Science of the Total Environment 514 (2015) 467–491

Contents lists available at ScienceDirect

Science of the Total Environment

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

Review

What have we learned from worldwide experiences on the management and treatment of hospital effluent? — An overview and a discussion on perspectives

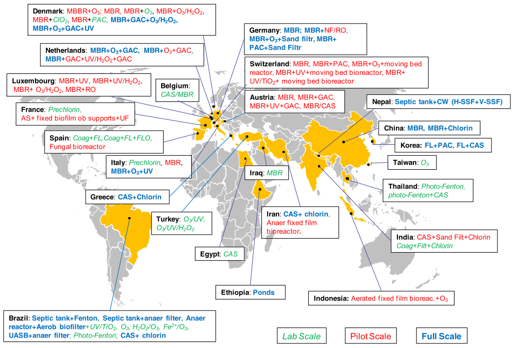
P. Verlicchi [a,b,*], M. Al Aukidy [a], E. Zambello [a]

[a] Department of Engineering, University of Ferrara, Via Saragat 1, I-44122 Ferrara, Italy
[b] Terra&Acqua Tech Technopole of the University of Ferrara, Via Borsari 46, 44123 Ferrara, Italy

HIGHLIGHTS

- Different technologies for a dedicated treatment of hospital effluent are discussed.
- Photo-Fenton process seems to be a promising preliminary treatment. Membrane bioreactor is a proper secondary treatment for hospital effluent.
- AOPs showed a good removal efficiency for most classes of pharmaceuticals.
- UV irradiation is a promising technology in the removal of X-ray contrast media.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 13 January 2015
Received in revised form 5 February 2015
Accepted 5 February 2015
Available online 16 February 2015

Editor: D. Barcelo

ABSTRACT

This study overviews lessons learned from experimental investigations on dedicated treatment systems of hospital effluent carried out worldwide in the last twenty years. It includes 48 peer reviewed papers from 1995 to 2015 assessing the efficacy of different treatment levels (preliminary, primary, secondary and polishing) of hospital wastewater in removing a wide spectrum of pharmaceutical compounds as well as conventional contaminants. Moreover, it highlights the rationale and the reasons for each study: reducing the discharge of micropollutants in surface water, improving existing wastewater treatment technologies and reducing the risk of spread of pathogens causing endemic diseases and finally, it offers a critical analysis of the conclusions and

---

Abbreviations: AOP, advanced oxidation process; AOXs, adsorbable organic compounds; ARB, antibiotic resistant bacteria; ARG, antibiotic resistant genes; AS, activated sludge; BAT, best available technology; CAS, conventional activated sludge; Chlorin, chlorination; Coag, coagulation; CPCs, cancerogenic platinum compounds; CWs, constructed wetlands; D617, N-dealkylverapamil; D_{ow}, octanol water distribution coefficient; DNA, deoxyribonucleic acid; DO, dissolved oxygen; DOC, dissolved organic carbon; EE2, ethinyl estradiol or 17-α ethinyl estradiol; EQS, environmental quality standard; FL, flocculation; FLO, flotation; GAC, granular activated carbon; HDPE, high density polyethylene; HRT, hydraulic retention time; H-SSF, horizontal subsurface flow; HWW, hospital wastewater; ICM, iodinated contrast media; K_a, dissociation constant; k_{biol}, biological degradation rate; K_{ow}, octanol water partition coefficient; LP, low pressure; MBBR, moving bed biofilm reactor; MBR, membrane biological reactor; MCWO, molecular weight cut off; MP, medium pressure; NF, nanofiltration; O&M, maintenance and operation; PAC, powdered activated carbon; PhC, pharmaceutical compound; RO, reverse osmosis; SARS, severe acute respiratory syndrome; SRT, sludge retention time; T, temperature; TDS, total dissolved solids; TOC, total organic carbon; TSS, total suspended solids; UASB, upflow anaerobic sludge blanket; UF, ultrafiltration; UV, ultraviolet; UWW, urban wastewater; v_f, filtration velocity; V-SSF, vertical subsurface flow; WWTP, wastewater treatment plant.

* Corresponding author at: Department of Engineering, University of Ferrara, Via Saragat 1, I-44122 Ferrara, Italy.
E-mail addresses: paola.verlicchi@unife.it (P. Verlicchi), mustafakether.alaukidi@unife.it (M. Al Aukidy), elena.zambello@unife.it (E. Zambello).

http://dx.doi.org/10.1016/j.scitotenv.2015.02.020

Keywords:
Advanced oxidation processes
Environmental risk assessment
Hospital effluent
Pharmaceutical removal
Toxicity
Treatment costs

suggestions of each study. The most investigated technologies are membrane bioreactors equipped with ultrafiltration membranes in the secondary step, ozonation followed by activated carbon filtration (in powder and in granules) in the polishing step. Interesting research projects deal with photo-Fenton processes acting as primary treatments to enhance biodegradation before biological treatment, and as a polishing step, thus further reducing micro-contaminant occurrence. Investment and operational costs are also presented and discussed for the different treatment technologies tested worldwide, in particular membrane bioreactors and various advanced oxidation processes.

This study also discusses the need for further research to evaluate toxicity resulting from advanced oxidation processes as well as the need to develop an accurate feasibility study that encompasses technical, ecotoxicological and economic aspects to identify the best available treatment in the different situations from a global view point.

Contents

1. Introduction

In recent years, hospital effluent has been the object of study and research in various countries throughout the world facing different issues. The specific driving and inspiring force has been to improve the knowledge of the chemical and physical characterization of such wastewater for conventional parameters, namely BOD_5, COD, TSS, N and P compounds, pH and T (Sarafraz et al., 2007; Verlicchi et al., 2012a); the microbiological load of hospital effluent and also the risk of the spread of antibiotic resistant bacteria (Boillot et al., 2008; Chitnis et al., 2004); differences in composition between hospital effluent and urban wastewater (UWW) (Verlicchi et al., 2010); seasonal variation of hospital effluent compositions (Verlicchi et al., 2012a, 2012c); strategies in their management (co-treatment or dedicated treatment with UWW) (Pauwels and Verstraete, 2006; Verlicchi et al., 2010); evaluation of the adequacy of adopted treatment strategies with respect to the removal of specific contaminants (Mesdaghinia et al., 2009; Beier et al., 2010); technical and economic feasibility of dedicated treatment trains for hospital wastewater (HWW) (PILLS Report, 2012); and contribution of hospital effluent to the influent of a municipal wastewater treatment plant (WWTP) (Verlicchi et al., 2012a; Santos et al., 2013).

On occasion, the occurrence of disease outbreaks due to pathogens occurring in sewage, such as SARS (severe acute respiratory syndrome) in China in 2003, has led scientists to develop specific research projects to identify safety measures to rapidly adopt in existing WWTPs, in particular in plants receiving hospital effluent, not only to deal with the current emergency, but also to prevent further ones (Wang et al., 2005).

Quite rarely, national (or regional) legal regulations have been established to define how to manage and treat hospital effluent before its disposal (discharge in public sewage for treatment at a municipal WWTP or discharge into a surface water body) (Boillot et al., 2008; Verlicchi et al., 2010). Indeed, hospital effluent was and (still) is generally considered of the same pollutant nature as UWW and thus it is commonly discharged in public sewage systems, conveyed to an urban WWTP where it is subjected to conventional treatment, often consisting in primary clarification, activated sludge process and sometimes disinfection. This practice is very common although recent studies (Verlicchi et al., 2010; Santos et al., 2013; McArdell et al., 2011) highlighted that higher concentrations of pharmaceuticals (PhCs), disinfectants and X-ray contrast media occur in hospital effluent as well as a microbiological load exhibiting a higher resistance to treatment (Chitnis et al., 2004).

Municipal WWTPs were conceived and, in some cases, recently upgraded to guarantee a high removal efficiency of carbon, nitrogen and phosphorus compounds, as well as microorganisms (mainly bacteria): pollutants regularly arriving with and occurring in the WWTP influent at concentrations in the order of units (P compounds), tens (NH_4, TKN) and hundreds (COD, BOD_5) of mg/L and thousands of MPN/100 mL (*Escherichia coli*).

Commonly adopted treatments at municipal WWTPs include: preliminary treatments, (sometimes) primary clarification, secondary biological (usually consisting in a conventional activated sludge – CAS – process), and polishing treatments (chemical disinfection or sometimes rapid filtration followed by UV disinfection). Unfortunately, these WWTPs are not adequate enough to reach high removal efficiencies for the wide spectrum of micropollutants (PhCs, adsorbable organic compounds commonly known with the acronym AOXs) commonly present in hospital effluent. They are also among the main sources of antibiotic release into the environment and thus they may promote the selection of antibiotic resistant genes (ARG) and antibiotic resistant bacteria (ARB), as deeply investigated in Rizzo et al. (2013). Moreover, in some circumstances, conventional treatments have been adopted for HWW, but they are not well managed and very low efficiencies are achieved even for common parameters, namely BOD_5, COD, TSS and total coliform (Mesdaghinia et al., 2009). Sometimes, a simple primary treatment is adopted for hospital effluent (primary clarification, prechlorination) but it is not efficient (Martins et al., 2008).

In other cases, no treatment is adopted at all and direct discharge of raw HWW into surface rivers is a common practice (Liu et al., 2010).

The main focus of this study is to present and discuss lessons learned from previous investigations and studies carried out on dedicated treatment of HWW in the different countries worldwide. It offers a critical analysis of data collected from lab, pilot and full scale treatment plants acting as primary, secondary and tertiary steps. Attention is paid to the removal efficiencies observed for contaminants, including conventional parameters but in particular emerging ones: mainly PhCs, detergents and disinfectants. The analysis also compares the assessment of investment and operational costs for each applied technology.

2. Object and framework of the survey

This study is based on 48 publications regarding investigations into the *dedicated* treatment of hospital effluent in lab, pilot and full scale plants acting as primary, secondary and tertiary steps. They were carried out in 24 different countries all over the world between 1995 and 2015.

Collected data that are presented and discussed herein mainly refer to observed removal efficiencies for 108 PhCs belonging to 17 different classes: analgesics and anti-inflammatories (20), anaesthetics (1), anthelmintics (5), antibiotics (23), antifungals (1), antihypertensives (6), antineoplastics (6), antiseptics (1), antivirals (5), beta-blockers (6), contrast media (9), fragrances (3), hormones (4), lipid regulators (4), psychiatric drugs (12), receptor antagonists (1) and stimulants (1). Table SD-2 in the Supplementary data compiles all the selected compounds grouped according to their class. Moreover, conventional pollutants (BOD_5, COD, SS, N and P compounds, microorganisms…) are also reported and discussed.

In discussing removal efficiencies of selected PhCs observed for the different treatment technologies and steps, particular attention is paid to the potential capacity of each technology in retaining/degrading specific compounds and, when possible, to the operational conditions which could maximize them. Data are presented in graphs in the manuscript and further details are provided in tables in the Supplementary data.

Table 1
Main chemical characteristics of hospital effluent in terms of conventional parameters and pharmaceuticals and other emerging compounds.

Parameter	Range of concentrations	Reference
Conductivity, μS/cm	300–1000	Boillot et al. (2008), Verlicchi et al. (2012c)
pH	6–9	PILLS Report (2012), Kosma et al. (2010)
Redox potential, mV	850–950	Verlicchi et al. (2010), Boillot et al. (2008)
Fat and oil, mg/L	50–210	Al-Hashimia et al. (2013), Verlicchi et al. (2010)
Chlorides, mg/L	80–400	Emmanuel et al. (2004), Verlicchi et al. (2012c)
Total N, mg N/L	60–98	PILLS Report (2012), Beyene and Redaie (2011)
NH_4, mgNH_4/L	10–68	McArdell et al. (2011), Verlicchi et al. (2012c), Wen et al. (2004)
Nitrite, mg NO_2/L	0.1–0.58	Al-Hashimia et al. (2013), McArdell et al. (2011)
Nitrate, mg NO_3/L	1–2	Lopez et al. (2010), McArdell et al. (2011), Venditti et al. (2011)
Phosphate, mg P-PO_4/L	6–19	Al-Hashimia et al. (2013), Verlicchi et al. (2010, 2012c)
Suspended solids, mg/L	120–400	Verlicchi et al. (2012c)
COD, mg/L	1350–2480	Kajitvichyanukul and Suntronvipart (2006), Berto et al. (2009)
Dissolved COD, mg/L	380–700	McArdell et al. (2011)
DOC, mg/L	120–130	McArdell et al. (2011);
TOC, mg/L	31–180	Beier et al. (2012), Nardi et al. (1995)
BOD_5/COD (biodegradability index)	0.3–0.4	Kajitvichyanukul and Suntronvipart (2006)
AOX, μg/L	550–10000	Kummerer et al. (1998), Nardi et al. (1995)
Microorganisms, MPN/100 mL		
E. coli	10^3–10^6	Beier et al. (2012), Nielsen et al. (2013)
Enterococci	10^3–10^6	Beier et al. (2012)
Faecal coliform	10^3–10^4	Beier et al. (2012)
Total coliform	10^5–10^7	Lopez et al. (2010), Beyene and Redaie (2011)
EC_{50} (*Daphnia*), TU	9.8–117	Emmanuel et al. (2004), Machado et al. (2007)
Total surfactants, mg/L	4–8	Verlicchi et al. (2008, 2010)
Total disinfectants, mg/L	2–200	Kummerer (2001), Verlicchi et al. (2012c)
Specific disinfectants[a]:		
BAC_C12–18, μg/L	49	Kovalova et al. (2012)
BAC_C12, μg/L	34	Kovalova et al. (2012)
DDAC-C10, μg/L	102	Kovalova et al. (2012)
Antibiotics, μg/L	30–200	Verlicchi et al. (2012c)
Antinflammatories, μg/L	5–1500	Verlicchi et al. (2012c)
Lipid regulators, μg/L	1–10	Verlicchi et al. (2012c)
Cytostatic agents, μg/L	5–50	Suarez et al. (2009), Verlicchi et al. (2012c)
ICM, μg/L	0.2–2600	Verlicchi et al. (2012c)
Beta-blockers, μg/L	0.4–25	Verlicchi et al. (2012c)

[a] Disinfectants: quaternary ammonia disinfectant: BAC_C12–18: benzalkonium chloride; DDAC-C10: dimethyldidecylammonium chloride.

All removal values reported and discussed (in the following graphs and tables) must be considered with the necessary caution, bearing in mind their origin and that they may be affected by many factors, namely:

- influent characteristics (macro- and micro-pollutant concentrations),
- operational conditions (sludge concentration, sludge retention time (SRT), hydraulic retention time (HRT), pH, temperature (T), feeding

Table 2
List of the studies included in the overview together with a brief description of the corresponding investigations and rationale.

Reference	Main characteristics of experimental investigations and treatment plants	Rationale	Investigated parameters
Abd El-Gawad and Aly (2011)	Investigation carried out at four hospitals in Egypt to assess hospital effluent quality and quantity, as well as the impact on the environment in terms of common parameters and pollutants when a CAS system is adopted as treatment prior to discharge into surface water.	Suitable HWW management based on standard set for conventional pollutants in UWW	Conventional parameters: BOD_5, DO, TSS, total coliform, faecal coliform and trace elements (metals)
Al-Hashimia et al. (2013)	Investigation carried out on real wastewater collected from a hospital located in Iraq to assess the performance of a lab-scale *sequencing* anoxic/anaerobic MBR for nutrient removal under different internal recycling time modes between anoxic and anaerobic conditions operating with an SRT = 58.5–116 d, internal recycle rate of 39 L/h, a flux of 15.12 L/(m^2 h).	Enhancement in nutrient removal in hospital effluent	Conventional parameters: COD, BOD_5, PO_4, NH_4, NO_3, NO_2, TSS, oil and grease, total and faecal coliforms
Andersen et al. (2014)	Investigation regarding to the treatment of the oncological ward effluent by means of a pilot plant consisting in a moving bed biofilm reactor (MBBR) followed by ozonation carried out in Denmark. System performances were provided for six pharmaceutical model substrates each representing different biological and chemical degradation.	Optimization of the removal of selected compounds by means of a MBBR and ozonation	PhCs: triclosan, mefenamic acid, diclofenac, naproxen, gemfibrozil, ketoprofen, ibuprofen, clofibric acid
Arslan et al. (2014)	Investigation carried out on raw hospital effluent in Turkey. Ozonation, O_3/UV and $O_3/UV/H_2O_2$ were tested as a *pretreatment* option in a batch reactor in order to evaluate the removal of COD and UV absorbance and the improvement in biodegradation.	Options in pretreatments	Conventional parameters: COD and absorbance
Azar et al. (2010)	Investigation carried out on real HWW collected from two hospitals located in Iran, by means of biological oxidation (aerobic/anaerobic) in an 80-litre pilot plant.	Recommended treatment for hospital effluent in Iran, based on an analysis of conventional parameter removals	Conventional parameters: COD, BOD_5, TSS, NO_2, NO_3, PO_4, detergents, oil and grease, total coliform, *Escherichia coli*, Ag, Hg and Ni
Beier et al. (2010)	Investigation carried out at Waldbrol hospital (Germany) by means of nanofiltration (NF) and reverse osmosis (RO) membrane (pilot plant) for the treatment of a (full scale) MBR permeate. The molecular weight cut off (MWCO) of NF membranes was 300–400 Da and of RO membranes was 100–150 Da. For the tests, the pump pressure was 7 bar for NF and 14 bar for RO and the maximum fed flux to NF/RO modules was between 20 and 36 L/(m^2 h).	Dedicated polishing treatment for HWWs to remove PhCs	PhCs: bezafibrate, bisoprolol, carbamazepine, clarithromycin, ciprofloxacin, diclofenac, ibuprofen, metronidazole, moxifloxacin, telmisartan, tramadol
Beier et al. (2011)	Investigation carried out at the full-scale MBR in operation at Waldbrol hospital in Germany to assess PhCs removal from hospital wastewater. The permeate is then sent to the municipal WWTP. The main design parameters are: Q = 130 m^3/d; maximum flow 250 m^3/d; 5 Kubota EK 400 flat sheet membrane modules, total membrane area 1600 m^2, cut off value 0.2 μm; biomass concentration in the bioreactor 10–12 g/L; biological reactor volume 56 m^3. The main average operating parameters: hydraulic retention time 31.3 h, temperature in aerated tank 24.6 °C, biomass concentration 13.6 g/L, flux 10–20 L/(m^2 h).	Separate treatment of HWWs will allow evaluation of the appropriateness of MBR for hospital effluent in high density urban areas, contributing to minimizing the operating and financial expenditure for municipal WWTP.	PhCs: bezafibrate, bisoprolol, carbamazepine, clarithromycin, ciprofloxacin, diclofenac, ibuprofen, metronidazole, moxifloxacin, tramadol
Beier et al. (2012)	Investigation carried out at a hospital in Waldbrol (Germany) to assess the performance of a full-scale wastewater treatment plant equipped with a MBR and to evaluate the characteristics of the activated sludge. For design and operational parameters see Beier et al. (2011).	Evaluation of MBR as a dedicated treatment of HWWs to reduce the environmental input of chemical and microbiological parameters in the environment	Conventional parameters: COD, TOC, AOX, NH_4, total P, *E. coli* and enterococci
Berto et al. (2009)	Investigation carried out at a hospital in Brazil to evaluate the effectiveness of "advanced" pretreatments consisting in a biological (full-scale septic tank, 45 m^3) and a chemical stage (lab-scale Fenton reactor) to remove organic matter and pathogenic microbiota from HWW.	Adequate advanced (pre)treatments for hospital effluents to reduce their environmental impact	Conventional parameters: COD, BOD_5, P and N compounds, suspended solids, total coliform and thermotolerant coliforms
Beyene and Redaie (2011)	Investigation carried out at Hawassa University Referral Hospital (Ethiopia) to examine the suitability of a series of (full scale) ponds for the treatment of HWW. The treatment train consists of two facultative ponds (each of them: surface area 667 m^2, depth 1.5 m and retention time 14 d) followed by two maturation ponds (each of them surface area of about 400 m^2, depth 1.1 m, retention time 3 d) and a final fish pond (surface area 862 m^2, depth 1.5 m, retention time 9 d).	Evaluation of the risk posed by HWWs in terms of conventional pollutants and a proposal to upgrade existing WWTP in order to reduce it.	Conventional parameters: COD, BOD_5, P, PO_4, total Nitrogen, NH_3, NO_3, NO_2 TSS, TDS, Cl, S_2, total coliforms and faecal coliforms

Table 2 (*continued*)

