumption per bed, and excretion percentage. Measured concentrations are determined by sample collection and subsequent analysis with analytical instrumentation in a laboratory setting. Predicted and measured concentrations of pharmaceuticals in hospital effluents might present different results. These differences can be partially attributed to the time scales considered. While predicted concentrations are extrapolated in most cases by using yearly pharmaceutical consumption data, measured concentrations are determined at a certain point in time and for a limited period of time. Measured concentrations may present higher variability than predicted concentrations, depending on the compound [9, 37]. Some authors consider predicted concentrations a better option to determine discharge of pharmaceuticals over longer time periods [9]. Each approach has merits and shortfalls and should be considered when developing a source characterization effort, as discussed in another chapter of this book. Ultimately the defining factors to use one or the other are dependent on cost, access to consumption information, and/or access to sewage systems and research goals. Predicted and measured concentrations are used in this chapter to illustrate the significance of these analytes in hospital effluents.

In most instances research groups not only intend to characterize effluent sources but also assess their impact in WWTP performance [3, 4, 6–8, 10]. As there are thousands of pharmaceuticals commercially available and many can be found in the environment in their parent form and as conjugates, prioritization strategies have been developed. These prioritization strategies take into consideration different criteria (e.g., consumption/sales, physico-chemical properties, (eco)toxicity, risk, degradability/persistence, resistance to treatment) [3, 12].

To date over 300 pharmaceutical residues, conjugates, and other chemical residues have been screened in hospital effluents and the latest investigations have been incorporating an increasing number of compounds for assessment due to the commercial availability of more analytical standards and the improvement of analytical instrumentations. These pollutants are of particular concern due to the mounting evidence of potential impact to aquatic organisms (e.g., genetic lesions, organ and reproductive abnormalities, behavioral changes) and the production of antibiotic-resistant bacteria and genes once released into the environment [13–18].

This chapter intends to summarize the current knowledge on the occurrence of common pollutants and pharmaceuticals in hospital effluent.

2 Hospital Effluent Characterization

Hospital effluents have been characterized in different geographic regions for conventional and non-conventional parameters by several research groups. A summary of the ranges of concentrations measured for several chemical, biological, and microbiological parameters is presented in Table 1.

2.1 Physico-Chemical Characterization

The physico-chemical characterization of hospital effluents includes the assessment of different parameters. Among these parameters, the most routinely used to assess the presence and loads of inorganic/organic matter in the effluent are electric conductivity (EC), biochemical oxygen demand (BOD), chemical oxygen demand (COD), total suspended solids (TSS), and total nitrogen. The concentration ranges for these parameters measured in hospital effluents collected in different countries over a 20-year span are summarized in Table 1. The concentration ranges measured demonstrate the relevance of hospital effluents as a source of inorganic/organic matter loads particularly when compared with municipal effluents (whose variability intervals usually observed are: BOD₅ between 100 and 400 mg L⁻¹, COD between 43 and 270 mg L⁻¹, TSS between 150 and 500 mg L⁻¹, and total N between 30 and 100 mg L⁻¹) [2]. Verlicchi et al. [5] indicate that hospital effluents typically present BOD₅, COD, and TSS 2–3 times higher than in municipal effluents corresponding to specific contributions of 160 g BOD₅ patient⁻¹ day⁻¹, 260–300 g COD patient⁻¹ day⁻¹, and 120–150 g TSS patient⁻¹ day⁻¹.

2.2 Bacteriological Characterization

The bacteriological characterization of hospital effluents typically includes the assessment of indicators of fecal contamination and pathogens.

Fecal coliforms are typically determined by analyzing *E. coli* since they represent 80 to 90% of detected thermo-tolerant coliforms [2]. *E. coli* are a facultative anaerobic bacteria species predominant in the gut and feces. The presence of these bacteria in wastewater is regarded as an indication of fecal contamination and therefore the presence of pathogenic fecal micro-organisms. Other less commonly analyzed parameters in hospital effluent include: a) bacteria such as spores of sulfite-reducing anaerobes, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella*; and b) pathogenic virus such as enterovirus, norovirus, adenovirus, rotavirus, and hepatitis A virus [1, 2].

Fecal contamination (total and fecal coliforms) load is generally more relevant in municipal effluents than hospital effluents. This is resultant of the higher dilution

Table 1 Hospital effluent characterization parameters

Parameter (unit of measure)	Concentration(s)
Electrical conductivity ($\mu\text{S cm}^{-1}$)	300–2,700
pH	6–9
Redox potential (mV)	850–950
Fat and oil (mg L^{-1})	50–210
Chlorides (mg L^{-1})	80–400
Total N (mg N L^{-1})	60–230
NH_4 ($\text{mg NH}_4 \text{L}^{-1}$)	10–68
Nitrite ($\text{mg NO}_2 \text{L}^{-1}$)	0.1–0.6
Nitrate ($\text{mg NO}_3 \text{L}^{-1}$)	1–2
Phosphate ($\text{mg P-PO}_4 \text{L}^{-1}$)	6–19
Total suspended solids (mg L^{-1})	116–3,260
COD (mg L^{-1})	39–7,764
Dissolved COD (mg L^{-1})	380–700
DOC (mg L^{-1})	120–130
TOC (mg L^{-1})	31–180
BOD_5 (mg L^{-1})	16–2,575
BOD_5/COD	0.3–0.4
AOX ($\mu\text{g L}^{-1}$)	550–10,000
<i>E. coli</i> (MPN 100 mL^{-1})	10^3 – 10^6
Enterococci (MPN 100 mL^{-1})	10^3 – 10^6
Fecal coliform (MPN 100 mL^{-1})	10^3 – 10^4
Total coliform (MPN 100 mL^{-1})	10^4 – 10^7
EC_{50} (<i>Daphnia</i>) (TU)	9.8–117
Total surfactants (mg L^{-1})	4–8
Total disinfectants (mg L^{-1})	2–200
Norovirus (genomic copies L^{-1})	2.4×10^6
Adenovirus (genomic copies L^{-1})	2.8×10^6
Rotavirus	1.9×10^6
Hepatitis A virus	10^4
Gd ($\mu\text{g L}^{-1}$)	<1–300
Hg ($\mu\text{g L}^{-1}$)	0.3–8
Pt ($\mu\text{g L}^{-1}$)	0.01–289
Hg ($\mu\text{g L}^{-1}$)	0.04–5
Ag ($\mu\text{g L}^{-1}$)	150 – 437×10^3
As ($\mu\text{g L}^{-1}$)	0.8–11
Cu ($\mu\text{g L}^{-1}$)	50–230
Ni ($\mu\text{g L}^{-1}$)	7–71
Pb ($\mu\text{g L}^{-1}$)	3–19
Zn ($\mu\text{g L}^{-1}$)	70–670

Adapted from [1, 2, 5, 20, 22–26, 33]

of the hospital effluent due to significant water consumption per bed [1]. The opposite has been reported for enterovirus concentration being 2–3 times higher in hospital effluent than in municipal effluent [1].

2.3 *Heavy Metals and Other Toxic Chemical Compounds Characterization*

The main heavy metals found in hospital effluents are gadolinium (Gd), mercury (Hg), and platinum (Pt) [5, 20]. Other heavy metals such as Cd, Cu, Fe, Ni, Pb, and Zn typically present similar concentrations as the reported in municipal effluent [20].

Gadolinium containing substances (e.g., gadodiamide, gadopentetic acid, Gd-diethylenetriamine pentaacetate) are applied (orally or intravenously) during magnetic resonance imaging (MRI) because of its high magnetic moment imaging of the digestive tract, brain, and spine.

The contrast media are excreted non-metabolized into hospital sewage within a few hours after application. With a residence time of 70 min and with an excretion of 85–98% within 24 h, it is estimated that approximately 90% of Gd is excreted during the patient hospital stay [5, 21].

Kümmerer and Helmers measured Gd in effluent originated in Freiburg University Hospital (Germany) with three MRI systems serving 15–25 patients per day. The Gd concentrations measured ranged between <1 and $55 \mu\text{g L}^{-1}$ and presented low concentrations overnight with a noticeable increase in the morning (around 10 a.m.) and also exhibited two peaks later in the day (6 p.m. and 10 p.m.). Daouk et al. [22] assessed Gd temporal variability during 1 week in the Geneva University Hospital main building (741 beds – Switzerland) and reported a noticeable increase at the end of the week (Friday). They measured Gd concentrations within the range <1 – $300 \mu\text{g L}^{-1}$.

Mercury is usually found in diagnostic agents, active ingredients of disinfectants and diuretic agents. Hg concentrations in hospital effluent range between 0.3 and $7.5 \mu\text{g L}^{-1}$ [23, 24]. Since the early 2000s, there has been an effort in industrialized countries to reduce Hg contamination by using diagnostic agents without this heavy metal and by implementing better waste management practices.

Platinum containing substances (e.g., carboplatin and cisplatin) have been used as antineoplastics for oncological treatment since the mid-1970s. After being administered, these antineoplastics are excreted at different rates (patient dependent). Carboplatin is excreted at a rate of 50–75% within the first 24 h after being administered. Cisplatin is excreted at a rate of 31–85% within the first 51 days after being administered. The biological half-lives for the two long-term phases of renal platinum excretion are 160 and 720 days. It is estimated that 70% of the administered Pt is excreted into the hospital effluents [25].