Reference	Main characteristics of experimental investigations and treatment plants	Rationale	Investigated parameters
Chiang et al. (2003)	Investigation carried out in Taiwan on the disinfection by continuous ozonation of hospital effluent and in particular of the effluent from the kidney dialysis unit and on the increment of hospital effluent biodegradability.	Disinfection effect and improvement in biodegradability of hospital effluent by ozonation	Conventional parameters: COD, BOD, total coliforms
Chitnis et al. (2004)	Investigation carried out in India in a pilot plant consisting in preliminary and primary treatments, a conventional activated sludge system, sand filtration and chlorination.	Investigation into the microbiological community and evaluation of the risk of multidrug resistant bacteria spread	Different microbiological parameters: total coliforms, faecal enterococci, staphylococci, *Pseudomonas*, multidrug resistant bacteria
Cruz-Morato et al. (2014)	Investigation carried out in Spain in a batch fluidized bed bioreactor (lab scale) under sterile and non-sterile conditions with *Trametes versicolor* pellets to examine the removal of a wide group of pharmaceutical compounds from HWW. Samples were collected from the main sewer of Girona University Hospital (Spain).	Evaluation of the capacity of a treatment by fungal bioreactor in reducing pharmaceutical concentration from HWW	99 PhCs of different classes
de Almeida et al. (2013)	Investigation carried out at the University hospital of Santa Maria (Brazil) by means of a septic tank and anaerobic filter (full scale).	Environmental risks of PhCs and adequateness of treatment trains	PhCs: 5 anti-anxiety and anti-epileptic compounds
Emmanuel et al. (2004)	Toxicity evaluation after prechlorination (NaClO addition) of the effluent from the infectious and tropical disease department at the hospital in Lyon, France.	Toxicity evaluation due to prechlorination	Conventional parameters: COD, TOC, AOX, chlorides
Gautam et al. (2007)	Investigation carried out at the hospital located in Vellore, Tamil Nadu (India), by means of a lab-scale plant consisting of coagulation (by adding $FeCl_3$ up to 300 mg/L), rapid filtration and disinfection (by adding a bleaching powder solution) steps.	Options for hospital effluent pretreatment before discharge in public sewage	Conventional parameters: COD, BOD_5, SS and P
Grundfos Biobooster (2012)	Report from an on-going project in Denmark to evaluate the best available technologies (BATs) for the separated treatment of hospital effluent. Two sequences are being tested: MBR followed by O_3, GAC and/or H_2O_2 and UV, MBR followed by GAC and UV.	Evaluation of the BAT for hospital treatment	.
Kajitvichyanukul and Suntronvipart (2006)	Investigation carried out in Bangkok, Thailand, on the pretreament of hospital effluent by using a lab-scale photo-Fenton process.	Improvement in biodegradability of hospital effluent by using the photo-Fenton process as a pretreatment	Conventional parameters: COD, BOD_5, TOC, turbidity, TSS, conductivity and toxicity
Kist et al. (2008)	Investigation carried out on the treatment of wastewater produced in a hospital laundry in the Rio Pardo Valley (Brazil), by means of a (lab scale, 4 L) ramp type reactor for catalytic photoozonation ($UV/TiO_2/O_3$).	Reduction of the risk posed by hazardous substances occurring in HWWs due to adequate pretreatments	Conventional parameters: COD, BOD_5, turbidity, surfactants, *Escherichia coli* and thermotolerant coliforms
Kohler et al. (2012)	Investigation carried out at the Hospitalier Emil Mayrisch (Luxembourg) by means of a pilot plant (MBR + UV; MBR + H_2O_2 + UV) to assess the removal of some pharmaceutical compounds. Details of the MBR are reported in Venditti et al. (2011).	Technical and economical feasibility for hospital effluent treatment.	13 PhCs
Kosma et al. (2010)	Investigation carried out on the occurrence and removal of PhCs at the hospital (full scale) WWTP (CAS, 600 m^3, HRT = 6 h) in Ioannina (Greece).	Impact of pharmaceuticals on the environment	11 PhCs; COD, BOD_5, NO_3, PO_4 and TSS
Kovalova et al. (2012)	Investigation carried out in Switzerland, on a pilot-scale primary clarifier + MBR installed and operated for one year at Cantonal Hospital in Baden. The bioreactor consisted of an anoxic tank (0.5 m^3) and an aerobic one (1 m^3) equipped with submerged ultrafiltration flat sheet membrane plates (15–30 L/m^2 h, 38 nm pore size, nominal cut-off 150 kDa). Biomass concentration was 2 g/L, SRT 30–50 d, temperature 29 °C.	Analysis of performance and removal in MBR of many PhCs. Reduction of the spread of multi resistant or pathogenic bacteria, virus, parasite eggs and PhCs	56 PhCs
Kovalova et al. (2013)	Investigation carried out at the Cantonal Hospital in Baden (Switzerland) in a pilot plant consisting in a primary clarifier, MBR (see Kovalova et al. (2012)), and five post-treatment technologies: O_3, O_3/H_2O_2, powdered activated carbon (PAC), and low pressure UV light with and without TiO_2.	Removal of typical pollutants in hospital effluent (disinfectants, pathogens and antibiotic resistant bacteria) by advanced treatments	56 PhCs
Lenz et al. (2007a)	Investigation carried out at a hospital in Vienna (Austria), by means of a pilot MBR (150 L) installed and fed with oncologic in-patient treatment ward effluent. Ultrafiltration membranes (nominal cut-off of 100 kDa) were used.	Risk of cancerostatic platinum compounds to humans	Cancerostatic platinum compounds
Lenz et al. (2007b)	Investigation carried out at the oncological ward in a hospital in Vienna (Austria), by means of a pilot MBR (see Lenz et al. (2007a)) followed by granular activated carbon (GAC) and UV. Biomass concentration was 12–15 g/L, the average hydraulic load 260 L/d	Environmental risk of cytostatic	Cancerostatic platinum compounds.

(continued on next page)

Table 2 (*continued*)

Reference	Main characteristics of experimental investigations and treatment plants	Rationale	Investigated parameters
Liu et al. (2010)	Investigation carried out in China on operating conditions, MBR efficiency in treating hospital effluent.	To avoid the spread of pathogenic microorganisms and viruses, especially following the outbreak of SARS in 2003	Conventional parameters: COD, BOD$_5$, NH$_3$, TSS, bacteria and faecal coliform
Machado et al. (2007)	Investigation carried out in Brazil, on a lab-scale advanced oxidation process (UV/TiO$_2$/O$_3$) operating as a tertiary treatment, fed with secondary HWW.	Proposal of a (sustainable) treatment schematic to reduce microorganisms and toxicity from hospital effluent	Conventional parameters: COD, BOD$_5$, turbidity, total nitrogen, total phosphorus, surfactants, thermotolerant coliforms, toxicity and AOX
Mahnik et al. (2007)	Occurrence and treatability of cytostatics in the effluent from the oncologic in-patient treatment ward of the Vienna University Hospital was investigated as well as their removal by an MBR (pilot scale, 150 L of aeration tank, hydraulic load 100–200 L/d, HRT = 20–24 h, biomass concentration 12–15 g/L, UF membranes: active area 1 m^2, nominal cut-off 100 kDa).	Pollution level of the effluent from particular hospital wards	4 PhCs: 5-fluorouracil, doxorubicin, epirubicin and daunorubicin
Mahvi et al. (2009)	Analysis of the performance of seven WWTPs (CAS + chlorination) in Kerman Province (Iran) receiving hospital effluent in terms of removal of main conventional parameters and malfunctions.	Malfunctions in WWTPs receiving hospital effluents	Conventional parameters: COD, BOD$_5$, DO, TSS, pH, NO$_2$, NO$_3$, PO$_4$, Cl and SO$_4^{2-}$
Martins et al. (2008)	Investigation carried out in Brazil into the pretreatment of hospital effluent by using a septic tank and an anaerobic filter. Analysis was referred to occurrence, removal of ciprofloxacin and the resulting risk due to its residue in the treated effluent.	Evaluation of the adequateness of specific pretreatment in Brazil	PhC: ciprofloxacin
McArdell et al. (2011)	Report including all the details of the investigations described in Kovalova et al. (2012, 2013) and in PILLS Report (2012) referring to the Swiss investigations on MBR and MBR+ AOPs applied to a hospital effluent.	Testing and comparing the removal of PhCs from HWW by different technologies	Conventional parameters, PhCs
Mousaab et al. (2015)	Investigation into the removal ability of PhCs and conventional pollutants in an upgraded UF membrane system coupled with an activated sludge (AS) reactor by the addition of biofilm support media in the aeration tank in case of hospital effluent treatment. The aeration bioreactor had a volume of 400 L, the UF membrane system consisted of a hollow fibre module (1 m^2 surface area, pore size 0.2 μm). HRT = 22 h and SRT = 20 d.	Improvement in PhC removal from hospital effluent and in membrane functioning resulting in a reduction of operation costs	PhCs
Nardi et al. (1995)	Investigation into disinfection of the effluent of an Italian infectious disease ward by means of different doses of ClO$_2$ and evaluation of AOX production.	Disinfection performance of ClO$_2$ with respect to NaClO in case of hospital effluent and evaluation of AOX production	Conventional parameters: COD, TOC, total and faecal coliforms, streptococci, AOX
Nielsen et al. (2013)	Investigation carried out in Denmark with pilot and lab scale plants into the ability of different technologies acting as a secondary (MBR) or a tertiary (O$_3$, O$_3$/H$_2$O$_2$, ClO$_2$, PAC) treatment in removing common PhCs from hospital effluent. The MBR was equipped with ceramic UF membranes (surface area 3.75 m^2, pore size 60 nm). The average daily flow was 2.2 m^3/d and 24.6 L/(m^2 h), SRT = 35 d.	Risk to human health posed by HWWs during combined sewers overflow	PhCs; *E. coli*, total coliforms, total enterococci
Pauwels et al. (2006)	Investigation carried out in Ghent (Belgium) to compare the performance of two lab-scale plants (CAS and MBR) in treating hospital effluent. The MBR consisted of a 25 L tank equipped with 3 plate membrane modules (pore size 0.4 μm; total surface area 0.3 m^2) HRT = 12 h in both reactors.	Potential risk of HWW-correlation between PhC and conventional parameters removal	COD, total ammonium nitrogen, total coliforms, faecal coliforms, total aerobic bacteria, total anaerobic bacteria and enterococci; ethinylestradiol
Pharmafilter report (2013)	Report on the characteristics and the performance of a full-scale system (Pharmafilter) installed and tested in the Reinier de Graaf Gasthuis in Delft (Netherlands) in the period 2010–2012. The system is an integral concept for the optimization of care, processing waste and purifying wastewater in hospitals. It consists in: pretreatment (sieve), biological process (UF MBR), ozonation, GAC filtration. The sludge discharged from the MBR is fed back into the digester and any excess sludge water from the digestate formed in the digester can be transported to the MBR. The fate and removal of about 100 PhCs were observed.	Potential health risk posed by HWWs	Potential health risk posed by HWWs PhCs
PILLS Report (2012)	Report of the main results achieved within the European PILLS project developed in 2010–2012 involving four research units in different countries that investigated the removal of PhCs from HWW by means of MBR + PAC, MBR + O$_3$ + moving bed bioreactor, MBR + UV + moving bed bioreactor in Switzerland, MBR + RO, MBR + UV, MBR + O$_3$/H$_2$O$_2$ in Luxembourg, MBR + O$_3$ + sand filtration, MBR +	Effects of pharmaceuticals on environment water and potential measures to reduce their occurrence	PhCs

Table 2 (*continued*)

Reference	Main characteristics of experimental investigations and treatment plants	Rationale	Investigated parameters
	PAC + sand filtration in Germany, MBR + O_3 + GAC, MBR + GAC + UV/H_2O_2 + GAC in the Netherlands. Monitored parameters were PhCs and toxicity. See also Kovalova et al. (2012, 2013), Kohler et al. (2011) and McArdell et al. (2011).		
Prado et al. (2011)	Investigation carried out in Brazil involving detection of some enteric viruses and hepatitis A in hospital effluent and in the effluent from two different full scale treatment plants. The removal efficiencies observed in the two sequences: upflow anaerobic sludge blanket (UASB) + three serial anaerobic filters and CAS system followed by a chlorination tank were investigated and compared.	Quantification of enteric viruses and hepatitis A in the effluent of different hospital WWTPs	Enteric viruses and hepatitis A
Prayitno et al. (2014)	Investigation on a pilot scale plant consisting in an aerated fixed film biofilter (AF2B reactor) coupled with an ozonation reactor fed by the effluent from Malang City hospital in Indonesia.	Pollution and health problems for humans being caused by the discharge of HWWs	Conventional pollutants: BOD_5, phenols, faecal coliform and Pb
Rezaee et al. (2005)	Investigation carried out in Iran on a pilot-scale system consisting in an integrated anaerobic–aerobic fixed film reactor fed with hospital effluent before co-treatment with urban wastewater.	Potential reduction of the organic load in hospital effluent by biological pretreatment before its cotreatment	Conventional parameters: COD, BOD_5, NH_4, turbidity, bacteria and *Escherchia coli*
Shrestha et al. (2001)	Analysis of the removal performance in a full scale two stage constructed wetland (CW) designed and constructed in Nepal to treat hospital effluent (20 m^3/d). The system consists in a three chambered septic tank, a horizontal flow bed (140 m^2), with 0.65 to 0.75 m depth and a vertical flow bed (120 m^2) with 1 m depth. The beds were planted with local reeds (*Phragmites karka*).	Transfer CW technology to developing countries to reduce pollution in aquatic environments	Conventional parameters: TSS, BOD_5, COD, NH_4, PO_4^{2-}, total coliforms, *E. coli*, streptococci
Sim et al. (2013)	Investigation carried out at two hospital WWTPs located in Korea to assess the occurrence and removal of selected pharmaceutical and personal care products. The wastewater treatment plants consist of (i) flocculation (FL) + activated carbon filtration (AC); (ii) flocculation + CAS.	Potential risks of anthelmintics on non-target organisms in the environment and their resistance to biodegradation	33 PhCs and personal care products
Suarez et al. (2009)	Investigation carried out in Spain into the pretreatment of hospital effluent. The efficacy of coagulation–flocculation (Coag-FL) and flotation (FLO) processes in removing PhCs was investigated in case of two kinds of hospital effluent: one from radiotherapy and outpatient consultation wards and one from hospitalized patients, surgery, laboratories, radiology and general services. Coagulation–flocculation assays were performed in a jar-test device and in a continuous pilot-scale plant. Ferric chloride ($FeCl_3$) and aluminium sulphate ($Al_2(SO_4)_3$) were added.	Potential risk of hospital wastewater to the environment	13 PhCs and personal care products; TSS, COD, fat
Vasconcelos et al. (2009)	Investigation carried out in Brazil into the potential pretreatment of hospital effluent to degrade persistent compounds. In particular the study investigated the performance of a lab-scale photo-induced oxidation, heterogeneous photocatalysis, ozonation and peroxone in degrading the antimicrobial ciprofloxacin.	Environmental impact of ciprofloxacin and analysis of its degradation by ozone and photoprocesses	Ciprofloxacin, COD.
Venditti et al. (2011)	Investigation carried out in Luxembourg on the removal of conventional pollutants and selected PhCs by means of a pilot MBR fed with hospital effluent (2 m^3/d on average). The bioreactor consists of an anoxic/oxic compartment (0.175 m^3, 0.515 m^3 respectively) and is equipped with two submerged microfiltration membrane modules (pore size 0.4 μm, total surface area 9.6 m^2). Average HRT 8 h, temperature 16–18 °C, biomass concentration 10–13.2 g/L, SRT > 30 d.	Adequateness of MBR as a pretreatment for hospital effluent	10 common PhCs, DOC, COD, BOD_5, NH4, NO_3, total N total P
Verlicchi et al. (2010)	Investigation carried out at an Italian hospital by means of a pilot-scale MBR equipped with UF membranes.	Hospitals are the main source of PhCs. Guidelines for a full scale plant for hospital effluent	Monitored parameters were COD, BOD_5, SS, NH_4, total P and *Escherchia coli*
Wen et al. (2004)	Investigation carried out at Haidian community hospital (China), where a full-scale submerged hollow fibre MBR was installed.	Efficiency and operation stability of MBR equipped with microfiltration membranes in treating HWWs	Monitored pollutants were COD, BOD_5, NH_4, turbidity and *Escherchia coli*
Wilde et al. (2014)	Investigation carried out in Brazil into the degradation of a mixture of beta-blockers in hospital effluent by ozonation and Fenton reaction.	Optimization of the operational condition in the degradation of a mixture of PhCs in hospital effluent	Atenolol, propranolol and metoprolol

mode, dosage of ozone, H_2O_2, UV irradiation, catalyst type and contact time),
- reactor types (conventional activated sludge system or membrane bioreactor (MBR); compartmentalization),
- environmental conditions (temperature, irradiation), and
- water sampling mode and frequency.

Before discussing the main results derived from these studies, a snapshot of the main chemical, physical and microbiological characteristics of HWW is provided in Table 1. References are also provided for each compiled parameter or class of compounds of PhCs.

To ease the reading of the manuscript, a brief presentation of each investigation is reported in Table 2 and the list of all the investigated treatment trains is provided in Table 3 with the corresponding references.

3. Technologies and treatment trains for HWW under review

Table 2 reports the main characteristics of the studies included in this review referring to the dedicated treatment of hospital effluent and the *rationale* behind each one.

A rapid glance at Table 2 points out that hospital effluent was subjected to different treatment levels: just a preliminary/primary (potential or actual) dedicated treatment before its co-treatment with UWW at a municipal WWTP, sometimes conventional secondary biological treatments (CAS) or modified CAS processes that are systems combining attached and suspended biomass, but also MBRs, and advanced oxidation processes (AOPs). In some countries AOPs were investigated as preliminary–primary treatments in order to enhance biodegradation in the stream.

In order to help in the reading of this review, Table 3 lists all the types of investigated technologies and treatment trains with the corresponding references. Their distribution in the different countries in the world can be found in the graphical abstract, as well as on a larger scale in Fig. SD-1 in the Supplementary data.

Most of the investigations referred to pilot/lab scale plants (69%) and the remaining 31% to full scale dedicated facilities (see Table SD-1 in the Supplementary data). The latter include the following treatment trains: septic tank followed by an anaerobic filter (Brazil, de Almeida et al., 2013; Martins et al., 2008); UASB + anaerobic filters (Brazil, Prado et al., 2011); series of maturation and facultative ponds (Ethiopia, Beyene and Redaie, 2011); septic tank + constructed wetlands (H-SSF + V-SSF beds) (Nepal, Shrestha et al., 2001); MBR (in Germany, Beier et al., 2011, 2012; in China: Liu et al., 2010; Wen et al., 2004); CAS + chlorination (in Greece, Kosma et al., 2010; in Brazil, Prado et al., 2011; in Iran, Mahvi et al., 2009); MBR + chlorination (in China, Liu et al., 2010); flocculation + activated carbon or flocculation + CAS (Republic of Korea, Sim et al., 2013); MBR + O_3 + UV (Italy, Verlicchi et al., 2010); MBR + O_3 or PAC and then sand filtration (in Germany, PILLS Report, 2012); MBR + O_3 + GAC (a full scale demo plant called Pharmafilter operating in the Netherlands, Pharmafilter report, 2013); and MBR + GAC + O_3/H_2O_2 and MBR + GAC + UV (in Denmark, Grundfos biobooster, 2012).

Moreover, 53% of the studies were carried out in European countries (Austria, Belgium, Denmark, France, Germany, Greece, Italy, Luxembourg, Netherlands, Switzerland and Turkey), 27% in Asiatic countries (China, India, Indonesia, Iran, Iraq, Nepal, Republic of Korea, Thailand and Taiwan), 16% in South America (Brazil) and 4% in Africa (Egypt and Ethiopia). PhCs were detected and removal efficiencies were evaluated in 60% of the studies included, whereas the remaining ones only refer to conventional parameters. All the studies developed in Europe investigated PhCs with the only exception of Nardi et al. (1995) (referring to prechlorination of raw hospital effluent), and Arslan et al. (2014) regarding AOPs applied on a raw HWW.

Table 3
Dedicated treatment trains for hospital effluent included in the review.

Investigated treatment/treatment train	Reference
(Pre)disinfection with ozone[1]	Chiang et al. (2003)
(Pre)disinfection with chlorine[1]	Emmanuel et al. (2004), Nardi et al. (1995), Liu et al. (2010)
(Pre)photo-Fenton[1]	Kajitvichyanukul and Suntronvipart (2006)
Coagulation–flocculation; Coagulation–flocculation + flotation	Suarez et al. (2009)
Coagulation + filtration + disinfection	Gautam et al. (2007)
Screening + O_3/UV or $O_3/UV/H_2O_2$ (+biological step)[2]	Arslan et al. (2014)
Septic tank + anaerobic filter	de Almeida et al. (2013), Martins et al. (2008)
Septic tank + HSF + VSF	Shrestha et al. (2001)
Septic tank + Fenton	Berto et al. (2009)
Flocculation + CA	Sim et al. (2013)
Flocculation + CAS	Sim et al. (2013)
Anaerobic–aerobic fixed film reactor	Rezaee et al. (2005)
Facultative and polishing ponds (II + III)[2]	Beyene and Redaie (2011)
Aerated fixed film biofilter + O_3	Prayitno et al. (2014)
CAS	Abd El-Gawad and Aly (2011), Azar et al. (2010)
CAS + support media + UF	Mousaab et al. (2015)
CAS + chlorination	Kosma et al. (2010), Mahvi et al. (2009), Prado et al. (2011)
Fungal bioreactor	Cruz-Morato et al. (2014)
UASB + anaerobic filter	Prado et al. (2011)
MBBR + ozonation	Andersen et al. (2014)
MBR	Al-Hashimia et al. (2013), Beier et al. (2012), Kovalova et al. (2012), Lenz et al. (2007a), Liu et al. (2010), Mahnik et al. (2007), Nielsen et al. (2013), Venditti et al. (2011), Wen et al. (2004)
MBR + chlorination	Liu et al. (2010), Nielsen et al. (2013)
MBR + GAC	Lenz et al. (2007b)
MBR + GAC + O_3 and or H_2O_2 + UV	Grundfos Biobooster (2012),
MBR + GAC + UV	Lenz et al. (2007b)
MBR + H_2O_2 + UV	Kohler et al. (2011), Kovalova et al. (2013)
MBR + O_3 + GAC	Pharmafilter report (2013)
MBR + O_3 + GAC+ UV	Grundfos Biobooster (2012),
MBR + public sewage + cotreatment	Beier et al. (2011)
MBR + UV	Lenz et al. (2007b)
MBR + H_2O_2	Kohler et al. (2011)
(MBR+) PAC[3]	Kovalova et al. (2013), Nielsen et al. (2013)
(MBR+) O_3[3]	Kovalova et al. (2013), Nielsen et al. (2013)
(MBR+) O_3/H_2O_2[3]	Nielsen et al. (2013)
(MBR+) UV with/without TiO_2[3]	Kovalova et al. (2013)
$UV/O_3/TiO_2$	Kist et al. (2008)
(Septic tank + anaerobic filter+) O_3, H_2O_2/O_3 [3]	Vasconcelos et al. (2009)
(Septic tank + anaerobic filter+) O_3, Fe^{+2}/O_3[3]	Wilde et al. (2014)
(Septic tank + anaerobic filter+) UV [3]	Vasconcelos et al. (2009)
(Septic tank + anaerobic filter+)TiO_2/UV[3]	Vasconcelos et al. (2009)
NF/RO (polishing)[4]	Beier et al. (2010)

[1] (Pre): means preliminary treatment.

[2] (Biological treatment) means that the investigated treatment is upstream of a biological step.

[3] Upstream treatments reported in brackets have to better define the step of the treatment considered and reported data on the removal efficiencies of PhCs do *not* include their contribution in the cited investigations.

[4] (II + III) means a series of secondary and tertiary ponds.

It is worth noting that often in Asian countries, the main reason for investigating hospital effluent treatment is the need to guarantee "safe" treatment for this kind of wastewater and to evaluate the possibility of directly reusing the treated effluent due to water scarcity for various requirements, in particular for irrigation (Al-Hashimia et al., 2013). As discussed below, although it is highly appreciable that this problem has been tackled, their common conclusion, based on an analysis of conventional contaminants whereby a secondary biological treatment followed by chlorination may be considered adequate treatment even in case of direct reuse, is not backed up by comprehensive research into micropollutants or ecotoxicology.

In European countries, the main reason for research is generally an awareness of the potential risk posed by the occurrence of PhC residues in secondary effluent and the need to reduce the PhC load discharged into the environment via WWTP effluent. There is a lively debate on the need to adopt dedicated and proper treatments for hospital effluents (Ort et al., 2010; Verlicchi et al., 2012a; Santos et al., 2013) based on the evaluation of the contribution of the health care structure and the corresponding catchment area in the discharge of PhCs.

4. Results and discussion

The following sections present and discuss collected data on the removal efficiencies of selected PhCs as well as conventional parameters from HWW by different systems acting as primary, secondary and tertiary steps. A specific section is devoted to the removal ability of microorganisms observed in the different technologies and on measures suggested to reduce the spread of pathogens and also of antibiotic resistant bacteria. Supplementary data provides a brief overview on the main reactions taking place during AOPs and might help in reading the following discussion.

4.1. Preliminary and primary treatments — pharmaceutical removal

Preliminary treatments are generally adopted and tested with the aim of removing rough and coarse material from raw wastewater, thus protecting mechanical and electrical parts in the downstream treatment steps. Specific treatments have also been tested in lab and pilot plants to reduce the toxicity of chemical mixtures occurring in hospital effluent and to enhance biodegradability (namely to increase the BOD_5/COD ratio) and to improve downstream biological processes.

Coagulation–flocculation and flotation are processes that satisfy the first objective as they promote the removal of suspended solids and colloids from wastewater which do not settle spontaneously (Gautam et al., 2007; Suarez et al., 2009), whereas ozonation (Chiang et al., 2003) and AOPs (Kajitvichyanukul and Suntronvipart, 2006) satisfy the second objective.

COD removal was found greater than 70% when 200 mg/L of ferric chloride was added to raw hospital effluent and removal increased to over 98% if the coagulant was added to settled HWW. A following step of disinfection by calcium hydrochloride not only reduces microorganisms, but also COD. It was found that with a contact time of 30 min, the $Ca(ClO)_2$ break point dose is 20 mg/L (Gautam et al., 2007).

A few studies have been carried out on the effectiveness of coagulation, flocculation and flotation in removing PhCs from hospital effluent (Suarez et al., 2009; Martins et al., 2008). Fig. 1 shows the main results when common coagulants $Al_2(SO_4)_3$ and $FeCl_3$ at a dosage of 25 mg/L are added to the raw wastewater, with and without flotation. These processes are not particularly efficient in removing PhCs, confirming the considerations reported in Verlicchi et al. (2012b). In fact, only diclofenac and some fragrances are removed by more than 60%. Fig. 1 also reports the somewhat modest removal efficiency (17%) observed for ciprofloxacin using a septic tank followed by an anaerobic filter fed with raw effluent from a hospital in Brazil (Martins et al., 2008).

Attempts to improve COD removal and increase biodegradability in *raw* hospital effluent were made by applying ozonation, O_3/UV and $O_3/UV/H_2O_2$ as a pretreatment (Arslan et al., 2014). Based on lab scale tests on effluent from a diagnostic centre, nuclear medicine, oncology, radiology and medical genetics departments, it was found that the highest COD removal (47.5%) was obtained in a system $O_3/UV/H_2O_2$ operating at pH 6.0, O_3 concentration 10 mg/L, monochromatic UV lamp (254 nm) and dosage of H_2O_2 1.8 mL within 60 min. As for absorbance removal, the best AOP is O_3/UV: in fact the addition of H_2O_2 led to a scavenger effect on hydroxyl radicals resulting in a lower removal efficiency (see Supplementary data for more details).

The results achieved from the ozonation of effluent from a kidney dialysis unit are quite interesting: at a dose of 25 mg/L of ozone and a contact time of 20 min, COD was reduced from 132 mg/L to 97 mg/L and the

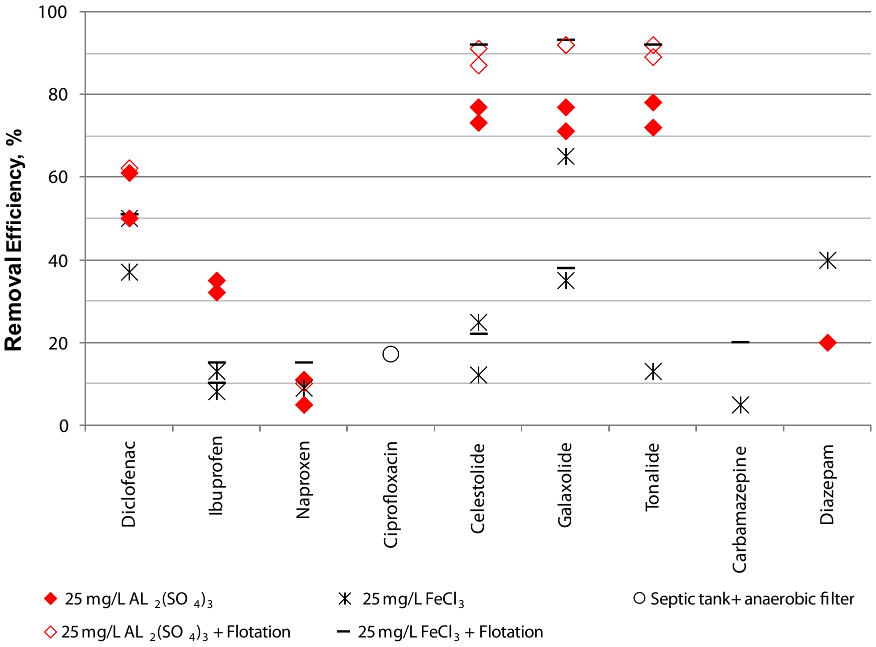


Fig. 1. Observed removal efficiencies from HWW for selected PhCs in different primary treatments.
Data from: Suarez et al., 2009; Martins et al., 2008.

ratio BOD_5/COD increased from 0.15 to 0.26 confirming a consistent increment in the biodegradability of the stream (Chiang et al., 2003).

Another option to improve biodegradability is achieved using photo-Fenton processes (see Supplementary data for the main reactions involved). It was found that in hospital effluent of average pollutant strength (COD 1350–2250 mg/L, BOD_5/COD 0.30) with a dosage ratio COD:H_2O_2:Fe^{+2} equal to 1:4:0.1, a reaction pH of 3 and a reaction time of 2 h, the removal efficiencies for BOD_5, COD and TOC were: 61%, 77% and 52% and the BOD_5/COD ratio increased from 0.30 to 0.52. It was also found that for higher COD values, optimum reaction conditions have to be tested to guarantee good mineralization of organic compounds and to enhance biodegradability (Kajitvichyanukul and Suntronvipart, 2006). The increased biodegradability of the wastewater was also confirmed by batch experiments on raw and pretreated effluent subjected to a biological process using activated sludge. It was found that in the case of pretreated wastewater, the removal of COD amounted to 90% after a 72 h treatment time, whereas it was only 30% in the case of raw hospital effluent (Kajitvichyanukul and Suntronvipart, 2006).

A Fenton process may also act as a disinfectant step: in fact it greatly removes total coliforms and thermotolerant coliforms as documented by Berto et al. (2009). The cases of complete removal observed in their investigation were ascribed to acidic conditions and the occurrence of hydroxyl radicals. Low pH values would cause bacteria death and HO• would assure DNA denaturation.

These studies led to suggest ozonation, Fenton as well as photo-Fenton processes as suitable solutions for the preliminary treatment of hospital wastewater from a technical viewpoint. An economic analysis would be necessary to assess investment, operational and maintenance costs. Moreover, the adequateness of adopting these advanced technologies as "pretreatment" also needs to be confirmed from a toxicological view point, but unfortunately, there is no available research to investigate.

4.2. Secondary treatments — pharmaceutical removal

Most of the studies investigated the capacity of MBRs as a biological stage for the treatment of HWW. Other systems analyzed include: CAS systems in Iran (Mahvi et al., 2009), Greece (Kosma et al., 2010), Egypt (Abd El-Gawad and Aly, 2011) and Belgium (Pauwels et al., 2006), an anaerobic–aerobic fixed film bioreactor in Iran (Rezaee et al., 2005), an aerated fixed film biofilter in Indonesia (Prayitno et al., 2014), a moving bed biofilm reactor in Denmark (Andersen et al., 2014), ultrafiltration membranes coupled with a modified CAS reactor by the addition of biofilm supports in France (Mousaab et al., 2015), maturation and polishing ponds in Ethiopia (Beyene and Redaie, 2011), horizontal and vertical subsurface flow systems in Nepal (Shrestha et al., 2001), and a fungal bioreactor in Spain (Cruz-Morato et al., 2014). In the first part of this section MBRs and CAS are critically analyzed and compared, the remaining systems are analyzed and compared in the second part.

4.2.1. MBR

Lessons learned from the reviewed studies, carried out all over the world, regarding the efficacy of MBRs applied to UWW in the removal of macro- and micro-pollutants (Verlicchi et al., 2012b) are certainly useful in an analysis of the performance of an MBR fed with hospital effluent. As regards this type of wastewater, special attention must be paid to evaluate the potential inhibition effect on the biological activities of PhCs, heavy metals, disinfectants, detergents that occur at higher concentrations in HWW rather than UWW thus, the risk that they could negatively affect the degradation processes of micro contaminants has to be assessed.

In the studies included herein, hospital effluent is generally subjected to a coarse screening (2 mm), sometimes through a fine screen or a sieve (0.5–1 mm), whereas a primary clarifier is only rarely adopted (HRT 2–10 h). Adequate pretreatments are extremely useful in guaranteeing continuous operation of MBRs. As reported in the investigation by Verlicchi et al. (2008), the raw HWW may contain rags, filaments, pieces of cardboard that can adversely interfere with moving parts within the WWTPs or clog membranes and thus they have to be efficiently removed at the start of the treatment train. This is in agreement with suggestions by Gabarron et al. (2013) which investigated different pretreatment processes to find the most adequate technology that would consistently contribute in minimizing the ragging impact over MBR performance.

A storage/equalization tank before an MBR guarantees homogeneous feeding avoids damage to the membrane units and may also promote sorption removal mechanisms due to the contact between solid particles and micropollutants. This is the case of cancerogenic platinum compounds (CPCs), such as cisplatin, that show a high affinity for suspended solids (Lenz et al., 2007a). In this study, the feed from the oncological ward was first collected in a tank (24 h residence time), then processed through a sieve (1 μm, to separate suspended solids from the liquid phase) and finally sent to an MBR treatment. The CPC concentration was significantly reduced after passing through the sieve and the membranes due to particle and biomass sorption onto the surface.

A biological reactor usually consists in an anoxic/oxic compartments to promote complete nitrification and denitrification. P removal, when necessary, is achieved by a co-precipitation with $FeCl_2$. Biomass concentration in the aerated compartment varied between 2 and 20 g/L, the sludge retention time ranged between 20 and 100 d with the only exception of an MBR operating in parallel with a CAS system whose SRTs were 12–15 d in each (Pauwels et al., 2006).

Ultrafiltration membranes (tubular or flat sheet, 0.03–0.06 μm) were more frequently investigated (Nielsen et al., 2013; Lenz et al., 2007a; PILLS Report, 2012 — at the Swiss, German and Dutch units within the project) than microfiltration membranes (sheet, 0.4 μm; Pauwels et al., 2006; Beier et al., 2011; Luxembourg unit within the PILLS project — PILLS Report, 2012). Submerged membrane modules integrated in the bioreactor were the most commonly adopted configuration; side stream modules were equipped only in the Dutch unit within the PILLS project and in the Austrian investigation where the MBR was fed by the oncological ward effluent (Lenz et al., 2007a).

A rapid glance at the macro-pollutant removal observed in the different MBRs shows that notably high values were found (94% for DOC, 99% for COD, 93–99% for NH_4^+, around 85% for nitrates) resulting in a high quality permeate, with reduced variability intervals for the different pollutants: DOC 6–11 mg/L, COD 20–30 mg/L and total N 3–17 mg/L with a few exceptions (McArdell et al., 2011; Wen et al., 2004).

Good biological activity was in general guaranteed and maintained throughout each observation period in the different investigations. Chemical or physical parameter shocks could occasionally occur resulting in disturbances at the biological reactors and, from a macroscopic point of view, reduced removal of macro-pollutants, namely COD, SS and N compounds, from a microscopic point of view changes, modification or disintegration of the activated sludge flocks (Pauwels et al., 2006; McArdell et al., 2011).

In this context, quaternary ammonia disinfectants are potential critical parameters, as their consumption may greatly vary from one hospital to another as remarked by Kovalova et al. (2012). As for the common quaternary ammonia disinfectant BAC C12, tolerable concentrations may reach up to 150 μg/L without inducing negative effects on the biomass (Kovalova et al., 2012; McArdell et al., 2011).

Moreover, hospital laundrette effluent represents a hotspot for certain pollutants (Kist et al., 2008). A sudden increase in formic acid concentrations may occur as reported by Pauwels et al. (2006), leading to a pH shock (2.5) in the bioreactor. This results in a process performance decrease due to the disintegration of the sludge and consequently in a dramatic decrease in COD removal.

Figs. 2 and 3 report all collected data on removal of PhCs in hospital effluent by an MBR operating at different SRT values.

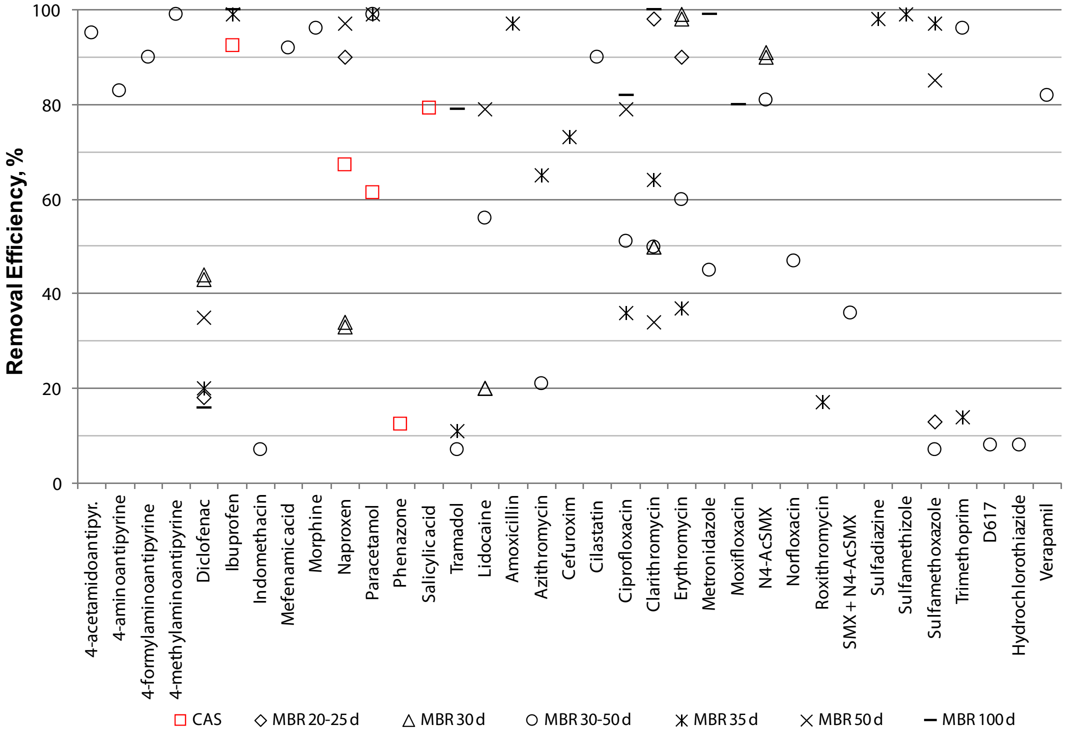


Fig. 2. Observed removal efficiencies for a group of selected compounds in MBRs and CAS operating at different SRTs.
Data from: Kosma et al., 2010; Kovalova et al., 2012; PILLS Report, 2012, Nielsen et al., 2013; Beier et al., 2011; Kohler et al, 2012.