Kümmerer et al. [25] measured Pt in five European hospitals of different size (from 174 to 2,514 beds). They found concentrations varying between <0.01 and $3.5 \mu\text{g L}^{-1}$. They also analyzed Pt concentration variation in the Freiburg University Hospital (Germany) during a 24-h period and found two concentration peaks, at 4 a.m. and 10 a.m. Daouk et al. [22] assessed Pt temporal variability during 1 week in the Geneva University Hospital main building (741 beds – Switzerland) and reported a noticeable increase at the end of the week (on Thursdays). They measured Pt concentrations within the range <0.01 – $2 \mu\text{g L}^{-1}$. Lenz et al. [26] measured Pt in an oncological in-patient treatment ward in Vienna (Austria) and reported concentrations ranging between 2.0 and $289 \mu\text{g L}^{-1}$. They conducted Pt speciation analysis and identified carboplatin as the main contributor to Pt loads.

2.4 Pharmaceuticals Residues Characterization

The consumption of pharmaceuticals is variable among healthcare facilities [9, 27]. As an example, in Germany the total pharmaceutical consumption has been estimated for a psychiatric hospital, a nursing home, and a general hospital. The total pharmaceutical consumption ranged between 32 (psychiatric hospital) and $1,263 \text{ kg year}^{-1}$ (general hospital) with annual average consumption of individual pharmaceuticals ranging between 0.1 and $1,000 \text{ g bed}^{-1}$ [9]. In general, the main therapeutic categories consumed in hospitals are contrast media, laxatives, analgesics, anti-inflammatories, antibiotics, and cytostatic drugs [6, 22]. Once consumed, the pharmaceuticals are excreted mainly via urine (55–80%) and at a lower rate via feces (4–30%), as non-metabolized substances, metabolites, or conjugated with inactivating substances [1, 38].

The concentration of pharmaceutical residues in hospital effluents are the result of the combination of three main factors: administered quantity, excreted percentage, and chemical characteristics (mainly stability and biodegradability) of the specific compounds [5]. Hospital effluents have been screened for pharmaceutical residues in different geographic regions (e.g., Asia – [28]; Europe – [4, 11, 29]; North-America – [6, 39, 40]).

The total load of pharmaceuticals in the effluents of the hospitals in these geographic regions ranged between $78 \mu\text{g L}^{-1}$ [28] and 5 mg L^{-1} [29] with 12 therapeutic categories being regularly measured (Table 2). These therapeutic categories comprise $\geq 94\%$ of the total concentrations measured.

The therapeutic categories percentage distribution is very dependent on the analytes targeted for analysis. Within the therapeutic categories regularly measured in hospital effluents, contrast media agents, cytostatics, analgesics, and anti-bacterials and anti-infectives are the most relevant. When prevailing, these categories can individually reach $>40\%$ of the total concentration measured [4, 11, 28, 29]. Other relevant therapeutic categories include anti-epileptic, anti-inflammatory, psychoanaleptic, and β -blocker drugs reaching a maximum of 20% of the total concentration measured [4, 6, 28].

Table 2 Therapeutic classes and range of concentration measured in healthcare facilities effluents

Therapeutic class	Investigated compounds	Concentration(s) $\mu\text{g L}^{-1}$
Analgesics/anti-inflammatories	Codeine	0.02–50
	Diclofenac	0.24–15
	Ibuprofen	0.07–43
	Naproxen	10–11
	Paracetamol	5–1,368
	Salicylic acid	23–70
Antibiotics	Ciprofloxacin	0.03–125
	Clarithromycin	0.20–3
	Copropofloxacin	0.85–2
	Doxycycline	0.1–7
	Erythromycin	27–83
	Lincomycin	0.3–2
	Metronidazole	0.1–90
	Norfloxacin	0.03–44
	Ofloxacin	0.35–35
	Oxytetracycline	0.01–4
	Penicillin G	0.85–5
	Sulfamethoxazole	0.04–83
	Tetracycline	0.01–4
	Trimethoprim	0.01–15
Psychiatric drugs	Carbamazepine	0.54–2
Anti-hypertensives	Diltiazem	0.71–2
Beta-blockers	Metoprolol	0.42–25
Hormones	17 β -estradiol, E2	0.03–0.04
	Estriol, E3	0.35–0.50
	Estrone, E1	0.02–0.03
	Ethinylestradiol, EE2	0.02–0.02
Contrast media	Iopromide	0.2–2,500
	Iomeprol	0.01–1,392
Anti-diabetics	Glibenclamide	0.05–0.11
Anti-viral	Aciclovir	0.02–0.60
	Famciclovir	N.D.-0.11
	Penciclovir	N.D.-0.01
	Valaciclovir	N.D.-0.01
Anti-cancerdrugs	4-Hydroxy tamoxifen	N.D.-0.01
	5-fluorouracil	5–124
	Azathioprine	blq-0.09
	Bicalutamide	N.D.-0.08
	Capecitabine	N.D.-0.05
	Cyclophosphamide	0.008–2
	Docetaxel	blq-0.08
Doxifluridine	N.D.-0.08	
	Etoposide	blq-0.7

(continued)

Table 2 (continued)

Therapeutic class	Investigated compounds	Concentration(s) $\mu\text{g L}^{-1}$
	Ifosfamide	0.01–2
	Methotrexate	blq-0.02
	Paclitaxel	blq-0.10
	Tamoxifen	0.004–0.17
	Tegafur	N.D.-0.09

Adapted from [22, 33, 34]

Note: country-specific prescription habits influence the compounds present in the effluent

N.D. not detected, blq below limit of quantification

Most pharmaceuticals screened in hospital effluents present maximum concentrations $<10 \mu\text{g L}^{-1}$. Higher concentrations are typically measured for specific compounds some of which are presented in Table 2 (e.g., acetaminophen, caffeine, ciprofloxacin, gabapentin, ibuprofen, iomeprol, iopamidol, iopromide, metformin, theobromine) reaching concentrations within the low mg L^{-1} range for several contrast media agents [4, 6, 11, 28, 29].

Daouk et al. [22] investigated pharmaceuticals belonging to different categories in effluents originated in the Geneva University Hospital main building (741 beds – Switzerland) and calculated mean daily loads for 15 pharmaceuticals ranging mainly between 0.1 and 14 g day^{-1} , except for acetaminophen (143 g day^{-1}), piperacillin (0.08 g day^{-1}), and diclofenac (0.04 g day^{-1}). The weekly variability of these pharmaceuticals was assessed and the daily load remained with the 50–150% of the average for compounds which are widely consumed on a regular basis such as acetaminophen, morphine, and ibuprofen.

Pharmaceuticals consumed at lower extent such as the analgesics diclofenac, mefenamic acid or the anti-epileptics gabapentin and carbamazepine presented on the contrary a higher variability, up to 400% of the average value with the highest concentrations being measured throughout the week. For the investigated antibiotics, a higher variability was observed for metronidazole than for sulfamethoxazole and ciprofloxacin. Metronidazole presented highest concentrations earlier in the week.

Specialized hospitals and wards (e.g., oncologic in-patient care, intensive care, geriatric care, psychiatric care) use a different range of drugs than general hospitals. The effluents originated by an oncological in-patient care ward (18 beds) in Vienna University Hospital (Austria) have been characterized for antimetabolites and anthracyclines [26, 30]. The antimetabolite 5-fluorouracil is administered in the treatment of breast, skin, bladder, and lung cancer in dosages ranging from 200 to $1,000 \text{ mg m}^{-2}$ body surface [30]. Approximately 2–35% of the administered drug is excreted un-metabolized via urine within 24 h [30]. The anthracyclines doxorubicin, epirubicin, and daunorubicin are frequently used in the treatment of hematological and solid neoplasms, including acute leukemia, high grade lymphoma, breast cancer, and bladder cancer in dosages ranging from 15 to 120 mg m^{-2}

body surface. Approximately 3.5–5.7% of administered doxorubicin, 11% of epirubicin, and 13–15% of daunorubicin are excreted un-metabolized via urine within 24 h. [30]. Of the administered cytostatics, 5-fluorouracil and doxorubicin have been measured in the effluent at $<8.6\text{--}124\ \mu\text{g L}^{-1}$ and $<0.26\text{--}1.35\ \mu\text{g L}^{-1}$, respectively [30]. In total, 0.5–4.5% of the administered amount of 5-fluorouracil and 0.1–0.2% of the administered amount of doxorubicin were found in the effluent of the oncological in-patient treatment ward [26].

Lopes de Souza et al. [31] investigated intravenous antibiotics consumed in an intensive care unit (16 beds) in a Brazilian hospital, calculated the predicted environmental concentration (PEC), and performed an environmental risk assessment. The consumption of these antibiotics in the intensive care unit was identified as being relevant since this unit with only 10% of the total number of beds available in the hospital used 25% of the total antibiotic consumption. Several intravenous antibiotic classes were used and the highest consumption was identified for the antibiotics ceftriaxone, meropenem, ceftazidime, cefazolin, clindamycin, piperacillin, cefepime, ampicillin, vancomycin, trimethoprim, sulbactam, and ceftazidime [31]. The highest consumption was identified for ceftriaxone with $3.13\ \text{g year}^{-1}$. These authors calculated PECs factoring in dilution of effluent by surface water flow (10 times). If the dilution factor is not considered, the predicted concentrations released by the intensive care unit range between $1.15\ \mu\text{g L}^{-1}$ for quinolones and $701\ \mu\text{g L}^{-1}$ for cephalosporins. Within cephalosporins, the highest predicted concentrations were calculated for ceftazidime ($280\ \mu\text{g L}^{-1}$) and ceftriaxone ($320\ \mu\text{g L}^{-1}$). Other classes with significant predicted concentrations include carbapenems and penicillins with $229\ \mu\text{g L}^{-1}$ and $262\ \mu\text{g L}^{-1}$, respectively. Within these two classes, the highest predicted concentrations were calculated for meropenem ($220\ \mu\text{g L}^{-1}$) and ampicillin ($222\ \mu\text{g L}^{-1}$). Lopez de Souza and colleagues [31] indicate that most of the intravenous antibiotics investigated present a high risk to the environment. Some of the risks associated with the release of antibiotics is related with the high potential to generate antibiotic-resistant bacteria [1, 13–19].