As underlined by different studies (Clara et al., 2005; Verlicchi et al., 2012a, 2012b; Monteiro and Boxall, 2010), SRT greatly affects the removal performance of many PhCs. Long SRT values promote adaptation of different kinds of microorganisms and the presence of slower growing species which could have a greater capacity for removing more recalcitrant compounds while simultaneously improving suspended solid separation (Kreuzinger et al., 2004). Based on data shown in Figs. 2 and 3 involving removal efficiencies of compounds

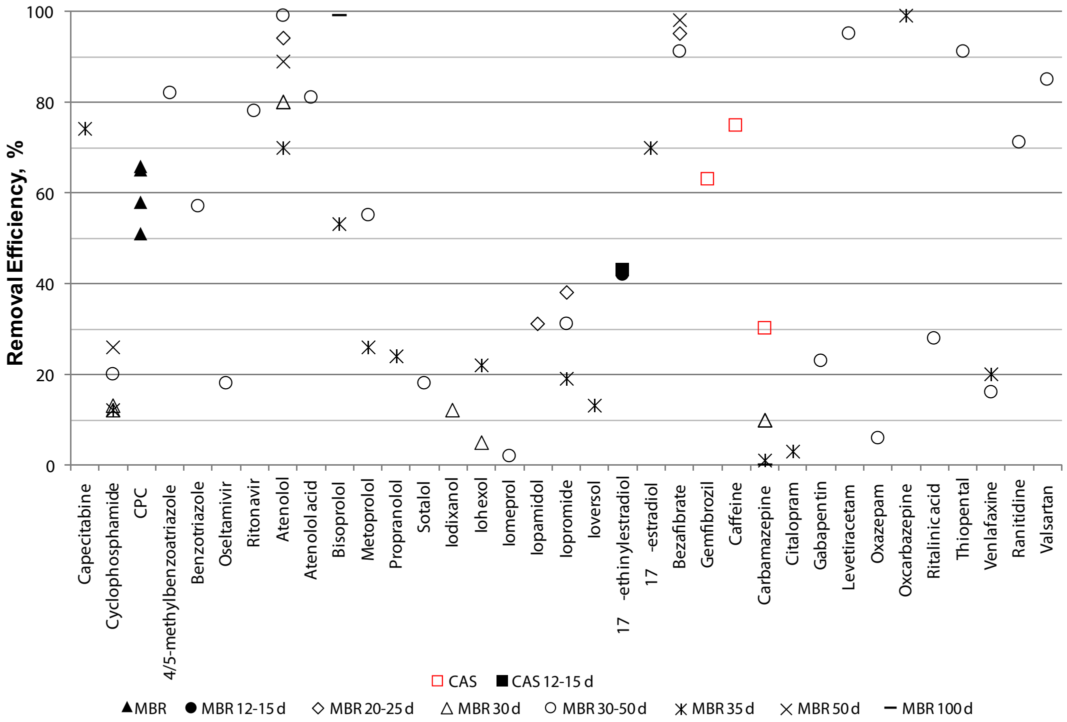


Fig. 3. Observed removal efficiencies for a group of selected compounds in MBRs and CAS operating at different SRTs.
Data from: Kosma et al., 2010; Pauwels et al., 2006; Lenz et al., 2007a, 2007b; Kovalova et al., 2012; PILLS Report, 2012; Nielsen et al., 2013; Beier et al., 2011; Kohler et al., 2012.

observed at different sludge ages, it emerges that an SRT equal to 20–25 d promotes the removal of atenolol and clarithromycin, slightly higher values (around 30 d) enhance diclofenac and erythromycin removal and around 50 d a larger number of compounds are better removed: naproxen, lidocaine, ciprofloxacin, sulfamethoxazole and cyclophosphamide.

Very good removal efficiencies of over 90% were in general observed at a SRT greater than 30 d for many of the selected compounds.

Modest removal efficiencies (<50%) were observed for metoprolol, iopamidol, carbamazepine, gabapentin and ritalinic acid.

Unfortunately, removal efficiency was always scarce (<25%) for various PhCs, namely: indomethacin, phenazone, roxithromycin, D617 (N-dealkylverapamil, a metabolite of Verapamil), cyclophosphamide, oseltamivir carboxylate, propranolol, sotalol, iodixanol, iohexol, iomeprol, ioversol and oxazepam.

The antineoplastic agents included in the CPC group show a higher removal efficiency with respect to cyclophosphamide, due to their higher affinity to sorbing onto particles and activated sludge flocks within the MBR (Lenz et al., 2007a,b).

Releases sometimes occur for diclofenac, phenazone, ciprofloxacin, clarithromycin, sulfadiazine, sulfamethoxazole, propranolol, iopamidol and carbamazepine, probably due to deconjugation during biological treatment (Kovalova et al., 2012; Nielsen et al., 2013). These are not reported in the graph in Figs. 2 and 3. An in-depth discussion of the potential release of many PhCs is reported in Verlicchi et al. (2012b) as well as in Monteiro and Boxall (2010).

Based on the Swiss research carried out within the PILLS project involving 56 compounds of different therapeutic classes, it emerged that an MBR (SRT equal to 30–50 d) is able to remove up to 90% of pharmaceuticals and metabolite *load* (X-ray contrast media excluded), although removal of some of the selected compounds was very poor (in particular, clindamycin, diclofenac and furosemide). Only 2% of the influent contrast media load was removed in the investigated MBR.

An MBR is not a satisfactory treatment process for the removal of AOX: in the permeate, AOXs occur in the range of 0.56–0.85 mg/L (Beier et al., 2011; McArdell et al., 2011) and further advanced treatment is necessary to reduce their content in the final effluent (Machado et al., 2007).

The absence of suspended solids in the MBR effluent represents a strength as it is the most important condition required by many advanced technologies in the removal of trace contaminants, as suspended solids may negatively interfere with the removal performance of said technologies.

An MBR appears to be an adequate secondary treatment for hospital effluent as it produces very good quality and stable effluent throughout the running time, and is thus suitable for advanced technologies (Venditti et al., 2011; Beier et al., 2011), including NF/RO and AOPs. Full scale MBRs have been adopted for the treatment of HWW in Italy (Verlicchi et al., 2010), Germany (PILLS Report, 2012) and China (Liu et al., 2010).

4.2.2. CAS

Only two research projects were found dealing with the removal of PhCs from hospital effluent involving "dedicated" CAS systems: one lab scale (Pauwels et al., 2006) and one full scale (Kosma et al., 2010). Pretreatment was only reported in the second case, consisting in a grit removal and mixing tank. Biological reactors had anoxic/aerobic compartments in the first case and only aerobic in the second. In the research by Kosma et al., 2010 removal efficiencies were provided for PhCs after CAS (HRT 6 h) + chlorination.

Only 10 PhCs were monitored in these dedicated CAS systems. High removal efficiencies were observed for ibuprofen (92%), salicylic acid (79%) and caffeine (75%), naproxen, gemfibrozil, paracetamol and ethynyl estradiol (EE2) were moderately removed (67%, 63%, 61% and 43% respectively), whereas scant removal was found for carbamazepine and phenazone (30% and 13% respectively). A modest release (−17%) was observed for diclofenac.

4.2.3. Comparison between CAS and MBR

In the research by Pauwels et al. (2006), CAS and an MBR were operating in parallel, fed with the same hospital effluent (spiked with EE2 up to 1 mg/L). With respect to the MBR, the CAS system exhibited a slower start up and was more prone to bulking. Moreover, COD removal was worse in the CAS system (88% in CAS vs. 93% in an MBR) as was the removal of various bacterial groups: total coliforms, faecal coliforms and total anaerobic bacteria (about 2 log units less) and total aerobic bacteria (1.4 log units less). No differences were found in the removal of EE2 between CAS and MBR.

The higher removal efficiencies observed for some bacterial groups in the MBR permeate are due to membrane retention. Their occurrence in the MBR effluent may instead be explained by unavoidable bacteria regrowth from the effluent vessel into the permeate collecting tube and also by the absence of proper membrane cleaning while the system was running, as disinfection was not applied (Pauwels et al., 2006).

Lessons learned from previous studies on removal of PhCs by means of CAS and an MBR fed with UWW (Verlicchi et al., 2012a,b) highlighted that in the MBR, the combination of higher biomass concentration in the aerated basin, development of different bacterial species within the biomass, smaller sludge flocks that may enhance sorption on the surface of different contaminants, higher SRTs and higher removal of suspended solids, greatly contributes to the removal of PhCs from the stream. Moreover, as discussed below, passage through ultrafiltration membranes guarantees disinfection of the wastewater, thus reducing the risk of spread of pathogenic bacteria and of multi-drug resistant bacteria.

4.2.4. MBR upgrade

Recently, an upgrade of the MBR system was researched by Mousaab et al. (2015) with the aim of improving PhC removal efficiencies and membrane function. The system consisted in an activated sludge basin coupled with an external ultrafiltration membrane module (0.2 μm), operating at a SRT 20 d, HRT 22 h, T 18–20 °C and pH 6.8–7.9. In the first 75 d, it worked under "usual" conditions. Then, HDPE support media were added to the biological reactor (specific area: 600 m^2/m^3; diameter: 12.2 mm; length: 12 mm, density: 0.95–0.98 kg/m^3) promoting the development of a hybrid (attached and suspended) biomass and a longer SRT of fixed organisms. In the modified bioreactor, higher removal efficiencies were observed for soluble COD (91.8% vs. 86.9%), TSS (100% vs. 99.6%) and VSS (93.2% vs. 87.9%) and removal efficiencies greater than 95% for codeine, pravastatin, ketoprofen, diclofenac, roxithromycin, gemfibrozil and iohexol, whereas in the unmodified MBR their removal was either absent or very low. The presence of biofilm supports also enhanced particle sorption and improved effluent quality, thus offering better protection of the membranes against fouling and reducing cleaning operations.

Enhanced removal of P compounds from hospital effluent could be obtained by sequencing anoxic/anaerobic MBRs. Al-Hashimia et al. (2013) found that the optimal phase for this type of system is operating with an internal recycling mode of 2 h anoxic followed by 2 h anaerobic. These conditions provide an optimal simultaneous removal efficiency of 93% for N compounds and 83% for P compounds (expressed as $P\text{-}PO_4^-$).

4.2.5. Other investigated biological systems

In Nepal, in 1997 a dedicated treatment plant was built for hospital effluent. It consists of a three chambered septic tank (16.7 m^3) providing pretreatment, followed by CW systems: a horizontal subsurface flow bed (140 m^2, 0.65 m deep and 0.75 m high, filled with 5 mm crushed gravel) and a vertical flow bed (120 m^2, 1 m deep, filled with clean sand) as a secondary step. Very good removal efficiencies were observed for TSS and BOD_5 (97–99%), COD (94–97%), $N\text{-}NH_4$ (80–

99%), total coliform (99.87–99.999%), *E. coli* (99.98–99.999%) and *Streptococcus* (99.3–99.99%) (Shrestha et al., 2001).

In Ethiopia, a series of waste stabilisation ponds (2 facultative ponds, 2 maturation ponds and 1 fish pond covering an area of about 3000 m^2 with a total retention time of 43 d) was found to be reasonably efficient in the removal of BOD_5, COD, sulphide, suspended solids and N compounds from hospital effluent (Beyene and Redaie, 2011). Despite the satisfactory removal of total and faecal coliforms (99.7 and 99.4% respectively), their final concentrations do not fulfil WHO recommendations for restricted and unrestricted irrigation. Options to improve the quality of the final effluent were considered: for instance adoption of (*i*) constructed wetlands; (*ii*) two successive lagoons followed by infiltration into the land; (*iii*) MBR advanced oxidation treatment to better remove all the parameters as well as pharmaceuticals; and (*iv*) photo-Fenton process to reduce toxicity. Only the first option was considered feasible, whereas the second could lead to groundwater contamination and the applicability of the remaining options was found difficult in terms of cost, installation, operation and maintenance.

In Iran, hospital effluents are generally discharged into a public sewage system and then co-treated with urban effluents. Usually they are subjected to a secondary treatment; disinfection is mandatory in case of disease outbreaks and in critical periods (in the summer and autumn due to reduced river water flow) (Mahvi et al., 2009). The most common malfunctions are due to operator inexperience at the WWTP and negligent WWTP management by the authorities. Investigations were carried out on pilot plants with the aim of evaluating (*i*) proper pretreatment of hospital effluent before discharge into a public sewage system followed by co-treatment (Rezaee et al., 2005) and (*ii*) a (co)-treatment train able to respect Iranian legal requirements for physical, chemical and microbiological parameters for direct discharge into the surface body, disposal to wells and reuse in agriculture (Azar et al., 2010). These investigations found that an integrated anaerobic/aerobic fixed film bioreactor can greatly remove organic and nitrogen compounds from raw hospital wastewater and when followed by co-treatment consisting in primary treatment, an aerobic/anaerobic activated sludge reactor fulfils the legal requirements for conventional parameters. These conclusions however do not consider any kind of more recalcitrant compounds (pharmaceuticals, contrast agents, disinfectants) whose removal is poor in the investigated biological systems.

Another treatment train was investigated in Indonesia consisting in an aerated fixed film biofilter followed by an ozone reactor. Satisfactory removal efficiencies were observed for BOD_5 (97.5%), faecal coliform (99.23%), Pb and phenol (100%), but there was no chemical analysis involving pharmaceuticals, disinfectants or detergents (Prayitno et al., 2014).

As for preliminary treatments, in addition to what has already been reported in Section 4.1, chemical flocculation followed by a CAS process represents an efficient barrier for anthelmintic drugs (albendazole and flubendazole) considering that overall removal is in the range of 67–75% (Sim et al., 2013).

Modifications to biological reactors to enhance micropollutant removal have undergone in-depth analysis during the last years. This is the case of Andersen et al. (2014) where on a pilot scale, the combination of a moving bed biofilm reactor followed by an ozonation stage was investigated. A biological system was developed (called a staged MBBR) to attempt to improve the creation of fixed biofilms where slow-growing bacteria would stand a better chance of development (these bacteria are very efficient in removing pharmaceuticals) compared to biomass developed in CAS systems. Higher removal efficiencies were observed for ketoprofen and gemfibrozil and occasionally for diclofenac and clofibric acid.

Interesting and promising results were observed for many PhCs in a batch fluidized bed bioreactor under sterile and non-sterile conditions with *Trametes versicolor* pellets (Cruz-Morato et al., 2014) fed with hospital effluent, operating at pH 4.5, T 25 °C, 1.4 g dry weight biomass per litre and with a continuous addition of glucose and ammonium tartrate as a nutrient source for the biomass. Sterile conditions showed that *T. versicolor* is responsible for the removal of the detected compounds. Very good removal efficiencies were observed for analgesics and anti-inflammatory drugs after 1 d and complete removal of most was observed after 8 d, with the only exception of salicylic acid and dexamethasone. Although antibiotics were partially removed and required longer times (5 d against 1 d for analgesics), the fungal treatment achieved better results than conventional activated sludge (CAS) processes (Verlicchi et al., 2012a,b) for the most part. This is the case of ciprofloxacin (69% and 99% in sterile and non-sterile conditions respectively, vs. 58–78% in CAS) and clarithromycin (80% in non-sterile conditions vs. 46–62% in CAS). Higher removal efficiencies were also observed for the anti-hypertensives: valsartan (90 and 95% after 8 d in sterile and non-sterile conditions), irbesartan (73 and 98% in sterile and non-sterile conditions) and diuretic furosemide (100% and 80% in sterile and non-sterile conditions vs. 33–54% in CAS). As for diclofenac, complete removal was observed. This is an important result as it is one of the most persistent compounds in CAS and also a potential candidate for regulation by European legislation. On the other hand, a disadvantage of this process is that after treatment, pH neutralization is necessary as secretion of organic acids by the fungus lowers the overall pH.

As concerns the investigations carried out in Iran, Iraq and Indonesia, it is important to underline that final effluent from treatment trains including CAS or ponds generally should not be directly reused for irrigation purposes due to the occurrence of residues of PhCs and other emerging contaminants. AOPs should be included in the treatment trains and in any case, further research into the ecotoxicological characteristics of the final effluent should be carried out.

4.3. Tertiary treatments — pharmaceutical removal

4.3.1. Filtration through powdered or granular activated carbon (PAC and GAC)

Filtration through PAC and GAC has undergone in-depth investigation by different European research groups. Figs. 4 and 5 report all the collected data. In all cases included in this study, PAC/GAC treatment followed an MBR fed only with hospital effluent. In the permeate DOC was in the range of 6–8 mg/L and TOC around 20 mg/L (McArdell et al., 2011; Nielsen et al., 2013).

The adsorbent used in the Swiss research was PAC (McArdell et al., 2011) with a surface area of 1300 m^2/g, a particle size d_{50} 15 μm and a zero surface charge point pH_{PZC} equal to 8.8 (this last value represents the pH at which on the carbon surface there are as many positively as negatively charged functional groups; below this value the carbon surface is positively charged). In the PAC reactor, good mixing guaranteed a constant concentration of the adsorbent, its retention time was 2 d as a few differences were found with longer times. Good separation between loaded PAC and treated effluent was achieved by *filtration* through UF membrane flat sheets (pore size 0.04 μm) in the PILLS project plants (McArdell et al., 2011; PILLS Report, 2012) and through a 1 μm glass fibre filter in the Dutch research (Nielsen et al., 2013). Nanofiltration opposed to ultrafiltration would certainly be convenient from a technical view point (improved PhC removal), but not from an economic one, as nanofiltration concentrate would require dedicated treatment due to the high concentrations of micropollutants. Another option could be pumping the loaded activated carbon from the PAC reactor to the MBR for recycling: a consistent improvement in the removal of contaminants could result. But neither of these processes were researched.

The investigated doses of PAC ranged between 8 and 23 mg/L in the Swiss and German research studies (PILLS Report, 2012) and between 150 and 450 mg/L in Dutch studies (Nielsen et al., 2013). The former range, which is absolutely more sustainable from an economic view point, was defined on the basis of costs and reasonable removal rates for a wide spectrum of micropollutants (56 compounds), the latter

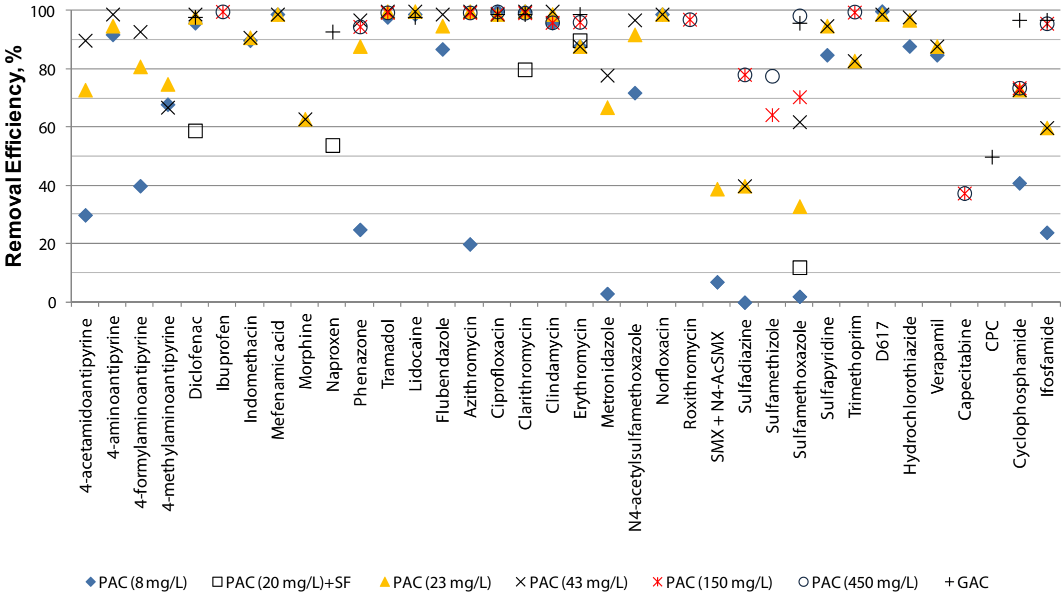


Fig. 4. Observed removal efficiencies for a group of selected PhCs in HWW by PAC and GAS systems.
Data from: Kovalova et al., 2013; PILLS Report, 2012; Nielsen et al., 2013; Lenz et al., 2007b.

was based on a Swedish study on the removal of micropollutants in aquatic environments (Walhberg et al., 2010).

In the PAC filter effluent, DOC occurred at about 4–4.5 mg/L (PAC dose 8 mg/L), 2.7–3.7 (PAC dose 23 mg/L) and about 2 mg/L (PAC dose 43 mg/L).

Within the Swiss campaigns, at the applied PAC dose of 8 mg/L, 25 out of the 56 investigated pharmaceuticals were subjected to high removal efficiencies (>80%) whereas 10 compounds exhibited removal efficiencies below 20%; at the intermediate value of 23 mg/L a removal efficiency greater than 80% was observed for 36 compounds and less than 20% for only two contrast media (diatrizoate and ioxitalamic acid). When 43 mg/L of PAC was dosed, 38 compounds had high removal efficiencies (>80%) and the same two contrast agents still had scant removal efficiencies (<20%).

A rapid glance at the results achieved within the Dutch research (Nielsen et al., 2013) shows that no significant differences were observed in the removal of the 30 selected pharmaceuticals by applying 150 mg/L or 450 mg/L of PAC.