Herrmann et al. [9] investigated the pharmaceutical contributions by a psychiatric hospital (146 beds) and a nursing home (286 beds) in Germany. In these facilities, most of the pharmaceuticals consumed act on the nervous system and include anti-epileptics, psycholeptics, and psychoanaleptics. Anti-epileptics are commonly used to treat epilepsy, but some substances in this therapeutic category, such as gabapentin, pregabalin and valproic acid, are also used to treat bipolar disorders or neuropathic pain, hence their relevance in the psychiatric hospital and the nursing home. Valproic acid was identified as the pharmaceutical with the highest consumption in the psychiatric hospital with $33.1 \pm 4.8\ \text{g bed}^{-1}\ \text{year}^{-1}$. In the psychiatric hospital, psycholeptics (antipsychotics, tranquilizers, and hypnotics) were consumed more frequently than psychoanaleptics (antidepressants) because individuals suffering from depression are, in general, treated more often as outpatients [9]. The antipsychotic quetiapine was found to be consumed in high quantities in either facility (e.g., psychiatric hospital – $25.8 \pm 3.6\ \text{g bed}^{-1}\ \text{year}^{-1}$). Other relevant pharmaceuticals included two analgesics/anti-inflammatories (ibuprofen

– $22.6 \pm 1.1 \text{ g bed}^{-1} \text{ year}^{-1}$ and metamizole – $24.7 \pm 2.4 \text{ g bed}^{-1} \text{ year}^{-1}$) and the antidiabetic metformin – $12.3 \pm 4.5 \text{ g bed}^{-1} \text{ year}^{-1}$ [9].

Santos et al. [11] screened 78 pharmaceuticals and other chemical residues in Portuguese hospitals and estimated total mass loads ranging between 1.5 g day^{-1} (Maternity hospital with 96 beds) and 306 g day^{-1} (University hospital with 1,456 beds) and Oliveira et al. [6] screened 185 pharmaceuticals and other chemical residues in the US hospitals and estimated total mass loads ranging between 180 and 310 g day^{-1} for general hospitals (250 to 600 beds).

Besides the number and size of the healthcare facilities, the impact of healthcare facilities pharmaceuticals and chemical residues loads into WWTP is related with the size of the sewer network. Sewer networks treating effluent volumes originating from different sources result in increased dilution of the loads originating from healthcare facilities. Oliveira and co-authors [6] investigated sewer networks with variable number of hospitals (1–2) and inflows ($1,300\text{--}103,000 \text{ m}^3 \text{ day}^{-1}$) and estimated that the pharmaceuticals and other chemical residues loads originating from 6 general hospitals at the WWTPs influents ranged between 1 and 59%. Additionally, estimates of individual pharmaceuticals contributions from healthcare facilities at WWTP influent indicate that higher inflows ($\geq 10,000 \text{ m}^3 \text{ day}^{-1}$) result in a lower individual pharmaceutical contribution from healthcare facilities ($<15\%$) [6, 32] and that lower inflows ($<10,000 \text{ m}^3 \text{ day}^{-1}$) individual pharmaceutical can reach $>80\%$ [6].

High concentrations of some anti-cancer drugs were found in HWWs than the influent of a WWTP in Girona, Spain [33], highlighting the importance of applying decentralized solutions to treat hospital effluent *on-site* before being discharged into the urban sewage collection system to reduce the environmental risks posed by pharmaceuticals [33, 35].

3 Hospital Effluent Treatment Guidelines and Regulatory Efforts

Guidelines for the management of hospital effluents have been set forth by international organizations (e.g., World Health Organization, WHO [41]). These guidelines have been summarized by Carraro et al. [1] and also discussed in a chapter in this book. In general, the WHO guidelines recommend pre-treatment of effluents originated from specific departments (e.g., medical laboratories, dental) and indicate the minimum requirements for the discharge of hospital effluent into municipal sewer systems. These requirements include the existence of a WWTP with tertiary treatment with the treated effluent bacterial removal rate $\geq 95\%$ and anaerobically produced digested sludge with no more than one helminth egg per liter. In addition, the waste management system of the healthcare facilities should ensure that only low quantities of toxic chemicals, pharmaceuticals, radionuclides, cytostatic drugs, and antibiotics are present in the discharged sewage.

The WHO guidelines also recommend monitoring the sewer system and the effluent quality. Effluent quality is recommended to be assessed by monitoring common parameters such as temperature, pH, BOD₅, COD, nitrate, total phosphorus, total suspended solids, presence and concentration of *E. coli*. In general, many countries have the infrastructures recommended and their legislation requires the assessment of these same effluent quality parameters.

For effluents originated by specific sources such as healthcare facilities the legislation might require the measurement of additional parameters such as adsorbable organic halogens (AOX), total and free chlorine, detergents, disinfectants, surfactants, oil and grease, sulfates, cyanides, organophosphates, total nitrogen, heavy metals, microbiological parameters (total coliform), and toxicity.

The research contributions identifying micropollutants (pharmaceuticals and other chemical residues) sources, their predicted and measured concentrations in effluents and the environment, and risk assessment have had an important contribution to have regulatory institutions considering the need to investigate some of these organic compounds.

In addition, some of these substances (erythromycin, clarithromycin, azithromycin, 17- α -ethinylestradiol (EE2), 17- β -estradiol (E2), estrone (E1), diclofenac) have been included in the European watch list and in the US contaminant candidate list (erythromycin, 17- α -ethinylestradiol, 17 β -estradiol, 17- α -estradiol, equilenin, equilin, estriol, estrone, mestranol, and norethindrone) that concerns new substances for priority action. Priority action involves additional research to determine the risk associated with the release into the environment and the potential need to set regulatory limits on these pharmaceuticals.

4 Conclusions

Hospital effluents have been characterized in different geographic regions. These involved monitoring physico-chemical parameters, biological pollutants, inorganic pollutants, and organic pollutants.

Healthcare facilities effluents physico-chemical parameters demonstrate the relevance of these facilities as a source of organic/inorganic loads when compared with municipal effluents. Some authors reported that healthcare facilities effluents typically present physico-chemical parameters such as BOD₅, COD, and TSS 2–3 times higher than municipal effluents.

Bacteriological characterization in hospital effluents is frequently performed by determining fecal contamination (e.g., *E. coli*) and less commonly by analyzing other bacteria and viruses (e.g., enterovirus). As healthcare facilities consume considerable amounts of water (200–1,200 L bed⁻¹ day⁻¹), fecal contamination is normally less relevant than in municipal effluents due to higher dilution. The opposite has been reported for enterovirus with the concentration being 2–3 times higher in hospital effluents.

Heavy metal characterization in hospital effluents demonstrates the relevance of gadolinium (Gd) and platinum (Pt) with concentrations reaching $\leq 300 \mu\text{g L}^{-1}$.

Pharmaceutical residues characterization demonstrates their presence in effluents originated in general hospitals operating in different geographic regions and the relevance of 12 therapeutic categories. Within these therapeutic categories the highest total percentage has been measured for analgesics, anti-bacterials, and anti-infectives, contrast media and cytostatics ($>40\%$). Other relevant therapeutic categories include anti-epileptics, anti-inflammatories, psychoanaleptics, and β -blockers ($\leq 20\%$). With some exceptions, most pharmaceuticals quantified in healthcare facilities effluents present maximum concentrations $< 10 \mu\text{g L}^{-1}$.

Specialized hospitals and wards effluent characterization/consumption patterns demonstrate the relevance of a different range of pharmaceuticals between different hospitals.

Total mass loads for pharmaceutical and other chemical residues have been estimated for hospitals with varying sizes and types of treatment in different geographic regions. The total mass loads reported ranged between 1.5 and 310 g day^{-1} . Besides the healthcare facilities characteristics their potential presence at the WWTP influent is also related with the size of the sewer network and the presence of other discharging sources. The investigation of sewer networks with variable number of hospitals and inflows estimated that pharmaceuticals and other chemical residues loads originating from general hospitals at the WWTP influents can reach up to 65%. Additionally, estimates of pharmaceutical individual contributions originating from healthcare facilities at WWTP influent indicate that at lower flows they can reach $>80\%$.

Healthcare facilities are a source of an array of pollutants which can reach the WWTP influent, resist treatment, and enter the environment with potential effects on aquatic organisms and water quality. To minimize these effects, it is recommended to implement effluent treatment prior to their release, when the sewer system is dimensioned to treat $< 10,000 \text{ m}^3 \text{ day}^{-1}$ inflow, has multiple healthcare facilities connected to the system and the WWTP is performing secondary treatment. Additionally, further research is required for the: (a) characterization of effluents originated from specific wards and specialized hospitals; (b) assessment of concentration variability during larger periods of time (monthly, yearly); and (c) risk assessment of many of the pollutants already measured in the effluents for potential inclusion in priority/candidate lists and subsequent inclusion in specific source regulations.