A comparison between the Dutch campaign and the PILLS project, referring only to the 24 compounds monitored in all the cited studies,

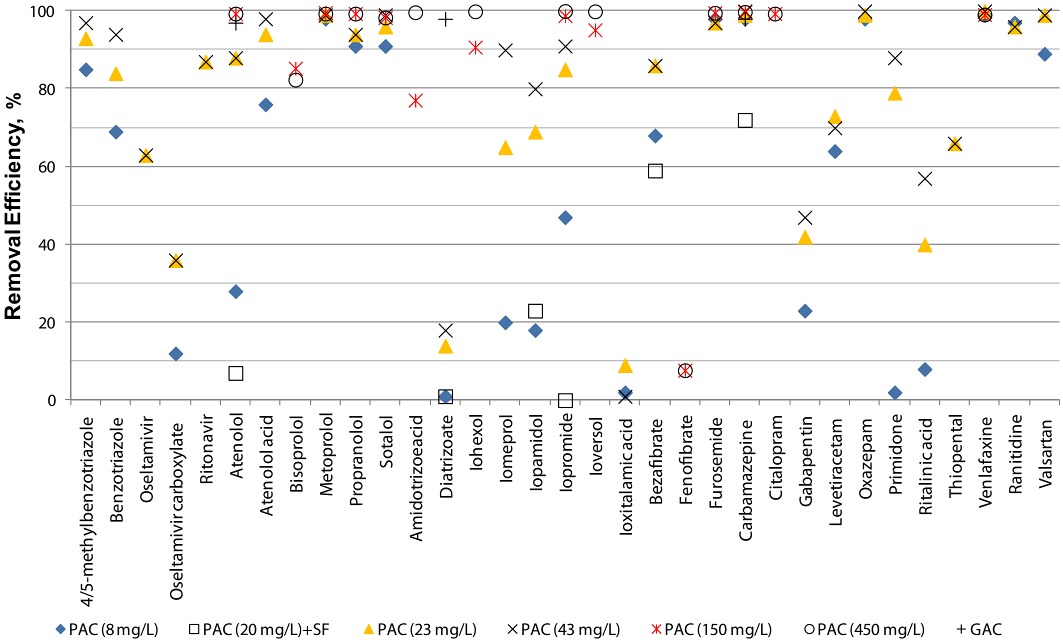


Fig. 5. Observed removal efficiencies for a group of selected PhCs in HWW by PAC and GAC systems.
Data from: Kovalova et al., 2013; PILLS Report, 2012; Nielsen et al., 2013.

highlights that only for 5 PhCs a higher removal efficiency was achieved with the (extremely high) Dutch dosages. This occurred for the antibiotics sulfadiazine (40% vs. 78% at both high doses), sulfamethoxazole (62% vs. 71% and 99% at the two doses) and trimethoprim (83% vs. 99.9% at both doses), the contrast agent ifosfamide (60 vs. 96%), and the beta blocker atenolol (88 vs. 99%).

Attempts to correlate the observed removal efficiency of PhCs by using PAC and their sorption potential expressed in terms of K_{ow} or D_{ow} (also accounting for acid–base speciation) were done by the Swiss research group (Kovalova et al., 2013; McArdell et al., 2011). As regards neutral (i.e., not charged) compounds at pH 8.8 (namely carbamazepine, oxazepam, 4-acetamidoantipyrine, cyclophosphamide, iomeprol, iopamidol, iopromide, metronidazole, phenazone and primidone), it was found that the higher the D_{ow} value, the higher the observed removal by sorption. On the contrary there is no agreement between experimental data and prediction from Log D_{ow} of sorption removal for *charged* compounds.

These results confirm that removal mechanisms consist in nonspecific dispersive interactions and electrostatic interactions as well as between the charged adsorbent surface and ionic adsorbate. Moreover, not only Log D_{ow} influences the behaviour of a pharmaceutical, but also its pK_a, molecular size and aromaticity/aliphaticity potential as well as the presence of functional groups. As regards PAC, effective removal mechanisms depend on surface area, pore size and texture, surface chemistry (in particular functional groups and point of zero charge) and mineral matter content.

As a rule of thumb, adsorption is most effective for compounds which are uncharged and apolar.

An interesting analysis and discussion of the behaviour of many compounds is reported in Kovalova et al. (2013) and McArdell et al. (2011).

A consistent improvement in the removal of contrast media may be achieved by recycling PAC to biological treatment as documented in the MicroPoll projects (Zwickenpflug et al., 2010).

GAC filtration was investigated at the Netherlands research unit within the PILLS project (PILLS Report, 2012) and also in Austria where the oncological ward effluent in a hospital was subjected first to an MBR then to GAC treatment (Lenz et al., 2007b). In the first case, the filter bed had a height of 3.0 m and an empty bed contact time of 51 min. It was fed by MBR permeate (TOC equal to 8.7 mg/L). After GAC filtration, all investigated pharmaceuticals were found below their detection limits. Also sulfamethoxazole, reluctant to PAC sorption, was removed by more than 96%. Unfortunately data referring to contrast agents were not collected.

In the second case, the GAC filter had a height of 36.7 cm, a cross surface of 19.6 cm^2 and a flow rate of 7.6 L/h. Antineoplastic compounds (the cancerostatic platinum compounds CPC cisplatin, carboplatin, oxaliplatin and 5-fluorouracil) were monitored in the GAC influent (corresponding to an MBR permeate) and effluent. Referring to total Pt content, it was observed that GAC contributed to a removal rate of about 50%. As discussed below, a combination of UV with GAC leads to a lesser removal rate of total Pt. This may be due to the fact that the photodegradation products of CPCs exhibit lower affinity to activated carbon than the parent compounds.

It is interesting to observe that with PAC and GAC no byproducts occur, with respect to all oxidation processes (ozonation and AOPs in general) where oxidation and photodegradation compounds are unavoidable and often they have ecotoxicological effects.

4.3.2. Ozonation

In ozonation investigations, the influent to each ozone reactor was always an MBR permeate (McArdell et al., 2011; Nielsen et al., 2013), with a COD ranging from 12 to 30 mg/L, a DOC ranging from 6 to 11 mg/L, pH 8–8.5 and T 20–22 °C (Kovalova et al., 2012). Contact time within the ozone reactor was between 12 and 23 min and the applied dose of ozone was between 0.45 and 2 g O_3/g DOC (PILLS project) and between 4.1 and 7.8 g O_3/g TOC in the study by Nielsen et al. (2013). Higher concentrations of ozone were not tested as they would lead to the formation of potentially toxic bromates, according to literature (von Gunten, 2003).

As is clearly shown in Figs. 6 and 7, the higher the applied ozone dose, the greater the number of compounds with a removal efficiency >90%. At the lowest tested value of 0.45 g O_3/g DOC (German unit within the PILLS project, PILLS Report, 2012), 3 out of the 11 investigated compounds were efficiently removed (namely diclofenac, sulfamethoxazole and erythromycin), the number increases to 26 out of

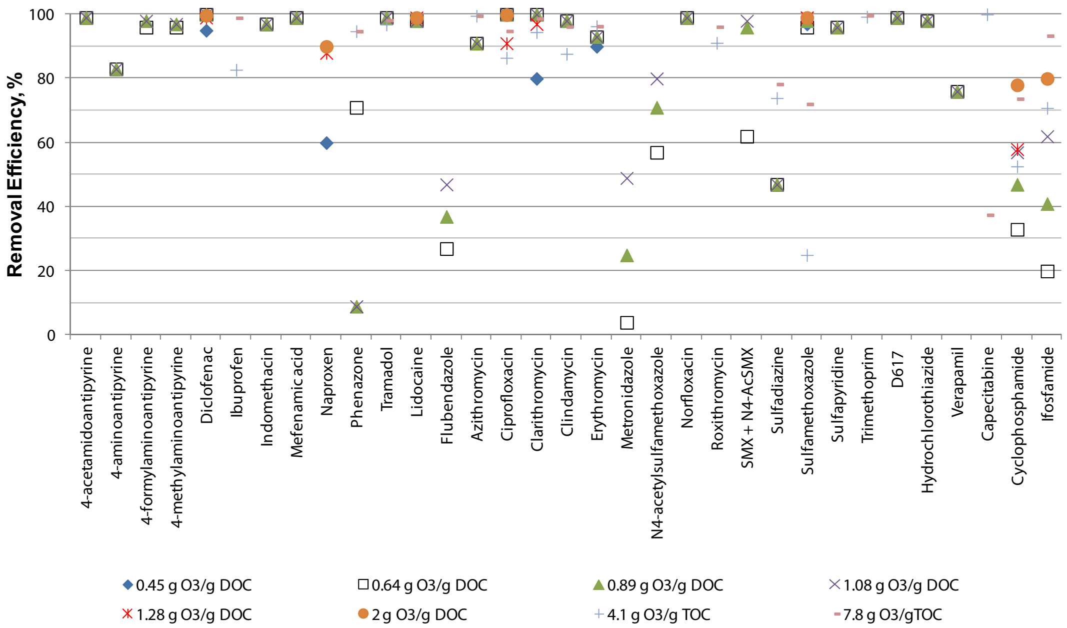


Fig. 6. Observed removal efficiencies for a group of selected PhCs in HWW by ozonation.
Data from: PILLS Report, 2012; Kovalova et al., 2013; Nielsen et al., 2013; Lenz et al., 2007b.

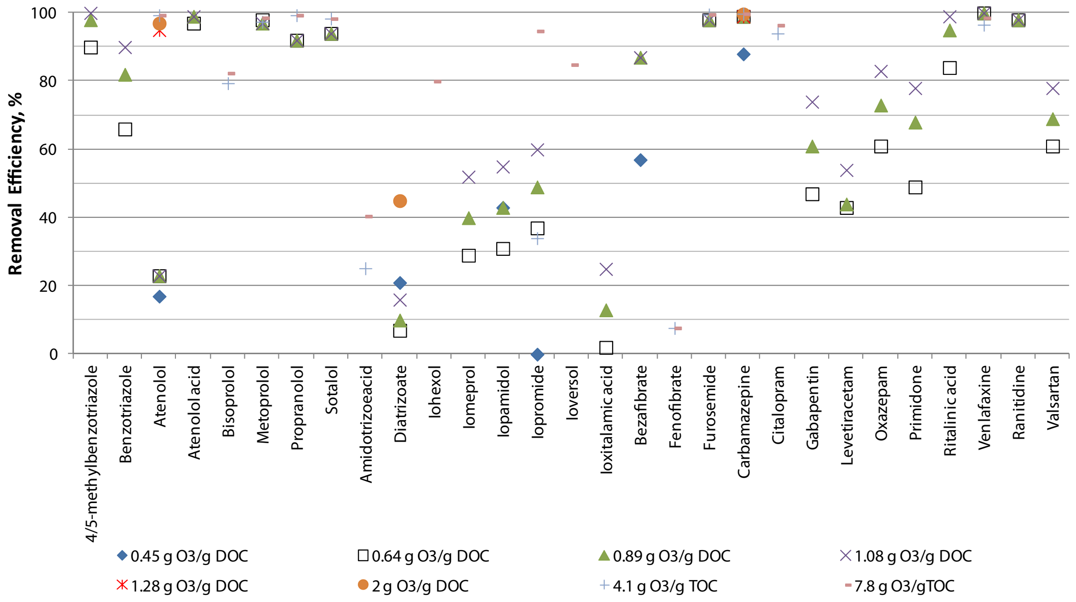


Fig. 7. Observed removal efficiencies for a group of selected PhCs in HWW by ozonation.
Data from: PILLS Report, 2012; Kovalova et al., 2013; Nielsen et al., 2013; Lenz et al., 2007b.

the 48 selected compounds at 0.64 g O3/g DOC (Kovalova et al., 2013), to 28 out of 49 at 0.89 and 29 out of 49 at 1.08 g O_3/g DOC (Kovalova et al., 2013).

The classes of cytostatics and contrast agents were quite reluctant to removal by ozonation: the average removal efficiencies observed were always lower than those observed for other classes. At medium-high ozone doses, only some compounds of these two classes were removed by about 50–60%. This occurred to cyclophosphamide, ifosfamide, iopamidol and iopromide at doses of about 1.1 g O_3/g DOC and 4.1–7.8 g O_3/g TOC (Nielsen et al., 2013). The most reluctant compounds to be removed by ozone were the contrast agents diatrizoate and ioxitalamic acid, the antibiotic metronidazole and the anthelmintic flubendazole whose average observed removal efficiencies were between 13 and 27%.

This treatment did not consistently decrease COD and DOC as ozonation does not *eliminate* (that is, *mineralize*) organic matter and micropollutants but rather transforms them into other more degradable compounds also measured as COD and DOC.

It is quite interesting to point out that ozonation seems to be a quite promising treatment for the abatement of most of the micropollutant load in hospital effluent. It is important to bear in mind one of the lessons learned by the PILLS project: based on a Swiss research referring to the top 100 administered pharmaceuticals in the investigated large hospital (McArdell et al., 2011), a removal efficiency of 90% was observed for all the PhCs and metabolite *load* (ICM excluded) by ozone (1.08 g O_3/g DOC, pH 8.5, T = 22 °C). This removal reduces to 50% if contrast agents are included. This could lead to the consideration that sewage conveying radiological ward effluent could be separated and treated by a dedicated WWTP, so it could also be possible to recover iodium.

The main disadvantage in adopting ozonation, and more in general AOPs, is the formation of oxidation byproducts (like bromates) due to the matrix compounds (for instance bromides). As these products could have ecotoxicological effects, it is advisable to adopt a biological step (namely a sand filter or an MBBR) that will act as a barrier. In the Swiss research, the concentration of bromide in the permeate was 30–40 μg/L and after the addition of the highest dose of ozone (1.08 g O_3/g DOC, corresponding to 7 mg O_3/L), bromate was found at a concentration of 1 μg/L, well below the Swiss drinking water standard set at 10 μg/L.

Ozonation reactions were due to the very selective attack of ozone to specific functional moieties of organic substances and to the less selective attacks of hydroxyl radicals ($HO^\cdot$), formed during ozone decomposition, to a wider spectrum of functional groups within the molecules. Ozone decomposition is favoured by the presence of hydroxyl ions (OH^-) at alkaline pH (pH > 9).

The following rules of thumb could lead to a rough prediction of the efficacy of ozonation in removing different types of micropollutants resulting from studies on the kinetics of ozonation reactions and on the potential correlation between molecular structure (presence of

Table 4
Main operational parameters in the UV reactors included in this study.

Unit→ ↓Parameter	Austria	Switzerland	Luxembourg
Plant type	Pilot	Pilot	Pilot
Lamp	LP	LP	LP and MP
Actual fluence, J/m^2	110,000	800, 2400, 7200	7400–29,700 (LP) 10,125–506,250 (MP), λ = 200–280 nm 5400–270,000 (MP), λ = 280–315 nm 4725–236,250 (MP), λ = 200–280 nm and 315–400 nm
Residence time, s	120	18, 54,162	18–71 (LP), 1.3–64 (MP)

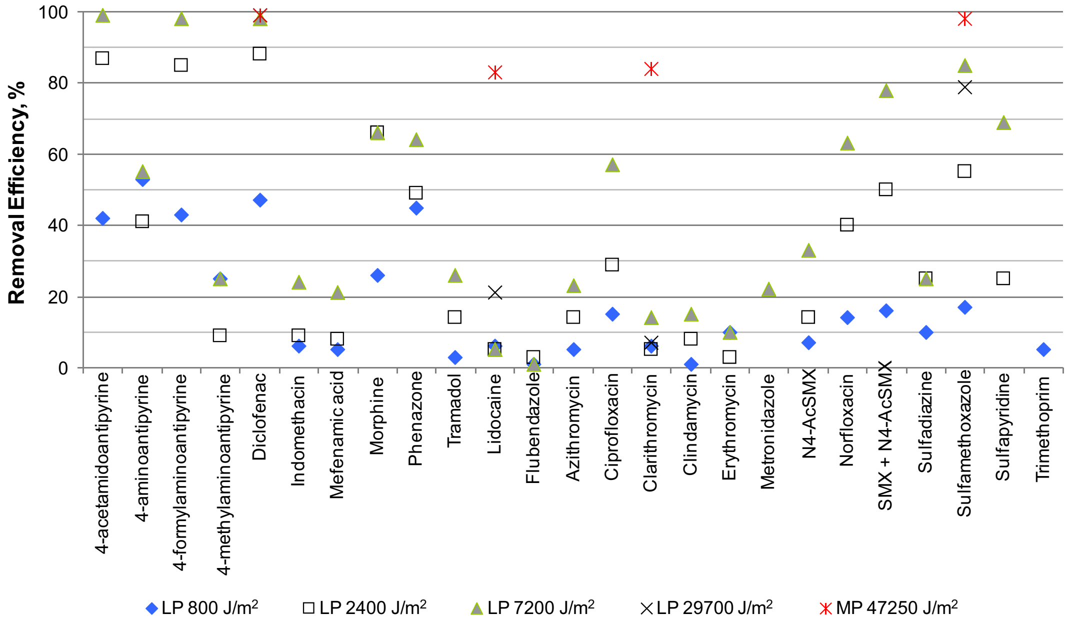


Fig. 8. Observed removal efficiency for a group of selected PhCs in HWW by UV treatment.
Data from: Kovalova et al., 2013; PILLS Report, 2012; Kohler et al., 2012.

moieties within the molecule) of a compound and its reactivity with ozone (Lee and Von Gunten, 2010):

(i) olefin, phenol, aniline, thiophenol, thiol and tertiary amine exhibit a high reactivity with ozone,
(ii) secondary amines, thioester and anisol an intermediate reactivity,
(iii) primary amines and nitro group a slow reactivity and
(iv) amides do not react with ozone.

Compounds with a high reactivity to ozone are already removed to a high extent at the lowest dose of 0.64 g O_3/g DOC. For compounds with intermediate reactivity, such as benzotriazole and ritalinic acid, higher removal efficiencies were observed with higher ozone doses. Lowest removal efficiency was found in contrast agents without moieties.

4.3.3. UV radiation

Only a few investigations (within the PILLS project (PILLS Report, 2012) and at the oncologic ward in a hospital in Vienna (Lenz et al., 2007b)) dealt with the ability and the contribution of an UV irradiation process in the removal of PhCs from (pretreated) hospital effluent: in each one, the UV reactor was always fed by an MBR permeate (DOC = 6–8 mg/L). The main characteristics of the tested equipment are reported in Table 4 (PILLS Report, 2012, McArdell et al., 2011; Lenz et al., 2007b): in particular different fluence values were tested and, in

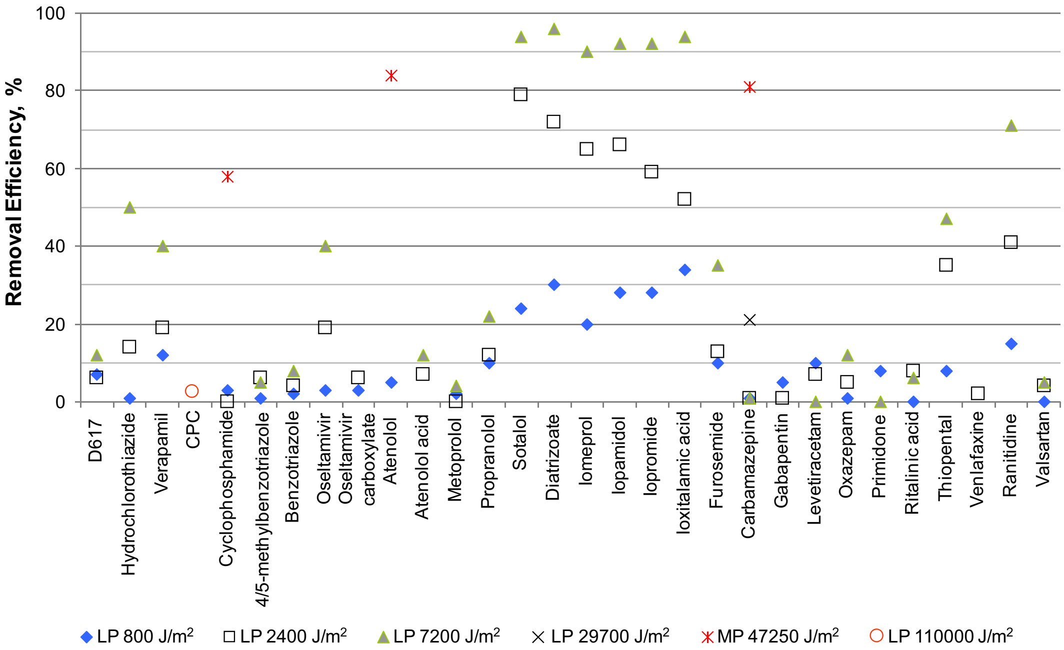


Fig. 9. Observed removal efficiency for a group of selected PhCs in HWW by UV treatment.
Data from: Lenz et al., 2007b; Kovalova et al., 2013; PILLS Report, 2012; Kohler et al., 2012.

the Luxembourg unit, low and medium pressure (LP, MP) UV lamps were used and for some runs, a polychromatic light was applied to the water stream. The collected data are reported in Figs. 8 and 9 referring to the lamp type and the applied fluence.