References

1. Carraro E, Si B, Bertino C, Lorenzi E, Sa B, Gilli G (2016) Hospital effluents management: chemical, physical, microbiological risks and legislation in different countries. *J Environ Manage* 168:185–199
2. El-Ogri F, Ouazzani N, Boraâm F, Mandi L (2016) A survey of wastewaters generated by a hospital in Marrakech city and their characterization. *Desalin Water Treat* 57 (36):17061–17074

3. Al AM, Verlicchi P, Voulvoulis N (2014) A framework for the assessment of the environmental risk posed by pharmaceuticals originating from hospital effluents. *Sci Total Environ* 493:54–64
4. Verlicchi P, Al AM, Galletti A, Petrović M, Barceló D (2012) Hospital effluent: investigation of the concentrations and distribution of pharmaceuticals and environment risk assessment. *Sci Total Environ* 430:109–118
5. Verlicchi P, Galletti A, Petrović M, Barceló D (2010) Hospital effluents as a source of emerging pollutants: an overview of micropollutants and sustainable treatment options. *J Hydrol* 389:416–428
6. Oliveira TS, Murphy M, Mendola N, Wong V, Carlson D, Waring L (2015) Characterization of pharmaceuticals and personal care products in hospital effluent and waste water influent/effluent by direct-injection LC-MS-MS. *Sci Total Environ* 518–519:459–478
7. Verlicchi P, Al AM, Zambello E (2015) What have we learned from worldwide experiences on the management and treatment of hospital effluent? – an overview and a discussion on perspectives. *Sci Total Environ* 514:467–491
8. Verlicchi P, Al AM, Zambello E (2012) Occurrence of pharmaceutical compounds in urban wastewater: removal, mass load and environmental risk after a secondary treatment – a review. *Sci Total Environ* 429:123–155
9. Hermann M, Olsson O, Fiehn R, Herrel R, Herrel M, Kümmerer K (2015) The significance of different health institutions and their respective contributions of active pharmaceutical ingredients to wastewater. *Environ Int* 85:61–76
10. Luo Y, Guo W, Ngo HH, Nghiem LD, Hai FI, Zhang J, Liang S, Wang XC (2014) A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. *Sci Total Environ* 473–474:619–641
11. Santos L, Gros M, Rodriguez-Mozaz S, Delerue-Matos C, Pena A, Barceló D, Montenegro C (2013) Contribution of hospital effluents to the load of pharmaceuticals in urban wastewaters: identification of ecologically relevant pharmaceuticals. *Sci Total Environ* 461–462:302–316
12. De Voogt P, Janex-Habibi M-L, Sacher F, Puijker L, Mons M (2009) Development of a common priority list of pharmaceuticals relevant for the water cycle. *Water Sci Technol* 59:1
13. Cizmas L, Sharma VK, Gray CM, McDonald TJ (2015) Pharmaceuticals and personal care products in waters: occurrence, toxicity, and risk. *Environ Chem Lett*. doi:[10.1007/s10311-015-0524-4](https://doi.org/10.1007/s10311-015-0524-4)
14. Brodin T, Fick J, Jonsson M, Klaminder J (2013) Dilute concentration of a psychiatric drug alter behavior of fish from natural populations. *Science* 339:814–815. doi:[10.1126/science.1226850](https://doi.org/10.1126/science.1226850)
15. Galus M, Jeyaranjan J, Smith E, Li H, Metcalfe C, Wilson JY (2013) Chronic effects of exposure to a pharmaceutical mixture and municipal wastewater in zebrafish. *Aquat Toxicol* 132–133:212–222
16. Galus M, Kirischian N, Higgins S, Purdy J, Chow J, Ranganarjan S, Li H, Metcalfe C, Wilson JY (2013) Chronic, low concentration exposure to pharmaceuticals impacts multiple organ systems in zebrafish. *Aquat Toxicol* 132–133:200–211
17. Parolini M, Pedriali A, Binelli A (2013) Application of a biomarker response index for ranking the toxicity of five pharmaceuticals and personal care products (PPCP) to the bivalve *Dreissena polymorpha*. *Arch Environ Contam Toxicol* 64:439–447
18. Boxall ABA, Rudd MA, Brooks BW, Caldwell DJ, Choi K, Hickmann S, Innes E, Ostapyk K, Staveley JP, Verslycke T (2012) Pharmaceuticals and personal care products in the environment: what are the big questions? *Environ Health Perspect* 120:1221–1229
19. Guardabassi L, Petersen A, Olsen JE, Dalsgaard A (1998) Antibiotic resistance in *Acinetobacter* spp. isolated from sewers receiving waste effluent from a hospital and a pharmaceutical plant. *Appl Environ Microbiol* 64(9):3499–3502
20. Kümmerer K (2001) Drugs in the environment: emission of drugs, diagnostic aids and disinfectants into wastewater by hospitals in relation to other sources – a review. *Chemosphere* 45(6–7):957–969