Observed removal efficiencies for the investigated compounds were always less than 50% when the UV fluence of 800 J/m^2 was applied. At 2400 J/m^2, 12 out of 31 PhCs were removed at more than 50% and with 7200 J/m^2, 18 out of 31 compounds exceeded the 50% removal threshold. If the UV is irradiated at higher fluence values, removal increases (for instance at 29700 J/m^2 or 47250 J/m^2). When MP lamps were used, a polychromatic light was produced and all the seven investigated compounds were successfully removed. Figs. 8 and 9 clearly show, with the exception of cyclophosphamide ($\eta = 58\%$), that the removal efficiency of the other compounds ranged between 81 and 98%, on average 83%.

Compounds with the highest removal efficiencies were: 4-acetamidoantipyrine (99% with LP and 7200 J/m^2), diclofenac (99% with LP lamp and 29,700 and 47,250 J/m^2), diclofenac and 4-formylaminoantipyrine (98%, with LP and 7200 J/m^2), sulfamethoxazole (98% with LP lamp and 47,250 J/m^2), diatrizoate (97% with LP and 7200 J/m^2), sotalol (95% with LP and 7200 J/m+) and the remaining X ray contrast media (iomeprol 90%, iopamidol, iopromide and ioxitalamic acid 92% with LP and 7200 J/m^2). This last result is quite interesting, as the UV process seems to be the most effective treatment to remove these from the wastewater.

The contribution of an UV process in the removal of antineoplastic compounds was found to be negligible. This was concluded by Lenz et al. (2007b) who monitored the cancerostatic platinum compounds (CPCs) cisplatin, carboplatin, oxaliplatin and 5-fluorouracil in the effluent of a hospital oncological ward. They found that oxidation of CPC by UV leads to a marginal reduction of total Pt as, even if the substances are transformed by oxidation, the total amount of Pt remains the same. As for cyclophosphamide, removal efficiency was found higher in the case of medium pressure UV lamps than in the case of LP lamps (58% vs. 3%).

It was observed that UV irradiation is a promising technology in the removal of X-ray contrast media. Very appreciable results were observed when a fluence of 7200 J/cm^2 was applied. At higher values the removal of different analgesics, antibiotics and beta-blockers increased (Kovalova et al., 2013).

Transmission of UV in water is strictly correlated to water turbidity. Very low turbidity is recommended in order to greatly reduce potential interferences with the water matrix. Excessive dosages of chemical oxidisers may act as a scavenger thus inhibiting contaminant destruction efficiency.

UV transmission is subject to decrease due to lamp fouling. To reduce lamp fouling, adequate pretreatments are necessary, insoluble oil and grease concentrations should be minimized and heavy metal ion concentration should be maintained at a concentration less than 10 mg/L.

4.3.4. Advanced oxidation processes (AOPs)

4.3.4.1. Removal of pharmaceuticals. Advanced oxidation processes include different technologies aiming to completely oxidize and/or destroy different kinds of organic pollutants in water and wastewater streams into H_2O, CO_2 and mineral salts.

Each one is characterized by a variety of *radical reactions* due to highly reactive species (mainly hydroxyl radical HO•, but also superoxide radical anion O_2^-•, hydroperoxyl radicals HO_2•, ROO^-), generated on site in different ways, involving combinations of chemical agents (namely ozone, hydrogen peroxide, transition metals, metal oxides) and auxiliary energy sources (namely UV irradiation, electronic current, y-radiation and ultrasound). This study includes combinations between O_3 and H_2O_2 as chemical agents and UV irradiation as an energy source.

HO• is the primary oxidant in AOPs and unlike many other radicals it is non-selective, it readily reacts with many organic pollutants occurring in the water, converting them into more hydrophilic compounds than the original ones.

A brief presentation of each, including the main reactions occurring during AOPs is reported in the Supplementary data, whereas below, the results obtained in the different investigations into AOPs applied to hospital effluents as polishing treatments are presented (Fig. 10) and discussed.

In the experimental setup tested in Switzerland within the PILLS project (McArdell et al., 2011), the photocatalysis process UV/TiO_2 was compared to the UV process alone. This setup includes a reaction

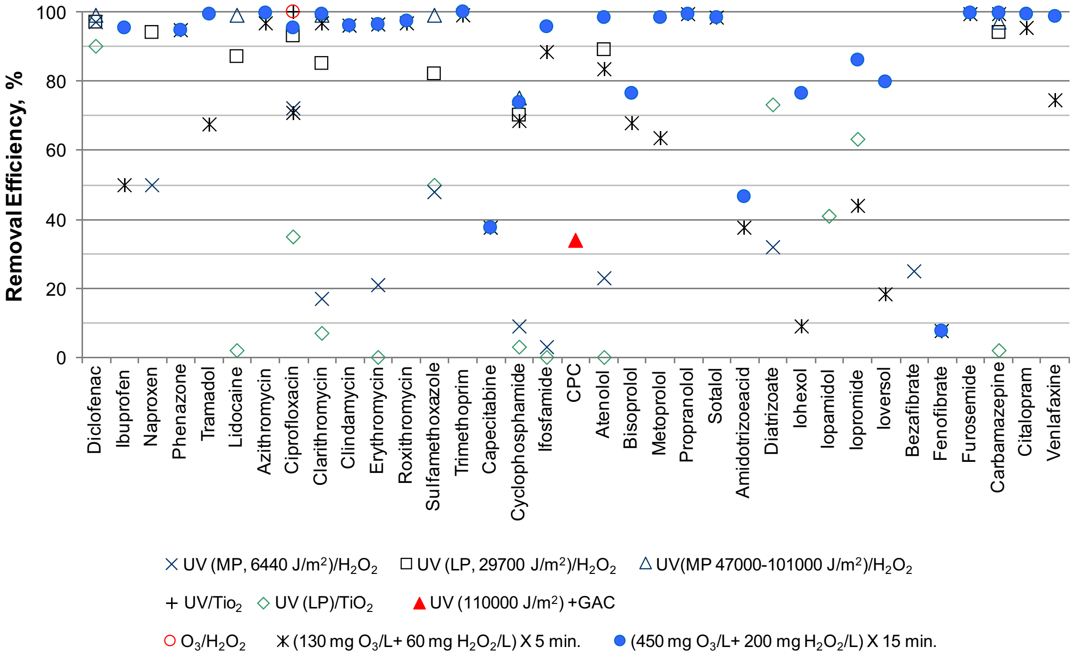


Fig. 10. Observed removal efficiencies for a group of selected PhCs in HWW by AOPs.
Data from: Lenz et al., 2007b; Vasconcelos et al., 2009; PILLS Report, 2012; Nielsen et al., 2013.

column containing four conical cartridges, consisting in a photocatalytic fibre (titanium-dispersed silica-based fibre with a sintered anatase-TiO_2 layer on the surface), around a low pressure UV lamp (254 nm, 220 V, 100–400 W overall energy consumption, 10 mW/cm^2 nominal fluence rate). To protect the fibre from particle contamination, two pre-filters with a mesh width of 25 and 5 μm were installed. The elimination rate was evaluated after 1, 3 and 9 cycles with the photocatalytic chamber (UV/TiO_2) and with UV only. Removal obtained with one cycle was marginal.

Another interesting investigation was carried out by Vasconcelos et al. (2009), aiming to compare the degradation of just ciprofloxacin in hospital effluent by ozonation, UV irradiation, UV/TiO_2 and O_3/H_2O_2. As to TiO_2/UV lab scale equipment was used and TiO_2 was added as a suspension (400 mg TiO_2/700 mL) to the hospital effluent set at pH = 3 to enhance photocatalyst activity (see Supplementary data for process details). After the treatment, the samples were filtered through a 0.22 μm membrane to separate TiO_2 particles from the solution. Complete removal of ciprofloxacin was observed after 60 min within the photocatalytic reactor. The same result was obtained after 300 min in an UV reactor (equipped with a 125 W medium pressure mercury lamp).

UV/TiO_2 exhibited a better removal than UV only for a few compounds, in particular for 4-aminoantipyrine, 4-methylaminoantipyrine and sulfapyridine. In general the removal efficiencies increased by a factor of two for most of the compounds without a photocatalyst.

An increment in the cycles slightly improved the removal of contaminants. Only X-ray contrast agents achieved higher removal efficiencies than in the other post-treatments (20–70%). These results led to the consideration that direct phototransformation with UV dominated the micropollutant removal and indirect phototransformation due to the presence of the embedded TiO_2 did not occur.

Generally the removal efficiencies observed with TiO_2/UV in 9 cycles were observed in only 3 cycles when using UV alone.

The lower removal efficiency observed by UV/TiO_2 might also be due to the fact that photocatalytic fibre could have adsorbed UV light and shaded part of the reaction chamber, thus the water could have been exposed to less UV irradiation.

An improvement in the removal of PhCs was observed when H_2O_2 was added to the UV reactor. No consistent differences were found between a dosage of 0.56 g/L and 1.11 g/L (Kohler et al., 2012). It was also found that the optimum light wavelength for the UV/H_2O_2 system is 254 nm as it guarantees the lowest background absorbance of the investigated water and high H_2O_2 absorbance resulting in an efficient generation of hydroxyl radicals. As a consequence, LP lamps are recommended as about 90% of their irradiated light is emitted at 254 nm, whereas MP lamps emit 254 nm light for 5–10% of the total emission.

The good results obtained with LP UV irradiation in AOPs lead to the consideration that for many PhCs, degradation processes are mainly due to chemical oxidation (between the molecule and the generated radicals) rather than to direct photolysis (Kohler et al., 2012).

Wilde et al. (2014) achieved promising results thanks to the degradation of a mixture of beta-blockers (atenolol, propranolol and metoprolol) in hospital effluent (pretreated in a septic tank followed by an anaerobic filter) by O_3 and Fe^{+2}/O_3: they showed that, in 120 min, complete degradation of the parent compounds was observed but not their complete elimination. The degradation process was found strictly correlated to pH. Alkaline pH values promote the removal of metoprolol and propranolol, whereas acidic values enhance the removal of organic load (expressed as COD). The investigation also highlighted the risk of undesired byproducts due to ozonolysis with a more intense degree of recalcitrance with respect to their parent compounds. This lead to better investigated ecotoxicological characteristics of the polished effluent.

Table 5
Disinfection performance by means of AOPs.

Method	Secondary effluent Thermotolerant coliforms Machado et al. (2007)	Laundry effluent Thermotolerant coliforms Kist et al. (2008)
Secondary effluent	1.1 10^6	9 10^6
UV/O_3	17,000	110
UV	9000	
TiO_2	170	
O_3	170	
O_3/TiO_2	120	1700
UV/TiO_2	40	20
$UV/TiO_2/O_3$	<2	<20

A slight increment in the removal of micropollutants was observed by adding H_2O_2 into the system. H_2O_2 accelerates the decomposition of ozone and partially increases the amount of hydroxyl radicals. Two different application modes were tested within the PILLS project (McArdell et al., 2011):

- addition of H_2O_2 into the ozone reactor influent;
- pre-ozonation of the MBR permeate with 1.2 g O_3/g DOC, addition of 2.5 mg/L H_2O_2 to half of the treated wastewater and both parts again treated with 0.7 g O_3/g DOC.

Differences were observed of about ± 20% which were not considered significant because within experimental error, in agreement with data already published confirming that little improvement was found especially in water with relatively high DOC (Acero and von Gunten, 2001) and that hydroxyl radicals attack is less effective than O_3 attack.

A significant removal efficiency is observed if very high doses of ozone and H_2O_2 are applied to the permeate as tested by Nielsen et al. (2013) (130 mg O_3/L and 60 mg H_2O_2/L 5 min; 450 mg O_3/L and 200 mg H_2O_2/L 15 min): in these operational conditions with few exceptions (sulfamethoxazole) all the selected micropollutants were removed below their PNEC/EQS (environmental quality standard) value.

In order to guarantee a clear, polished effluent, sometimes a "trap" step follows the AOP reactor. In this context, the effluent of a PAC reactor was filtered through UF membrane flat sheets (pore size 0.04 μm) (Switzerland, McArdell et al., 2011). Moreover within the PILLS project units, a moving bed bioreactor (HRT = 0.3–1 d) was used following PAC, O_3 or TiO_2/UV and a sand filter (filtration velocity $v_f < 12$ m/h) was equipped after ozone or the PAC unit.

4.3.4.2. Removal of microorganisms. Disinfection efficiency is strictly correlated to the applied technologies. Table 5 reports the efficacy of 7 different treatments applied to a secondary hospital effluent (Machado et al., 2007) or a secondary hospital laundry effluent (Kist et al., 2008) carried out in Brazil:

The main influent characteristics to the disinfection step were: 25 °C, pH = 9.5, upstream treatments: septic tank + anaerobic/aerobic treatment fed with hospital/laundry effluent. A dose of 12 mg O_3/L was applied and equipped with a UV lamp with an emission at 254 and 365 nm, radiating an energy of 31.9 J/cm^2. Catalyst fixation was obtained by preparing a suspension of TiO_2 in $CHCl_3$ (10% m/v) and by spreading it on a plate (2.96 mg TiO_2/cm^2). The contact time was 60 min for each.

The best disinfection efficiency was observed for the combination $UV/TiO_2/O_3$, that also provides very good turbidity removal (from 234 to 36.5 NTU), surfactants (8.0 10^6 mg/L to < detection limit) and toxicity (EC_{50} *Daphnia magna* from 65 to 100). A contact time of 10 min will result in a concentration of 330 MPN/100 mL and of 30 min of about 70 MPN/100 mL.

The disinfection performance is due to damage of the microorganism's cell wall and cytoplasmatic membrane. Thus cell permeability increases allowing intracellular content to flow through the membrane leading to cell death.

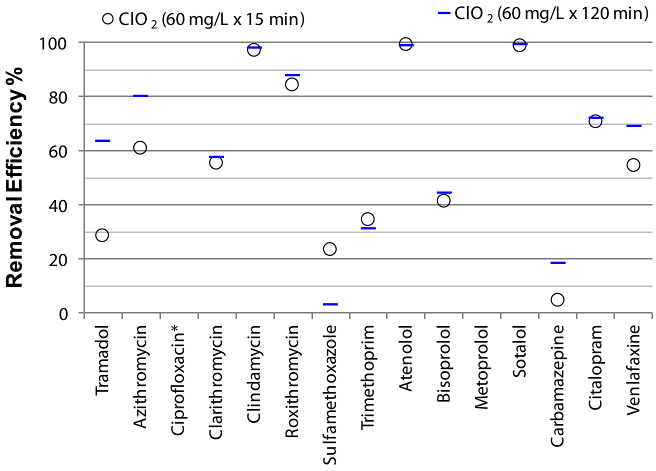


Fig. 11. Removal of PhCs by final chlorination.
Data from: Nielsen et al., 2013.

4.3.5. Nanofiltration and reverse osmosis

Nanofiltration (NF) and reverse osmosis (RO) processes are considered potential polishing treatments for hospital effluent, pretreated in an MBR from a technical view point. Residues of PhCs, still present in the permeate, may be retained due to molecular weight and size, sorption onto the membrane and also charge. Each membrane is characterized by a molecular weight cut off (MWCO) that represents the weight of those substances retained between 60 and 90%. Sorption is a potential removal mechanism for poorly soluble non-polar compounds, negatively charged compounds are rejected by NF/RO membranes due to electrostatic repulsion between the compounds and the negatively charged membrane surface (Kimura et al., 2004). Moreover, water characteristics such as pH, ionic strength, hardness, organic matter and membrane biofouling also have an influence on solute rejection.

In the study by Beier et al. (2010) the permeate of an MBR (COD < 30 mg/L, 5–10 mg N/L) equipped with microfiltration membranes was then subjected to NF and RO processes, characterized by a MWCO of 300–400 Da and 100–150 Da, respectively. It was found that RO exhibited a higher removal for all selected PhCs with respect to NF. However, RO presents major disadvantages due to the limited yield and the retentates that have to be properly disposed of. However, no suitable prediction model has been developed up to now as the rejection of the different micropollutants in NF/RO processes is specific for each membrane (Siegrest and Joss, 2012).

4.3.6. Chlorination

Only a few data are available regarding the removal efficiency of PhCs observed after a final chlorination. These are reported in Fig. 11 and refer to the investigation carried out by Nielsen et al. (2013). The added amount of ClO_2 was 60 mg/L in each run, and two different contact times were adopted: 15 min and 60 min. Ciprofloxacin showed higher concentrations in the effluent rather than in the influent to the treatment. In addition, chlorination seems to be able to remove diclofenac: in the study by Nielsen et al. (2013), its concentration in the influent (MBR permeate) was quite low (<5 ng/L) and in the effluent it was 1 ng/L (15 min as contact time). But it was found that under lab scale controlled chlorination with surface water, diclofenac exhibited a large degree of reactivity and its final concentration was below detection limit (Westerhoff et al., 2005).

4.4. Disinfection performance

In some countries disinfection is mandatory for the effluent generated in infectious disease wards or in health care specialized in infectious diseases (Nardi et al., 1995; Emmanuel et al., 2004). Faecal and total coliforms were found in the ranges 10^2–10^4 MPN/100 mL and 10^4–10^6 MPN/100 mL respectively (Table 1). These values are lower than those usually found in raw urban wastewater (Verlicchi et al., 2012a), probably due to the antimicrobial activity of antibiotic and disinfectant residues present in the infectious disease ward effluent.

At a dosage of 10 mg/L of ClO_2 and a contact time of 30 min faecal and total coliforms drop to less than 12,000 and 20,000 MPN/100 mL and a complete removal of viruses was always observed (Nardi et al., 1995).

Predisinfection of raw hospital effluent is still an issue of great concern: based on a theoretical hypothesis, Korzeniewska et al. (2013) recommend a preliminary disinfection of the hospital effluent before its immission into public sewage in order to minimize the spread of antibiotic resistant bacteria, on the other hand, research by Emmanuel et al. (2004) found that disinfection by means of NaOCl of the effluent from infectious and tropical disease departments can reduce the content of microorganisms, but at the same time it has toxic effects on aquatic organisms.

In many countries, including China, direct chlorination or primary treatment followed by chlorination represents the most widely used methods to treat and, in particular, disinfect hospital effluent in order to prevent the spread of pathogenic microorganisms (Liu et al., 2010). Despite the fact that chlorine disinfection has a broad spectrum of activities against bacteria, virus and fungi and it is simple to use, it may produce toxic byproducts, its performance depends on the water quality and only a low removal efficiency is achieved for viruses as they have a greater tolerability against chlorine compounds than bacteria. As a consequence, a high excess of disinfectant is generally applied to guarantee a (rough) disinfection of the hospital effluent, but inevitably extremely high concentrations of residual chloride (as high as 100–130 mg/L) will occur, resulting in serious pollution problems to the receiving aquatic environment, as remarked by Emmanuel et al. (2004) who investigated the effect of the addition of NaClO to hospital effluent: it can greatly reduce bacteria population, but it has toxic effects on aquatic organisms.

In China, to avoid an excessive use of chlorine, the removal of different types of microorganisms from hospital effluent is dealt with by means of an MBR, mostly employing submerged membranes (pore size about 0.2–0.4 μm), followed by a chlorination step with a dosage of NaClO of 1–2 mg/L as free chlorine with a contact time of 1.5 min. Since 2000, many plants based on membrane technologies have been built for the treatment of hospital effluent, with a capacity ranging between 20 and 2000 m^3/d, in compliance with the severe limits of 50 PFU/100 mL such as *E. coli* (Liu et al., 2010).

While a (UF) MBR followed by a specific disinfection step may be considered a viable option for the removal of a wide group of bacteria occurring in hospital effluent, studies into their performance in reducing pathogenic viruses are still scarce. The removal of viruses in an MBR is substantially due to three mechanisms: virus rejection depending on the cake generating on the membrane surface, viral inactivation of the biomass, and adsorption onto the surface of suspended solids which makes these microorganisms more stable.

In a Brazilian investigation (Prado et al., 2011) the removal of some enteric viruses (rotavirus A, human adenovirus, norovirus genogroups I and II and hepatitis A viruses) was compared in two different treatment trains: an anaerobic one including a UASB followed by three anaerobic filters and an aerobic one consisting of a conventional activated sludge process followed by chlorination. It was found that both systems are not suited to their removal. Their frequencies of detection and quantification results varied according to the virus type and effluents coming from different health care structures.

An MBR, equipped with ultrafiltration membranes, is able to remove groups of bacteria as reported above mainly due to membrane retention, reducing the spread of multiple antibiotic resistant strains, usually occurring in hospital effluent. But specific disinfection is advisable, in order to avoid regrowth of (survival) bacteria as discussed in Pauwels et al. (2006). For inactivation of pathogens and possible removal of

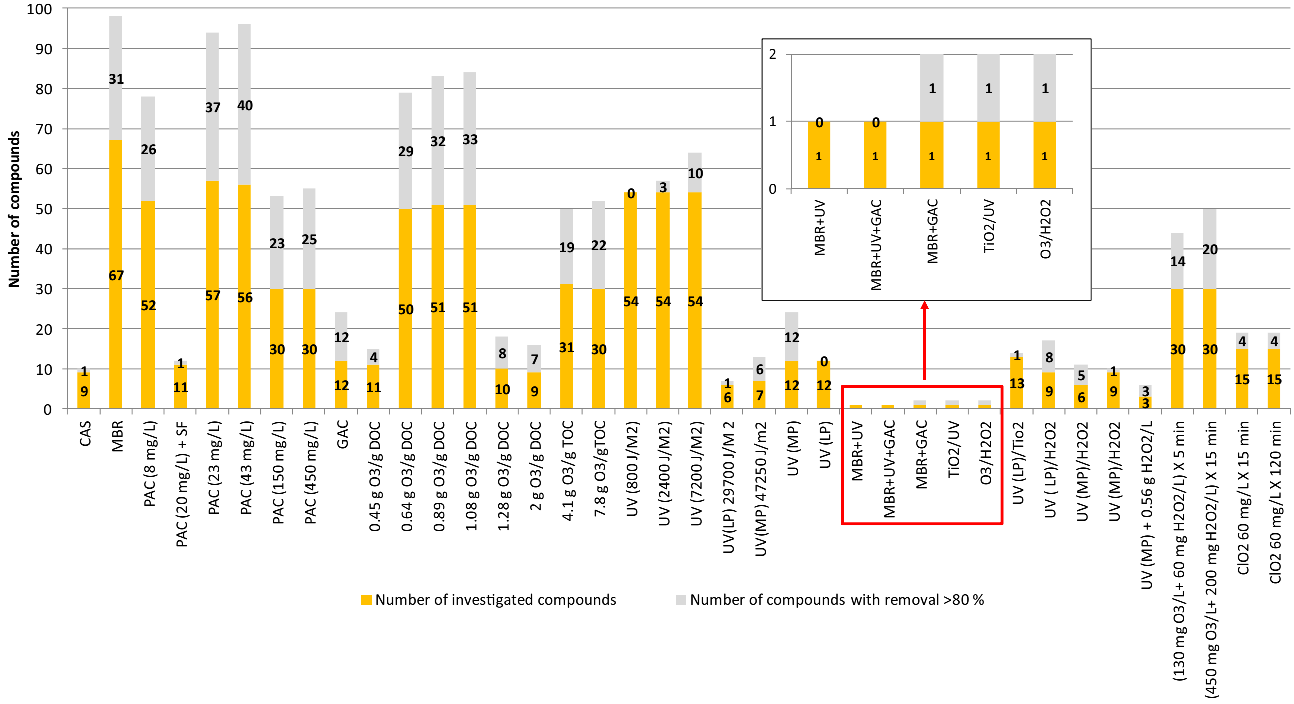


Fig. 12. Comparison among secondary and tertiary treatments of HWW with a view of the number of investigated compounds and of compounds exhibiting a removal efficiency greater than 80%.

antibiotic resistant bacteria, UV and ozonation are more efficient with respect to PAC and GAC.

In wastewater disinfection, the fluence to apply depends on the required microorganism limits (Verlicchi et al., 2011). For instance 100 J/m^2 is applied if the aim is to guarantee 1000 MPN/100 mL of total coliforms, 750–850 J/m^2 if a concentration of 23 MPN/100 mL of total coliform has to be guaranteed and finally a fluence greater than 1000 J/m^2 if the residual concentration of total coliform is $<$2.2 MPN/100 mL, thus allowing an unrestricted irrigation of the disinfected effluent (Crites and Tchobanoglous, 1998).

To inactivate specific microorganisms, oocysts or viruses, the requested fluence could be higher. To inactivate 3 log of Adenovirus type 40, a fluence of 1670 J/m^2 is required, whereas to inactivate up to 3 log of Cryptosporidium and Giardiasis, a fluence of 120 J/m is required (Hijnen et al., 2006).

These considerations lead to the consideration that when ozonation, UV, AOPs in general are applied to hospital effluent to remove recalcitrant compounds, at the same time it is disinfected to a very high degree. But in order to guarantee safe reuse of the disinfected effluent for unrestricted irrigation, a higher fluence is required (as well as further studies into the ecotoxicologic characteristics of the water).

Table 6
Removal efficiencies expected for the different groups of compounds.

Group	PAC	AOP	UV	Cl_2/ClO_2	Coag/Floc
Antibiotics	40–90	20–90	40–90	20–90	<20
Antidepressants	70–90	20–90	40–90	20–70	<20–40
Analgesics/anti-inflammatories	>90	20–90	70–90	20–70	<20
Lipid regulator	>90		>90	20–70	<20
X-ray contrast media	70–90	70–90	20–90	20–70	<20–40
Disinfectants/detergents	>90	>90	40–90	>20	<20–40

4.5. Comparison between the different treatments

A comparison of the performance of the different analyzed secondary and tertiary dedicated treatments for HWW is depicted in Fig. 12 in terms of number of investigated compounds and the number of compounds exhibiting a removal efficiency greater than 80%. It is based on all the data collected about PhCs in the peer reviewed papers included in this manuscript. What clearly emerges is that the most investigated technologies are MBR, PAC, ozonation and UV. The best results were performed by MBR (secondary step) and PAC (tertiary step).

Moreover Table SD-3 in the Supplementary data compiles compounds that exhibited a removal efficiency greater than 80% during secondary and tertiary treatments, with the corresponding references.

An in-depth analysis of the comparison of pairs of treatment is performed in Kovalova et al. (2013) with respect to the different classes of PhCs. They found that iodinated contrast media were better removed by MBR + UV (66% of the total influent load), all the selected PhCs except iodinated contrast media by MBR + PAC or MBR + UV (99%).

Lessons learned from these campaigns led to consider 1.08 g O_3/g DOC, 23 mg/L PAC and 2400 J/m^2 UV the values that best satisfy the two following choice criteria: relatively good abatement for most micropollutants and reasonable running costs (Kovalova et al., 2013).

Table 6 reports a rough estimation of the global removal of the different kinds of classes with respect to different technologies, based on all the collected data.

It is important to observe that the choice of the best technologies for treatment of hospital effluent should not necessarily lead to the complete removal of specific parent compounds, but to the removal of the estrogenic activity of the effluent itself, or more generally, a reduction in its ecotoxicological effects.

Bearing this concept in mind, processes including TiO_2 photocatalysis seem to be promising technologies as they are able to remove estrogenic activity of 17-β-estradiol (Byrne et al., 1998) and 17-α-ethinylestradiol (Coleman et al., 2000).

AOPs seem to be the most promising technologies as they can be effective in removing compounds not affected by other technologies as discussed above, reactions are generally fast, resulting in more compact reactors, finally (no or) low chemical doses are required leading to (no or) lower residuals, but they may have undesirable drawbacks, namely: unselective hydroxyl radicals, production of more hydrophiles and more difficult to treat byproducts than the original ones; as have been clearly listed by Suty et al. (2004).

The spread of disease due to pathogens and of specific strains of antibiotic resistant bacteria can be countered by a disinfection step (Korzeniewska et al., 2013). Some laws and regulations (including the Italian Deliberation by the Inter-ministerial Committee dated 4 February 1977) require treatment of the effluent from health care structures, blood analysis laboratories, and in particular, for the effluent from infectious disease wards. As an example, the effluent produced by the very large laboratory for blood analysis in Pievesestina (Cesena, North Italy, effluent flow-rate about 10^3 m^3/year) is subjected to ozonation and filtration through activated carbon prior to being immitted into the public sewage system and is then co-treated at the municipal WWTP. Alternatively, the addition of 10 mg/L of ClO_2 and a contact time of 30 min guarantee an efficient removal of faecal and total coliforms, with a negligible increment of AOX (Nardi et al., 1995). This increment is consistent if the applied disinfectant is NaClO (Emmanuel et al., 2004).

Due to the different nature of pollutants that may be present in hospital effluent (residues of PhCs, their metabolites, disinfectants and antiseptics, heavy metals, radio-elements, pathogens), the risk posed by this effluent may be toxic, radioactive and infectious.

Proper management of hospital effluent has to be considered and must include measures to mitigate the consequences at a WWTP level as well as towards the environment.

4.6. Removal efficiencies vs. physical–chemical properties of investigated compounds

Many studies were developed in order to investigate potential correlations between observed pharmaceutical removal efficiencies achieved by the different wastewater treatments and pharmaceutical molecular properties (among them Cunningham, 2008; Joss et al., 2006; Rogers, 1996; Tadkaew et al., 2011). They underlined that it is always very difficult to find reliable correlations, because many factors (i.e., operational and environmental conditions) affect removal mechanisms of such complex molecules thus a wide range of variability is generally observed for the removal of a specific compound during a treatment. Studies referring to UWW led to rules of thumb that try to correlate the behaviour of a specific molecule on the basis of its properties: k_{biol}, K_d, K_{ow} and pK_a, as discussed and reported in Tadkaew et al. (2011) and Verlicchi et al. (2013). Lessons learned from UWW may be also useful in making a rough prediction of efficacy of specific treatments in HWW managing.

Moreover attempts to correlate the behaviour of common parameters, such as COD or SS, and specific pharmaceuticals during hospital wastewater treatment were carried out, but unfortunately they did not suggest any reliable relationship (Emmanuel et al., 2004; Pauwels et al., 2006; Vasconcelos et al., 2009; Wilde et al., 2014).

5. Hospital effluent toxicity and environmental risk assessment

Interesting and useful research has been accomplished dealing with hospital effluent toxicity and assessment of the environmental risk posed by pharmaceutical residues in treated hospital effluent (Boillot et al., 2008; Perrodin et al., 2013; Emmanuel et al., 2004). This is quite a complex problem and is beyond the aim of this manuscript, but some lessons learned from published studies are discussed herein to point out concerns that merit further research.

It is well known that hospital effluent is 5–15 more toxic than urban wastewater due to the high concentrations of detergent and disinfectants, often containing chlorine or aldehydes (such as sodium hypochlorite and glutaraldehyde), iodinated contrast media that lead to the generation of AOX in the drainage network, heavy metals (namely silver used in radiology departments), radio-elements injected or administered in nuclear medicine studies and completely excreted in urine and PhC residues. That being said, hospital effluent can inhibit the activity of the biomass in the aeration tank of a sewage facility by 7–8% as documented in Boillot et al. (2008) and Panouillères et al. (2007).

Investigations are often based on Microtox and acute *D. magna* tests (Emmanuel et al., 2004; Boillot et al., 2008), but also to batteries including different kinds of test (Perrodin et al., 2013).

Lessons learned from these studies suggest that different pollutants may induce or contribute to toxicity: namely free chlorine, AOX (Emmanuel et al., 2004), ethanol, propanol and metals including Zn, Cu, As and Pb (Boillot et al., 2008).

Environmental risk assessment of hospital wastewater is generally based on the risk quotient *RQ*, defined as the ratio between PhC concentration in the effluent and its predicted non-effect concentration (PNEC). According to the classification that was adopted in many studies (Straub, 2002; Verlicchi et al., 2012a; Santos et al., 2013) the risk is classified high if $RQ \geq 1$, medium if $1 < RQ < 0.1$ and low if $RQ \leq 0.1$.

Based on *measured* effluent concentrations Verlicchi et al. (2012a) and Santos et al. (2013) found that in raw hospital effluent a high risk is posed by azithromycin, clarithromycin, erythromycin, ofloxacin, sulfamethoxazole, metronidazole fluoxetine, ibuprofen, acetaminophen and iopromide. This fact pinpoints that adequate treatment is necessary for hospital wastewater to reduce its negative effect on the environment. Bearing this in mind, the frameworks provided by Al Aukidy et al. (2014), Emmanuel et al. (2005), Escher et al. (2011), Lienert et al. (2011) and Mullot et al. (2010) might help in evaluating and comparing the efficacy of different treatment trains.

5.1. Antibiotic resistance bacteria

Another source of risk in hospital effluent is correlated to the occurrence of antibiotics and consists in the potential development and release of antibiotic-resistant bacteria (ARB) and genes (ARG). The PILLS project pinpoints that the risk of the spread of resistance to specific antibiotic molecules is higher in hospital effluent than in urban WW. The efficiency of advanced biological and chemical processes varies in the range of 1–5 log units. Ultrafiltration MBRs guarantee a consistent reduction of this risk, whereas a following step including ozonation, sand or PAC filtration does not contribute to further reduction.

6. Costs

A summary of the investment and operational and maintenance (O&M) costs for the different scenarios is reported in Table 7 referring to economic evaluations carried out in the cited studies in a design step. Unfortunately they are not homogeneous and not always investment and operational and maintenance data are available. The investments are amortized over 10 or 15 years depending on the investigations. Table 7 just offers a rapid comparison of the different technologies and of the order of magnitude of the different treatment trains.

Many considerations may arise from these reported values. For example, it emerged from previous discussion of collected removal data of PhCs that activated carbon seems a promising technology in reducing their occurrence in the final effluent. But activated carbon requires expensive maintenance operations in order to guarantee proper performance. In this context, investment cost for an activated carbon filter is lower than that of another AOP treatment, but if DOC levels in the stream fed to the carbon filter are above 10 mg/L, carbon treatment could become uncompetitive against AOPs, due to frequent change out, regeneration and disposal of the exhausted carbon. Moreover,

Table 7
Investment and O&M costs for hospital effluent treatment by different technologies.

Author	Kajitvichyanukul and Suntronvipart (2006)	Liu et al. (2010)	Verlicchi et al. (2010)	Beier et al. (2012)	PILLS Report, 2012				Kovalova et al. (2013)		Nielsen et al. (2013)							
Place	Thailand	China	Italy	Germany	Netherlands				Switzerland		Denmark							
											O_3	O_3	$O_3 + H_2O_2$	$O_3 + H_2O_2$	PAC	PAC	ClO_2	MBR + O_3
Type of treatment	Photo-Fenton	MBR	MBR + O_3 + UV	MBR + GAC	MBR + O_3 + GAC	MBR + MBR + PAC	MBR + O_3	82 mg/L × 10 min	156 mg/L × 20 min	(130 + 60) mg/L × 5 min	(450 + 200) mg/L × 15 min	150 mg/L	450 mg/L	60 mg/L × 120 min	156 mg/L			
Investment cost (€/m^3)			3.6		3.25	3.35	3.5	3.65										
O&M cost (€/m^3)	0.38[a]	0.45–0.163[a]			1.45	1.65	1.75	1.85			0.22	0.4	0.34	1.08	0.31	1.06	0.3	1
Total cost €/m^3				4.1	4.7	5	5.3	5.5	2.7	2.4								

[a] Exchange rate refers to December 20th 2014.

GAC and PAC do not destroy microcontaminants, but they allow their transfer from a liquid phase to a solid one. Operational costs should also include costs of final disposal of GAC and PAC.

To have an idea of the potential cost of dedicated treatment of hospital effluent, total costs range between 4.1 €/m^3 and 5.5 €/m^3 in case of secondary treatment by means of an MBR and polishing AOPs with the exception of Kovalova et al. (2013) that reported lower total costs ranging around 2.4–2.7 €/m^3. These differences were not commented by the two research groups within the PILLS projects.

7. Current strategies and future perspectives in the treatment of hospital effluent — conclusions

Management and treatment of hospital effluent greatly vary in different countries. In developed ones they may be completely absent, meaning that HWW is directly discharged into a surface water body or they consist in simple chlorination, or primary clarification followed by a chlorination or primary and secondary treatments followed by chemical disinfection (Prayitno et al., 2014).

Various research projects have been carried out in these countries, aiming to evaluate the suitability of some (simple) treatment trains for hospital effluent. They generally refer to a discussion of the observed removal efficiencies of *conventional* contaminants and microorganisms, and the possibilities to directly re-use this reclaimed water for irrigation purposes as they have to face problems arising from water shortage (among them Chitnis et al., 2004; Shrestha et al., 2001; Beyene and Redaie, 2011; Abd El-Gawad and Aly, 2011). Suggestions to improve the adopted treatment are also provided with a view to their applicability in terms of land requirement, footprint, costs, installation, operation and maintenance. Some case studies are reported herein. Direct reuse of reclaimed water should be evaluated, including the risk posed by persistent emerging contaminants and their (acute and chronic) effects on the environment and human health.

In European countries efforts are made to improve removal of these persistent compounds by means of end-of pipe treatments and in this context, AOP technologies are the most researched ones. Studies generally refer to occurrence and removal of a consistent number of PhCs, as well as ecotoxicological evaluation by means of the risk quotient ratio, i.e., the ratio between maximum measured concentrations and predicted no-effect concentration (Verlicchi et al., 2012a; Escher et al., 2011). Different full scale WWTPs have already been constructed for the dedicated treatment of hospital effluent. Each one consists in preliminary treatment, MBR (Beier et al., 2011), MBR followed by ozonation and UV (Verlicchi et al., 2010), ozonation and PAC (PILLS Report, 2012) and ozonation and GAC (Pharmafilter report, 2013; Grundfos Biobooster, 2012).

An interesting approach has been adopted in France to manage and treat the effluent of the Centre Hospitalier Alpes Léman in Annemasse. Thanks to dedicated piping, the HWW is conveyed to the near municipal WWTP where it is treated in a specific line and subjected to continuous monitoring to improve the removal of persistent compounds. This was a decision taken by the local authorities who have even drawn up a specific law for this site (Sipibel Report, 2014).

The best option in the management and treatment of hospital effluent is strictly correlated to hospital size and catchment area dimension and must be defined on the basis of a technical and economical feasibility study that would focus on the most appropriate measures able to reduce the (macro and micro) pollutant load discharged into the surface water environment. Dedicated treatments for hospital effluent are recommended by many authors worldwide, segregation and special treatment seem adequate for specific effluent including effluent generated in radiology wards, containing ICMs, the most recalcitrant compounds, at extremely high concentrations, but also for the effluent from laundries, oncological wards and clinical analysis laboratories, as in the case of the large and centralized Italian lab services discussed above. In any case, dilution with surface water should not represent the proper action to mitigate potential adverse negative effects of PhC residues in the environment.

A final remark is suggested by studies promoting the implementation of energy-intensive systems with indirect solar energy by aggregating photovoltaic cells for the generation of electrical energy. This may result in energy storage and in a balanced use of energy during periods in which light incidence is lower.

Appendix A. Supplementary data

The Supplementary data includes figures and tables referring to: worldwide distribution of all treatment trains and technologies, investigated in lab, pilot and full scale plants, included in this study together with the corresponding reference; list of pharmaceuticals included in this study; reactions involved in AOPs processes, list of compounds exhibiting a removal higher than 80% in secondary and tertiary treatment steps, according to studies examined in this review study. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.scitotenv.2015.02.020.

References

Abd El-Gawad, H.A., Aly, A.M., 2011. Assessment of aquatic environmental for wastewater management quality in the hospitals: a case study. Aust. J. Basic Appl. Sci. 5, 474–482.

Acero, J.L., Von Gunten, U., 2001. Characterization of oxidation processes: ozonation and the AOP O-3/H2O2. J. Am. Water Works Assoc. 93, 90–100.

Al Aukidy, M., 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.

Al-Hashimia, M., Abbas, T.R., Jasema, Y.I., 2013. Performance of sequencing anoxic/anaerobic membrane bioreactor (SAM) system in hospital wastewater treatment and reuse. Eur. Sci. J. 9, 169–180.

Andersen, H.R., Chhetri, R.K., Hansen, M.S., Christensson, M., Sundmark, K., Sund, C., et al., 2014. Staged MBBR optimized for pharmaceutical biodegradation and ozonation of hospital wastewater. Poster presentation at the 8th World Water Congress, Lisbon.

Arslan, A., Veli, S., Bingol, D., 2014. Use of response surface methodologies for pretreatment of hospital wastewater by O_3/UV and O_3/UV/H_2O_2 processes. Sep. Purif. Methods 132, 561–567.

Azar, A.M., Jelogir, A.G., Bidhendi, G.N., Mehrdadi, N., Zaredar, N., Poshtegal, M.K., 2010. Investigation of optimal method for hospital wastewater treatment. J. Food Agric. Environ. 8, 1199–1202.

Beier, S., Köster, S., Veltmann, K., Schröder, HFr, Pinnekamp, J., 2010. Treatment of hospital wastewater effluent by nanofiltration and reverse osmosis. Water Sci. Technol. 61, 1691–1698.