21. Kümmerer K, Helmerts E (2000) Hospital effluents as a source of Gadolinium in the aquatic environment. *Environ Sci Technol* 34:573–577
22. Daouk S, Chèvre N, Vernaz N, Widmer C, Daali Y, Fleury-Souverain S (2016) Dynamics of active pharmaceutical ingredients loads in a Swiss university hospital wastewaters and prediction of the related environmental risk for the aquatic ecosystems. *Sci Total Environ* 537:244–253
23. Nour-eddine A, Lahcen B (2014) Estimate of the metallic contamination of the urban effluents by the effluents of the Mohamed V Hospital of Meknes. *Eur Sci J* 10(3):71–78
24. Amouei A, Asghamia H, Fallah H, Faraji H, Barari R, Naghipour D (2015) Characteristics of effluent wastewater in hospitals of Babol University of Medical Sciences, Babol, Iran. *Health Scope* 4(2):e23222. 1–4
25. Kümmerer K, Helmerts E, Hubner P, Mascart G, Milandri M, Reinthaler F, Zwakenberg M (1999) European hospitals as a source for platinum in the environment in comparison with other sources. *Sci Total Environ* 225:155–165
26. Lenz K, Mahnik SN, Weissenbacher N, Mader RM, Krenn P, Hann S, Koellensperger G, Uhl M, Knasmüller S, Ferk F, Bursch W, Fuerhacker M (2007) Monitoring, removal and risk assessment of cytostatic drugs in hospital wastewater. *Water Sci Technol* 56(12):141–149
27. Escher BI, Baumgartner R, Koller M, Treyer K, Linert J, McArdell CS (2011) Environmental toxicology and risk assessment of pharmaceuticals from hospital wastewater. *Water Res* 45:75–92
28. Lin AY-C, Yu T-H, Lin C-F (2008) Pharmaceutical contamination in residential, industrial, and agricultural waste streams: risk to aqueous environments in Taiwan. *Chemosphere* 74:131–141
29. Kovalova L, Siegrist H, Singer H, Wittmer A, McArdell C (2012) Hospital wastewater treatment by membrane bioreactor: performance and efficiency for organic micropollutant elimination. *Environ Sci Technol* 46:1536–1545
30. Mahnik SN, Lenz K, Weissenbacher N, Mader RM, Fuerhacker M (2007) Fate of 5-fluorouracil, doxorubicin, epirubicin, and daunorubicin in hospital wastewater and their elimination by activated sludge and treatment in a membrane-bio-reactor system. *Chemosphere* 66:30–37
31. Lopes de Souza SM, Carvalho de Vasconcelos E, Dziedzic M (2009) Environmental risk assessment of antibiotics: an intensive care unit analysis. *Chemosphere*:962–967
32. Ort C, Lawrence MG, Reungoat J, Eaglesham G, Carter S, Keller J (2010) Determining the fraction of pharmaceutical residues in wastewater originating from a hospital. *Water Res* 44:605–615
33. Ferrando-Climent L, Rodriguez-Mozaz S, Barcelò D (2014) Incidence of anticancer drugs in an aquatic urban system: From hospital effluents through urban wastewater to natural environment. *Environ Pollut* 193:216–223
34. Verlicchi P, Galletti A, Al Aukidy M (2013) Hospital wastewaters: Quali-quantitative characterization and strategies for their management and treatment. In: Sharma SK, Sanghi R (eds) *Wastewater reuse and management*. Springer, New York
35. Azuma T, Arima N, Tsukada A, Hirami S, Matsuoka R, Moriwake R, Ishiuchi H, Inoyama T, Teranishi Y, Yamaoka M, Mino Y, Hayashi T, Fujita Y, Masada M (2016) Detection of pharmaceuticals and phytochemicals together with their metabolites in hospital effluents in Japan, and their contribution to sewage treatment plant influents. *Sci Total Environ* 548–549:189–197
36. Verlicchi P, Galletti A, Masotti L (2010) Management of Hospital Wastewaters: the case of the effluent of a large hospital situated in a small town. *Water Sci Technol* 61(10):2507–2519
37. Verlicchi P, Zambello E (2016) Predicted and measured concentrations of pharmaceuticals in hospital effluents. Examination of the strengths and weaknesses of the two approaches through the analysis of a case study. *Sci Total Environ* 565:82–94

38. Lienert J, Güdel K, Escher BI (2007) Screening method for ecotoxicological hazard assessment of 42 pharmaceuticals considering human metabolism and excretory routes. *Environ Sci Technol* 41(12):4471–4478
39. Riazul HM, Metcalfe C, Li H, Parker W (2012) Discharge of pharmaceuticals into municipal sewers from hospitals and long-term care facilities. *Water quality research. J Canada* 47 (2):140–152
40. Kleywegt S, Pileggi V, Lam YM, Elises A, Puddicomb A, Purba G, Di Caro J, Fletcher T (2016) The contribution of pharmaceutically active compounds from healthcare facilities to a receiving sewage treatment plant in Canada. *Environ Toxicol Chem* 35(4):850–862
41. World Health Organisation (WHO) (2014). In: Chartier Y, Emmanuel Y, Pieper U, Prüss A, Rushbrook P, Stringer R, Townend W, Wilburn S, Zghondi R (eds) *Safe management of wastes from health-care activities*, 2 edn. Available at the web site http://www.searo.who.int/srilanka/documents/safe_management_of_wastes_from_healthcare_activities.pdf?ua=1. Accessed 26 Feb 2017