Beier, S., Cramer, C., Köster, S., Mauer, C., Palmowski, L., Schröder, HFr, et al., 2011. Full scale membrane bioreactor treatment of hospital wastewater as forerunner for hot-spot wastewater treatment solutions in high density urban areas. Water Sci. Technol. 63, 66–71.

Beier, S., Cramer, C., Mauer, C., Köster, S., Schröder, HFr, Pinnekamp, J., 2012. MBR technology: A promising approach for the (pre-)treatment of hospital wastewater. Water Sci. Technol. 65, 1648–1653.

Berto, J., Rochenbach, G.C., Barreiros, M.A.B., Corrêa, A.X.R., Peluso-Silva, S., Radetski, C.M., 2009. Physico-chemical, microbiological and ecotoxicological evaluation of a septic tank/Fenton reaction combination for the treatment of hospital wastewaters. Ecotoxicol. Environ. Saf. 72, 1076–1081.

Beyene, H., Redaie, G., 2011. Assessment of waste stabilization ponds for the treatment of hospital wastewater: the case of Hawassa University Referral Hospital. World Appl. Sci. J. 15, 142–150.

Boillot, C., Bazin, C., Tissot-Guerraz, F., Droguet, J., Perraud, M., Cetre, J.C., et al., 2008. Daily physicochemical, microbiological and ecotoxicological fluctuations of a hospital effluent according to technical and care activities. Sci. Total Environ. 403, 113–129.

Byrne, J.A., Eggins, B.R., Brown, N.M.D., McKinney, B., Rouse, M., 1998. Immobilisation of TiO_2 powder for the treatment of polluted water. Appl. Catal. B Environ. 17, 25–36.

Chiang, C.F., Tsai, C.T., Lin, S.T., Huo, C.P., Lo, K.W., 2003. Disinfection of hospital wastewater by continuous ozonation. J. Environ. Sci. Health A A38 (12), 2895–2908.

Chitnis, V., Chitnis, S., Vaidya, K., Ravikant, S., Patil, S., Chitnis, D.S., 2004. Bacterial population changes in hospital effluent treatment plant in central india. Water Res. 38, 441–447.

Clara, M., Strenn, B., Gans, O., Martinez, E., Kreuzinger, N., Kroiss, H., 2005. Removal of selected pharmaceuticals, fragrances and endocrine disrupting compounds in a membrane bioreactor and conventional wastewater treatment plants. Water Res. 39, 4797–4807.

Coleman, H.M., Eggins, B.R., Byrne, J.A., Palmer, F.L., King, E., 2000. Photocatalytic degradation of 17-β-oestradiol on immobilised TiO_2. Appl. Catal. B Environ. 24, L1–L5.

Crites, R.W., Tchobanoglous, G., 1998. Small and Decentralized Wastewater Management Systems. WCB/McGraw-Hill Editor, New York.

Cruz-Morato, C., Lucas, D., Llorca, M., Rodriguez-Mozaz, S., Gorga, M., Petrovic, M., et al., 2014. Hospital wastewater treatment by fungal bioreactor: removal efficiency for pharmaceuticals and endocrine disruptor compounds. Sci. Total Environ. 493, 365–376.

Cunningham, V.L., 2008. Special characteristics of pharmaceuticals related to environmental fate. In: Kummerer, K. (Ed.), Pharmaceutical in the Environment — Sources, Fate, Effects and Risks, III ed. Springer Berlin Heidelberg, pp. 23–34.

De Almeida, C.A.A., Brenner, C.G.B., Minetto, L., Mallmann, C.A., Martins, A.F., 2013. Determination of anti-anxiety and anti-epileptic drugs in hospital effluent and a preliminary risk assessment. Chemosphere 93, 2349–2355.

Emmanuel, E., Keck, G., Blanchard, J.M., Vermande, P., Perrodin, Y., 2004. Toxicological effects of disinfections using sodium hypochlorite on aquatic organisms and its contribution to AOX formation in hospital wastewater. Environ. Int. 30, 891–900.

Emmanuel, E., Perrodin, Y., Keck, G., Blanchard, J., Vermande, P., 2005. Ecotoxicological risk assessment of hospital wastewater: a proposed framework for raw effluents discharging into urban sewer network. J. Hazard. Mater. 117, 1–11.

Escher, B.I., Baumgartner, R., Koller, M., Treyer, K., Lienert, J., McArdell, C.S., 2011. Environmental toxicology and risk assessment of pharmaceuticals from hospital wastewater. Water Res. 45, 75–92.

Gabarron, S., Gómez, M., Monclús, H., Rodríguez-Roda, I., Comas, J., 2013. Ragging phenomenon characterisation and impact in a full-scale MBR. Water Sci. Technol. 67, 810–816.

Gautam, A.K., Kumar, S., Sabumon, P.C., 2007. Preliminary study of physico-chemical treatment options for hospital wastewater. J. Environ. Manag. 83, 298–306.

Grundfos biobooster, 2012. Wastewater Treatment at Herlev Hospital, Denmark. available at the web site:, http://www.herlevhospital.dk/NR/rdonlyres/74234BCB-4E38-4B84-9742-80FFCDB416AF/0/10988_Biobooster_Herlev_LOW_opslag.pdf (last access on January 12th, 2015).

Hijnen, W.A.M., Beerendonk, E.F., Medema, G.J., 2006. Inactivation credit of UV radiation for viruses, bacteria and protozoan (oo)cysts in water: a review. Water Res. 40, 3–22.

Joss, A., Zabczynski, S., Göbel, A., Hoffmann, B., Löffler, D., McArdell, C.S., et al., 2006. Biological degradation of pharmaceuticals in municipal wastewater treatment: proposing a classification scheme. Water Res. 40, 1686–1696.

Kajitvichyanukul, P., Suntronvipart, N., 2006. Evaluation of biodegradability and oxidation degree of hospital wastewater using photo-Fenton process as the pretreatment method. J. Hazard. Mater. B138, 384–391.

Kimura, K., Toshima, S., Amy, G., Watanabe, Y., 2004. Rejection of neutral endocrine disrupting compounds (EDCs) and the pharmaceutical active compounds (PhACs) by RO membranes. J. Membr. Sci. 245, 71–78.

Kist, L.T., Albrech, C., Machado, Ê.L., 2008. Hospital laundry wastewater disinfection with catalytic photoozonation. Clean Soil Air Water 36, 775–780.

Kohler, C., Venditti, S., Igos, E., Klepiszewski, K., Benetto, E., Cornelissen, A., 2012. Elimination of pharmaceutical residues in biologically pre-treated hospital wastewater using advanced UV irradiation technology: a comparative assessment. J. Hazard. Mater. 239–240, 70–77.

Korzeniewska, E., Korzeniewska, A., Harnisz, M., 2013. Antibiotic resistant *Escherichia coli* in hospital and municipal sewage and their emission to the environment. Ecotoxicol. Environ. Saf. 91, 96–102.

Kosma, C.I., Lambropoulou, D.A., Albanis, T.A., 2010. Occurrence and removal of PPCPs in municipal and hospital wastewaters in Greece. J. Hazard. Mater. 179, 804–817.

Kovalova, L., Siegrist, H., Singer, H., Wittmer, A., McArdell, C.S., 2012. Hospital wastewater treatment by membrane bioreactor: performance and efficiency for organic micropollutant elimination. Environ. Sci. Technol. 46, 1536–1545.

Kovalova, L., Siegrist, H., Von Gunten, U., Eugster, J., Hagenbuch, M., Wittmer, A., et al., 2013. Elimination of micropollutants during post-treatment of hospital wastewater with powdered activated carbon, ozone, and U. Environ. Sci. Technol. 47, 7899–7908.

Kreuzinger, N., Clara, M., Strenn, B., Kroiss, H., 2004. Relevance of the sludge retention time (SRT) as design criteria for wastewater treatment plants for the removal of endocrine disruptors and pharmaceuticals from wastewater. Water Sci. Technol. 50, 149–156.

Kummerer, K., 2001. Drugs in the environment: emission of drugs, diagnostic aids and disinfectants into wastewater by hospital in relation to other sources — a review. Chemosphere 45, 957–969.

Kummerer, K., Erbe, T., Gartiser, S., Brinker, L., 1998. AOX-emissions from hospital into municipal wastewater. Chemosphere 36, 2437–2445.

Lee, Y., Von Gunten, U., 2010. Oxidative transformation of micropollutants during municipal wastewater treatment: comparison of kinetic aspects of selective (chlorine, chlorine dioxide, ferrate VI, and ozone) and non-selective oxidants (hydroxyl radical). Water Res. 44, 555–566.

Lenz, K., Koellensperger, G., Hann, S., Weissenbacher, N., Mahnik, S.N., Fuerhacker, M., 2007a. Fate of cancerostatic platinum compounds in biological wastewater treatment of hospital effluents. Chemosphere 69, 1765–1774.

Lenz, K., Mahnik, S.N., Weissenbacher, N., Mader, R.M., Krenn, P., Hann, S., et al., 2007b. Monitoring, removal and risk assessment of cytostatic drugs in hospital wastewater. Water Sci. Technol. 56, 141–149.

Lienert, J., Koller, M., Konrad, J., McArdell, C.S., Schuwirth, N., 2011. Multiple-criteria decision analysis reveals high stakeholder preference to remove pharmaceuticals from hospital wastewater. Environ. Sci. Technol. 45, 3848–3857.

Liu, Q., Zhou, Y., Chen, L., Zheng, X., 2010. Application of MBR for hospital wastewater treatment in China. Desalination 250, 605–608.

Lopez, N., Deblonde, T., Hartemann, Ph., 2010. Les effluents liquids hospitaliers. Hygiènes 18, 405–410.

Machado, Ê.L., Kist, L.T., Schmidt, R., Hoeltz, J.M., Dalberto, D., Alcayaga, E.L.A., 2007. Secondary hospital wastewater detoxification and disinfection by advanced oxidation processes. Environ. Technol. 28, 1135–1143.

Mahnik, S.N., Lenz, K., Weissenbacher, N., Mader, R.M., 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.

Mahvi, A., Rajabizadeh, A., Fatehizadeh, A., Yousefi, N., Hosseini, H., Ahmadian, M., 2009. Survey wastewater treatment condition and effluent quality of Kerman Province hospitals. World Appl. Sci. J. 7, 1521–1525.

Martins, A.F., Vasconcelos, T.G., Henriques, D.M., Frank, C.S., König, A., Kümmerer, K., 2008. Concentration of ciprofloxacin in Brazilian hospital effluent and preliminary risk assessment: a case study. Clean Soil Air Water 36, 264–269.

McArdell, C.S., Kovalova, L., Siegrist, H., 2011. Input and elimination of pharmaceuticals and disinfectants from hospital wastewater. Final Report (July).

Mesdaghinia, A.R., Naddafi, K., Nabizadeh, R., Saeedi, R., Zamanzadeh, M., 2009. Wastewater characteristics and appropriate Method for wastewater management in the hospitals. Iran J. Public Health 38, 34–40.

Monteiro, S.C., Boxall, A.B.A., 2010. Occurrence and fate of human pharmaceuticals in the environment. Rev. Environ. Contam. Toxicol. 202, 53–154.

Mousaab, A., Claire, C., Magali, C., Christophe, D., 2015. Upgrading the performances of ultrafiltration membrane system coupled with activated sludge reactor by addition of biofilm supports for the treatment of hospital effluents. Chem. Eng. J. 262, 456–463.

Mullot, J., Karolak, S., Fontova, A., Levi, Y., 2010. Modeling of hospital wastewater pollution by pharmaceuticals: first results of mediflux study carried out in three French hospitals. Water Sci. Technol. 62, 2912–2919.

Nardi, G., Feretti, D., Bracchi, U., Dorè, F., Francesconi, A., Grottolo, M., et al., 1995. Acque reflue ospedaliere. Valutazione di un trattamento di disinfezione con biossido di cloro. Inquinamento 7, 77–83.

Nielsen, U., Hastrup, C., Klausen, M.M., Pedersen, B.M., Kristensen, G.H., Jansen, J.L.C., et al., 2013. Removal of APIs and bacteria from hospital wastewater by MBR plus O_3, $O_3 + H_2O_2$, PAC or ClO_2. Water Sci. Technol. 67, 854–862.

Ort, C., Lawrence, M., Reungoat, J., Eagleham, G., Carter, S., Keller, J., 2010. Determination of the fraction of pharmaceutical residues in wastewater originating from a hospital. Water Res. 44, 605–615.

Panouillères, M., Boillot, C., Perrodin, Y., 2007. Study of the combined effects of a peracetic acid-based disinfectant and surfactants contained in hospital effluents on daphnia magna. Ecotoxicology 16, 327–340.

Pauwels, B., Verstraete, W., 2006. The treatment of hospital wastewater: an appraisal. J. Water Health 4, 405–416.

Pauwels, B., Fru Ngwa, F., Deconinck, S., Verstraete, W., 2006. Effluent quality of a conventional activated sludge and a membrane bioreactor system treating hospital wastewater. Environ. Technol. 27, 395–402.

Perrodin, Y., Bazin, C., Bony, S., Devaux, A., Bertrand-Krajewski, J.L., Cren-Olivé, C., et al., 2013. A priori assessment of ecotoxicological risks linked to building a hospital. Chemosphere 90, 1037–1046.

Pharmafilter report, 2013. Evaluation report Pharmafilter Full scale demonstration in the Reinier de Graaf Gasthuis (Hospital) Delft. 9789057735936 (Available at the web site: http://nieuwesanitatie.stowa.nl/upload/publicaties/STOWA%202013%2016%20LR.pdf (last access on January 12th 2015)).

PILLS Report, 2012. Pharmaceutical residues in the aquatic system: — a challenge for the future. Final Report of the European Cooperation Project PILLS (available at the address: www.pills-project.eu (last access on January 5th 2015), Gelsenkircken September 2012).

Prado, T., Silva, D.M., Guilayn, W.C., Rose, T.L., Gaspar, A.M.C., Miagostovich, M.P., 2011. Quantification and molecular characterization of enteric viruses detected in effluents from two hospital wastewater treatment plants. Water Res. 45, 1287–1297.

Prayitno, Kusuma Z., Yanuwiadi, B., Laksmono, R.W., Kamahara, H., Daimon, H., 2014. Hospital wastewater treatment using aerated fixed film biofilter — ozonation (Af2b/O3). Adv. Environ. Biol. 8, 1251–1259.

Rezaee, A., Ansari, M., Khavanin, A., Sabzali, A., Aryan, M.M., 2005. Hospital wastewater treatment using an integrated anaerobic aerobic fixed film bioreactor. Am. J. Exp. Sci. 1, 259–263.

Rizzo, L., Manaia, C., merlin, C., Schwartz, T., Dagot, C., Ploy, M.C., Michael, I., Fatta-Kassinos, D., 2013. Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: a review. Sci. Total Environ. 447, 345–360.

Rogers, H.R., 1996. Sources, behaviour and fate of organic contaminants during sewage treatment and in sewage sludges. Sci. Total Environ. 185, 3–26.

Santos, L.H.M.L.M., Gros, M., Rodriguez-Mozaz, S., Delerue-Matos, C., Pena, A., et al., 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.

Sarafraz, Sh., Khani, M.R., Yaghmaeian, K., 2007. Quality and quantity survey of hospital wastewater in Hormozgan Province. Iran. J. Environ. Health Sci. Eng. 4, 43–50.

Shrestha, R.R., Haberl, R., Laber, J., 2001. Constructed wetland technology transfer to Nepal. Water Sci. Technol. 43, 345–350.

Siegrest, H., Joss, A., 2012. Review on the fate of organic micropollutants in wastewater treatment and water reuse with membranes. Water Sci. Technol. 66, 1369–1376.

Sim, W.J., Kim, H.Y., Choi, S.D., Kwon, J.H., Oh, J.E., 2013. Evaluation of pharmaceuticals and personal care products with emphasis on anthelmintics in human sanitary waste, sewage, hospital wastewater, livestock wastewater and receiving water. J. Hazard. Mater. 248–249, 219–227.

Sipibel Report, 2014. Effluents hospitaliers et stations d'épuration urbaines: caractérisation, risques et traitabilité- Presentation and premiers resultants. June, available at the web site, http://www.graie.org/Sipible/publications.html (last access on January 2nd, 2015).

Straub, J.O., 2002. Environmental risk assessment for new human pharmaceuticals in the European Union according to the draft guideline/discussion paper of January 2001. Toxicol. Lett. 131, 137–143.

Suarez, S., Lema, J.M., Omil, F., 2009. Pre-treatment of hospital wastewater by coagulation–flocculation and flotation. Bioresour. Technol. 100, 2138–2146.

Suty, H., De Traversay, C., Cost, M., 2004. Application of advanced oxidation processes: present and future. Water Sci. Technol. 49, 227–233.

Tadkaew, N., Hai, F.I., McDonald, J.A., Khan, S.J., Nghiem, L.D., 2011. Removal of trace organics by MBR treatment: the role of molecular properties. Water Res. 45, 2439–2451.

Vasconcelos, T.G., Kümmerer, K., Henriques, D.M., Martins, A.F., 2009. Ciprofloxacin in hospital effluent: degradation by ozone and photoprocesses. J. Hazard. Mater. 169, 1154–1158.

Venditti, S., Köhler, C., Arenz-Leufen, M., O'Nagy, O., Cornelissen, A., Klepiszewski, K., 2011. Membrane bioreactor process as pre-treatment for hospital effluents. Proceedings 8th IWA Leading-Edge Conference on Water and Wastewater Technologies, Amsterdam.

Verlicchi, P., Galletti, A., Masotti, L., 2008. Caratterizzazione e trattabilità di reflui ospedalieri: indagine sperimentale (con sistemi MBR) presso un ospedale dell'area ferrarese. Proceedings Sidisa Conference, Florence (Italy), June 2008 (in Italian).

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, 2507–2519.

Verlicchi, P., Galletti, A., Al Aukidy, M., Masotti, L., 2011. New perspectives in wastewater disinfection. Water Disinfection. Nova Publisher, pp. 77–108.

Verlicchi, P., Al Aukidy, M., Galletti, A., Petrovic, M., Barceló, D., 2012a. Hospital effluent: investigation of the concentrations and distribution of pharmaceuticals and environmental risk assessment. Sci. Total Environ. 430, 109–118.

Verlicchi, P., Al Aukidy, M., Zambello, E., 2012b. 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.

Verlicchi, P., Galletti, A., Petrovic, M., Barcelò, D., 2012c. Micro-pollutants in hospital effluent: their fate, risk and treatment options. In: Barcelò, D., Kostianoy, A.G. (Eds.), Emerging Organic Contaminants and Human Health, the Handbook of Environmental Chemistry. Springer, pp. 139–172.

Verlicchi, P., Zambello, E., Al Aukidy, M., 2013. Removal of pharmaceuticals by conventional wastewater treatment plants. In: Barcelò, D., Petrovic, M. (Eds.), Comprehensive Analytical Chemistry. Elsevier, pp. 231–286.

von Gunten, U., 2003. Ozonation of drinking water: part II. Disinfection and by-product formation. Water Res. 37, 1469–1487.

Walhberg, C., Biorlenius, B., Paxeus, N., 2010. Pharmaceuticals Residues in Stockholm Water Environment — Occurrence Mitigations and Treatment of Wastewater. Stockolm Vatten (in Swedish).

Wang, X.W., Li, J., Guo, T., Zhen, B., Kong, Q., Yi, B., et al., 2005. Concentration and detection of SARS coronavirus in sewage from Xiao Tang Shan hospital and the 309th Hospital of the Chinese People's Liberation Army. Water Sci. Technol. 52, 213–221.

Wen, X., Ding, H., Huang, X., Liu, R., 2004. Treatment of hospital wastewater using a submerged membrane bioreactor. Process Biochem. 39, 1427–1431.

Westerhoff, P., Yoon, Y., Snyder, S., Wert, E., 2005. Fate of endocrine-disruptor, pharmaceutical and personal care product chemicals during simulated drinking water treatment processes. Environ. Sci. Technol. 39, 6649–6663.

Wilde, M.L., Montipo, S., Martins, A.F., 2014. Degradation of b-blockers in hospital wastewater by means of ozonation and Fe^{2+}/ozonation. Water Res. 48, 280–295.

Zwickenpflug, B., Böhler, M., Sterkele, B., Joss, A., Siegrist, H., Traber, J., Gujer, W., Behl, M., Dorusch, F., Hollender, J., Ternes, T., Fink, G., 2010. Einsatz von Pulveraktivkohle zur Elimination von Mikroverunreinigungen aus kommunalem Abwasser. Final report of the MicroPoll project EAWAG on behalf of the Swiss Federal Office for the Environment, Dübendorf, CH (http://www.eawag.ch/forschung/eng/schwerpunkte/ (last access on January 12th 2015)).